Simple Derivatives of Natural Amino Acids as Chiral Ligands in the Catalytic Asymmetric Addition of Phenylacetylene to Aldehydes

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Optically active propargylic alcohols are important chiral building blocks in asymmetric synthesis, and asymmetric addition of terminal alkynes to aldehydes is one of the most important and interesting procedures by which to prepare these chiral building blocks. In this work we have identified some simple derivatives of (*S*)-proline and other natural amino acids as chiral ligands that can be combined with $Ti(OiPr)_4$ and then used to catalyze the asymmetric addition of zinc acetylide, produced in situ by the reaction of phenylacetylene with diethylzinc, to aldehydes. The *ee* value was as high as 90%.

Introduction

Optically active propargylic alcohols are important building blocks in asymmetric synthesis as they are used in the preparation of a diverse range of molecules, including natural products, pharmaceuticals, and macromolecules.[1] The addition of asymmetric terminal alkynes to aldehydes is one of the most important methods for producing chiral secondary propargylic alcohols. In recent years, great progress has been made in the addition reactions of alkynylzinc to aldehydes and the enantioselectivity has been as high as 99%.[2] Carreira and co-workers found that zinc acetylides, generated in situ from the reaction of terminal alkynes and $Zn(OTf)_2$ in the presence of triethylamine, could enantioselectively add to alphatic aldehydes when promoted by chiral ligand *N*-methylephedrine and a high *ee* up to 99% was achieved.[3] Chan and co-workers[4] have disclosed that a combination of chiral BINOL and sulfonamide with $Ti(OiPr)_4$ generates a highly enantioselective catalyst which catalyzes the addition of alkynylzinc, produced in situ from the reaction of phenylacetylene and dimethylzinc, to aromatic aldehydes. Pu and co-workers developed a more convenient process, the BINOL/$Ti(OiPr)_4$/Et_2Zn method, to produce highly optically active secondary propargylic alcohols in which alkyl and aromatic aldehydes are both suitable substrates.[5] By using this process, chiral BINOL and its derivatives have successfully been used in this asymmetric reaction and highly enantioselective propargylic alcohols were afforded. Wang and co-workers[6] recently found that complexes of sulfonamide alcohols and $Ti(OiPr)_4$ also catalyze the highly enantioselective addition of phenylacetylene to both alkyl and aromatic aldehydes. Other chiral ligands, including amino alcohols[7] and oxazoline,[8] have also recently been reported to catalyze this asymmetric addition reaction. Although progress has been made, more effort is needed to develop cheap and highly enantioselective chiral ligands.

Our group has been developing chiral ligands that can be synthesized conveniently in simple, short reactions and from cheap, available chiral resources.[9] Recently we disclosed that simple L-Boc-proline could be combined with $Ti(OiPr)_4$ to effectively catalyze the addition of zinc acetylide to aromatic aldehydes with moderate-to-good enantioselectivity.[10] This phenomenon has spurred our continued interest in this field. Consequently we have investigated whether other simple *N*-substituted derivatives of (*S*)-proline could be used as ligands in this reaction, if they would be highly enantioselective, and if simple derivatives of other natural amino acids would also catalyze this asymmetric reaction. The answers to these questions are given in this paper.

Results and Discussion

For this study, we chose five derivatives of L-proline **1a**–**e**, two derivatives of phenylalanine **2a**,**b**, Boc-valine (**3**) and Cbz-threonine (**4**) (Figure 1). With the exception of **1c**, **1d**,**1e** and **2b**, these compounds are cheap and commercially available. Compounds **1c** and **2b** can be conveniently prepared in a single step according to the typical process reported in the literature[11] (for example, see Scheme 1). The L-amino acids were dissolved in aqueous NaOH at 0 °C and

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an ethereal solution of *p*-toluenesulfonyl chloride was added dropwise while stirring over several hours to give the tosyl amino acids **1c** and **2b**.

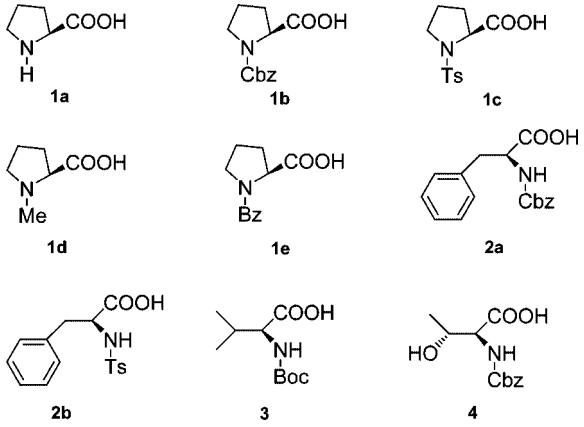
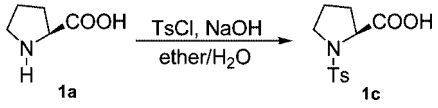
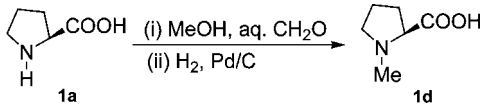


Figure 1. L-Proline and its *N*-substituted derivatives.



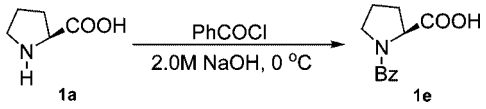
Scheme 1. Synthesis of *N*-tosylproline (**1c**).

Following the reported method,[12] L-proline in methanol was allowed to react with a solution of 40% aqueous formaldehyde and then reduced with hydrogen catalyzed by Pd/C. This produced *N*-methylproline (**1d**) in high yield (Scheme 2).



Scheme 2. Preparation of *N*-methylproline (**1d**).

The ligand **1e** was readily prepared by adding benzoyl chloride to a solution of L-proline in 2.0 M NaOH (Scheme 3).



Scheme 3. Synthesis of L-Bz-proline (**1e**).

Because of the special structure of proline, we initially focused on the enantioselective addition of phenylacetylene to benzaldehyde with simple *N*-substituted derivatives of proline as ligands (Table 1, entries 1–5). The results show that the reaction with *N*-tosylproline **1c** was the most enantioselective and that *N*-methylproline (**1d**) resulted in the poorest asymmetric induction. Natural proline has rather poor solubility in organic solvents. However, because proline, a small molecule, has successfully been used as a chemical enzyme in some asymmetric reactions,[13] we perservered in our attempts to determine the enantioselectivity of this reaction. To our surprise we found that it readily catalyzes this reaction when Ti(O*i*Pr)$_4$ is introduced into the reaction mixture. Clearly the reactions with *N*-acyl (**1b** and **1e**) and *N*-sulfonyl (**1c**) derivatives of L-proline gave products with higher enantioselectivity. We have also observed that the reaction with *N*-tosylproline was more enantioselective than that with Boc-proline.[10] Considering the configuration of the products, L-proline gave an (*S*)-configured product whilst the other proline derivatives gave (*R*)-configured alcohols.

Table 1. Reaction data from the enantioselective addition of phenylacetylene to benzaldehyde[a] with derivatives of amino acids as chiral ligands.

Entry	Ligand	Time [h]	Yield [%]	*ee* [%][b]	Config.[c]
1	**1a**	10	62	20	*S*
2	**1b**	10	70	60	*R*
3	**1c**	10	85	71	*R*
4	**1d**	10	50	11	*R*
5	**1e**	10	66	51	*R*
6	**2a**	10	56	25	*R*
7	**2b**	10	60	15	*R*
8	**3**	10	60	40	*R*
9	**4**	10	65	45	*R*

[a] Reagents: 20% ligands, 3.0 equiv. Ti(O*i*Pr)$_4$, and 2.0 equiv. Et_2Zn wth respect to benzaldehyde were used; toluene was used as solvent. [b] Determined by chiral HPLC on a Daicel Chiralcel OD column. [c] The absolute configurations were based on determination of the specific rotation and in comparison with literature, see ref.[14]

After studying the addition reactions with simple derivatives of L-proline, we then investigated the feasibility of this reaction with other derivatives of amino acids. We chose two phenylalanine derivatives **2a** and **2b**, the noncyclic Boc-valine (**3**), and Cbz-Thr (**4**), which possesses two chiral centers. We found that each of these four ligands could combine with Ti(O*i*Pr)$_4$ to catalyze the reaction (Table 1, entries 6–9), although the products were obtained with poor enantioselectivity. The reaction with *N*-tosyl-Phe (**2b**) had a lower *ee* than that with Cbz-Phe (**2a**). Of these four ligands, the reactions involving the alkyl amino acids were more enantioselective.

To improve the enantioselectivity of these reactions, we explored the conditions that influenced the asymmetric induction. The results are given in Table 2. The enantioselectivity was influenced by the amount of Ti(O*i*Pr)$_4$ used in the reaction (Table 2, entries 1–4); the highest *ee* was obtained when 3.0 equiv. of Ti(O*i*Pr)$_4$, with respect to the ligand, was used. On increasing the amount of diethylzinc in the reaction, the *ee* decreased, so 2.0 equiv. diethylzinc, with respect to the substrate, was optimal (entries 3, 5, and 6). Solvents had a significant effect on the asymmetric reaction. The results show that both diethyl ether and toluene were promising, but toluene gave the best results (entries 3 and 7–10). As for the amount of the ligand used (entries 3, 11, and 12), 20% equiv. with respect to the substrate gave good results; increasing the amount of ligand from 20 to 30%, led to an increase of only 1% in the *ee*.

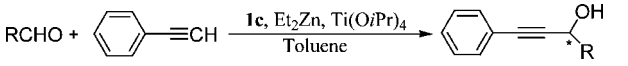
Table 2. Reaction data from the enantioselective addition of phenylacetylene to benzaldehyde with *N*-tosylproline as the chiral ligand.

Entry	Ligand[a] [%]	$Ti(OiPr)_4$[b] [equiv.]	Et_2Zn[a] [equiv.]	Solvent	Time [h]	Yield [%]	*ee* [%][c]	Config.
1	20	1.0	2.0	toluene	10	66	60	*R*
2	20	2.0	2.0	toluene	10	70	70	*R*
3	20	3.0	2.0	toluene	10	85	71	*R*
4	20	4.0	2.0	toluene	10	80	69	*R*
5	20	3.0	3.0	toluene	10	82	67	*R*
6	20	3.0	4.0	toluene	10	80	61	*R*
7	20	3.0	2.0	diethyl ether	10	75	67	*R*
8	20	3.0	2.0	THF	10	50	55	*R*
9	20	3.0	2.0	CH_2Cl_2	10	40	23	*R*
10	20	3.0	2.0	hexane	10	40	10	*R*
11	10	3.0	2.0	toluene	10	50	41	*R*
12	30	3.0	2.0	toluene	10	82	72	*R*

[a] The amount equivalent with respect to the substrate. [b] The amount equivalent of $Ti(OiPr)_4$ with respect to the ligand **1c**. [c] The *ee* was determined by chiral HPLC on a Daicel Chiracel OD column.

Because the reaction with ligand **1c** gave the highest enantioselecitvity of the ligands under these optimal reaction conditions, we next investigated its asymmetric catalytic activity in reactions with other aromatic and alkyl aldehydes as substrates. The conclusions are shown in Table 3. Except for 2-chlorobenzaldehyde (entry 13), the reactions with aromatic aldehydes gave good-to-high enantioselectivity (entries 1–13); 3-nitrobenzaldehyde gave the highest *ee* of 90% (entry 10) whilst 4-fluorobenzaldehyde and 4-methylbenzaldehyde also gave high *ee*s (entries 4 and 5). With the alkyl aldehydes, the reaction with α,β-unsaturated *trans*-cinnamaldehyde gave good enantioselectivity (entry 17); the other alkyl aldehydes only achieved moderate *ee*s.

Table 3. Reaction data from the phenylacetylene asymmetric addition to aldehydes catalyzed by **1c**–$Ti(OiPr)_4$.



Entry	Aldehyde	Time [h]	Yield [%] [a]	*ee* [%][b]
1	benzaldehyde	10	85	71
2	4-chlorobenzaldehyde	20	92	71
3	4-bromobenzaldehyde	24	80	75
4	4-fluorobenzaldehyde	10	85	80
5	4-anisaldehyde	10	80	80
6	4-tolualdehyde	24	70	66
7	3-bromobenzaldehyde	8	90	59
8	3-anisaldehyde	20	80	63
9	3-tolaldehyde	10	82	71
10	3-nitrobenzaldehyde	10	60	90
11	α-naphthaldehyde	10	84	77
12	β-naphthaldehyde	8	80	75
13	2-chlorobenzaldehyde	8	80	20
14	cyclohexanecarbaldehyde	8	70	35
15	butyraldehyde	20	70	40
16	isobutyraldehyde	20	70	25
17	cinnamaldehyde	10	60	68

[a] Isolated yield. [b] Determined by chiral HPLC on a Daicel Chiracel OD column.

Conclusions

In conclusion, some simple derivatives of natural amino acids were successfully used as chiral ligands in the catalytic asymmetric addition of phenylacetylene to aldehydes. The reactions with derivatives of proline were more enantioselective on account of its special structure. Ligand **1c**, derived from L-proline, showed the highest enantioselectivity with 90% *ee*.

Experimental Section

General Remarks: All the asymmetric reactions were carried out under argon and solvents were dried according to established procedures. Reactions were monitored by thin-layer chromatography (TLC). Purification by column chromatography was carried out using silica gel. All aldehydes, aminoacids, and their Boc and Cbz derivatives were purchased from Acros or Fluka. Diethylzinc was prepared from EtI and Zn and then diluted with toluene to form a 1.0 M solution. Melting points were recorded with an X-4 melting point apparatus and are uncorrected. ^1H NMR spectra were measured with a Bruker Am 400M spectrometer (samples in $CDCl_3$ with TMS as the internal standard). IR spectra were obtained with a Nicolet AVATAR 360 FT-IR spectrometer. Optical rotations were recorded with a Perkin-Elmer 341 polarimeter. ESI-MS were recorded with a Mariner® Biospectrometer. The *ee* values were determined by chiral HPLC (eluent: Hexane/IPA 10:1) with a Daicel Chiracel® OD column on Waters® and a 996 UV detector.

General Procedure for the Synthesis of *N*-Tosylproline (1c): L-Proline (5.76 g, 50 mmol) was dissolved in aqueous 2.0 M NaOH (50 mL, 100 mmol) at 0 °C. An ethereal solution of *p*-toluenesulfonyl chloride (9.53 g, 50 mmol) was added dropwise while stirring over 4 h. The ethereal solution was then separated and the aqueous solution acidified to pH 2.0 with hydrochloric acid. The aqueous layer was extracted with ethyl acetate three times; the organic layers were combined, washed with a little brine, dried with anhydrous $MgSO_4$, and then concentrated under reduced pressure to give the product as a pale yellow oil (12.8 g, 95% yield). $[\alpha]_D^{26}$ –83.9 (*c* = 3.05, MeOH) {lit.[15] $[\alpha]_D^{10}$ –92.5 (*c* = 1.78, EtOH)}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.93–2.14 (m, 4 H, CH_2), 2.44 (s, 3 H, CH_3), 3.23–3.29 (m, 1 H, CHN), 3.49–3.55 (m, 1 H, CHN), 4.18–4.28 (dd, *J* = 8.4 Hz, *J* = 4.4 Hz, 1 H, CHCO), 7.33–7.35 (d, *J* = 8.4 Hz, 2 H,

Ph-H), 7.76–7.78 ppm (d, J = 8.0 Hz, 2 H, Ph-H). IR (KBr): $\tilde{\nu}$ = 3541, 3214, 2981, 2880, 2740, 2642, 1730, 1597, 1491, 1449, 1402, 1344, 1286, 1198, 1157, 1094, 1012, 818, 708, 664, 590, 548 cm^{-1}. ESI-MS for $[C_{12}H_{15}NO_4S - H]^-$: 268.

General Procedure for the Synthesis of *N*-Tosylphenylalanine (2b): L-Phenylalanine (8.26 g, 50 mmol) was dissolved in 2.0 M aqueous NaOH (50 mL, 100 mmol) at 0 °C. An ethereal solution of *p*-toluenesulfonyl chloride (9.53 g, 50 mml) was added dropwise with stirring over 4 h. The ethereal solution was then separated and the aqueous solution was acidified to pH 2.0 with hydrochloric acid. The aqueous layer was extracted three times with ethyl acetate; the organic layers were combined, washed with a little brine, dried with anhydrous $MgSO_4$, and then concentrated under reduced pressure. The residue was crystallized with toluene to give **2b** as needle-shaped crystals (15.2 g, 95% yield). M.p. 158–159 °C; $[\alpha]_D^{28}$ +2.0 (c = 1.50, MeOH) {lit.[16] m.p. 164–165 °C; $[\alpha]_D^{28}$ +2.4 (CH_3COCH_3)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, CH_3), 2.96–3.01 (m, 1 H, $PhCH_2$), 3.06–3.11 (dd, J = 5.2 Hz, J = 13.6 Hz, 1 H, $PhCH_2$), 4.19–4.21 (dd, J = 3.2 Hz, J = 6.0 Hz, 1 H, CHCO), 7.06–7.07 (d, J = 7.2 Hz, 2 H, Ph-H), 7.20–7.26 (m, 5 H, Ph-H), 7.57–7.59 ppm (d, J = 8.4 Hz, 2 H, Ph-H). ESI-MS for $[C_{16}H_{17}NO_4S - H]^-$: 318.

General Procedure for the Synthesis of *N*-Methylproline (1d): L-Proline (2.0 g, 17.4 mmol) was dissolved in methanol (20 mL) and 40% aqueous formaldehyde (1.4 mL, 19.1 mmol) was added to this solution. Next, 10% Pd/C catalyst (500 mg) was added to he reaction mixture and the resulting slurry was stirred under hydrogen overnight. The slurry was then filtered through a Celite pad to remove the catalyst. The pad was washed with methanol and the combined filtrates were concentrated under reduced pressure. The residue was dissolved in ethanol/benzene (1:1, 100 mL) and concentrated a second time to provide a solid that was recrystallized from methanol/diethyl ether. In this way *N*-methylproline (**1d**) was isolated as fine needles (2.1 g, 92% yield). M.p. 143–144 °C; $[\alpha]_D^{23}$–78.0 (c = 1.5, MeOH) {lit.[12] m.p. 142–145 °C; $[\alpha]_D^{23}$ –78.0 (c = 2.0, MeOH)}. ^{1}H NMR (400 MHz, D_2O): δ = 1.78–2.01 (m, 2 H, CH_2), 2.28–2.35 (m, 1 H, CH_2), 2.75 (s, 3 H, CH_3), 2.94–3.01 (m, 1 H, NCH), 3.52–3.58 (m, 1 H, NCH), 3.69–3.73 ppm (dd, J = 7.2 Hz, J = 9.2 Hz, 1 H, CHCO). IR (KBr): $\tilde{\nu}$ = 3422, 3066, 2879, 1625, 1457, 1398, 1331, 1016 cm^{-1}. ESI MS for $[C_6H_{11}NO_2 + Na]^+$: 152; for $[C_6H_{11}NO_2 + K]^+$: 168.

General Procedure for the Synthesis of *N*-Benzoylproline (1e): L-Proline (1.15g, 10 mmol) was dissolved in 2 M NaOH (5 mL) at 0 °C and treated alternately with benzoyl chloride (1.3 mL, 11 mmol) and 2 M NaOH (5 mL) at the same temperature. The solution was vigorously stirred and cooled throughout, and it was kept alkaline by addition of more alkali. After 30 min the solution was acidified. The aqueous layer was extracted three times with chloroform (90 mL); the organic layers were combined, dried with anhydrous Na_2SO_4, and then concentrated under reduced pressure. The residue was crystallized with ethanol/water to give a needle crystal (1.36 g, 62% yield). M.p. 156–157 °C; $[\alpha]_D^{21}$ –98.0 (c = 1.00, EtOH) {lit.[17] m.p. 154–156 °C; $[\alpha]_D^{25}$ –97.0 (c = 1.0, MeOH)}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88–1.94 (m, 1 H, CH), 2.00–2.07 (m, 1 H, CH), 2.19–2.23 (m, 1 H, CH), 2.26–2.47 (m, 1 H, CH), 3.52–3.64 (m, 2 H, CH_2N), 4.77–4.80 (dd, J = 5.2 Hz, J = 8.0 Hz, 1 H, CHCO), 7.39–7.57 ppm (m, 5 H, Ph-H).

Typical Procedure for the Catalytic Asymmetric Addition of Phenylacetylene to Aldehydes: Under argon, ligand **1c** (20.2 mg, 0.075 mmol) was dissolved in dry toluene (2 mL) in a 10 mL round-bottomed flask and $Ti(OiPr)_4$ (66.6 μL, 0.225 mmol) was added at room temperature. The reaction was allowed to stir for 1 h. Then a solution of Et_2Zn (0.5 mL, 0.5 mmol, 1.0 mmol/mL dry toluene) was introduced and the mixture was stirred for 1 h. Phenylacetylene (33 μL, 0.3 mmol) was added to the flask and the reaction continued for another 1 h at the same temperature. Then the flask was put into an ice-water bath and the mixture cooled to 0 °C. Benzaldehyde (25 μL, 0.25 mmol) was then introduced. The reaction mixture was allowed to warm to room temperature and stirred to completion, as determined by TLC. The flask was cooled to 0 °C, and the reaction quenched with 5% aqueous HCl. The aqueous layer was extracted with diethyl ether three times; the organic layers were combined, washed with a little brine (3 mL), dried with anhydrous Na_2SO_4, and then concentrated to dryness. The resulting crude product was purified by preparative TLC to afford the desired alcohol as a pale yellow oil.

(*R*)-1,3-Diphenylprop-2-yn-1-ol: 85% yield, 71% *ee*. Retention time: t_{major} = 13.49 min, t_{minor} = 22.22 min.

1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-ol: 92% yield; 71% *ee*. Retention time: t_{major} = 10.36 min, t_{minor} = 31.49 min.

1-(4-Bromophenyl)-3-phenylprop-2-yn-1-ol: 80% yield; 75% *ee*. Retention time: t_{major} = 11.08 min, t_{minor} = 34.67 min.

1-(4-Fluorophenyl)-3-phenylprop-2-yn-1-ol: 85% yield; 80% *ee*. Retention time: t_{major} = 9.94 min, t_{minor} = 28.06 min.

1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-ol: 80% yield; 80% *ee*. Retention time: t_{major} = 16.38 min, t_{minor} = 31.44 min.

1-(4-Methylphenyl)-3-phenylprop-2-yn-1-ol: 70% yield; 66% *ee*. Retention time: t_{major} = 10.60 min, t_{minor} = 20.79 min.

1-(3-Bromophenyl)-3-phenylprop-2-yn-1-ol: 90% yield; 59% *ee*. Retention time: t_{major} = 10.82 min, t_{minor} = 37.15 min.

1-(3-Methoxyphenyl)-3-phenylprop-2-yn-1-ol: 80% yield; 63% *ee*. Retention time: t_{major} = 18.49 min, t_{minor} = 29.96 min.

1-(3-Methylphenyl)-3-phenylprop-2-yn-1-ol: 82% yield; 71% *ee*. Retention time: t_{major} = 11.98 min, t_{minor} = 27.30 min.

1-(3-Nitrophenyl)-3-phenylprop-2-yn-1-ol: 60% yield; 90% *ee*. Retention time: t_{minor} = 11.80 min, t_{major} = 17.13 min.

1-(1-Naphthyl)-3-phenylprop-2-yn-1-ol: 84% yield; 77% *ee*. Retention time: t_{major} = 17.45 min, t_{minor} = 36.05 min.

1-(2-Naphthyl)-3-phenylprop-2-yn-1-ol: 80% yield; 75% *ee*. Retention time: t_{major} = 16.94 min, t_{minor} = 52.98 min.

1-(2-Chlorophenyl)-3-phenylprop-2-yn-1-ol: 80% yield; 20% *ee*. Retention time: t_{major} = 10.61 min, t_{minor} = 11.64 min.

1-Cyclohexyl-3-phenylprop-2-yn-1-ol: 70% yield; 35% *ee*. Retention time: t_{major} = 6.41 min, t_{minor} = 14.62 min.

1-Phenylhex-1-yn-3-ol: 70% yield; 40% *ee*. Retention time: t_{major} = 6.28 min, t_{minor} = 15.93 min.

4-Methyl-1-phenylpent-1-yn-3-ol: 70% yield; 25% *ee*. Retention time: t_{major} = 6.13 min, t_{minor} = 10.68 min.

***trans*-1,5-Diphenylpent-1-en-4-yn-3-ol:** 60% yield; 68% *ee*. Retention time: t_{major} = 19.03 min, t_{minor} = 67.19 min.

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[1] a) N. Cohen, G. Saucy, *J. Org. Chem.* **1980**, *45*, 582–588; b) R. A. Gibbs, W. H. Okamura, *J. Am. Chem. Soc.* **1988**, *110*, 4062–4063; c) B. Trost, M. J. Krisch, *J. Am. Chem. Soc.* **1999**, *121*, 6131–6141; d) A. G. Myers, B. Zheng, *J. Am. Chem. Soc.* **1996**, *118*, 4492–4493; e) W. Oppolzer, R. N. Radinov, E. El-Sayed, *J. Org. Chem.* **2001**, *66*, 4766–4770.

[2] For reviews, see: a) P. Z. Cozzi, R. Hilgraf, N. Zimmermann, *Eur. J. Org. Chem.* **2004**, 4095–4105; b) L. Pu, *Tetrahedron* **2003**, *59*, 9873–9886; c) D. E. Frantz, R. Fässler, C. S. Tomooka, E. M. Carreira, *Acc. Chem. Res.* **2000**, *33*, 373–381.

[3] a) D. E. Frantz, R. Fässler, E. M. Carreira, *J. Am. Chem. Soc.* **2000**, *122*, 1806–1807; b) E. El-Sayed, N. K. Anand, E. M. Carreira, *Org. Lett.* **2001**, *3*, 3017–3020; c) D. Boyall, F. López, H. Sasaki, D. Frantz, E. M. Carriera, *Org. Lett.* **2000**, *2*, 4233–4236; d) N. K. Anad, E. M. Carreira, *J. Am. Chem. Soc.* **2001**, *123*, 9687–9688.

[4] a) G. Lu, X. Li, W. L. Chan, A. S. C. Chan, *Chem. Commun.* **2002**, 172–174; b) X. Li, G. Lu, W. H. Kwok, A. S. C. Chan, *J. Am. Chem. Soc.* **2002**, *124*, 12636–12637.

[5] a) D. Moore, L. Pu, *Org. Lett.* **2002**, *4*, 1855–1857; b) G. Gao, D. Moore, R.-G. Xie, L. Pu, *Org. Lett.* **2002**, *4*, 4143–4146; c) M.-H. Xu, L. Pu, *Org. Lett.* **2002**, *4*, 4555–4557; d) D. Moore, W.-S. Huang, M.-H. Xu, L. Pu, *Tetrahedron Lett.* **2002**, *43*, 8831–8834; e) Z.-B. Li, L. Pu, *Org. Lett.* **2004**, *6*, 1065–1068.

[6] a) Z. Xu, R. Wang, J. Xu, C.-s. Da, W.-j. Yan, C. Chen, *Angew. Chem. Int. Ed.* **2003**, *42*, 5747–5749; b) Z. Xu, C. Chen, J.-k. Xu, M.-b. Miao, W.-j. Yan, R. Wang, *Org. Lett.* **2004**, *6*, 1193–1195.

[7] a) B. Jiang, Y. Feng, *Tetrahedron Lett.* **2002**, *43*, 2975–2977; b) G. Lu, X. Li, Z. Zhou, W. L. Chan, A. S. C. Chan, *Tetrahedron: Asymmetry* **2001**, *12*, 2147–2152.

[8] a) A. L. Braga, H. R. Appelt, C. C. Silveria, L. A. Wessjohann, P. H. Schneider, *Tetrahedron* **2002**, *58*, 10413–10416; b) M. Li, X.-Z. Zhu, K. Yuan, B.-X. Cao, X.-L. Hou, *Tetrahedron: Asymmetry* **2004**, *15*, 219–222.

[9] a) X.-w. Yang, J.-h. Shen, C.-s. Da, R. Wang, M. C. K. Choi, L. Yang, K.-y. Wong, *Tetrahedron: Asymmetry* **1999**, *10*, 133–138; b) X.-w. Yang, J.-h. Shen, C.-s. Da, H.-s. Wang, W. Su, R. Wang, A. S. C. Chan, *J. Org. Chem.* **2000**, *65*, 295–296; c) X.-w. Yang, W. Su, D.-x. Liu, H.-s. Wang, J.-h. Shen, C.-s. Da, R. Wang, A. S. C. Chan, *Tetrahedron* **2000**, *56*, 3511–3516; d) X.-w. Yang, J.-h. Shen, C.-s. Da, H.-s. Wang, W. Su, D.-x. Liu, R. Wang, M. C. K. Choi, A. S. C. Chan, *Tetrahedron Lett.* **2001**, *42*, 6573–6575; e) D.-x. Liu, L.-c. Zhang, Q. Wang, C.-s. Da, Z.-q. Xin, R. Wang, M. C. K. Choi, A. S. C. Chan, *Org. Lett.* **2001**, *3*, 2733–2735; f) C.-s. Da, Z.-j. Han, M. Ni, F. Yang, D.-x. Liu, Y.-f. Zhou, R. Wang, *Tetrahedron: Asymmetry* **2003**, *14*, 659–665; g) Y.-f. Kang, L. Liu, R. Wang, W.-j Yan, Y.-f. Zhou, *Tetrahedron: Asymmetry* **2004**, *15*, 3155–3159.

[10] Y.-f. Zhou, R. Wang, Z.-q. Xu, W.-j. Yan, L. Liu, Y.-f. Gao, C.-s. Da, *Tetrahedron: Asymmetry* **2004**, *15*, 589–591.

[11] J.-S. You, M.-Y. Shao, H.-M. Gau, *Tetrahedron: Asymmetry* **2001**, *12*, 2971–2975.

[12] L. Aurelio, J. S. Box, R. T. C. Brownlee, A. B. Hughes, M. M. Sleebs, *J. Org. Chem.* **2003**, *68*, 2652–2667.

[13] B. List, *Tetrahedron* **2002**, *58*, 5573–5590.

[14] P. V. Ramachandran, A. V. Teodorovic, M. V. Rangaishenvi, H. C. Brown, *J. Org. Chem.* **1992**, *57*, 2379–2386.

[15] N. Izumiya, *Bull. Chem. Soc. Jpn.* **1953**, *26*, 53–58.

[16] J. I. G. Cadogan, S. V. Ley, G. Pattenden, *Dictionary of Organic Compounds*, 6th ed., Chapman & Hall, London, **1996**, vol. 5, p. 5190 (P-0-01247).

[17] J. S. Davies, W. A. Thomas, *J. Chem. Soc., Perkin Trans. 2* **1978**, 1157–1163.

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