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Biocatalytic Asymmetric Synthesis of Optically Pure Aromatic Propargylic Amines Employing ω-Transaminases

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Abstract: The asymmetric reductive bio-amination of prochiral aromatic propargyl ketones led to the corresponding amines in optically pure form (*ee* > 99%). The (*R*)- as well as the (*S*)-enantiomers of the propargylic amines were obtained, employing either (*R*)-selective ω-transaminases (ω-TAs) originating from *Arthrobacter* sp. and *Aspergillus terreus* or an (*S*)-selective ω-TA from *Chromobacterium violaceum*. The product propargylic amines were obtained with high conversions (up to 99%). To simplify product isolation, protection of the free amino group to the corresponding acetamides or benzamides was performed without loss of optical puritiy. The final products were isolated in moderate to good yields (33–67% over two steps) in optical pure form without additional purification steps. Although propargyl ketones are described in the literature to be irreversible inhibitors for aminotransferases, suitable ω-transaminases were identified for the amination of these compounds.

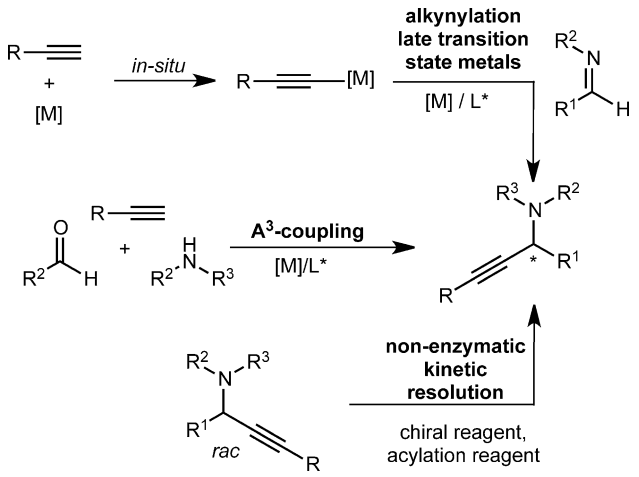
Keywords: amines; asymmetric catalysis; biotransformations; enzymes; propargylic amines

Introduction

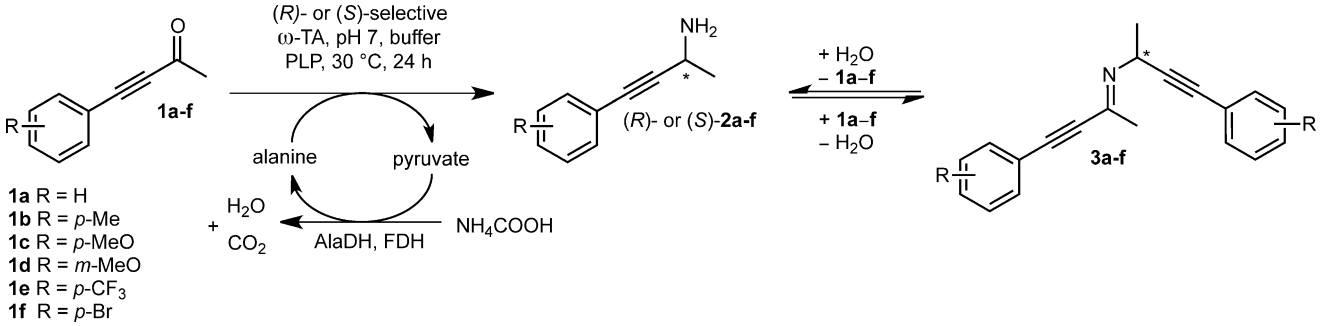
Propargylic amines unite the nucleophilic properties of an amine group and the moderate electrophilicity of a triple bond in a single molecule. These features make substituted propargylic amines versatile building blocks for organic synthesis, especially for the preparation of nitrogen-containing heterocycles such as 2-aminoimidazoles,[1] oxazolidones,[2] pyrimidones[3] or triazoles.[4] Additionally, they constitute a key scaffold in various pharmaceuticals and biologically active compounds,[5] including monoamine oxidase B (MAO-B) and HIV-1 reverse transcriptase inhibitors.[6]

Due to the broad applicability of chiral propargylic amines, a convenient straight-forward procedure for their preparation in optical pure form is highly demanded. Thereby, the combination of late transition state metals and chiral ligands for the alkynylation of aldimines can be seen as state of the art (Scheme 1).[7] This reaction requires the use of activated C=N species such as nitrones, *N*-acyl-, *N*-sulfonyl-, *N*-tosyl- or *N*-mesylimines.[8] To circumvent the need of externally prepared, activated electrophiles, this classical methodology was extended to a three-component coupling reaction of an aldehyde, alkyne and amine, also referred to as A^3-coupling.[9]

While the nucleophilic 1,2-addition allows the asymmetric synthesis of chiral propargylic amines



Scheme 1. Conventional routes for the preparation of chiral propargylic amines, including the nucleophilic 1,2-additon to activated aldimines and the non-enzymatic kinetic resolution of racemic propargylic amines.



Scheme 2. Asymmetric amination of ketones **1a–f** using (*R*)- or (*S*)-selective ω-transaminases.

from scratch, the non-enzymatic kinetic resolution employs chiral reagents in combination with acylation reagents to resolve racemic propargylic amines.[10] Although this approach gives rise to a broad range of free propargylic amines, its main drawback is the limitation to a maximum possible yield of 50%. Besides these numerous chemical approaches for the synthesis of optically pure propargylic amines, no biocatalytic methodology has been reported to access propargylic amines to the best of our knowledge; only propargylic alcohols have been prepared by biocatalytic approaches.[11]

The application of enzymes in organic synthesis has proven to be an alternative for established chemical processes.[12] Important benefits of biocatalysts are mild operation conditions such as aqueous media, temperatures between 20 °C and 40 °C and physiological pH values. In general, they are air- and water-stable and apart from the environmental benefits, enzymes display high chemo-, regio- and stereoselectivities. Consequently, chiral primary amines have already been successfully accessed *via* biocatalysis.[13] In this context, ω-transaminases or aminotransferases (E.C. 2.6.1.X), which catalyse the transfer of an amino group from an amine donor to a ketone (i.e., amine acceptor), have gained significant attention as they exhibit a broad substrate spectrum.[14] However, the preparation of propargylic amines from propargyl ketones has not been reported as yet.

Results and Discussion

Firstly, prochiral propargyl ketones **1b–f** bearing electron-donating or electron-withdrawing substituents at the phenyl moiety were prepared *via* a single-step synthesis from commercially available aromatic acetylenes as previously described[11b] (see the Supporting Information).

Then various enantiocomplementary ω-transaminases were tested for the reductive amination of model substrate **1a** (Scheme 2). The (*R*)-selective ω-TAs from *Arthrobacter* sp. (ArR-ω-TA)[15] and *Aspergillus terreus* (AT-ω-TA)[16] as well as the (*S*)-selective ω-TA from *Chromobacterium violaceum* (CV-ω-TA)[17] successfully converted **1a** to the chiral propargylic amine **2a**.

It is worth mentioning that other ω-TAs like the one from *Bacillus megaterium*,[18] *Paracoccus denitrificans*,[19] *Pseudomonas putida*, *Vibrio fluvialis*[20] or *Arthrobacter citreus*[21] did not transform **1a**, although they have been described to possess a broad substrate tolerance, involving bulky and long chained substrates.[22] Having identified a suitable (*S*)-selective ω-TA and two (*R*)-selective ω-TAs, the reaction conditions were optimised with respect to substrate concentration and co-solvent. Optimum substrate concentrations ranged from 10 mM to 25 mM. At higher concentrations of **1a**, a side product was detected in significant amounts, which was proposed to be imine **3a** according to mass spectroscopy. Imine **3a** is in equilibrium with substrate ketone **1a** and product amine **2a**. Furthermore, extended reaction times (>24 h) resulted in the degradation of the product amine as deduced from non-identified products observed by GC and a colour change of the reaction mixture. On comparing the time courses of the bioreduction of **1a** at 25 and 50 mM with ArR-ω-TA up to 72 h, imine formation was highest within the first 3 h of the reaction (Figure 1). Due to the transformation of ketone **1** to amine **2** and the equilibrium between imine **3** and ketone/amine, the concentration of imine **3** depleted over time.

As the reaction proceeded, the amount of imine decreased to a minimum of 4% in the case of 25 mM substrate concentration whereas at 50 mM, the amount of imine remained at 20%. In both cases the starting ketone **1a** was not detectable anymore after 24 h. Prolonging the reaction time did not result in imine depletion; however degradation of product **2a** became predominant.

Consequently, various phenyl-substituted propargyl ketones **1a–f** were subjected to the bioamination in the presence of CV-, ArR- or AT-ω-TA. All substrates were successfully transformed with high conversions and perfect stereoselectivity (*ee* >99%)

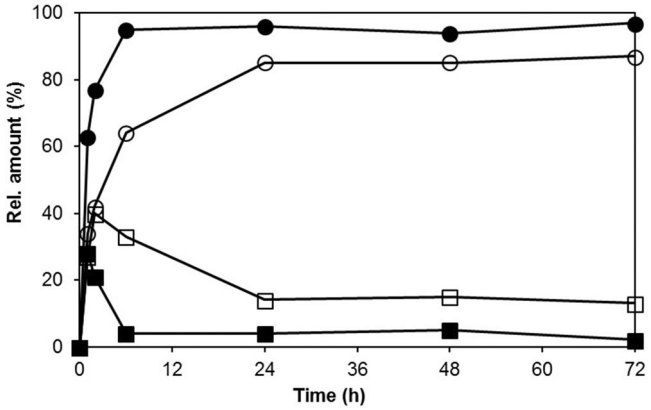


Figure 1. Time course for the formation of amine **2a** (○, ●) and imine **3a** (□, ■) during the ArR-ω-TA-catalysed amination of ketone **1a** at 25 mM (filled symbols) and 50 mM (open symbols).

(Table 1, Table 2, and Table 3). For substrates bearing an electron-donating group in *para* or *meta* positions in particular, the conversion to the desired optically pure propargylic amines was over 90% (Table 1, Table 2, and Table 3 entries 2–4). In most cases, the starting material was completely consumed within 24 h and the amount of detected imine **3a–d** was always below 10%. However, if the substrates carried an electron-withdrawing group at the phenyl ring (i.e.. substrates **1e** and **1f**), conversions to products **2e** and **2f** were lower, independent of the ω-TA used.

In more detail, the (*S*)-selective ω-transaminase CV-ω-TA (Table 1) transformed all *para*-substituted substrates with perfect stereoselectivity (*ee* >99%) to the corresponding (*S*)-amine (*S*)-**2** (entries 1–3, 5, and 6) and the *meta*-methoxy-substituted ketone **1d** to (*S*)**-2d** with 96% *ee* (entry 4). The addition of co-solvent (10% v v^{-1}) had a positive effect on the formation of amine **2**, particularly for substrate **1d**, leading to an increase of product formation of **2d** from 82% to 97%. Additionally, in the presence of DMSO the *ee* for **2d** improved from 96% to >99%. On the other hand, DMSO led to decreased conversions for **1c**, **1e** and **1f**, whereas for **1a** and **1b** the conversion remained at 99%.

The (*R*)-selective ω-TA variant originating from *Arthrobacter* sp. transformed all ketones to the (*R*)-

Table 1. Asymmetric reductive amination of ketones **1a–f** catalysed by CV-ω-TA.[a]

Entry	Substrate	Without co-solvent				DMSO (10% v/v)			
		1 [%]	**2** [%]	*ee* **2** [%][c]	**3** [%]	**1** [%]	**2** [%]	*ee* **2** [%][c]	**3** [%]
1	**1a**	<1	99	>99 (*S*)	<1	<1	99	>99 (*S*)	<1
2	**1b**	<1	99	>99 (*S*)	<1	<1	99	>99 (*S*)	<1
3	**1c**	3	97	>99 (*S*)	<1	10	89	>99 (*S*)	1
4	**1d**	18	82	96 (*S*)	<1	3	97	>99 (*S*)	<1
5	**1e**	<1	83[b]	>99 (*S*)	<1	32	19[b]	>99 (*S*)	37
6	**1f**	21	58[b]	>99 (*S*)	<1	10	54[b]	>99 (*S*)	<1

[a] *Reaction conditions:* substrate **1** (10 mM), lyophilised *E. coli* cells containing the (*S*)-selective CV-ω-TA (20 mg), L-alanine (250 mM), ammonium formate (150 mM), phosphate buffer (100 mM, pH 7), PLP (1 mM), NAD^+ (1 mM), FDH (11 U), AlaDH (12 U), 24 h, 30 °C, in the case of DMSO: 10% v/v. Reaction volume = 1 mL.

[b] An unidentified side product was detected by GC analysis; therefore, the percentages of **1**, **2** and **3** do not sum up to 100%.

[c] Determined by GC on a chiral phase after acetylation to the corresponding acetamide derivative **4**.

Table 2. Asymmetric reductive amination of ketones **1a–f** catalysed by ArR-ω-TA.[a]

Entry	Substrate	Without co-solvent				DMSO (10% v/v)			
		1 [%]	**2** [%]	*ee* **2** [%][b]	**3** [%]	**1** [%]	**2** [%]	*ee* **2** [%][b]	**3** [%]
1	**1a**	<1	99	>99 (*R*)	<1	<1	98	>99 (*R*)	1
2	**1b**	<1	92	>99 (*R*)	8	1	90	>99 (*R*)	9
3	**1c**	<1	96	>99 (*R*)	4	<1	96	>99 (*R*)	4
4	**1d**	2	95	>99 (*R*)	3	3	97	>99 (*R*)	3
5	**1e**	9	64	98 (*R*)	27	<1	65	98 (*R*)	34
6	**1f**	34	46	>99 (*R*)	20	<1	76	>99 (*R*)	23

[a] *Reaction conditions:* substrate (25 mM), lyophilised *E. coli* cells (20 mg) containing the (*R*)-selective ArR-ω-TA, D-alanine (250 mM), ammonium formate (150 mM), phosphate buffer (100 mM, pH 7.0), PLP (1 mM), NAD^+ (1 mM), FDH (11 U), AlaDH (12 U), 24 h, 30 °C. Reaction volume = 1 mL.

[b] Determined by GC on a chiral phase after acetylation to the corresponding acetamide derivative **4**.

Table 3. Asymmetric reductive amination of ketones **1a–f** catalysed by AT-ω-TA.[a]

Entry	Substrate	Without co-solvent				DMSO (10% v/v)			
		1 [%]	**2** [%]	*ee* **2** [%][c]	**3** [%]	**1** [%]	**2** [%]	*ee* **2** [%][c]	**3** [%]
1	**1a**	<1	>99	>99 (*R*)	<1	<1	>99	>99 (*R*)	<1
2	**1b**	<1	>99	>99 (*R*)	<1	<1	>99	>99 (*R*)	<1
3	**1c**	<1	95[b]	>99 (*R*)	<1	<1	97[b]	>99 (*R*)	<1
4	**1d**	<1	97[b]	>99 (*R*)	<1	<1	97[b]	>99 (*R*)	<1
5	**1e**	59	35	>99 (*R*)	6	<1	90	>99 (*R*)	10
6	**1f**	25	70[b]	>99 (*R*)	1	<1	94[b]	>99 (*R*)	2
Entry	Substrate	1,2-Dimethoxyethane (10% v/v)				DMF (10% v/v)			
		1 [%]	**2** [%]	*ee* **2** [%][c]	**3** [%]	**1** [%]	**2** [%]	*ee* **2** [%][c]	**3** [%]
1	**1a**	1	98	>99 (*R*)	1	<1	>99	>99 (*R*)	<1
2	**1b**	1	93	>99 (*R*)	6	<1	>99	>99 (*R*)	<1
3	**1c**	1	95[b]	>99 (*R*)	<1	<1	97[b]	>99 (*R*)	<1
4	**1d**	<1	96[b]	>99 (*R*)	<1	<1	97[b]	>99 (*R*)	<1
5	**1e**	<1	62	>99 (*R*)	38	<1	95	>99 (*R*)	5
6	**1f**	<1	85[b]	>99 (*R*)	11	<1	96[b]	>99 (*R*)	1

[a] *Reaction conditions:* substrate (10 mM), lyophilised *E. coli* cells (20 mg) containing the (*R*)-selective AT-ω-TA, D-alanine (250 mM), ammonium formate (150 mM), phosphate buffer (100 mM, pH 7), PLP (1 mM), NAD^+ (1 mM), FDH (11 U), AlaDH (12 U), 24 h, 30 °C. Reaction volume = 1 mL.

[b] An unidentified side product was detected by GC-analysis; that is why the percentages of **1**, **2** and **3** do not sum up to 100%.

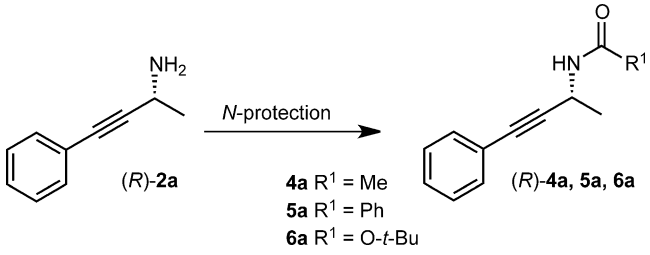
[c] Determined by GC on a chiral phase after acetylation to the corresponding acetamide derivative **4**.

propargylic amines with perfect *ee* (>99%) at 25 mM (Table 2), except for **1e**, which led to the corresponding amine (*R*)-**2e** with 98% *ee*. The enzyme preserved its excellent stereoselectivity also in the presence of DMSO (10% vv^{-1}), thus in all cases identical *ee*s were obtained as in the absence of DMSO. The second (*R*)-selective ω-transaminase from *Aspergillus terreus* (AT-ω-TA) aminated all substrates to the desired (*R*)-propargylic amines with perfect stereoselectivity (*ee* >99%) (Table 3). Studying the influence of different co-solvents such as DMSO, 1,2-dimethoxyethane (DME) and dimethylformamide (DMF) on the conversion, it was noticed that their addition improved the biotransformation of all substrates compared to reactions run without co-solvent.[23]

The obtained results clearly indicate that propargyl ketones can be aminated and are therefore not necessarily aminotransferase inhibitors acting *via* the formation of a covalent bond to an active site amino acid residue as previously proposed.[24]

To enable the application of the propargylic amines as building blocks for further syntheses as well as the isolation on preparative scale, derivatisation of the free amino group was required. Attempts to directly isolate the chiral amines **2a–f** from an up-scaled biotransformation failed, due to the quick degradation of the propargylic amines which had already been reported previously.[25] Consequently, various *N*-protection strategies were investigated to obtain the chiral products without loss of optical purity (Table 4). Particular attention was devoted to the *N*-acylation of (*R*)-**2a** to yield the acetylated (*R*)-**4a** and the benzoylated derivative (*R*)-**5a** for two reasons: first and foremost, the required acid chlorides/anhydrides are

Table 4. Derivatisation experiments of (*R*)-**2a**.



Entry	(*R*)-**2a** [mmol]	Reagents	Temp. [°C]	Time [h]	Yield[a] [%]
1	0.25	Ac_2O, pyr	21	15	45
2	0.10	Ac_2O, Et_3N	0–21[b]	15	65
3	0.25	AcCl, Et_3N	0–21[b]	3	43[c]
4	0.25	BzCl, Et_3N	0–21[b]	3	26[c]
5	0.25	Boc_2O, Et_3N	0–21[b]	15	58[d]

[a] Isolated yields over two reaction steps, i.e., biotransformation and acylation.

[b] The reaction was started at 0 °C and after all reagents were added the mixture was allowed to warm to 21 °C.

[c] Reaction was performed under an inert atmosphere, with freshly distilled acid chlorides and dry solvents.

[d] Residual Boc_2O impurities after flash chromatography.

Table 5. Isolated yields for acetamides and benzamides after asymmetric amination of ketone **1** and derivatisation.[a]

Entry	ω-TA	Amide[a]	R	Yield[b] [%]	*ee* [%]
1	AT	**4a**	H	65	>99 (*R*)
2	CV	**4a**	H	67	>99 (*S*)
3	AT	**4b**	*p*-Me	54	>99 (*R*)
4	AT	**4c**	*p*-MeO	64	>99 (*R*)
5	AT	**4d**	*m*-MeO	45	>99 (*R*)
6	AT	**5e**	*p*-CF_3	33	>99 (*R*)
7	AT	**4f**	*p*-Br	36	>99 (*R*)

[a] *Reaction conditions:* for amines **2a–d**, **f** (0.1–0.2 mmol), Et_3N (6.0 equiv.), Ac_2O (2.0 equiv.) in CH_2Cl_2, 0 °C to room temperature, overnight; for amine **2e**, Et_3N (1.5 equiv.), BzCl (1.0 equiv.) in absolute CH_2Cl_2, 0 °C to room temperature, 2 h, N_2.

[b] Isolated yields over two reaction steps, i.e., biotransformation and acylation. DMSO (10% v/v) supported preparative biotransformations were performed using AT-ω-TA (200 mg), substrate **1a–f** (0.1–0.2 mmol). Theoretical yields for **4a–f** were calculated based on the conversions for (*R*)-**2a–f** (Table 3).

cheap and readily available; furthermore, the generated amides are stable solids that can be easily isolated.

Acetylation was more efficient than the benzoylation when applying acid chlorides (entries 3 and 4). Regarding the acetylation with acetic anhydride, it was observed that a decreased amine concentration (10 mM instead of 25 mM, calculated based on the conversion of the biotransformation), as well as the switch from pyridine to Et_3N positively influenced the reaction as higher yields of acetamide (*R*)-**4a** were obtained (entries 1 and 2). Additionally, it has to be noted that the application of acetic anhydride allowed a simplified work-up procedure *via* extraction, while flash chromatography was required to purify reactions using the acid chlorides. Alternatively to the acylation, carbamate (*R*)-**6a** was successfully obtained by *N*-Boc protection. Since Boc_2O required more purification steps, acetylation using acetic anhydride and Et_3N was favoured. After having identified an appropriate protection procedure, preparative asymmetric bioamination was performed for substrates **1a–f** employing AT-ω-TA.

The chiral product amines (*R*)-**2a–f** were directly derivatised to (*R*)-**4a–d** and **4f** as well as (*R*)-**5e** which were obtained with reasonable yields (Table 5). It is worth mentioning that converting the propargylic amines to the corresponding amides did not affect the optical purity, thus the *ee*s remained >99%. Just to have one (*S*)-product prepared as well, (*S*)-**4a** was isolated with *ee* >99% (entry 2). The absolute configurations of (*R*)- or (*S*)-**4a–f** and (*R*)-**5e** were determined *via* measurement of the optical rotations and comparison to values recently published (see the Supporting Information).[10a,b]

Conclusions

In summary, the first asymmetric reductive amination of a set of prochiral aromatic propargyl ketones has been reported. Although propargylic amines have previously been reported to be irreversible inhibitors for aminotransferases,[24] suitable ω-transaminases were identified for this reaction. Different substrates, bearing an electron-donating or electron-withdrawing group attached to the phenyl ring could be successfully transformed to the (*S*)- or (*R*)-propargylic amines by three known ω-transaminases. In general, the (*S*)- and (*R*)-amine products **2a–f** were obtained with perfect *ee* (>99%) after optimisation of the reaction conditions and depending on the choice of the enzyme. Conversions ranged from moderate for substrates **1e–f** to (almost) completion for **1a–d**. Employing water miscible co-solvents (10% $v v^{-1}$) such as DMSO, DME or DMF led to enhanced conversions in selected cases. Due to the low stability of unprotected propargylic amines, derivatisation to the stable propargylic amides was performed following the preparative biotransformation without loss of optical purity. The procedure presented represents a reliable and simple approach for the asymmetric synthesis of optically pure propargylic amines, which are important chiral building blocks.

Experimental Section

General Remarks

All chemicals used in this study were purchased from commercial suppliers and used as received unless stated otherwise. Preparative chromatographic separations were performed by column chromatography on Merck silica gel 60 (0.063–0.200 μm). Optical rotations at the sodium D-line were measured at 25 °C on a Perkin–Elmer polarimeter 341. GC and GC-MS were recorded with an Agilent 7890A GC system. The GC-MS system was equipped with an Agilent 5975C mass selective detector and an HP-5 MS column (30 m × 0.25 mm × 0.25 μm; helium as carrier gas [flow = 0.55 mL min^{-1}]). ^1H and ^{13}C NMR spectra were recorded at 20 °C on a 300 Bruker NMR unit; chemical shifts are given in ppm relative to Me_4Si or relative to the resonance of the solvent. Formate dehydrogenase (2.1 U mg^{-1}) was purchased from Evocatal (Evo 1.1.230). All ω-transaminases were overexpressed in *E. coli* BL21 (DE3) and used as lyophilised cell preparations as reported previously.[14b,23e,26] L-Alanine dehydrogenase from *Bacillus subtilis* was prepared and purified as described recently.[23e] All biotransformations were carried out in an Infors Unitron shaker.

Representative Procedure for the Synthesis of (*R*)-Phenylbut-3-yn-2-yl-amine (*R*)-2a (Analytical Scale)

Lyophilised cells of *E. coli* containing the overexpressed AT-ω-TA (20 mg) were rehydrated in sodium phosphate buffer (pH 7.0, 100 mM, 334 μL) at 30 °C for 30 min. Buffer

solutions of PLP (50 μL, 20 mM), NAD^+ (50 μL, 20 mM), NH_4COOH (100 μL, 1.5 M), D-alanine (250 μL, 1 M), FDH (5 mg, 11 U), and AlaDH (15 μL, 12 U) were added to the reaction vessel. Finally, addition of substrate **1a** (1.44 mg, 0.01 mmol) – if required in solution with the co-solvent (100 μL, 10% v/v) – started the bio-transformation which was shaken at 120 rpm and 30 °C for 24 h. The reaction mixture was quenched by addition of saturated Na_2CO_3 solution (200 μL) and vigorous shaking. After extraction with EtOAc (2 × 500 μL) the combined organic layers were dried over $MgSO_4$ and the conversion was measured by GC.

Representative Procedure for the Synthesis of (*R*)-Phenylbut-3-yn-2-yl-amine (*R*)-2a (Preparative Scale)

For the preparative biotransformation, the lyophilised *E. coli*/ω-TA preparation (200 mg) and substrate **1a** (14.4 mg, 0.1 mmol) were incubated in sodium phosphate buffer (pH 7.0, 100 mM, 3.34 mL) containing PLP (1 mM), NAD^+ (1 mM), NH_4COOH (150 mM), D-alanine (250 mM), FDH (110 U), Ala-DH (120 U) and DMSO (10% v/v) under the same conditions as described above. The reaction was stopped by adding 2 N HCl (2.5 mL), followed by extraction with CH_2Cl_2 (5 mL) in order to remove any remaining starting material. The aqueous layer was basified with 6 N NaOH (1 mL) to pH 10–11 and extracted with Et_2O (2 × 5 mL). The collected organic layers were dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residual oil was immediately used for derivatisation.

Representative Procedure for the Synthesis of (*R*)-*N*-(4-Phenylbut-3-yn-2-yl)acetamide (*R*)-(4a)

The freshly isolated propargylic amine (*R*)-**2a** (0.1 mmol) was dissolved in CH_2Cl_2 (5 mL). The mixture was placed on ice and Et_3N (83 μL, 0.6 mmol) was added under vigorous stirring. Then, Ac_2O (20 μL, 0.2 mmol) was added dropwise and stirring was continued at room temperature overnight. Addition of water (3 mL) and stirring for another 30 min stopped the reaction. The organic layer was washed with 5% H_2SO_4 (2 × 25 mL) and saturated Na_2CO_3 (2 × 25 mL) prior to drying over $MgSO_4$. The solvent was removed under reduced pressure to the yield the optically pure acetamide (*R*)-**4a** as a colourless solid; yield: 12.2 mg (0.065 mmol, 65%); R_f = 0.3 (CH_2Cl_2/EtOAc, 90:10); mp 90–95 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 1.48 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3), 2.01 (s, 3 H, CH_3), 5.05 (dq, $^3J_{H,H}$ = 6.9 Hz, 1 H, CH), 5.93 (brd, $^3J_{H,H}$ = 6.7 Hz, 1 H, NH), 7.30 (m_c, 3 H, Ar), 7.40 (m_c, 2 H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.6 (CH_3), 23.3 (CH_3), 37.7 (CH), 82.2 (C), 89.4 (C), 122.5 (C), 128.3 (CH), 128.4 (CH), 131.7 (CH), 168.9 (C); IR (ATR-film): ν = 3287, 3056, 2977, 2927, 1636 (C=O), 1539, 1367, 1275, 1132, 976, 760, 712, 689, 601 cm^{-1}; GC-MS (70 eV, EI): *m/z* (%) = 187 (18) [M^+−H], 172 (100) [$C_{11}H_{10}NO^+$]; $[\alpha]_D^{25}$: +183 (*c* 0.51, $CHCl_3$), >99% *ee*; Lit.[10a] for (*S*)-amine $[\alpha]_D^{20}$: −163 (*c* 0.6, $CHCl_3$), 91% *ee*.

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