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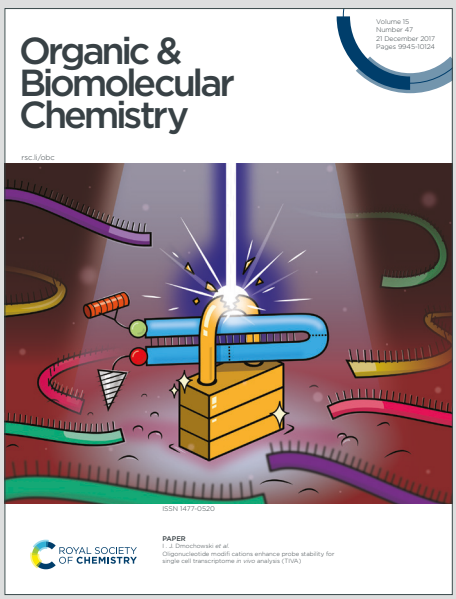

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ARTICLE

Dimethylzinc-mediated enantioselective addition of terminal alkynes to 1,2-diketones using perhydro-1,3-benzoxazines as ligands

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A conformationally restricted perhydro-1,3-benzoxazine derived from (-)-8-aminomenthol behaves as a good chiral ligand in the dimethylzinc-mediated enantioselective monoaddition of aromatic and aliphatic terminal alkynes to 1,2-diketones. The corresponding α-hydroxyketones were achieved in good yields with high enantioselectivities starting from both aromatic and aliphatic 1,2-diketones. The alkynylation of unsymmetrically 1,2-diketones with electronically different substituents also proceed with high regio- and enantioselectivity. This reaction provides a practical way to synthesize ketones bearing a chiral tertiary propargylic alcohol.

Introduction

The construction of chiral tertiary alcohol functionalities is a continuing challenge in the synthesis of pharmacologically active compounds, natural products and organic building blocks.[1] The catalytic enantioselective addition of nucleophilic reagents to carbonyl compounds is an extended method for the construction of optically active alcohols and there are several catalytic enantioselective reactions to access chiral secondary alcohols, such as the deeply studied and highly developed addition of organozinc reagents to aldehydes.[2] In contrast, the formation of optically active tertiary alcohols through the addition of nucleophilic organozinc reagents to simple ketones still remains a challenge. This attends to the lower reactivity of ketones and the difficulties in stereodifferentiation of their two enantiotopic faces.[3]

The utilization of activated ketones bearing an electron-withdrawing-group in alpha position to the carbonyl group overcome these problems of lack of reactivity, as shown in the enantioselective alkylation and alkynylation to α-ketoesters[4,5] fluorinated ketones,[6,7] and isatines.[8,9] However, this excess of reactivity along with the fact that, many times, this particular kind of electrophile may act as a chelating ligand and enhance the reactivity of the nucleophilic species, might be a problem due to the competing non-catalyzed reaction pathway, which would have a detrimental effect on the enantioselectivity.
Recently, we have shown that chiral conformationally restricted perhydro-1,3-benzoxazines derived from (-)-8-aminomenthol behave as excellent ligands for the enantioselective addition of organozinc reagents to carbonyl compounds,[10] including α-ketoesters.[11]

Apart from the previously mentioned substrates, 1,2-diketones have emerged as suitable electrophilic reagents for the enantioselective addition of organozinc compounds, allowing to obtain chiral tertiary alcohols contained in α-hydroxyketone moieties, which have an important role in biological processes such as the inhibition of urease[12] and the regulation of the gene expression of Legionella pneumophila.[13]

Being aware of the relevance of these structures, in a previous communication we employed our chiral perhydro-1,3-benzoxazine ligands in the dimethylzinc-mediated addition of phenylacetylene to benzils to afford the corresponding chiral tertiary alcohols in high yields with high enantioselectivity.[14] Herein we present the complete study of the enantioselective dimethylzinc-mediated addition of terminal alkynes to aromatic, aliphatic and unsymmetrically substituted 1,2-diketones in the presence of perhydro-1,3-benzoxazines as chiral ligands.[15, 16]

Results and discussion

Conformationally restricted perhydro-1,3-benzoxazines have proved their efficiency as chiral ligands for the enantioselective alkynylation of α-ketoesters promoted by dimethylzinc.[11b] Considering this, we decided to employ 1,2-diketones as substrates for the enantioselective alkynylzinc addition reaction, in which represents the first enantioselective organozinc addition to ketones activated by another carbonyl group in alpha position.

We first tested our chiral perhydro-1,3-benzoxazines **1a**-**f** in the model reaction of 1,2-diphenylethane-1,2-dione **2a** with phenylacetylene in toluene at 0 ºC (Table 1).

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Electronic Supplementary Information (ESI) available: NMR spectra data (^{1}H and ^{13}C) and chiral HPLC chromatograms for new synthesized compounds. See DOI: 10.1039/x0xx00000x

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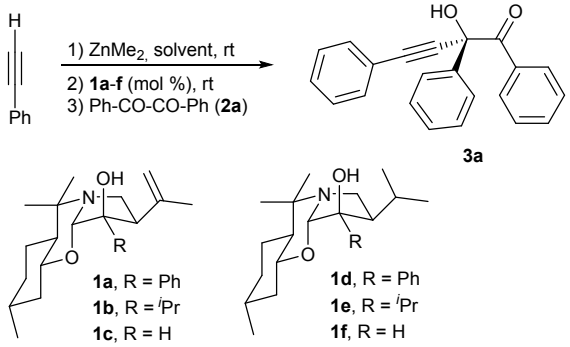
Table 1. Screening studies of enantioselective addition of phenylacetylene to 1,2-diphenylethane-1,2-dione **2a**.[a]



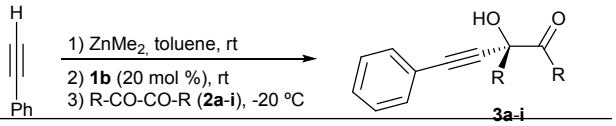
Entry	Ligand (mol %)	Solvent	T (ºC)	t (h)	Yield (%)[b]	er[c]
1	**1a** (20)	toluene	0	20	44	84:16
2	**1b** (20)	toluene	0	20	33	96:4
3	**1c** (20)	toluene	0	20	42	46:54
4	**1d** (20)	toluene	0	20	36	79:21
5	**1e** (20)	toluene	0	20	40	67:33
6	**1f** (20)	toluene	0	20	50	49:51
7	**1b** (20)	toluene	-10	20	76	92:8
8	**1b** (20)	toluene	-20	20	88	94:6
9	**1b** (20)	toluene	-30	30	70[d]	94:6
10	**1b** (20)	toluene	0	0.5	59[d]	87:13
11	**1b** (20)	toluene	0	2.25	70	89:11
12	**1b** (20)	toluene	0	6.5	40	92:8
13	**1b** (20)	toluene	0	48	18	>99:1
14	**1b** (20)	hexane	-20	20	15[d]	---
15	**1b** (20)	CH_2Cl_2	-20	20	68[d]	92:8
16	**1b** (20)	THF	-20	20	66	77:23
17	**1b** (20)	Et_2O	-20	20	56[d]	65:35
18	**1b** (15)	toluene	-20	20	84	93:7
19	**1b** (10)	toluene	-20	20	80	89:11
20[e]	**1b** (20)	toluene	-20	30	58[d]	92:8

[a] Reaction conditions: 0.15 mmol (1.0 equiv) of **2a**, 0.6 mmol (4.0 equiv.) of dimethylzinc and 0.63 mmol (4.2 equiv.) of phenylacetylene. [b] Yield of isolated product after purification by flash column chromatography. [c] Enantiomeric ratio determined by HPLC on a chiral stationary phase. [d] Variable amounts of the starting diketone **2a** were recovered. [e] Only 0.3 mmol of dimethylzinc (2.0 equiv) and 0.31 mmol (2.1 equiv) of phenylacetylene were used.

We found that a kinetic resolution takes place on the reaction product above -20 ºC due to a second addition of the alkynylzinc derivative to the α-hydroxy ketone. Under the reaction conditions, the minor enantiomer of the hydroxy ketone reacts faster than the major enantiomer and the enantioselectivity improves but a large loss of chemical yield occurs.[14] Fortunately, in the optimized reaction conditions (4 equiv of phenylacetylene and dimethylzinc, 20 mol % of **1b** as ligand, at -20 °C in toluene for 20 h) this process is slow enough to allow obtaining the α-hydroxyketone in high yield with good enantioselectivity.

With these conditions in hand, we moved on to explore the substrate scope of the addition of phenylacetylene to symmetrically substituted 1,2-diketones **2a**-**k** (Table 2).

Table 2. Substrate Scope of the alkynylation of 1,2-diketones **2a**-**i**.[a]



Entry	Diketone, R	Yield (%)[b]	er[c]
1	**2a**, Ph	**3a** (88)	94:6
2[d]	**2a**, Ph	**3a** (58)	97:3
3	**2b**, 4-Me-C_6H_4	**3b** (85)	91:9
4[d]	**2b**, 4-Me-C_6H_4	**3b** (52)	95:5
5	**2c**, 4-OMe-C_6H_4	**3c** (48)	90:10
6[e]	**2c**, 4-OMe-C_6H_4	**3c** (70)	88:12
7	**2d**, 3-OMe-C_6H_4	**3d** (85)	92:8
8	**2e**, 2-Cl-C_6H_4	**3e** (83)	88:12
9[e]	**2f**, 4-Cl-C_6H_4	**3f** (69)	97:3
10[e]	**2g**, 4-Br-C_6H_4	**3g** (48)	93:7
11	**2h**, 2-furyl	**3h** (77)	97:3
12[e]	**2i**, 2-naphthyl	**3i** (62)	89:11

[a] Reaction conditions: (1) 1.05 mmol (4.2 equiv.) of phenylacetylene, 1.0 mmol (4.0 equiv) of dimethylzinc, toluene, rt, 1 h; (2) ligand **1b** 0.05 mmol (20 mol %, 0.2 equiv.), toluene, rt, 30 min; (3) diketone 0.25 mmol (1.0 equiv.), toluene, −20 °C, 20 h. [b] Yield of isolated product after purification by flash column chromatography. [c] Enantiomeric ratio determined by HPLC on a chiral stationary phase. [d] Reaction was stirred for an additional 4 h at 0 °C. [e] Diketone was dissolved and added in CH_2Cl_2 because of their insolubility in toluene at -20 ºC.

The enantiocontrol seemed not to be influenced by electronic effects and *ortho*-, *meta*-, and *para*-substituted aromatic α-diketones bearing electron-donating and electron-withdrawing substituents afforded the corresponding α-hydroxyketones without significant changes in the enantiocontrol, with moderate to good yields (Table 2, entries 3-10). Neither steric effects made any variation in the enantioselectivity, even when a bulkier diketone **2i** was employed (Table 2, entry 12). We also tested the heteroaromatic diketone **2h** and pleasingly achieved the product in good yield with excellent enantioselectivity (Table 2, entry 11).

On the other hand, enantioselectivity can be improved if once the hydroxyl ketones **3** are formed at -20 °C, the kinetic resolution is allowed to occur at 0 °C for 4 h (Table 2, entries 2 and 4). However, under these conditions a significant loss of chemical yield occurs.

Then, we studied the influence of electronic effects of some phenylacetylene derivatives, as well as the addition of aliphatic alkynes (Table 3).

The α-hydroxyketones **3j**-**l** were obtained in good yield and with high enantioselectivity both for phenylacetylene derivatives substituted with electron-donating and electron-withdrawing groups (Table 3, entries 1-3). The use of aliphatic terminal alkynes such as octyne and 4-phenyl-1-butyne afforded the products **3m** and **3n** with a decrease of the enantioselectivity with respect to the aromatic substituted alkynes (Table 3, entries 4 and 5); although the enantioselectivity in the alkynylation of diketone **2a** with 3-((*tert*-butyldimethylsilyl)oxy)-1-propyne was as good as showed for aromatic substituted terminal alkynes (Table 3, entry 7).

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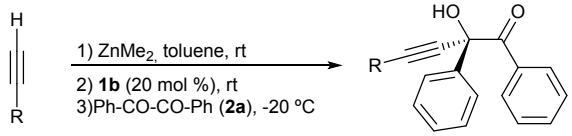
Only the addition of trimethylsilylacetylene occurred in poor yield with moderate enantioselectivity (Table 3, entry 6).

The scope of the reaction was further explored and enolizable aliphatic 1,2-diketones were subjected to the alkynylation protocol (Table 4). Diketones **2j** and **2k** afforded the corresponding alkynylated products **4a**-**k** with good chemical yield and excellent enantiocontrol, both for aromatic and aliphatic alkynes. For aliphatic diketones kinetic resolution occurs at -20 ºC[14] and higher enantioselectivities are obtained than with aromatic diketones, although the chemical yield slightly decreases. We did not find any competitive enolization process that could decrease the yield of desired products. Again, the enantiocontrol seemed not to be influenced by electron-donating and electron-withdrawing substituents in different positions in the aromatic ring of the alkyne (Table 4, entries 3-7). When aliphatic terminal alkynes were employed the enantioselectivity decreases slightly, although the enantioselectivity levels remain higher than the alkynylation of aromatic diketone **2a** (compare entries 8-11 in Table 4 versus entries 4-7 in Table 3).

Encouraged by these results, we decided to study the regio- and enantioselectivity of the reaction when unsymmetrically substituted 1,2-diketones**5a**-**f** were employed. The alkynylation of diketones with electronically different substituents on the aromatic rings occurred preferably on the carbonyl group attached to the ring with the electron-withdrawing group and proceeded with high regio- and enantioselectivity. (Table 5).

Table 3. Alkyne scope of the alkynylation of **2a**.[a]



3j-**p**

Entry	Alkyne, R	Yield (%)[b]	er[c]
1	4-Me-C_6H_4	**3j** (88)	95:5
2	4-Br-C_6H_4	**3k** (78)	91:9
3	2-F-C_6H_4	**3l** (65)	97:3
4	C_6H_5-$(CH_2)_2$	**3m** (79)	82:18
5	$CH_3(CH_2)_5$	**3n** (69)	86:14
6	TMS	**3o** (37)	82:18
7	TBDMSO-CH_2	**3p** (73)	93:7

[a] Reaction conditions: (1) alkyne 1.05 mmol (4.2 equiv), dimethylzinc 1.0 mmol (4.0 equiv), toluene rt, 1 h; (2) ligand **1b** 0.05 mmol (20 mol %, 0.2 equiv), toluene, rt, 30 min; (3) diketone 0.25 mmol (1.0 equiv), toluene, -20 °C, 20 h. [b] Yield of isolated product after purification by flash column chromatography. [c] Enantiomeric ratio determined by HPLC on a chiral stationary phase.

Table 4. Substrate Scope of the alkynylation of 1,2-diketones **2a**-**i**.[a]

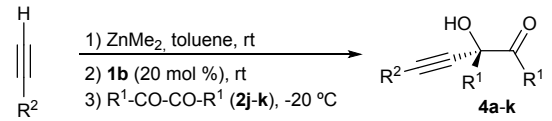
Entry	Diketone, R^1	AlKyne, R^2	Yield (%)[b]	er[c]
1	**2j**, Me	C_6H_5	**4a** (68)	99:1
2	**2k**, Et	C_6H_5	**4b** (72)	>99:1
3	**2k**, Et	4-Me-C_6H_4	**4c** (71)	>99:1
4	**2k**, Et	4-Br-C_6H_4	**4d** (63)	>99:1
5	**2k**, Et	2-F-C_6H_4	**4e** (79)	95:5
6	**2k**, Et	3-OMe-C_6H_4	**4f** (80)	96:4
7	**2k**, Et	3-Cl-C_6H_4	**4g** (84)	95: 5
8	**2k**, Et	C_6H_5-$(CH_2)_2$	**4h** (56)	90:10
9	**2k**, Et	$CH_3(CH_2)_5$	**4i** (60)	94:6
10	**2k**, Et	TMS	**4j** (50)	92:8
11	**2k**, Et	TBDMSO-CH_2	**4k** (58)	97:3

[a] Reaction conditions: (1) 1.05 mmol (4.2 equiv.) of phenylacetylene, 1.0 mmol (4.0 equiv) of dimethylzinc, toluene, rt, 1 h; (2) ligand **1b** 0.05 mmol (20 mol %, 0.2 equiv.), toluene, rt, 30 min; (3) diketone 0.25 mmol (1.0 equiv.), toluene, −20 °C, 20 h. [b] Yield of isolated product after purification by flash column chromatography. [c] Enantiomeric ratio determined by HPLC on a chiral stationary phase. [d]

The alkynylation of diketone **5a** with an electron-donating methoxy group on one of the aromatic rings and an electron-withdrawing chlorine on the other occurs preferably on the carbonyl group attached to the ring with the chlorine group. After 20 h of reaction at -20 °C, a mixture of hydroxy ketones **6a** and **17a** was obtained in a ratio 93:7 and 72% of chemical yield. The enantioselectivity for **6a** was 92:8 er (Table 5, entry 1). A kinetic resolution could be observed again when the alkynylation reaction of diketone **5a** was left to stir for additional 4 h at 0 ºC, which resulted in an increase of the regio- and enantioselectivity due to the consumption of the minor enantiomer (entry 2).

On the other hand, when 1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)phenyl)ethane-1,2-dione **5b** acted as the electrophile, the product **6b** was obtained as a single regioisomer, as a result of the alkynylation of the carbonyl attached to the electronically deficient aromatic ring (Table 5, entry 3). The alkynylation also proceeds with total regioselectivity if there are two electron-withdrawing chlorine substituent group (Table 5, entries 8-10) or two electron-donating methoxy groups in one of the aromatic rings (Table 5, entries 4-7). In all cases the enantioselectivity was good.

The alkynylation of a simple alkyl aryl diketone as **5e** provided a mixture of hydroxy ketones **6j** and **7j** without regioselectivity although with high enantioselectivity (97:3 er for **6j** and 95:5 er for **7j**). However, the alkynylation of the alkyl aryl diketone **5f** with an electron-withdrawing chlorine substituent at the aromatic ring and a bulky isopropyl group proceeded with total regioselectivity, and only the formation of hydroxy ketone **6k** (93:7 er) was observed in the ^{1}H NMR spectra of the reaction mixture after 20 h of reaction at −20 °C.



4a-**k**

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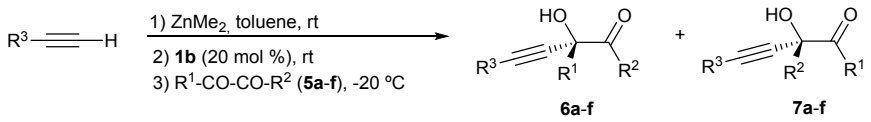
Table 5. Scope of the alkynylation of asymmetrical 1,2-diketones **5a-f**.



Entry	Ketone	R^1	R^2	Alkyne, R^3	Yield (%)[b]	Ratio **6**:**7**	er **6**[c]
1	**5a**	4-Cl-C_6H4	4-OMe-C_6H_4	C_6H_5	72	**6a** (93):**7a** (7)	92:8
2[d]	**5a**	4-Cl-C_6H_4	4-OMe-C_6H_4	C_6H_5	48	**6a** (>98%)[e]	96:4
3	**5b**	4-CF_3-C_6H_4	4-OMe-C_6H_4	C_6H_5	79	**6b** (>98%)[e]	96:4
4	**5c**	2-Cl-C_6H_4	3,4-$(OMe)_2$-C_6H_3	C_6H_5	72	**6c** (>98%)[e]	95:5
5	**5c**	2-Cl-C_6H_4	3,4-$(OMe)_2$-C_6H_3	4-Me-C_6H_4	91	**6d** (>98%)[e]	95:5
6	**5c**	2-Cl-C_6H_4	3,4-$(OMe)_2$-C_6H_3	4-Br-C_6H_4	90	**6e** (>98%)e	94:6
7	**5c**	2-Cl-C_6H_4	3,4-$(OMe)_2$-C_6H_3	$CH_3(CH_2)_5$	62	**6f** (>98%)[e]	97:3
8	**5d**	2,4-Cl_2-C_6H_3	4-OMe-C_6H_3	C_6H_5	95	**6g** (>98%)[e]	93:7
9	**5d**	2,4-Cl_2-C_6H_3	4-OMe-C_6H_3	4-Me-C_6H_4	85	**6h** (>98%)[e]	92:8
10	**5d**	2,4-Cl_2-C_6H_3	4-OMe-C_6H_3	4-Br-C_6H_4	81	**6i** (>98%)[e]	89:11
11	**5e**	C_6H_5	Me	C_6H_5	85	**6j** (46):**7j** (54)	97:3 (95:5)[f]
12	**5f**	2-Cl-C_6H_4	^{i}Pr	C_6H_5	79	**6k** (>98%)[e]	93:7

[a] Reaction conditions: (1) alkyne 1.05 mmol (4.2 equiv), dimethylzinc 1.0 mmol (4.0 equiv), toluene rt, 1 h; (2) ligand **1b** 0.05 mmol (20 mol %, 0.2 equiv), toluene, rt, 30 min; (3) diketone 0.25 mmol (1.0 equiv), toluene, -20 °C, 20 h. [b] Yield of isolated product after purification by flash column chromatography. [c] Enantiomeric ratio determined by HPLC on a chiral stationary phase. [d] Reaction was stirred for an additional 4 h at 0 °C. [e] Only regioisomer **6** was detected by 1H NMR. [f] In parentheses the er in regioisomer **7j**

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The configuration of the newly formed stereogenic center of **6a** was established by X-ray diffraction analysis[14] and has been extended to all of the other hydroxyketones **3a**-**p**, **4a**-**k**, and **6a**-**k** based on mechanistic analogy.

Although a detailed mechanistic discussion is difficult at present, we propose the model shown in Figure 1, in agreement with the anti-transition state structure proposed by Noyori,[17] to account for the stereoselectivity observed with chiral ligand **1b**. In this model, the transfer of the alkynyl group occurs to the Si face of the ketone carbonyl.

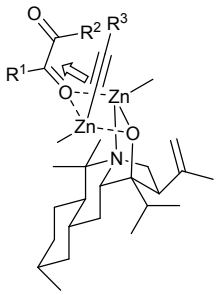

Figure 1. Proposed model for the addition of alkynylzinc derivatives to 1,2-diketones catalyzed by ligand **1b**.

Conclusions

In conclusion, a wide range of propargylic alcohols have been prepared through a highly efficient dimethylzinc-mediated enantioselective addition of terminal alkynes to symmetrical and asymmetrical 1,2-diketones in the presence of the chiral perhydro-1,3-benzoxazine ligand 1b. Starting from aromatic 1,2-diketones the chiral tertiary alcohols were achieved in good yields with high enantioselectivity with independence of the electronic effects or steric hindrance on the aromatic ring when phenylacetylene derivatives were employed as the nucleophiles. Aliphatic alkynes and the challenging enolizable aliphatic diketones were also tolerated and no detrimental effect on the enantiocontrol was observed.

Experimental section

General information

All reactions were carried out in anhydrous solvents under nitrogen atmosphere in dried glassware by means of Schlenk techniques. Flash chromatography was carried out using silica gel (230–240 mesh). Chemical yields refer to pure isolated substances. TLC analysis was performed on glassbacked plates coated with silica gel 60 and an F254 indicator and visualized by either UV irradiation or by staining with I_2 or phosphomolybdic acid solution. ^{1}H NMR (400 or 500 MHz) and ^{13}C NMR (100 or 126 MHz) spectra were recorded in $CDCl_3$. Chemical shifts for protons are reported in ppm from tetramethylsilane with the residual $CHCl_3$ resonance as internal reference. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants, in Hertz, and integration. Specific rotations were measured using a 5-mL cell with a 1-dm path length, and a sodium lamp, and concentration is given in g per 100 mL. High resolution mass spectrometry analysis (HRMS) was performed on a quadrupole spectrometer with TOF analyzer. Chiral HPLC analysis was performed using Daicel Chiralcel OD, Chiralcel OD-H, Chiralcel OJ, Chiralpak AD-H, Chiralpak AS-H, Lux-Amylose-1, Lux-Cellulose-2 or Lux-Cellulose-2 columns. UV detection was monitored at 254, 220 or 210 nm. Dimethylzinc (1.2 M solution in toluene) was purchased from Acros Organics. Diketones **2a-e**, **2g**, **2h**, **2j**, **2k**, **5c** and **5e** were purchased from commercial sources and used as received. Diketones **2f,**[18] **2i,**[19] and **5a**,[20] and ligands **1a-f**[21] were prepared according to the methods described in literature. Compounds **3a-i**, **3m**, **3o**, **3p**, **4a**, **4b**, **6a**, **7a**, **6c**, **6j** and **7j** have been described previously.[14] For the synthesis of diketones **5b**, **5d** and **5f** see the supporting information for this article.

General Procedure for the enantioselective alkynylation Addition of α-Diketones

To a 1.2 M solution of $ZnMe_2$ in anhydrous toluene (0.83 mL, 1.0 mmol) under nitrogen atmosphere was added the terminal alkyne (1.05 mmol) at room temperature. After stirring the mixture for 1 h, a solution of ligand **1b** (16 mg, 0.05 mmol) in anhydrous toluene (0.5 mL) was added. The resulting mixture was stirred for another 30 min at the same temperature and then was cooled to -20 ºC. Once this solution was cooled, a solution of the corresponding diketone (0.25 mmol) in anhydrous toluene (2 mL) was added and the reaction mixture was stirred at this temperature for 20 h. Diketones **2c**, **2f**, **2g** and **2i** were dissolved and added to CH_2Cl_2 (2 mL) because of their insolubility in toluene at -20 ºC. Afterwards, the mixture was quenched under nitrogen atmosphere with an aqueous saturated solution of ammonium chloride, extracted with ethyl acetate (3 x 15 mL), washed with brine, dried over $MgSO_4$, filtered and concentrated. Purification by silica gel column chromatography with different mixtures of ethyl acetate:hexane or dichloromethane:hexane gave the pure α-hydroxy ketones.

(*S*)-2-hydroxy-1,2-diphenyl-4-(p-tolyl)but-3-yn-1-one (3j)

This compound was obtained from **2a** (52 mg, 0.25 mmol) and purified by flash chromatography (ethyl acetate:hexane = 1:45); colorless oil; yield: 71 mg, 88%; $[\alpha]_D^{25}$ = -146.8 (*c* = 1.5, CH_2Cl_2, 90% ee); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 2.34 (s, 3H), 5.56 (s, 1H), 7.11 (d, *J* = 7.9 Hz, 2H), 7.28-7.42 (m, 7H), 7.46 (m, 1H), 7.66 (m, 2H), 8.08 (dd, J_1 = 8.5 Hz, J_2 = 1.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 21.5, 76.4, 86.6, 90.7, 118.8, 126.8 (2C), 128.1 (2C), 128.8, 129.0 (2C), 129.1 (2C), 131.1 (2C), 131.6 (2C), 133.7, 139.3, 140.3, 195.1; IR (neat) *v*: 3387, 3067, 2227, 1671, 1595, 1449, 962, 764, 701, 680 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{23}H_{18}NaO_2$ 349.1199, found 349.1206; HPLC (Lux-Amylose-1, hexane:isopropanol = 90:10, 1.0 mL·min^{-1}, *λ* = 254 nm): t_R = 31.2 min for *S* enantiomer, t_R = 34.9 min for *R* enantiomer.

(*S*)-4-(4-bromophenyl)-2-hydroxy-1,2-diphenylbut-3-yn-1-one (3k)

This compound was obtained from **2a** (54 mg, 0.26 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:3); colorless oil; yield: 79 mg, 78%; $[\alpha]_D^{25}$ = -149,5 (*c* = 1.0, CH_2Cl_2, 82% ee); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.56 (s, 1H), 7.25-7.40 (m, 7H), 7.41-7.49 (m, 3H), 7.53 (d, *J* = 8.3 Hz, 2H), 8.05 (dd, J_1 = 8.6 Hz, J_2 =1,2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 76.4, 88.4, 89.3, 120.8, 123.4, 126.7 (2C), 128.2 (2C), 128.9, 129.0 (2C), 131.0 (2C), 131.5, 131.7 (2C), 133.1 (2C), 133.9, 140.0, 194.7; IR (neat) *v*: 3415,3061, 3028, 2226, 1680, 1596, 1486, 960, 698, 653 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{22}H_{15}BrNaO_2$ 413.0148, found 413.0148; HPLC (Chiralcel OD-H, hexane:isopropanol = 90:10, 1 mL·min^{-1}, *λ* = 254 nm): t_R = 7.9 min for *S* enantiomer, t_R = 12.7 min for *R* enantiomer.

(*S*)-4-(2-fluorophenyl)-2-hydroxy-1,2-diphenylbut-3-yn-1-one (3l)

This compound was obtained from **2a** (54 mg, 0.26 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:3); colorless oil; yield: 55 mg, 65%; $[\alpha]_D^{25}$ = -136.4 (*c* = 0.8, CH_2Cl_2, 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.58 (s, 1H), 7.02-7.14 (2H), 7.27-7.40 (m, 6H), 7.41-7.49 (m, 2H) 7.66 (d, *J* = 7.1 Hz, 2H), 8.09 (dd, J_1 = 8.5 Hz, J_2 = 1.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 76.4, 83.9, 92.3, 110.6 (d, *J* = 15.6 Hz), 115.5(d, *J* = 20.6 Hz), 124.0 (d, *J* =3.7 Hz), 126.8 (2), 128.1 (2), 128.8, 129.0 (2), 130.7 ((d, *J* = 8.0 Hz), 131.2 (2C), 131.3, 133.4, 133.8, 140.0, 163.1 (d, *J* = 253 Hz), 194.7; IR (neat) *v*: 3397, 3067, 2227, 1723, 1673, 1597, 1490, 965, 761, 700, 683, 640 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{22}H_{15}F$ Na O_2 353.0948, found 353.0957; HPLC (Chiralcel OD, hexane:isopropanol = 96:4, 1 mL·min^{-1}, *λ* = 254 nm): t_R = 10.2 min for *R* enantiomer, t_R = 11.5 min for *S* enantiomer.

(*S*)-2-hydroxy-1,2-diphenyldec-3-yn-1-one (3n)

This compound was obtained from **2a** (53 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:3); colorless oil; yield: 56 mg, 69%; $[\alpha]_D^{25}$ = -143.3 (*c* = 0.8, CH_2Cl_2, 72% ee); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 0.84 (t, *J* = 6.8 Hz, 3H), 1.15-1.34 (m, 6H), 1.50 (m, 2H), 2.30 (m, 2H), 5.41 (s, 1H), 7.23-7.36 (m, 5H), 7.43 (m, 1H), 7.57 (dd, J_1 = 7.0 Hz, J_2 = 1.5 Hz, 2H),

7.99 (d, J_1 = 8.4 Hz, J_2 = 1.3 Hz 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 19.0, 22.5, 28.1, 28.5, 31.2, 76.0, 78.6, 92.1, 126.8 (2C), 128.0 (2C), 128.6, 128.8 (2C), 131.1 (2C), 131.6, 133.5, 140.5, 195.5; IR (neat) *v*: 3428, 3067, 3029, 2232, 2204, 1679, 1594, 759, 698, 684, 642, 605 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{22}H_{24}NaO_2$ 343,1669, found 343.1667; HPLC (Chiralpak AD-H, hexane:isopropanol = 90:10, 1 mL·min^{-1}, λ = 254 nm): t_R = 9.0 min for *S* enantiomer, t_R = 17.7 min for *R* enantiomer.

(*S*)-4-ethyl-4-hydroxy-6-(*p*-tolyl)hex-5-yn-3-one (4c)

This compound was obtained from **2k** (57 mg, 0.50 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 82 mg, 71%; $[\alpha]_D^{25}$ = +246.3 (*c* = 1.0, CH_2Cl_2, 99% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.99 (t, *J* = 7.4 Hz, 3H), 1.17 (t, *J* = 7.3 Hz, 3H), 1.85 (dq, J_1 = 14.7 Hz, J_2 = 7.3 Hz, 1H), 2.08 (dq, J_1 = 14.7 Hz, J_2 = 7.4 Hz, 1H), 2.32 (s, 3H), 2.62 (dq, J_1 = 18.0 Hz, J_2 = 7.3 Hz, 1H), 3.01 (dq, J_1 = 18.0 Hz, J_2 = 7.3 Hz, H), 4.16 (s, 1H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.8, 8.2, 21.5, 29.3, 33.3, 76.3, 85.9, 87.0, 119.0, 129.0 (2C), 131.6 (2C), 138,0, 209.1; IR (neat) *v*: 3460, 2975, 2939, 2225, 1717, 1510, 1459, 1173, 1021, 959, 816, 959, 709 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{15}H_{18}NaO_2$ 253.1199, found 253.1200; HPLC (Chiralcel OJ, hexane:isopropanol = 96:4, 0.8 mL·min^{-1}, λ = 254 nm): t_R = 12.2 min for *S* enantiomer, t_R = 13.8 min for *R* enantiomer.

(*S*)-6-(4-bromophenyl)-4-ethyl-4-hydroxyhex-5-yn-3-one (4d)

This compound was obtained from **2k** (57 mg, 0.50 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 93 mg, 63%; $[\alpha]_D^{25}$ = +208.8 (*c* = 1.0, CH_2Cl_2, 99% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.98 (t, *J* = 7.4 Hz, 3H), 1.16 (t, *J* = 7.4 Hz, 3H), 1.85 (dq, J_1 = 14.6 Hz, J_2 = 7.4 Hz, 1 H), 2.07 (dq, J_1 = 14.6 Hz, J_2 = 7.4 Hz, 1 H), 2.62 (dq, J_1 =18.1 Hz, J_2 = 7.4 Hz, 1H), 2.97 (dq, J_1 = 18.1 Hz, J_2 = 7.4 Hz, 1H), 4.17 (s, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.8, 8.2, 29.4, 33.2, 76.2, 84.7, 88.9, 121.0, 123.1, 129.0, 131.6 (2C), 133.2 (2C), 208.7; IR (neat) *v*: 3450, 2982, 2941, 2219, 1721, 1486, 1113, 1011, 960, 821, 778 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{15}BrNaO_2$ 317.0148, found 317.0152; HPLC (Chiralcel OJ, hexane:isopropanol = 96:4, 0.8 mL·min^{-1}, λ = 254 nm): t_R = 13.7 min for *S* enantiomer, t_R = 14.8 min for *R* enantiomer.

(*S*)-4-ethyl-6-(2-fluorophenyl)-4-hydroxyhex-5-yn-3-one (4e)

This compound was obtained from **2k** (58mg, 0.51 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:3); colorless oil; yield: 94 mg, 79%; $[\alpha]_D^{25}$ = +204.9 (*c* = 0.8, CH_2Cl_2, 90 % ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.01 (t, *J* = 7.3 Hz, 3H), 1.18 (t, *J* = 7.3 Hz, 3H), 1.86 (dq, J_1 = 14.7 Hz, J_2 = 7.3 Hz, 1H), 2.10 (dq, J_1 = 14.7 Hz, J_2 = 7.3 Hz, 1H), 2.64 (dq, J_1 = 18.1 Hz, J_2 = 7.3 Hz, 1H), 3.05 (dq, J_1 = 18.1, J_2 = 7.3 Hz, 1H), 4.18 (s, 1H), 7.01-7.10 m, (2H), 7.29 (m, 2H), 7.41 (td, J_1 = 7.3 Hz, J_2 = 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.8, 8.1, 29.3, 33.2, 76.3, 79.2, 92.9, 110.7 (d, *J* = 15.6 Hz), 115.5 (d, *J* = 20.8 Hz), 123.9 (d, *J* = 3.8 Hz), 130.5 (d, *J* = 8.0 Hz), 133.5 , 162.9 (d, *J* = 252 Hz), 208.8; IR (neat) *v*: 3455, 2977, 2940, 2231, 1719, 1419, 1492, 1451, 1255, 1102, 961, 839, 755 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{15}FNaO_2$ 257.0948, found 257.0952; HPLC (Lux-Amylose-1, hexane:isopropanol = 96:4, 1 mL·min^{-1}, λ = 254 nm): t_R = 6.2 min for *R* enantiomer, t_R = 6.8 min for *S* enantiomer.

(*S*)-4-ethyl-4-hydroxy-6-(3-methoxyphenyl)hex-5-yn-3-one (4f)

This compound was obtained from **2k** (58 mg, 0.51 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); pale yellow oil; yield: 100 mg, 80%; $[\alpha]_D^{25}$ = +112.9 (*c* = 0.74, $CHCl_3$, 92% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.01 (t, *J* = 7.4 Hz, 3H), 1.19 (t, *J* = 7.4 Hz, 3H), 1.87 (dq, J_1 = 14.7 Hz, J_2 = 7.4 Hz, 1H), 2.10 (dq, J_1 = 14.7 Hz, J_2 = 7.4 Hz, 1H), 2.64 (dq, J_1 = 18.1 Hz, J_2 = 7.4 Hz, 1H), 3.02 (dq, J_1 = 18.1 Hz, J_2 = 7.4 Hz, 1H), 3.79 (s, 3H), 4.18 (s, 1H), 6.89 (ddd, J_1 = 8.3 Hz, J_2 = 2.5 Hz, J_3 = 1.1 Hz, 1H), 6.95 (dd, J_1 = 2,5 Hz, J_2 = 1.1 Hz, 1H), 7.02 (dt, J_1 = 7.8 Hz, J_2 = 1.1 Hz, 1H), 7.21 (dd, J_1 = 8.3 Hz, J_2 = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 7.8, 8.2, 29.4, 33.3, 55.3, 76.3, 85.7, 87.6, 115.3, 116.6, 123.0, 124.3, 129.4, 159.3, 209.0; IR (neat) *v*: 3454, 2973, 2939, 2878, 2223, 1719, 1593, 1576, 1460, 1289, 1204, 1177, 1042, 958, 784, 686 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for calcd. for $C_{15}H_{18}NaO_3$ 269.1148, found 269.1154; HPLC (Chiralcel OD, hexane:isopropanol = 99:1, 1.0 mL·min^{-1}, λ = 254 nm): t_R = 11.7 min for *S* enantiomer, t_R = 15.7 min for *R* enantiomer.

(*S*)-6-(3-chlorophenyl)-4-ethyl-4-hydroxyhex-5-yn-3-one (4g)

This compound was obtained from **2k** (58 mg, 0.51 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 107 mg, 84%; $[\alpha]_D^{25}$ = +160.1 (*c* = 0.68, $CHCl_3$, 90% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.01 (t, *J* = 7.4 Hz, 3H), 1.20 (t, *J* = 7.3 Hz, 3H), 1.88 (dq, J_1 = 14.9 Hz, J_2 = 7.4 Hz, 1H), 2.10 (dq, J_1 = 14.9 Hz, J_2 = 7.4 Hz, 1H), 2.64 (dq, J_1 = 18.1 Hz, J_2 = 7.3 Hz, 1 H), 3.00 (dq, J_1 = 18.1 Hz, J_2 = 7.3 Hz, 1H), 4.18 (s, 1H), 7.22-7.27 (m, 2H), 7.30-7.34 (m, 2H), 7.42 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ:* 7.8, 8.2, 29.4, 33.2, 76.2, 84.3, 89.0, 123.7, 129.1, 129.6, 129.9, 131.6, 134.2, 208.7; IR (neat) *v*: 3464, 2972, 2935, 2884, 1722, 1593, 1562, 1474, 1464, 1101, 958, 782, 684 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{15}ClNaO_2$ 273.0653, found 273.0650; HPLC (Lux-Cellulose-2, hexane:isopropanol = 98:2, 1.0 mL·min^{-1}, λ = 254 nm): t_R = 5.5 min for *R* enantiomer, t_R = 6.4 min for *S* enantiomer.

(*S*)-4-ethyl-4-hydroxy-8-phenyloct-5-yn-3-one (4h)

This compound was obtained from **2k** (57 mg, 0.50 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 68 mg, 56%; $[\alpha]_D^{25}$ = +125.8 (*c* = 1.0, CH_2Cl_2, 80% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (t, *J* = 7.3 Hz, 3H), 1.05 (t, *J* = 7.3 Hz, 3H), 1.68 (dq, J_1 = 14.6 Hz, J_2 = 7.3 Hz, 1H), 1.90 (dq, J_1 = 14.6 Hz, J_2 = 7.3 Hz, 1H), 2.40 (dq, J_1 = 18.2 Hz, J_2 = 7.3 Hz, 1H), 2.52 (t, *J* = 7.3 Hz, 2H), 2.70 (dq, J_1 = 18.2 Hz, J_2 = 7.3Hz, 1H), 2.81 (t, *J* = 7.3 Hz, 2H), 4.02 (s, 1H), 7.16-7.22 (3H), 7.24-7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.7, 8.0, 20.8, 28.9, 33.3, 34.6, 75.8, 79.9, 85.8, 126.3, 128.3 (2C), 128.4 (2C), 140.3, 209.5; IR (neat) *v*: 3462, 2976, 2938, 2231, 1717, 1496, 1454, 1342, 1185, 1106,1031, 970, 747, 698 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{16}H_{20}NaO_2$ 267.1356, found

267.1356,; HPLC (Chiralpak AD-H, hexane:isopropanol = 95:5, 1.0 mL·min^{-1}, λ = 220 nm): t_R = 7.2 min for *S* enantiomer, t_R = 8.4 min for *R* enantiomer.

(*S*)-4-Ethyl-4-hydroxydodec-5-yn-3-one (4i)

This compound was obtained from **2k** (55 mg, 0.48 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 65 mg, 60%; $[\alpha]_D^{25}$ = +119.6 (*c* = 0.8, CH_2Cl_2, 88% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.86 (t, *J* = 6.9 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 1.13 (t, *J* = 7.3 Hz, 3H), 1.22-1.40 (6H), 1.48 (m, 2H), 1.73 (dq, J_1 =14.6 Hz, J_2 = 7.3 Hz, 1H), 1.94 (dq, J_1 = 14.6 Hz, J_2 = 7.3 Hz, 1H), 2.19 (t, *J* = 7.3 Hz, 2H), 2.53 (dq, J_1 = 18.0 Hz, J_2 = 7.0 Hz, 1H), 2.93 (dq, J_1 = 18.0 Hz, J_2 = 7.0 Hz, 1H), 4.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.7, 8.1, 14.0, 18.7, 22.5, 28.3, 28.5, 29.1, 31.2, 33.3, 75.9, 79.0, 86.8, 209.6; IR (neat) *v*: 3465, 2921, 2851, 1739, 1721, 1463, 1373, 1238, 1185, 1110, 1021, 974, 722, 609 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{14}H_{24}NaO_2$ 247.1669, found 247.1667; HPLC (Chiralpak AD-H, hexane:isopropanol = 99:1, 0.5 mL·min^{-1}, λ = 210 nm): t_R = 17.9 min for *S* enantiomer, t_R = 20.9 min for *R* enantiomer.

(*S*)-4-ethyl-4-hydroxy-6-(trimethylsilyl)hex-5-yn-3-one (4j)

This compound was obtained from **2k** (57 mg, 0.50 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 53 mg, 50%; $[\alpha]_D^{25}$ = +178.5 (*c* = 0.6, CH_2Cl_2, 84% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.14 (s, 9H), 0.92 (t, *J* = 7.6 Hz, 3H), 1.14 (t, *J* = 7.4 Hz, 3H), 1.74 (dq, J_1 = 14.6 Hz, J_2 = 7.6 Hz, 1H), 1.97 (dq, J_1 = 14.6 Hz, J_2 = 7.6 Hz, 1H), 2.54 (dq, J_1 = 17.9 Hz, J_2 = 7.6 Hz, 1H), 2.93 (dq, J_1 = 17.9 Hz, J_2 = 7.6 Hz, 1H), 4.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: -0.3 (3C), 7.7, 8.3, 29.1, 33.2, 76.2, 90.9, 103.8, 208.9; IR (neat) *v*: 3464, 2966, 2935, 2171, 1719, 1345, 1251, 1103, 1005, 962, 840, 760, 700 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{11}H_{20}NaO_2Si$ 235.1125, found 235.1124; HPLC (Chiralpak AD-H, hexane:isopropanol = 99:1, 0.5 mL·min^{-1}, λ = 210 nm): t_R = 12.4 min for *S* enantiomer, t_R = 13.8 min for *R* enantiomer.

(*S*)-7-((*tert*-butyldimethylsilyl)oxy)-4-ethyl-4-hydroxyhept-5-yn-3-one (4k)

This compound was obtained from **2k** (55 mg, 0.50 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 79 mg, 58%; $[\alpha]_D^{25}$ = +83.6 (*c* = 0.8, CH_2Cl_2, 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.08 (s, 6H), 0.87 (s, 9H), 0.91 (t, *J* = 7.4 Hz, 3H), 1.12 (t, *J* = 7.4 Hz, 3H), 1.76 (dq, *J* = 14.7, 7.4 Hz, 1 H), 1.97 (dq, J_1 = 14.7 Hz, J_2 = 7.4 Hz, 1 H), 2.53 (dq, J_1 = 18.1 Hz, J_2 = 7.4 Hz, 1H), 2.93 (dq, J_1 = 18.1 Hz, J_2 = 7.4 Hz, 1H), 4.05 (s, 1H), 4.32 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: -5.2 (2C), 7.6, 8.0, 18.2, 25.7 (3C), 29.2, 33.0, 51.6, 75.8, 83.4, 84.5, 208.9; IR (neat) *v*: 3457, 2931, 2858, 1721, 1463, 1363, 1254, 1182, 1092, 966, 833, 777 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{15}H_{28}NaO_3Si$ 307.1700, found 307.1703; HPLC (Chiralpak AD-H, hexane:isopropanol = 95:5, 1.0 mL·min^{-1}, λ = 210 nm): t_R = 11.0 min for *S* enantiomer, t_R = 12.5 min for *R* enantiomer.

(*S*)-2-hydroxy-1-(4-methoxyphenyl)-4-phenyl-2-(4-(trifluoromethyl)phenyl)but-3-yn-1-one (6b)

This compound was obtained from **5b** (77 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2), Pale yellow oil; yield: 81 mg 79%; $[\alpha]_D^{25}$ = -139.2 (*c* = 0.4, $CHCl_3$, 92% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.82 (s, 3H), 5.76 (s, 1H), 6.83 (ddd, J_1 = 9.1Hz, J_2 = 2.8 Hz, J_3 = 2.1 Hz, 2H), 7.31-7.38 (3H), 7.47 (m, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2 H), 8.08 (ddd, J_1 = 9.1Hz, J_2 = 2.8 Hz, J_3 = 2.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 55.5, 75.4, 86.9, 90.6, 113.7 (2C), 121.6, 123.6, 125.9 (q, *J* = 3.7 Hz, 2C), 127.2 (2C), 128.4 (2C), 129.2, 130.8 (q, *J* = 32.5 Hz), 131.7 (2C), 133.7 (2C), 144.6, 164.3, 192.5; IR (neat) *v*: 3315, 2974, 2883, 2242, 1642, 1543, 1383, 1288, 1217, 1087,1049, 878, 708, 655 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{24}H_{17}F_3NaO_3$ 433.1022, found 433.1020; HPLC (Lux-Amylose-1, hexane:isopropanol = 88:12, 1.0 mL·min^{-1}, λ = 254 nm): t_R = 21.8 min for *R* enantiomer, t_R = 25.1 min for *S* enantiomer.

(*R*)-2-(2-chlorophenyl)-1-(3,4-dimethoxyphenyl)-2-hydroxy-4-(*p*-tolyl)but-3-yn-1-one (6d)

This compound was obtained from **5c** (75 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 94 mg, 91%; $[\alpha]_D^{25}$ = -336.4 (*c* = 1.5, CH_2Cl_2, 90% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.32 (s, 3H), 3.72 (s, 3H), 3.85 (s, 3H), 5.69 (s, 1H), 6.71 (d, *J* = 8.6 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 2H), 7.24-7.33 (m, 4H), 7.40 (td, J_1 = 7.7 Hz, J_2 = 2.0 Hz, 2H), 7.52 (d, *J* = 2.0 Hz, 1 H), 7.59 (dd, J_1 = 8.6 Hz, J_2 = 2.0 Hz, 1H), 8.44 (dd, J_1 = 7.7 Hz, J_2 =1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 55.8 (2C), 76.3, 86.7, 91.7, 109.9, 112.7, 118.6, 124.6, 125.4, 127.0, 129.1 (2C), 130.3, 130.4, 131.4, 131.6 (2), 133.4, 138.2, 139.4, 148.2, 153.6, 192.8; IR (neat) *v*: 3396, 2934, 2838, 2218, 1673, 1594, 1510, 1439, 1263, 1170, 1020, 816, 766, 753, 732, 682, 631 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{25}H_{21}ClNaO_4$ 443.1021, found 433.1037; HPLC (Chiralcel OD, hexane:isopropanol = 90:10, 1.0 mL·min^{-1}, λ = 254 nm): t_R = 13.3 min for *S* enantiomer, t_R = 15.6 min for *R* enantiomer.

(*R*)-4-(4-bromophenyl)-2-(2-chlorophenyl)-1-(3,4-dimethoxyphenyl)-2-hydroxybut-3-yn-1-one (6e)

This compound was obtained from **5c** (76 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 109 mg, 90%; $[\alpha]_D^{25}$ = -270.7 (*c* = 2.5, CH_2Cl_2, 88% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.72 (s, 3H), 3.85 (s, 3H), 5.71 (s, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 7.23-7.32 (m, 4H), 7.36-7.45 (m, 3H), 7.50 (d, *J* = 2.0 Hz, 1H), 7.55 (dd, J_1 = 8.6 Hz, J_2 = 2.0 Hz, 1H), 7.55 (dd, J_1 = 7.8 Hz, J_1 = 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.8, 56.0, 76.3, 88.5, 90.3, 109.9, 112.6, 120.5, 123.6, 124.4, 125.4, 127.1, 130.2, 130.4, 131.4, 131.7 (2C), 133.1 (2C), 133.3, 137.9, 148.4, 153.8, 192.5; IR (neat) *v*: 3395, 2934, 2834, 2221, 1673, 1594, 1583, 1514, 1486, 1134, 1070, 823, 761, 732, 704 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{24}H_{18}BrClNaO_4$ 506.9969, found 506.9973; HPLC (Chiralpak AD-H, hexane:isopropanol = 80:20, 1.5 mL·min^{-1}, λ = 254 nm): t_R = 37.6 min for *S* enantiomer, t_R = 40.3 min for *R* enantiomer.

(*R*)-2-(2-chlorophenyl)-1-(3,4-dimethoxyphenyl)-2-hydroxydec-3-yn-1-one (6f)

This compound was obtained from **5c** (75 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2);

colorless oil; yield: 63 mg, 62%; $[\alpha]_D^{25}$ = -248.3 (*c* = 0.2, $CHCl_3$, 94% ee); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 0.84 (t, *J* = 6.8 Hz, 3H), 1.16-1.26 (m, 4H), 1.27-1.33 (m, 2H), 1.50 (m, 2H), 2.31 (m, 2H), 3.72 (s, 3H), 3.86 (s, 3H), 5.58 (s, 1H), 6.71 (d, *J* = 8.6 Hz, 1H), 7.22-7.29 (m, 2H), 7.39 (td, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H), 7.46 (d , *J* = 2.0 Hz, 1H), 7.53 (dd, J_1 = 8.6Hz, J_2 = 2.0 Hz, 1H), 8.39 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 14.0, 19.0, 22.5, 28.2, 28.5, 31.2, 55.8, 55.93, 75.9, 78.9, 93.3, 109.8, 112.7, 124.6, 125.4, 126.9, 130.1, 130.3, 131.2, 133.4, 138.4, 148.2, 153.5, 193.3; IR (neat) *ν*: 3386, 2970, 2933, 2862, 1677, 1596, 1517, 1465, 1268, 1145, 1135, 951, 816, 764 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{24}H_{27}ClNaO_4$ 437.1490, found 437.1495; HPLC (Lux-Cellulose-2, hexane:isopropanol = 90:10, 1.0 mL·min^{-1}, *λ* = 254 nm): t_R = 15.7 min for *S* enantiomer, t_R = 30.8 min for *R* enantiomer.

(R)-2-(2,4-dichlorophenyl)-2-hydroxy-1-(4-methoxyphenyl)-4-phenylbut-3-yn-1-one (6g)

This compound was obtained from **5d** (77 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil; yield: 98 mg, 95%; $[\alpha]_D^{25}$ = -168.7 (*c* = 1.68, $CHCl_3$, 86% ee); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 3.81 (s, 3H), 5.71 (s, 1H), 6.80 (d, *J* = 9.0 Hz, 2H), 7.25-7.44 (m, 7H), 7.95 (d, *J* = 9.0 Hz, 2H), 8.37 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 55.5, 75.7, 86.9, 91.6, 113.6 (2C), 121.5, 124.4, 127.3, 128.4 (2C), 129.3, 131.1, 131.4, 131.7 (2C), 132.8 (2C), 134.0, 135.5, 136.7, 164.0, 192.2; IR (neat) *ν*: 3368, 2975, 2928, 2844, 2221 1675, 1600, 1510, 1467, 1252, 1170, 965, 946, 785, 757, 690, 604 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{23}H_{16}Cl_2NaO_3$ 433.0369, found 433.0361; HPLC (Chiralpak AS-H, hexane:isopropanol = 98:2, 1.0 mL·min^{-1}, *λ* = 254 nm): t_R = 26.1 min for *S* enantiomer, t_R = 32.1 min for *R* enantiomer.

(*R*)-2-(2,4-dichlorophenyl)-2-hydroxy-1-(4-methoxyphenyl)-4-(*p*-tolyl)but-3-yn-1-one (6h)

This compound was obtained from **5d** (76 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); pale yellow oil; yield: 89 mg, 85%; $[\alpha]_D^{25}$ = -259.3 (*c* = 1.1, $CHCl_3$, 84% ee); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 2.34 (s, 3H), 3.81 (s, 3H), 5.71 (s, 1H), 6.80 (dt, J_1 = 9.0 Hz, J_2 = 2.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 2.1 Hz, 1H), 7.33 (dt, *J* = 8.0 Hz, 2 H), 7.40 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.95 (dt, J_1 = 9.0 Hz, J_2 = 2.0 Hz, 2H), 8.38 (dd, J_1 = 8.5 Hz, J_2 = 2.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 21.5, 55.4, 75.7, 86.3, 91.9, 113.6 (2C), 118.4, 124.4, 127.3, 129.1 (2C), 131.0, 131.5, 131.6 (2), 132.8 (2C), 134.0, 135.5, 136.8, 139.6, 164.0, 192.3; IR (neat) *ν*: 3376, 2977, 2926, 2219, 1677, 1600, 1510, 1251, 1171, 1080, 1044, 965 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{24}H_{18}Cl_2NaO_3$ 447.0525, found 447.0527; HPLC (Chiralcel OD, hexane:isopropanol = 95:5, 1.0 mL·min^{-1}, *λ* = 254 nm): t_R = 9.3 min for *S* enantiomer, t_R = 13.9 min for *R* enantiomer.

(*R*)-4-(4-bromophenyl)-2-(2,4-dichlorophenyl)-2-hydroxy-1-(4-methoxyphenyl)but-3-yn-1-one (6i)

This compound was obtained from **5d** (75 mg, 0.24 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); colorless oil, yield: 93 mg, 81%; $[\alpha]_D^{25}$ = -267.1 (*c* = 1.14, $CHCl_3$, 78% ee); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 3.81 (s, 3H), 5.73 (s, 1H), 6.81 (d, *J* = 9.0 Hz, 2H), 7.25-7.30 (m, 3H), 7.40 (dd, J_1 = 8.4 Hz, J_2 = 2.1 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 9.0 Hz, 2H), 8.32 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 55.5, 75.7, 88.1, 90.5, 113.7 (2C), 120.4, 123.7, 124.2, 127.4, 131.1, 131.3, 131.7 (2C), 132.8 (2C), 133.1 (2C), 134.0, 135.6, 136.5, 164.1, 192.0; IR (neat) *ν*: 3395, 2928, 2871, 2222, 1676, 1600, 1510, 1486, 1250, 1170, 1070, 1012, 964, 824, 753, 608 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{23}H_{15}BrCl_2NaO_3$ 510.9474, found: 510.9473; HPLC (Lux-Cellulose-2, hexane:isopropanol = 95:5, 1.0 mL·min^{-1}, *λ* = 254 nm): t_R = 16.1 min for *S* enantiomer, t_R = 36.3 min for *R* enantiomer.

(*R*)-4-(2-chlorophenyl)-4-hydroxy-2-methyl-6-phenylhex-5-yn-3-one (6k)

This compound was obtained from **5f** (55 mg, 0.25 mmol) and purified by flash chromatography (CH_2Cl_2:hexane = 1:2); white solid; yield: 64 mg, 79%; mp 130-132 ºC (from hexane); $[\alpha]_D^{25}$ = +38.6 (*c* = 1.42, $CHCl_3$, 86%); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 0.97 (d, *J* = 6.8 Hz, 3H), 1.32 (d, *J* = 6.8 Hz, 3H), 2.93 (sp, *J* = 6.8 Hz, 1H), 5.10 (s, 1 H), 7.33-7.41 (m, 6H), 7.53 (m, 2H), 8.26 (ddd, J_1 = 8.0 Hz, J_2 = 1.9 Hz, J_3 = 0.8 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$): *δ* 19.7, 22.1, 35.8, 78.8, 85.8, 90.3, 121.5, 127.0, 128.5 (2C), 129.3, 130.5, 131.3, 131.6, 131.8 (2C), 133.2, 135.1, 208.3; IR (neat) *ν*: 3448, 2974, 2935, 2875, 2222, 1725, 1590, 1570, 1468, 1443, 1020, 988, 912, 756, 690 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $C_{19}H_{17}ClNaO_2$ 335.0809, found 335.0814; HPLC (Chiralpak AS-H, hexane:isopropanol = 97:3, 1.0 mL·min^{-1}, *λ* = 254 nm): t_R = 8.8 min for *S* enantiomer, t_R = 11.5 min for *R* enantiomer.

Conflicts of interest

There are no conflicts to declare.

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