DOI: 10.1002/adsc.201200185

Enantiocontrolled Synthesis of Tertiary α-Hydroxy-α-ynyl Esters by Dimethylzinc-Mediated Addition of Alkynes to α-Keto Esters

Rebeca Infante,[a] Alfonso Gago,[a] Javier Nieto,[a,*] and Celia Andrés[a,*]

[a] Instituto CINQUIMA and Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid, 47011 Valladolid, Spain
Fax: (+34)-983-423-013; e-mail: javiernr@qo.uva.es or celian@qo.uva.es

Received: March 5, 2012; Revised: May 17, 2012; Published online: September 28, 2012

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201200185.

Abstract: A perhydro-1,3-benzoxazine behaves as an excellent chiral ligand in the nucleophilic addition of alkynylzinc derivatives, prepared from terminal alkynes and dimethylzinc, to α-keto esters without using other Lewis acids. The enantioselectivity is excellent and homogeneous for a wide variety of aromatic and heteroaromatic α-keto esters. Aliphatic enolizable α-keto esters were alkynylated with moderate enantioselection.

Keywords: alkynylation; asymmetric catalysis; enantioselectivity; ketones; propargylic alcohols; zinc

Introduction

Among the enantioselective catalytic transformations that involve the generation of a carbon-carbon bond, the addition of organometallic reagents to carbonyl compounds has attracted special interest and constitutes a valuable method for the obtention of chiral secondary and tertiary alcohols.[1] Particularly interesting are the optically active propargylic alcohols, which are versatile building blocks in asymmetric synthesis[2] and whose structure is present in numerous drugs and natural products.[3]

The most common methods for the preparation of optically active propargylic alcohols involve (i) the asymmetric reduction of the corresponding propargylic ketone[4] or (ii) the asymmetric alkynylation of carbonyl compounds catalyzed by metal complexes.[5–7] Although numerous examples of the first method have been reported, two major limitations are present: the starting alkynyl ketones are usually prone to decompose and isomerize and tertiary alcohols are inaccessible by this method. Conversely, both problems are solved by the addition of a terminal acetylide to simple aldehydes or ketones. Nevertheless, although the asymmetric alkynylation of aldehydes has been well developed, few studies concerning the alkynylation of ketones have been disclosed, probably due to their low reactivity toward alkynylides and the difficulties for high enantiocontrol. An interesting class of carbonyl compounds which might overcome this weakness are the more reactive α-keto esters. However, this excess of reactivity might be a problem due to the competing non-catalyzed reaction pathway. In fact, although some reports of catalytic enantioselective addition of dialkylzinc to α-keto esters have been disclosed,[8] as far as we know only one study has been reported concerning the preparation of chiral propargylic alcohols through nucleophilic addition of alkynylzinc to α-keto esters.[9] In this report the alkynylzinc derivative was prepared *in situ* by the protocol described by Carreira,[10] using catalytic amounts of zinc triflate in the presence of triethylamine and an amino alcohol. The alkynylation reaction was performed neat at 70 °C, and a relatively large amount of chiral ligand (22 mol%) was required. Under these conditions, high yields and good enantioselectivities are obtained for the alkynylation of aromatic and cyclic keto esters, while enolizable α-keto esters provide poor results. In this context, we decided to embark on the synthesis of chiral tertiary propargylic alcohols through addition of organometallic species to α-keto esters.

Recently, it has been found that the conformationally restricted perhydro-1,3-benzoxazines **1a–f** (Figure 1) behave as excellent ligands for the enantioselective alkylation and arylation of carbonyl compounds,[11] and in this way we envisioned their utilization as ligands for the enantioselective alkynylation of α-keto esters with alkynylzinc derivatives.

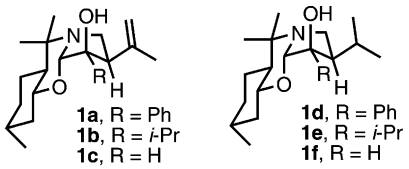


Figure 1. Structures of perhydro-1,3-benzoxazine-based ligands **1a–f**.

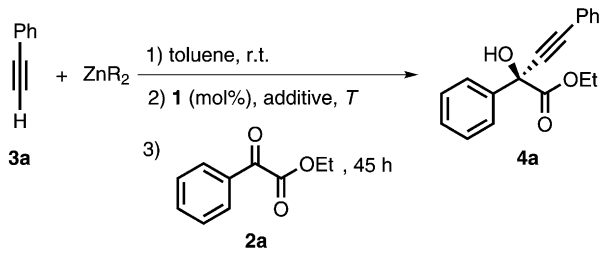
Results and Discussion

The alkynylation of ethyl 2-oxo-2-phenylacetate **2a** with phenylacetylene **3a** was chosen as a model reaction. We initially proposed a different procedure for the preparation of the alkynylzinc species, which involved the pre-formation of zinc phenylacetylide by treatment of the alkyne (2 equiv.) with dimethylzinc (2 equiv.) in toluene at room temperature.[12] The alkynylzinc derivative was treated with 20 mol% of ligand **1a** and, after cooling at 0 °C, it was reacted with ethyl 2-oxo-2-phenylacetate **2a** (see entry 1, Table 1).

To our delight, although the chemical yield after 20 h was poor under these conditions, the enantioselectivity of the process was significantly attractive (75% *ee*). Encouraged by this result, we carried out a set of experiments for the optimization of the reaction conditions using the protocol described above, by considering parameters such as (i) nature of ligand, (ii) nature of alkynylzinc derivative, (iii) temperature of the addition of keto ester, (iv) ligand and reactive loadings and (v) the use of additives. The results obtained are summarized in Table 1 and Table 2.

Although longer reaction times (45 h) did not improve considerably the chemical yield (entry 2, Table 1), the use of 4 equiv, of phenylacetylene and dimethylzinc under the same conditions led to an acceptable chemical yield, and more interestingly, to an improvement of enantioselectivity (80% *ee*, entry 3, Table 1). The chemical yield was further improved when diethylzinc was used instead of dimethylzinc, although the enantioselectivity was eroded (64% *ee*, entry 4, Table 1), probably due to the higher reactivity of the alkynylzinc derivative (competition between non-catalyzed and catalyzed reaction pathway). When the effect of the temperature was later explored (en-

Table 1. Enantioselective addition of alkynylzinc derivatives to **2a**: optimization of reaction conditions and screening of ligands **1a–f**.



Entry	Ligand (mol%)	ZnR_2 (equiv.)[a]	Temp. *T* [°C]	Yield [%][b]	*ee* [%][c]
1[d]	**1a** (20)	$ZnMe_2$ (2)	0	20	75
2	**1a** (20)	$ZnMe_2$ (2)	0	38	76
3	**1a** (20)	$ZnMe_2$ (4)	0	68	80
4	**1a** (20)	$ZnEt_2$ (4)	0	92	64
5	**1a** (20)	$ZnMe_2$ (4)	23	78	73
6	**1a** (20)	$ZnMe_2$ (4)	−10	75	81
7	**1a** (20)	$ZnMe_2$ (4)	−20	80	83
8	**1a** (20)	$ZnMe_2$ (4)	−35	58	66
9	**1a** (20)	$ZnMe_2$ (4)	−50	62	70
10	**1b** (20)	$ZnMe_2$ (4)	−20	89	93
11	**1c** (20)	$ZnMe_2$ (4)	−20	58	35
12	**1d** (20)	$ZnMe_2$ (4)	−20	75	71
13	**1e** (20)	$ZnMe_2$ (4)	−20	81	85
14	**1f** (20)	$ZnMe_2$ (4)	−20	60	48
15	**1b** (10)	$ZnMe_2$ (4)	−20	89	92
16	**1b** (5)	$ZnMe_2$ (4)	−20	56	90

[a] Same equiv. of phenylacetylene.
[b] Yield of product after chromatographic purification.
[c] Determined by HPLC (OD column).
[d] Reaction time was 20 h.

Table 2. Enantioselective addition of alkynylzinc derivatives to **2a** in the presence of **1b**. Screening of additives.

Entry[a]	**1b** (mol%)	Additive (mol%)	Temp. *T* [°C]	Yield [%][b]	*ee* [%][c]
1	20	DiMPEG (20)	−20	78	86
2	20	*i*-PrOH (10)	−20	84	87
3	20	Ti(O-*i*-Pr)$_4$ (25)	−20	54	93
4	20	B(OEt)$_3$ (25)	−20	79	93
5	20	B(OEt)$_3$ (40)	−20	74	93
6	10	B(OEt)$_3$ (25)	−20	56	91

[a] $ZnMe_2$/phenylacetylene/keto ester 4:4:1.
[b] Yield of product after chromatographic purification.
[c] Determined by HPLC (OD column).

tries 3, 5–9, Table 1) it was found that the reaction proceeded with good enantiocontrol in the range of 0 to −20 °C. At room temperature or below −20 °C, the enantioselectivity decreased significantly. The optimal temperature was determined to be −20 °C, and a good level of enantiocontrol was obtained (83% *ee*, entry 7, Table 1).

Under the best reaction conditions found so far (4 equiv. of phenylacetylene and dimethylzinc, 20 mol% ligand, −20 °C, 45 h) a screening of ligands (**1a–f**) was carried out (entries 7, 10–14, Table 1). The presence of a tertiary stereocenter on the carbon that bears the hydroxy group in the ligand is crucial to obtain good enantioselectivity, since the secondary alcohols **1c** and **1f** led to a considerable decrease of enantiocontrol (entries 11 and 14, Table 1). The best result was achieved with ligand **1b** (entry 10, 89% yield and 93% *ee*), which bears a sterically bulky isopropyl group on the mentioned tertiary stereocenter.

In addition, the ligand loading could be reduced from 20 to 10 mol%, without any substantial changes in either chemical yield or enantioselectivity (entries 10 *vs.* 15, Table 1), and even with 5 mol% of ligand the enantioselectivity was maintained at good levels (90% *ee*, entry 16, Table 1).

Finally, the influence of different additives on the enantiocontrol of the process was also studied (Table 2).[13] The addition of DiMPEG (MW 2000) or 2-propanol led to a reduction of the selectivity (entries 1 and 2, Table 2), whereas the addition of a Lewis acid, such as Ti(O-*i*-Pr)$_4$ or B(OEt)$_3$, in different proportions afforded the product in essentially the same enantiomeric excess, although the chemical yields were reduced (entries 3–6, Table 2).

After determining the optimal reaction conditions (4 equiv. of phenylacetylene and dimethylzinc, 10 mol% of **1b** as ligand, at −20 °C), the substrate scope was explored in the alkynylation of a series of α-keto esters with different electronic and steric nature, and the results are collected in Table 3.

It is noteworthy that the efficiency of our catalytic system was maintained at high levels for all aromatic α-keto esters in terms of enantiocontrol (91–96% *ee*,), with the exception of the *ortho*-substituted derivative **2g** (entry 7), which led to the corresponding alcohol with good yield and moderate enantioselectivity. Keto esters **2a–c** bearing alkoxy groups (OR[1]) of different steric volumes afforded the corresponding products with high enantioselectivities (91–93% *ee*, entries 1–3)

The enantiocontrol seemed not to be influenced by electronic effects, as both electron-donating (entries 4 and 5) and electron-withdrawing substituents (entry 6) were tolerated in the aromatic ring without significant changes of the selectivity. Also a more bulky keto ester such as the 2-naphthyl derivative **2i** and the heteroaromatic derivative **2j** were alkynylated with excellent enantioselectivity (94% *ee*).

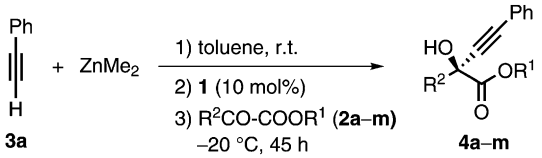
When enolizable aliphatic keto esters were employed instead of aromatic derivatives (entries 11–13), the enantiomeric excesses diminished slightly. Although the chemical yields were moderate for these substrates, they were clearly superior to the only previously reported result.[9a] When keto esters **2l** and **2m**, bearing an isopropyl and a phenethyl substituent, respectively, the corresponding alcohols were obtained with moderate enantioselectivities (77% and 75% *ee*, respectively, entries 12 and 13). However, with ethyl pyruvate **2k** the enantioselection was maintained at a good level (86% *ee*, entry 11).

A screening of ligands **1a–f** showed again that ligand **1b** provides the highest enantioselectivity among the six ligands in the alkynylation of alkyl derivatives (entries 13–18, Table 3).

On the other hand, the alkynylation of keto ester **2a** with an aliphatic terminal alkyne was also performed (Scheme 1). The less reactive 3-(*tert*-butyldimethylsilyloxy)-1-propyne **3b** was used and the corresponding product **4n** was isolated in a moderate yield (45%) with excellent enantioselectivity (93% *ee*).

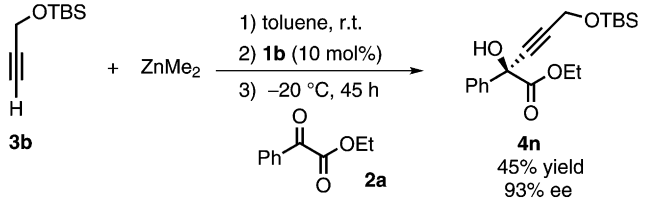
Although a detailed mechanistic discussion is difficult at present, we propose the model shown in Figure 2, in agreement with the *anti*-transition state structure proposed by Noyori,[14] to account for the stereoselectivity observed with chiral ligand **1b**. In this model, the transfer of the alkynyl group occurs to the *Si* face of the ketone carbonyl.

Table 3. Enantioselective addition of phenylacetylene to α-keto esters in the presence of **1b**.



Entry	Ligand	2	R^1	R^2	4	Yield [%][a]	*ee* [%][b]
1	**1b**	**2a**	Et	Ph	**4a**	89	92
2	**1b**	**2b**	Me	Ph	**4b**	96	91
3	**1b**	**2c**	*i*-Pr	Ph	**4c**	65	93
4	**1b**	**2d**	Et	*p*-Me-C_6H_4	**4d**	50	96
5	**1b**	**2e**	Et	*p*-MeO-C_6H_4	**4e**	89	96
6	**1b**	**2f**	Et	*p*-Cl-C_6H_4	**4f**	71	93
7	**1b**	**2g**	Et	*o*-Me-C_6H_4	**4g**	87	81
8	**1b**	**2h**	Et	*o*-MeO-C_6H_4	**4h**	92	91
9	**1b**	**2i**	Et	2-naphthyl	**4i**	84	94
10	**1b**	**2j**	Et	2-furyl	**4j**	60	94
11	**1b**	**2k**	Et	Me	**4k**	66	86
12	**1b**	**2l**	Et	*i*-Pr	**4l**	50	77
13	**1b**	**2m**	Et	$PhCH_2CH_2$	**4m**	73	75
14	**1a**	**2m**	Et	$PhCH_2CH_2$	**4m**	68	66
15	**1c**	**2m**	Et	$PhCH_2CH_2$	**4m**	62	46
16	**1d**	**2m**	Et	$PhCH_2CH_2$	**4m**	60	50
17	**1e**	**2m**	Et	$PhCH_2CH_2$	**4m**	65	65
18	**1f**	**2m**	Et	$PhCH_2CH_2$	**4m**	49	42

[a] Yield of product after chromatographic purification.
[b] Determined by HPLC (OD, AD-H, AS-H columns). The absolute configurations of **4b** and **4k** were assigned by comparison of the sign of specific rotation with literature data, whereas the absolute configurations of **4a**, **4c–j** and **4l–m** were assigned by assuming an analogous mechanism for the phenylacetylene transfer



Scheme 1. Asymmetric addition of aliphatic alkynes to ethyl 2-oxo-2-phenylacetate.

In summary, chiral tertiary propargylic alcohols were afforded through a mild enantioselective zinc-mediated alkynylation of α-keto esters, which was efficiently promoted by perhydro-1,3-benzoxazines derived from 8-aminomenthol, without using other Lewis acids. Under optimal conditions, the enantioselectivity was excellent and homogeneous for a wide variety of aromatic and heteroaromatic α-keto esters, with independence of the electronic effects or steric hindrance on the aromatic ring. Aliphatic alkynes were also tolerated and no detrimental effect on enantioselectivity was observed, and even the challenging aliphatic enolizable α-keto esters were alkynylated with moderate enantioselection.

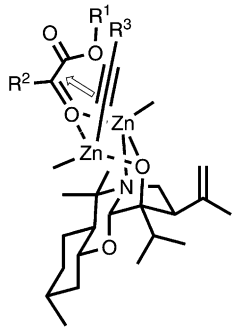


Figure 2. Proposed model for the addition of alkynylzinc derivatives to α-keto esters catalyzed by ligand **1b**.

Experimental Section

General Remarks

All reactions were carried out in anhydrous solvents under an argon atmosphere in dried glassware by means of Schlenk techniques. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 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 sol-

vent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet sp = septet, 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. Flash chromatography was carried out using silica gel (230–240 mesh). Chemical yields refer to pure isolated substances. TLC analysis was performed on glass-backed plates coated with silica gel 60 and an F_{254} indicator, and visualized by either UV irradiation or by staining with I_2 or phosphomolybdic acid solution. Chiral HPLC analysis was performed using a Daicel Chiralcel OD Column, Chiralpak AD-H or Chiralpak AS-H. UV detection was monitored at 220 nm or at 254 nm. High resolution mass spectrometry analysis (HR-MS) were performed on a quadrupole spectrometer with TOF analyzer.

Keto esters **2a**, **2b**, **2k**, **2l**, **2m** were purchased from commercial sources and used as received. Phenylacetylene **3a** and *tert*-butyldimethyl(2-propynyloxy)silane **3b** were purchased and distilled prior to use. Keto esters **2c–j** were prepared according to described procedures.[8d,15] Racemic hydroxy esters were synthesized by addition of the corresponding freshly prepared lithium acetylide solution in THF (1 equiv.) to the corresponding keto esters (1 equiv.) in THF at low temperature (−78 °C). Ligands **1a–f** were prepared according to the literature.[11,16]

Typical Procedure for Enantioselective Acetylene Addition to α-Keto Esters

To a solution of acetylene **3** (1.05 mmol) in anhydrous toluene (1.0 mL) under an argon atmosphere was added dropwise a 1.2 M solution of Me_2Zn in toluene (0.83 mL, 1.0 mmol) at room temperature. After stirring the mixture for 1 h at that temperature, a solution of ligand **1b** (8.0 mg, 0.025 mmol) in anhydrous toluene (1 mL) was added. The resulting mixture was stirred for another 30 min at the same temperature and was then cooled to −20 °C. Once this solution was cooled, the corresponding keto ester (0.25 mmol) was added and the reaction mixture was stirred at this temperature for 45 h. Afterwards, the mixture was quenched with an aqueous HCl solution (5%), extracted with Et_2O (4 × 15 mL), washed with brine, dried over $MgSO_4$, filtered off, and the solvents were evaporated. Purification by silica gel column chromatography with different mixtures of ethyl acetate/hexane gave the pure hydroxy esters. Enantiomeric excess was determined by chiral HPLC.

(*S*)-Ethyl 2-hydroxy-2,4-diphenylbut-3-ynoate (4a): This compound was obtained from **2a** (42 μL, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 89%; $[\alpha]_D^{20}$: −23.9 (*c* 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3H), 4.22 (dq, J_1 = 10.7 Hz, J_2 = 7.1 Hz, 1H), 4.32 (dq, J_1 = 10.7 Hz, J_2 = 7.1 Hz, 1H), 4.34 (br s, 1H, OH), 7.31–7.44 (m, 6H), 7.51–7.56 (m, 2H), 7.74–7.80 (m, 2H);[17] ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 63.5, 73.2, 86.1, 87.1, 121.9, 126.2 (2), 128.3 (2), 128.3 (2), 128.6, 128.9, 131.9 (2), 139.4, 171.9; IR (neat): ν = 3416, 2997, 2923, 2853, 2233, 1741, 1235, 1068, 765, 743, 698, 654, 600 cm^{-1}; HR-MS: *m/z* = 303.0993, calcd. for $C_{18}H_{16}O_3$ + Na^+: 303.0992; HPLC (Chiralcel OD, hexane:2-propanol = 99:01, 0.6 mL min^{-1}, λ = 220 nm): t_R = 37.5 min for enantiomer *R*, t_R = 40.5 min for enantiomer *S*.

(*S*)-Methyl 2-hydroxy-2,4-diphenylbut-3-ynoate (4b): This compound was obtained from **2b** (37 μL, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 96%; $[\alpha]_D^{20}$: −15.4 (*c* 1.2, $CHCl_3$), (lit.[9] $[\alpha]_D^{20}$: +19.56, *c* 4.04, $CHCl_3$, *R*). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 3H), 4.38 (s, 1H, OH), 7.32–7.46 (m, 6H), 7.53–7.58 (m, 2H), 7.76–7.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 54.2, 73.2, 86.2, 86.9, 121.8, 126.2 (2), 128.2 (2), 128.3 (2), 128.7, 128.9, 131.9 (2), 139.2, 172.3; IR (neat): ν = 3492, 2951, 2228, 1737, 1255, 1096, 1071, 766, 753, 694, 650 cm^{-1}; HR-MS: *m/z* = 289.0831, calcd. for $C_{17}H_{14}O_3$ + Na^+: 289.0835; HPLC (Chiralpak AS-H, hexane:2-propanol = 99:01, 1 mL min^{-1}, λ = 220 nm): t_R = 32.6 min for enantiomer *R*, t_R = 41.7 min for enantiomer *S*.

(*S*)-Isopropyl 2-hydroxy-2,4-diphenylbut-3-ynoate (4c): This compound was obtained from **2c** (48.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 65%; $[\alpha]_D^{20}$: −27.9 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14 (d, J = 6.3 Hz, 3H), 1.33 (d, J = 6.3 Hz, 3H), 4.40 (s, 1H, OH), 5.11 (hept, J = 6.3 Hz, 1H), 7.31–7.44 (m, 6H), 7.50–7.56 (m, 2H), 7.74–7.79. (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 21.1, 63.4, 73.1, 85.9, 87.3, 122.0, 126.1 (2), 128.3 (2), 128.8, 129.0 (2), 131.9 (2), 136.5, 138.5, 172.0; IR (neat): ν = 3475, 2987, 2923, 2858, 2238, 1845, 1713, 1276, 1254, 1098, 1070, 762, 758, 726, 693, 653 cm^{-1}; HR-MS: *m/z* = 317.1153, calcd. for $C_{19}H_{18}O_3$ + Na^+: 317.1148; HPLC (Chiralpak AD-H, hexane:2-propanol = 99:01, 1 mL min^{-1}, λ = 220 nm): t_R = 21.8 min for enantiomer *R*, t_R = 26.7 min for enantiomer *S*.

(*S*)-Ethyl 2-hydroxy-4-phenyl-2-*p*-tolylbut-3-ynoate (4d): This compound was obtained from **2d** (48.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 50%; $[\alpha]_D^{20}$: −22.9 (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, J = 7.1 Hz, 3H), 2.38 (s, 3H), 4.21 (dq, J_1 = 10.7 Hz, J_2 = 7.1 Hz, 1H), 4.29 (br s, 1H, OH), 4.32 (dq, J_1 = 10.7 Hz, J_2 = 7.1 Hz, 1H), 7.21 (d, J = 8.2 Hz, 2H), 7.30–7.39 (m, 3H), 7.50–7.56 (m, 2H), 7.64 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 21.1, 63.4, 73.1, 85.9, 87.3, 122.1, 126.1 (2), 128.3 (2), 128.8, 129.0 (2), 131.9 (2), 136.6, 138.5, 172.0; IR (neat): ν = 3478, 2923, 2853, 2233, 1736, 1238, 1172, 1080, 1040, 826, 762, 694 cm^{-1}; HR-MS: *m/z* = 317.1157, calcd. for $C_{19}H_{18}O_3$ + Na^+: 317.1148; HPLC (Chiralpak AD-H, hexane:2-propanol = 80:20, 1 mL min^{-1}, λ = 220 nm): t_R = 9.5 min for enantiomer *R*, t_R = 14.4 min for enantiomer *S*.

(*S*)-Ethyl 2-hydroxy-2-(*p*-methoxyphenyl)-4-phenylbut-3-ynoate (4e): This compound was obtained from **2e** (52.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 89%; $[\alpha]_D^{20}$: −30.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3H), 3.82 (s, 3H), 4.23 (dq, J_1 = 10.7 Hz, J_2 = 7.1 Hz, 1H), 4.29 (s, 1H, OH), 4.34 (dq, J_1 = 10.7 Hz, J_2 = 7.1 Hz, 1H), 6.92 (d, J = 9.0 Hz, 2H), 7.29–7.40 (m, 3H), 7.47–7.56 (m, 2H), 7.66 (d, J = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 55.3, 63.4, 72.8, 85.9, 87.3, 113.6 (2), 122.0, 127.5 (2), 128.3 (2), 128.8, 131.6, 131.9 (2), 159.8, 172.0; IR (neat): ν = 3473, 2981, 2837, 2228, 1731, 1608, 1509, 1245, 1170, 1086, 1031,

835, 757, 691, 621 cm^{-1}: HR-MS: $m/z = 333.1101$, calcd. for $C_{19}H_{18}O_4 + Na^+$: 333.1097; HPLC (Chiralpak AD-H, hexane:2-propanol = 90:10, 1 mL min^{-1}, $\lambda = 220$ nm): $t_R =$ 23.5 min for enantiomer *R*, $t_R = 33.0$ min for enantiomer *S*.

(*S*)-Ethyl 2-(*p*-chlorophenyl)-2-hydroxy-4-phenylbut-3-ynoate (4f): This compound was obtained from **2f** (53.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 71%; $[\alpha]_D^{20}$: −26.0 (*c* 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7.1$ Hz, 3H), 4.23 (dq, $J_1 =$ 10.7 Hz, $J_2 = 7.1$ Hz, 1H), 4.32 (dq, $J_1 = 10.7$ Hz, $J_2 = 7.1$ Hz, 1H), 4.35 (br s, 1H, OH), 7.31–7.40 (m, 5H), 7.50–7.54 (m, 2H), 7.70 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 13.8$, 63.7, 72.7, 86.3, 86.8, 121.7, 127.8 (2), 128.3 (2), 128.4 (2), 129.0, 131.9 (2), 134.7, 138.0, 171.5; IR (neat): $\nu =$ 3474, 2982, 2231, 1733, 1489, 1240, 1089, 108, 1015, 835, 756, 690, 611 cm^{-1}; HR-MS: $m/z = 337.0615$, calcd. for $C_{18}H_{15}ClO_3 + Na^+$; 337.0602; HPLC (Chiralcel OD, hexane:2-propanol = 99:01, 0.6 mL min^{-1}, $\lambda = 220$ nm): $t_R =$ 33.4 min for enantiomer *R*, $t_R = 37.9$ min for enantiomer *S*.

(*R*)-Ethyl 2-hydroxy-4-phenyl-2-*o*-tolylbut-3-ynoate (4g): This compound was obtained from **2g** (43.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 87%; $[\alpha]_D^{20}$: −2.4 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.27$ (t, $J = 7.1$ Hz, 3H), 2.39 (s, 3H), 4.10 (s, 1H, OH), 4.28 (dq, $J_1 = 10.7$ Hz, $J_2 = 7.1$ Hz, 1H), 4.39 (dq, $J_1 = 10.7$ Hz, $J_2 = 7.1$ Hz, 1H), 7.16–7.20 (m, 1H), 7.22–7.30 (m, 2H), 7.31–7.39 (m, 3H), 7.49–7.56 (m, 2H), 7.97–8.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 13.8$, 19.9, 63.3, 74.5, 87.3, 87.8, 121.9, 125.7, 128.3 (2), 128.7, 128.9, 128.9, 131.8 (3), 136.1, 136.6, 172.3; IR (neat): $\nu = 3475$, 2981, 2226, 1729, 1239, 1072, 1054, 1033, 754, 725, 690, 650 cm^{-1}; HR-MS: $m/z = 317.1151$, calcd. for $C_{19}H_{18}O_3 + Na^+$: 317.1148; HPLC (Chiralpak AD-H, hexane:2-propanol = 80:20, 1 mL min^{-1}, $\lambda = 220$ nm): $t_R = 8.9$ min for enantiomer *S*, $t_R =$ 10.1 min for enantiomer *R*.

(*R*)-Ethyl 2-hydroxy-2-(*o*-methoxyphenyl)-4-phenylbut-3-ynoate (4h): This compound was obtained from **2h** (52.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 92%; $[\alpha]_D^{20}$: +19.0 (*c* 2.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7.1$ Hz, 3H), 3.81 (s, 3H), 4.31 (q, $J = 7.1$ Hz, 2H), 4.44 (br s, 1H, OH), 6.91 (dd, $J_1 =$ 8.2 Hz, $J_2 = 0.9$ Hz, 1H), 7.04 (td, $J_1 = 7.5$ Hz, $J_2 = 1.1$ Hz, 1H), 7.31–7.39 (m, 4H), 7.52–7.58 (m, 2H), 8.00 (dd, $J_1 =$ 7.6 Hz, $J_2 = 1.7$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 13.9, 55.4, 62.7, 72.6, 86.1, 87.4, 111.1, 120.7, 121.9, 127.8, 128.2 (2), 128.8, 129.3, 130.3, 131.8 (2), 156.3, 171.9; IR (neat): $\nu = 3463$, 2956, 2923, 2853, 2233, 1732, 1257, 1235, 1076, 1035, 759, 745, 693, 647 cm^{-1}; HR-MS: $m/z = 333.1100$, calcd. for $C_{19}H_{18}O_4 + Na^+$: 333.1097; HPLC (Chiralpak AD-H, hexane:2-propanol = 90:10, 1 mL min^{-1}, $\lambda = 220$ nm): $t_R =$ 25.0 min for enantiomer *S*, $t_R = 48.7$ min for enantiomer *R*.

(*S*)-Ethyl 2-hydroxy-2-(naphthalen-2-yl)-4-phenylbut-3-ynoate (4i): This compound was obtained from **2i** (57.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 84%; $[\alpha]_D^{20}$: −44.8 (*c* 0.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7.1$ Hz, 3H), 4.24 (dq, $J_1 =$ 10.7 Hz, $J_2 = 7.1$ Hz, 1H), 4.36 (dq, $J_1 = 10.7$ Hz, $J_2 = 7.1$ Hz, 1H), 4.47 (s, 1H, OH), 7.33–7.43 (m, 3H), 7.49–7.55 (m, 2H), 7.56–7.61 (m, 2H), 7.79–7.94 (m, 4H), 8.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 13.8$, 63.6, 73.3, 86.3, 87.1, 122.0, 123.9, 125.6, 126.3, 126.5, 127.6, 128.2, 128.3 (2), 128.5, 128.9, 132.0 (2), 132.9, 133.3, 136.7, 171.8; IR (neat): $\nu =$ 3474, 3059, 2981, 2231, 1731, 1235, 1092, 1038, 858, 820, 756, 690 cm^{-1}; HR-MS: $m/z = 353.1145$, calcd. for $C_{22}H_{18}O_3 +$ Na^+: 353.1148; HPLC (Chiralpak AD-H, hexane:2-propanol = 99:01, 1 mL min^{-1}, $\lambda = 220$ nm): $t_R = 89.9$ min for enantiomer *R*, $t_R = 97.4$ min for enantiomer *S*.

(*R*)-Ethyl 2-(2-furyl)-2-hydroxy-4-phenylbut-3-ynoate (4j): This compound was obtained from **2j** (42.0 mg, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (dichloromethane/hexane = 1/2); colorless oil; yield: 60%; $[\alpha]_D^{20}$: +7.2 (*c* 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.30$ (t, $J = 7.1$ Hz, 3H), 4.29 (s, 1H, OH), 4.30–4.43 (m, 2H), 6.39 (dd, $J_1 = 3.3$ Hz, $J_2 = 1.8$ Hz, 1H), 6.70 (dd, $J_1 = 3.3$ Hz, $J_2 = 0.9$ Hz, 1H), 7.31–7.38 (m, 3H), 7.42 (dd, $J_1 = 1.8$ Hz, $J_2 = 0.9$ Hz, 1H), 7.50–7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 13.9$, 63.9, 68.5, 84.7, 85.3, 109.4, 110.5, 121.6, 128.3 (2), 129.1, 132.0 (2), 143.4, 151.2, 169.8; IR (neat): $\nu = 3476$, 2923, 2853, 2233, 1732, 1489, 1446, 1244, 1206, 1070, 1065, 1039, 1007, 760, 748, 694 cm^{-1}; HR-MS: $m/z = 293.0783$, calcd. for $C_{16}H_{14}O_4 +$ Na^+: 293.0784; HPLC (Chiralpak AD-H, hexane:2-propanol = 99:01, 1 mL min^{-1}, $\lambda = 220$ nm): $t_R = 57.0$ min for enantiomer *S*, $t_R = 84.0$ min for enantiomer *R*.

(*S*)-Ethyl 2-hydroxy-2-methyl-4-phenylbut-3-ynoate (4k): This compound was obtained from **2k** (29 μL, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 66%; $[\alpha]_D^{20}$: +28.6 (*c* 0.9, $CHCl_3$), (lit.[9] $[\alpha]_D^{20}$: −15.3, *c* 0.38, $CHCl_3$, 92% *ee* for *R*). H NMR (400 MHz, $CDCl_3$): $\delta = 1.35$ (t, $J = 7.1$ Hz, 3H), 1.78 (s, 3H), 3.64 (s, 1H, OH), 4.33 (q, $J = 7.1$ Hz, 2H), 7.27–7.35 (m, 3H), 7.40–7.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.0$, 27.1, 62.9, 68.3, 83.8, 88.4, 122.0, 128.2 (2), 128.7, 131.8 (2), 172.7; IR (neat): $\nu =$ 3476, 2987, 2238, 1840, 1733, 1246, 1146, 1123, 1015, 756, 691, 615 cm^{-1}; HR-MS: $m/z = 241.0829$, calcd. for $C_{13}H_{14}O_3 + Na^+$: 241.0835; HPLC (Chiralcel OD, hexane:2-propanol = 99:01, 0.6 mL min^{-1}, $\lambda = 220$ nm): $t_R = 33.0$ min for enantiomer *S*, $t_R = 41.6$ min for enantiomer *R*.

(*S*)-Ethyl 2-hydroxy-2-isopropyl-4-phenylbut-3-ynoate (4l): This compound was obtained from **2l** (38 μL, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/30); colorless oil; yield: 50%; $[\alpha]_D^{20}$: +28.8 (*c* 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.95$ (d, $J = 6.8$ Hz, 3H), 1.19 (d, $J =$ 6.8 Hz, 3H), 1.36 (t, $J = 7.1$ Hz, 3H), 2.32 (hept, $J = 6.8$ Hz, 1H), 3.51 (s, 1H, OH), 4.29–4.41 (m, 2H), 7.27–7.35 (m, 3H), 7.42–7.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 14.1, 16.3, 16.9, 37.0, 62.9, 74.7, 84.7, 87.6, 122.3, 128.2 (2), 128.5, 131.8 (2), 172.8; IR (neat): $\nu = 3501$, 2971, 2935, 2873, 2228, 1840, 1731, 1244, 1146, 1027, 1013, 756, 723, 691 cm^{-1}; HR-MS: $m/z = 269.1140$, calcd. for $C_{15}H_{18}O_3 + Na^+$: 269.1148; HPLC (Chiralpak AD-H, hexane:2-propanol = 99:01, 1 mL min^{-1}, $\lambda = 220$ nm): $t_R = 13.6$ min for enantiomer *R*, $t_R = 16.2$ min for enantiomer *S*.

(*S*)-Ethyl 2-hydroxy-2-phenethyl-4-phenylbut-3-ynoate (4m): This compound was obtained from **2m** (48 μL, 0.25 mmol) and **3a** (117 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 73%; $[\alpha]_D^{20}$: +36.9 (*c* 0.6, $CHCl_3$). ^{1}H NMR

(400 MHz, $CDCl_3$): $\delta = 1.37$ (t, $J = 7.1$ Hz, 3H), 2.25–2.50 (m, 2H), 2.71–2.85 (m, 1H), 2.94–3.07 (m, 1H), 3.72 (br s, 1H, OH), 4.27–4.39 (m, 2H), 7.18–7.28 (m, 3H), 7.28–7.37 (m, 5H), 7.43–7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.1$, 30.1, 41.7, 63.0, 71.0, 84.7, 87.4, 122.0, 126.0, 128.2 (2), 128.4 (2), 128.5 (2), 128.7, 131.8 (2), 141.1, 172.4; IR (neat): $\nu = 3489$, 3028, 2977, 2932, 2873, 2228, 1840, 1733, 1239, 1186, 1097, 1016, 755, 690 cm^{-1}; HR-MS: $m/z =$ 331.1294, calcd. for $C_{20}H_{20}O_3 + Na^+$: 331.1305; HPLC (Chiralcel OD, hexane:2-propanol = 99:01, 0.6 mL min^{-1}, $\lambda =$ 220 nm): $t_R = 36.5$ min for enantiomer *S*, $t_R = 42.8$ min for enantiomer *R*.

(*S*)-Ethyl 5-(*tert*-butyldimethylsilyloxy)-2-hydroxy-2-phenylpent-3-ynoate (4n): This compound was obtained from **2a** (42 μL, 0.25 mmol) and **3b** (219 μL, 1.05 mmol), and purified by flash chromatography (ethyl acetate/hexane = 1/45); colorless oil; yield: 45%. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.14$ (s, 6H), 0.92 (s, 9H), 1.22 (t, $J = 7.1$ Hz, 3H), 4.15–4.31 (m, 3H), 4.45 (s, 2H), 7.30–7.40 (m, 3H), 7.64–7.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = -5.1$ (2), 13.8, 18.2, 25.7 (3), 51.7, 63.5, 72.7, 82.8, 85.0, 126.2 (2), 128.2 (2), 128.6, 139.2, 171.7: IR (neat): $\nu = 3453$, 2956, 2930, 2858, 1734, 1251, 1145, 1063, 1008, 834, 778, 729, 696, 668 cm^{-1}; HR-MS: $m/z = 371.1639$, calcd. for $C_{19}H_{28}O_4Si + Na^+$: 371.1649; HPLC (Chiralcel OD, hexane:2-propanol = 99:01, 0.6 mL min^{-1}, $\lambda = 254$ nm): $t_R = 21.9$ min for enantiomer *R*, $t_R = 26.3$ min for enantiomer *S*.

Acknowledgements

We acknowledge the financial support from the Spanish Ministerio de Ciencia e Innovación (MICINN) (Project CTQ2011-28487/BQU) and Junta de Castilla y León (GR168). R. I. also thanks Junta de Castilla y León for a predoctoral fellowship.

References

[1] a) M. Beller, C. Bolm, in: *Transition Metals for Organic Synthesis*, 2nd edn., Wiley-VCH, Weinheim, **2004**, pp 519–551; b) J. Christoffers, A. Baro, in: *Quaternary Stereocentres: Challenges and Solutions for Organic Synthesis*, Wiley-VCH, Weinheim, **2005**.

[2] J. S. Yadav, S. Chandrasekhar, in: *Enantioselective Synthesis of Propargyl Alcohols as Multifunctional Synthons*, in *Drug Discovery and Development: Drug Development*, Vol. 2, (Ed.: M. S. Chorghade), Wiley, Hoboken, **2006**.

[3] a) L. Tan, C. Chen, R. D. Tillyer, E. J. J. Grabowski, P. J. Reider, *Angew. Chem.* **1999**, *111*, 724–727; *Angew. Chem. Int. Ed.* **1999**, *38*, 711–713; b) K. K. Chauhan, C. G. Frost, *J. Chem. Soc. Perkin Trans. 1* **2000**, 3015–3019; c) P. A. Roethle, D. Trauner, *Org. Lett.* **2006**, *8*, 345-347.

[4] Selected examples: a) A. Blake, A. Cunningham, A. Ford, S. Teat, S. Woodward, *Chem. Eur. J.* **2000**, *6*, 3586–3594; b) K. Tanaka, T. Shoji, *Org. Lett.* **2005**, *7*, 3561–3563; c) S. Eagon, C. DeLieto, W. J. McDonald, D. Haddenham, J. Saavedra, J. Kim, B. Singaram, *J. Org. Chem.* **2010**, *75*, 7717–7725.

[5] Reviews: a) K. Soai, S. Niwa, *Chem. Rev.* **1992**, *92*, 833–856; b) L. Pu, *Tetrahedron* **2003**, *59*, 9873–9886; c) P. G. Cozzi, R. Hilgraf, N. Zimmermann, *Eur. J. Org. Chem.* **2004**, 4095–4105; d) B. M. Trost, A. H. Weiss, *Adv. Synth. Catal.* **2009**, *351*, 963–983; e) E. M. Carreira, D. E. Frantz, in: *Science of Synthesis, Stereoselective Synthesis*, (Eds.: J. G. De Vries, G. A. Molander, P. A. Evans), Georg Thieme Verlag, Stuttgart, **2011**, Vol. 2, pp 497–515.

[6] For selected recent examples of alkynylation of aldehydes, see: a) M. Turlington, A. M. DeBerardinis, L. Pu, *Org. Lett.* **2009**, *11*, 2441–2444; b) J. Zhong, S. Hou, Q. Bian, M. Yin, R. Na, B. Zheng, Z. Li, S. Liu, M. Wang, *Chem. Eur. J.* **2009**, *15*, 3069-3071; c) G. Blay, L. Cardona, I. Fernández, A. Marco-Aleixandre, M. C. Muñoz, J. R. Pedro, *Org. Biomol. Chem.* **2009**, *7*, 4301–4308; d) J. Ito, R. Asai, H. Nishiyama, *Org. Lett.* **2010**, *12*, 3860–3862; e) E. R. Graham, R. R. Tykwinski, *J. Org. Chem.* **2011**, *76*, 6574–6583; f) N. Kojima, S. Nishijima, K. Tsuge, T. Tanaka, *Org. Biomol. Chem.* **2011**, *9*, 4425-4428.

[7] For recent examples of alkynylation of ketones, see: a) R. Motoki, M. Kanai, M. Shibasaki, *Org. Lett.* **2007**, *9*, 2997–3000; b) P. K. Dhondi, P. Carberry, L. B. Choi, J. D. Chisholm, *J. Org. Chem.* **2007**, *72*, 9590–9596; c) T. Ueda, K. Tanaka, T. Ichibakase, Y. Orito, M. Nakajima, *Tetrahedron* **2010**, *66*, 7726-7731; d) G.-W. Zhang, W. Meng, H. Ma, J. Nie, W.-Q. Zhang, J.-A. Ma, *Angew. Chem.* **2011**, *123*, 3600–3604; *Angew. Chem. Int. Ed.* **2011**, *50*, 3538–3542; e) K. Tanaka, K. Kukita, T. Ichibakase, S. Kotani, M. Nakajima, *Chem. Commun.* **2011**, *47*, 5614–5616.

[8] a) E. F. DiMauro, M. C. Kozlowski, *Org. Lett.* **2002**, *4*, 3781–3784; b) K. Funabashi, M. Jachmann, M. Kanai, M. Shibasaki, *Angew. Chem.* **2003**, *115*, 5647–5650; *Angew. Chem. Int. Ed.* **2003**, *42*, 5489–5492; c) L. C. Wieland, H. Deng, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 15453–15456; d) G. Blay, I. Fernandez, A. Marco-Aleixandre, J. R. Pedro, *Org. Lett.* **2006**, *8*, 1287–1290; e) H.-L. Wu, P.-Y. Wu, Y.-Y. Shen, B.-J. Uang, *J. Org. Chem.* **2008**, *73*, 6445–6447; f) B. Zheng, S. Hou, Z. Li, H. Guo, J. Zhong, M. Wang, *Tetrahedron: Asymmetry* **2009**, *20*, 2125–2129.

[9] a) B. Jiang, Z. Chen, X. Tang, *Org. Lett.* **2002**, *4*, 3451-3453. For two recent examples of enantioselective alkynylation of trifluoropyruvate, see: b) K. Aikawa, Y. Hioki, K. Mikami, *Org. Lett.* **2010**, *12*, 5716–5719; c) T. Ohshima, T. Kawabata, Y. Takeuchi, T. Kakinuma, T. Iwasaki, T. Yonezawa, H. Murakami, H. Nishiyama, K. Mashima, *Angew. Chem.* **2011**, *123*, 6420–6424; *Angew. Chem. Int. Ed.* **2011**, *50*, 6296–6300.

[10] For a review, see: D. E. Frantz, R. Fässler, C. S. Tomooka, E. M. Carreira, *Acc. Chem. Res.* **2000**, *33*, 373–381.

[11] a) C. Andrés, R. Infante, J. Nieto, *Tetrahedron: Asymmetry Tetrahedron:Asymmetry* **2010**, *21*, 2230–2237; b) R. Infante, J. Nieto, C. Andrés, *Org. Biomol. Chem.* **2011**, *9*, 6691-6699; c) R. Infante, J. Nieto, C. Andrés, *Chem. Eur. J.* **2012**, *18*, 4375–4379; d) R. Infante, J. Nieto, C. Andrés, *Synthesis* **2012**, *44*, 1343-1348.

[12] P. G. Cozzi, J. Rudolph, C. Bolm, P.-O. Norrby, C. Tomasini, *J. Org. Chem.* **2005**, *70*, 5733–5736.
[13] It is known that the presence of additives of different nature might improve the enantioselectivity in additions of organozinc reagents to carbonyl compounds, see: a) E. M. Volg, H. Gröger, M. Shibasaki, *Angew. Chem. Int. Ed. Angew. Chem. Ind. Ed.* **1999**, *38*, 1570–1577; b) C. Bolm, J. Rudolph, *J. Am. Chem. Soc.* **2002**, *124*, 14850-14851; c) S. Dahmen, *Org. Lett.* **2004**, *6*, 2113–2116; d) J. Rudolph, N. Hermanns, C. Bolm, *J. Org. Chem.* **2004**, *69*, 3997–4000; e) J. Rudolph, M. Lormann, C. Bolm, S. Dahmen, *Adv. Synth. Catal.* **2005**, *347*, 1361–1368.
[14] a) M. Yamakawa, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 6327; b) M. Yamakawa, R. Noyori, *Organometallics* **1999**, *18*, 128.
[15] X. Creary, *J. Org. Chem.* **1987**, *52*, 5026–5030.
[16] a) R. Pedrosa, C. Andrés, C. D. Rosón, M. Vicente, *J. Org. Chem.* **2003**, *68*, 1852–1858; b) C. Andrés, I. González, J. Nieto, C. D. Rosón, *Tetrahedron* **2009**, *65*, 9728–9736.
[17] a) A. Meyer, M. Flammang, C. G. Wermuth, *Synthesis* **1976**, 832–833; b) W. L. White, K. L. Ricciardelli, M. K. Chaguturu, U.S. Patent 4,704,161A, **1986**; c) Z. W. Just, R. C. Larock, *J. Org. Chem.* **2008**, *73*, 2662–2667.

