CHEMISTRY
A EUROPEAN JOURNAL

COMMUNICATION

DOI: 10.1002/chem.201201765

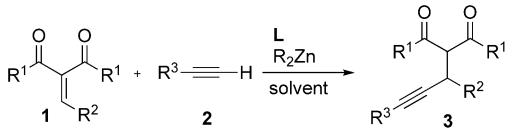
Enantioselective Zinc-Mediated Conjugate Addition of Terminal Alkynes to Enones

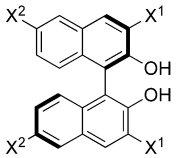
Gonzalo Blay,* Luz Cardona, José R. Pedro,* and Amparo Sanz-Marco[a]

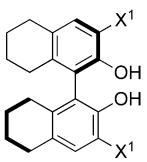
The conjugate addition of carbanionic species to electrophilic double bonds, that is, unsaturated carbonyl compounds, is one of the most attractive methods for constructing a new C–C bond. Among the different kinds of carbon nucleophiles, terminal alkynes are of interest to create functionalized internal alkynes.[1] The alkynyl groups can be readily transformed into other functional groups, thus, increasing the value of these compounds as versatile building blocks.[2] An interesting outcome results from the reaction with unsaturated carbonyl and related compounds bearing β-substituents, in which a new stereogenic centre is formed. The asymmetric alkynylation of enones has been carried out by using preformed 1,1′-Bi-2,2′-naphthol (BINOL)-derived alkynylboronates[3] and alkynylalanes in the presence of Ni catalysts.[4] On the other hand, the direct asymmetric conjugate alkynylation of electrophilic alkenes with terminal alkynes has been scarcely studied and remains a challenging problem.

A first example was reported by Carreira by using 5-alkylidene Meldrum's acids (2,2-dimethyl-1,3-dioxane-4,6-dione) as electrophiles and a PINAP–copper complex (PINAP = 1-(2-(diphenylphosphino)naphthalen-1-yl)phthalazine) as catalyst.[5] Shibasaki also used copper catalysis for the asymmetric alkynylation of α,β-unsaturated thioamides.[6] A diphosphine–rhodium complex was used by Fillion and Zorzitto for the conjugate addition of silylacetylenes to 5-benzylidene Meldrum's acids,[7] while Hayashi and Nishimura described the rhodium-catalyzed alkynylation of simple enones, enals, and nitroalkenes with silylacetylenes.[8] Recently, the same group reported the asymmetric catalytic addition of silylacetylenes to α,β-enones in the presence of a biphosphine–cobalt(I) complex, generated in situ by the reduction of a cobalt(II) salt with Zn.[9] Finally, a few examples of conjugate alkynylations mediated by zinc have been reported, which required equivalent or higher amounts of chiral material in all cases. Thus, Walker and Cui carried out the conjugate alkynylation of 5-benzylidene Meldrum's acid derivatives with alkynyl Grignard reagents in the presence of a superstoichiometric amount of a cinchonidine–Me_2Zn complex.[10] Carreira reported the diastereoselective alkynylation of chiral oxazepanedione acceptors with zinc alkynylides, generated by treating terminal alkynes with $Zn(OTf)_2$ and an amine base,[11] and Tomioka reported the asymmetric reaction of nitroolefins with arylalkynes mediated by dimethylzinc and 1.5 equivalents of a chiral amino alcohol.[12] Herein, we describe the first zinc-mediated conjugate alkynylation of enones by employing catalytic amounts of a chiral inducer, which is promoted by diethylzinc. Previously, our group has described the dialkylzinc-mediated addition of terminal alkynes to aldehydes[13] and imines[14] in the presence of catalytic amounts of hydroxyamides and BINOL-type ligands, respectively.

In our study we used arylidenediketones **1** as electrophiles (Scheme 1), because these compounds are readily available by Knoevenagel condensation of 1,3-diketones and aldehydes and show high electrophilicity. For the optimization of the conditions, we studied the reaction between enone **1a**

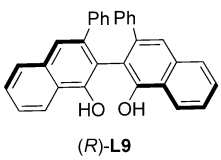




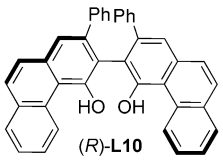


(*R*)-**L1** $X^1 = X^2 = H$
(*R*)-**L2** $X^1 = H$, $X^2 = Br$
(*R*)-**L3** $X^1 = Br$, $X^2 = H$
(*R*)-**L6** $X^1 = 3,5\text{-}(CF_3)_2C_6H_3$, $X^2 = H$
(*R*)-**L7** $X^1 = 2,4,6\text{-}i\text{Pr}_3C_6H_2$, $X^2 = H$
(*R*)-**L8** $X^1 = 9\text{-phenanthrenyl}$, $X^2 = H$

(*R*)-**L4** $X^1 = H$
(*R*)-**L5** $X^1 = Br$



(*R*)-**L9**



(*R*)-**L10**

Scheme 1. Conjugate alkynylation of enones and binaphthol ligands used.

[a] Prof. Dr. G. Blay, Dr. L. Cardona, Prof. Dr. J. R. Pedro, A. Sanz-Marco
Departament de Química Orgànica
Facultat de Química, Universitat de València
C/Dr. Moliner 50, E-46100 Burjassot (València), Spain
Fax: (+34) 963544328
E-mail: gonzalo.blay@uv.es
jose.r.pedro@uv.es

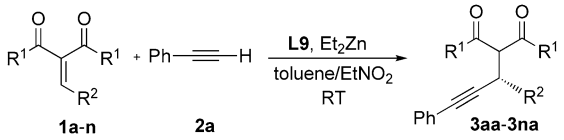
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201201765.

Table 1. Conjugate addition of phenylacetylene (**2a**, R^3 = Ph) to enone **1a** (R^1 = Me, R^2 = Ph). Screening of ligands and conditions.[a]

Entry	L	R_2Zn	Co-solvent	T [°C]	t [h]	Yield [%][b]	*ee* [%][c]
1	**L1**	Me_2Zn[d]	toluene	70	2	40	10 (*S*)
2	**L2**	Me_2Zn[d]	toluene	70	4	52	20 (*S*)
3	**L3**	Me_2Zn[d]	toluene	70	2	58	29 (*R*)
4	**L4**	Me_2Zn[d]	toluene	70	2	65	6 (*R*)
5	**L5**	Me_2Zn[d]	toluene	70	2	70	26 (*R*)
6	**L6**	Me_2Zn[d]	toluene	70	2	55	28 (*S*)
7	**L7**	Me_2Zn[d]	toluene	70	2	81	0
8	**L8**	Me_2Zn[d]	toluene	70	1	62	0
9	**L9**	Me_2Zn[d]	toluene	70	1	87	64 (*R*)
10	**L10**	Me_2Zn[d]	toluene	70	2	50	32 (*R*)
11	**L9**	Et_2Zn[e]	toluene	70	1	92	63 (*R*)
12	**L9**	Et_2Zn[e]	toluene	RT	4	69	74 (*R*)
13	**L9**	Et_2Zn[e]	toluene	0	5	30	68 (*R*)
14	**L9**	Et_2Zn[e]	CH_2Cl_2	RT	4	49	80 (*R*)
15	**L9**	Et_2Zn[e]	$MeNO_2$	RT	4	45	91 (*R*)
16	**L9**	Et_2Zn[e]	$EtNO_2$	RT	4	69	87 (*R*)
17	**L9**	Et_2Zn[e]	$PhNO_2$	RT	4	68	86 (*R*)
18	**L9**	Et_2Zn[e]	$iPrNO_2$	RT	4	48	75 (*R*)
19	**L9**	Et_2Zn[f]	$EtNO_2$	RT	4	72	87 (*R*)

[a] **L** (20 mol%), R_2Zn (2 equiv), **2a** (7.5 equiv) in toluene (0.48 mL) at 70°C for 1.5 h, followed by addition of **1a** (0.125 mmol) in co-solvent (1 mL) at the indicated *T*. [b] Yield of isolated product. [c] Determined by HPLC. [d] Me_2Zn in toluene (2 M). [e] Et_2Zn in hexane (1 M). [f] Et_2Zn in toluene (1.5 M).

Table 2. Conjugate addition of phenylacetylene (**2a**, R^3 = Ph) to enones **1**.[a]



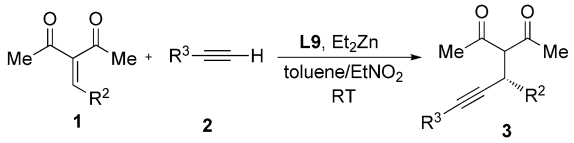
Entry	1	R^1	R^2	t [h]	3	Yield [%][b]	*ee* [%][c]
1	**1a**	Me	Ph	4	**3aa**	72	87
2	**1b**	Me	4-BrC_6H_4	4	**3ba**	68 (74)[d]	88 (99)[d]
3	**1c**	Me	4-ClC_6H_4	4	**3ca**	67	88
4	**1d**	Me	4-MeC_6H_4	4	**3da**	69	85
5	**1e**	Me	4-$MeOC_6H_5$	4	**3ea**	65 (50)[d]	86 (97)[d]
6	**1f**	Me	4-$NO_2C_6H_5$	4	**3fa**	53	82
7	**1g**	Me	3-ClC_6H_5	4	**3ga**	64	83
8	**1h**	Me	2-naphthyl	4	**3ha**	52 (71)[d]	80 (99)[d]
9	**1i**	Me	3-furyl	4	**3ia**	53	83
10	**1j**	Me	2-furyl	4	**3ja**	48	80
11	**1k**	Me	3-thienyl	4	**3ka**	52	83
12	**1l**	Me	Me	4	**3la**	68	64
13	**1m**	Et	Ph	5	**3ma**	55	76

[a] **L9** (20 mol%), Et_2Zn in toluene (1.5 M, 2 equiv), **2a** (7.5 equiv) in toluene (0.48 mL) at 70°C for 1.5 h, followed by addition of **1** (0.125 mmol) in $EtNO_2$ (1 mL) at RT. [b] Yield of isolated product. [c] Determined by HPLC. [d] Yield and *ee* after single crystallization from hexane/CH_2Cl_2.

(R^1 = Me, R^2 = Ph) and phenylacetylene (**2a**) by using different binaphthol ligands (Table 1). The starting conditions were similar to those used by us for the alkynylation of aldehydes:[13] the reactive species were generated by heating the chiral ligand, phenylacetylene, and dimethylzinc in toluene at 70°C for 1.5 h, followed by addition of the electrophile at the same temperature. Following this protocol, different binaphthol-type ligands were screened (entries 1–10), the best result being obtained with the vaulted ligand (*R*)-VANOL (**L9**, (*R*)-3,3′-Diphenyl-2,2′-bi-1-naphthalol). The use of Et_2Zn (hexane solution) instead of Me_2Zn slightly improved the yield. The enantioselectivity could be increased by adding the electrophile to the reaction mixture at RT, but with a detrimental effect on the yield. A dramatic improvement on the enantioselectivity of the reaction was achieved when nitromethane was used as co-solvent, although the expected product was obtained in lower yield. An examination of the reaction mixture showed the presence of a significant amount of 5-phenylisoxazole, resulting from a 1,3-dipolar cycloaddition between nitromethane and phenylacetylene.[15] To minimize this side reaction, other nitroalkanes were studied. A compromise between yield and enantioselectivity was obtained with nitroethane (entry 16). Finally, a slight improvement was achieved by using a diethylzinc solution in toluene instead of hexane. In this way, product **1aa** was obtained in 72% yield with 87% *ee* (entry 19).

With these optimized conditions in hand, we studied the scope of the reaction. Good yields and enantiomeric excesses above 80% were obtained in the reaction of phenylacetylene (**2a**) with a number of enones **1** that are substituted at the β carbon with an aryl group, regardless of the electron-withdrawing or electron-donating nature of the substituent on the aromatic ring (Table 2, entries 1–7). Larger aromatic (2-naphthyl) and heteroaromatic substituents were also tolerated (entries 8–11). Finally, the reaction with enone **1l**, bearing an aliphatic group (Me), gave the expected product **3la** with moderate enantioselectivity (entry 12). We also tested the effect of the substituent on the carbonyl group: 4-benzylideneheptane-3,5-dione (**1m**, R^1 = Et, R^2 = Ph) reacted with **2a** to give the corresponding alkynylation product **3ma** in lower yield (55%) and enantioselectivity (76%) than its analogous **1a** (Table 2, entry 13).[16] Next, the addition of other terminal alkynes **2** was investigated (Table 3).

Table 3. Enantioselective conjugate addition of other terminal alkynes **2** to enones **1**.[a]

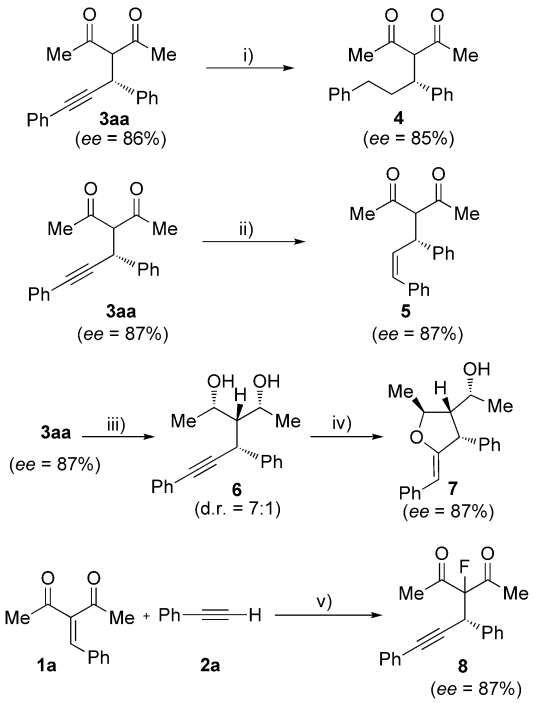


Entry	1	R^2	2	R^3	3	Yield [%][b]	*ee* [%][c]
1	**1a**	Ph	**2b**	4-FC_6H_4	**3ab**	61 (80)[d]	86 (99)[d]
2	**1a**	Ph	**2c**	4-ClC_6H_4	**3ac**	56	87
3	**1a**	Ph	**2d**	4-$MeOC_6H_4$	**3ad**	53 (44)[d]	84 (99)[d]
4	**1b**	4-BrC_6H_4	**2b**	4-FC_6H_4	**3bb**	80	86
5	**1c**	4-ClC_6H_4	**2b**	4-FC_6H_4	**3cb**	76	86
6[e]	**1c**	4-ClC_6H_4	**2b**	4-FC_6H_4	**3cb**	45	93
7	**1d**	4-MeC_6H_4	**2b**	4-FC_6H_4	**3db**	67	87
8	**1a**	Ph	**2e**	3-thienyl	**3ae**	62	80
9[f]	**1a**	Ph	**2f**	Et	**3af**	45	27

[a] **L9** (20 mol%), Et_2Zn in toluene (1.5 M, 2 equiv), **2a** (7.5 equiv) in toluene (0.48 mL) at 70°C for 1.5 h, followed by addition of **1** (0.125 mmol) in $EtNO_2$ (1 mL) at RT, 4 h. [b] Yield of isolated product. [c] Determined by HPLC. [d] Yield and *ee* after single crystallization from hexane/CH_2Cl_2. [e] $MeNO_2$ was used instead of $EtNO_2$. [f] Reaction was carried out at 70°C.

Alkynes bearing substituted aromatic rings reacted with several enones **1** to give the expected products with enantioselectivities similar to those observed with phenylacetylene (entries 1–7). 3-Thienylacetylene, bearing a heteroaromatic ring, also reacted under these conditions to give compound **3ae** with 80% *ee* (entry 8). However, 1-butyne required a higher reaction temperature and gave the expected product in 43% yield with 27% *ee* (entry 9), while trimethylsilylacetylene gave a complex mixture of products that was not characterized. Finally, it is worth noting that most products **3** are crystalline solids, which can be obtained almost enantiomerically pure by a single crystallization from hexane/CH_2Cl_2 (Table 2, entries 2, 5 and 8; Table 3, entries 1 and 3).

The absolute configuration of the stereogenic centre of **3aa** was determined to be *R* after complete hydrogenation ($Pd/CaCO_3$) of the triple bond (Scheme 2) and comparison



Scheme 2. Modifications of compound **3aa** and tandem 1,4-addition–fluorination: i) H_2, $Pd/CaCO_3$, EtOH, 30 min, 99%; ii) H_2, Lindlar catalyst, benzene, 1 h, 99%; iii) $LiAlH_4$ (4 equiv), THF, 0°C, 1 h, 86%; iv) Ag(OTf) (cat.), THF, 0°C, 77%; v) **L9**, Et_2Zn, toluene/$EtNO_2$, 4 h, then NFSI (3 equiv), RT, 77 h, 48%.

of the resulting product **4** with the hydrogenation product of the known compound (+)-3-[(*S,E*)-1,3-diphenylallyl]pentane-2,4-dione,[17] which was obtained by Pd-catalyzed enantioselective allylic alkylation of (*E*)-1,3-diphenylallyl acetate with pentane-2,4-dione (see the Supporting Information). For the other products **3**, the stereochemistry was assigned by analogy.

On the other hand, reduction of the triple bond with Lindlar catalyst quantitatively provided compound **5** with a *Z*-double bond and an allylic stereogenic centre. This procedure is complementary to the Pd-catalyzed allylic substitution of 1,3-diphenylallyl acetate with pentane-2,4-dione, which favours the formation of the compound with an *E*-double bond (see the Supporting Information).[17] Furthermore, compound **3aa** could be reduced with $LiAlH_4$ with good diastereoselectivity, which, followed by silver-catalyzed cyclization, gave access to chiral tetrahydrofuran **7** having four stereogenic centres. Finally, we achieved an asymmetric tandem 1,4-addition–fluorination reaction by quenching the alkynylation mixture with *N*-fluorobenzenesulfonimide (NFSI) as the terminal electrophile to give **8**.[18]

In conclusion, we have reported the first zinc-mediated asymmetric conjugate addition of terminal alkynes **2** to arylidene-1,3-diketones **1** by using a catalytic amount of a chiral inducer. The products **3** are obtained in good yields and enantioselectivities (up to 99% *ee* after a single crystallization). The reaction can be applied to differently substituted enones and terminal alkynes with aromatic or heteroaromatic groups. The potential synthetic applicability of the resulting products was shown by diverse transformations. Further studies to enlarge the scope of the reaction as well as mechanistic studies are underway.

Experimental Section

General: Reactions were carried out under nitrogen in round-bottomed flasks that were oven-dried overnight at 120°C. Commercial reagents were used as purchased. Arylidene-1,3-diketones **1** were prepared from the corresponding aldehydes and 1,3-diketones as described in the literature. Toluene was distilled from CaH_2. Nitroethane was dried and stored on 4 Å molecular sieves. Reactions were monitored by TLC analysis using Merck silica gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040–0.063 mm. Melting points were determined in capillary tubes. NMR spectra were recorded at 300 MHz for ^1H and at 75 MHz for ^{13}C NMR spectroscopy by using residual nondeuterated solvent ($CHCl_3$) as internal standard ($\delta = 7.26$ and 77.0 ppm), and at 282 MHz for ^{19}F NMR spectroscopy by using $CFCl_3$ as internal standard. Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments. High resolution mass spectra (ESI) were recorded on a Q-TOF spectrometer equipped with an electrospray source with a capillary voltage of 3.3 kV. Mass spectra (EI) were recorded at 70 eV. Specific optical rotations were measured by using sodium light (D line 589 nm). Chiral HPLC analyses were performed in a chromatograph equipped with a UV diode-array detector by using chiral stationary columns from Daicel.

General procedure for the enantioselective alkynylation reaction: A solution of Et_2Zn in toluene (1.5 M, 0.17 mL, 0.25 mmol) was added dropwise to a solution of (*R*)-VANOL (**L9**, 11.3 mg, 0.025 mmol) and phenylacetylene (**2a**, 103 μL, 0.94 mmol) in toluene (0.48 mL) at RT under nitrogen, and the mixture was stirred for 1.5 h at 70°C. Then, the reaction mixture was cooled to RT. A solution of arylidene-1,3-diketone **1a** (23.5 mg, 0.125 mmol) in nitroethane (1.0 mL) was added by using a syringe. The solution was stirred until the reaction was complete (monitored by TLC). The reaction mixture was quenched with aqueous NH_4Cl (20%, 1.0 mL), extracted with CH_2Cl_2 (2×15 mL), washed with brine (15 mL), dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane/EtOAc mixtures afforded compound **3aa** (26.2 mg, 72%). M.p. 75–77°C; $[\alpha]_D^{20} = +46.7$ ($c = 0.73$ in $CHCl_3$, 87% *ee*); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.42$–7.27 (m, 10H), 4.67 (d, $J = 11.1$ Hz, 1H), 4.22 (d, $J = 11.1$ Hz, 1H), 2.39 (s, 3H), 1.93 ppm (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) $\delta = 201.6$ (C), 201.6 (C), 138.2 (C), 131.6 (2CH), 128.9 (2CH), 128.3 (CH), 128.2 (2CH), 128.1

(2CH), 127.7 (CH), 122.6 (C), 88.0 (C), 84.9 (C), 75.6 (CH), 38.0 (CH), 31.1 (CH_3), 28.7 ppm (CH_3); MS (EI) *m/z* (%): 290 $[M]^+$ (1), 248 (22), 247 (100), 191 (34), 189 (15); HRMS: *m/z* calcd for $C_{20}H_{18}O_2$: 290.1307 $[M]^+$; found: 290.1303; HPLC (Chiralcel OD-H, hexane/*i*PrOH 99:01, 1 mL min^{-1}): $t_r = 9.2$ min (major), $t_r = 10.9$ min (minor); *ee*: 87%.

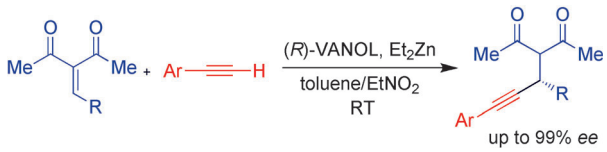
Acknowledgements

Financial support from the Ministerio de Ciencia e Innovación and FEDER (CTQ2009–13083) and from Generalitat Valenciana (ACOMP/2012/212 and ISIC 2012/001) is acknowledged. A.S-M. thanks the MICINN for a pre-doctoral grant (FPI).

Keywords: alkynes · conjugate addition · enantioselectivity · enones · zinc

[1] B. M. Trost, A. H. Weiss, *Adv. Synth. Catal.* **2009**, *351*, 963–999.
[2] P. F. Hudrlik, A. M. Hudrlik in *The Chemistry of the Carbon–Carbon Triple Bond*, Part 1 (Ed: S. Patai), Wiley, Chichester, **1978**, pp. 199–273.
[3] a) J. M. Chong, L. Shen, N. J. Taylor, *J. Am. Chem. Soc.* **2000**, *122*, 1822–1823; b) T. R. Wu, J. M. Chong, *J. Am. Chem. Soc.* **2005**, *127*, 3244–3245.
[4] a) Y.-S. Kwak, E. J. Corey, *Org. Lett.* **2004**, *6*, 3385–3388; b) O. V. Larionov, E. J. Corey, *Org. Lett.* **2010**, *12*, 300–302.
[5] a) T. F. Knöpfel, P. Zarotti, T. Ichikawa, E. M. Carreira, *J. Am. Chem. Soc.* **2005**, *127*, 9682–9683; b) for a copper-catalyzed diastereoselective alkynylation with ethyl propiolate, see: S. Fujimori, E. M. Carreira, *Angew. Chem.* **2007**, *119*, 5052–5055; *Angew. Chem. Int. Ed.* **2007**, *46*, 4964–4967.
[6] a) R. Yazaki, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2010**, *132*, 10275–10277; b) R. Yazaki, N. Kumagai, M. Shibasaki, *Chem. Asian J.* **2011**, *6*, 1778–1790; c) R. Yazaki, N. Kumagai, M. Shibasaki, *Org. Lett.* **2011**, *13*, 952–955.
[7] E. Fillion, A. K. Zorzitto, *J. Am. Chem. Soc.* **2009**, *131*, 14608–14609.
[8] a) T. Nishimura, X.-X. Guo, N. Uchiyama, T. Katoh, T. Hayashi, *J. Am. Chem. Soc.* **2008**, *130*, 1576–1577; b) T. Nishimura, T. Sawano, T. Hayashi, *Angew. Chem.* **2009**, *121*, 8201–8203; *Angew. Chem. Int. Ed.* **2009**, *48*, 8057–8059; c) T. Nishimura, S. Tokuji, T. Sawano, T. Hayashi, *Org. Lett.* **2009**, *11*, 3222–3225; d) T. Nishimura, T. Sawano, S. Tokuji, T. Hayashi, *Chem. Commun.* **2010**, *46*, 6837–6839.
[9] T. Nishimura, T. Sawano, K. Ou, T. Hayashi, *Chem. Commun.* **2011**, *47*, 10142–10144.
[10] a) S. Cui, S. D. Walker, J. C. S. Woo, C. J. Borths, H. Mukherjee, M. J. Chen, M. M. Faul, *J. Am. Chem. Soc.* **2010**, *132*, 436–437; b) J. C. S. Woo, S. Cui, S. D. Walker, M. M. Faul, *Tetrahedron* **2010**, *66*, 4730–4737.
[11] T. F. Knöpfel, D. Boyall, E. M. Carreira, *Org. Lett.* **2004**, *6*, 2281–2283.
[12] M. Yamashita, K. Yamada, K. Tomioka, *Org. Lett.* **2005**, *7*, 2369–2371.
[13] a) G. Blay, I. Fernández, A. Marco-Aleixandre, J. R. Pedro, *J. Org. Chem.* **2006**, *71*, 6674–6677; b) G. Blay, I. Fernández, A. Marco-Aleixandre, M. C. Muñoz, J. R. Pedro, *Org. Biomol. Chem.* **2009**, *7*, 4301–4308.
[14] a) G. Blay, L. Cardona, E. Climent, J. R. Pedro, *Angew. Chem.* **2008**, *120*, 5675–5678; *Angew. Chem. Int. Ed.* **2008**, *47*, 5593–5596; b) G. Blay, A. Brines, A. Monleón, J. R. Pedro, *Chem. Eur. J.* **2012**, *18*, 2440–2444; c) G. Blay, E. Ceballos, A. Monleón, J. R. Pedro, *Tetrahedron* **2012**, *68*, 2128–2134.
[15] F. Machetti, L. Cecchi, E. Trogu, F. De Sarlo, *Eur. J. Org. Chem.* **2007**, 4352–4359.
[16] In some cases, enolized products **3** were obtained to some extent depending on the structure of R^2.
[17] a) T. Imamoto, M. Nishimura, A. Koide, K. Yoshida, *J. Org. Chem.* **2007**, *72*, 7413–7416; b) T. Noël, K. Bert, E. Van der Eycken, J. Van der Eycken, *Eur. J. Org. Chem.* **2010**, 4056–4061.
[18] L. Wang, W. Meng, C.-L. Zhu, Y. Zheng, J. Nie, J.-A. Ma, *Angew. Chem.* **2011**, *123*, 9614–9618; *Angew. Chem. Int. Ed.* **2011**, *50*, 9442–9446.

Received: May 18, 2012
Published online: ■■ ▮▮, 0000



Zinc for conjugate alkynylation: The enantioselective conjugate addition of terminal alkynes to 2-arylidene-1,3-diketones in the presence of diethylzinc and a catalytic amount of (*R*)-VANOL has been developed. The reaction can be applied to different aromatic and heteroaromatic alkynes and enones, giving the expected products in good yield and with enantiomeric excesses up to 91%. The products can be enantiomerically enriched up to 99% *ee* by crystallization (see scheme).

Asymmetric Catalysis

G. Blay, L. Cardona, J. R. Pedro,* A. Sanz-Marco* ..... ▮▮▮▮–▮▮▮▮

Enantioselective Zinc-Mediated Conjugate Addition of Terminal Alkynes to Enones