DOI: 10.1002/ejoc.201100282

Quinine-Catalysed Double Michael Addition of Malononitrile to 1,5-Disubstituted Pentadien-3-ones: A Stereoselective Route to Cyclohexanones

Claudia De Fusco[a] and Alessandra Lattanzi*[a]

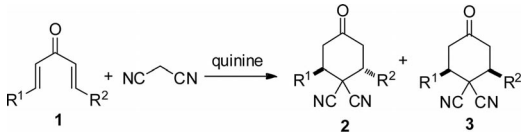
Keywords: Organocatalysis / Alkaloids / Michael addition / Cascade reactions / Diastereoselectivity / Enantioselectivity

The stereoselective synthesis of 4-oxo-2,6-diaryl-cyclohexane-1,1-dicarbonitriles has been developed through double Michael addition of malononitrile to 1,5-disubstituted pentadien-3-ones catalysed by quinine. This simple cascade process affords cyclohexanones in moderate-to-good yields, excellent diastereoselectivity and up to 86 % *ee*. The isolation of the monoaddition product helps to shed light on the stereochemical outcome of the two-step process.

Introduction

The employment of organic promoters in cascade processes is a fast growing and highly appealing field in asymmetric synthesis.[1] Complex molecular structures are selectively constructed in a stereocontrolled fashion by using simple reagents in a single operation, thus successfully addressing efficiency and economic concerns.[2] Carbon–carbon and carbon–heteroatom bonds are consecutively formed to afford multifunctionalised cyclic derivatives with different stereocentres. In the young area of organocascade processes, covalent catalysis, through iminium–enamine and enamine–iminium formation, has been the highly preferred activation strategy that uses secondary and primary amines as promoters.[3] On the other hand, relatively few examples of cascade processes have been reported that exploit noncovalent catalysis. Successful examples include the use of chiral phosphoric acids[4] or bifunctional promoters, such as cinchona-based and Takemoto-type thioureas.[5]

Organocatalytic Michael addition reactions that combine several carbon and heteroatom-based nucleophiles with common acceptors such as enals, enones and nitro alkenes have received a lot of attention in the past years.[6] In this context, malononitrile was scarcely explored as a donor for this process in comparison to malonate esters, nitro alkanes and 1,3-dicarbonyl compounds.[7] We recently reported that quinine promotes the highly enantioselective conjugate addition of malononitrile to chalcones.[8] On these grounds and by considering the clear advantages associated with the development of a process that uses low-cost and easily available catalysts and reagents, the Michael addition of malononitrile to 1,5-disubstituted pentadien-3-ones was investigated (Scheme 1). We envisaged that quinine could stereoselectively promote a double conjugate addition to directly afford cyclohexanones.



Scheme 1. Double Michael addition of malononitrile to 1,5-disubstituted pentadien-3-ones catalysed by quinine.

Interestingly, from a literature survey, we disclosed that cyclic 1,3-dicarbonyl compounds were used as donors by Wynberg in a pioneering study of double conjugate addition with compounds **1** catalysed by quinine.[9] The corresponding cyclohexanone spiranes were obtained in moderate yield (<50%) as a mixture of *trans*/*cis* isomers (*trans*/*cis* ≥ 2:1), and an optical yield of 30% was determined for the *trans* isomer in a specific case.[10] While this manuscript was in preparation, a similar approach starting from compounds **1** and malononitrile was reported by Yan and co-authors.[11] Covalent catalysis through iminium ion generation, provided by 9-amino-9-deoxyepiquinine and trifluoroacetic acid as co-catalyst, proved to be a viable route for the stereoselective synthesis of products **2**.

Herein, we illustrate a double Michael addition process of malononitrile to *trans*-1,5-disubstituted pentadien-3-ones promoted by quinine, which proceeds with excellent diastereoselectivity and good enantiocontrol.

Results and Discussion

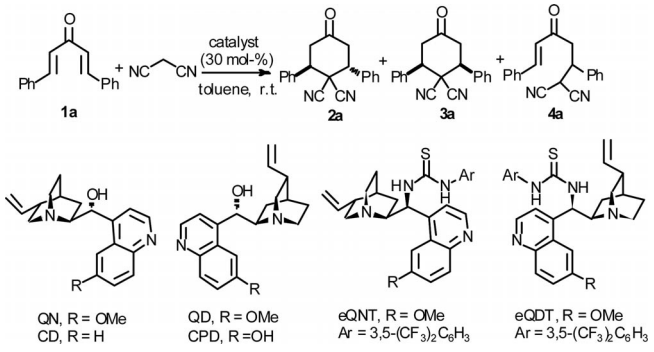
For the optimisation study, *trans*,*trans*-dibenzylideneacetone **1a** was used as a model compound with toluene as solvent and cinchona alkaloids or their derivatives as cata-

[a] Dipartimento di Chimica e Biologia, Università di Salerno, via Ponte don Melillo, 84084 Fisciano, Italy
Fax: +39-089-969603
E-mail: lattanzi@unisa.it

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201100282.

lysts (Table 1). When quinine was used, the *trans* isomer **2**[12] was formed in 44% yield, with a good diastereoselective ratio and 65% *ee* (Entry 1). The reaction carried out by using stoichiometric amounts of quinine under more diluted conditions afforded compound **2a** in 43% yield and 72% *ee* (Entry 2).

Table 1. Double conjugate addition of malononitrile to compound **1a** with cinchona-based catalysts ($R^1 = R^2 = Ph$).[a]



Entry	Catalyst	*C* [M]	*t* [h]	**2a/3a**[b]	Yield **2a** (**4a**) [%][c]	*ee* **2a** (**4a**) [%][d]
1	QN	0.2	87	9:1	44	65
2[e]	QN	0.1	42	2:1	43	72
3[f]	QN	0.1	48	5:1	48	77
4[g]	QN	0.04	66	10:1	70	79
5[g,h]	QD	0.04	52	24:1	61	–51
6[g]	CD	0.04	54	30:1	17 (46)	80 (52)
7[g]	CPD	0.04	71	–	– (37)	– (45)
8[g]	eQNT	0.04	66	n.d.[i]	<5 (76)	n.d.[i] (86)
9[g]	eQDT	0.04	66	>30:1	15 (57)	–86 (–76)

[a] Reaction conditions: **1a** (0.1 mmol), malononitrile (0.12 mmol), quinine (0.03 mmol). [b] Determined by ^{1}H NMR analysis. [c] Yield of isolated product; yield of **4a** in parenthesis. [d] Determined by chiral HPLC analysis; *ee* of **4a** in parenthesis. [e] 1 equiv. quinine was used. [f] 0.05 mmol malononitrile was used. [g] 0.1 mmol malononitrile was used. [h] Negative *ee* indicates the formation of the opposite enantiomer. [i] Not determined.

In both cases the starting material was almost consumed, and the formation of a coloured solid was also observed. The unidentified mixture of side products could derive from intermolecular Michael addition reactions to afford oligomers. Indeed, when 0.5 equiv. malononitrile was used the yield and the enantioselectivity of compound **2a** significantly improved (Entry 3). In order to favour the cyclisation of the firstly formed Michael adduct, the reaction mixture was further diluted with **1a**/malononitrile in a 1:1 ratio (Entry 4). We were pleased to observe the formation of *trans*-cyclohexanone **2a** in 70% yield and 79% *ee*. Under these conditions, quinidine afforded the opposite enantiomer of *trans*-**2a** in higher diastereocontrol, although a significantly lower *ee* was observed (Entry 5). As expected, cinchonidine proved to be a less active, although selective, catalyst for the reaction, as *trans*-cyclohexanone **2a** was obtained in 17% yield and 80% *ee* (Entry 6). Moreover, the monoaddition adduct **4a** was isolated in 46% yield. In the presence of cupreidine (CPD), the adduct **4a** was exclusively formed in modest yield and enantioselectivity (Entry 7). Finally, quinine-derived and quinidine-derived thioureas (eQNT and eQDT, respectively) were also screened as promoters for this process (Entries 8 and 9). They proved to be less effective than natural cinchona alkaloids QN and QD, although a good level of stereoselectivity was observed. The monoaddition product **4a** was isolated as the prevalent compound, whereas *trans*-cyclohexanone **2a** was obtained in low amounts. The poor activity shown by cinchona-derived thioureas was found to be in agreement with findings previously reported in the enantioselective Michael addition of malononitrile to *trans*-chalcones promoted by these catalysts.[7b]

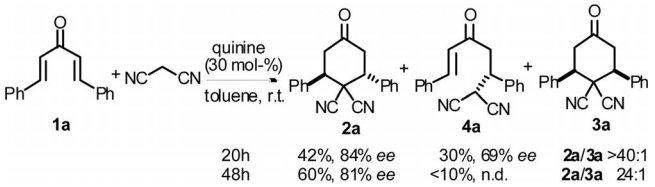
By taking into account the results illustrated in Table 1, quinine was chosen as the most effective catalyst for further studies of the cascade process; the solvent effect was briefly investigated (Table 2). Although in chlorobenzene a faster conversion to the product was observt lower temperatures (Entries 1 and 2). *m*-Xylene gave a comparable result to toluene (Entry 3), whereas halogenated and ethereal solvents afforded inferior results (Entries 4 and 5). Toluene was confirmed to be the best medium in which to perform the reaction. Pleasingly, working at higher dilution gave essentially the exclusive formation of the *trans* isomer **2a** in satisfactory yield and with 86% *ee* (Entry 6). Slightly inferior results were achieved when working under more concentrated conditions at lower temperature and when using 20 mol-% of catalyst loading (Entries 7 and 8).

Table 2. Optimisation study for the double conjugate addition of malononitrile to compound **1a** with quinine at room temperature.[a]

Entry	Solvent	*t* [h]	**2a/3a**[b]	Yield **2a** [%][c]	*ee* **2a** [%][d]
1	ClC_6H_5	36	14:1	66	72
2[e]	ClC_6H_5	47	>30:1	61	76
3	*m*-xylene	70	20:1	66	80
4	$CHCl_3$	67	18:1	50	62
5	THF	67	n.d.	<5	n.d.
6[f]	toluene	103	>50:1	55	86
7[g]	toluene	91	>30:1	54	83
8[h]	toluene	74	>30:1	56	80

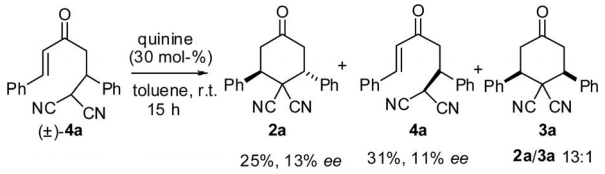
[a] Reaction conditions: **1a** (0.1 mmol), malononitrile (0.1 mmol), quinine (0.03 mmol) in 2.5 mL solvent. [b] Determined by ^{1}H NMR analysis. [c] Yield of isolated product. [d] Determined by chiral HPLC analysis. [e] Reaction performed at –18 °C. [f] *C* = 0.02 M. [g] Reaction performed at 4 °C. [h] 20 mol-% of catalyst was used.

In order to shed some light on the stereochemical outcome of the entire process, the reaction performed under conditions reported in Entry 4 of Table 1 was quenched after 20 h. In addition to compound *trans*-**2a**, the adduct **4a** was isolated in 69% *ee* (Scheme 2).



Scheme 2. Monitoring of the double Michael addition over time.

According to our previous findings on the quinine-promoted Michael addition of malononitrile to *trans*-chalcones, the first adduct **4a** should be *S* configured.[8] An amplification of the enantiomeric excess of compound **2a** was observed, which is expected on the basis of Horeau's principle.[13] After 48 h, *trans*-**2a** was isolated in 60% yield and with 81% *ee*, whereas adduct **4a** was nearly consumed. Moreover, compound **3a** was detected, although in very low amount. Unreacted **1a** was still present in the crude reaction mixture in both experiments. On the basis of the data illustrated in Scheme 2, it appears that the course of the second Michael addition reaction, to give the cyclised product **2a**, is also influenced by the chiral non-racemic adduct **4a**. If the opposite were true, according to Horeau's principle, compound **2a** would be expected to achieve 92% *ee* and *cis*-**3a** product would be formed in about a 25% yield at full conversion. Racemic **4a** was then reacted under the same reaction conditions (Scheme 3). After 15 h, unreacted **4a** was isolated in 11% *ee* and product **2a** in 13% *ee*. A poorly effective process of kinetic resolution occurs during cyclisation, which indicates that this step is also subjected to substrate control, although to a minor extent.[14]



Scheme 3. Kinetic resolution of the monoadduct **4a** in the second conjugate addition.

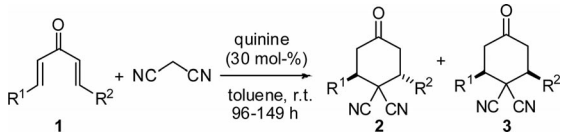
On the basis of all the experimental findings, the organocatalyst seems to predominantly control the stereoselectivity of the cascade process.

The scope of the double Michael addition was next investigated by reacting symmetrically- and unsymmetrically substituted dienones **1** with malononitrile (Table 3).

Symmetrically substituted *trans* products **2** were obtained in high-to-excellent diastereoselectivity and up to 86% *ee* (Entries 1–3). Unsymmetrically aryl-substituted dienones with electron-donating and electron-withdrawing groups were also suitable substrates for the process and afforded the *trans* isomer **2** in satisfactory yield, with excellent diastereocontrol and good *ee* (Entries 4–6). The heteroaromatic derivative **1g** furnished compound *trans*-**2g** in modest yield, with excellent diastereoselectivity and fairly good enantiomeric excess (Entry 7). An improvement in the yield for *trans*-**2g** could be obtained after a prolonged reaction time, although with a slightly decreased level of diastereo- and enantiocontrol (Entry 8). Dimethyl malonate and nitromethane were also checked as donors, but they did not react (Entries 9 and 10).

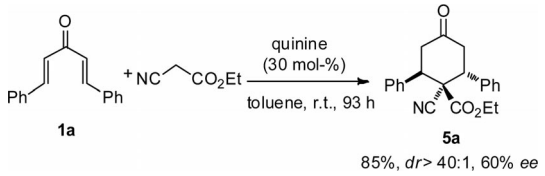
By assuming adducts **4** to be *S* configured, the absolute configuration of the major enantiomer of compounds *trans*-**2** should be 2*R*,6*R*. In order to confirm this hypothesis, model compound **1a** was treated with ethyl cyanoacetate in the presence of quinine (Scheme 4).

Table 3. Stereoselective double conjugate addition of malononitrile to compounds **1** catalysed by quinine.[a]



Entry	R^1, R^2	Donor	Yield **2** [%][b]	*ee* **2** [%][c] (**2**/**3**[d])
1	Ph, Ph (**a**)	$NCCH_2CN$	55	86 (>50:1)
2	4-MeC_6H_4, 4-MeC_6H_4 (**b**)	$NCCH_2CN$	54	85 (>50:1)
3	4-$CF_3C_6H_4$, 4-$CF_3C_6H_4$ (**c**)	$NCCH_2CN$	62	83 (19:1)
4	4-MeC_6H_4, Ph (**d**)	$NCCH_2CN$	68	82 (>30:1)
5	4-$MeOC_6H_4$, Ph (**e**)	$NCCH_2CN$	48	85 (>40:1)
6	4-ClC_6H_4, Ph (**f**)	$NCCH_2CN$	53	80 (>40:1)
7	2-thienyl, Ph (**g**)	$NCCH_2CN$	32	86 (>40:1)
8[e]	2-thienyl, Ph (**g**)	$NCCH_2CN$	47	80 (16:1)
9	Ph, Ph (**h**)	$CH_2(CO_2Me)_2$	–	–
10	Ph, Ph (**i**)	CH_3NO_2	–	–

[a] Reaction conditions: **1a** (0.1 mmol), malononitrile (0.1 mmol), quinine (0.03 mmol) in 5 mL solvent. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] Determined by ^1H NMR analysis. [e] Reaction quenched after a longer reaction time.



Scheme 4. Stereoselective quinine-catalysed double Michael addition of ethyl cyanoacetate to **1a**.

Cyclic compounds of this type have recently been obtained in high diastereo- and enantioselectivity by Melchiorre and co-authors by using 9-amino(9-deoxy)-*epi*-hydroquinine and 2-fluoro benzoic acid as co-catalyst in a Michael–Michael cascade process that combines enamine–iminium activation of enones.[15]

The double Michael addition, illustrated in Scheme 4, proceeded with an excellent control of the diastereoselectivity, and *trans*-cyclohexanone **5a** was isolated in high yield and 60% *ee*.

The absolute configuration of compound **5a** was determined to be (2*R*,6*R*) by comparing HPLC retention times and optical rotation values with those previously reported.[15] This result confirms that the stereochemical outcome of the first conjugate addition on compounds **1**, to give adducts **4**, is consistent with our previous findings.[8,16]

Conclusions

In conclusion, we developed a simple organocatalytic cascade process to *trans*-4-oxo-2,6-diaryl-cyclohexane-1,1-dicarbonitriles by double Michael addition of malononitrile to 1,5-disubstituted pentadien-3-ones by using low-cost and easily available quinine as the catalyst. The *trans*-cyclohexanones have been isolated in moderate-to-good yield, with excellent diastereocontrol and good enantioselectivity. In

this study, it has been demonstrated that noncovalent catalysis provided by quinine can be considered an alternative strategy to enamine–iminium activation of enones to access functionalised diaryl-substituted cyclohexanones. Further investigations on the synthesis of cyclohexanone derivatives by double Michael addition are under way in our laboratory.

Experimental Section

General Procedure for the Double Michael Addition of Malononitrile to Compounds 1: A solution of **1** (0.1 mmol), malononitrile (6.6 mg, 0.1 mmol) and quinine (9.7 mg, 0.03 mmol) in toluene (5 mL) was stirred at room temperature until the pentadien-3-one was consumed as monitored by TLC (petroleum ether/diethyl ether, 60:40). The crude reaction mixture was directly purified by flash chromatography on silica gel eluting with petroleum ether and mixtures of petroleum ether/diethyl ether (90:10 to 70:30) to afford cyclohexanones **2**.[17]

Supporting Information (see footnote on the first page of this article): General experimental methods, experimental procedures, characterisation data, HPLC traces, ^{1}H and ^{13}C NMR spectra for new compounds are presented.

Acknowledgments

Ministero dell'Università e della Ricerca (MIUR) and University of Salerno are acknowledged for financial support. Dr. P. Iannece is thanked for the MS analyses.

[1] a) L. F. Tietze, G. Brasche, K. Gericke (Eds.), *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**; b) D. Enders, C. Grondal, M. R. M. Hüttl, *Angew. Chem.* **2007**, *119*, 1590; *Angew. Chem. Int. Ed.* **2007**, *46*, 1570–1581; c) G. Guillena, D. J. Ramón, M. Yus, *Tetrahedron: Asymmetry* **2007**, *18*, 693–700; d) C. Grondal, C. Jeanty, D. Enders, *Nat. Chem.* **2010**, *2*, 167–178.

[2] a) P. A. Wenders, V. A. Verma, T. J. Paxton, T. H. Pillow, *Acc. Chem. Res.* **2008**, *41*, 40–49; b) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695–705.

[3] For selected examples, see: a) N. Halland, P. S. Aburel, K. A. Jørgensen, *Angew. Chem.* **2004**, *116*, 1292; *Angew. Chem. Int. Ed.* **2004**, *43*, 1272–1277; b) D. Gryko, *Tetrahedron: Asymmetry* **2005**, *16*, 1377–1383; c) J. W. Yang, M. T. Hechavarria Fonseca, B. List, *J. Am. Chem. Soc.* **2005**, *127*, 15036–15037; d) Y. Huang, A. M. Walji, C. H. Larsen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 15051–15053; e) W. Wang, H. Li, J. Wang, L. Zu, *J. Am. Chem. Soc.* **2006**, *128*, 10354–10355; f) Y. Yamamoto, N. Momiyama, H. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 5962–5963; g) H. Sundén, I. Ibrahem, L. Eriksen, A. Córdova, *Angew. Chem.* **2005**, *117*, 4955; *Angew. Chem. Int. Ed.* **2005**, *44*, 4877–4880; h) D. Enders, M. R. M. Hüttl, C. Grondal, G. Raabe, *Nature* **2006**, *441*, 861–863; i) D. Enders, M. R. M. Hüttl, J. Runsink, G. Raabe, B. Wendt, *Angew. Chem.* **2007**, *119*, 471; *Angew. Chem. Int. Ed.* **2007**, *46*, 467–469; j) Y. Hayashi, T. Okano, S. Aratake, D. Hazelard, *Angew. Chem.* **2007**, *119*, 5010; *Angew. Chem. Int. Ed.* **2007**, *46*, 4922–4925; k) S. Cabrera, J. Alemán, P. Bolze, S. Bertelsen, K. A. Jørgensen, *Angew. Chem.* **2008**, *120*, 127; *Angew. Chem. Int. Ed.* **2008**, *47*, 121–125; l) B. Tan, Z. Shi, P. J. Chua, G. Zhong, *Org. Lett.* **2008**, *10*, 3425–3428; m) H. Ishikawa, T. Suzuki, Y. Hayashi, *Angew. Chem.* **2009**, *121*, 1330; *Angew. Chem. Int. Ed.* **2009**, *48*, 1304–1307; n) P. Galzerano, F. Pesciaioli, A. Mazzanti, G. Bartoli, P. Melchiorre, *Angew. Chem.* **2009**, *121*, 8032; *Angew. Chem. Int. Ed.* **2009**, *48*, 7892–7894; o) T. Urushima, D. Sakamoto, H. Ishikawa, Y. Hayashi, *Org. Lett.* **2010**, *12*, 4588–4591.

[4] For selected examples, see: a) M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem.* **2006**, *118*, 3765; *Angew. Chem. Int. Ed.* **2006**, *45*, 3683–3686; b) J. Zhou, B. List, *J. Am. Chem. Soc.* **2007**, *129*, 7498–7499; c) M. Terada, K. Machioka, K. Sorimachi, *J. Am. Chem. Soc.* **2007**, *129*, 10336–10337; d) M. Rueping, A. P. Antonchick, *Angew. Chem.* **2008**, *120*, 5920; *Angew. Chem. Int. Ed.* **2008**, *47*, 5836–5838.

[5] For selected examples, see: a) S. Kaneko, T. Yoshino, T. Katoh, S. Terashima, *Tetrahedron* **1998**, *54*, 5471–5484; b) Y. Hoashi, T. Yabuta, Y. Takemoto, *Tetrahedron Lett.* **2004**, *45*, 9185–9188; c) J. Xie, K. Yoshida, K. Takasu, Y. Takemoto, *Tetrahedron Lett.* **2008**, *49*, 6910–6913; d) Y.-K. Liu, H. Liu, W. Du, L. Yue, Y.-C. Chen, *Chem. Eur. J.* **2008**, *14*, 9873–9877; e) R. Dodda, J. J. Goldman, T. Mandal, C.-G. Zhao, G. A. Broker, E. R. T. Tiekink, *Adv. Synth. Catal.* **2008**, *350*, 537–541; f) J. Wang, H. Xie, H. Li, L. Zu, W. Wang, *Angew. Chem.* **2008**, *120*, 4245; *Angew. Chem. Int. Ed.* **2008**, *47*, 4177–4179; g) C. Yu, Y. Zhang, A. Song, Y. Ji, W. Wang, *Chem. Eur. J.* **2011**, *17*, 770–774.

[6] For reviews, see: a) D. Almaşi, D. A. Alonso, C. Nájera, *Tetrahedron: Asymmetry* **2007**, *18*, 299–365; b) S. Sulzer-Mossé, A. Alexakis, *Chem. Commun.* **2007**, 3123–3135; c) D. Enders, K. Lüttgen, A. A. Narine, *Synthesis* **2007**, 959–980; d) S. B. Tsogoeva, *Eur. J. Org. Chem.* **2007**, 1701–1716; e) A. Córdova (Ed.), *Catalytic Asymmetric Conjugate Reactions*, Wiley-VCH, Weinheim, **2010**.

[7] a) T. Inokuma, Y. Hoashi, Y. J. Takemoto, *J. Am. Chem. Soc.* **2006**, *128*, 9413–9419; b) J. Wang, H. Li, L. Zu, W. Jiang, H. Xie, W. Duan, W. Wang, *J. Am. Chem. Soc.* **2006**, *128*, 12652–12653; c) X.-F. Li, L.-F. Cun, C.-X. Lian, L. Zhong, Y.-C. Chen, J. Liao, J. Zhu, J.-G. Deng, *Org. Biomol. Chem.* **2008**, *6*, 349–353; d) S.-L. Zhao, C.-W. Zheng, G. Zhao, *Tetrahedron: Asymmetry* **2009**, *20*, 1046–1051; e) Ren, Y.-J. Gao, J. Wang, *Chem. Eur. J.* **2010**, *16*, 13594–13598.

[8] A. Russo, A. Perfetto, A. Lattanzi, *Adv. Synth. Catal.* **2009**, *351*, 3067–3071.

[9] W. ten Hoeve, H. Wynberg, *J. Org. Chem.* **1979**, *44*, 1508–1514.

[10] For the stereoselective amino acid catalysed cascade reactions to cyclohexanone spiranes, see: a) D. B. Ramachary, N. S. Chowdari, C. F. Barbas III, *Synlett* **2003**, 1910–1914; b) D. B. Ramachary, K. Anebouselvy, N. S. Chowdari, C. F. Barbas III, *J. Org. Chem.* **2004**, *69*, 5838–5849.

[11] X.-m. Li, B. Wang, J.-m. Zhang, M. Yan, *Org. Lett.* **2011**, *13*, 374–377.

[12] a) A. T. Rowland, B. C. Jill, *J. Org. Chem.* **1988**, *53*, 434–437; b) A. T. Rowland, S. A. Filla, M. L. Coutlangus, M. D. Winemiller, M. J. Chamberlin, G. Czulada, S. D. Johnson, *J. Org. Chem.* **1998**, *63*, 4359–4365.

[13] a) J. P. Vigneron, M. Dhaenens, A. Horeau, *Tetrahedron* **1973**, *29*, 1055–1059; b) K. Soai, H. Hori, M. Kawahara, *J. Chem. Soc., Chem. Commun.* **1992**, 106–108; c) S. E. Baba, K. Sartor, J.-C. Poulin, H. B. Kagan, *Bull. Chim. Soc. Fr.* **1994**, *131*, 525–533.

[14] For an organocatalytic Michael–Michael cascade process involving an interplay of stereocontrol and dynamic kinetic resolution see ref. [5g]

[15] L.-Y. Wu, G. Bencivenni, M. Mancinelli, A. Mazzanti, G. Bartoli, P. Melchiorre, *Angew. Chem.* **2009**, *121*, 7332; *Angew. Chem. Int. Ed.* **2009**, *48*, 7196–7199.

[16] The (2*R*,6*R*) absolute configuration of compounds **2** is in agreement with data reported in ref. [11]

[17] Characterisation data of new compounds are reported in the Supporting Information.

Received: February 28, 2011
Published Online: April 26, 2011

