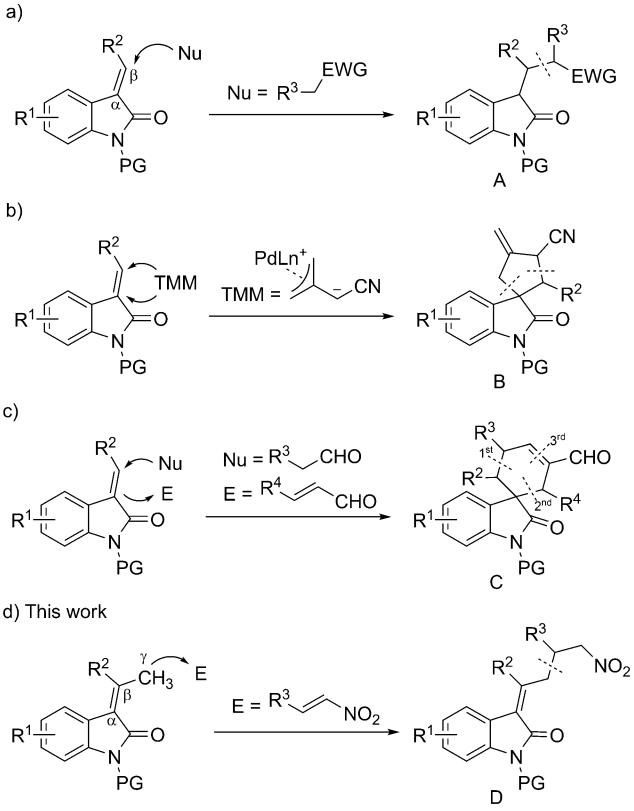
Organocatalysis

DOI: 10.1002/anie.201202027

Bifunctional Cinchona Alkaloid/Thiourea Catalyzes Direct and Enantioselective Vinylogous Michael Addition of 3-Alkylidene Oxindoles to Nitroolefins**

Claudio Curti, Gloria Rassu,* Vincenzo Zambrano, Luigi Pinna, Giorgio Pelosi, Andrea Sartori, Lucia Battistini, Franca Zanardi, and Giovanni Casiraghi**

3-Alkylidene oxindoles (methyleneindolinones), be they natural or man-made substances, occupy a preeminent position among the various classes of chemically and medicinally relevant small-molecule scaffolds.[1] Their plural functional architecture featuring a lactam carbonyl flanked by a highly substituted exocyclic double bond renders them enabling intermediates to be elaborated into a myriad of useful nitrogen heterocycles of varied complexity.[2] For example, 3-alkylidene oxindoles can be viewed as electrophilic Michael acceptors, which react with carbon-centered anions to give β-substituted oxindoles of type A (Scheme 1 a). In addition, they can act as electron-poor components in synchronous (Scheme 1 b) or stepwise (Scheme 1 c) cycloadditive functionalizations, thus opening the way to a wide range of highly valuable 3,3-spirocyclic structures of type B or C. Whereas these protocols have been largely pursued and formed the basis of many synthetic achievements,[2] an "umpolung" option could also be envisaged (Scheme 1 d), and capitalizes on the vinylogous pro-nucleophilic character of the alkyl group attached at the β-position of the ylidene. By reacting with the proper acceptors, these nucleophiles furnish olefinic oxindoles of type D, which are functionalized at the most distant point of the molecule (C_γ). However, despite the potential synthetic utility this method promises in terms of product complexity and atom economy, this opportunity has arguably been rather overlooked by the organic synthesis community,[3] and only very recently has an inaugural asymmetric vinylogous aldolization study been disclosed by our own research group.[4] Continuing this program, we report herein that a varied repertoire of γ-substituted α-ylidene oxindoles of type D can be assembled in high yield and excellent enantioselectivity in the first example of a direct, organocatalytic asymmetric vinylogous Michael (AVM) addition reaction of olefinic oxindoles to nitroolefins.[5,6] Reactions were perfectly guided by the chiral cinchona alkaloid/thiourea catalysts (Figure 1),[7] whose progeny was originally conceived and exploited by the research groups of Chen,[8] Soós,[9] Connon,[10] and Dixon.[11]



Scheme 1. Reactivity of 3-alkylidene oxindoles. a) Michael-type C_β functionalization.[2d,e] b) A [3 + 2] trimethylenemethane (TMM) cycloaddition.[2a,b] c) Michael/Michael/aldol annulation cascade.[2d,e] d) Vinylogous Michael-type C_γ functionalization (this work). PG = protecting group; EWG = electron-withdrawing group.

[*] Dr. C. Curti, Dr. A. Sartori, Dr. L. Battistini, Prof. Dr. F. Zanardi, Prof. Dr. G. Casiraghi
Dipartimento Farmaceutico, Università degli Studi di Parma
Parco Area delle Scienze 27A, I-43124 Parma (Italy)
E-mail: claudio.curti@unipr.it
giovanni.casiraghi@unipr.it
Prof. Dr. G. Pelosi
Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica, Università degli Studi di Parma, Parma (Italy)
Dr. G. Rassu, Dr. V. Zambrano
Istituto di Chimica Biomolecolare del CNR
Traversa La Crucca 3, I-07100 Li Punti, Sassari (Italy)
E-mail: gloria.rassu@icb.cnr.it
Dr. L. Pinna
Dipartimento di Chimica e Farmacia, Università degli Studi di Sassari, I-07100 Sassari (Italy)

[**] We thank the Università degli Studi di Parma and the Regione Autonoma della Sardegna (L.R. 07.08.2007, n.7) for funding. Thanks are due to Centro Interdipartimentale Misure "G. Casnati" for instrumental facilities.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201202027.

© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

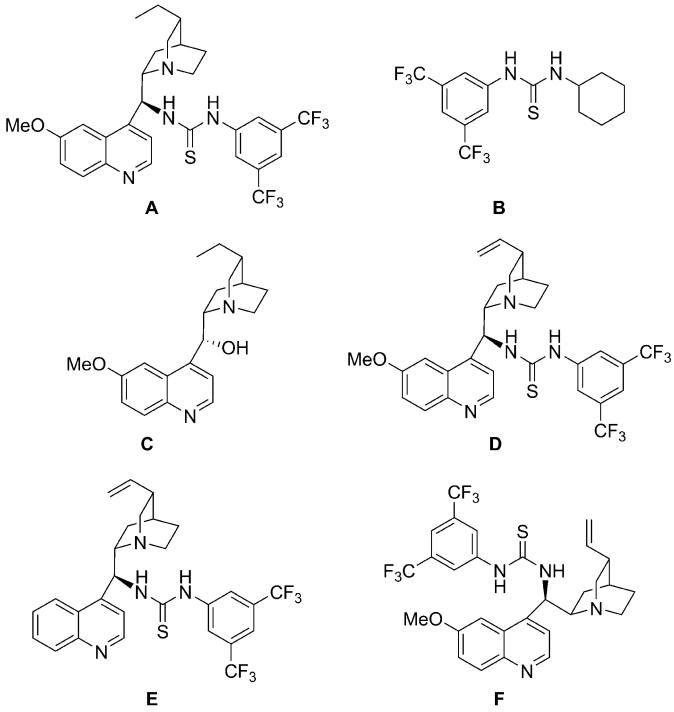
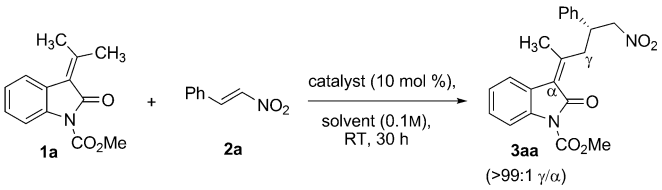


Figure 1. Catalysts for the AVM addition of 3-alkylidene oxindoles to nitroolefins.

Table 1: Survey of catalysts and conditions for the direct AVM addition of oxindole **1a** to olefin **2a**.[a]



Entry	Catalyst	Solvent	Yield [%][b]	d.r. [*Z*:*E*][c]	*ee* [%][d]
0	DABCO	CH_2Cl_2	16	5:1	racemic
1	**A**	CH_2Cl_2	60	10:1	95
2	**B**	CH_2Cl_2	0	–	–
3	**C**	CH_2Cl_2	18	10:1	−24
4	**D**	CH_2Cl_2	52	10:1	96
5	**E**	CH_2Cl_2	53	10:1	95
6	**F**	CH_2Cl_2	58	10:1	−96
7	**A**	toluene	68[e]	10:1	97
8	**A**	THF	42	12:1	94
9	**A**	MeOH	24	9:1	77
10[f]	**A**	toluene	85	20:1	98
11[f,g]	**A**	toluene	76	20:1	98
12[f,h]	**A**	toluene	90	>20:1	>99
13[f,h,i]	**A**	toluene	98	>20:1	>99
14[f,h,j]	**A**	toluene	73	>20:1	>99

[a] Unless otherwise stated, all AVM reactions were carried out on a 0.2 mmol scale using 1:1 **1a**/**2a** molar ratio and 10 mol% of catalyst in 2 mL of solvent at RT for 30 h. [b] Yield of isolated product after column chromatography. [c] Determined by ^{1}H NMR analysis of the crude reaction mixture. [d] Determined by chiral HPLC analysis. [e] 10% of an over-reaction by-product was also obtained. [f] Reaction carried out at −15 °C for 24 h followed by 12 h at RT. [g] **1a**/**2a** molar ratio was 1:1.2. [h] **1a**/**2a** molar ratio was 1.2:1. [i] 5 mol% of **A** was used. [j] 1 mol% of **A** was used in 72 h. DABCO = 1,4-diazabicyclo[2.2.2]octane, THF = tetrahydrofuran.

Initiating our work, we investigated the possible carbon–carbon bond-formation between readily available isopropylidene oxindole **1a** and *trans*-β-nitrostyrene (**2a**) in the presence of the dihydroquinine-derived thiourea **A** at ambient temperature (Table 1, entry 1). It was pleasing that the AVM reaction proceeded efficiently in CH_2Cl_2 with a 10 mol% catalyst loading, and the expected Michael adduct **3aa** (>99:1 γ/α) was isolated in 60% yield after 30 hours. Notably, both diastereoselectivity and enantioselectivity were good (10:1 *Z*/*E* d.r. and 95% *ee*). Although this first result was rewarding insofar as the *ee* value was concerned, a systematic catalyst screening and refinement of the reaction parameters were performed to identify even more productive and selective reaction conditions. To exclude any uncertainty that the use of the cinchona/thiourea catalysts might be decisive for positive reaction progress and an efficient catalyst-to-product transfer of chirality, control experiments were performed using the same reaction conditions of entry 1 in Table 1, but switching catalyst **A** to thiourea **B** and dihydroquinine **C** (Table 1, entries 2 and 3). Similar to several precedents in this field, both experiments failed, thus substantiating the principle that cooperativity between the basic and acidic moieties within the catalyst is indeed a stringent prerequisite for an effective asymmetric induction and reactivity.

On this basis, we felt compelled to explore alternative cinchona/thiourea catalysts **D**–**F** derived from quinine, cinchonidine, and quinidine, respectively (Table 1, entries 4–6). With respect to the initial attempt with catalyst **A**, the data did not show significant variation in the reaction outcome and, in these cases, the vinylogous Michael adduct **3aa** was obtained with almost equal ease and only slightly reduced yields upon isolation. As expected, quasienantiomers **E** and **F** did produce compounds which were enantiomers at the newly created stereocenters (entries 5 versus 6). Overall this trial identifies catalyst **A** as the catalyst of choice to be advanced for further optimization.

Of the solvents scrutinized, toluene was shown to be the ideal candidate as **3aa** was delivered in an improved 68% yield with 10:1 *Z*/*E* d.r. and 97% *ee* (Table 1, entry 7). The only cloud shadowing this notable result was the presence of a marginal amount of an over-reaction by-product (ca. 10% yield) arising from bilateral Michael addition at both the methyl termini of the isopropylidene oxindole **1a**.[12] Gratifyingly, by lowering the reaction temperature to −15 °C and increasing the donor/acceptor molar ratio to as little as 1.2:1 at a 0.1M concentration (entry 12), the reaction returned **3aa** in 90% yield upon isolation, with virtually complete selectivity and little, if any, by-product generation. Conveniently, the catalyst loading was reduced to 5 mol% with no erosion of selectivity (entry 13). However, additional lowering to 1 mol% prolonged the reaction time, thus rendering this option less practical (entry 14). Thus, by comprehensive comparison, the optimal reaction conditions in view of reactivity and global selectivity were those unveiled in entry 13 of Table 1.

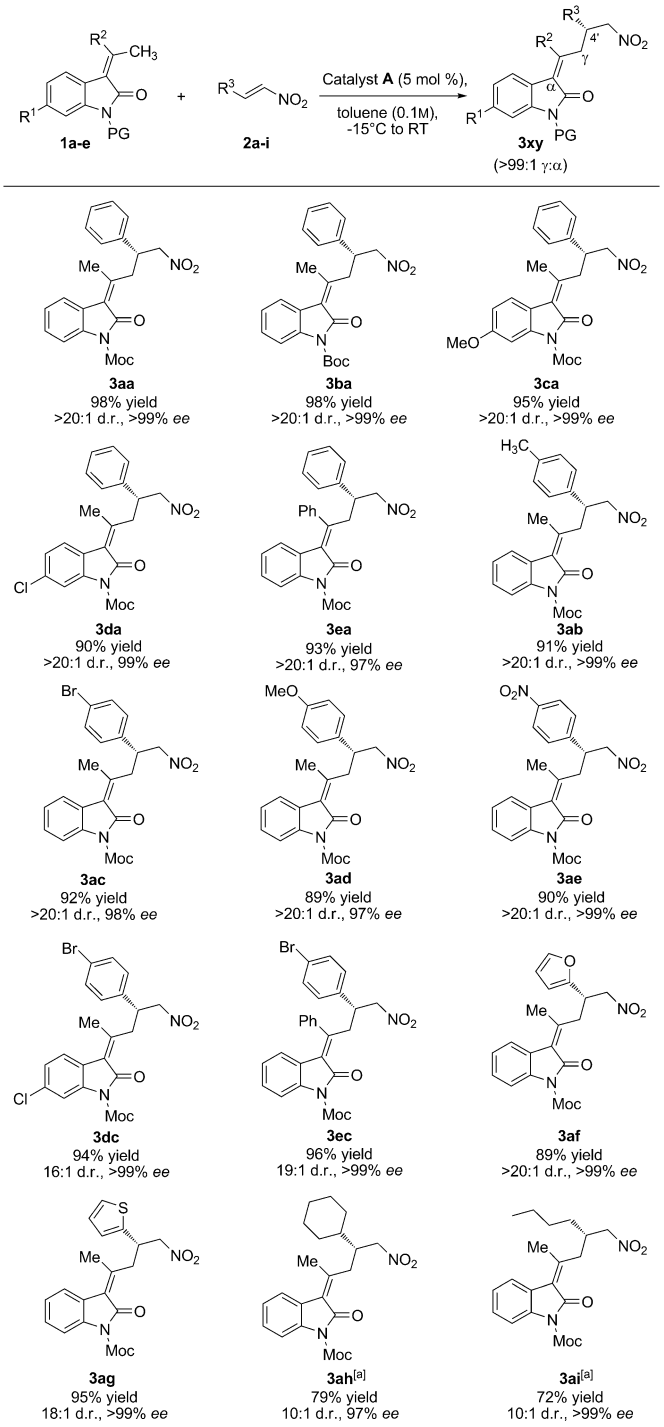
 © 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

At this point, with the optimal reaction conditions in hand, the scope and limitations of this unprecedented, direct AVM addition were surveyed with respect to both the indole donor and the alkene acceptor components. The results are summarized in Scheme 2. A number of indole nucleophiles carrying diverse nitrogen protecting groups and substituents at both the benzo and the olefin moieties were first studied. Excellent results were achieved with carbamoyl oxindoles **1a** and **1b** having methoxycarbonyl (Moc) and *tert*-butoxycarbonyl (Boc) substituents, thus leading to adducts **3aa** and **3ba**, respectively, in very high yields and selectivities. In sharp contrast, with protecting-group-free oxindoles and benzyl-protected derivatives the reactions stalled; and this substantiated that the presence of an electron-withdrawing group at the indole nitrogen atom, capable of engaging in supplementary hydrogen-bonding interactions with the catalyst, is an indispensable prerequisite for the reaction to occur efficiently and selectively (see below).[13] Even indoles carrying electron-releasing or electron-withdrawing substituents at the aromatic ring, such as the methoxy derivative **1c** and chlorine derivative **1d**, nicely served as Michael donors, thus giving rise to the corresponding vinylogous adducts **3ca** and **3da**, respectively, in high yields and excellent levels of diastereo- and enantioselectivity. Equally, benzylidene oxindole **1e**, carrying an aromatic ring at the C_β-position, was a competent donor, and delivered *E* configured adduct **3ea** solely in 93% yield and 97% *ee*.[14,15]

A variety of nitroalkene acceptors were then investigated. Irrespective of the electronic and steric demand of the aromatic ring within styrenes **2b–e**, all reactions went to completion, and the respective adducts **3ab–3ae**, as well as **3dc** and **3ec**, were isolated in good yields and very good margins of diastereo- and enantioselectivities. Nitroalkenes **2f** and **2g** bearing a heteroaromatic ring could also be used as proper Michael acceptors, thus giving **3af** and **3ag**, respectively, in excellent yields with diastereo- and enantioselectivies close to 100%. Finally, to explore the substrate generality further, AVM additions of **1a** to nitroalkenes carrying aliphatic side chains, such as β-cyclohexylnitroethene (**2h**) and β-*n*-butylnitroethene (**2i**), were evaluated. To our delight, with a 10 mol% catalyst loading at room temperature, the same remarkable stereocontrol was attained, thereby affording products **3ah** and **3ai**, respectively with 10:1 d.r. and 97 to greater than 99% *ee*, albeit in slightly lower yields (isolated) because of decreased reactivity of these nitroolefins.

Based on the above results and several precedents with these catalysts,[7] a possible model of dual activation of both the nucleophile and the electrophile by means of catalyst **A** was proposed (see Figure S5 in the Supporting Information). **A** serves as the chiral bifunctional catalyst: the thiourea unit activates the nitroalkene by double hydrogen bonding, while the quinuclidine base deprotonates the oxindole to afford an active dienolate species. An extra hydrogen bond between the carbonyl of the indole N-protecting group and the protonated quinuclidine base of the catalyst further contributes to stabilization of the transition state, thus ensuring preferential approach of the dienolate to the alkene Re face.[16,17] At the same time, the favorable *s-cis* alignment of the indole dienolates during the approach to the activated nitroolefins



Scheme 2. Generality of the direct AVM addition with respect to the donor and acceptor components. Unless otherwise stated, all AVM reactions were carried out on a 0.4 mmol scale using 1.2:1 **1/2** molar ratio, and 5 mol% of catalyst in 4 mL of solvent at −15°C for 24 h, followed by 12 h at RT. The reported yields are those of the isolated products. The d.r. and *ee* values were determined by ^{1}H NMR spectroscopy and chiral HPLC analysis, respectively. The origin of the adducts can be derived by the formula abbreviation **3xy**: the first letter identifies the oxindole donor, while the second letter identifies the nitroolefin acceptor. [a] 10 mol% catalyst was used, at RT for 72 h.

 © 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

controls the geometry of the newly formed double bond within the oxindole products, as indicated.

The absolute configuration of brominated adduct **3ac**, as well as the geometry of the alkene subunit were firmly established to be (3*Z*,4′*R*) by X-ray anomalous dispersion analysis (see Figure S6 in the Supporting Information),[18] and they are in accordance with those predicted by the proposed catalytic models. The absolute configurations of the other Michael adducts in Scheme 2 were assigned by analogy; their *Z*/*E* geometry was established by 2D-NOESY NMR experiments. In addition, the absolute configuration of Michael adducts **3aa**, *ent*-**3aa**, **3ea**, **3ag**, and **3ah** was also determined by OsO_4/PhI(OAc)$_2$-assisted oxidative fragmentation of the exocyclic double bond to afford known nitroketones (see the Supporting Information for details).

In conclusion, driven by lack of precedent for exploiting α-ylidene oxindoles as vinylogous carbon nucleophiles, we have realized the first and sole example of a direct, organocatalytic AVM addition of 3-alkylidene oxindoles to nitroolefins. The reactions were admirably orchestrated by the bifunctional cinchona alkaloid/thiourea catalyst **A**, to deliver almost enantiopure γ-substituted 3-alkylidene oxindoles with outstanding levels of regio-, diastereo-, and enantioselectivity. Provided that N-carbamoyl-protected oxindoles were used, the reaction scope and generality were substantial, regardless of the presence of neutral, electron-withdrawing, or electron-releasing substituents on the reaction components. Additional investigations into the utility and scope of 3-alkylidene oxindoles as electron-rich substrates in catalytic, asymmetric vinylogous carbon–carbon and carbon–heteroatom bond formations are currently underway.

Received: March 14, 2012
Published online: ■■ ■■, ■■■■

Keywords: asymmetric synthesis · heterocycles · Michael reaction · organocatalysis · umpolung

[1] a) C. Marti, E. M. Carreira, *Eur. J. Org. Chem.* **2003**, 2209 – 2219; b) C. Marti, E. M. Carreira, *J. Am. Chem. Soc.* **2005**, *127*, 11505 – 11515; c) C. V. Galliford, K. A. Scheidt, *Angew. Chem.* **2007**, *119*, 8902 – 8912; *Angew. Chem. Int. Ed.* **2007**, *46*, 8748 – 8758; d) A. Millemaggi, R. J. K. Taylor, *Eur. J. Org. Chem.* **2010**, 4527 – 4547; e) H.-L. Wang, Z. Li, G.-W. Wang, S.-D. Yang, *Chem. Commun.* **2011**, *47*, 11336 – 11338.

[2] For selected examples, see: a) B. M. Trost, N. Cramer, H. Bernsmann, *J. Am. Chem. Soc.* **2007**, *129*, 3086 – 3087; b) B. M. Trost, N. Cramer, S. M. Silverman, *J. Am. Chem. Soc.* **2007**, *129*, 12396 – 12397; c) X.-H. Chen, Q. Wei, S.-W. Luo, H. Xiao, L.-Z. Gong, *J. Am. Chem. Soc.* **2009**, *131*, 13819 – 13825; d) G. Bencivenni, L.-Y. Wu, A. Mazzanti, B. Giannichi, F. Pesciaioli, M.-P. Song, G. Bartoli, P. Melchiorre, *Angew. Chem.* **2009**, *121*, 7336 – 7339; *Angew. Chem. Int. Ed.* **2009**, *48*, 7200 – 7203; e) K. Jiang, Z.-J. Jia, S. Chen, L. Wu, Y.-C. Chen, *Chem. Eur. J.* **2010**, *16*, 2852 – 2856; f) Q. Wei, L.-Z. Gong, *Org. Lett.* **2010**, *12*, 1008 – 1011; g) F. Pesciaioli, P. Righi, A. Mazzanti, G. Bartoli, G. Bencivenni, *Chem. Eur. J.* **2011**, *17*, 2842 – 2845; h) Z.-J. Jia, H. Jiang, J.-L. Li, B. Gschwend, Q.-Z. Li, X. Yin, J. Grouleff, Y.-C. Chen, K. A. Jørgensen, *J. Am. Chem. Soc.* **2011**, *133*, 5053 – 5061; i) B. Tan, G. Hernández-Torres, C. F. Barbas III, *J. Am. Chem. Soc.* **2011**, *133*, 12354 – 12357; j) Y. Cao, X. Jiang, L. Liu, F. Shen, F. Zhang, R. Wang, *Angew. Chem.* **2011**, *123*, 9290 – 9293; *Angew. Chem. Int. Ed.* **2011**, *50*, 9124 – 9127; k) I. Allous, S. Comesse, M. Sanselme, A. Daïch, *Eur. J. Org. Chem.* **2011**, 5303 – 5310; l) B. Tan, N. R. Candeias, C. F. Barbas III, *Nat. Chem.* **2011**, *3*, 473 – 477; m) X. Li, Y.-M. Li, F.-Z. Peng, S.-T. Wu, Z.-Q. Li, Z.-W. Sun, H.-B. Zhang, Z.-H. Shao, *Org. Lett.* **2011**, *13*, 6160 – 6163; n) F. Zhong, X. Han, Y. Wang, Y. Lu, *Angew. Chem.* **2011**, *123*, 7983 – 7987; *Angew. Chem. Int. Ed.* **2011**, *50*, 7837 – 7841; o) C. Palumbo, G. Mazzeo, A. Mazziotta, A. Gambacorta, M. A. Loreto, A. Migliorini, S. Superchi, D. Tofani, T. Gasperi, *Org. Lett.* **2011**, *13*, 6248 – 6251; p) L. Liu, D. Wu, S. Zheng, T. Li, X. Li, S. Wang, J. Li, H. Li, W. Wang, *Org. Lett.* **2012**, *14*, 134 – 137; q) B. Tan, X. Zeng, W. W. Y. Leong, Z. Shi, C. F. Barbas III, G. Zhong, *Chem. Eur. J.* **2012**, *18*, 63 – 67; r) X.-F Xiong, Q. Zhou, J. Gu, L. Dong, T.-Y Liu, Y.-C Chen, *Angew. Chem.* **2012**, *124*, 4477 – 4480; *Angew. Chem. Int. Ed.* **2012**, *51*, 4401 – 4404.

[3] For an early example of vinylogous Claisen-type condensation, see: L. Horner, *Justus Liebigs Ann. Chem.* **1941**, *548*, 117 – 146.

[4] G. Rassu, V. Zambrano, R. Tanca, A. Sartori, L. Battistini, F. Zanardi, C. Curti, G. Casiraghi, *Eur. J. Org. Chem.* **2012**, 466 – 470.

[5] For general reviews on vinylogous aldol, Mannich, and Michael addition reactions, see: a) G. Casiraghi, F. Zanardi, G. Appendino, G. Rassu, *Chem. Rev.* **2000**, *100*, 1929 – 1972; b) M. Kalesse, *Top. Curr. Chem.* **2005**, *244*, 43 – 76; c) S. E. Denmark, J. R. Heemstra Jr., G. L. Beutner, *Angew. Chem.* **2005**, *117*, 4760 – 4777; *Angew. Chem. Int. Ed.* **2005**, *44*, 4682 – 4698; d) G. Casiraghi, F. Zanardi, L. Battistini, G. Rassu, *Synlett* **2009**, 1525 – 1542; e) T. Brodmann, M. Lorenz, R. Schäckel, S. Simsek, M. Kalesse, *Synlett* **2009**, 174 – 192; f) G. Casiraghi, L. Battistini, C. Curti, G. Rassu, F. Zanardi, *Chem. Rev.* **2011**, *111*, 3076 – 3154; g) S. V. Pansare, E. K. Paul, *Chem. Eur. J.* **2011**, *17*, 8770 – 8779.

[6] For recent reports on organocatalytic, direct AVM additions of activated alkene nucleophiles, including α,β-unsaturated carbonyls, see: a) G. Bencivenni, P. Galzerano, A. Mazzanti, G. Bartoli, P. Melchiorre, *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 20642 – 20647; b) Y. Zhang, Y.-L. Shao, H.-S. Xu, W. Wang, *J. Org. Chem.* **2011**, *76*, 1472 – 1474; c) L. Lin, J. Zhang, X. Ma, X. Fu, R. Wang, *Org. Lett.* **2011**, *13*, 6410 – 6413; d) A. Quintard, A. Lefranc, A. Alexakis, *Org. Lett.* **2011**, *13*, 1540 – 1543; e) M. Terada, K. Ando, *Org. Lett.* **2011**, *13*, 2026 – 2029. Further references in Chapter 5.2.2, p. 3144 *ff* of [5f].

[7] For general reviews on the use of cinchona alkaloid/urea and cinchona alkaloid/thiourea organocatalysts, see: a) S. J. Connon, *Chem. Commun.* **2008**, 2499 – 2510; b) C. E. Song in *Cinchona Alkaloids in Synthesis and Catalysis*, Wiley-VCH, Weinheim, **2009**; c) P. R. Schriner, *Chem. Soc. Rev.* **2009**, *38*, 1187 – 1198; d) Y. Takemoto, *Chem. Pharm. Bull.* **2010**, *58*, 593 – 601; e) E. M. O. Yeboah, S. O. Yeboah, G. S. Sing, *Tetrahedron* **2011**, *67*, 1725 – 1762; f) Q. L. Zhou in *Privileged Chiral Ligands and Catalysts*, Wiley-VCH, Weinheim, **2011**.

[8] B.-J. Li, L. Jiang, M. Liu, Y.-C. Chen, L.-S. Ding, Y. Wu, *Synlett* **2005**, 603 – 606.

[9] B. Vakulya, S. Varga, A. Csámpai, T. Soós, *Org. Lett.* **2005**, *7*, 1967 – 1969.

[10] S. H. McCooey, S. J. Connon, *Angew. Chem.* **2005**, *117*, 6525 – 6528; *Angew. Chem. Int. Ed.* **2005**, *44*, 6367 – 6370.

[11] J. Ye, D. J. Dixon, P. S. Hynes, *Chem. Commun.* **2005**, 4481 – 4483.

[12] Of note, only one stereoisomer of the bis(adduct) by-product could be detected.

[13] In addition, the Moc/Boc protecting groups may enhance the acidity of the γ-methyl protons in **1**, thereby allowing the enolization of the substrates to be more facile.

[14] According to IUPAC nomenclature, adducts **3ea**, as well as **3ec**, are indeed *E* configured, but the actual disposition of the

 © 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

double-bond substituents is the same as for all adducts portrayed in Scheme 2.
[15] Reactions performed with monosubstituted 3-ethylidene oxindole (R^2=H) failed because of extensive substrate decomposition under the scrutinized reaction conditions.
[16] The crucial role played by the indole carbamoyl protecting group is additionally supported by the low enantiocontrol obtained when a 3-ylidene benzofuranone analogue was utilized in lieu of the present indole matrices.
[17] An alternative transition-state model involving electrophile activation by the protonated amine group of the catalyst cannot, in principle, be ruled out. See structure II in Figure S5 of the Supporting Information. See, for example: a) T. Okino, Y. Hoashi, T. Furukawa, X. Xu, Y. Takemoto, *J. Am. Chem. Soc.* **2005**, *127*, 119 – 125; b) A. Hamza, G. Schubert, T. Soós, I. Pápai, *J. Am. Chem. Soc.* **2006**, *128*, 13151 – 13160.
[18] CCDC 870537 (**3ac**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

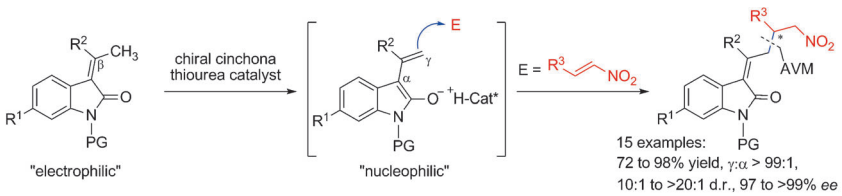
 © 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Communications

Organocatalysis

C. Curti,* G. Rassu,* V. Zambrano, L. Pinna, G. Pelosi, A. Sartori, L. Battistini, F. Zanardi, G. Casiraghi* ____ ▮▮▮▮–▮▮▮▮

Bifunctional Cinchona Alkaloid/Thiourea Catalyzes Direct and Enantioselective Vinylogous Michael Addition of 3-Alkylidene Oxindoles to Nitroolefins



Vinylogy: Advances in asymmetric catalysis using the bifunctional cinchona alkaloid/thioureas enabled an umpolung of the classical C_β reactivity of 3-alkylidene oxindoles, thus allowing the development of the first and sole example of a direct, organocatalytic asymmetric vinylogous Michael (AVM) reaction with nitroolefins.

© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!