ORGANIC
LETTERS

2013
Vol. 15, No. 17
4338–4341

Enantioselective Intermolecular Formal [3 + 3] Cycloaddition of 2,3-Disubstituted Indoles with Acrolein

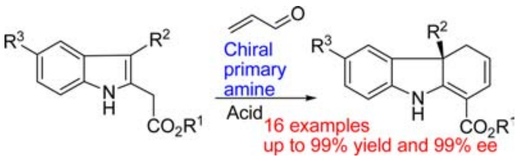
Jianbiao Huang, Long Zhao, Yong Liu, Weiguo Cao, and Xiaoyu Wu*

*Department of Chemistry, Shanghai University, 99 Shangda Road,
Shanghai 200444, China*

wuxy@shu.edu.cn

Received June 27, 2013

ABSTRACT



An expedient enantioselective synthesis of highly substituted hydrocarbazoles has been realized by an organocatalyzed formal [3 + 3] cycloaddition between acrolein and 2,3-disubstituted indoles. Tricyclic hydrocarbazoles were obtained from a broad range of 2,3-disubstituted indoles and acrolein in good to excellent yields and excellent enantioselectivites.

Chiral hydrocarbazoles bearing a quaternary stereocenter at C3 in the indoline substructure constitute the framework of quite a number of alkaloids. The stereochemical diversity and structural complexity as well as biological activities of such alkaloids have rendered them highly attractive synthetic targets.[1] In the past few decades, tremendous synthetic efforts have been devoted to the construction of these structural frameworks both in racemic and in optically pure form (Figure 1).[2,3]

From the point of biogenesis, this type of alkaloid is presumed to arise from the conjunction of tryptamine and secologanin, followed by skeleton rearrangements and functional transformations.[4] Thus, it is not surprising that tryptamine and other indole derivatives have been frequently chosen as starting materials for the chemical synthesis of such alkaloids. A survey of the synthetic work on this class of alkaloids reveals that the most challenging task, assembling the densely substituted cyclohexane moiety embedded in the hydrocarbazoles, has been solved by means of Diels–Alder reactions and related formal [4 + 2] cycloadditions.[5] This process has been rendered asymmetric by organocatalysis.[6] Recent examples include the following: (1) MacMillan and co-workers reported an asymmetric intermolecular Diels–Alder/elimination/conjugate addition cascade sequence for the synthesis of a key intermediate, which greatly facilitated the synthesis of a number of complex alkaloids;[3h,j] (2) You et al. employed an intramolecular Michael/Mannich organocascade

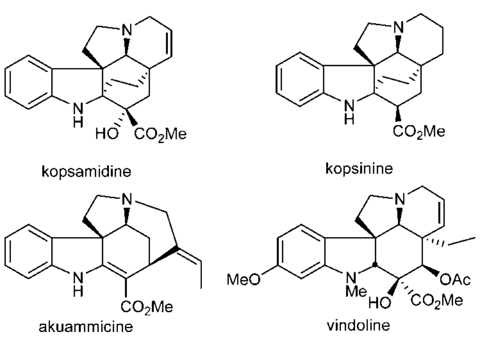


Figure 1. Examples of alkaloids bearing hydrocarbazole unit.

---

(1) (a) Saxton, J. E. In *The Alkaloids*; Cordell, G. A. Ed.; Academic Press: New York, 1998; Vol. 50, Chapter 9. (b) Saxton, J. E. In *The Alkaloids*; Cordell, G. A. Ed.; Academic Press: New York, 1998; Vol. 51, Chapter 1. (c) Ramirez, A.; Garcia-Rubio, S. *Curr. Med. Chem.* **2003**, *10*, 1891. (d) Jordan, M. A.; Wilson, L. *Nat. Rev. Cancer* **2004**, *4*, 253.

(2) (a) For reviews see: Zhang, D.; Song, H.; Qin, Y. *Acc. Chem. Res.* **2011**, *44*, 447. (b) Attorusso, E.; Taglialatela-Scafati, O. *Modern Alkaloids: Structure, Isolation, Synthesis and Biology*, Wiley-VCH: Weinheim, Germany, 2008. (c) Greig, N. H.; Pei, X.-F.; Soncrant, T. T.; Ingram, D. K.; Brossi, A. *Med. Res. Rev.* **1995**, *15*, 3. (d) Bonjoch, J.; Solé, D. *Chem. Rev.* **2000**, *100*, 3455. (e) Mori, M. *Heterocycles* **2010**, *81*, 259. (f) Jeffrey, S. C.; Overman., L. E. *Angew. Chem., Int. Ed.* **2012**, *51*, 4288. (g) Shibasaki, M.; Ohshima, T. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: San Diego, CA, 2007; Vol. 64, Chapter 3.

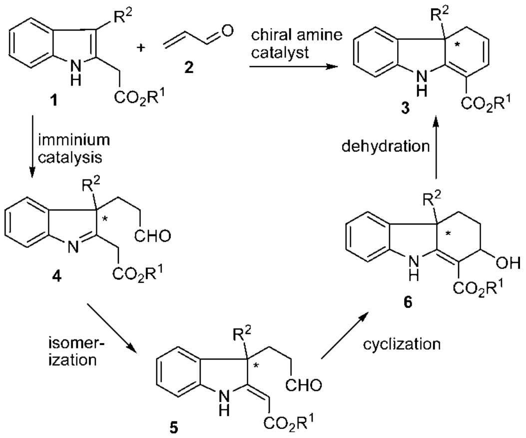
10.1021/ol401809d

catalyzed by a quinine-derived primary amine for the enantioselective synthesis of tetracyclic indolines.[5d] Despite these achievements, the development of new strategies for efficient and asymmetric construction of such hydrocarbazoles that can serve as suitable precursors for the synthesis of alkaloids and their analogues is still highly desirable.[7]

In our ongoing search for a new efficient one-pot cascade sequence for the asymmetric synthesis of hydrocarbazoles (Scheme 1), we envisioned that 2,3-disubstituted indole **1** would be a suitable nucleophile for the conjugate addition to acrolein **2**, providing an asymmetric access to hydrocarbazoles. As outlined in Scheme 1, condensation of indole derivative **1** with acrolein **2** is promoted through the activation of the enal by formation of an imminium intermediate to afford indolenine intermediate **4** after release of the catalyst.[8] Intermediate **4** undergoes isomerization to afford enamino-ester **5**, which after an intramolecular cyclization and following dehydration affords highly functionalized hydrocarbazole **3**.

Of concern are two major issues inherent in this sequence: the first is the possible competitive reaction between N(1) and C(3), although the latter is the most reactive site toward electrophilic substitution;[9−11] while the second is the further conjugate addition(s) of cyclized product **3** due to the nucleophilic nature of the dienamine moiety.[12] Presumably, the first issue could be solved by careful tuning of the reaction conditions, while the second one could be tackled by introducing an ester

Scheme 1. Conceptual Cascade Sequence to Chiral Hydrocarbazoles



---

(3) For selected recent examples on total synthesis of alkaloids containing hydrocarbazole substructure in optically pure form: (a) Yang, R. W.; Qiu, F. G. *Angew. Chem., Int. Ed.* **2013**, *52*, 6015. (b) Li, Z. Q.; Zhang, S. X.; Wu, S. T.; Shen, X. L.; Zou, L. W.; Wang, F. Q.; Li, X.; Peng, F. Z.; Zhang, H. B.; Shao, Z. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 4117. (c) Horning, B. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2013**, *135*, 6442. (d) Harada, S.; Sakai, T.; Takasu, K.; Yamada, K.; Yamamoto, Y.; Tomioka, K. *Chem. Asian J.* **2012**, *7*, 2196. (e) Medley, J. W.; Movassaghi, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 4572. (f) Zi, W. W.; Xie, W. Q.; Ma, D. W. *J. Am. Chem. Soc.* **2012**, *134*, 9126. (g) Pandey, G.; Kumara, P. *Org. Lett.* **2011**, *13*, 4672. (h) Jones, S. B.; Simmons, B.; Mastracchio, A.; MacMillan, D. W. C. *Nature* **2011**, *475*, 183. (i) Kato, D.; Sasaki, Y.; Boger, D. L. *J. Am. Chem. Soc.* **2010**, *132*, 3685. (j) Jones, S. B.; Simmons, B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 13606. (k) Dounay, A. B.; Overman, L. E.; Wrobleski, A. D. *J. Am. Chem. Soc.* **2005**, *127*, 10186. For selected recent examples on total synthesis of alkaloids containing hydrocarbazole substructure in racemic: (l) Martin, D. B. C.; Nguyen, L. Q.; Vanderwal, C. D. *J. Org. Chem.* **2012**, *77*, 17. (m) Jiao, L.; Herdtweck, E.; Bach, T. *J. Am. Chem. Soc.* **2012**, *134*, 14563. (n) Tan, S. H.; Banwell, M. G.; Willis, A. C.; Reekie, T. A. *Org. Lett.* **2012**, *14*, 5621. (o) Jing, P.; Yang, Z.; Zhao, C. G.; Zheng, H. J.; Fang, B. W.; Xie, X. G; She, X. G. *Chem.—Eur. J.* **2012**, *18*, 6729. (p) McMurray, L.; Beck, E. M.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2012**, *51*, 9288. (q) Zu, L.; Boal, B. W.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *133*, 8877. (r) Zhang, M.; Huang, X.; Shen, L.; Qin, Y. *J. Am. Chem. Soc.* **2009**, *131*, 6013. (s) Éles, J.; Kalaus, G.; Greiner, I.; Kajtár-Peredy, M.; Szabó, P.; Szabó, L.; Szántay, C. *Tetrahedron* **2002**, *58*, 8921.

(4) (a) Rueffer, M.; Nagakura, N.; Zenk, M. H. *Tetrahedron Lett.* **1978**, *19*, 1593. (b) Nagakura, N.; Rüffer, M.; Zenk, M. H. *J. Chem. Soc. Perkin Trans. 1* **1979**, 2308. (c) Hudlicky, T.; Reed, J. W. *The Way of Synthesis: Evolution of Design and Methods for Natural Products*; Wiley-VCH: Weinheim, Germany, 2007.

(5) For examples see: (a) Heureux, N.; Wouters, J.; Norberg, B.; Markó, I. E. *Org. Biomol. Chem.* **2006**, *4*, 3898. (b) Heureux, N.; Wouters, J.; Markó, I. E. *Org. Lett.* **2005**, *7*, 5245. (c) Kawano, M.; Kiuchi, T.; Negishi, S.; Tanaka, H.; Hoshikawa, T.; Matsuo, J.; Ishibashi, H. *Angew. Chem., Int. Ed.* **2013**, *52*, 906. (d) Cai, Q.; Zheng, C.; Zhang, J. W.; You, S. L. *Angew. Chem., Int. Ed.* **2011**, *50*, 8665. (e) Cai, Q.; You, S. L. *Org. Lett.* **2012**, *14*, 3040. (f) Zheng, C. W.; Lu, Y. P.; Zhang, J. K.; Chen, X. K.; Chai, Z.; Ma, W. Y.; Zhao, G. *Chem.—Eur. J.* **2010**, *16*, 5853. (g) Edwankar, R. V.; Edwankar, C. R.; Namjoshi, O. A.; Deschamps, J. R.; Cook, J. M. *J. Nat. Prod.* **2012**, *75*, 181. (h) Cao, Y. J.; Cheng, H. G.; Lu, L. Q.; Zhang, J. J.; Cheng, Y.; Chen, J. R.; Xiao, W. J. *Adv. Synth. Catal.* **2011**, *353*, 617 Also see references 3c, 3e, 3h, 3j, 3l, and 3s.

(6) For examples on construction of hydrocarbazoles by organocatalyzed [4 + 2] cyclization, see references 3c, 3e, 3h, 3j, 5d, 5e, 5f, and 5h. For reviews on organocatalysis, see: (a) Berkessel, A.; Groger, H. *Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis*; Wiley-VCH: Weinheim, Germany, 2004. (b) List, B.; Yang, J.-W. *Science* **2006**, *313*, 1584. (c) List, B. *Chem. Commun.* **2006**, 819. (d) Marigo, M.; Jørgensen, K. A. *Chem. Commun.* **2006**, 2001. (e) Dalko, P. I. *Enantioselective Organocatalysis: Reactions and Experimental Procedures*; Wiley—VCH: Weinheim, Germany, 2007. (f) Dondoni, A.; Massi, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 4638. (g) Melchiorre, P.; Marigo, M.; Carlone, A.; Bartoli, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 6138.

(7) During the progress of this work, List and co-workers reported an acid catalyzed interrupted indolization for enantioselective synthesis of hydrocarbazoles bearing quaternary stereocenter: Martínez, A.; Webber, M. J.; Müller, S.; List, B. *Angew. Chem., Int. Ed.* **2013** DOI: 10.1002/anie.201301618.

(8) For selected reviews on iminium catalysis, see: (a) Lelais, G.; MacMillan, D. W. C. *Aldrichim. Acta* **2006**, *39*, 79. (b) Erkkila, A.; Majander, I.; Pihko, P. M. *Chem. Rev.* **2007**, *107*, 5416.

(9) Lakhdar, S.; Westermaier, M.; Terrier, F.; Goumont, R.; Boubaker, T.; Ofial, A. R.; Mayr, H. *J. Org. Chem.* **2006**, *71*, 9088.

(10) For examples of N(1) addition of 3-substituted indoles: (a) Trost, B. M.; Krische, M. J.; Berl, V.; Grenzer, E. M. *Org. Lett.* **2002**, *4*, 2005. (b) Bandini, M.; Eichholzer, A.; Tragni, M.; Umani-Ronchi, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 3238. (c) Cui, H. L.; Feng, X.; Peng, J.; Lei, J.; Jiang, K.; Chen, Y. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 5737. (d) Stanley, L. M.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2009**, *48*, 7841. (e) Enders, D.; Wang, C.; Raabe, G. *Synthesis* **2009**, 4119. (f) Hong, L.; Sun, W. S.; Liu, C. X.; Wang, L.; Wang, R. *Chem.—Eur. J.* **2010**, *16*, 440. (g) Cai, Q.; Zheng, C.; You, S. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 8666.

(11) For examples of C(3) addition of 3-substituted indoles: (a) Kimura, M.; Futamata, M.; Mukai, R.; Tamaru, Y. *J. Am. Chem. Soc.* **2005**, *127*, 4592. (b) Trost, B. M.; Quancard, J. *J. Am. Chem. Soc.* **2006**, *128*, 6314. (c) Kagawa, N.; Malerich, J. P.; Rawal, V. H. *Org. Lett.* **2008**, *10*, 2381. (d) Austin, J. F.; Kim, S.-G.; Sinz, C. J.; Xiao, W.-J.; MacMillan, D.W. C. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5482. (e) Cai, Q.; Liu, C.; Liang, X. W.; You, S. L. *Org. Lett.* **2012**, *14*, 4588. (f) Zhang, Z. H.; Antilla, J. C. *Angew. Chem., Int. Ed.* **2012**, *51*, 11778.

(12) For examples of nucleophilic addition of dienamine, see: (a) Bertelsen, S.; Marigo, M.; Brandes, S.; Dinér, P.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 12973. (b) Bencivenni, G.; Galzerano, P.; Mazzanti, A.; Bartoli, G.; Melchiorre, P. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20642. (c) Bergonzini, G.; Vera, S.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2010**, *49*, 9685. (d) Stiller, J.; Marqués-López, E.; Herrera, R. P.; Frçhlich, R.; Strohmann, C.; Christmann, M. *Org. Lett.* **2011**, *13*, 70.

functionality at the β-position to reduce the nucleophilicity of the dienamine.

To test the feasibility of the above-mentioned working hypothesis, our study was carried out with 2,3-disubstituted indole **1a** and acrolein **2** as model substrates for screening reaction conditions (Scheme 2). At the beginning, L-proline derived secondary amine[13] **7a** and L-phenylalanine derived imidazolidinone **8a** were evaluated using reaction conditions similar to those reported by MacMillan and co-workers.[3h] Although the reactions proceeded smoothly and **1a** was consumed quickly, to our dismay, **7a** resulted in a mixture of unidentified products besides a trace amount of **3a**, while **8a** led to the formation of **3a** in 17% yield with 81% ee and a mixture of **9** and its diastereoisomers. The relative configuration of **9** was determined by X-ray diffraction.[14]

The initial frustrations caused by secondary amine catalysts prompted us to turn our attention to chiral primary amines[15] as alternative catalysts for this cascade. To our delight, with quinine-derived primary amine[16] **10a** (15 mol %) as the catalyst and perfluorobenzoic acid (PFBA, 30 mol %) as the cocatalyst, the cascade reaction proceeded smoothly in dioxane at 15 °C to afford the cyclized product **3a** in 88% yield and 90% ee (Table 1, entry 1). Attempts to improve the performance of this reaction by screening of the acid cocatalysts (Table 1, entries 2−6) revealed that ortho-nitrobenzoic acid (2-NBA) was the best, providing **3a** in 95% yield and 95% ee (Table 1, entry 2).

Scheme 2. Reaction between **1a** and **2** Catalyzed by a Chiral Secondary Amine

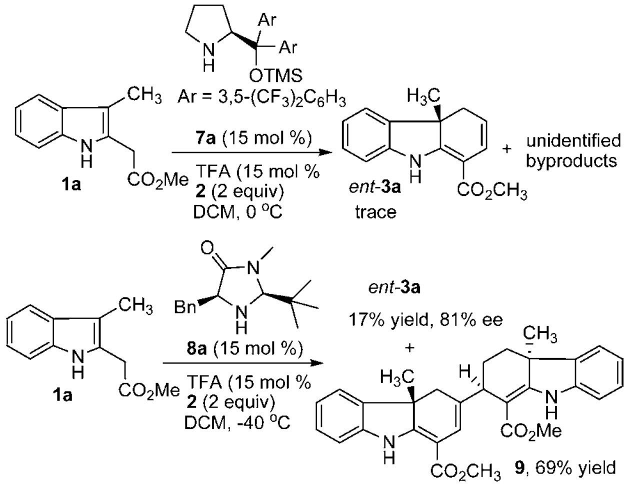
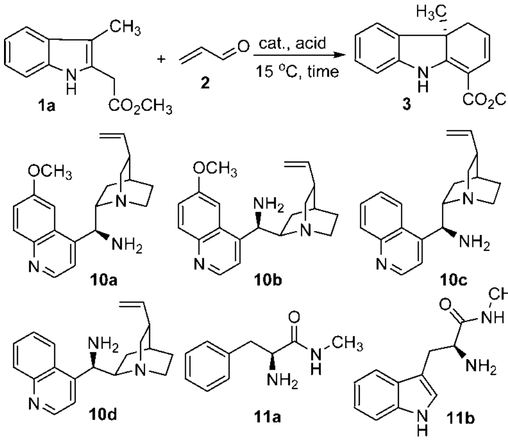


Table 1. Screening of Reaction Conditions[a]



entry	cat.	acid[b]	solvent	time (h)	yield (%)[c]	ee (%)[d]
1	**10a**	PFBA	dioxane	4	88	90
2	**10a**	2-NBA	dioxane	6	95	95
3	**10a**	4-NBA	dioxane	12	90	92
4	**10a**	3,5-$(CF_3)_2$-BA	dioxane	12	90	88
5	**10a**	4-CF_3−BA	dioxane	15	90	89
6	**10a**	BA	dioxane	20	20	ND[e]
7	**10a**	2-NBA	toluene	2	98	53
8	**10a**	2-NBA	Et_2O	15	60	75
9	**10a**	2-NBA	THF	15	60	97
10	**10a**	2-NBA	DCM	2	99	86
11	**10a**	2-NBA	DCE	3	86	90
12	**10a**	2-NBA	EA	4	98	95
13	**10a**	2-NBA	DMF	48	49	75
14	**10a**	2-NBA	MeOH	6	73	90
15	**10b**	2-NBA	EA	12	90	−60
16	**10c**	2-NBA	EA	18	98	87
17	**10d**	2-NBA	EA	20	10	ND[e]
18	**11a**	2-NBA	EA	6	62	−9
19	**11b**	2-NBA	EA	6	69	−9

[a] General conditions: **1a** (0.2 mmol), **2** (0.40 mmol), cat. (15 mol %) and acid additive (30 mol %) in solvent (1 mL) at 15 °C. [b] PFBA, perfluorobenzoic acid; 2-NBA, 2-NO_2−$C_6H_4CO_2H$; 4-NBA, 4-NO_2−$C_6H_4CO_2H$; 3,5-$(CF_3)_2$-BA, 3,5-$(CF_3)_2$-$C_6H_3CO_2H$; 4-CF_3−BA, 4-(CF_3)-$C_6H_4CO_2H$; BA, benzoic acid. [c] Yield referred to isolated pure **3a**. [d] Enantiomeric excess of **3a** was determined by chiral HPLC analysis. [e] Enantiomeric excess not determined.

A brief screening of solvents indicated that the reaction was quite solvent-dependent (Table 1, entries 7−14). EA proved to be the best in terms of both yield and ee (entry 12). Solvents such as THF, DCE, and MeOH provided the product in excellent enantioselectivity albeit in lower yields (entries 9, 11, and 14). With the use of toluene or DCM as a solvent, significant acceleration in the reaction rate was observed and high yield was attained, whereas the enantioselectivity was inferior as compared to

---

(13) For reviews on chiral secondary amine catalysis, see: (a) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471. (b) Mielgo, A.; Palomo, C. *Chem. Asian J.* **2008**, *3*, 922. (c) Jensen, K. L.; Dickmeiss, G.; Jiang, H.; Albrecht, Ł.; Jørgensen, K. A. *Acc. Chem. Res.* **2012**, *45*, 248.

(14) CCDC-937785 (**9**) and CCDC-937778 (**13**) contain 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.

(15) For reviews on chiral primary amine catalysis, see: (a) Bartoli, G.; Melchiorre, P. *Synlett* **2008**, 1759. (b) Chen, Y. C. *Synlett* **2008**, 1919. (c) Peng, F.; Shao, Z. *J. Mol. Catal. A* **2008**, *285*, 1. (d) Xu, L. W.; Lu, Y. *Org. Biomol. Chem.* **2008**, *6*, 2047. (e) Xu, L. W.; Luo, J.; Lu, Y. *Chem. Commun.* **2009**, 1807.

(16) For a review on cinchona-based primary amine catalysis: Melchiorre, P. *Angew. Chem., Int. Ed.* **2012**, *51*, 9748.

the use of EA (entries 7, 10). The catalytic performance of the other three primary amines (**10b**–**d**) derived from cinchona alkaloids and two amino acid-based primary amines (**11a**, **11b**) were also evaluated; however, the results were not as good as that of **10a** (entries 15–19).

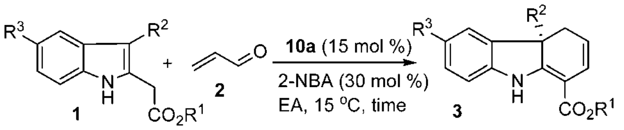
With the optimized reaction conditions established (Table 1, entry 12), the substrate scope of this cascade reaction was then extended to other 2,3-disubstituted indoles. As shown in Table 2, a broad range of 2,3-disubstituted indoles reacted to afford the corresponding hydrocarbazoles in good to excellent yields and high ee values. It should be noted that the size of the alkoxy group of the ester moiety in the substrate did not exhibit a marked influence on the outcome of this reaction, since **1b** with an ethoxy group and **1c** with a benzyloxy group furnished the corresponding cyclized products **3b** and **3c** in comparable yields and ees as **1a** (entries 1–3). A comparative study revealed that bulkiness of the substituent on the indolic C(3) did not affect the enantioselectivity of this reaction, while longer reaction time was needed for a substrate with a larger substituent on C(3) than methyl group (entries 4–9). Furthermore, the electronic nature of the substituent on indolic C(5) was found to have no influence on the results of this cascade (entries 10–15).

Attempts to extend the scope of α,*β*-unsaturated enal to substituted ones such as cinnaldehyde, crotonaldehyde, and methyl acrolein were unsuccessful, providing no desired cyclized products even at elevated temperatures in prolonged reaction times. The proton on the indolic nitrogen is necessary in the current research, as N-methyl protected **1a** is inactive for this transformation.

The synthetic utility of chiral hydrocarbazoles thus prepared was explored in a Diels–Alder reaction[17] and in electrophilic substitution, and satisfactory results were obtained. Treatment of **3a** with *N*-(4-bromophenyl)-maleimide **12** in toluene at 110 °C for 1.5 h gave the endo product **13** in 95% yield;[14] when exposed to a mixture of DMF and $POCl_3$ (Vilsmeier–Haack reaction),[18] **3a** was converted into aldehyde **14** quantitatively (Scheme 3).

The absolute configuration of hydrocarbazole **3a** was unambiguously determined to be 4a*R* by single-crystal X-ray diffraction analysis of its Diels–Alder adduct **13** (see Supporting Information). The absolute configuration of other tricyclic products could be assigned by analogy.

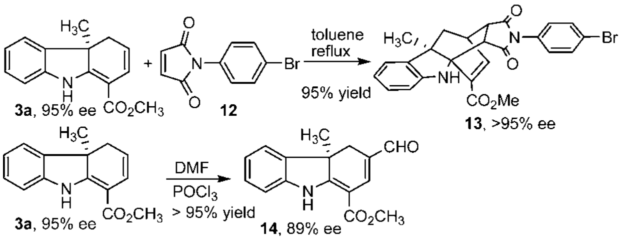
Table 2. Cascade Reaction between 2,3-Disubstituted Indoles and Acrolein[a]



entry	R_1, R_2, R_3, **1**	**3**	time (h)	yield (%)[b]	ee (%)[c]
1	Me, Me, H, **1a**	**3a**	4	98	95
2	Et, Me, H, **1b**	**3b**	6	86	91
3	Bn, Me, H, **1c**	**3c**	6	93	90
4	Me, n-Pr, H, **1d**	**3d**	12	93	95
5	Me, allyl, H, **1e**	**3e**	6	99	90
6	Me, Bn, H, **1f**	**3f**	24	63	89
7	Me, $BnCH_2$, H, **1g**	**3g**	12	92	96
8	**1h**[d]	**3h**	18	67	99
9	**1i**[d]	**3i**	18	73	92
10	Me, Me, Me, **1j**	**3j**	1.5	99	94
11	Me, Me, MeO, **1k**	**3k**	3	94	92
12	**1l**[d]	**3l**	8	87	96
13	Et, $BnCH_2$, MeO, **1m**	**3m**	4	85	98
14	Me, Me, F, **1n**	**3n**	2.5	99	94
15	Me, Me, Br, **1o**	**3o**	18	93	90

[a] Genreal conditions: **1a** (0.2 mmol), **2** (0.40 mmol), cat. (15 mol %) and acid additive (30 mol %) in solvent (1 mL) at 15 °C. [b] Yield referred to isolated pure **3**. [c] Enantiomeric excess of **3** was determined by chiral HPLC analysis. [d] R^1 = Et, R^2 = CH_2CH_2NHBoc, R^3 = H, **1h**; R^1 = Me, R^2 = $CH_2CH_2NHCO_2Et$, R^3 = H, **1i**; R^1 = Me, R^2 = $CH_2CH_2NHCO_2Et$, R^3 = Me, **1l**.

Scheme 3. Additional Derivatization of **3**



In summary, we have developed formal [3 + 3] organocatalytic cascade sequences for the asymmetric preparation of tricyclic hydrocarbazoles **3** from a broad range of 2,3-disubstituted indoles and acrolein in good to excellent yields and excellent enantioselectivites. The synthetic potential of these advanced structures was demonstrated by further derivatization via a Diels–Alder reaction and Vilsmeier–Haack reaction.

Acknowledgment. The generous financial support from the National Natural Science Foundation of China (No. 21072125 and No. 21272150) is acknowledged. Dr Hanwei Hu at Shanghai Medicilon is also gratefully acknowledged for helpful discussions.

Supporting Information Available. General experimental conditions, NMR spectra, and HPLC analysis of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

---

(17) (a) Kuehne, M. E.; Seaton, P. J. *J. Org. Chem.* **1985**, *50*, 4790. (b) Wenkert, E.; Pestchanker, M. J. *J. Org. Chem.* **1988**, *53*, 4875. (c) Magnus, P.; Payne, A. H.; Hobson, L. *Tetrahedron Lett.* **2000**, *41*, 2077. (d) Magnus, P.; Gazzard, L.; Hobson, L.; Payne, A. H.; Rainey, T. J.; Westlund, N.; Lynch, V. *Tetrahedron* **2002**, *58*, 3423.

(18) For selected reviews on Vilsmeier–Hacck reaction: (a) Kantlehner, W. *Eur. J. Org. Chem.* **2003**, 2530. (b) Jones, G.; Stanforth, S. P. *Org. React.* **2000**, *56*, 355.