Organocatalysis

International Edition: DOI: 10.1002/anie.201701947
German Edition: DOI: 10.1002/ange.201701947

Catalytic Asymmetric N-Alkylation of Indoles and Carbazoles through 1,6-Conjugate Addition of Aza-*para*-quinone Methides

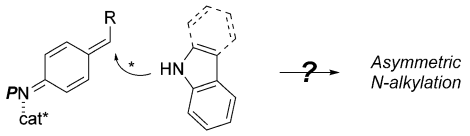
*Min Chen and Jianwei Sun**

Abstract: *Catalytic asymmetric N-alkylation of indoles and carbazoles represents a family of important but underdeveloped reactions. Herein, we describe a new organocatalytic strategy in which in situ generated aza-para-quinone methides are employed as the alkylating reagent. With the proper choice of a chiral phosphoric acid and an N-protective group, the intermolecular C–N bond formation with various indole and carbazole nucleophiles proceeded efficiently under mild conditions with excellent enantioselectivity and functional-group compatibility. Control experiments and kinetic studies provided important insight into the reaction mechanism.*

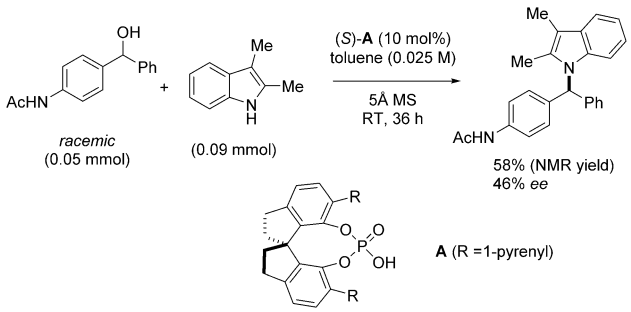
Asymmetric N-alkylation of indoles and carbazoles represents a family of important reactions in organic synthesis owning to the prevalence of these subunits in natural products and biologically active molecules.[1–4] However, these reactions, particularly intermolecular ones, have remained underdeveloped, presumably owing to difficult regiocontrol as a result of the low nucleophilicity of the N-H motif. Indeed, direct asymmetric indole N-alkylation has been mainly limited to substrates with certain substituents.[2] To overcome these limitations, some indirect strategies have also been devised.[3] Nevertheless, most of these reactions are limited to allylation. Furthermore, asymmetric N-alkylation of carbazoles has been much less studied,[4] which is in sharp contrast to the wide utility of carbazoles in medicinal chemistry and materials science.[1f] In this context, we report herein a highly efficient strategy for the asymmetric intermolecular N-alkylation of indoles and carbazoles by means of a 1,6-addition of aza-*p*-quinone methides (aza-*p*-QMs).

Aza-QMs are useful species in organic synthesis, biological processes, materials science, and drug development.[5] Having noticed their high reactivity toward nucleophiles, we envisioned that these species may serve as versatile alkylating reagents for the difficult asymmetric *N*-alkylation of indoles and carbazoles, provided that asymmetric induction by a suitable chiral catalyst could be achieved (Scheme 1).[6–8]

We started our exploration of the reaction with 2,3-dimethylindole, hoping to intrinsically favor N-alkylation over the more common C-alkylation (Scheme 2). An N-acetyl *para*-aminobenzylic alcohol was employed as the model precursor to aza-*p*-QM. Different chiral phosphoric acids based on BINOL and SPINOL backbones were evaluated as potential catalysts to catalyze not only the dehydration for in situ generation of the aza-*p*-QM intermediate, but also the subsequent asymmetric alkylation.[9] After considerable optimization efforts (see the Supporting Information for details), we were delighted to find that the reaction proceeded to form the desired N-alkylation product, albeit with moderate efficiency and enantioselectivity (Scheme 2). Of particular note is the absolute regioselectivity. The indole unit reacted at the 1-position exclusively, thus representing a new example of asymmetric N-alkylation of indoles. Among all the catalysts evaluated, catalyst **A** exhibited the best catalytic performance with regard to efficiency and enantioselectivity.[10] However, further tuning of the parameters did not improve the results.



Scheme 1. Development of an asymmetric N-alkylation of indoles and carbazoles with *para*-aza-quinone methides (***P*** = protective group).



Scheme 2. Preliminary results.

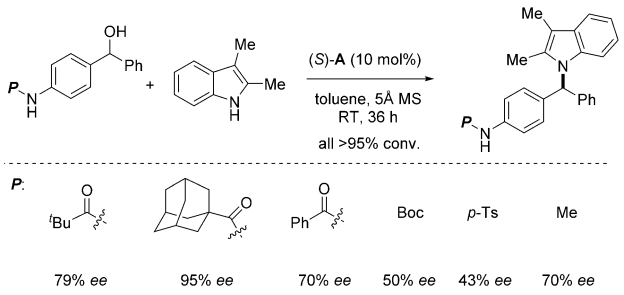
With the aim of further improving the reaction efficiency and enantioselectivity, we envisioned the possibility of changing the N-protective group of the alkylating reagent. As shown in Scheme 3, bulky aliphatic acyl groups, such as pivaloyl and 1-adamantanecarbonyl groups, proved superior, with the latter giving excellent enantioselectivity (95% *ee*). Other typical N-protective groups, such as Bz, Boc, and Ts, gave moderate enantioselectivity (see the Supporting Information for details). It is worth noting that protection with a methyl group also resulted in good reactivity, but not excellent enantioselectivity.

With the optimized conditions in hand, next we examined the reaction scope. A wide range of substituted indoles participated smoothly in the intermolecular C–N bond

[*] Dr. M. Chen, Prof. J. Sun
Department of Chemistry
The Hong Kong University of Science and Technology
Clear Water Bay, Kowloon, Hong Kong SAR (China)
E-mail: sunjw@ust.hk

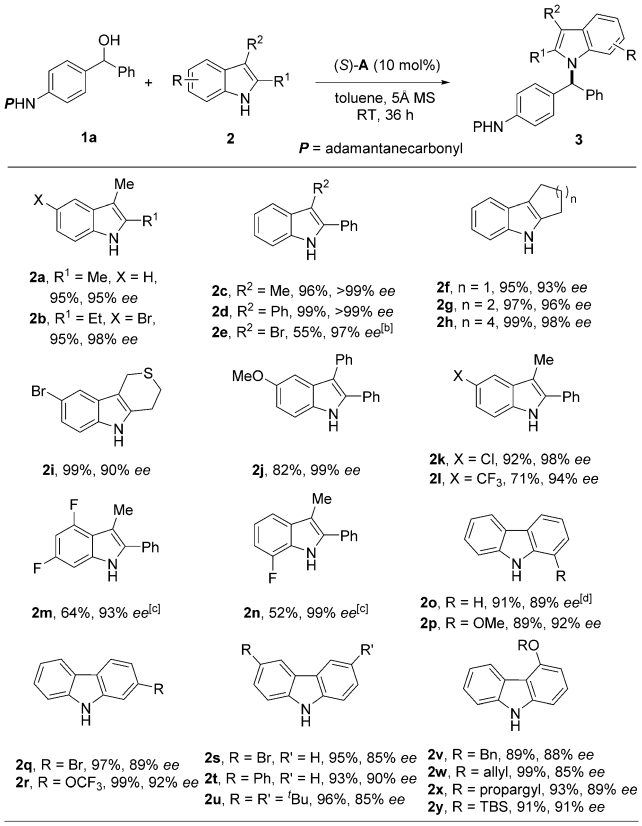
Supporting information for this article can be found under: http://dx.doi.org/10.1002/anie.201701947.

 © 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 3. Evaluation of different protective groups.

formation reaction, providing the corresponding indole-derived chiral anilines with excellent efficiency and enantioselectivity (Scheme 4). More importantly, a range of variously substituted carbazoles are also suitable nucleophiles (**2o**–**2y**). The scope with respect to the aza-*p*-QM precursors is equally broad (Scheme 5). Heterocycles like thiophene can also be incorporated into the product. Substitution with an aliphatic group at the benzylic position also provided good enantioselectivity. The mild conditions mean that a diverse set of functional groups is tolerated, including aryl halides, esters, nitriles, ethers, olefins, alkynes, and silyl-protected alcohols.



Scheme 4. Scope with respect to indoles and carbazoles.[a] [a] **1a** (0.2 mmol), **2** (0.28 mmol), 5 Å MS (50 mg), toluene (8.0 mL). The reactions for **2o**–**2y** were run with **2** (0.4 mmol) and (*R*)-**B1** without MS at 0 °C, which led to products with opposite configuration. Yields of isolated product are shown. [b] Run in the dark. [c] Run with 0.6 mmol of **2** for 72 h. [d] Run at 0 °C.

The product absolution configuration was confirmed by X-ray crystallography (**3u**). Notably, many of these products were obtained in essentially enantiopure form. It is also worth noting that the *p*-aminobenzylamine motif is a widely observed subunit in many biologically important molecules.[11]

While 3-substituted indoles use the 1-position as the nucleophilic site for the reaction, we were interested in knowing how 3-unsubstituted indoles react. Indeed, with the above standard conditions, the reaction with 2-phenylindole gives exclusive reaction at the 3-position, but with diminished enantioselectivity (75 % *ee*). Nevertheless, we further optimized the reaction and found that the use of dichloromethane as the solvent and 3 Å molecular sieves as additive led to improved enantioselectivity (Table 1). A brief survey of some analogous nucleophiles indicated that aryl, alkenyl, and alkyl substitution at the 2-position of the indole nucleophile does not significantly influence on the efficiency and enantioselectivity.[12] Steric hindrance in close proximity to the reactive site is also well tolerated.

Table 1: Scope with respect to 3-unsubstituted indoles.[a]

Entry	R	5	Yield [%][b]	*ee* [%][b]
1	Ph	**5a**	99	84
2	1-cyclohexenyl	**5b**	99	82
3	Bn	**5c**	98	88
4	^{i}Pr	**5d**	95	89
5	^{t}Bu	**5e**	96	94

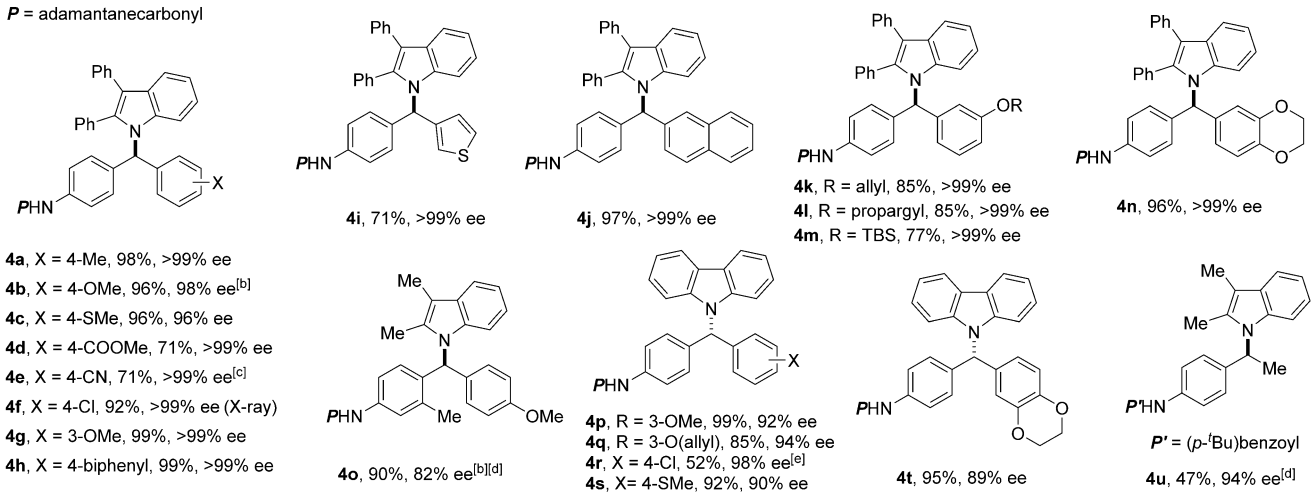
[a] **1a** (0.2 mmol), **4** (0.23 mmol), 3 Å MS (10 mg), CH_2Cl_2 (8.0 mL). [b] Yield of isolated product.

To further demonstrate the utility of the process, we carried out representative derivatizations of the product **3d**. Reduction of the amide smoothly gave chiral aniline **6** (Scheme 6). The N-acyl protective group can be efficiently removed in the presence of SmI_2 and Et_3N to form the free amine **7** (Scheme 6). Notably, the optical purity remained unchanged after these transformations.

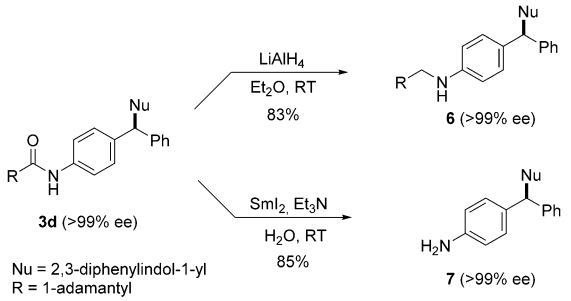
To probe the reaction mechanism, particularly whether the key aza-*p*-QM intermediate is involved, we carried out some control experiments. We synthesized the N-methylated substrate **1a′**, which is not capable of generating the aza-*p*-QM intermediate. In fact, **1a′** did not react under the standard conditions, which is consistent with the intermediacy of aza-*p*-QM (Scheme 7). Furthermore, when substrate **1a** was subjected to the standard conditions in the absence of a nucleophile, we were able to isolate a dimeric product **9**, which was presumably formed through alcohol addition to the aza-*p*-QM intermediate (Scheme 8). Further addition of a nucleophile to the reaction mixture still led to the desired product formation with comparably high enantioselectivity, albeit with slow conversion compared with the standard method. This observation indicates that the formation of **9** is reversible and the reverse conversion of **9** into the aza-*p*-QM is slow.

 © 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

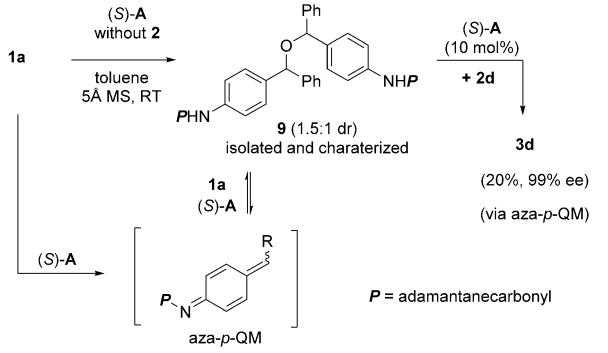
These are not the final page numbers!



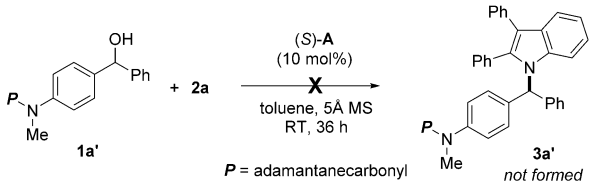
Scheme 5. Scope with respect to aza-*p*-QMs.[a] [a] **1a** (0.2 mmol), **2** (0.28 mmol), 5 Å MS (50 mg), toluene (8.0 mL). Yield of isolated product is provided. The reactions for **4p–4t** were run with **2** (0.4 mmol) and (*R*)-**A** without MS at 0 °C, which led to products with opposite configuration. Yield of isolated product is provided. [b] Run at 0 °C. [c] Run with 2 equivalents of nucleophile and 15 mol% of (*S*)-**A** for 72 h. [d] Run with 0.6 mmol of 2,3-dimethylindole. [e] The remained substrate accounts for the mass balance.



Scheme 6. Representative derivatizations of the product **3d**.



Scheme 8. Mechanistic evaluation of the involvement of aza-p-QM.



Scheme 7. Mechanistic evaluation using N-methylated substrate **1a'**.

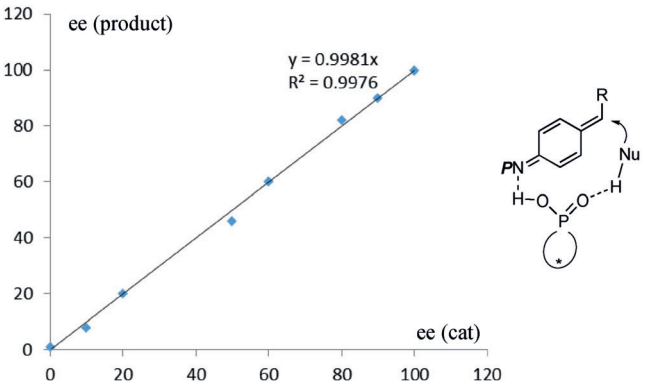


Figure 1. Absence of nonlinear effects and the proposed transition state.

To gain further insight into the mode of catalyst activation, we found that the enantiopurity of the product shows a linear relationship with that of the catalyst (Figure 1). This result may suggest that only one catalyst molecule is involved in the enantiodetermining transition state. We thus propose a transition state in which the catalyst plays a bifunctional role to activate both the aza-*p*-QM and the nucleophile. In this way, remote stereocontrol is expected. Indeed, this remote control is highly effective in view of the observed excellent enantiocontrol.[13]

In summary, we have developed a new strategy for the efficient asymmetric N-alkylation of indoles and carbazoles, an important but underdeveloped reaction. This process employs highly reactive in situ generated aza-*para*-quinone methides as the alkylating reagent. With the proper choice of a chiral phosphoric acid and N-protective group, the intermolecular C–N bond formation with various indole and carbazole nucleophiles proceeded with excellent efficiency and enantioselectivity. The mild reaction conditions mean

 © 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

that the reaction tolerates a wide range of functional groups. The use of alcohol precursors for in situ generation of the unstable aza-*para*-quinone methide intermediates makes this process particularly easy to handle. Control experiments provided important insight into the reaction mechanism, suggesting that the chiral acid catalyst serves not only as a promoter for the in situ formation of the key aza-*para*-quinone methide intermediate, but also as a bifunctional catalyst in the subsequent enantiodetermining step.

Acknowledgements

Financial support was provided by Hong Kong RGC (16311616, 16304115, ECS605812, M-HKUST607/12) and Shenzhen STIC (JCYJ20160229205441091). We thank Dr. Herman Sung for assistance in structure determination.

Conflict of interest

The authors declare no conflict of interest.

Keywords: alkylation · asymmetric catalysis · aza-quinone methides · nucleophilic addition · organocatalysis

[1] Selected reviews on the utility of indoles and carbazoles: a) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2005**, *105*, 2873 – 2920; b) M. Shiri, *Chem. Rev.* **2012**, *112*, 3508 – 3549; c) M. Bandini, A. Eichholzer, *Angew. Chem. Int. Ed.* **2009**, *48*, 9608 – 9644; *Angew. Chem.* **2009**, *121*, 9786 – 9824; d) R. J. Sundberg, *Indoles*, Academic Press, London, **1996**; e) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev.* **2010**, *110*, 4489 – 4497; f) A. W. Schmidt, K. R. Reddy, H.-J. Knölker, *Chem. Rev.* **2012**, *112*, 3193 – 3328.

[2] Selected examples of asymmetric N-alkylation of indoles: a) M. Bandini, A. Eichholzer, M. Tragni, A. Umani-Ronchi, *Angew. Chem. Int. Ed.* **2008**, *47*, 3238 – 3241; *Angew. Chem.* **2008**, *120*, 3282 – 3285; b) L. M. Stanley, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2009**, *48*, 7841 – 7844; *Angew. Chem.* **2009**, *121*, 7981 – 7984; c) H.-L. Cui, X. Feng, J. Peng, J. Lei, K. Jiang, Y.-C. Chen, *Angew. Chem. Int. Ed.* **2009**, *48*, 5737 – 5740; *Angew. Chem.* **2009**, *121*, 5847 – 5850; d) B. M. Trost, M. Osipov, G. Dong, *J. Am. Chem. Soc.* **2010**, *132*, 15800 – 15807; e) Q. Cai, C. Zheng, S.-L. You, *Angew. Chem. Int. Ed.* **2010**, *49*, 8666 – 8669; *Angew. Chem.* **2010**, *122*, 8848 – 8851; f) Y. Xie, Y. Zhao, B. Qian, L. Yang, C. Xia, H. Huang, *Angew. Chem. Int. Ed.* **2011**, *50*, 5682 – 5686; *Angew. Chem.* **2011**, *123*, 5800 – 5804; g) H.-G. Cheng, L.-Q. Lu, T. Wang, Q.-Q. Yang, X.-P. Liu, Y. Li, Q.-H. Deng, J.-R. Chen, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 3250 – 3254; *Angew. Chem.* **2013**, *125*, 3332 – 3336.

[3] Examples of indirect formation of chiral *N*-alkyl indoles: a) W.-B. Liu, X. Zhang, L.-X. Dai, S.-L. You, *Angew. Chem. Int. Ed.* **2012**, *51*, 5183 – 5187; *Angew. Chem.* **2012**, *124*, 5273 – 5277; b) X. Dou, W. Yao, C. Jiang, Y. Lu, *Chem. Commun.* **2014**, *50*, 11354 – 11357; c) K. Xu, T. Gilles, B. Breit, *Nat. Commun.* **2015**, *6*, 7616; d) Q.-A. Chen, Z. Chen, V. M. Dong, *J. Am. Chem. Soc.* **2015**, *137*, 8392 – 8395.

[4] We are only aware of one general study on asymmetric N-alkylation of carbazoles: Q. M. Kainz, C. D. Matier, A. Bartoszewicz, S. L. Zultanski, J. C. Peters, G. C. Fu, *Science* **2016**, *351*, 681 – 684.

[5] Reviews and highlights of QMs and aza-QMs: a) A. B. Turner, *Q. Rev. Chem. Soc.* **1964**, *18*, 347 – 360; b) H.-U. Wagner, R. Gompper in *The Chemistry of the Quinonoid Compounds*, *Vol. 2* (Ed.: S. Patai), Wiley, New York, **1974**, chap. 18, pp. 1145 – 1178; c) M. G. Peter, *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 555 – 570; *Angew. Chem.* **1989**, *101*, 572 – 587; d) K. Wojciechowski, *Eur. J. Org. Chem.* **2001**, 3587 – 3605; e) T. Itoh, *Prog. Polym. Sci.* **2001**, *26*, 1019 – 1059; f) *Quinone Methides* (Ed.: S. E. Rokita), Wiley, Hoboken, NJ, **2009**; g) M. M. Toteva, J. P. Richard, *Adv. Phys. Org. Chem.* **2011**, *45*, 39 – 91; h) A. Parra, M. Tortosa, *ChemCatChem* **2015**, *7*, 1524 – 1544; i) A. A. Jaworski, K. A. Scheidt, *J. Org. Chem.* **2016**, *81*, 10145 – 10153.

[6] We are not aware of any asymmetric reactions of aza-*p*-QMs. Achiral and racemic examples: a) P. Bongsup, R. Lonnie, D. Joanna, *Tetrahedron* **2000**, *56*, 7379 – 7388; b) M. Canepa, M. A. Fox, J. K. Whitesell, *J. Org. Chem.* **2001**, *66*, 3886 – 3892; c) K. Tanaka, W. Ohashi, H. Okada, Y. Chujo, *Tetrahedron Lett.* **2014**, *55*, 1635 – 1639; d) M. S. Markoulides, C. G. Efthymiou, A. J. Tasiopoulos, N. Chronakis, *Synlett* **2015**, 2659 – 2662.

[7] Representative reviews (a–b) and examples of *o*-QMs (c–o) and *p*-QMs (p–t): a) L. Caruana, M. Fochi, L. Bernardi, *Molecules* **2015**, *20*, 117333 – 111764; b) Z. Wang, J. Sun, *Synthesis* **2015**, 3629 – 3644; c) D. Wilcke, E. Herdtweck, T. Bach, *Synlett* **2011**, 1235 – 1238; d) O. El-Sepelgy, S. Haseloff, S. K. Alamsetti, C. Schneider, *Angew. Chem. Int. Ed.* **2014**, *53*, 7923 – 7927; *Angew. Chem.* **2014**, *126*, 8057 – 8061; e) C.-C. Hsiao, H.-H. Liao, M. Rueping, *Angew. Chem. Int. Ed.* **2014**, *53*, 13258 – 13263; *Angew. Chem.* **2014**, *126*, 13474 – 13479; f) C.-C. Hsiao, S. Raja, H.-H. Liao, I. Atodiresei, M. Rueping, *Angew. Chem. Int. Ed.* **2015**, *54*, 5762 – 5765; *Angew. Chem.* **2015**, *127*, 5854 – 5857; g) W. Zhao, Z. Wang, B. Chu, J. Sun, *Angew. Chem. Int. Ed.* **2015**, *54*, 1910 – 1913; *Angew. Chem.* **2015**, *127*, 1930 – 1933; h) Z. Wang, F. Ai, Z. Wang, W. Zhao, G. Zhu, Z. Lin, J. Sun, *J. Am. Chem. Soc.* **2015**, *137*, 383 – 389; i) G. C. Tsui, L. Liu, B. List, *Angew. Chem. Int. Ed.* **2015**, *54*, 7703 – 7706; *Angew. Chem.* **2015**, *127*, 7814 – 7818; j) J.-J. Zhao, S.-B. Sun, S.-H. He, Q. Wu, F. Shi, *Angew. Chem. Int. Ed.* **2015**, *54*, 5460 – 5464; *Angew. Chem.* **2015**, *127*, 5550 – 5554; k) Y. Luan, S. E. Schaus, *J. Am. Chem. Soc.* **2012**, *134*, 19965 – 19968; l) J. Izquierdo, A. Orue, K. A. Scheidt, *J. Am. Chem. Soc.* **2013**, *135*, 10634 – 10637; m) H. Lv, W.-Q. Jia, L.-H. Sun, S. Ye, *Angew. Chem. Int. Ed.* **2013**, *52*, 8607 – 8610; *Angew. Chem.* **2013**, *125*, 8769 – 8772; n) Y. Huang, T. Hayashi, *J. Am. Chem. Soc.* **2015**, *137*, 7556 – 7559; o) W. Guo, B. Wu, X. Zhou, P. Chen, X. Wang, Y.-G. Zhou, Y. Liu, C. Li, *Angew. Chem. Int. Ed.* **2015**, *54*, 4522 – 4526; *Angew. Chem.* **2015**, *127*, 4605 – 4609; p) W. D. Chu, L. F. Zhang, X. Bao, X. H. Zhao, C. Zeng, J. Y. Du, G. B. Zhang, F. X. Wang, X. Y. Ma, C. A. Fan, *Angew. Chem. Int. Ed.* **2013**, *52*, 9229 – 9233; *Angew. Chem.* **2013**, *125*, 9399 – 9403; q) L. Caruana, F. Kniep, T. K. Johansen, P. H. Poulsen, K. A. Jørgensen, *J. Am. Chem. Soc.* **2014**, *136*, 15929 – 15932; r) Z. Wang, Y. F. Wong, J. Sun, *Angew. Chem. Int. Ed.* **2015**, *54*, 13711 – 13714; *Angew. Chem.* **2015**, *127*, 13915 – 13918; s) N. Dong, Z.-P. Zhang, X.-S. Xue, X. Li, J.-P. Cheng, *Angew. Chem. Int. Ed.* **2016**, *55*, 1460 – 1464; *Angew. Chem.* **2016**, *128*, 1482 – 1486; t) K. Zhao, Y. Zhi, T. Shu, A. Valkonen, K. Rissanen, D. Enders, *Angew. Chem. Int. Ed.* **2016**, *55*, 12104 – 12108; *Angew. Chem.* **2016**, *128*, 12283 – 12287.

[8] Examples of asymmetric reactions of aza-*o*-QMs: a) C. Wang, J. A. Tunge, *J. Am. Chem. Soc.* **2008**, *130*, 8118 – 8119; b) Q.-Q. Yang, Q. Wang, J. An, J.-R. Chen, L.-Q. Lu, W.-J. Xiao, *Chem. Eur. J.* **2013**, *19*, 8401 – 8404; c) A. Lee, A. Younai, C. K. Price, J. Izquierdo, R. K. Mishra, K. A. Scheidt, *J. Am. Chem. Soc.* **2014**, *136*, 10589 – 10592; d) G. Li, H. Liu, G. Lv, Y. Wang, Q. Fu, Z. Tang, *Org. Lett.* **2015**, *17*, 4125 – 4127; e) H.-H. Liao, A. Chatupheeraphat, C.-C. Hsiao, I. Atodiresei, M. Rueping,

 © 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

Angew. Chem. Int. Ed. **2015**, *54*, 15540 – 15544; *Angew. Chem.* **2015**, *127*, 15760 – 15765; f) A. Chatupheeraphat, H.-H. Liao, S. Mader, M. Sako, H. Sasai, I. Atodiresei, M. Rueping, *Angew. Chem. Int. Ed.* **2016**, *55*, 4803 – 4807; *Angew. Chem.* **2016**, *128*, 4882 – 4887; g) M. Kretzschmar, T. Hodík, C. Schneider, *Angew. Chem. Int. Ed.* **2016**, *55*, 9788 – 9792; *Angew. Chem.* **2016**, *128*, 9941 – 9946; h) K. Bera, C. Schneider, *Chem. Eur. J.* **2016**, *22*, 7074 – 7078.

[9] Seminal reports and selected reviews on chiral phosphoric acid catalysis: a) T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem. Int. Ed.* **2004**, *43*, 1566 – 1568; *Angew. Chem.* **2004**, *116*, 1592 – 1594; b) D. Uraguchi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 5356 – 5357; c) T. Akiyama, *Chem. Rev.* **2007**, *107*, 5744 – 5758; d) M. Terada, *Synthesis* **2010**, 1929 – 1982; e) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev.* **2014**, *114*, 9047 – 9153; f) T. James, M. van Gemmeren, B. List, *Chem. Rev.* **2015**, *115*, 9388 – 9409.

[10] Catalyst **A** was first reported by List and co-workers: L. Kötzner, M. J. Webber, A. Martínez, C. De Fusco, B. List, *Angew. Chem. Int. Ed.* **2014**, *53*, 5202 – 5205; *Angew. Chem.* **2014**, *126*, 5303 – 5306.

[11] a) P. L. Kotian, Y. S. Babu, M. Wu, V. R. Chintareddy, V. S. Kumar, W. Zhang, Patent CA2941380 A1, **2015**; b) S. E. Draheim, N. J. Bach, R. D. Dillard, D. R. Berry, D. G. Carlson, N. Y. Chirgadze, D. K. Clawson, L. W. Hartley, L. M. Johnson, N. D. Jones, E. R. McKinney, E. D. Mihelich, J. L. Olkowski, R. W. Schevitz, A. C. Smith, D. W. Snyder, C. D. Sommers, J.-P. Wery, *J. Med. Chem.* **1996**, *39*, 5159 – 5175; c) A. Tafi, R. Costi, M. Botta, R. Di Santo, F. Corelli, S. Massa, A. Ciacci, F. Manetti, M. Artico, *J. Med. Chem.* **2002**, *45*, 2720 – 2732.

[12] With the standard method, unsubstituted indole reacted at the 3-position with excellent yield but moderate enantioselectivity (94 % yield, 56 % *ee*).

[13] Substrate kinetic resolution was observed ($s = 6.3$). During the progress of the reaction, the product *ee* remained constant. The absolute stereochemistry of the product is influenced by the configuration of the catalyst, but not that of the substrate. These observations are consistent with the intermediacy of aza-*p*-QM.

Manuscript received: February 22, 2017
Revised: March 1, 2017
Final Article published: ■■ ■■, ■■■■

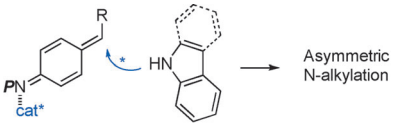
 © 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Communications

Organocatalysis

M. Chen, J. Sun* _____ ■■■■–■■■■

Catalytic Asymmetric N-Alkylation of Indoles and Carbazoles through 1,6-Conjugate Addition of Aza-*para*-quinone Methides



An organocatalytic strategy for the asymmetric N-alkylation of indoles and carbazoles was developed in which in situ generated aza-*para*-quinone methides are employed as the alkylating reagent. With the proper choice of a chiral phosphoric acid and N-protective group (***P***), the intermolecular C–N bond formation with various indole and carbazole nucleophiles proceeds under mild conditions with excellent efficiency and enantioselectivity.

 © 2017 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!