Photochemistry

DOI: 10.1002/anie.201102306

Visible-Light-Induced Oxidation/[3+2] Cycloaddition/Oxidative Aromatization Sequence: A Photocatalytic Strategy To Construct Pyrrolo[2,1-*a*]isoquinolines**

*You-Quan Zou, Liang-Qiu Lu, Liang Fu, Ning-Jie Chang, Jian Rong, Jia-Rong Chen, and Wen-Jing Xiao**

The development of new and highly efficient strategies for the rapid construction of intricate molecular architectures is of great importance and remains a preeminent goal in current synthetic chemistry.[1] Compared with traditional stepwise chemical processes, tandem reactions have proven to be extremely useful in achieving these goals owing to their high reaction efficiency, atom economy, and operational simplicity.[2] In this context, a considerable number of tandem reactions for the synthesis of complex molecular systems have been established over the past century.[2,3] However, one fundamental impediment associated with the chemical industries is the exhaustion and nonrenewal of fossil fuels. The search for clean and renewable energy[4] in the preparation of valuable synthetic building blocks and biologically important molecules has become one of the most challenging tasks in this century. In this endeavor, photocatalysis using visible light represents a unique strategy because of its inherent "green chemistry" features.[5] In 2008 a milestone was reached in the field of catalysis using visible light when two seminal publications appeared almost simultaneously: one on direct asymmetric alkylation of aldehydes,[6] and one on intramolecular formal [2+2] cycloaddition.[7] Since then, photochemical synthesis using visible light has received much attention,[8] and some fundamental chemical transformations have been elegantly carried out under irradiation with visible light.[9] Despite these advances, tandem reactions initiated by visible light remain largely unexplored, and the development of such methods for the highly efficient and practical synthesis of natural products and analogues is greatly desirable.

The vast majority of biologically active molecules and pharmaceutical compounds contain nitrogen heterocycles.[10] For example, lamellarin alkaloids, a new family of marine natural products that contain a pyrrolo[2,1-*a*]isoquinoline core, were found to exhibit a wide spectrum of biological activities (Figure 1).[11] For instance, lamellarin D, which was

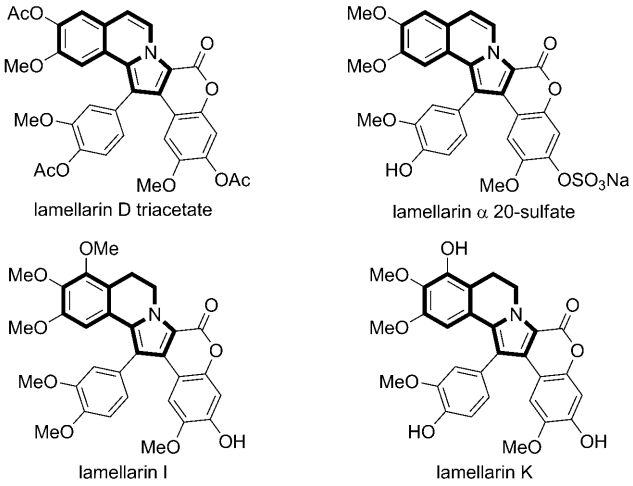


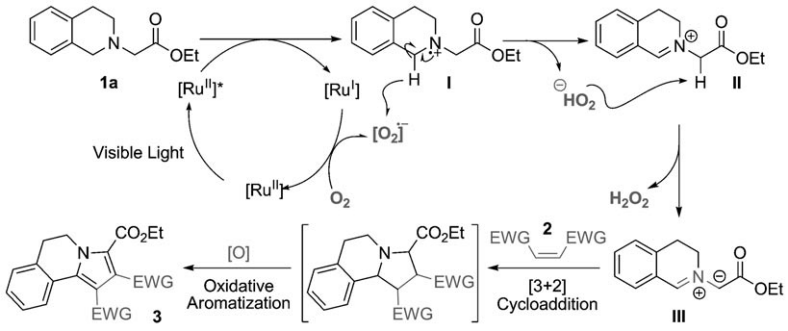
Figure 1. Representative examples of novel marine natural lamellarin alkaloids.

isolated from prosobranch mollusk *Lamellaria* sp., is a potent inhibitor of human topoisomerase I,[12] and lamellarin α 20-sulfate is a drug candidate for the inhibition of HIV integrase.[13] Other members of this family, such as lamellarin I and lamellarin K, displayed potential antitumor activities.[14] This biological activity has made the synthesis of these compounds attractive, and several straightforward and robust methods for their syntheses have been established.[15] Notably, Wang and co-workers have recently disclosed a highly efficient approach to the core structure of lamellarin by employing a copper(II)-catalyzed oxidation/[3+2] cycloaddition/aromatization cascade.[16] As part of our ongoing research program addressing carbo- and heterocycle-oriented method development,[17] we herein report a mechanistically distinct method for the construction of pyrrolo[2,1-*a*]isoquinolines using a photoredox strategy. We envisioned that ethyl 2-(3,4-dihydroisoquinolin-2(1*H*)-yl) acetate (**1a**) could be oxidized to generate the iminium ion **II** in the presence of $[Ru(bpy)_3]^{2+}$ under irradiation by visible light.[5d,e] Subsequently, the iminium intermediate **II** affords 1,3-dipole azomethine **III** by a deprotonation process; **III** then undergoes [3+2] cycloaddition reactions and sequential oxidation

[*] Y.-Q. Zou, L.-Q. Lu, L. Fu, N.-J. Chang, J. Rong, Dr. J.-R. Chen, Prof. Dr. W.-J. Xiao
Key Laboratory of Pesticide & Chemical Biology
Ministry of Education, College of Chemistry
Central China Normal University
152 Luoyu Road, Wuhan, Hubei 430079 (China)
Fax: (+86) 27-6786-2041
E-mail: wxiao@mail.ccnu.edu.cn
Homepage: http://chem-xiao.ccnu.edu.cn/default.aspx

[**] We are grateful to the National Science Foundation of China (NO.20872043, 21072069 and 21002036), the National Basic Research Program of China (2011CB808600), and the Program for Changjiang Scholars and Innovative Research Team in University (IRT0953) for support of this research.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201102306.

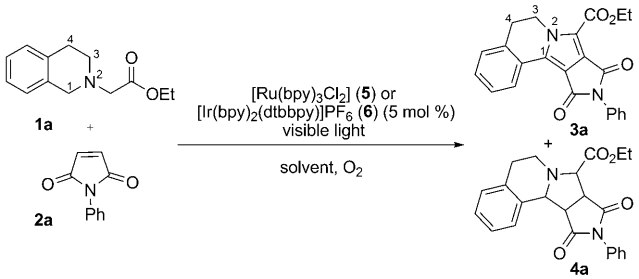


Scheme 1. Photocatalytic oxidation/cycloaddition/aromatization sequence. EWG = electron-withdrawing group.

to form the pyrrolo[2,1-*a*]isoquinoline (Scheme 1). Although the reductive quenching of the excited species $[Ru(bpy)_3]^{2+*}$ by tertiary amines has been applied in a few synthetic methods,[8,9] this strategy, to the best of our knowledge, has not been examined in a tandem reaction involving a [3+2] cycloaddition.

Our initial investigations were focused on examining the feasibility of the reaction of dihydroisoquinoline ester **1a** with *N*-phenylmaleimide (**2a**) and optimizing the reaction conditions for application to a variety of dihydroisoquinoline derivatives and electron-deficient components. To our delight, the proposed reaction between **1a** and **2a** does indeed occur in the presence of $[Ru(bpy)_3Cl_2]$ (5 mol%) and dioxygen in DMF (*N*,*N*′-dimethylformamide) under irridation by visible light to afford dihydropyrrolo[2,1-*a*]isoquinoline **3a** and hexahydropyrrolo[2,1-*a*]isoquinoline **4a** in 26% and 15% yields, respectively, upon isolation (Table 1, entry 1). Encouraged by these results, we then started to optimize the reaction conditions to improve the chemical yield. With CH_3CN as the solvent, the yield of **3a** was increased to 47%, although there was still a significant amount of **4a** formed as well (Table 1, entry 2). In order to further improve the reaction efficiency and selectivity, *N*-bromosuccinimide (1.1 equiv) was added to the crude reaction mixture when **2a** was completely consumed. Remarkably, this tandem reaction was completed within 9–10 hours and gave the corresponding product **3a** in high yield (Table 1, entries 3–5). Under the same reaction conditions, $[Ir(ppy)_2(dtbbpy)]PF_6$ can also catalyze this transformation to give an 86% yield, but with a prolonged reaction time (Table 1, entry 6). Interestingly, when the catalyst loading was reduced to 2.5 mol% or even 1 mol%, the reaction also gave comparable results (Table 1, entries 7 and 8). Notably no reaction occurred in the absence of a photocatalyst, such as visible light or oxygen, thus indicating that the photoredox catalysis is essential for this tandem process (Table 1, entries 9–11).

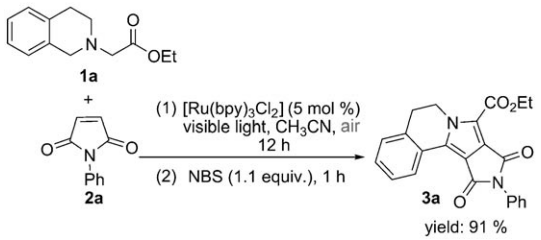
Table 1: Optimization of the reaction conditions.[a]



Entry	Catalyst	Solvent	*t* [h]	Yield [%][b] **3a**/**4a**
1	**5** (5 mol%)	DMF	72	26/15
2	**5** (5 mol%)	CH_3CN	72	47/27
3[c]	**5** (5 mol%)	CH_3CN	9	94/0
4[c]	**5** (5 mol%)	DMF	10	69/0
5[c]	**5** (5 mol%)	EtOH	10	60/0
6[c]	**6** (5 mol%)	CH_3CN	24	86/0
7[c]	**5** (2.5 mol%)	CH_3CN	13	90/0
8[c]	**5** (1 mol%)	CH_3CN	13	90/0
9[d]	**5** (5 mol%)	CH_3CN	72	0/0
10[e]	–	CH_3CN	72	0/0
11[f]	**5** (5 mol%)	CH_3CN	72	0/0

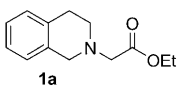
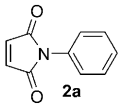
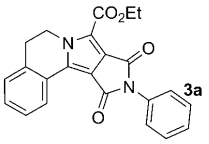
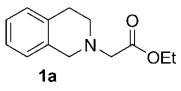
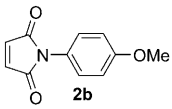
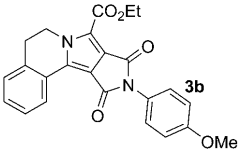
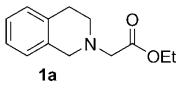
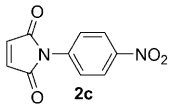
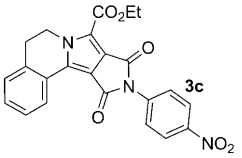
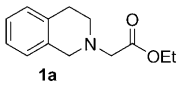
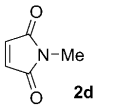
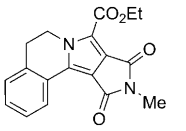
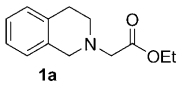
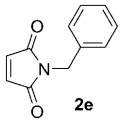
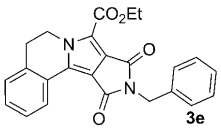
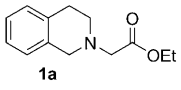
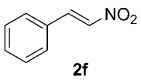
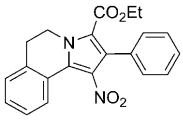
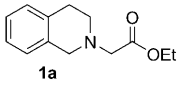
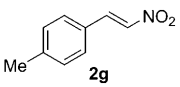
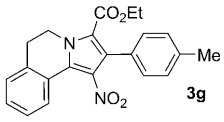
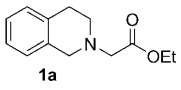
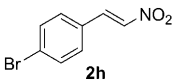
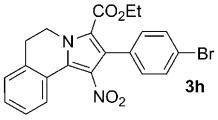
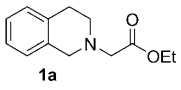
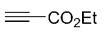
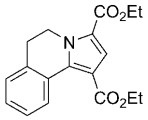
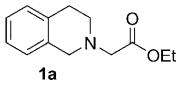
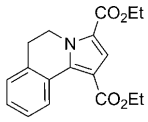
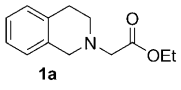
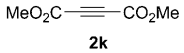
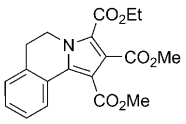
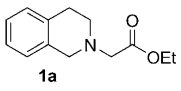
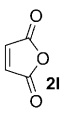
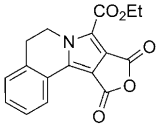
[a] Reaction conditions: **1a** (0.36 mmol), **2a** (0.20 mmol), catalyst **5** or **6** (1–5 mol%), O_2 balloon, visible-light irradiation, and solvent (3.0 mL). [b] Yield of the isolated product. [c] NBS (1.1 equiv) was added to the reaction mixture when **2a** was completely consumed, and stirring continued for another 1 h. [d] Reaction was carried out in the dark. [e] Reaction was carried out without catalyst. [f] Reaction mixture was degassed and the reaction was carried out under an inert atmosphere. bpy = 2,2′-bipyridine, dtbbpy = 4,4′-di-tert-butyl-2,2′-bipyridine, NBS = *N*-bromosuccinimide.

With the optimal reaction conditions established, we then examined the substrate scope of this tandem reaction. As highlighted in Table 2, a variety of N-substituted maleimides **2a**–**2e** can react efficiently with **1a** to give the corresponding products in good to excellent yields upon isolation (Table 2, entries 1–5). The reaction appears quite general with respect to the dipolarophile components. It was found that the reaction proceeded smoothly with nitroolefins **2f**–**2h** bearing electron-neutral, electron-donating, and electron-withdrawing groups on the aromatic ring and the corresponding products were obtained in 53–64% yields (Table 2, entries 6–8). More importantly, other dipolarophiles, such as activated alkynes, acrylates, and maleic anhydrides, reacted smoothly even without the addition of NBS (Table 2, entries 9–11). Notably, this tandem reaction exhibited excellent regioselectivity and only one regioisomer was formed in the reaction of **1a** and the unsymmetrical dipolarphiles (e.g. **2h**, **2i**, etc.). The structures of products **3h** and **3i** were unambiguously established by X-ray crystallographic analysis.[18,19]



Scheme 2. Reaction system was open to air.

Table 2: Oxidation/[3+2] cycloaddition/aromatization sequence.[a]

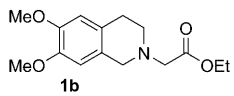
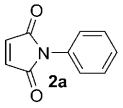
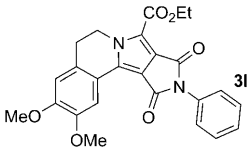
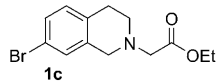
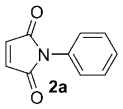
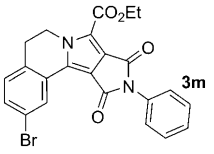
Entry	Dihydroisoquinoline esters **1**	Dipolarophile **2**	Product **3**	*t* [h]	Yield[b] [%]
1	 **1a**	 **2a**	 **3a**	12	94
2	 **1a**	 **2b**	 **3b**	12.5	81
3	 **1a**	 **2c**	 **3c**	12.5	68
4	 **1a**	 **2d**	 **3d**	11	94
5	 **1a**	 **2e**	 **3e**	11	76
6	 **1a**	 **2f**	 **3f**	15	64(16)[c]
7	 **1a**	 **2g**	 **3g**	12	62(13)[c]
8	 **1a**	 **2h**	 **3h**	12	53(11)[c]
9[d]	 **1a**	 **2i**	 **3i**	24	52
10[d]	 **1a**	 **2j**	 **3i**	24	52
11[d]	 **1a**	 **2k**	 **3j**	22	65
12	 **1a**	 **2l**	 **3k**	25	51

Structural variation in dihydroisoquinoline esters can also be realized without loss in reaction efficiency. Incorporation of two methoxy substituents at the C6- and C7-positions in the dihydroisoquinoline, and a bromo group at the C7-position reveals that electronic modification of the substrate can be accomplished (Table 2, entries 13 and 14). Importantly, the photocatalytic system also works well when the oxygen is replaced by air (Scheme 2).

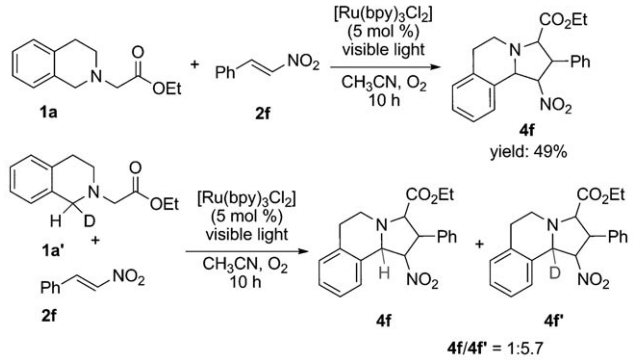
Notably the cycloadduct **4f** was isolated when nitroolefins were employed as dipolarphiles (Scheme 3). The formation of **4a** (Table 1, entries 1 and 2) and **4f** revealed that this tandem reaction proceeds through [3+2] cycloaddition with a subsequent oxidative aromatization. To get more insight into the mechanism of the present transformation (Scheme 1), the kinetic isotopic effect (KIE) was investigated by the reaction of deuterated ethyl 2-(3,4-dihydroisoquinolin-2(1*H*)-yl) acetate (**1a′**) with nitrostyrene (**2f**; Scheme 2).[19] Results showed that the abstraction of a hydrogen in the α position of the radical cation **I** by the superoxide radical anion is 5.7 times faster than the abstraction of deuterium; this result revealed that this process might play an important role in the current visible-light-induced reaction. A precise reaction mechanism awaits further study.

In conclusion, we have developed a photocatalytic tandem oxidation/[3+2] cycloaddition/oxidative aromatization sequence using visible light. This novel protocol provides a rapid and efficient access to biologically important pyrrolo[2,1-*a*]isoquinolines in a highly concise fashion. The application of this powerful strategy to the synthesis of natural products, lamellarin I and K, and more detailed mechanistic investigations are currently underway in our laboratory.

Table 2: (Continued)

Entry	Dihydroisoquinoline esters **1**	Dipolarophile **2**	Product **3**	*t* [h]	Yield[b] [%]
13	 **1b**	 **2a**	 **3l**	24	93
14	 **1c**	 **2a**	 **3m**	15	89

[a] Reaction conditions: **1a** (0.36 mmol), **2a** (0.20 mmol), catalyst **5** (5 mol%), O_2 balloon, visible-light irridation, and CH_3CN (3.0 mL). [b] Yield of the isolated product. [c] Yield of the oxidation products of **3** (oxidized at the C3- and C4-positions)[20] is in parentheses. [d] Without NBS.



Scheme 3. Mechanistic studies.

Experimental Section

Representative procedure: *N*-Phenylmaleimide (**2a**; 0.30 mmol) was added to a mixture of ethyl 2-(3,4-dihydroisoquinolin-2(1*H*)-yl) acetate (**1a**; 0.36 mmol) and $[Ru(bpy)_3Cl_2]$ (**5**; 0.015 mmol) in CH_3CN (3.0 mL) under an oxygen atmosphere. The solution was stirred at room temperature under irridation by visible light (distance app. 10 cm). After **2a** was completely consumed (monitored by TLC), the light source was removed and *N*-bromosuccinimide (1.1 equiv) was added to the reaction mixture. The resulting mixture was stirred for another 1 h. The crude mixture was concentrated under reduced pressure and then purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 10:1) to furnish the desired compound **3a**.

Received: April 3, 2011
Published online: June 22, 2011

Keywords: alkaloids · oxygen · photochemistry · tandem reactions · visible light

[1] For selected references, see: a) P. A. Wender, B. L. Miller, *Org. Synth. Theory Appl.* **1993**, *2*, 27; b) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695; c) L. F. Tietze, F. Haunert, *Stimulating Concepts in Chemistry*, Wiley-Interscience, New York, **2000**; d) H. Jiang, P. Elsner, K. L. Jensen, A. Falcicchio, V. Marcos, K. A. Jørgensen, *Angew. Chem.* **2009**, *121*, 6976; *Angew. Chem. Int. Ed.* **2009**, *48*, 6844; e) A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208; f) A. Deagostino, C. Prandi, S. Tabasso, P. Venturello, *Molecules* **2010**, *15*, 2667; g) N. T. Jui, E. C. Y. Lee, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2010**, *132*, 10015; h) A. Quintard, A. Alexakis, C. Mazet, *Angew. Chem.* **2011**, *123*, 2402; *Angew. Chem. Int. Ed.* **2011**, *50*, 2354.

[2] For selected reviews on tandem reactions, see: a) D. E. Fogg, E. N. dos Santos, *Coord. Chem. Rev.* **2004**, *248*, 2365; b) A. Ajamian, J. L. Gleason, *Angew. Chem.* **2004**, *116*, 3842; *Angew. Chem. Int. Ed.* **2004**, *43*, 3754; c) L. F. Tietze, N. Rackelmann, *Pure Appl. Chem.* **2004**, *76*, 1967; d) P. de Meijere, A. von Zezschwitz, S. Bräse, *Acc. Chem. Res.* **2005**, *38*, 413; e) J. C. Wasilke, S. J. Obrey, R. T. Baker, G. C. Bazan, *Chem. Rev.* **2005**, *105*, 1001; f) K. C. Nicolaou, D. J. Edmonds, P. G. Bulger, *Angew. Chem.* **2006**, *118*, 7292; *Angew. Chem. Int. Ed.* **2006**, *45*, 7134; g) S. Arns, L. Barriault, *Chem. Commun.* **2007**, 2211; h) B. B. Touré, D. G. Hall, *Chem. Rev.* **2009**, *109*, 4439; i) K. C. Nicolaou, J. S. Chen, *Chem. Soc. Rev.* **2009**, *38*, 2993; j) L. F. Tietze, G. Brasche, K. M. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-Interscience, New York, **2006**.

[3] For some of the most recent examples, see: a) 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; b) G. Chai, S. Wu, C. Fu, S. Ma, *J. Am. Chem. Soc.* **2011**, *133*, 3740; c) D. Belmessieri, L. C. Morrill, C. Simal, A. M. Z. Slawin, A. D. Smith, *J. Am. Chem. Soc.* **2011**, *133*, 2714; d) Y. Li, X. Xu, J. Tan, C. Xia, D. Zhang, Q. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 1775; e) K. Saito, H. Sogou, T. Suga, H. Kusama, N. Iwasawa, *J. Am. Chem. Soc.* **2011**, *133*, 689; f) T. Achard, A. Lepronier, Y. Gimbert, H. Clavier, L. Giordano, A. Tenaglia, G. Buono, *Angew. Chem.* **2011**, *123*, 3614; *Angew. Chem. Int. Ed.* **2011**, *50*, 3552; g) S. Yasuhara, M. Sasa, T. Kusakabe, H. Takayama, M. Kimura, T. Mochida, K. Kato, *Angew. Chem.* **2011**, *123*, 3998; *Angew. Chem. Int. Ed.* **2011**, *50*, 3912; h) D. Shu, X. Li, M. Zhang, P. J. Robichaux, W. Tang, *Angew. Chem.* **2011**, *123*, 1382; *Angew. Chem. Int. Ed.* **2011**, *50*, 1346.

[4] G. Ciamician, *Science* **1912**, *36*, 385.

[5] For pioneering works, see: a) H. Cano-Yelo, A. Deronzier, *J. Chem. Soc. Perkin Trans. 2* **1984**, 1093; b) H. Cano-Yelo, A. Deronzier, *Tetrahedron Lett.* **1984**, *25*, 5517; c) J.-M. Zen, S.-L. Liou, A. S. Kumar, M.-S. Hsia, *Angew. Chem.* **2003**, *115*, 597; *Angew. Chem. Int. Ed.* **2003**, *42*, 577. For selected reviews, see: d) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102; e) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, *2*, 527; f) K. Zeitler, *Angew. Chem.* **2009**, *121*, 9969; *Angew. Chem. Int. Ed.* **2009**, *48*, 9785; g) D. Gust, T. A. Moore, *Acc. Chem. Res.* **1993**, *26*, 198.

[6] D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77.

[7] M. A. Ischay, M. E. Anzovino, J. Du, T. P. Yoon, *J. Am. Chem. Soc.* **2008**, *130*, 12886.

[8] For examples, see: a) Y. Su, L. Zhang, N. Jiao, *Org. Lett.* **2011**, *13*, 2168; b) Z. Lu, M. Shen, T. P. Yoon, *J. Am. Chem. Soc.* **2011**, *133*, 1162; c) M. Neumann, S. Fuldner, B. Konig, K. Zeitler, *Angew. Chem.* **2011**, *123*, 981; *Angew. Chem. Int. Ed.* **2011**, *50*, 951; d) H.-W. Shih, M. N. Vander Wal, R. L. Grange, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2010**, *132*, 13600; e) R. S. Andrews, J. J. Becker, M. R. Gagne, *Angew. Chem.* **2010**, *122*, 7432; *Angew. Chem. Int.*

Ed. **2010**, *49*, 7274; f) L. Furst, B. S. Matsuura, J. M. R. Narayanam, J. W. Tucker, C. R. J. Stephenson, *Org. Lett.* **2010**, *12*, 3104; g) J. W. Tucker, J. D. Nguyen, J. M. R. Narayanam, S. W. Krabbe, C. R. J. Stephenson, *Chem. Commun.* **2010**, *46*, 4985; h) A. G. Condie, J. C. Gonzalez-Gomez, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2010**, *132*, 1464; i) J. W. Tucker, J. M. R. Narayanam, S. W. Krabbe, C. R. J. Stephenson, *Org. Lett.* **2010**, *12*, 368; j) J. M. R. Narayanam, J. W. Tucker, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2009**, *131*, 8756; k) D. A. Nagib, M. E. Scott, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 10875.

[9] a) C. Dai, J. M. R. Narayanam, C. R. J. Stephenson, *Nat. Chem.* **2011**, *3*, 140; b) F. Su, S. C. Mathew, G. Lipner, X. Fu, M. Antonietti, S. Blechert, X. Wang, *J. Am. Chem. Soc.* **2010**, *132*, 16299; c) M. Rueping, C. Vila, R. M. Koenigs, K. Poscharny, D. C. Fabry, *Chem. Commun.* **2011**, *47*, 2360; d) F. Su, S. C. Mathew, L. Mohlmann, M. Antonietti, X. Wang, S. Blechert, *Angew. Chem.* **2011**, *123*, 683; *Angew. Chem. Int. Ed.* **2011**, *50*, 657.

[10] a) T. Eicher, S. Hauptmann, *The Chemistry of Heterocycles*, Wiley-VCH, Weinheim, **2003**; b) J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, *Org. Biomol. Chem.* **2006**, *4*, 2337.

[11] For recent reviews on lamellarins and related alkaloids, see: a) C. Bailly, *Curr. Med. Chem. Anti-Cancer Agents* **2004**, *4*, 363; b) S. T. Handy, Y. Zhang, *Org. Prep. Proced. Int.* **2005**, *37*, 411; c) H. Fan, J. Peng, M. T. Hamann, J. F. Hu, *Chem. Rev.* **2008**, *108*, 264; d) D. Pla, F. Albericio, M. Alvarez, *Anti-Cancer Agents Med. Chem.* **2008**, *8*, 746.

[12] E. Marco, W. Laine, C. Tardy, A. Lansiaux, M. Iwao, F. Ishibashi, C. Bailly, F. Gago, *J. Med. Chem.* **2005**, *48*, 3796.

[13] a) M. V. R. Reddy, M. R. Rao, D. Rhodes, M. S. T. Hansen, K. Rubins, F. D. Bushman, Y. Venkateswarlu, D. J. Faulkner, *J. Med. Chem.* **1999**, *42*, 1901; b) A. Aubry, X-S. Pan, L. M. Fisher, V. Jarlier, E. Cambau, *Antimicrob. Agents Chemother.* **2004**, *48*, 1281.

[14] a) S. Malla Reddy, M. Srinivasulu, N. Satyanarayana, A. K. Kondapi, Y. Venkateswarlu, *Tetrahedron* **2005**, *61*, 9242; b) A. R. Quesada, M. D. G. Gravalos, J. L. F. Puentes, *Br. J. Cancer* **1996**, *74*, 677.

[15] For representative examples, see: a) A. Heim, A. Terpin, W. Steglich, *Angew. Chem.* **1997**, *109*, 158; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 155; b) P. Ploypradith, C. Mahidol, P. Sahakitpichan, S. Wongbundit, S. Ruchirawat, *Angew. Chem.* **2004**, *116*, 884; *Angew. Chem. Int. Ed.* **2004**, *43*, 866; c) T. Ohta, T. Fukuda, F. Ishibashi, M. Iwao, *J. Org. Chem.* **2009**, *74*, 8143.

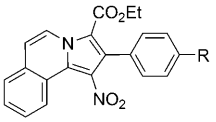
[16] During the preparation of this manuscript, Wang and co-workers reported a nice route to pyrrolo[2,1-a]isoquinolines. See: C. Yu, Y. Zhang, S. Zhang, H. Li, W. Wang, *Chem. Commun.* **2011**, *47*, 1036.

[17] a) J.-R. Chen, C.-F. Li, X.-L. An, J.-J. Zhang, X.-Y. Zhu, W.-J. Xiao, *Angew. Chem.* **2008**, *120*, 2523; *Angew. Chem. Int. Ed.* **2008**, *47*, 2489; b) L.-Q. Lu, Y.-J. Cao, X.-P. Liu, J. An, C.-J. Yao, Z.-H. Ming, W.-J. Xiao, *J. Am. Chem. Soc.* **2008**, *130*, 6946; c) L.-Q. Lu, F. Li, J. An, J.-J. Zhang, X.-L. An, Q.-L. Hua, W.-J. Xiao, *Angew. Chem.* **2009**, *121*, 9706; *Angew. Chem. Int. Ed.* **2009**, *48*, 9542; d) L.-Q. Lu, J.-J. Zhang, F. Li, Y. Cheng, J. An, J.-R. Chen, W.-J. Xiao, *Angew. Chem.* **2010**, *122*, 4597; *Angew. Chem. Int. Ed.* **2010**, *49*, 4495; e) X.-F. Wang, Q.-L. Hua, Y. Cheng, X.-L. An, Q.-Q. Yang, J.-R. Chen, W.-J. Xiao, *Angew. Chem.* **2010**, *122*, 8557; *Angew. Chem. Int. Ed.* **2010**, *49*, 8379.

[18] CCDC 822857 (**3h**) and CCDC 823097 (**3i**) 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.

[19] See the Supporting Information for details.

[20] Structures of the oxidation products of **3f**–**3h**:



3f': R = H
3g': R = Me
3h': R = Br

