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Metal-free synthesis of polycyclic quinazolinones enabled by a $(NH_4)_2S_2O_8$-promoted intramolecular oxidative cyclization

Lijuan Xie, Cong Lu, Dong Jing, Xinrui Ou, and Ke Zheng*

Dedication ((optional))

Abstract: An efficient metal-free, $(NH_4)_2S_2O_8$ mediated intramolecular oxidative cyclization for the construction of polycyclic heterocycles was disclosed. A series of polycyclic quinazolinone derivatives with good functional group tolerance were obtained in high yields. The natural products tryptanthrin and rutaecarpine, as well as their derivatives, were easily synthesized by this strategy. A preliminary mechanism study suggested the carbon-centered radical was involved in the catalytic cycle.

Introduction

The quinazolinone is an attractive scaffold that widely exists in many pharmaceutical relevant natural products and assigned as privileged structure in medicinal chemistry (Figure 1).[1-2] Hundreds of natural alkaloids containing the quinazolinone core have been found and many of them play a significant role in drug discovery for their versatile biological activities, such as antibacterial, antifungal, antiviral, antimalarial, and antiparkinsonian.[2-3] Over the past decades, the synthesis of these privileged scaffolds has attracted a lot of interest for both synthetic and medicinal chemists owing to their important applications, and a variety of methods have been developed.[4] The traditional synthetic routes to quinazolinone compounds are based on 2-aminobenzoic acids or their derivatives as starting materials.[5] Typically, 2-aminobenzamides react with one-carbon reagents, such as aldehydes, aromatic alcohols, toluene, tertiary amines and methyl radical sources, to form the iminium intermediates, followed by the intramolecular nucleophilic addition to construct quinazolinone framework is one of the most common methods (Scheme 1-A1).[6-8] The Ullmann-type cascade reactions by using 2-halobenzamides or 2-halobenzoic

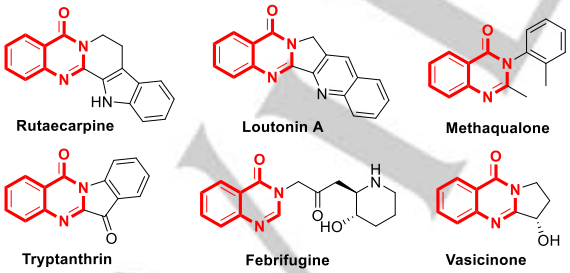
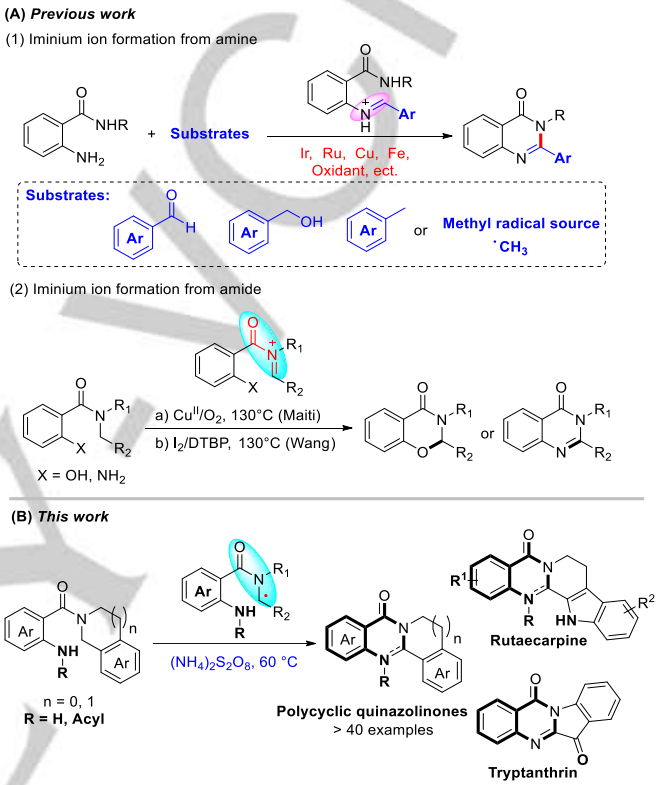


Figure 1. Natural products and drug molecules containing quinazolinone.



Scheme 1. Pathways to synthesize quinazolinones.

acids as the starting materials also have been proven highly efficient for the synthesis of quinazolinones by Fu and other research groups.[9] Compared to the amine, the formation of iminium ion from amide is more challenging and still far less studied due to its delocalization of the nitrogen lone pair to the carbonyl oxygen of amide.[10a] Recently, the Cu^{II}/O$_2$ and I$_2$/DTBP catalysis were demonstrated as efficient systems for the intramolecular C-O or C-N cross dehydrogenative coupling via amide iminium intermediates to synthesize benzoxazinones and quinazolinones under high temperature (130 °C) by the Maiti group and the Wang group, respectively (Scheme 1-A2).[10] Despite significant advances that have been made in this field, the method for the synthesis of fused polycyclic quinazolinone derivatives is rare, especially in a metal-free fashion.[11] Herein, we developed a metal-free, $(NH_4)_2S_2O_8$ mediated C-H/N-H cross dehydrogenative coupling via amide iminium intermediate under mild condition, providing an efficient and facile approach to synthesize a series of polycyclic quinazolinone derivatives (>40 examples), as well as the natural products tryptanthrin, rutaecarpine and their analogues (Scheme 1B).

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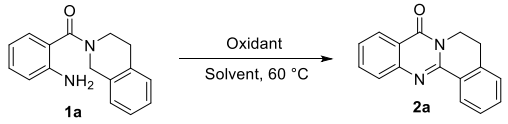
Results and Discussion

Initially, the 2-aminobenzamide **1a** was selected as the model substrate for the optimization studies. As shown in Table 1, the reaction proceeded smoothly when using 2.0 equiv of $K_2S_2O_8$ as the oxidant in DMSO at 60 °C, furnished the quinazolinone product **2a** in 30% yield (Table 1, entry 1). The yield was further improved, when $Na_2S_2O_8$ or $(NH_4)_2S_2O_8$ was used as oxidant and the $(NH_4)_2S_2O_8$ gave the best result (77% yield, entries 2-3). Other oxidants such as DDQ and DTBP were also explored and no target product was formed (entries 4-5). The solvents had a great influence on the reaction, and the DMSO had been indentified as optimal for the reaction (entries 6-10). The yield of **2a** decreased to 55% when reducing the amount of $(NH_4)_2S_2O_8$ to 1.0 equiv (entry 11). Finally, we found that the best result was obtianed by using 4.0 equiv of $(NH_4)_2S_2O_8$ as the oxidant at 60 °C for 2.5 h, furnishing the product **2a** in 92% yield (entries 12-13).

Table 1. Optimization of reaction conditions.[a]

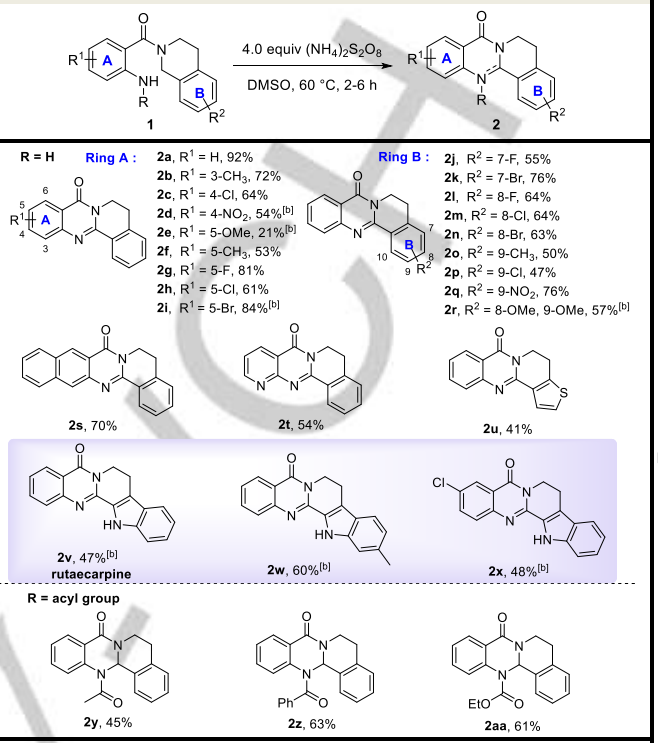


Entry	Oxidant	Solvent	Yield (%)[b]
1	$K_2S_2O_8$ (2.0 equiv)	DMSO	30
2	$Na_2S_2O_8$ (2.0 equiv)	DMSO	70
3	$(NH_4)_2S_2O_8$ (2.0 equiv)	DMSO	77
4	DDQ (2.0 equiv)[c]	DMSO	NR
5	TBHP (2.0 equiv)[c]	DMSO	NR
6	$(NH_4)_2S_2O_8$ (2.0 equiv)	CH_3CN	27
7	$(NH_4)_2S_2O_8$ (2.0 equiv)	DCE	20
8	$(NH_4)_2S_2O_8$ (2.0 equiv)	Dioxane	NR
9	$(NH_4)_2S_2O_8$ (2.0 equiv)	DMF	11
10	$(NH_4)_2S_2O_8$ (2.0 equiv)	Toluene	20
11	$(NH_4)_2S_2O_8$ (1.0 equiv)	DMSO	55
12	$(NH_4)_2S_2O_8$ (3.0 equiv)	DMSO	86
13	**$(NH_4)_2S_2O_8$ (4.0 equiv)**	**DMSO**	**92**

[a] **1a** (0.05 mmol), solvent (1.0 mL), under an air atmosphere. [b] Isolated yield. [c] DDQ: 2,3-Dichloro-5,6-Dicyano-1,4-Benzoquinone, TBHP: Tert-Butyl Hydroperoxide. NR = no reaction.

Based on the optimal conditions, the substrates scope of the reaction was investigated. As shown in Table 2, this method exhibited excellent functional group tolerance, and a wide range of 2-aminobenzamides were compatible in the reaction, yielding the polycyclic quinazolinone derivatives in good to high yields (up to 92% yield, **2a**-**2aa**). Both the electron-withdrawing and electron-donating substituents at different positions of benzene ring A furnished the desired products **2b**-**2i** in good yields, while the 5-OMe substrate **1e** gave a low yield. Similarly, benzene ring B of the tetrahydroisoquinoline moiety bearing various electronic properties at different positions also be successfully applied to the reaction, leading to the corresponding products **2j**-**2r** in good yields. The 2-aminonaphthamide furnished the product **2s** in high yield (70% yield, Table 2). In addition, the heterocyclic

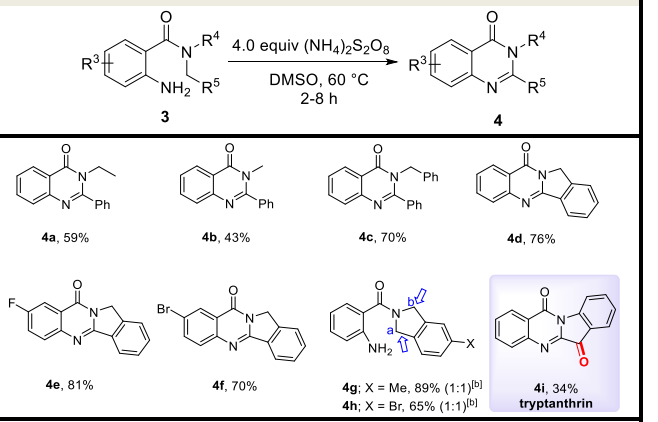
Table 2. Scope for the synthesis of quinazolinone derivatives. [a]



[a] **1** (0.05 mmol), 4.0 equiv $(NH_4)_2S_2O_8$, solvent (1.0 mL), under an air atmosphere. Isolated yield. [b] 2.0 equiv $(NH_4)_2S_2O_8$.

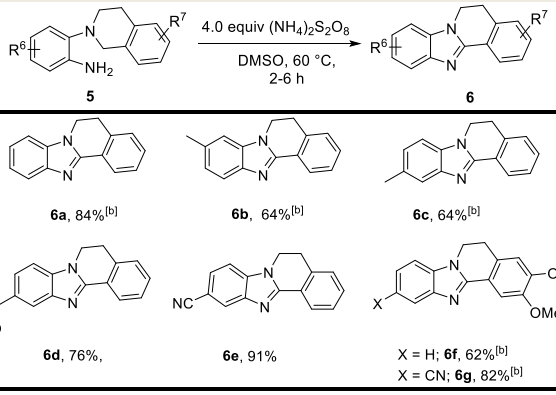
substrates were also tolerable in the reaction, affording the desired polycyclic quinazolinones **2t** and **2u** in 54% and 41% yields, respectively. Notably, the natural product rutaecarpine **2v** and its analogues (**2w**-**2x**) were achieved in 47-60% yields under the optimal conditions, which provided an efficient and facile approach to construct rutaecarpine analogues. More significantly, this method can be applied to the synthesis of *N*-substituted quinazolinones, which represent new chemical entities and never been achieved before, demonstrating the generality of this method (**2y**-**2aa**, Table 2). Next, we further

Table 3. Scope for the synthesis of quinazolinone derivatives. [a]



[a] **3** (0.05 mmol), 4.0 equiv $(NH_4)_2S_2O_8$, solvent (1.0 mL), under an air atmosphere. Isolated yield. [b] Isolated combined yields. Isomer ratios were determined by analysis of the ^1H NMR spectra of isolated products.

Table 4. Scope for the synthesis of imidazole compounds. [a]

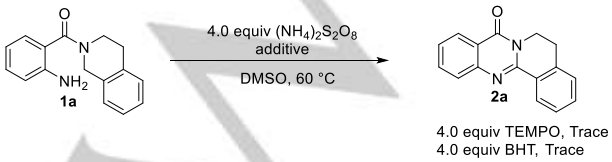


[a] **5** (0.05 mmol), 4.0 equiv $(NH_4)_2S_2O_8$, solvent (1.0 mL), under an air atmosphere. Isolated yield. [b] 2.0 equiv $(NH_4)_2S_2O_8$.

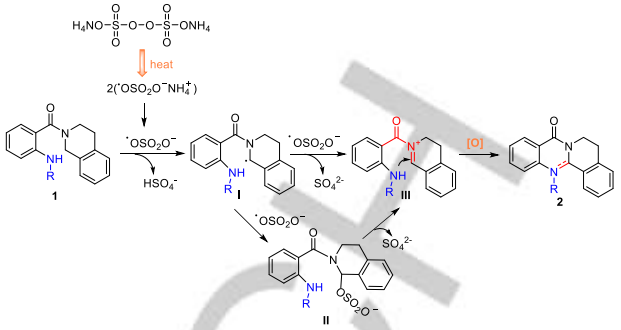
applied this system to the cyclization of 2-amino-*N*-benzylbenzamides, furnished the corresponding products **4a**-**4c** in moderate yields (Table 3). To our delight, it was found that the cyclization of the isoindoline derivatives was also tolerated, providing the desired products in high yields (65-89% yields, **4d**-**4h**). To our surprise, the natural product tryptanthrin **4i** was observed in moderate yield by the sequentially oxidation of cyclization product under the optimal conditions (Table 3).

Furthermore, this method could be further extended to the synthesis of polycyclic benzimidazole derivatives by using 2-(3,4-dihydroisoquinolin-2(1H)-yl)aniline **5** as the substrates. As shown in Table 4, the corresponding tetracyclic imidazole products **6a**-**6g** were observed in good to high yields (62-91% yields) under the optimal conditions, offering further synthetic utility of this method.

To identify the mechanism of this reaction, control experiments were performed (Scheme 2). When 4.0 equiv of TEMPO (2,2,6,6-tetramethylpiperidin-1-oxy) or BHT (2,6-*di*-tert-butyl-4-methylphenol) was added under the standard condition, only trace amount of product **2a** was obtained. These results suggested that the radical intermediates were involved in the catalytic cycle. Similar result was observed under N_2 atmosphere compared to that performed under air conditions, indicating that the O_2 was not necessary for this transformation. Based on these experimental results and literature precedences,[12] a proposed mechanism involving an intramolecular nucleophilic addition of amide iminium ion was depicted in Scheme 3. First, the homolysis of $S_2O_8^{2-}$ leads to the formation of $SO_4^{\cdot-}$ radical anion under thermolysis. Then the carbon-centered radical intermediate **I** was generated from the 2-aminobenzamide **1** by single-electron-transfer (SET) of $SO_4^{\cdot-}$



Scheme 2. Control experiments.



Scheme 3. Proposed mechanism.

radical anion. Sequentially, further oxidation of intermediate **I** by $SO_4^{\cdot-}$ radical anion could generate an amide iminium intermediate **III**. Finally, an intramolecular nucleophilic addition of intermediate **III**, followed by further oxidation gave the final product **2** and acyl substituents when employed did not need the further oxidation. In a competitive pathway, the recombination of the radical intermediate **I** and $SO_4^{\cdot-}$ radical anion could generate the sulfate intermediate **II**, followed by the formation of intermediate **III**, which can easily transform to quinazolinone product **2**.

Conclusions

In conclusion, we have developed a simple, metal-free protocol for the intramolecular dehydrogenative C-H/N-H cross-coupling reactions under mild condition. This method offered an efficient way to construct the fused polycyclic quinazolinone derivatives. The synthetic utility of this method was further demonstrated by the synthesis of the natural products tryptanthrin, rutaecarpine and their analogues. Preliminary mechanism studies suggested that the carbon-centered radical and amide iminium ion were the key intermediates in the catalytic cycle. The biological activity test of these polycyclic quinazolinone derivatives and further application of this strategy is ongoing in our laboratory.

Experimental Section

The oven-dried Schlenk tube (10 mL) containing a stirring bar was charged with 0.05 mmol **1a** and 0.2 mmol $(NH_4)_2S_2O_8$, 1.0 mL DMSO, and heated to 60 °C for 2-6 h. After the reaction was completed, the product was directly purified by column chromatography (PE/EA) to afford the desired products.

Acknowledgments

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Conflict of interest

The authors declare no conflict of interest.

Keywords: quinazolinones • metal-free • carbon radical • tryptanthrin • rutaecarpine

[1] a) D. He, M. Wang, S. Zhao, Y. Shu, H. Zeng, C. Xiao, C. Lu, Y. Liu, *Fitoterapia* **2017**, *119*, 136-149; b) A. Hameed, M. Al-Rashida, M. Uroos, S. A. Ali, Arshia, M. Ishtiaq, K. M. Khan, *Expert Opin. Ther. Pat.* **2018**, *28*, 281-297; c) S. Yin, L. Zhou, J. Lin, L. Xue, C. Zhang, *Eur. J. Med. Chem.* **2015**, *101*, 462-475; d) A. M. Alafeefy, A. E. Ashour, O. Prasad, L. Sinha, S. Pathak, F. A. Alasmari, A. K. Rishi, H. A. Abdel-Aziz, *Eur. J. Med. Chem.* **2015**, *92*, 191-201.

[2] a) E. Jafari, M. R. Khajouei, F. Hassanzadeh, G. H. Hakimelahi, G. A. Khodarahmi, *Res. Pharm. Sci.* **2016**, *11*, 1-14; b) S. B. Mhaske, N. P. Argade, *Tetrahedron* **2006**, *62*, 9787-9826.

[3] a) J. B. Koepfli, J. F. Mead, J. A. Brockman, *J. Am. Chem. Soc.* **1947**, *69*, 1837-1837; b) J. B. Koepfli, J. F. Mead, J. A. Brockman, *J. Am. Chem. Soc.* **1949**, *71*, 1048-1054; c) X. Wang, M. Wang, J. Yan, M. Chen, A. Wang, Y. Mei, W. Si, C. Yang, *ChemistrySelect* **2018**, *3*, 10663-10669; d) S. I. Kim, S. H. Lee, E. S. Lee, C. S. Lee, Y. Jahng, *Arch. Pharm. Res.* **2012**, *35*, 785-789.

[4] a) I. M. Abdou, S. S. Al-Neyadi, *Heterocycl. Commun.* **2015**, *21*, 115-132; b) D. J. Connolly, D. Cusack, T. P. O'Sullivan, P. J. Guiry, *Tetrahedron* **2005**, *61*, 10153-10202; c) L. He, H. Li, J. Chen, X.-F. Wu, *RSC Adv.* **2014**, *4*, 12065-12077; d) I. Khan, A. Ibrar, N. Abbas, A. Saeed, *Eur. J. Med. Chem.* **2014**, *76*, 193-244; e) I. Khan, S. Zaib, S. Batool, N. Abbas, Z. Ashraf, J. Iqbal, A. Saeed, *Bioorg. Med. Chem.* **2016**, *24*, 2361-2381; f) R. S. Rohokale, U. A. Kshirsagar, *Synthesis* **2016**, *48*, 1253-1268; g) T. M. M. Maiden, J. P. A. Harrity, *Org. Biomol. Chem.* **2016**, *14*, 8014-8025.

[5] a) T. Abe, K. Kida, K. Yamada, *Chem. Commun.* **2017**, *53*, 4362-4365; b) Y. Yang, C. Zhu, M. Zhang, S. Huang, J. Lin, X. Pan, W. Su, *Chem. Commun.* **2016**, *52*, 12869-12872; c) M. Dabiri, P. Salehi, M. Bahramnejad, M. Alizadeh, *Monatsh Chem.* **2010**, *141*, 877-881; d) F. Ji, M. F. Lv, W. B. Yi, C. Cai, *Org. Biomol. Chem.* **2014**, *12*, 5766-5772; e) F. C. Jia, Z. W. Zhou, C. Xu, Y. D. Wu, A. X. Wu, *Org. Lett.* **2016**, *18*, 2942-2945; f) W. Phakhodee, S. Wangngae, M. Pattarawarapan, *J. Org. Chem.* **2017**, *82*, 8058-8066; g) K. R. Rao, A. Raghunadh, R. Mekala, S. B. Meruva, T. V. Pratap, T. Krishna, D. Kalita, E. Laxminarayana, B. Prasad, M. Pal, *Tetrahedron Lett.* **2014**, *55*, 6004-6006.

[6] a) C. Zhang, C. K. De, R. Mal, D. Seidel, *J. Am. Chem. Soc.* **2008**, *130*, 416-417; b) M. Rueping, A. P. Antonchick, E. Sugiono, K. Grenader, *Angew. Chem. Int. Ed.* **2009**, *48*, 908-910; *Angew. Chem.* **2009**, *121*, 925-927; c) H. R. Safaei, M. Shekouhy, S. Khademi, V. Rahmanian, M. Safaei, *J. Ind. Eng. Chem.* **2014**, *20*, 3019-3024; d) W. Yu, X. Zhang, B. Qin, Q. Wang, X. Ren, X. He, *Green Chem.* **2018**, *20*, 2449-2454; e) R. Cheng, L. Tang, T. Guo, D. Zhang-Negrerie, Y. Du, K. Zhao, *RSC Adv.* **2014**, *4*, 26434-26438; f) S. R. Vemula, D. Kumar, G. R. Cook, *Tetrahedron Lett.* **2018**, *59*, 3801-3805.

[7] a) J. Zhou, J. Fang, *J. Org. Chem.* **2011**, *76*, 7730-7736; b) H. Hikawa, Y. Ino, H. Suzuki, Y. Yokoyama, *J. Org. Chem.* **2012**, *77*, 7046-7051; c*)* A. J. A Watson, A. C. Maxwell, J. M. J. Williams, *Org. Biomol. Chem.* **2012**, *10*, 240-243; d) W. Ge, X. Zhu, Y. Wei, *RSC Adv.* **2013**, *3*, 10817-10822; e) H. Wang, X. Cao, F. Xiao, S. Liu, G.-J. Deng, *Org. Lett.* **2013**, *15*, 4900-4903; f) M. Sharif, J. Opalach, P. Langer, M. Beller, X.-F. Wu, *RSC Adv.* **2014**, *4*, 8-17; g) S. M. A. H. Siddiki, K. Kon, A. S. Touchy, K. Shimizu, *Catal. Sci. Technol.* **2014**, *4*, 1716-1719; h) D. Zhao, Y.-R. Zhou, Q. Shen, J.-X. Li, *RSC Adv.* **2014**, *4*, 6486-6489; i) D. Qiu, Y. Wang, D. Lu, L. Zhou, Q. Zeng, *Monatsh. Chem.* **2015**, *146*, 1343-1347; j) Z. Zhang, M. Wang, C. Zhang, Z. Zhang, J. Lu, F. Wang, *Chem. Commun.* **2015**, *51*, 9205-9207; k) Y. Wang, X. Meng, G. Chen, P. Zhao, *Catal. Commun.* **2018**, *104*, 106-111; l) F. Li, L. Lu, P. Liu, *Org. Lett.* **2016**, *18*, 2580-2583.

[8] a) D. Zhao, T. Wang, J. X. Li, *Chem. Commun.* **2014**, *50*, 6471-6474; b) Y. Bao, Y. Yan, K. Xu, J. Su, Z. Zha, Z. Wang, *J. Org. Chem.* **2015**, *80*, 4736-4742; c) Y.-P. Zhu, Z. Fei, M.-C. Liu, F.-C. Jia, A.-X. Wu, *Org. Lett.* **2013**, *15*, 378-381; d) X. Chen, T. Chen, Y. Zhou, D. Han, L.-B. Han, S.-F. Yin, *Org. Biomol. Chem.* **2014**, *12*, 3802-3807; e) S. Guo, J. Zhai, X. Fan, *Org. Biomol. Chem.* **2017**, *15*, 1521-1529; f) V. Sriramoju, S. Kurva, S. Madabhushi, *New J. Chem.* **2018**, *42*, 3188-3191; g) Y. Yan, Y. Xu, B. Niu, H. Xie, Y. Liu, *J. Org. Chem.* **2015**, *80*, 5581-5587; h) L. Yang, X. Shi, B. Q. Hu, L. X. Wang, *Asian J. Org. Chem.* **2016**, *5*, 494-498; i) S. Mukhopadhyay, D. S. Barak, S. Batra, *Eur. J. Org. Chem.* **2018**, *2018*, 2784-2794.

[9] a) W. Xu, Y. Jin, H. Liu, Y. Jiang, H. Fu, *Org. Lett.* **2011**, *13*, 1274-1277; b) H. Chai, J. Li, L. Yang, H. Lu, Z. Qi, D. Shi, *RSC Adv.* **2014**, *4*, 44811-44814; c) T. Kotipalli, V. Kavala, D. Janreddy, V. Bandi, C. W. Kuo, C. F. Yao, *Eur. J. Org. Chem.* **2016**, *2016*, 1182-1193; d) M. Liu, M. Shu, C. Yao, G. Yin, D. Wang, J. Huang, *Org. Lett.* **2016**, *18*, 824-827; e) P. H. Pham, S. H. Doan, N. T. H. Vuong, V. H. H. Nguyen, P. T. M. Ha, N. T. S. Phan, *RSC Adv.* **2018**, *8*, 20314-20318; f) L.-X. Wang, J.-F. Xiang, Y.-L. Tang, *Eur. J. Org. Chem.* **2014**, *2014*, 2682-2685; g) C. Huang, Y. Fu, H. Fu, Y. Jiang, Y. Zhao, *Chem. Commun.* **2008**, 6333-6335; h) X. Liu, H. Fu, Y. Jiang, Y. Zhao, *Angew. Chem. Int. Ed.* **2009**, *48*, 348-351; *Angew. Chem.* **2009**, *121*, 354-357.

[10] a) A. Modak, U. Dutta, R. Kancherla, S. Maity, M. Bhadra, S. M. Mobin, D. Maiti, *Org. Lett.* **2014**, *16*, 2602-2605; b) K. Chen, B. Gao, Y. Shang, J. Du, Q. Gu, J. Wang, *Org. Biomol. Chem.* **2017**, *15*, 8770-8779; c) A. V. A. Gholap, S. Maity, C. Schulzke, D. Maiti, A. R. Kapdi, *Org. Biomol. Chem.* **2017**, *15*, 7140-7146; d) D. Maiti, A. Modak, U. Dutta, IN Pat., 1468/MUM/2014 (2015).

[11] a) Y. Ju, F. Liu, C. Li, *Org. Lett.* **2009**, *11*, 3582-3585; b) M. H. Larraufie, C. Courillon, C. Ollivier, E. Lacote, M. Malacria, L. Fensterbank, *J. Am. Chem. Soc.* **2010**, *132*, 4381-4387; c) D. S. Chen, G. L. Dou, Y. L. Li, Y. Liu, X. S. Wang, *J. Org. Chem.* **2013**, *78*, 5700-5704; d) Z. A. Fard, K. A. Dilmaghani, M. Soheilizad, B. Larijani, M. Mahdavi, *Tetrahedron* **2018**, *74*, 2197-2201.

[12] a) J. K. Laha, K. S. S. Tummalapalli, A. Nair, N. Patel, *J. Org. Chem.* **2015**, *80*, 11351-11359; b) J. K. Laha, K. S. S. Tummalapalli, K. P. Jethava, *Org. Biomol. Chem.* **2016**, *14*, 2473-2479.

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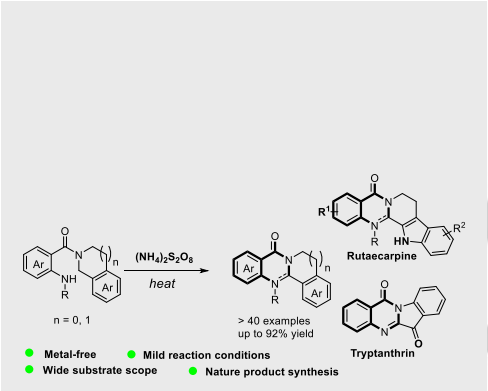

Key Topic* Synthetic Methods

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