ChemComm
Chemical Communications

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: M. Yan, R. Ma, R. Chen, L. Wang, Z. Wang and Y. Ma, *Chem. Commun.*, 2020, DOI: 10.1039/D0CC03820B.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemcomm

View Article Online
DOI: 10.1039/D0CC03820B

COMMUNICATION

Synthesis of 1,2-dihydro-1,3,5-triazines derivatives via Cu(II)-catalyzed C(SP^3)-H activation of *N,N*-dimethylethanolamine with amidines

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Min Yan[a,b], Renchao Ma[a], Rener Chen[a], Lei Wang[a], Zhiming Wang[a] and Yongmin Ma[a,b*]

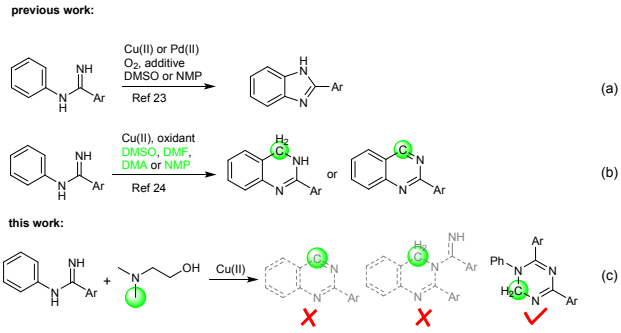
1,2-Dihydro-1,3,5-triazines and symmetrical 1,3,5-triazines were obtained in up to 81% yields from amidines and *N,N*-dimethylethanolamine catalyzed by $CuCl_2$. The reaction involves three C-N bond formations during the oxidative annulation process and the mechanism was proposed. This efficient synthesis of 1,2-dihydro-1,3,5-triazines was developed for the first time.

Transition-metal-catalyzed C-H activation is one of the hotspots in the field of organic synthesis with the concern about environmental impact and concept of atom and step economy.[1] For example, C-H activation/cyclization performs activation of the inert C-H bonds followed by cyclization with an introduced functional group.[1h,2] Oxidative functionalization of the C-H bond adjacent to nitrogen via cross-dehydrogenative coupling (CDC) is greatly successful and has attracted organic chemist's attentions in recent years.[3] However, cleavage of C-N bond is the least explored due to its relative stability.[4] This C-N bond cleavage of *N,N*-dimethylaniline[5], *N,N*-dimethylbenzylamine[6], *N,N,N′,N′*-tetramethylethylenediamine[7], *N,N*-dimethyl aliphatic amide[8] or *N*-methylpyrrolidone (NMP)[9] is usually catalyzed by Ru[10], Pd[11], Cu[12] or Fe[13] to offer one carbon source.

1,3,5-Triazines represent an important class of nitrogen-containing heterocycle. Compounds containing the triazine motif have widespread applications in pharmaceutical and agriculture industries, material science and organic synthesis.[14] 1,2-Dihydro-1,3,5-triazines, one derivative of 1,3,5-triazine species, have been extensively studied in the last few years due to their broad biological activity such as antitumor[15], antibacterial[16], anti-inflammatory[17] and antimalarial[18] properties. Consequently, the development of effective methods for constructing the dihydrotriazine skeleton has attracted considerable attention. Wurthwein et al. reported the synthesis of 1,2-dihydro-1,3,5-triazines by condensation of 1,3,5-triazapenta-1,3-dienes with aldehydes/ketones but with low yields.[19a] Eckert-Maksic et al. used guanidines and two equivalents of *N,N′*-diphenylcarbodiimide or *N,N′*-diisopropylcarbodiimide to construct the 1,2-dihydro-1,3,5-triazine scaffold.[19b] Hulme et al. developed a microwave-assisted protocol for the transformation of dihydrotriazines from aldehydes and aryl amidines.[20] Recently, Zhao et al. found copper supported on octahedral manganese oxide molecular sieve being an efficient catalyst for the synthesis of 1,2-dihydro-1,3,5-triazines directly from alcohols and amidines.[21] Chang et al. presented a direct annulation of *N*-benzimidazolyl amidines with aldehydes for the formation of *ortho*-fused 1,3,5-triazines.[22] However, the existing methods suffer from the disadvantages of harsh reaction conditions, low yields and not readily accessible raw materials. Thus, simple and efficient approaches to dihydrotriazines in a user-friendly manner remain highly demanded.

In 2008 and 2009 respectively, Buchwald and Shi independently reported the transformation of benzimidazoles from amidines under oxygen catalyzed by Cu(II) or Pd(II) using DMSO as the reaction medium (Scheme 1a).[23] With an addition of Selectfluor, DMSO acts not only as a solvent, also as a methylene donor and as a consequence, 3,4-dihydroquin--azolines or quinazolines were performed successfully (Scheme 1b).[24] Our previous work shows that *N,N*-dimethylethanolamine (DMEA) can offer one carbon donor.[25] As part of our continuing interest in using DMEA as the carbon

Scheme 1. Previous and present work for annulation of amidines.



[a] Institute of Advanced Studies and School of Pharmaceutical and Chemical Engineering, Taizhou University, 1139 Shifu Avenue, Taizhou, 318000, P R China
[b] School of Pharmaceutical Science, Zhejiang Chinese Medical University, Hangzhou, 310053, P R China

†Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

View Article Online DOI: 10.1039/D0CC03889B

synthon, we were wondering whether DMEA can offer a carbon to perform the annulation reaction for the synthesis of 3,4-dihydroquinazolines or quinazolines in same manner as DMSO did. Unfortunately, the target quinazolines were not successfully formed. ^{1}H NMR data also ruled out the possibility of the production of 3,4-dihydroquinazoline derivative. On the basis of its structural analysis and spectra, a novel 1,2-dihydro-1,3,5-triazine derivatives was assigned (Scheme 1c). Here we report the details.

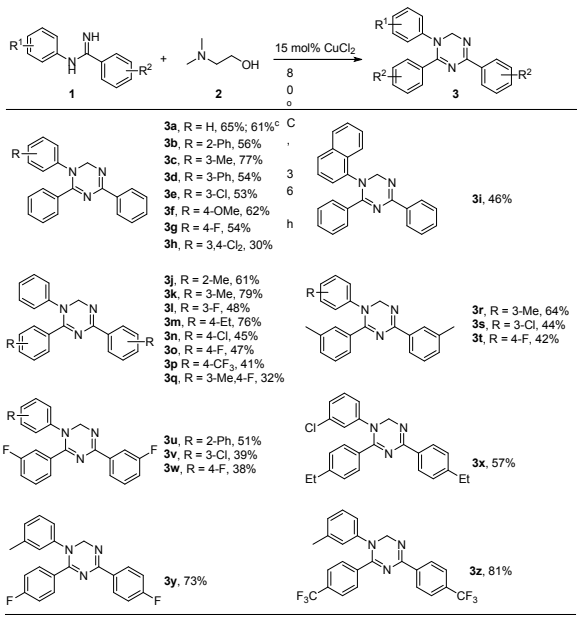
We started by selecting *N*-phenylbenzimidamide (**1a**) as the model substrate. The effect of different carbon sources, solvents, catalysts and temperatures on the product yields were investigated (see SI Table S1). After tedious optimization experiments, the optimal reaction condition is: *N*-phenylbenzimidamide (**1a**, 0.5 mmol), DMEA (0.5 mL) and $CuCl_2$ (15 mol%) at 80°C under air atmosphere for 36h.

Having affirmed the optimized reaction conditions, the scope of the reaction with a range of amidines **1** was investigated. We first employed the amidines with different substituents on the *N*-aryl side (**1a**-**1i**) as substrates and the results are presented in Table 1. In general, the presence of an electron-donating group (EDG) or electron-withdrawing group (EWG) at either *ortho*-, *meta*- or *para*- position was well tolerated and moderate to good yields of **3** were obtained. The position of both EDG and EWG on the aromatic ring had no significant influence on the yield (group of **3b**, **3d**, **3e** and **3g**). However, the electronic nature of the aromatic moiety appreciably influenced on the yield. For instance, the average yield of **3c** and **3f** which containing an EDG is 70%, whereas the average yield of **3b**, **3d**, **3e** and **3g** which containing an EWG is 54% only. In addition, moderate yields were achieved when di-substituted benzimidamide (**1h**) and naphthyl amidine (**1i**) were employed for the reaction. Having exhibited the scope of the amidines with substituents on the *N*-aryl side, the amidines with substituents on the benzimidamide side (**1j-1q**) under the optimized reaction conditions were next studied. Similarly, amidines bearing with an EDG gave appreciably higher yields compared to those with an EWG (**3j-3p**) and a di-substituted analogue provided only a moderate yield (**3q**). To further explore the universality of the reaction, amidines with substituents on both the *N*-aryl and the benzimidamide sides were also examined. Not surprisingly, moderate yields (38-64%) of the desired products (**3r**-**3x**) were achieved with two exceptions which gave delighted yields (73% for **3y** and 81% for **3z**). Unfortunately, heterocyclic analogues such as furan-2-yl and thiophen-3-yl substituted amidines did not work for the reaction. It is also noteworthy that the expected products were not successfully afforded when one of the aryl groups was replaced with an aliphatic group, such as using *N*-(*tert*-butyl)benzimidamide, *N*-benzylbenzimidamide and *N*-phenylacetimidamide as the starting materials.

Encouraged by these promising results, we further applied this method to assemble various symmetrical 2,4-disubstituted-1,3,5-triazines (**5**) started from *N*-unsubstituted benzimidamides (**4**) (Table 2). A series of amidines **4a-4i** bearing either an EDG or an EWG on the phenyl ring could be employed in the reaction, to afford the corresponding symmetrical heterocycles in moderate yields. Similar to the aforementioned results, amidines with an EDG gave relatively higher yields of **5** compared to those with an EWG (**5b**-**c** vs **5d**-**h**). On the other hand, *ortho*-substituted aryl amidine afforded much lower yield compared to *meta*- and *para*-substituted analogues (**5d** vs **5e-h**). This phenomenon is different from the results mentioned above for the conversion of *N*-substituted amidines. In addition, heterocyclic amidines was also tolerated in this reaction and the desired product 2,4-di(pyridin-4-yl)-1,3,5-triazine (**5i**) was achieved in a moderate yield. Again, when the aromatic group of the amidine was substituted with an aliphatic group such as ethyl, the desired product failed to be afforded.

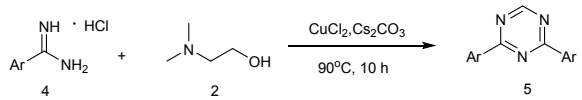
To gain an insight into the reaction mechanism, some controlled experiments were carried out. A radical inhibitor

Table 1. Substrate scope of amidines[a,b]



[a]Reaction conditions: **1** (0.5 mmol), $CuCl_2$ (0.15 equiv), in DMEA (0.5 mL) at 80 °C for 36 h; [b]Isolated yield; [c]Reaction performed in 6 mmol scale.

Table 2. Synthesis of symmetrical 2,4-disubstituted-1,3,5-triazines[a]

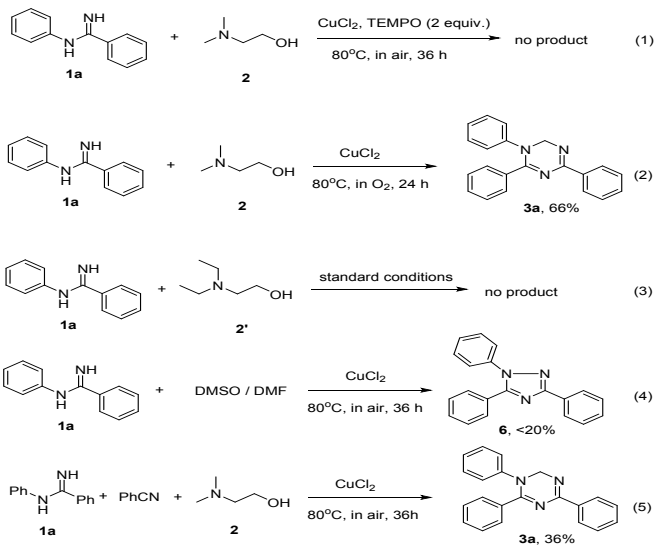


Entry	Product	Ar	Yield(%)[b]
1	**5a**	C_6H_5	66
2	**5b**	3-CH_3-C_6H_4	53
3	**5c**	4-CH_3-C_6H_4	51
4	**5d**	2-F-C_6H_4	18
5	**5e**	3-Br-C_6H_4	36
6	**5f**	4-Cl-C_6H_4	41
7	**5g**	4-Br-C_6H_4	38
8	**5h**	3,4-F_2-C_6H_3	29
9	**5i**	4-pyridin	58

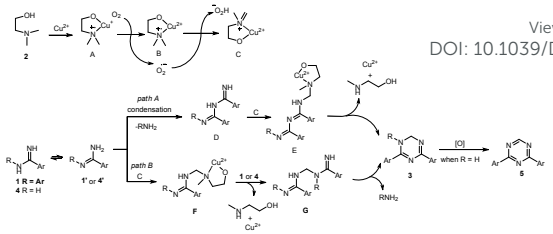
[a]Reaction conditions: **4** (0.5 mmol), $CuCl_2$ (0.15 equiv), Cs_2CO_3 (2.0 equiv) in DMEA (0.5 mL) at 90 °C for 10 h. [b]Isolated yield.

View Article Online
DOI: 10.1039/D0CC03820B

Scheme 2 Control experiments



2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) was added to the reaction system and the product yield was dramatically diminished and no product was observed when the amount of TEMPO reached 2 equivalents (Scheme 2, eq. 1). This obvious inhibiting effect indicates that the reaction may undergo a radical pathway. In addition, when the reaction was carried out under oxygen atmosphere, although the product yield was not significantly improved, the starting material **1a** was mostly consumed after 24 h reaction time, implied that oxygen atmosphere could accelerate the reaction process (Scheme 2, eq. 2). The kinetic studies were carried out under air and O_2 atmosphere, respectively, as illustrated in SI Figure S1. In the first 25 h, the yields of **3** in O_2 are much higher than those in air in the same reaction time. After 25 h, the reaction continued to afford **3** in air until the peak levelled to stable values, while yield of **3** in O_2 started to decrease slowly, most likely due to an over-oxidization of the resulting product. When the DMEA was replaced by *N,N*-diethylethanolamine, the reaction failed under such standard conditions, indicating that DMEA is critical to provide a carbon source for the annulation reaction (Scheme 2, eq. 3). On the other hand, when DMEA was replaced with DMSO or DMF which was used as a methylene donor widely, the desired 1,3,5-triazine was not obtained. Instead, DMSO/DMF was employed only as a solvent and 1,2,4-triazole (**6**) was afforded in less than 20% yield (Scheme 2, eq. 4). This result is similar to the literature report, where the reaction of amidines and benzonitriles was catalysed by $Cu(OAc)_2$[26] or CuI[27]. However, it is inconsistent with Buchwald's report[23a] that 2-aryl benzimidazoles were achieved from amidines in DMSO catalysed by $Cu(OAc)_2$. Considering that the reaction consumes 2 moles of **1** and the product **3** was achieved along with the byproduct aryl amine, based on the concept of atom economy, we attempted to replace 2 moles of **1a** with amidine and benzonitrile at one mole respectively. However, the reaction was less efficient and the benzonitrile was fully recovered after the reaction (Scheme 2, eq. 5).



cheme 3 Proposed reaction mechanism

Thus, the reaction mechanism for the annulation of the amidines with DMEA to obtain 1,2-dihydro-1,3,5-triazine derivatives was proposed based on the aforesaid results and literature reports[25, 28](Scheme 3). Initially, DMEA coordinates with Cu^{2+} to form an intermediate **A** which performs a Fenton-like reaction[29] to generate radical cation **B**. Removal of one proton from intermediate **B** leads to a reactive iminium ion **C**. Intermediate **C** couples with **D** which is performed by a condensation of compound **1** or **4** to afford the corresponding intermediate **E** (path A). Finally, intermediate **E** is annulated by removing *N*-methylethanolamine to give the final product **3**, regenerating copper salt for the next cycle. There is another possible pathway where intermediate **C** couples with **1** or **4** to afford intermediate **F**. **F** was nucleophilically attacked by **1** or **4** to form intermediate **G**, which followed by annulation to achieve the product **3** (path B). When *N*-unsubstituted amidines were employed as the starting material, **3** could be further oxidized in air to form an aromatic product **5**.

In summary, we have successfully developed a novel copper-mediated oxidative annulation for the synthesis of 1,4,6-triaryl-1,2-dihydro-1,3,5-triazines and symmetrical 2,4-diaryl 1,3,5-triazines. All of the 1,4,6-triaryl-1,2-dihydro-1,3,5-triazines are new compounds. DMAE was employed as a one carbon synthon in the reaction and the corresponding products are different from that using DMSO, DMF, DMA or NMP as the carbon source, rendering the method very attractive. Further studies utilizing this DMAE/metal salt system for the construction of various C-C and C-N bond formations are ongoing in our lab.

Financial support from the Leading Innovative and Entrepreneur Team Introduction Program of Zhejiang (No. 2019R01005) is gratefully acknowledged.

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 (a) G. Duarah, P. P. Kaishap, T. Begum and S. Gogoi, *Adv. Synth. Catal.*, 2019, **361**, 654-672. (b) H. Noh and J. Cho, *Coord. Chem. Rev.* 2019, **382**, 126-144. (c) A. Dhakshinamoorthy, A. M. Asiri and H. Garcia, *ACS Catal.*, 2019, **9**, 1081-1102. (d)E. P. Beaumier, A. J. Pearce, X. Y. See and I. A. Tonks, *Nat. Rev. Chem.*, 2019, **3**, 15-34. (e) M. A. Majewski and M. Stepien, *Angew. Chem. Int. Ed.*, 2019, **58**,

86-116. (f) K.-X. Tang, C.-M. Wang, T.-H. Gao, L. Chen, L. Fan and L.-P. Sun, *Adv. Synth. Catal.*, 2019, **361**, 26-38. (g) D. J. Abrams, P. A. Provencher and E. J. Sorensen, *Chem. Soc. Rev.*, 2018, **47**, 8925-8967. (h) S. M. Ujwaldev, N. A. Harry, M. A. Divakar and G. Anilkumar, *Catal. Sci. Technol.*, 2018, **8**, 5983-6018. (i) L. Dian and I. Marek, *Chem. Rev.*, 2018, **118**, 8415-8434.

2 (a) I. Khan, A. Ibrar and S. A. Shehzadi, *Coord. Chem. Rev.*, 2019, **380**, 440-470. (b) A. Peneau, C. Guillou and L. Chabaud, *Eur. J. Org. Chem.*, 2018, **2018**, 5777-5794. (c) Y.-F. Han and G.-X. Jin, *Chem. Soc. Rev.*, 2014, **43**, 2799-2823. (d) S.-S. Li, L. Qin and L. Dong, *Org. Biomol. Chem.*, 2016, **14**, 4554-4570. (e) Y. Yang, K. Li, Y. Cheng, D. Wan, M. Li and J. You, *Chem. Commun.*, 2016, **52**, 2872-2884.

3 (a) C.-J. Li, *Acc. Chem. Res.*, 2009, **42**, 335-344. (b) C. Yu and F. W. Patureau, *Angew. Chem. Int. Ed.*, 2018, **57**, 11807-11811. (c) Q. Yang, L. Zhang, C. Ye, S. Luo, L.-Z. Wu and C.-H. Tung, A*ngew. Chem. Int. Ed.*, 2017, **56**, 3694-3698.(d) B. V. Varun, J. Dhineshkumar, K. R. Bettadapur, Y. Siddaraju, K. Alagiri and K. R. Prabhu, *Tetrahedron Lett.*, 2017, **58**, 803-824. (e) Y. Liu, C. Wang, D. Xue, M. Xiao, C. Li and J. Xiao, *Chem. Eur. J.*, 2017, **23**, 3051-3061. (f) K. Gu, Z. Zhang, Z. Bao, H. Xing, Q. Yang and Q. Ren, *Eur. J. Org. Chem.*, 2016, **2016**, 3939-3942. (g) Z. Xie, X. Liu and L. Liu, *Org. Lett.*, 2016, **18**, 2982-2985. (h) C. Zhang, C. Tang and N. Jiao, *Chem. Soc. Rev.*, 2012, **41**, 3464-3484. (i) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215-1292.

4 (a) S.-Y. Baek, T. Kurogi, D. Kang, M. Kamitani, S. Kwon, D. P. Solowey, C.-H. Chen, M. Pink, P. J. Carroll, D. J. Mindiola and M.-H. Baik, *J. Am. Chem. Soc*., 2017, **139**, 12804-12814. (b) S. Hu, G. Luo, T. Shima, Y. Luo and Z. Hou, *Nat. Commun.*, 2017, **8**,1866. (c) W. Geng, W.-X. Zhang, W. Hao and Z. Xi*, J. Am. Chem. Soc.*, 2012, **134**, 20230-20233. (d) Y. Kuninobu, M. Nishi and K. Takai, *Chem. Commun.*, 2010, **46**, 8860-8862.

5 M.-N. Zhao, L. Yu, N.-F. Mo, Z.-H. Ren, Y.-Y. Wang and Z.-H. Guan, *Org. Chem. Front.*, 2017, **4**, 597-602.

6 W.-J. Yoo, A. Tanoue and S. Kobayashi, *Chem. Asian J.*, 2012, **7**, 2764-2767.

7 (a) G. Kibriya, A. K. Bagdi and A. Hajra, *Org. Biomol. Chem.*, 2018, **16**, 3473-3478. (b) L. Zhang, C. Peng, D. Zhao, Y. Wang, H.-J. Fu, Q. Shen and J.-X. Li, *Chem. Commun.*, 2012, **48**, 5928-5930. (c) Y. Yan, Z. Li, C. Cui, H. Li, M. Shi and Y. Liu, *Org. Biomol. Chem*., 2018, **16**, 2629-2633.

8 (a) H.-M. Xia, F.-L. Zhang, T. Ye and Y.-F. Wang, *Angew. Chem. Int. Ed.*, 2018, **57**, 11770-11775. (b) M.-N. Zhao, R.-R. Hui, Z.-H. Ren, Y.-Y. Wang and Z.-H. Guan, *Org. Lett.*, 2014, **16**, 3082-3085. (c) Y. Cao, D. Zhou and Y. Ma, *Can. J. Chem.*, 2019, **97**, 37-41. (d) J. Chen, Y. Ding, Y. Gao, D. Zhou, R. Hider and Y. Ma, *Chemistryselect*, 2019, **4**, 2404-2408.

9 A. Nunes, S. M. Marques, C. Quintanova, D. F. Silva, S. M. Cardoso, S. Chaves and M. Amelia Santos, *Dalton Trans.*, 2013, **42**, 6058-6073.

10 (a) N. Iqbal and E. J. Cho, *Adv. Synth. Catal.*, 2015, **357**, 2187-2192. (b) X.-Q. Hu, Z. Hu, G. Zhang, N. Sivendran and L. J. Goossen, *Org. Lett.*, 2018, **20**, 4337-4340.

11 (a) Z. Zhang, H. Wang, N. Qiu, Y. Kong, W. Zeng, Y. Zhang and J. Zhao, *J. Org. Chem.*, 2018, **83**, 8710-8715. (b) W.-J. Pan and Z.-X. Wang, *Asian J. Org. Chem.*, 2018, **7**, 1626-1634.

12 (a) F. Wang, Y. He, M. Tian, X. Zhang and X. Fan, *Org. Lett.*, 2018, **20**, 864-867. (b) H.-C. Cheng, W.-J. Hou, Z.-W. Li, M.-Y. Liu and B.-T. Guan, *Chem. Commun.*, 2015, **51**, 17596-17599.

13 (a) M.-N. Zhao, Z.-H. Ren, D.-S. Yang and Z.-H. Guan, *Org. Lett.*, 2018, **20**, 1287-1290. (b) L. Ma, Y. Li and Z. Li, *Sci. China Chem.*, 2015, **58**, 1310-1315.

14 (a) A. Junaid, F. P. L. Lim, E. R. T. Tiekink and A. V. Dolzhenko, *ACS Comb. Sci.*, 2019, **21**, 548-555. (b) G. Latacz, A. Lubelska, M. Jastrzebska-Wiesek, A. Partyka, M. A. Marc, G. Satala, D. Wilczynska, M. Kotanska, M. Wiecek, K. Kaminska, A. Wesolowska, K. Kiec-Kononowicz and J. Handzlik, *Int. J. Mol. Sci.*, 2019, **20**, 3420. (c) P. Barea, V. A. Barbosa, D. L. Bidoia, J. C. de Paula, T. F. Stefanello, W. F. da Costa, C. V. Nakamura and M. H. Sarragiotto, *Eur. J. Med. Chem.*, 2018, **150**, 579-590. (d) M. O. Sarhan, M. A. Motaleb, I. T. Ibrahim, M. M. Anwar and W. A. Zaghary, *Mini Rev. Med. Chem.*, 2018, **18**, 1302-1320. (e) S. Ren, M. J. Bojdys, R. Dawson, A. Laybourn, Y. Z. Khimyak, D. J. Adams and A. I. Cooper, *Adv. Mater.*, 2012, **24**, 2357-2361. (f) H. Tanaka, K. Shizu, H. Miyazaki and C. Adachi, *Chem. Commun.*, 2012, **48**, 11392-11394.

15 (a) H.-L. Ng, X. Ma, E.-H. Chew and W.-K. Chui, Eur. J. Med. Chem., 2017, **60**, 1734-1745. (b) A. M. Scherbakov, A. V. Komkov, A. S. Komendantova, M. A. Yastrebova, O. E. Andreeva, V. Z. Shirinian, A. Hajra, I. V. Zavarzin and Y. A. Volkova, *Front. Pharmacol.*, 2018, **8**, 979.

16 S. Maeda, T. Kita and K. Meguro, *J. Med. Chem.*, 2009, **52**, 597-600.

17 F.-F. Gan, R. Zhang, H.-L. Ng, M. Karuppasamy, W. Seah, W. H. Yeap, S.-M. Ong, E. Hadadi, S.-C. Wong, W.-K. Chui and E.-H. Chew, *Food Chem. Toxicol.*, 2018, **116**, 238-248.

18 (a) D. Gravestock, A. L. Rousseau, A. C. U. Lourens, S. S. Moleele, R. L. van Zyl and P. A. Steenkamp, *Eur. J. Med. Chem.*, 2011, **46**, 2022-2030. (b) T. Vilaivan, N. Saesaengseerung, D. Jarprung, S. Kamchonwongpaisan, W. Sirawaraporn and Y. Yuthavong, *Bioorg. Med. Chem.*, 2003, **11**, 217-224.

19 (a) N. Hesse, R. Froehlich, B. Wibbeling and E.-U. Wuerthwein, *Eur. J. Org. Chem.*, 2006, **2006**, 3923-3937. (b) V. Strukil, I. Dilovic, D. Matkovic-Calogovic, J. Saame, I. Leito, P. Sket, J. Plavec and M. Eckert-Maksic, *New J. Chem*., 2012, **36**, 86-96.

20 C. E. Bell, A. Y. Shaw, F. De Moliner and C. Hulme, *Tetrahedron*, 2014, **70**, 54-59.

21 X. Meng, X. Bi, Y. Wang, G. Chen, B. Chen, Z. Jing and P. Zhao, *Catal. Commun.*, 2017, **89**, 34-39.

22 M. Wang, Y. Meng, W. Wei, J. Wu, W. Yu and J. Chang, *Adv. Synth. Catal.*, 2018, **360**, 86-92.

23 (a) G. Brasche and S. L. Buchwald, *Angew. Chem. Int. Ed.*, 2008, **47**, 1932-1934. (b) Q. Xiao, W.-H. Wang, G. Liu, F.-K. Meng, J.-H. Chen, Z. Yang and Z.-J. Shi, *Chem. Eur. J.*, 2009, **15**, 7292-7296.

24 Y. Lv, Y. Li, T. Xiong, W. Pu, H. Zhang, K. Sun, Q. Liu and Q. Zhang, *Chem. Commun.*, 2013, **49**, 6439-6441.

25 M. Yan, R. C. Hider and Y. Ma, *Org. Chem. Front.*, 2019, **6**, 1168-1172

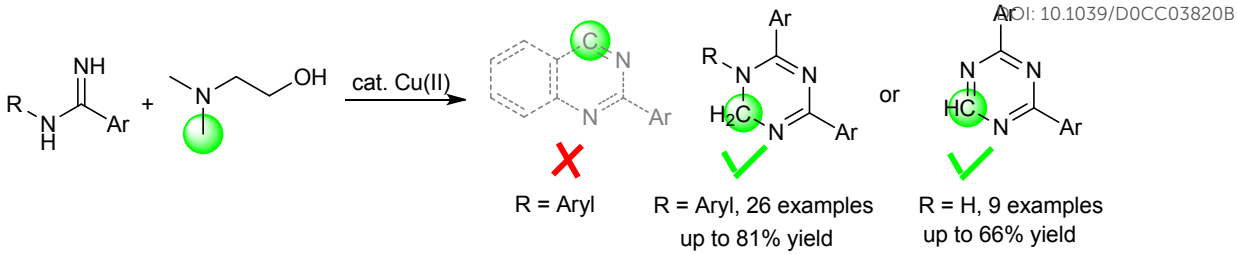
26 K. Sun, Y. Lv, Z. Zhu, L. Zhang, H. Wu, L. Liu, Y. Jiang, B. Xiao and X. Wang, *RSC Adv.*, 2015, **5**, 3094-3097.

27 K. Sun, X. Wang, Y. Jiang, Y. Lv, L. Zhang, B. Xiao, D. Li, Z. Zhu and L. Liu, *Chem. Asian J.*, 2015, **10**, 536-539.

28 (a) F. Wang, Q. You, C. Wu, D. Min, T. Shi, Y. Kong and W. Zhang, *RSC Adv.*, 2015, **5**, 78422-78426. (b) L. Zhang, D. Tang, J. Gao, J. Wang, P. Wu, X. Meng and B. Chen, *Synthesis*, 2016, **48**, 3924-3930. (c) S. A. Girard, T. Knauber and C.-J. Li, *Angew. Chem. Int. Ed.*, 2014, **53**, 74-100. (d) L. Zhang, C. Peng, D. Zhao, Y. Wang, H.-J. Fu, Q. Shen and J.-X. Li, *Chem. Commun.*, 2012, **48**, 5928-5930. (e) X. Wang, Y. Wang, Y. Yuan and C.-H. Xing, *Tetrahedron*, 2014, **70**, 2195-2202.

29 (a) N. Barrios-Bermudez, M. Gonzalez-Avendano, I. Lado-Tourino, A. Cerpa-Naranjo and M. L. Rojas-Cervantes, *Nanomaterials*, 2020, **10**. doi:10.3390/nano10040749 (b) A. D. Bokare and W. Choi, *J. Hazard. Mater.*, 2014, **275**, 121-135. (c) B. Ma, S. Wang, F. Liu, S. Zhang, J. Duan, Z. Li, Y. Kong, Y. Sang, H. Liu, W. Bu and L. Li, *J. Am. Chem. Soc.*, 2019, **141**, 849-857. (d) A. N. Pham, G. Xing, C. J. Miller and T. D. Waite, *J. Catal.*, 2013, **301**, 54-64. (e) R. Yamaguchi, S. Kurosu, M. Suzuki and Y. Kawase, *Chem. Eng. J.*, 2018, **334**, 1537-1549.

DOI: 10.1039/D0CC03820B



This efficient synthesis of 1,2-dihydro-1,3,5-triazine derivatives was developed for the first time using *N,N*-dimethylethanolamine as a new carbon donor.