View Article Online View Journal

ChemComm

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: R. D. Mule, A. C. Shaikh, A. B. Gade and N. Patil, *Chem. Commun.*, 2018, DOI: 10.1039/C8CC05743E.



This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the **author guidelines**.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard <u>Terms & Conditions</u> and the ethical guidelines, outlined in our <u>author and reviewer resource centre</u>, still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.



rsc.li/chemcomm

Published on 25 September 2018. Downloaded by Kaohsiung Medical University on 9/25/2018 7:24:30 AM



ChemComm

COMMUNICATION

A New Class of N-Doped Ionic PAHs via Intramolecular [4+2]-Cycloaddition between Arylpyridines and Alkynes

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

Ravindra D. Mule,^{ab} Aslam C. Shaikh,^{ab} Amol B. Gade^{ab} and Nitin T. Patil*^c

DOI: 10.1039/x0xx00000x

www.rsc.org/

Abstract. Reported herein, for the first time, is the copperpromoted intramolecular [4+2]-cycloaddition cascade to access ionic N-doped ionic polycyclic aromatic hydrocarbons (PAHs) with tunable emission wavelengths. It is showed that the reaction can be made catalytic with respect to Cu(OTf)₂ when external oxidant, Selectfluor, was used.

Polycyclic aromatic hydrocarbons (PAHs) with annulated aromatic rings have attracted considerable attention due to their fascinating structural features and wide application in organic, optical and electronic material.¹ It is known that the incorporation of heteroatoms in the aromatic framework of PAHs can modulate their physical, chemical and supramolecular properties.² As a subset of these compounds, nitrogen-doped PAHs represent an important class of molecules that have interesting applications in the field optoelectronics, light emitting-diodes, supercapacitors and bioimaging.³ Recently, it was shown that ionic N-doped PAHs exhibit interesting optical and aggregation behavior properties.⁴ Therefore, it is not surprising why several research group across the globe are engaged in the design and development of novel ionic N-doped PAHs (Figure 1a, Type A-D).⁵ However, most of the approaches to access N-doped ionic PAHs are based on Rh/Ru catalyzed C-H activation between arenes/heteroarenes and alkynes.⁶

During the last decades, Rh and Co-catalyzed reactions between alkynes and azadienes, involving C-H activation, have emerged as an important tool for accessing heterocyclic quaternary ammonium salts (Scheme 1a). For instance, the groups of Jones,⁷ Cheng,⁸ Huang,⁹ You¹⁰ and Jun¹¹ showed the utility of Rh-complexes for such reactions. Recently, Pérez-Temprano,¹² Cheng¹³ and Wang,¹⁴ in their independent reports, successfully demonstrated the use of Co-catalysts for the analogues transformations. Herein, we report

This journal is © The Royal Society of Chemistry 20xx

the design and development of new class of ionic N-doped PAHs i.e. Type **E** (Figure 1b) *via* Cu-mediated alkyne/azadiene [4+2]cycloaddition cascades (Scheme 1b). The reaction was proposed to proceed via initial amino-cupration followed by C-H activation/ reductive elimination sequence to produce ionic N-doped PAHs (Scheme 1b).



a) Formal [4+2]-cycloaddition via C-H activation (known work)



b) Formal intramolecular [4+2]-cycloaddition via aminocupration/C-H activation cascade (present work)



Scheme 1. Concepts for accessing heterocyclic quaternary ammonium salts *via* formal [4+2]-cycloadditions: Known and present work

Based on our previous report on gold-catalyzed oxidative intramolecular 1,2-amino-oxygenation reaction of alkynes,¹⁵ we

^a Division of Organic Chemistry, CSIR - National Chemical Laboratory, Dr. Homi Bhabha Road, Pune - 411 008, India.

^{b.} Academy of Scientific and Innovative Research (AcSIR), New Delhi – 110 025, India.

⁶ Department of Chemistry, Indian Institute of Science Education and Research (IISER) Bhopal, Bhopal Bypass Road, Bhauri, Bhopal - 462 066, India. Email: npatil@iiserb.ac.in.

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

Published on 25 September 2018. Downloaded by Kaohsiung Medical University on 9/25/2018 7:24:30 AM

DOI: 10.1039/C8CC05743E

Journal Name

envisioned that substrate of type **1** would undergo intramolecular [4+2]-cycloaddition reactions to produce ionic N-doped PAHs. Towards this end, several metal catalysts/oxidants were screened.¹⁶ Our systematic optimization studies revealed that refluxing **1a** (Ar' = 4-OMe-C₆H₄; R = Ph) in CH₃CN in the presence of stoichiometric amounts of Cu(OTf)₂ is the best the condition to achieve the desired PAH (**2a**) in 78% yield. Interestingly, Cu(OTf)₂ exhibits dual role by mediating the cascade transformation as well as providing counter ion. Be noted that the Cu-catalyzed reactions of alkenes, involving the simultaneous formation of C-C and C-N bonds, are known in the literature.¹⁷ However, to the best of our knowledge, the analogous reactions of alkynes have never been reported.

the alkyne terminal position of the pyridino alkynes were screened. For instance, the substrate with sterically demanding 1-Np and pyrenyl aromatic ring efficiently afforded desired PAHs **20** and **2p** in 80 and 85% yields, respectively. Further, in the cases where aliphatic substituents were placed on the alkyne terminus, the desired PAHs **2q-2s** obtained in good yields. Next, we directed our attention to examine the tolerance of the substituents on Ar ring. Pleasingly, the introduction of -Me, -F and -Cl substituents on the ring resulted in the formation of desired PAHs **2t-2x** in 60-70% yields. Similarly, the reaction tolerates di-substitutions at Ar ring to offer the products **2y-2aa** in moderate yields.



^{*a*}Reaction conditions: 0.13 mmol **1**, 1.0 equiv Cu(OTf)₂, CH₃CN (2 mL), 80 °C, 12 h. ^{*b*}Isolated yield. ^{*c*}Complex reaction mixture was obtained.

With the optimized reaction conditions in hand, we sought to explore the substrate scope for this reaction. The results are presented in Table 1. In general, substrates with variation in aryl ring at alkyne-terminus with varying functional groups, such as alkyl and –OMe were well tolerated (**2b-2d**). However, stronger electron donating group such as –NMe₂ was found to be unsuitable for the reaction. The reaction smoothly tolerated to varying substitution pattern (*ortho, meta, para*) on the aforementioned aryl moiety to furnish the corresponding PAHs in good yields (**2f-2n**). Next, substrates bearing bulky aromatics or long-chain/cyclic aliphatics at



^aReaction conditions: 0.13 mmol **1**, 1.0 equiv Cu(OTf)₂, CH₃CN (2 mL), 80 °C, 12 h. ^bIsolated yield. ^cCCDC for **2aj** – 1824191.

To understand the tolerance of substituents at Ar' ring, substrates **1ab-1am** were examined under the optimized reaction conditions (Table 2). It was observed that **1ab-1ah** underwent the smooth reactions to provide desired PAHs **2ab-2ah** in good yields (58-84%). Moreover, 1-Np, 2-Np, 9-phenanthryl groups were well tolerated under the present reaction conditions to produce desired PAHs **(2ai-2al)** in good yields. Even, the benzothiophenyl moiety was also well tolerated giving PAH **2am** in 65% yield. Scalability of the methods was demonstrated by the large-scale synthesis employing **1a** (2.7 mmol) as a starting material **(2a**, 76%).¹⁶



Interestingly, we found that the reaction can be made catalytic with respect to $Cu(OTf)_2$ when stoichiometric amount oxidant was used.¹⁶ When **1a**, **1b** and **1ag** was treated with 10 mol% $Cu(OTf)_2$ in the presence of Selectfluor, reaction proceeded smoothly to produce **2a'**, **2b'** and **2ag'** in 75, 63 and 65 % yields, respectively.

A plausible reaction pathway for the present transformation is depicted in Scheme 3. At first, activation of the alkyne by the $Cu(OTf)_2$ would occur to enable nucleophilic attack by the pyridyl nitrogen atom in 5-*exo-dig* fashion to generate vinyl copper intermediate I.¹⁸ This intermediate would activate C-H bond of proximal aryl ring and subsequently remove TfOH to generate copper (II) intermediate II.¹⁹ Further, reductive elimination would occur to form product **2a**. The fact that the yield of the reaction was not hampered in the presence of the radical scavenger such as 2,2,6,6-*tetra*-methylpiperidine-1-oxyl (TEMPO)¹⁶ rules out the possibility of radical mechanism.



The synthesised PAHs exhibit intense fluorescence and their photophysical properties were studied in CH₂Cl₂ solution (Table S1).¹⁶ The PL range covers the visible region, offering a palette of colors ranging from violet to orange (λ_{em} : 434-619 nm, Figure 2). These fluorophores have good photoluminescence capabilities with Φ_f values ranging from 0.06 to 0.88. Next, the electrochemical properties of representative PAHs were investigated by cyclic voltammetry and the result indicated that these PAHs have high electron-accepting abilities.¹⁶

Figure 2. Emission spectra of selected ionic PAHs in CH_2Cl_2



DOI: 10.1039/C8CC05743E COMMUNICATION

In conclusion, Cu(II)-mediated intramolecular alkynes/azadienes [4+2]-cycloaddition cascade has been disclosed. The reagent Cu(OTf)₂ exhibits dual role by mediating the cascade transformation as well as providing counter ion. Further, it is showed that the reaction can be made catalytic with respect to Cu(OTf)₂ in the presence of external oxidant, Selectfluor. The method provided an efficient access to ionic N-doped PAHs with tunable emission wavelengths.

Generous financial support by IISER Bhopal is gratefully acknowledged. We thank Saibal Bera and Dr. Rahul Banerjee for providing single crystal X-ray diffraction data. R.D.M., A.C.S. and A.B.G. thank CSIR for the award of senior research fellowship.

Notes and reference+

- (a) R. G. Harvey, Polycyclic Aromatic Hydrocarbons; Wiley-VCH: New York, 1997, 43; (b) A. Narita, X.-Y Wang, X. Feng and K. Müllen, *Chem. Soc. Rev.* 2015, **44**, 6616; (c) D. Pérez, D. Peña and E. Guitián, *Eur. J. Org. Chem.* 2013, 5981; (d) J. Wu, W. Pisula and K. Müllen, *Chem. Rev.* 2007, **107**, 718; (e) M. D. Watson, A. Fechtenkötter and K. Müllen, *Chem. Rev.* 2001, **101**, 1267.
- (2) For recent reviews, see: (a) M. Stępień, E. Gońka, M. Żyła and N. Sprutta, *Chem. Rev.* 2017, **117**, 3479; (b) X. Wang, G. Sun, P. Routh, D.-H. Kim, W. Huang and P. Chen, *Chem. Soc. Rev.* 2014, **43**, 7067; (c) W. Jiang, Y. Li and D. Wang, *Chem. Soc. Rev.* 2013, **42**, 6113.
- (3) Reviews: (a) Y. Deng, Y. Xie, K. Phou and X. Ji, J. Mater. Chem. A 2016, 4, 1144; (b) A. Mateo-Alonso, Chem. Soc. Rev. 2014, 43, 6311; (c) U. H. F. Bunz, J. U. Engelhart, B. D. Lindner and M. Schaffroth, Angew. Chem., Int. Ed. 2013, 52, 3810. For selected examples, see: (d) A. Skabeev, U. Eschieschang, Y. Zagranyarski, H. Klauk K. Müllen, and C. Li, Org. Lett. 2018, 20, 1409; (e) X.-Y. Wang, M. Richter, Y. He, J. Björk, A. Riss, R. Rajesh, M. Garnica, F. Hennersdorf, J. J. Weigand, A. Narita, R. Berger, X. Feng, W. Auwärter, J. V. Barth, C.-A. Palma and K. Müllen, Nat. Commun. 2017, 8, 1948; (f) S. Boldt, S. Parpart, A. Villinger, P. Ehlers and P. Langer, Angew. Chem., Int. Ed. 2017, 56, 4575; (g) C.-F. Liu, C. Cheng, Y. Jiang, W.-Y. Lai and W. Huang, New J. Chem. 2017, 41, 13619; (h) M. Richter, K. S. Schellhammer, P. Machata, G. Cuniberti, A. Popov, F. Ortmann, R. Berger, K. Müllen and X. Feng, Org. Chem. Front. 2017, 4, 847.

- (a) K. Xu, Y. Fu, Y. Dhou, F. Hennersdorf, P. Machata, I. Vincon, (4) J. J. Weigand, A. A. Popov, R. Berger and X. Feng, Angew. Chem., Int. Ed. 2017, 56, 15876; (b) D. Wu, R. Liu, W. Pisula, X. Feng and K. Müllen, Angew. Chem., Int. Ed. 2011, 50, 2791; (c) J. Fortage, F. Tuyèras, P. Ochsenbein, F. Puntoriero, F. Nastasi, S. Campagna, S. Griveau, F. Bedioui, I. Ciofini and P. P. Lainé, Chem. Eur. J. 2010, 16, 11047; (d) J. Fortage, C. Peltier, F. Nastasi, F. Puntoriero, F. Tuyèras, S. Griveau, F. Bedioui, C. Adamo, I. Ciofini, S. Campagna and P. P. Lainé, J. Am. Chem. Soc. 2010, 132, 16700; (e) D. Wu, W. Pisula, V. Enkelmann, X. Feng and K. Müllen, J. Am. Chem. Soc. 2009, 131, 9620; (f) D. Wu, L. Phi, G. J. Bodwell, G. Cui, N. Tsao, and K. Müllen, Angew. Chem., Int. Ed. 2007, 46, 5417.
- (5) For general reviews, see: (a) D. Sucunza, A. M. Cuadro, J. Alvarez-Builla and J. J. Vaquero, J. Org. Chem. 2016, 81, 10126; For selected examples, see: (b) F. Li, J. Cho, S. Tan, and S. Kim, Org. Lett. 2018, 20, 824; (c) N. Toriumi, N. Asano, K. Miyamoto, A. Muranaka, M. Uchiyama, J. Am. Chem. Soc. 2018, 140, 3858 ; (d) J.-R. Deng, C.-S. Tsang, W.-C. Chan, B. C.-B. Ko, N. C.-H. Lai, S. L.-F. Chan, B. Yang and M.-K. Wong, Chem. Sci. 2017, 8, 7537; (e) Y. Asanuma, H. Eguchi, H. Nishiyama, I. Tomita and S. Inagi, Org. Lett. 2017, 19, 1824; (f) J. M. Villar, J. Suárez, J. A. Varela and C. Saá, Org. Lett. 2017, 19, 1702; (g) Y. Yang, D. Liu, M. Song, D. Shi, B. Liu, K. Cheng, Y. Lu, H. Liu, M. Yang, W. Wang, J. Li and J. Wei, Chem. Eur. J. 2017, 23, 7409; (h) Q. Ge, Y. Hu, B. Li and B. Wang, Org. Lett. 2016, 18, 2483; (i) B. Feng, D. Wan, L. Yan, V. D. Kadam, J. You and G. Gao, RSC Adv. 2016, 6, 66407; (j) D. Ghorai, C. Dutta and J. Choudhury, ACS Catal. 2016, 6, 709; (k) D. Ghorai and J. Choudhury, ACS Catal. 2015, 5, 2692; (/) D. L. Davies, C. E. Ellul, S. A. Macgregor, C. L. McMullin and K. Singh, J. Am. Chem. Soc. 2015, 137, 9659; (m) D. Phao, Q. Wu, X. Huang, F. Song, T. Lv and J. You, Chem. Eur. J. 2013, 19, 6239; (n) G. Dhang, L. Yang, Y. Wang, Y. Xie, H. Huang, J. Am. Chem. Soc. 2013, 135, 8850.
- For recent reviews, see: (a) J. Jayakumar and C.-H. Cheng, J. (6) Chin. Chem. Soc. 2018, 65, 11; (b) P. Gandeepan and C.-H. Cheng, Chem. Asian J. 2016, 11, 448.
- (7) L. Li, W. W. Brennessel and W. D. Jones J. Am. Chem. Soc. 2008, 130, 12414.
- (8) (a) C.-2. Luo, J. Jayakumar, P. Gandeepan, Y.-C. Wu and C.-H. Cheng, Org. Lett. 2015, 17, 924; (b) C.-2. Luo, P. Gandeepan, J. Jayakumar, K. Parthasarathy, Y.-W. Chang and C.-H. Cheng, Chem. Eur. J. 2013, 19, 14181.
- (9) G. Ihang, L. Yang, Y. Wang, Y. Xie and H.Huang, J. Am. Chem. Soc. 2013, 135, 8850.
- (10) J. Tang, S. Li, D. Liu, Y. Dhao, D. She, V. D. Kadam, G. Gao, J. Lan and J. You, Org. Lett. 2017, 19, 604.
- (11) Y. R. Han, S.-H. Shim, D.-S. Kim and C.-H. Jun, Org. Lett. 2017, 19, 2941.
- (12) J. Sanjosé-Orduna, D. Gallego, A. Garcia-Roca, E. Martin, J. Benet-Buchholz and M. H. Pérez-Temprano, Angew. Chem., Int. Ed., 2017, 56, 12137.
- (13) S. Prakash, K. Muralirajan and C.-H. Cheng, Angew. Chem., Int. Ed., 2016, 55, 1844
- (14) Y.-X. Lao, S.-S. Phang, X.-G. Liu, C.-Y. Jiang, J.-Q. Wu, Q. Li, P.-S. Huang and H. Wang, Adv. Synth. Catal. 2016, 358, 2186.
- (15) A. C. Shaikh, D. S. Ranade, P. R. Rajamohanan, P. P. Kulkarni and N. T. Patil, Angew. Chem., Int. Ed., 2017, 56, 757.
- (16) See supporting information for more details.

- (17) For general reviews, see: (a) X. Dhu and S. Chiba, Chem. Soc. Rev. 2016, 45, 4504; (b) Y. Shimizu and M. Kanai, Tetrahedron Lett. 2014, 55, 3727; (c) J. P. Wolfe, Top. Heterocycl. Chem. 2013, 32, 1; (d) S.R. Chemler, J. Organomet. Chem, 2011, 696, 150; (e) S. R. Chemler and P. H. Fuller, Chem. Soc. Rev. 2007, 36, 1153. For pertinent reports, see: (f) E. S. Sherman and S. R. Chemler, Adv. Synth. Catal. 2009, 351, 467; (g) W. Deng and S. R. Chemler, J. Am. Chem. Soc. 2007, 129, 12948; (h) P. H. Fuller and S. R. Chemler, Org. Lett. 2007, 9, 5477; (i) E. S. Sherman, P. H. Fuller, D. Kasi and S. R. Chemler, J. Org. Chem. 2007, 72, 3896.
- (18) (a) L. Ouyang, X. Tang, H. He, C. Qi, W. Xiong, Y. Ren and H. Jiang, Adv. Synth. Catal. 2015, 357, 2556; (b) X. Phang, R. P. Hsung, H. Li, Chem. Commun., 2007, 23, 2420.
- (19) For selected reviews, see: (a) W.-H. Rao and B.-F. Shi, Org. Chem. Front., 2016, 3, 1028; (b) X. -X. Guo, D.-W. Gu, Z. Wu and W. Ihang, Chem. Rev., 2015, 115, 1622; (c) Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M. C. Chem. Rev., 2013, 113, 6234; (d) K. Hirano and M. Miura, Chem. Commun., 2012, 48, 10704.

This journal is C The Royal Society of Chemistry 20xx

COMMUNICATION

Published on 25 September 2018. Downloaded by Kaohsiung Medical University on 9/25/2018 7:24:30 AM

Published on 25 September 2018. Downloaded by Kaohsiung Medical University on 9/25/2018 7:24:30 AM.

Graphical Abstract

A New Class of N-Doped Ionic PAHs via Intramolecular [4+2]-Cycloaddition between Arylpyridines and Alkynes

Ravindra D. Mule, Aslam C. Shaikh, Amol B. Gade and Nitin T. Patil*

