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Iodine-mediated oxidative annulation for one-pot synthesis of pyrazines and quinoxalines using a multipathway coupled domino strategy†

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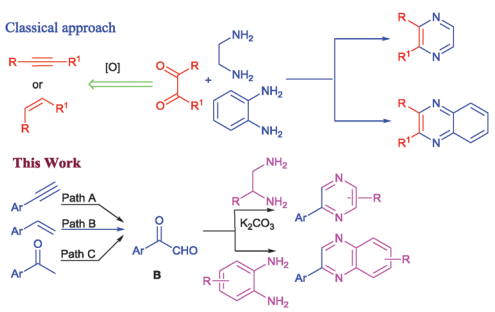
An efficient iodine-mediated oxidative annulation of aryl acetylenes–arylethenes–aromatic ketones with 1,2-diamines for the synthesis of pyrazines and regioselective synthesis of quinoxalines is presented. A multipathway coupled domino approach has been developed for the one-pot synthesis of 1,4-diazines with high functional group compatibility.

Unlike the conventional 'stop and go' synthesis, the domino strategy explores multiple bond-forming reactions under fixed reaction conditions, reducing the number of reagents or catalysts needed.[1a–d] Because of the step economy and reduced purification burden, these reactions are gaining more prominence. Various types of domino processes, including pericyclic,[1e] radical,[1f] photochemical,[1g] and transition metal-mediated[1h] reactions, have been reported. To make domino reactions more lucrative, recently, chemists have started coupling two or more domino processes in a one-pot operation.[2] Across the globe several research groups, including Wu's group, have successfully utilized the multiplicative effect of a coupled domino strategy for the synthesis of various different compounds.[3] Apart from these reports, Wu *et al.* demonstrated the significance of multi-pathway coupled domino (MPCD) strategies, a nature-inspired approach, for the synthesis of 2-acylbenzothiazoles.[3b] Inspired from these strategies, herein we report an MPCD approach for the synthesis of both pyrazines and quinoxalines.

Pyrazine and quinoxaline are prevalent heterocyclic units in pharmaceuticals and bioactive natural products (Fig. S1, ESI†).[4,5] For instance, pyrazine derivatives have been reported with antifungal,[6] antimycobacterial,[7] and herbicidal activity.[8] These derivatives are also used in the treatment of obesity, psychiatric and neurological disorders,[9] and in the food industry as a flavoring agents.[10] Recently, tetra-substituted pyrazines have been discovered as semiochemicals in orchids.[11]

Quinoxaline also possess significant biological activities including antiviral,[12] antibacterial,[13] anticancer,[14] and anti-inflammatory.[15] Moreover, quinoxalines have displayed practical utility in the fields of organic semiconductor materials[16] and organic synthons.[17]

For the preparation of these six-membered heterocycles, different type of reactions have been reported using 1,2-dicarbonyl compounds,[18,19] or epoxides,[20,21] or hydroxy ketones,[22,23] or their equivalents (Scheme 1).[24,25] Recently, Chen *et al.*,[26a] Hashmi *et al.*[26b] and Minakata's groups[26c] independently synthesized the quinoxalines from alkynes and 1,2-diamines in the presence of copper(II) or gold(I)[26d,e] or hypervalent iodine. Although such transformations are well developed, many of them require more than one step and employ expensive metal oxidants; the substrate scope is also limited. In addition, most of the methods are not applicable for pyrazines synthesis. Hence, developing a mild and efficient method for the synthesis of both pyrazine and quinoxalines with a high substrate scope is highly challenging and desirable. The iodine-mediated MPCD strategy reported by Wu *et al.*[3] appears to be an advantageous method for the synthesis of both pyrazine and quinoxalines with high substrate scope,



Scheme 1 Synthetic approaches to pyrazines and quinoxalines.

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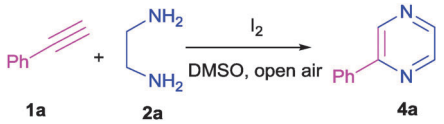
Table 1 Optimization of iodine-mediated annulation of phenyl acetylene and 1,2-diaminoethane[a]



1a 2a 4a

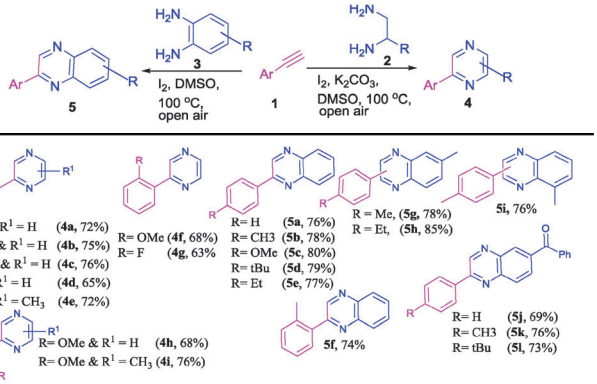
Entry	Reagent (equiv.)	Base (1.2 equiv.)	Temp. (°C)	Time (h)	Yield[b] (%)
1	I_2 (1.1)	—	80	12	n.r.
2	I_2 (1.1)	K_2CO_3	80	12	45
3	I_2 (1.1)	K_2CO_3	90	12	53
4	I_2 (1.1)	K_2CO_3	100	12	58
5	I_2 (1.1)	K_2CO_3	110	12	55
6	I_2 (1.1)	Et_3N	100	12	n.r.
7	I_2 (1.1)	Pyridine	100	12	n.r.
8	I_2 (1.1)	DIPEA	100	12	n.r.
9	I_2 (1.1)	NaOH	100	12	70
10	I_2 (2.0)	KOH	100	12	71
11	I_2 (2.0)	Na_2CO_3	100	12	70
12	I_2 (2.0)	CS_2CO_3	100	12	69
13	I_2 (2.0)	K_2CO_3	100	12	72
14	I_2 (2.5)	K_2CO_3	100	12	71
15	I_2 (2.0)	K_2CO_3	100	24	71
16	NIS (2.0)	K_2CO_3	100	12	38

[a] Reaction conditions: **1a** (1.0 mmol), **2a** (1.0 mmol), I_2 (2.0 mmol), K_2CO_3 (1.2 mmol), heated in DMSO, open air at 100 °C for 12 h. [b] Isolated yield. n.r. = no reaction.

because this reaction is metal free and generates 1,2-dicarbonyl compounds under identical reaction conditions from multiple substrates (aryl acetylenes–arylethenes–aromatic ketones). To initiate our study aimed at developing an iodine-mediated MPCD strategy for the preparation of proposed heterocycles, the test reaction between phenyl acetylene (**1a**) and 1,2-diaminoethane (**2a**) was carried out in the presence of iodine (1.1 mmol) and K_2CO_3 (1.2 mmol) in DMSO at 80 °C. As expected, the above combination of reagents resulted in the desired product (**4a**), but in low yields (45%) (entry 2 in Table 1). But the above transformation in DMSO at 100 °C in the presence of iodine (2 mmol) and K_2CO_3 (1.2 mmol) afforded the corresponding pyrazine **4a** in 72% yield (entry 13 in Table 1). However, this reaction did not work in the absence of inorganic base. Among various inorganic bases tested, Na_2CO_3, KOH, NaOH and Cs_2CO_3 were all effective, although affording the products with diminished yields, and K_2CO_3 appeared the best among them (Table 1, entries 10–13). Pyridine, triethylamine, and *N,N*-diisopropylethylamine (DIPEA) were also examined (Table 1, entries 6–8), but no product formation was observed. The screening experiments also showed that increasing the amount of iodine did not enhance the yield (Table 1, entry 14) and even after prolonging the reaction time to 24 h (Table 1, entry 15). We have also replaced the I_2 with *N*-iodosuccinimide (NIS) and examined the reaction progress, but it only inhibited the reaction. When the reaction was conducted at a lower temperature, it proceeded with a lower yield (Table 1, entries 1 and 2), and a higher reaction temperature did not increase the yield (Table 1, entry 5).

As depicted in Table 2, a broad variety of pyrazines could be readily obtained under the optimized conditions. The annulation of **2a** with various phenyl acetylenes was first examined.

Table 2 Synthesis of various pyrazines and quinoxalines from aryl acetylenes and 1,2-diamines[a]



[a] Reaction conditions: **1** (1.0 mmol), I_2 (2.0 mmol) and **2**/K_2CO_3 (1.0/1.2 mmol) or **3** (1.0 mmol) in DMSO, open air at 100 °C. Isolated yields provided.

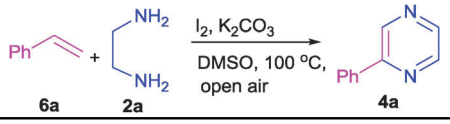
Phenyl acetylenes with electron-donating groups at either *ortho*-, *meta*- or *para*-positions on the phenyl ring all furnished the corresponding products in good yields (71–76%). The presence of an electron-withdrawing group on the phenyl acetylene was also tolerated. However, the product was obtained in moderate yield (65–68%).

As a next step different ethylenediamines were employed in this reaction. Propane-1,2-diamine reacts with both electron-rich and -poor phenyl acetylenes, affording products in good yields (72–76%). As expected, propane-1,2-diamine delivered two regioisomers (1 : 1).

Encouraged by the above results, we turned our attention towards the synthesis of quinoxalines using arylethenes **1** and benzene-1,2-diamine **3** as our next substrates. After several experimental iterations, the optimal reaction conditions emerged with phenyl acetylene **1a** (1.0 mmol), benzene-1,2-diamine **3a** (1.0 mmol), and I_2 (2.0 mmol) at 100 °C in DMSO. To probe the substrate scope for this reaction, a series of substituted phenyl acetylenes were subjected to the optimized reaction conditions (Table 2). Arylethenes with different substituents, such as Me, Et, *t*-Bu and OMe, could all provide the corresponding products with 74–80% yields (Table 2, **5b–f**). Next, the reaction scope of *o*-phenylenediamine was studied (Table 2). The compounds bearing an electron-donating group formed the products in good yields. Notably, mixtures of regioisomers (1 : 0.6) were formed in this transformation (Table 2, **5g–i**, 78–85%). Surprisingly, the reaction involving 3,4-diaminobenzophenone was found to be highly regioselective to produce corresponding products **5j–l** exclusively, in acceptable yields (69–76%). Uptill now, we do not know the reason for this selectivity. The structure of **5k** was unambiguously confirmed by X-ray crystallography (Fig. S2, ESI†).

To expand the scope of the substrates, terminal aryl alkenes were investigated using the conditions optimized for aryl acetylene, but reaction did not occur. To identify suitable conditions for the reaction, a series of oxidants were screened. Initially, the desired product **4** was obtained in 23% yield in the presence of hydrogen peroxide (H_2O_2) (Table 3, entry 3). The oxidants, such as *tert*-butyl hydroperoxide (TBHP) and cumene hydroperoxide (CMHP),

Table 3 Optimization of iodine mediated annulation of phenylethene and 1,2-diaminoethane[a]



6a 2a 4a

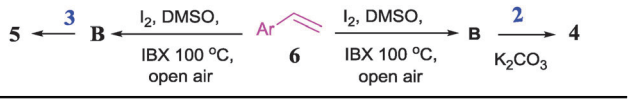
Entry	Reagent (equiv.)	Base (1.2 equiv.)	Oxidant (equiv.)	Temp. (°C)	Time (h)	Yield[b] (%)
1	I_2 (1.1)	—	—	80	12	n.r.
2	I_2 (1.1)	K_2CO_3	—	80	12	Trace
3	I_2 (1.1)	K_2CO_3	H_2O_2 (1.5)	80	12	23
4	I_2 (1.1)	K_2CO_3	H_2O_2 (1.5)	100	12	33
5	I_2 (1.1)	K_2CO_3	H_2O_2 (1.5)	110	12	29
6	I_2 (1.1)	K_2CO_3	TBHP (1.5)	100	12	26
7	I_2 (1.1)	K_2CO_3	CMHP (1.5)	100	12	27
8	I_2 (1.1)	K_2CO_3	IBX (1.5)	100	12	56
9	I_2 (1.1)	NaOH	IBX (1.5)	100	12	53
10	I_2 (2.0)	K_2CO_3	IBX (1.5)	100	12	61
11	I_2 (2.0)	K_2CO_3	IBX (2.0)	100	12	72
12	I_2 (2.0)	K_2CO_3	IBX (2.5)	100	12	68
13	I_2 (2.5)	K_2CO_3	IBX (2.0)	100	12	69
14	I_2 (2.0)	K_2CO_3	IBX (2.0)	100	24	68

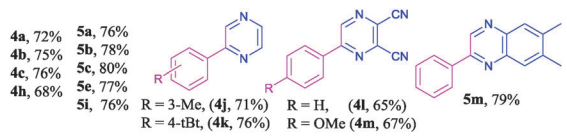
[a] Reaction conditions: **6** (1.0 mmol), I_2 (2.0 mmol), IBX (2.0 mmol) in DMSO at 100 °C for 2–3 h, and then added **2**/K_2CO_3 (1.0/1.2 mmol) or **3** (1.2 mmol) in DMSO, open air at 100 °C. [b] Isolated yields.

were screened. In all the reactions, product **4** was obtained but in lower yields (Table 3, entries 6 and 7). To our delight, the yield was increased to 56% when 2-iodoxybenzoic acid (IBX) was selected as an oxidant (Table 3, entry 8). After extensive optimization, it was found that the desired product could be obtained in 72% yield when **1a** (1 mmol) and I_2/IBX (2.0/2.0 mmol) were mixed and heated at 100 °C for 1.5 h, with the subsequent addition of 1,2-diaminoethane/K_2CO_3 to the mixture for another 10 h at 100 °C (Table 3, entry 11). This optimal condition (absence of base) is also used to synthesize quinoxalines. Then, the scope of both terminal aryl alkenes (**6**) and 1,2-diamines (**2**/**3**) was also explored (Table 4). The results demonstrated that the electronic nature of the aryl alkenes (**6** and **2**/**3**) had little influence on the reaction efficiency, as all the desired products were obtained in moderate to good yields (Table 4, 65–80%).

To further expand the substrate scope, substituted acetophenones **7** were also investigated. Furthermore, acetophenone **7a** in the presence of I_2 in DMSO could easily be transformed to arylglyoxals, which then reacted with 1,2-diaminoethane

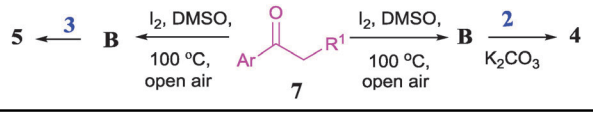
Table 4 Synthesis of various pyrazines and quinoxalines from arylethenes and 1,2-diamines[a]

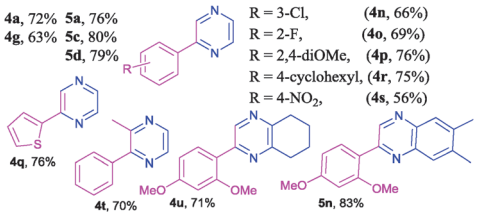




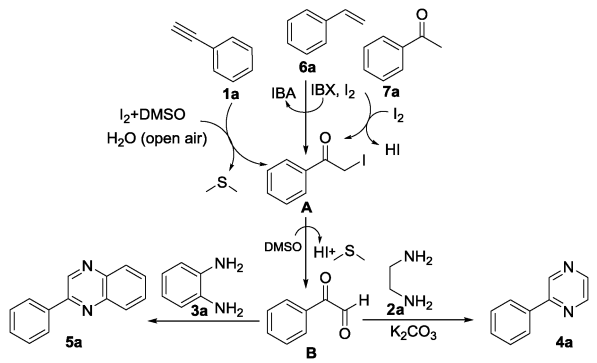
[a] Reaction conditions: **6** (1.0 mmol), IBX (2.0 mmol) I_2 (2.0 mmol) in DMSO at 100 °C for 2–3 h, and then added **2**/K_2CO_3 (1.0/1.2 mmol) or **3** (1.2 mmol) in DMSO, open air at 100 °C. Isolated yields provided.

Table 5 Synthesis of various pyrazines and quinoxalines from aromatic ketones and 1,2-diamines[a]





[a] Reaction conditions: **7** (1.0 mmol), I_2 (2.0 mmol) in DMSO at 100 °C for 2–3 h, and then added **2**/K_2CO_3 (1.0/1.2 mmol) or **3** (1.2 mmol) in DMSO, open air at 100 °C. Isolated yields provided.



Scheme 2 Proposed mechanism.

(**2a**)/K_2CO_3 or benzene-1,2-diamine (**3a**) to afford the corresponding products in one-pot. The electron withdrawing or donating groups present on aromatic ketones were well tolerated to produce **4** and **5** in good yields (Table 5).

As presented in Scheme 2, a possible reaction mechanism for this domino reaction is as follows, using phenyl acetylene **1a**, or styrene **6a**, or acetophenone **7a**, and 1,2-diaminoethane **2a**, or benzene-1,2-diamine **3a** as examples: initially, phenyl acetylene (**1a**) or styrene (**6a**) or acetophenone (**7a**) was converted into phenacyl iodide[27] (**A**) through consecutive iodination and oxidation with I_2 or I_2/IBX. Subsequently, phenacyl iodide (**A**) was further converted into phenylglyoxal (**B**) in DMSO.[3b] Finally, phenylglyoxal (**B**) reacted with **2a**/K_2CO_3 or **3a** *via* a condensation, and oxidative dehydrogenation sequence to afford the desired products **4a** and **5a**, respectively.

In summary, an I_2 promoted domino protocol has been developed to construct pyrazines and quinoxalines from simple and readily available aryl acetylenes–arylethenes–aromatic ketones and 1,2-diaminoethane–benzene-1,2-diamine, which could be useful for generation of a related compound library. The overall process involves three different reactions (iodination, Kornblum oxidation, and condensation) that were self-sequentially assembled in a single reactor. In addition, the protocol could exclusively provide single-regioisomer in the case of 3,4-diaminobenzophenone with different aryl acetylenes. Further studies on the application of this strategy for

the synthesis of pyrazine natural product botryllazine-A starting from **4m** will be reported in due course.

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Notes and references

1 (*a*) L. F. Tietze, G. Brasche and K. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, Germany, 2014; (*b*) H. Pellissier, *Chem. Rev.*, 2012, **113**, 442–524; (*c*) L. F. Tietze, T. Kinzel and C. C. Brazel, *Acc. Chem. Res.*, 2009, **42**, 367–378; (*d*) L. F. Tietze and N. Rackelmann, *Pure Appl. Chem.*, 2004, **76**, 1967–1983; (*e*) J. Poulin, C. M. Grisé-Bard and L. Barriault, *Chem. Soc. Rev.*, 2009, **38**, 3092–3101; (*f*) L. J. Sebren, J. J. Devery III and C. R. Stephenson, *ACS Catal.*, 2014, **4**, 703–716; (*g*) M. Horvat, H. Gorner, K.-D. Warzecha, J. R. Neudörfl, A. G. Griesbeck, K. Mlinaric-Majerski and N. Basaric, *J. Org. Chem.*, 2009, **74**, 8219–8231; (*h*) D.-C. Wang, H.-Y. Niu, M.-S. Xie, G.-R. Qu, H.-X. Wang and H.-M. Guo, *Org. Lett.*, 2013, **16**, 262–265.

2 (*a*) M. Gao, Y. Yang, Y.-D. Wu, C. Deng, W.-M. Shu, D.-X. Zhang, L.-P. Cao, N.-F. She and A.-X. Wu, *Org. Lett.*, 2010, **12**, 4026–4029; (*b*) Y. Yamamoto, H. Hayashi, T. Saigoku and H. Nishiyama, *J. Am. Chem. Soc.*, 2005, **127**, 10804–10805; (*c*) P. J. Alaimo, R. O'Brien III, A. W. Johnson, S. R. Slauson, J. M. O'Brien, E. L. Tyson, A.-L. Marshall, C. E. Ottinger, J. G. Chacon and L. Wallace, *Org. Lett.*, 2008, **10**, 5111–5114.

3 (*a*) W.-J. Xue, Y.-Q. Guo, F.-F. Gao, H.-Z. Li and A.-X. Wu, *Org. Lett.*, 2013, **15**, 890–893; (*b*) Y.-P. Zhu, F.-C. Jia, M.-C. Liu and A.-X. Wu, *Org. Lett.*, 2012, **14**, 4414–4417; (*c*) Y.-P. Zhu, M. Lian, F.-C. Jia, M.-C. Liu, J.-J. Yuan, Q.-H. Gao and A.-X. Wu, *Chem. Commun.*, 2012, **48**, 9086–9088; (*d*) Y.-P. Zhu, Q.-H. Gao, M. Lian, J.-J. Yuan, M.-C. Liu, Q. Zhao, Y. Yang and A.-X. Wu, *Chem. Commun.*, 2011, **47**, 12700–12702.

4 (*a*) L. E. Seitz, W. J. Suling and R. C. Reynolds, *J. Med. Chem.*, 2002, **45**, 5604–5606; (*b*) F. Palacios, A. M. Ochoa de Retana, J. I. Gil and R. Lopez de Munain, *Org. Lett.*, 2002, **4**, 2405–2408.

5 (*a*) A. Jaso, B. Zarranz, I. Aldana and A. Monge, *J. Med. Chem.*, 2005, **48**, 2019–2025; (*b*) M. Sato, T. Nakazawa, Y. Tsunematsu, K. Hotta and K. Watanabe, *Curr. Opin. Chem. Biol.*, 2013, **17**, 537–545.

6 M. Dolezal, M. Miletin, J. Kunes and K. Kralova, *Molecules*, 2002, **7**, 363–373.

7 M. H. Gezginci, A. R. Martin and S. G. Franzblau, *J. Med. Chem.*, 2001, **44**, 1560–1563.

8 M. Doležal and K. Král'ová, *Herbicides, Theory and Applications*, 2011, pp. 581–610.

9 A. R. Katritzky, C. W. Rees and K. T. Potts, *Comprehensive heterocyclic chemistry: the structure, reactions, synthesis and uses of heterocyclic compounds*, Pergamon Press, Oxford UK, 1984.

10 G. Buchbauer, C. T. Klein, B. Wailzer and P. Wolschann, *J. Agric. Food Chem.*, 2000, **48**, 4273–4278.

11 (*a*) B. R. Bohman, L. Jeffares, G. Flematti, L. T. Byrne, B. W. Skelton, R. D. Phillips, K. W. Dixon, R. Peakall and R. A. Barrow, *J. Nat. Prod.*, 2012, **75**, 1589–1594; (*b*) B. R. Bohman, L. Jeffares, G. Flematti, R. D. Phillips, K. W. Dixon, R. Peakall and R. A. Barrow, *Org. Lett.*, 2012, **14**, 2576–2578.

12 L. You, E. J. Cho, J. Leavitt, L.-C. Ma, G. T. Montelione, E. V. Anslyn, R. M. Krug, A. Ellington and J. D. Robertus, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 3007–3011.

13 L. E. Seitz, W. J. Suling and R. C. Reynolds, *J. Med. Chem.*, 2002, **45**, 5604–5606.

14 S. T. Hazeldine, L. Polin, J. Kushner, J. Paluch, K. White, M. Edelstein, E. Palomino, T. H. Corbett and J. P. Horwitz, *J. Med. Chem.*, 2001, **44**, 1758–1776.

15 A. Abu-Hashem, M. Gouda and F. Badria, *Eur. J. Med. Chem.*, 2010, **45**, 1976–1981.

16 S. Dailey, W. J. Feast, R. J. Peace, I. C. Sage, S. Till and E. L. Wood, *J. Mater. Chem.*, 2001, **11**, 2238–2243.

17 J. L. Sessler, H. Maeda, T. Mizuno, V. M. Lynch and H. Furuta, *J. Am. Chem. Soc.*, 2002, **124**, 13474–13479.

18 (*a*) J. Emmerich, Q. Hu, N. Hanke and R. W. Hartmann, *J. Med. Chem.*, 2013, **56**, 6022–6032; (*b*) A. Ohta, A. Imazeki, Y. Itoigawa, H. Yamada, C. Suga, C. Takagai, H. Sano and T. Watanabe, *J. Heterocycl. Chem.*, 1983, **20**, 311–320.

19 (*a*) V. Kunkuma, L. A. P. D. Bethala, Y. Bhongiri, B. N. P. Rachapudi and S. S. P. Potharaju, *Eur. J. Chem.*, 2011, **2**, 495–498; (*b*) H. K. Kadam, S. Khan, R. A. Kunkalkar and S. G. Tilve, *Tetrahedron Lett.*, 2013, **54**, 1003–1007.

20 (*a*) D. F. Taber, P. W. DeMatteo and K. V. Taluskie, *J. Org. Chem.*, 2007, **72**, 1492–1494; (*b*) A. Vidal-Albalat, S. Rodríguez and F. V. González, *Org. Lett.*, 2014, **16**, 1752–1755.

21 (*a*) S. Antoniotti and E. Duñach, *Tetrahedron Lett.*, 2002, **43**, 3971–3973; (*b*) A. Vidal-Albalat, S. Rodríguez and F. V. González, *Org. Lett.*, 2014, **16**, 1752–1755.

22 (*a*) S. A. Raw, C. D. Wilfred and R. J. Taylor, *Chem. Commun.*, 2003, 2286–2287; (*b*) S. A. Raw, C. D. Wilfred and R. J. Taylor, *Org. Biomol. Chem.*, 2004, **2**, 788–796.

23 (*a*) R. S. Robinson and R. J. Taylor, *Synlett*, 2005, 1003–1005; (*b*) S. A. Raw, C. D. Wilfred and R. J. Taylor, *Chem. Commun.*, 2003, 2286–2287.

24 (*a*) T. A. Elmaaty and L. W. Castle, *Org. Lett.*, 2005, **7**, 5529–5530; (*b*) P. P. Singh, S. K. Aithagani, M. Yadav, V. P. Singh and R. A. Vishwakarma, *J. Org. Chem.*, 2013, **78**, 2639–2648.

25 (*a*) B. C. Raju, K. V. Prasad, G. Saidachary and B. Sridhar, *Org. Lett.*, 2014, **16**, 420–423; (*b*) Y.-H. Cho, K.-H. Kim and C.-H. Cheon, *J. Org. Chem.*, 2014, **79**, 901–907; (*c*) C. F. Gers, J. Nordmann, C. Kumru, W. Frank and T. J. Müller, *J. Org. Chem.*, 2014, **79**, 3296–3310.

26 (*a*) W. Wang, Y. Shen, X. Meng, M. Zhao, Y. Chen and B. Chen, *Org. Lett.*, 2011, **13**, 4514–4517; (*b*) S. Shi, T. Wang, W. Yang, M. Rudolph and A. S. K. Hashmi, *Chem. – Eur. J.*, 2013, **19**, 6576–6580; (*c*) S. Okumura, Y. Takeda, K. Kiyokawa and S. Minakata, *Chem. Commun.*, 2013, **49**, 9266–9268; (*d*) M. Rudolph and A. S. K. Hashmi, *Chem. Commun.*, 2011, **47**, 6536–6544; (*e*) A. Hashmi and M. Buehrle, *Aldrichimica Acta*, 2010, **43**, 27–33.

27 To gain an insight into the mechanism of the iodine mediated pyrazines and quinoxalines synthesis *via* MPCD strategy, the following control experiment was performed. Intermediate '**A**' was obtained in 82% yield *via* reaction of **1a** with I_2 (2.0 mmol) in DMSO, open air conditions in the absence of 1,2-diaminoethane where the reaction is slow enough to allow its isolation. Subsequent conversion of phenacyl iodide (**A**) into phenylglyoxal (**B**) in DMSO was well proved by Wu *et al.*[3b]

