One-pot Synthesis of 2-(quinoxalin-2-yl)benzoate Through NBS-Mediated Sequential Reaction of 2-Alkynylbenozate and Aryl-1,2-diamine

Bin Huang, Lele Ma, Guanyinsheng Qiu

PII: S0040-4039(17)30516-6
DOI: http://dx.doi.org/10.1016/j.tetlet.2017.04.063
Reference: TETL 48855

To appear in: *Tetrahedron Letters*

Received Date: 19 March 2017
Revised Date: 14 April 2017
Accepted Date: 18 April 2017

Please cite this article as: Huang, B., Ma, L., Qiu, G., One-pot Synthesis of 2-(quinoxalin-2-yl)benzoate Through NBS-Mediated Sequential Reaction of 2-Alkynylbenozate and Aryl-1,2-diamine, *Tetrahedron Letters* (2017), doi: http://dx.doi.org/10.1016/j.tetlet.2017.04.063

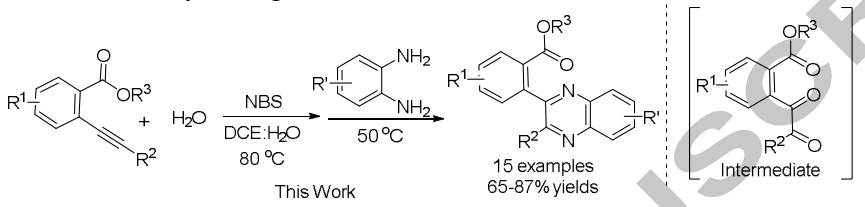
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

One-pot Synthesis of 2-(quinoxalin-2-yl)benzoate Through NBS-Mediated Sequential Reaction of 2-Alkynylbenozate and Aryl-1,2-diamine

Leave this area blank for abstract info.

Bin Huang,[+] LeLe Ma,[+] and Guanyinsheng Qiu*



Tetrahedron Letters
journal homepage: www.elsevier.com

One-pot Synthesis of 2-(quinoxalin-2-yl)benzoate Through NBS-Mediated Sequential Reaction of 2-Alkynylbenozate and Aryl-1,2-diamine

Bin Huang,[+] Lele Ma, [+] and Guanyinsheng Qiu[*]

College of Biological, Chemical Science and Engineering, Jiaxing University, 118 Jiahang Road, Jiaxing 314001, China.

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Benzil-o-carboxylate
N-bromosuccinimide
2-alkynylbenzoate
quinoxaline
Tandem reaction

ABSTRACT

A metal-free route involving a sequential reaction of 2-alknylbenzoate and aryl-1,2-diamine is described for the generation of 2-(quinoxalin-2-yl)benzoate. The sequential reaction combines NBS-mediated diketonization of 2-alknylbenzoate and condensation reaction with aryl-1,2-diamine, and proceeds smoothly under mild reaction conditions and an array of 2-(quinoxalin-2-yl)benzoate is achieved with high efficiency and excellent functional group tolerance. Mechanism studies indicate oxygen transfer reaction is observed and water is incorporated into neighboring ester group.

As a privileged structural motif, quinoxaline core has been in-depth investigation due to its excellent property in fluorescence chemistry and Biochemistry.[1] To improve and modify its property, it was highly desirable to install a pre-function into the quinoxaline core, which could be converted into expected building blocks by transitional-metal-catalyzed cross coupling reaction and other classical organic reactions. Therefore, tremendous efforts were made to develop synthetic methodology for introducing these pre-functions. Considering the nature of quinoxaline core behaving as a directing group, C-H functionalization with transitional metal catalysis was thus recognized as a powerful tool to derivatize the quinoxaline skeleton (scheme 1a).[2] By this strategy, numerous pre-functions such as nitro group, acyl group and halo group were efficiently incorporated. Basically, the established achievements were ascribed to a late-stage[3] functionalization of quinoxaline. In this paper, we would like to disclose a distinctive pathway that a synthetically useful handle in quinoxaline scaffold could be smuggled by an "early-stage" strategy. Given its versatility of ester group for further structural elaboration, we focused our attention on synthetic methodology development of ester-attached quinoxalines. The "early-stage" strategy proposed here represented a procedure that the ester group has been incorporated before the quinoxaline core was constructed.

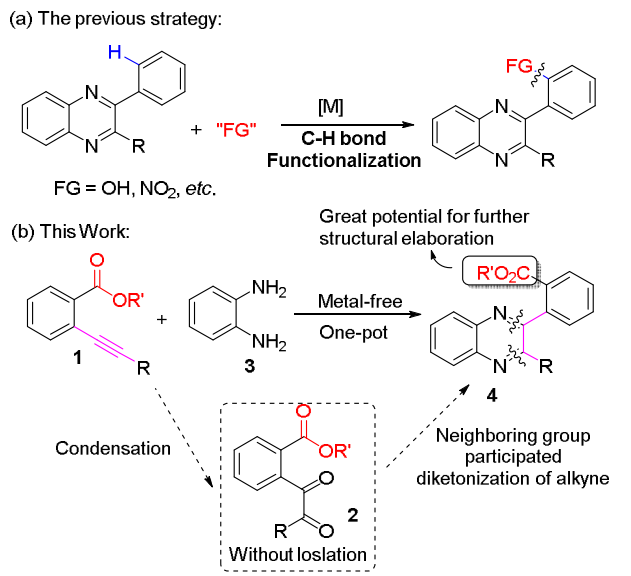
Retrosynthetically, the ester-connected quinoxalines **4** could be synthesized from a condensation of benzil-*o*-carboxylate **2** with aryl-1,2-diamine **3**. Benzil-*o*-carboxylate **2**, *in situ* generated from a neighbouring group-participated diketonization of triple bond in 2-alkynylbenzoate **1**, was proposed as an intermediate. In our design, the final quinoxalines **4** was achieved via a sequential reaction[4] (Scheme 1b). In principal, diketonization of 2-alkynylbenzoate should be an efficiency-determining step since the condensation of benzil-*o*-carboxylate with aryl-1,2-diamine was a well-known reaction.[5]

To the best of our knowledge, gold-catalyzed diketonization of 2-alkynylbenzoate was highlighted by Liu and co-workers in the presence of Selectfluor.[6a-6b] Mechanism investigation implied that the neighboring ester group served as a directing group to assist difluorohydration of triple bond in 2-alkynylbenzoate. The difluorohydrative intermediate was *in situ* hydrolyzed into benzil-*o*-carboxylate. Therefore, both of two oxygen atoms in keto group of benzil-*o*-carboxylate came from water. Additionally, the reaction scope exploration indicated that the reaction of 2-alkylethynylbenzoate did not give the desired product. Inspired by what mentioned above, we would like to develop a metal-free procedure for the diketonization of 2-alkynylbenzoate to provide benzil-*o*-carboxylate and be further applied into the construction of 2-(quinoxalin-2-yl)benzoate in an one-pot manner.[7]

As we know, a metal-free version on diketonization of 2-alkynylbenzaldehyde has been developed by Srinivasan and co-workers.[8] According to their findings, I_2 or ICl/water reaction

[+]: These authors contributed equally.

[*]: Corresponding author: G. Qiu, Tel.: +86-0573-83642057; fax: +86-0573-83642057; e-mail: 11110220028@fudan.edu.cn

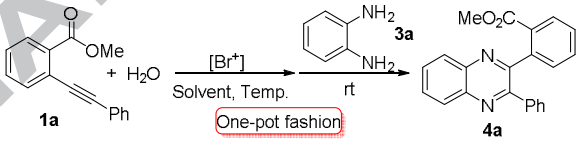


Scheme 1 Proposed route for the synthesis of 2-(quinoxalin-2-yl)benzoate from aryl-1,2-diamine and 2-alkynylbenzoate

system enabled diketonization of 2-alkynylbenzaldehyde to form tricarbonyl compounds. Mechanism studies indicated that a neighboring aldehyde group-participated electrophilic 6-*endo-dig* iodocyclization of 2-alkynylbenzaldehyde and another electrophilic iodohydration of the resulting isochromene cation intermediate gave rise to the tricarbonyl compounds. It was noteworthy that oxygen in aldehyde carbonyl of 2-alkynylbenzaldehyde already transferred into triple bond to produce one of keto carbonyl. In light of the above information,[9] we envisioned that this electrophilic 6-*endo-dig* halocyclization of 2-alkynylbenzoate and oxidative ring-opening of the resulting isocoumarin cation intermediate could be used in the diketonization for the formation of benzil-*o*-carboxylate. The *in situ* generated benzil-*o*-carboxylate condensed with aryl-1,2-diamine to offer the desired 2-(quinoxalin-2-yl)benzoate. To verify the practicality of this projected transformation, we started to optimize the reaction conditions. The reaction of methyl 2-phenylethynylbenzoate **1a** and benzene-1,2-diamine **3a** was employed as the model reaction.

Initially, various electrophiles were elaborated to mediate *6-endo-dig* cyclization of 2-alkynylbenzoate. Considering high efficiency of I_2 or ICl reaction system in diketonization of 2-alkynylbenzaldehyde, both I_2 and ICl were explored to trigger the model reaction. To our surprise, the model reaction did not provide the desired product **4a** but a compound 4-iodoisocoumarin (data not shown in table 1). The different result from the Srinivasan's findings promoted us to find a new reaction system. According to our previous findings, we were pleased to find that $K_2S_2O_8$ could oxidize bromide salt to bromo radical and hypobromite.[10] Consequently, *tetra-n*-butylammonium bromide (TBAB) and $K_2S_2O_8$ were employed as reaction system. To our disappoint, the model reaction still gave a negative result (entry 1, table 1). A similar result was observed when liquid bromine was used as the electrophile (entry 2, table 1). Pleasingly, *N*-bromosuccinimide (NBS) was an effective mediator to trigger diketonization of 2-alkynylbenzoate, and this sequential reaction provided the desired product **4a** in 12% total yield (entry 3, table 1). Encouraged by this promising outcome, we then examined other result-affecting factors. From the effect of reaction temperature, it seemed that temperature made great impact on the reaction. The reaction efficiency was greatly improved when the reaction temperature was increased to 50 °C, leading to the desired product **4a** in 49% yield (entry 4, table 1). Further increase of temperature to 80 °C afforded the desired product **4a** in 56% yield (entry 5, table 1). Solvent screening results indicated that DCE:H_2O (v/v, 1;1) was the best choice (entry 6, table 1). Other co-solvents such as *tetra*hydrofuran:water and *N*, *N*-dimethylformamide:water gave inferior yields (entries 7-8, table 1). Interestingly, Pure water was recognized as an efficient solvent to offer the desired product **4a** in 62% yield (entry 9, table 1). Screening on different ratios between DCE and water suggested that 1:1 was the best choice (entries 10-11, table 1). To improve reaction speed of condensation step, we also attempted to increase the condensation reaction temperature to 50 °C. To our delight, the total efficiency of this one-pot reaction was further improved, leading to the final product **4a** in 85% yield, and the total reaction time was reduced to 12 hrs (entry 12, table 1). The standard procedure using the optimized reaction conditions were following: NBS (2.1 equiv) was added into a mixture of 2-alkynylbenzoate **1a** (0.2 mmol) at DCE:H_2O (2 mL, 1:1, v/v). The resulting mixture was stirred at 80 °C. After completion of the reaction as indicated by TLC, benzene-1,2-diamine (1.2 equiv) was added. The mixture was stirred at 50 °C till the reaction completed.

Table 1 Initial studies for the synthesis of 2-(quinoxalin-2-yl)benzoate from aryl-1,2-diamine **3a** and 2-alkynylbenzoate **1a** [a]

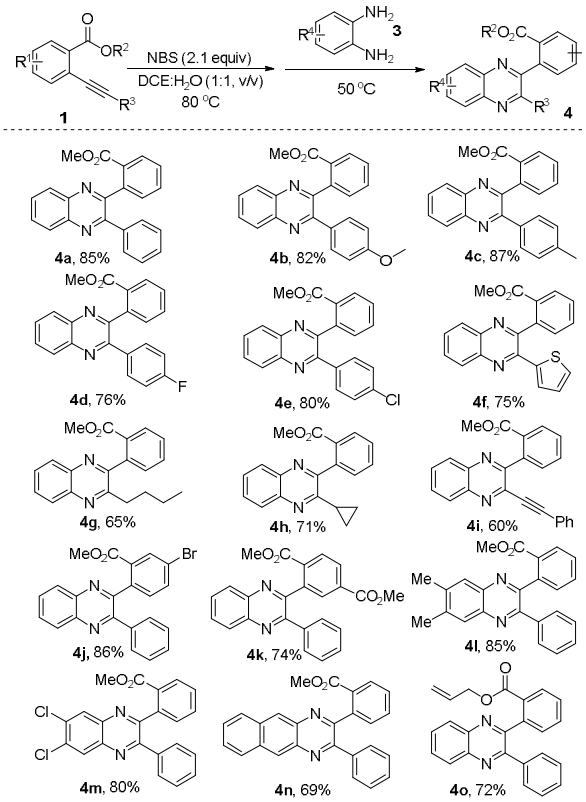


Entry	[Br$^+$]	Solvent	Temp. (°C)	Yield (%)[b]
1	TBAB/ $K_2S_2O_8$	DCM:H_2O (v/v, 1:1)	rt	complex
2	Br_2	DCM:H_2O (v/v, 1:1)	rt	trace[c]
3	NBS	DCM:H_2O (v/v, 1:1)	rt	12
4	NBS	DCM:H_2O (v/v, 1:1)	50	49
5	NBS	DCM:H_2O (v/v, 1:1)	80	56
6	NBS	DCE:H_2O (v/v, 1:1)	80	75
7	NBS	THF:H_2O (v/v, 1:1)	80	N.R.
8	NBS	DMF:H_2O (v/v, 1:1)	80	19
9	NBS	H_2O	80	62
10	NBS	DCE:H_2O (v/v, 5:1)	80	70
11	NBS	DCE:H_2O (v/v, 1:5)	80	61
12	**NBS**	**DCE:H_2O (v/v, 1:1)**	**80**	**85[d]**

[a] Reaction conditions: **1a** (0.2 mmol), [Br$^+$] (2.1 equiv), **3a** (1.2 equiv), solvent (2 mL); [b] Isolated yield based on 2-alkynylbenzoate **1a**. [c] 4-bromoisocoumarin was mainly observed. [d] The condensation reaction was conducted at 50 °C. DCE = 1,2-dichlorethane; N. R. = no reaction

With the optimized condition in hand (entry 12, table 1), we then examined the scope. The results were illustrated in Table 2. A series of 2-(quinoxalin-2-yl)benzoate **4** were achieved as expected. For example, the substrates with 4-methylphenylethynyl, 4-methoxylphenylethynyl, 4-fluorophenylethynyl, and 4-chlorophenylethynyl were

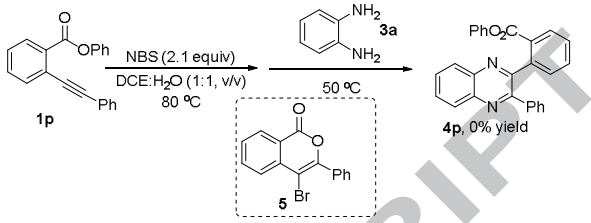
Table 2 2-(quinoxalin-2-yl)benzoate from aryl-1,2-diamine **3a** and 2-alkynylbenzoate **1a**[a]



a Isolated yield based on 2-alkynylbenzoate **1**.

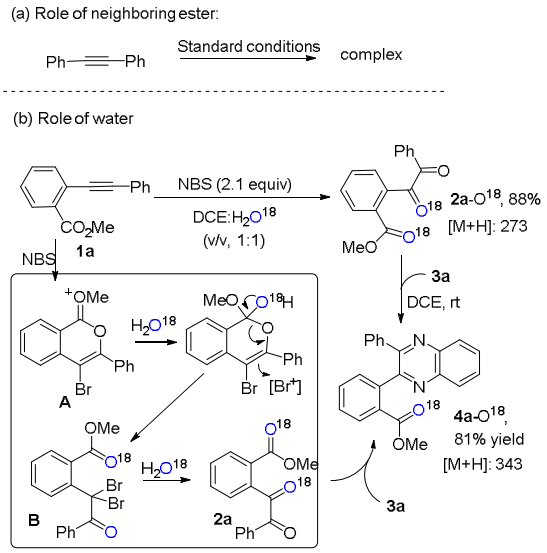
compatible for the reactions, producing corresponding 2-(quinoxalin-2-yl)benzoate **4a-4e** in 76-87% yields. Particularly, heteroarylethynyl-connected substrate proved to be an efficient reaction partner. For instance, under standard conditions the reaction of 2-thiophenylethynylbenzoate **1f** provided corresponding product **4f** in 75% yield. The alkyl-attached substrates on R^3 were suitable for the reaction. Under standard conditions the reactions of methyl 2-(hex-1-yn-1-yl)benzoate **1g** and methyl 2-(cyclopropylethynyl)benzoate **1h** gave rise to the corresponding 2-(quinoxalin-2-yl)benzoate **4g** and **4h** in 65% and 71% yield, respectively. Interestingly, the reaction of methyl 2-(phenylbuta-1,3-diyn-1-yl)benzoate **1i** afforded the desired sulphonate **4i** in 60% yield, where the C-C triple bond far away from ester group was survived, thus supporting the fact that neighboring ester-participation was required for the diketonization of alkynes. Additionally, the substituents attached on R^1 were also tested accordingly. To our delight, the corresponding products **4j** and **4k** were achieved in good yields when bromo and ester-linked substrates were used, respectively. Subsequently, we explored the effect of various aryl-1,2-diamines. To our delight, 4,5-dichloro and 4,5-dimethyl substituted benzene-1,2-diamine were efficient reaction partners, leading to the corresponding 2-(quinoxalin-2-yl)benzoate **4l** and **4m** in good yields. In particular, the reaction of methyl 2-alkynylbenzoate **1a** and naphthalene-2,3-diamine worked well, producing **4n** in 69% yield. Different esters were also explored. For example, the reaction of allyl 2-(phenylethynyl)benzoate **1o** proceeded smoothly under standard conditions, and the desired product **4o** was obtained in 72% yield. To our surprise, the reaction of phenyl 2-(phenylethynyl)benzoate **1p** did not give rise to the desired product **4p** (Table 3). A different compound 4-bromoisocoumarin **5** was isolated in the reaction. A blank experiment of **1p** without adding benzene-1,2-diamine **3a** provided the compound **5**, which suggested the diketonization failed to happened to the substrate **1p**.

Table 3 The reaction of phenyl 2-alkynylbenzoate**1p** [a]



[a] Isolated yield based on 2-alkynylbenzoate 1.

To make insight into the mechanism of the reaction, several control experiments were carried out. Firstly, a control experiment using the alkyne without neighboring ester group did not provide the desired quinoxaline core, and the reaction became complex. This reaction suggested an important role of neighboring ester in diketonization. Subsequently, we would like to identify the role of water. The solvent using DCE:H_2O^{18} was used under standard conditions. Electrospray ionization mass spectroscopic analysis showed that two equivalents of water were incorporated in the step of diketonization of 2-alkynylbenzoate **1a** since a strong signal at [M+H] = 273 was identified to be **2a**-O^{18}. To clarify exact site of oxygen-18, the condensation of **2a**-O^{18} with benzene-1,2-diamine **3a** was carried out. Electrospray ionization mass spectroscopic analysis of the product **4a** showed the quinoxaline **4a** contained an oxygen-18, showing one equivalent of water being transferred into ester group.



Scheme 2 Control experiments and proposed mechanism

In light of above results, a plausible mechanism was proposed in Scheme 2. For the diketonization step, an NBS-promoted 6-*endo* bromocyclization initiated the reaction with the formation of a 4-bromoisocoumarinium intermediate **A**. The intermediate **A** was attacked by water in the presence of another NBS to produce dibromohydrative product **B** through oxidative ring-opening reaction. The hydrolysis of **B** provided benzil-*o*-carboxylate intermediate **2**. The condensation of benzil-*o*-carboxylate with 1,2-diamine gave rise to quinoxaline **4**.

In conclusion, we have developed a metal-free route for the generation of 2-(quinoxalin-2-yl)benzoate from 2-alknylbenzoate and aryl-1,2-diamine. The sequential reaction combined a NBS-mediated diketonization of 2-alknylbenzoate and condensation reaction with aryl-1,2-diamine, and proceeded smoothly under mild reaction conditions and an array of 2-(quinoxalin-2-yl)benzoate was achieved with high efficiency and an excellent functional group tolerance. Mechanism studies indicated oxygen transfer reaction was observed and water was incorporated into the neighboring ester group.

Acknowledgments

Financial supports from the Natural Science Foundation of China (No: 21502069), the Natural Science Foundation of Zhejiang Province (No: LQ15B020006) and the Ph.D. Scientific Research Starting Foundation of Jiaxing University (No: 70515015) and Summit Program of Jiaxing University for Leading Talents are gratefully acknowledged.

References and notes

1. For the selected reviews on applications of quinoxaline chemistry, see: (a) Yuan, J.; Ouyang, J.; Cimrova, V.; Leclerc, M.; Najari, A.; Zou, Y. *J. Mater. Chem. C: Material for Option and Electronic Device* **2017**, *5*, 1858; (b) El Newahie, A. M. S.; Ismail, N. S. M.; Ahou El Ella, D. A.; Abouzid, K. A. M. *Archiv der Pharmazie* **2016**, *349*, 309; (c) Pareek, A.; Kishor, D. *International Journal of Pharma and Bio Sciences*, **2015**, *6*, 568; (d) Padvi, P. A.; Mahale, G. H.; Pawar, D. E.; Falak, C. S.; Kendre, A. V. *World J. Pharm. Res.* **2015**, *4*, 1892.
2. (a) Liu，Y.-K.; Lou, S.-J.; Xu, D.-Q.; Xu, Z.-Y. *Chem. Eur. J.* **2010**, *16*, 13590; (b) Zhang, W.; Lou, S.; Liu, Y.; Xu, Z. *J. Org. Chem.* **2013**, *78*, 5932; (c) Lou, S.-J.; Xu, D.-Q.; Xia, A.-B.; Wang, Y.-F.; Liu, Y.-K.; Du, X.-H.; Xu, Z.-Y. *Chem. Commun.* **2013**, *49*, 6218; (d) Santra, S. K.; Banerjee, A.; Khatun, N.; Samanta, A.; Patel, B. K. *RSC Adv.* **2015**, *5*, 11960; (e) Santra, S. K.; Banerjee, A.; Patel, B. K. *Tetrahedron* **2014**, *70*, 2422; (f) Khatun, N.; Banerjee, A.; Santra, S. K.; Behera, A.; Patel, B. K. *RSC Adv*. **2014**, *4*, 54532; (g) Kumar, S.; Saunthwal, R. K.; Mujahid, M.; Aggarwal, T.; Verma, A. K. *J. Org. Chem.* **2016**, *81*, 9912; (h) Santra, S. K.; Banerjee, K. N.; Patal, B. K. *Eur. J. Org. Chem.* **2015**, 350; (i) Reddy, B. V. S.; Ramesh, K.; Yadav, J. S. *Synlett* **2011**, 169; (j) Dong, J.; Long, Z.; Song, F.; Wu, N.; Guo, Q.; Lan, J.; You, J. *Angew. Chem. Int. Ed.* **2013**, *52*, 580; (k) Piechowska, J.; Vikki, K.; Sadowski, B.; Lemmetyinen, H.; Tkackenko, N. V.; Gryko, D. T. *J. Phys. Chem. A* **2014**, *118*, 144; (l) Santra, S. K.; Banerjee, A.; Mohanta, P. R.; Patel B. K. *J. Org. Chem.* **2016**, *81*, 6066;
3. For selected reviews on the strategy of "late-stage functionalization", see:(a) Vita, M. V.; Waser, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 5290; (b) Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2015**, *54*, 3216; (c) Besset, T.; Schneider, C.; Cahard, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 5048; (d) Barata-Vallejo, S.; Bonesi, S.; Postigo, A. *Org. Biomol. Chem.* **2016**, *14*, 7150;
4. For the selected reviews on sequential reaction, see: (a) Zeng, X.; *Chem. Rev.* **2013**, *113*, 6864; (b) Skrydstrup, T. *Angew. Chem., Int. Ed.* **1997**, *36*, 345; (c) Tietze, L. F.; Beifuse, U. *Angew. Chem., Int. Ed.* **1993**, *32*, 131.
5. For selected recent examples, see: (a) Ingale, A. P.; Netake, A. M.; Shinde, S. V. *Hetercyclic Lett.* **2016**, *6*, 333; (b) Harsha, K. B.; Rangappa, K. K. S. *RSC Adv.* **2016**, *6*, 57154; (c) Lassagne, F.; Chevallier, F. T.; Dorcet, V.; Mongin, F.; Domingo, L. R. *Synthesis* **2015**, *47*, 2680; (d) Aghapoor, K.; Mohsenzadeh, F.; Shakeri, A.; Darabi, H. R.; Ghassemzadeh, M.; Neumuller, B. *J. Organometallic Chem.* **2013**, *743*, 170; (e) Digwal, C. S.; Yadav, U.; Sakla, A. P.; Sri Ramya, P. V.; Aaghaz, S.; Kamal, A. *Tetrahedron Lett*. **2016**, *57*, 4012; (f) Pramanik, A.; Roy, A.; Khan, S.; Ghatak, A.; Bhar, S. *Tetrahedron Lett*. **2014**, *55*, 1771; (g) Zhang, C.; Xu, Z.; Zhang, L.; Jiao, N. *Tetrahedron* **2012**, *68*, 5258; (h) Lian, M.; Li, Q.; Zhu, P.; Yin, G.; Wu, A. *Tetrahedron* **2012**, *68*, 9598; (i) Cai, J.-J.; Zou, J.-P.; Pan, X.-Q.; Zhang, W. *Tetrahedron Lett*. **2008**, *49*, 7386; (j) Zhao, Z.; Wisnoski, D. D.; Wolkenberg, S. E.; Leister, W. H.; Wang, Y.; Lindsley, C. W. *Tetrahedron Lett*. **2004**, *45*, 4873; (k) Kaupp, G.; Naimi-Jamal, M. R. *Eur. J. Org. Chem.* **2002**, 1368; (l) More, S. V.; Sastry, M. N. V.; Wang, C.-C.; Yao, C. -F. *Tetrahedron Lett*. **2005**, *46*, 6345.
6. For *ortho*-group assisted diketonization of alkynes, see: (a) Liu, Y.; Chen, X.; Zhang, J.; Xu, Z.; *Synlett* **2013**, *24*, 1371; (b) Zhang, W.; Zhang, J.; Liu, Y.; Xu, Z. *Synlett* **2013**, *24*, 2709; (c) Majumdar, K. C.; Ansary, I.; De Narayan, R.; Roy, B. *Synthesis* **2011**, 2951; For transitional-metal-catalyzed diketonization of alkynes without *ortho*-group, see: (a) Xu, Y.; Wan, X. *Tetrahedron Lett.* **2013**, *54*, 642; (b) Gao, A.; Yang, F.; Li, J.; Wu, Y. *Tetrahedron* 2012, 68, 4950; (c) Ren, W.; Xia, Y.; Ji, S.-J.; Zhang, Y.; Wan, X.; Zhao, J. *Org. Lett.* **2009**, *11*, 1841; (d) Xu, C.-F.; Xu, M.; Jia, Y.-X.; Li, C.-Y. *Org. Lett*. **2011**, *13*, 1556; (e) Zhu, X.; Li, P.; Shi, Q.; Wang, L. *Green. Chem.* **2016**, *18*, 6373; (f) Jung, M. E.; Deng, G. *Org. Lett*. **2014**, *16*, 2142; Metal-free procedure, see:(a) Liu, M.; Fu, H.; Jiang, Y.; Zhao, Y. *Synthesis* **2008**, 2879; (b) Yusubov, M. S.-O.; Filimonov, V. D.. *Synthesis* **1991**, 131;
7. For selected review on one-pot synthesis, see: Hayashi, Y. *Chem. Sci.*, **2016**, *7*, 866. For our recent works on one-pot reaction, see: (a) Sheng, J.; Li, Y.; Qiu, G. *Org. Chem. Front.* **2017**, *4*, 95; (b) Li, Y.; Qiu, G.; Wang, H.; Sheng, J. *Tetrahedron Lett*. **2017**, *58*, 690.
8. (a) Sakthivel, K.; Srinivasan, K. *Eur. J. Org. Chem.* **2011**, 2781; (b) Sakthivel, K.; Srinivasan, K. *Eur. J. Org. Chem.* **2013**, 3386.
9. For electrophilic *6-endo* bromocyclization of *o*-alkynylbenzoates: Oliver, M. A.; Gandour, R. D. *J. Org. Chem.* **1984**, *49*, 558. For electrophilic *6-endo* Iodocyclization of *o*-alkynylbenzoates: (a) Yao, T.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5936; (b) Yao, T.; Larock, R. C. *Tetrahedron Lett.* **2002**, *43*, 7401; (c) Mehta, S.; Waldo, J. P.; Larock, R. C. *J. Org. Chem*. **2009**, *74*, 1141; (d) Peuchmaur, M.; Lisowski, V.; Gandreuil, C.; Maillard, L. T.; Martinez, J.; Hernandez, J.-F. *J. Org. Chem.* **2009**, *74*, 4158; (e) Verma, A. K.; Rustagi, V.; Aggarwal, T.; Singh, A. P. *J. Org. Chem.* **2010**, *75*, 7691; (f) Verma, A. K.; Aggarwal, T.; Rustagi, V.; Larock, R. C. *Chem. Commun*. **2010**, *46*, 4064; (g) Barluenga, J.; Llavona, L.; Yus, M.; Concellon, J. M. *Tetrahedron Lett*. **1991**, *47*, 7875.
10. (a) Qiu, G.; Liu, T.; Ding, Q. *Org. Chem. Front.*, **2016**, *3*, 510; (b) Qiu, G.; Li, Y.; Ma, L.; Zhou, H. *Org. Chem. Front.*, **2017**, *4*, DOI: 10.1039/C6QO00840B

Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.

Research Highlights:

1) Various ester-linked quinoxalines are synthesized from *o*-alkynylbenzoate.

2) Tandem NBS-mediated diketonization and condensation reaction are involved.

3) Ester Oxygen transfer reaction is recognized in the diketonization reaction.