

Metal-free syntheses of oxazoles and their analogues based on λ^3 -iodane-mediated cycloisomerization/functionalization reactions or [2+2+1] cycloaddition type reactions

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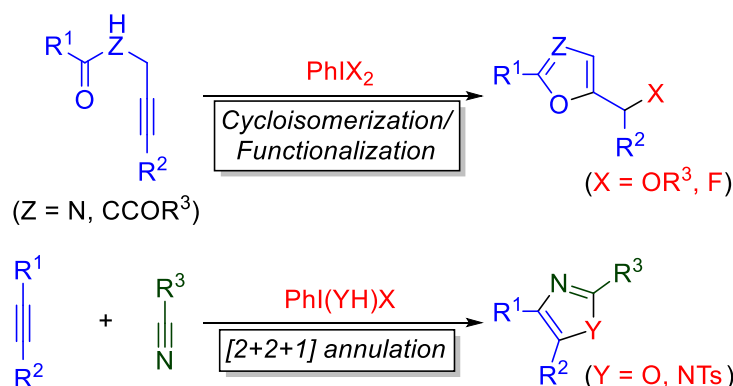
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Abstract

As a metal-free construction of oxazoles and furans concomitant with the introduction of oxygen functional groups or fluorine atoms into the side chains, we have developed λ^3 -iodane-mediated cycloisomerization/functionalization reactions of propargyl compounds. In these reactions, aryl- λ^3 -iodane ArI(X)Y works not only as a donor of heteroatomic functional groups but also as an activator of carbon-carbon triple bonds. Therefore, this methodology is not required any transition metal catalysts, which are frequently used in previous methods. Furthermore, this methodology can be extended to λ^3 -iodane-mediated [2+2+1] cycloaddition type reactions of alkynes, nitriles and heteroatoms for metal-free formation of oxazoles and imidazoles.



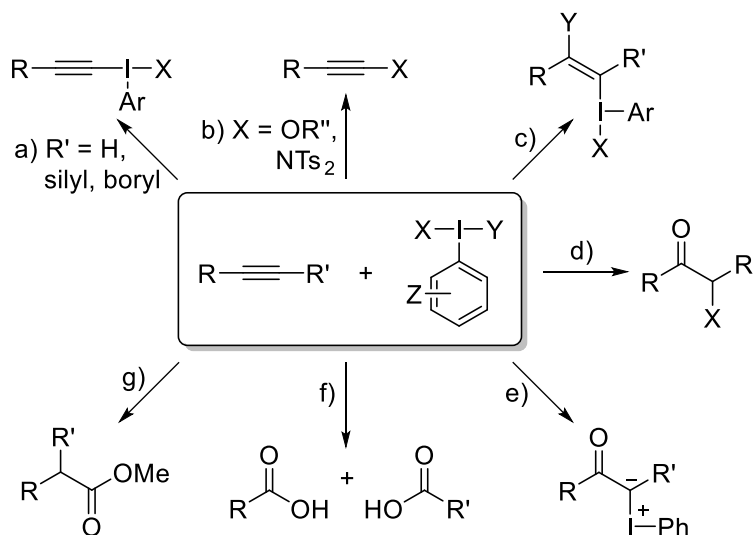
Keywords: Azole, cycloaddition, cycloisomerization, functionalization, iodine, metal-free

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1. Introduction

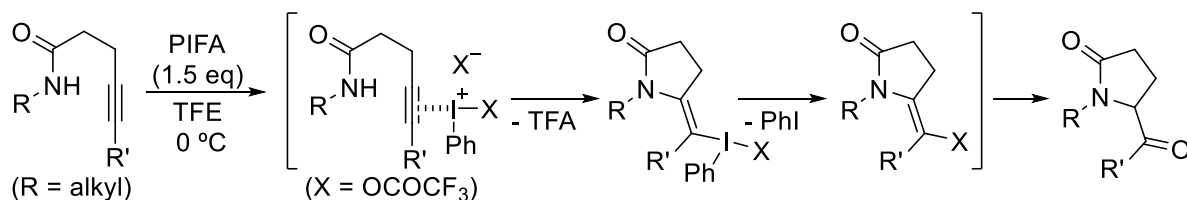
In recent years, hypervalent iodine reagents have been widely employed in organic syntheses because of their low toxicities, oxidizing abilities similar to heavy metal oxidants, and transition metal-like reactivities.¹ In particular, aryl- λ^3 -iodanes $\text{ArI}(\text{X})\text{Y}$ efficiently lead to metal-free oxidative transformations of alkynes to alkynyl- or alkenyl(aryl)iodonium salts (path a, c in Scheme 1), ynolates or -mides (path b) and α -functionalized ketones (path d, e), as well as the oxidative cleavage and rearrangement of alkynes to carboxylic acid derivatives (path f, g). Among these products, alkynyliodonium salt behave as a convenient synthetic intermediate of aromatic heterocycles such as thiazoles and so on,^{2,3} although the direct formation of these heterocycles from alkynes mediated by λ^3 -iodanes has not been achieved.



Scheme 1. Oxidative transformations of alkynes by aryl- λ^3 -iodanes $\text{ArI}(\text{X})\text{Y}$.

In addition to the abovementioned reactions, Tellitu and Domínguez's group have reported that phenyliodine(III) bis(trifluoroacetate) (PIFA) directly promote the oxidative cyclization of 4-alkynylcarboxamides (Scheme 2).⁴ In this procedure, PIFA works not only as a donor of oxygen function group but also as an activator for the triple bond ($\text{R}' = \text{alkyl}$). However, the similar approach to the aromatic

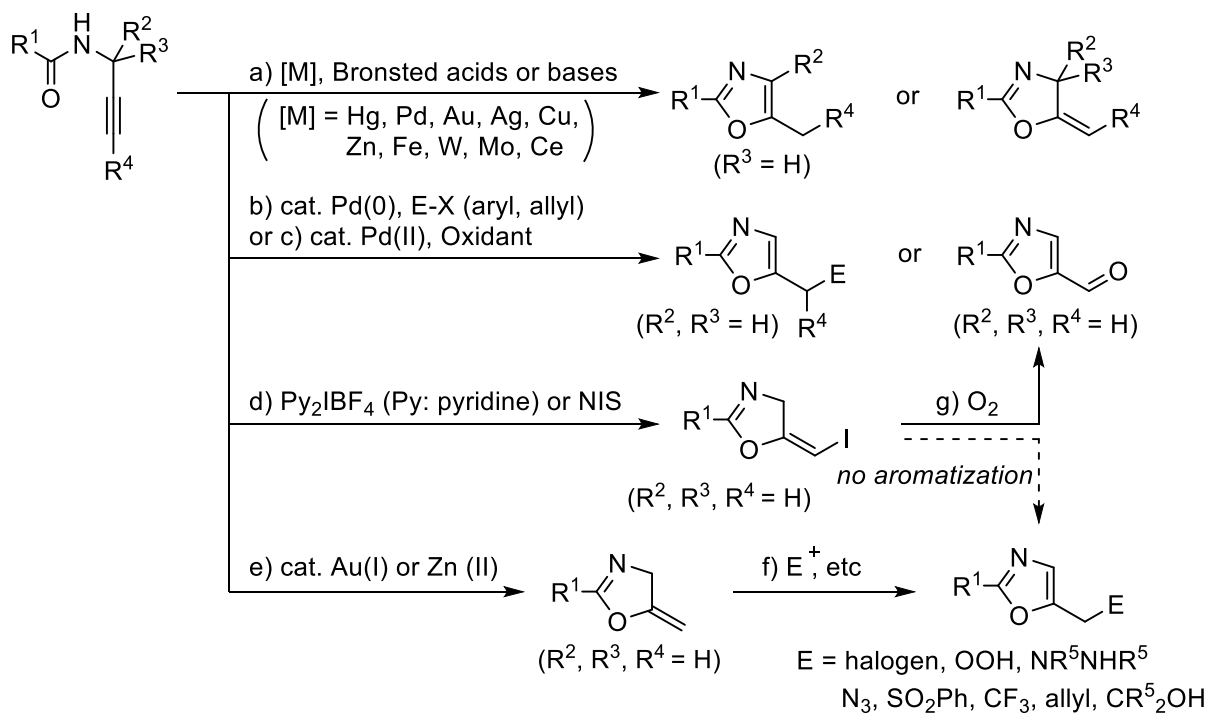
heterocycles by λ^3 -iodanes had not been reported, although oxidative cycloisomerization of enynols by 2-iodoxybenzoic Acid (IBX) had been known as the facile synthesis of 2-acylfurans.⁵ As a part of our study on the synthesis of heterocycles from propargyl compounds,^{6,7} we have developed the λ^3 -iodane-mediated oxidative cycloisomerization of *N*-propargyl amides for the preparation of oxazoles bearing oxygen functional group at their side chains (Section 2.1).⁸ Furthermore, this metal-free oxidative cycloisomerization approaches have been extended to the divergent synthesis of furfuryl alcohols and furfurals (Section 2.2)⁹ or catalytic synthesis of fluorinated oxazoles (Section 2.3)¹⁰ as well as [2+2+1] cycloaddition type reactions of alkynes, nitriles and heteroatoms (Section 3).^{11,12} The detailed synthetic and mechanistic study of these reactions will be discussed in the following sections.



Scheme 2. Oxidative cyclization of 4-alkynylcarboxamides.

2. λ^3 -Iodane-mediated Cycloisomerization/functionalization Reactions

Since oxazole nucleus has found widespread applications in fields of medicinal chemistry and synthetic chemistry, many strategies have been developed for the construction of oxazoles.^{13,14} Among them, the cycloisomerization of *N*-propargyl amides has been widely employed as the effective and versatile synthesis of oxazoles (Scheme 3).¹⁵



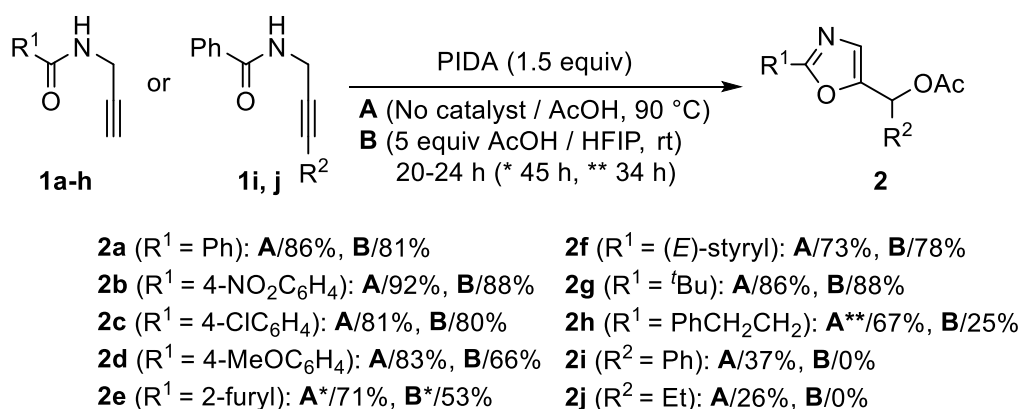
Scheme 3. Synthesis of oxazoles from *N*-propargyl amides.

These transformations have been achieved by transition metals such as Hg, Pd, Au, Ag, Cu, Zn, Fe, W, Mo, and Ce, as well as by Bronsted acids and strong bases (path a). In particular, Pd(0) complexes successfully catalyze the cycloisomerization–coupling reactions of *N*-propargyl amides with aryl iodides and allyl carbonates, thereby giving rise to the oxazoles having carbon functional groups in a single operation (path b).^{6,16} Also, Pd(II)-catalyzed conditions with oxidants lead to direct formation of 5-oxazolecarbaldehydes from propargylamides (path c).¹⁷ On the other hand, although iodocyclizations of various alkynes have been applied to the preparation of functionalized heterocycles, the halocyclizations of *N*-propargyl amides by general halogenating reagents hardly bring about aromatization to halogenated oxazoles (path d).¹⁸ Recently, Hashmi *et al.* reported an elegant synthesis of halogenated oxazoles via the gold-catalyzed formation of alkylideneoxazolines (path e)¹⁹ followed by the halogenation of them (path f).¹⁸ Such a method have been extended to oxazole synthesis with the introduction of heteroatomic or carbon functional groups^{20,21} as well as the further oxidation of iodinated alkylideneoxazolines (path g)²² by Hashmi's and other groups. However, before our report on λ^3 -iodane-mediated oxidative cycloisomerization,⁸ these two-step approaches to various functionalized oxazoles has been known. Also, the development of a metal-free cycloisomerization/functionalization sequence of *N*-propargyl amides still remains a challenging research theme.

2.1. Synthesis of oxazoles by cycloisomerization/oxy-functionalization reaction

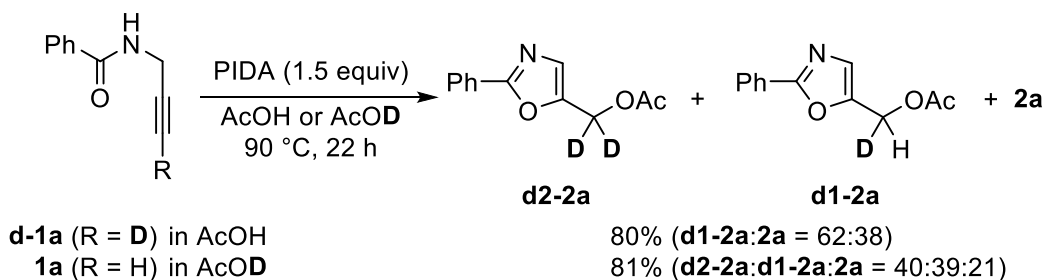
Our group has previously developed the Pd(0)-catalyzed cycloisomerization/allylation reaction of propargyl compounds with allyl carbonates (path b, Scheme 3), which proceeds via cyclization of *N*-propargyl amides through the activation of triple bonds by the *in situ* generated π -allyl Pd(II) species followed by the reductive elimination of the resulting Pd(II) species.^{6,7} Therefore, directed toward the development of the metal-free cycloisomerization/functionalization sequence of *N*-propargyl amides, we have focused on the activation mechanism by PIFA and the reductive elimination of iodobenzene (Scheme 2).⁴ Thus, the similar properties of λ^3 -iodane to metal catalyst would be expected to lead to the metal-free formation of oxazoles concomitant with the introduction of oxygen functional groups.

As shown in Scheme 4, the desired cycloisomerization/oxy-functionalization sequence of *N*-propargyl amides **1a** efficiently proceeded by phenyliodine(III) diacetate (PIDA) in AcOH (conditions **A**) or in the presence of AcOH (5 eq) in hexafluoroisopropanol (HFIP, conditions **B**).⁸ Thus, the both conditions gave the corresponding products **2a-g** in moderate to excellent yields (**A**: 67-92%, **B**: 25-88%) not only from aromatic amides **1a-f** but also from aliphatic amide **1g, h**. In cases of **1d, e** having electron-rich aromatic rings and **1h** having primary alkyl group, although requiring the thermal conditions (90 °C), the conditions **A** brought about the significantly good results. Also, the conditions **A** could be applied to the reaction of internal alkynes **1i** (R=Ph) and **1j** (R=Et), albeit lower yields than terminal alkynes **1a**.



Scheme 4. PIDA-mediated cycloisomerization/acetoxylation reactions of *N*-propargyl amides **1**.

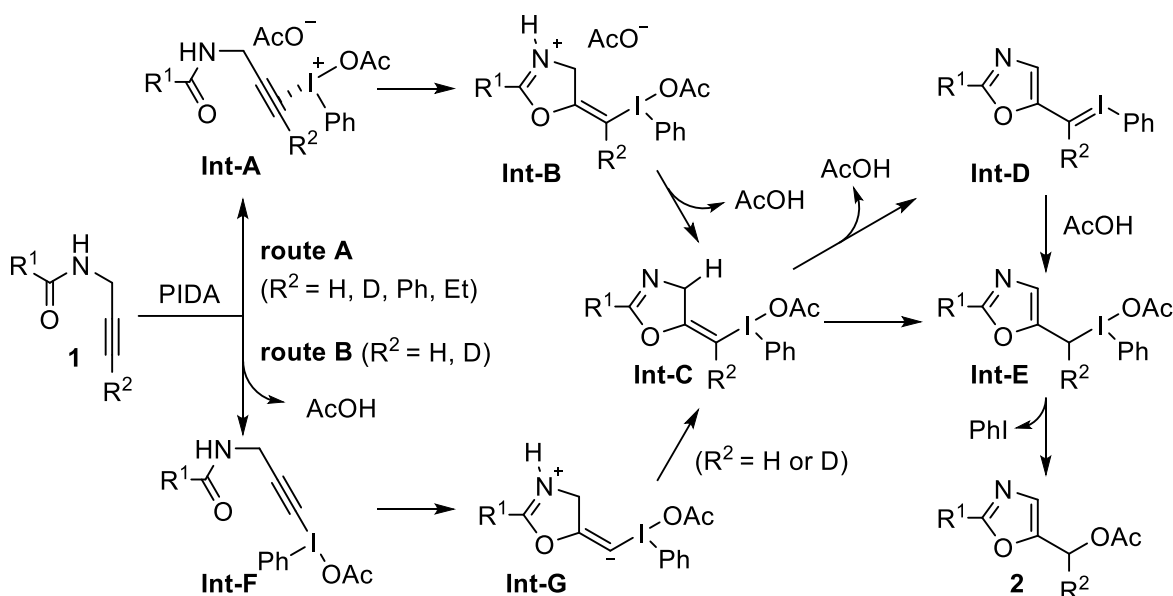
As the reason for the decrease in product yields of the inner alkynes **1i, j**, the following two points can be given: (i) PIDA would be hardly coordinated from alkyne π -bonds due to the steric effects, (ii) alkynyliodane intermediates could not be formed as shown in Scheme 1 (path a). Consequently, to check the involvement of alkynyliodane intermediates in the reaction of terminal alkynes, we have carried out H/D exchange experiments using deuterated alkyne **d-1a** (Scheme 5), which would lead to the formation of undeuterated oxazole **2a** if alkynyliodanes is involved. As expected, the treatment of **d-1a** with PIDA in AcOH under the optimized conditions afforded the undeuterated **2a** along with the mono-deuterated **d1-2a** in 80% yield (**d1-2a:2a** = 62:38). Interestingly, **1a** was exposed to PIDA in AcOD giving rise to di-deuterated product **d2-2a** as a mixture with **d1-2a** and **2a** (**d2-2a:d1-2a:2a** = 40:39:21). Notably, in the absence of PIDA, H-D exchange reaction of terminal hydrogen of **1a** with AcOD did not occur.



Scheme 5. H/D exchange experiments.

On the basis of these observations, the present formation of oxazole from terminal alkynes would proceed via two routes (Scheme 6). One consists of the cyclization of **Int-A** through the activation of the triple bond by PIDA followed by the deprotonation of **Int-B** (route **A**), and another consists of alkynyliodane **Int-F** followed by formal intramolecular proton transfer of **Int-G** (route **B**). And then, the common intermediate **Int-C** would be converted to **Int-E** via 1,4-elimination of AcOH and the subsequent addition of AcOH to the resulting **Int-D**, and/or via the direct isomerization induced under acidic conditions. The iodonium ylides like **Int-D** has been proposed as a key intermediate in the PIDA-mediated oxidation of terminal alkyne compounds to α -acetoxy ketones.²³ Also, alkylideneoxazoline has been known to be isomerized to oxazole by acid.²⁴ Finally, the substitution of phenyliodonium group of **Int-E** by AcOH and/or the reductive elimination of $\text{PhI}^{25,26}$ would give the target oxazoles **2**. Accordingly, the introduction of deuterium in the formation of **d1-2a** from **1a** (Scheme

5) would depend on (i) the deuteration of **Int-G** by AcOD or (ii) the addition of AcOD to iodonium ylide **Int-D**, both steps of which would be involved in the case of **d2-2a**.

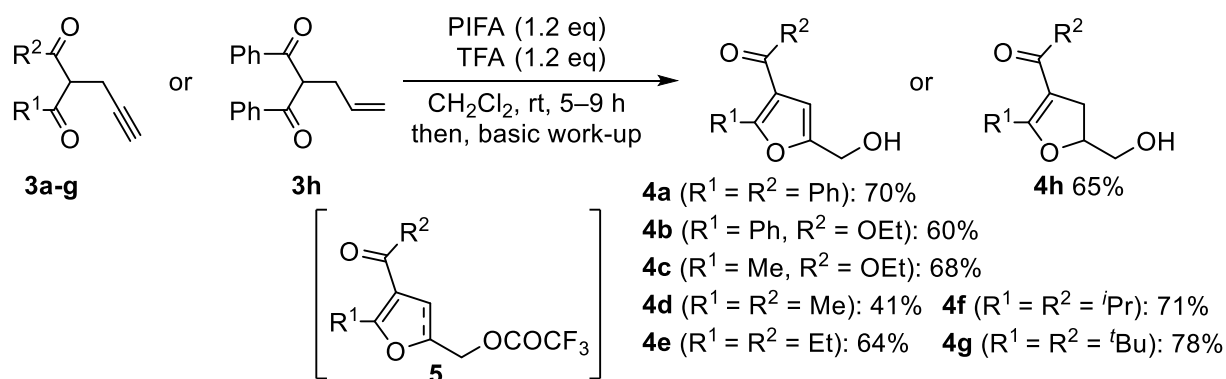


Scheme 6. Proposed mechanism for PIDA-mediated cycloisomerization/acetoxylation reactions.

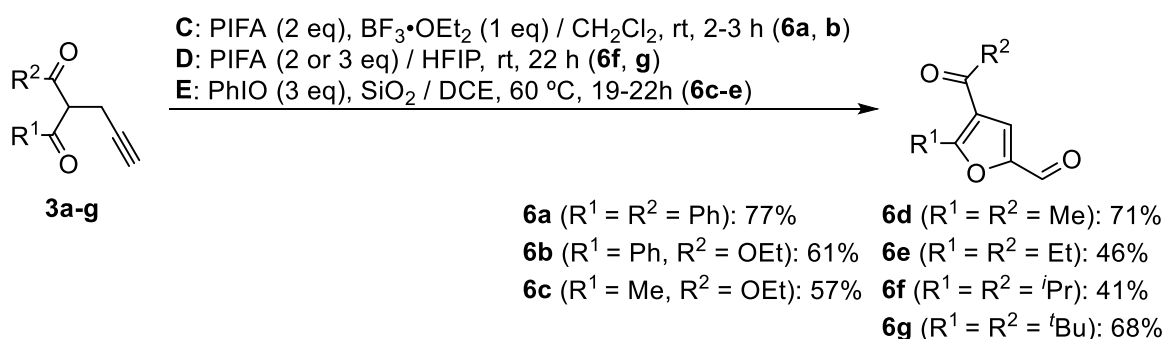
2.2. Synthesis of furans by cycloisomerization/oxy-functionalization reaction

Although oxidative cycloisomerization of enynols by IBX had been reported by Liu *et al.*⁵ as described in Section 1, the oxidative cycloisomerization reactions of alkynes including various metal-catalysis have been known only as preparations of 2-acylfurans.²⁷ Therefore, the PIDA-mediated oxidative cycloisomerization approach (Section 2.1) was extended to the formation of furfuryl alcohols from 2-propargyl 1,3-dicarbonyl compounds **3** (Scheme 7).⁹ In these transformations, PIFA was found to work well rather than PIDA (condition **A, B**) and IBX. Thus, in the presence of trifluoroacetic acid (TFA), not only diketones **4a, d-g** but also ketoester **4b, c** successfully reacted with PIFA in CH₂Cl₂. After the basic work-up, which leads to the alcoholysis of furfuryl trifluoroacetates **5**, furfuryl alcohols **4a-g** were obtained in 41-78% yields. Also, the present procedure could be applied to the reaction of allyl compound **4h**.

To our delight, the direct formation of furfurals **6** from **3** could be achieved by the increasing amounts of λ³-iodane reagents and by appropriate selection of additives and solvents (Scheme 8). Thus, the treatment of benzoyl compound **3a,b** or bulky aliphatic ketones **3f,g** with PIFA in the presence of BF₃•OEt₂ in CH₂Cl₂ (condition **C**) or in HFIP (condition **D**) gave the corresponding furfurals in good yields. In cases of **3c-e** having primary alkyl group, iodosylbenzene (PhIO) with silica gel in DCE (condition **E**) worked better. Although the formation mechanism of furfurals remains unclear, the formation of furfuryl trifluoroacetates **5** would proceed via the similar reaction pathway for the PIDA-mediated oxidative cycloisomerization of *N*-propargyl amides/acetoxylation reactions (Scheme 6).



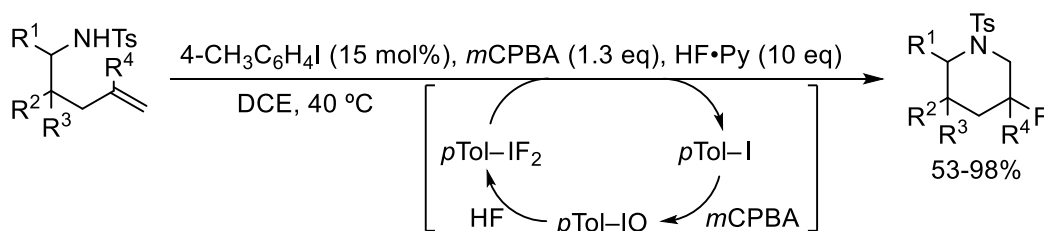
Scheme 7. PIFA-mediated formation of furfuryl alcohols.



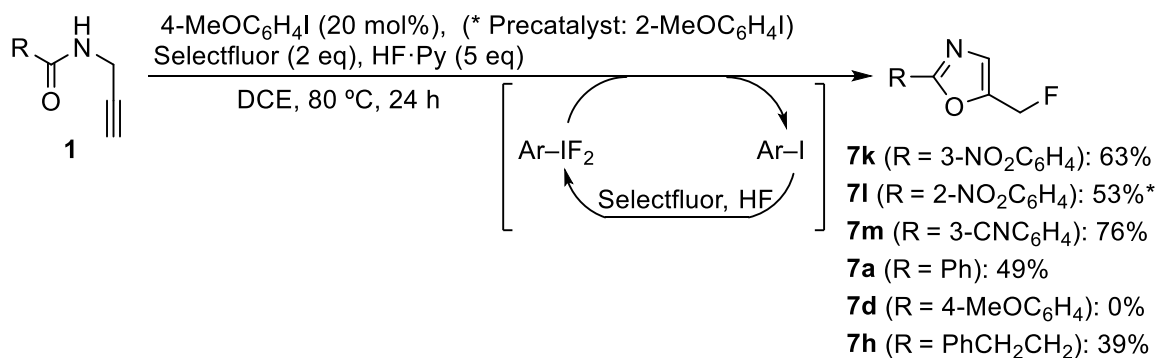
Scheme 8. PIFA- or PhIO-mediated formation of furfurals.

2.3. Synthesis of oxazoles by cycloisomerization/fluorination reaction

Recently, the efficient introduction method of fluorine into heterocycles has received much attention due to the improvement of properties (such as solubility, bioavailability and metabolic stability) by fluorine substituents.²⁸ As metal-free and efficient preparations of fluorinated heterocycles, cyclization/fluorination reactions of alkenes mediated by (difluoroiodo)-*p*-toluene (*p*-TolIF₂) with amine-HF complex have been demonstrated.²⁹ Very recently, catalytic fluorinative transformations using (difluoroiodo)arenes (ArIF₂) catalysts, which are *in situ* generated from ArI precatalyst, *m*-chloroperbenzoic acid (*m*CPBA) and HF·pyridine (HF·Py) or aq. HF, have been reported by Kitamura's³⁰ and Jacobsen's groups,³¹ and then have been extended to the aminofluorination of alkenyl amines by Shibata *et al* (Scheme 9).³² However, metal-free and catalytic fluorinative transformations of alkynes had been unknown.

Scheme 9. ArIF₂-catalyzed cyclization/fluorination reaction of alkenylamine.

Very recently, we could demonstrated the cycloisomerization/fluorination reaction of *N*-propargyl amides **1** catalyzed by ArIF_2 , which is *in situ* generated from 4- or 2-MeOC₆H₄I (20 mol%) as a precatalyst with Selectfluor and HF·Py (Scheme 10).¹⁰ This catalytic systems were relatively effective on the reactions of aromatic amides bearing electron-withdrawing groups such as nitro and cyano groups and no substituted **1a** giving rise to fluorinated oxazoles **7k-m** and **7a** in 49-76% yields, albeit no formation of MeO derivative **7d**. Surprisingly, although the facile preparation of ArIF_2 from and Selectfluor has been established by Shreeve *et al.* in 2005,³³ this procedure has been not applied to the iodine(III)-catalysis until 2015.^{34,35} It should be mentioned that the use of *m*CPBA instead of Selectfluor brought about the slow conversion to **7** along with the formation of side-products having oxygen functional group.



Scheme 10. ArIF_2 -catalyzed or -mediated cycloisomerization/fluorination reaction of **1**.

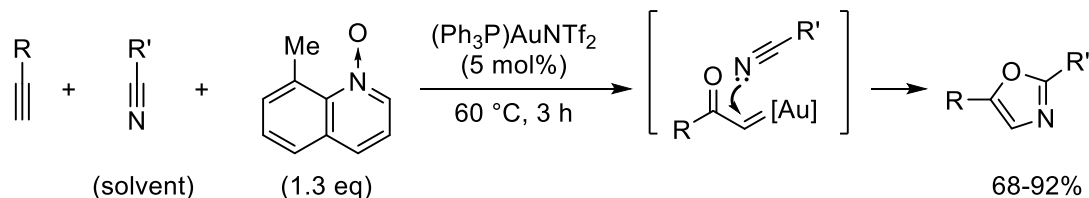
In the ArI /Selectfluor/HF·Py catalytic systems, similarly to PIDA-mediated cycloisomerization-acetoxylation sequence (route **A**, Scheme 6), the generated ArIF_2 would promote the cycloisomerization of **1** through the activation of triple bonds. And then, after the nucleophilic substitution of intermediate like **Int-E** by HF·Py, ArI is regenerated along with the formation of fluorinated oxazole **7**. Although alkynyl iodane intermediate like **Int-F** might be involved in the present reaction, the formation of alkynyl iodane from alkyne with ArIF_2 has been unknown.^{36,37} According to NMR studies using NO₂-substituted **1k** or MeO-substituted **1d** with *p*-TolIF₂, which also promoted cycloisomerization/fluorination reactions of **1k** (**1d**: no reaction), *p*-TolIF₂ would preferentially activate the triple bond rather than the amide group of **1k**. This result is indicative of the activation mechanism of the triple bond. In contrast, the triple bond of **1d** was not activated by *p*-TolIF₂ possibly due to the high Lewis basicity of the electron-rich amide group, and accordingly would not lead to the formation of intermediate like **Int-A**.

3. λ^3 -Iodane-mediated [2+2+1] Cycloaddition Type Reactions

3.1. [2+2+1] Synthesis of oxazoles

Multicomponent cycloaddition-type reactions, which allow for more bond formations in a single operation, can provide more atom-, step- and time-economical conversion of simple starting materials to complex and poly-functionalized cyclic compounds. Therefore, these processes of heteroatom-containing unsaturated compounds by various metal catalysts have been developed for mild and efficient approaches to heterocycles such as pyridines, furan, pyrroles, and some azoles.^{13,38} Regarding the cycloaddition-type synthesis of oxazoles, although oxidative [3+2] annulations of prefunctionalized ketones or aldehydes with nitriles or amines have been well studied,^{39,40,41} catalytic and regioselective [2+2+1] annulations of alkynes, nitriles, and oxygen atom

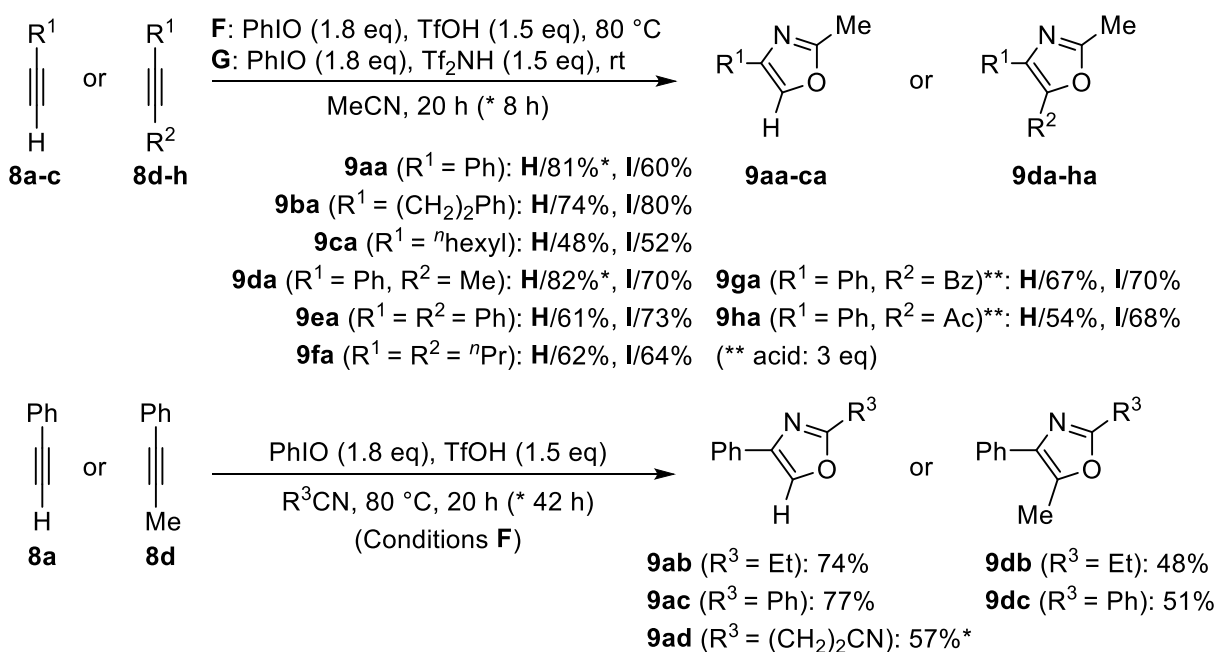
have reported by Zhang's and Jiang's group independently.^{42,43} These procedures are regarded as complementary methods: one is gold-catalyzed preparations of 2,5-disubstituted oxazoles from terminal alkynes (Scheme 11),⁴² and another is Cu-catalyzed preparations of 2,4,5-trisubstituted oxazoles from internal alkynes.⁴³ However, there had been no reports on the formation of 2,4-disubstituted oxazoles by [2+2+1] cycloaddition strategies and on applicable procedures to both terminal and internal alkynes.



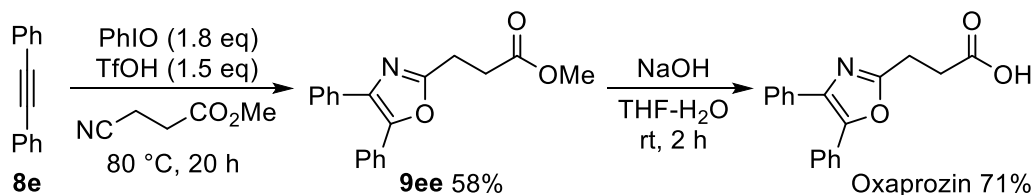
Scheme 11. Metal-catalyzed [2+2+1] cycloaddition-type synthesis of oxazoles.

Considering that our oxidative cycloisomerization approach could be applied to both terminal and internal alkynes (Section 2.1),⁸ we examined the [2+2+1] synthesis of oxazole from alkynes, nitriles, and oxygen atoms from iodine(III) reagents (Scheme 12).¹¹ Thus, we envisaged that $\text{PhI}(\text{OH})\text{X}$ generated *in situ* from PhIO and various Brønsted acids (H-X)⁴⁴ would promote an addition of nitriles to alkyne as a activator of triple bonds concomitant with an incorporation of O-atom into the ring as an O-donor, thereby leading to the metal-free [2+2+1] cycloaddition-type reactions.

Among the tested acid, triflic acid (TfOH) and bistriflylimide (Tf_2NH) were effective on the present reaction. Thus, in the presence of TfOH , not only terminal alkynes **8a-c** but also internal ones **8d-f** reacted with PhIO in MeCN at $80\text{ }^\circ\text{C}$ to give the corresponding 2,4-disubstituted oxazoles **9aa-ca**, which are different regioisomers from that of Zhang's gold-catalysis,⁴² and 2,4,5-trisubstituted oxazoles **9da-fa** in 48-82% yields (Conditions **F**). In cases of electron-withdrawing alkynes **8g,h**, 3 equivalent of TfOH showed good results. The use of Tf_2NH instead of TfOH brought about these conversion at room temperature, and then improved the yields of products except for **9aa** and **9da** (Conditions **G**). In cases of other nitriles such as EtCN , PhCN , and succinonitrile, conditions **F** showed superior results to conditions **G**. All the reactions proceeded regioselectively to give the corresponding products as a single isomer with the illustrated structures. Also, conditions **F** could be applied to a facile synthesis of an anti-inflammatory drug, Oxaproline from commercially available compounds in two steps including the hydrolysis of **9ee** (Scheme 13).

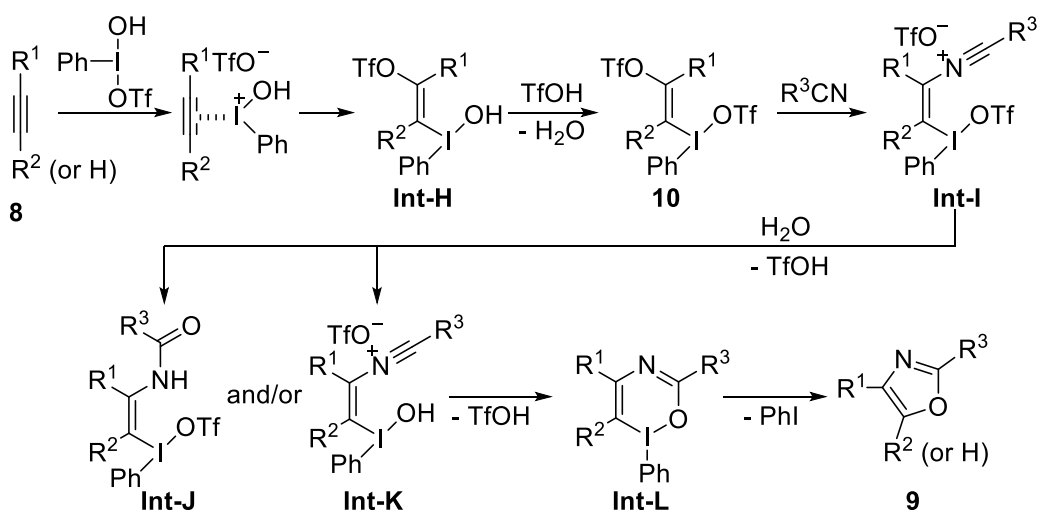


Scheme 12. Iodane-mediated [2+2+1] cycloaddition-type synthesis of oxazoles.



Scheme 13. A facile synthesis of anti-inflammatory drug, Oxaprozin.

Since we have observed the formation alkenyliodonium triflate **10c** (R¹ = ⁿhexyl, R² = H), which was determined by X-ray structure analysis, from **8c** in MeCN under the PhIO/TfOH-mediated conditions at 80 °C for 5 min,¹¹ we proposed a plausible mechanism for the present oxazole formation as shown in Scheme 14. That is, **10** would be formed through the iodooxidation of alkyne **8** with PhI(OH)OTf and the subsequent ligand exchange of OH group in **Int-H**.⁴⁴ After the nucleophilic vinylic substitution of **10** with R³CN arising from the Michael-acceptor ability of **10**,⁴⁵ the resulting **Int-I** would undertake the addition of H₂O and/or the ligand exchange with H₂O to generate **Int-J** and/or **Int-K**, which are converted to **Int-L**. Finally, the reductive elimination of **Int-L** would give the target oxazoles **9**.

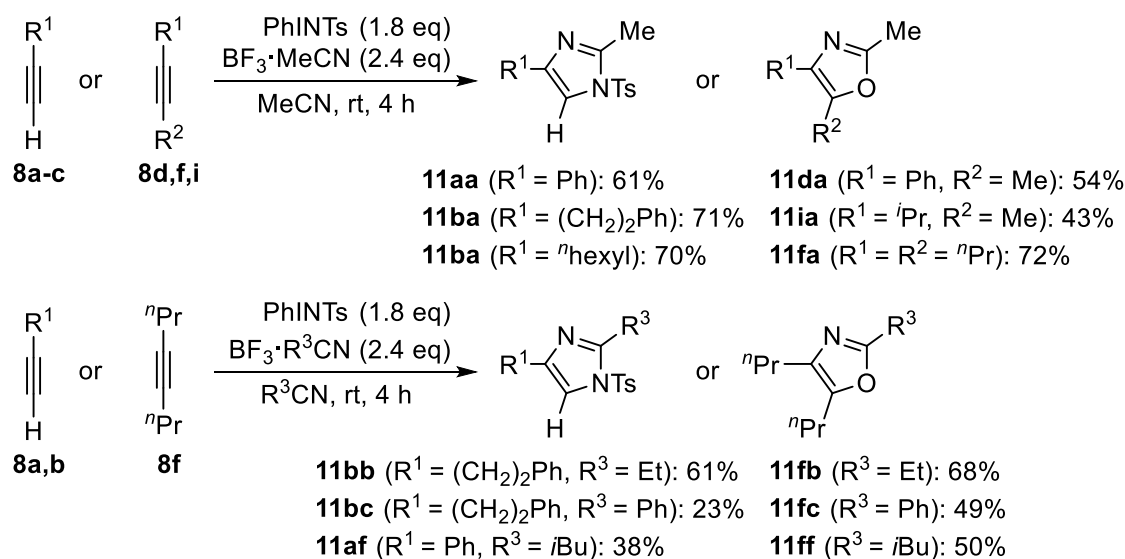


Scheme 14. Proposed mechanism for [2+2+1] synthesis of oxazoles.

Accordingly, the regiochemistry of oxazoles depends on the outcome of the iodooxidation step, in which the bulky iodonium ion would bind to the less sterically hindered R^2 side of the alkyne carbon in **8a-c** (R^1 =Ph, $(CH_2)_2Ph$, or $(CH_2)_5CH_3$, R^2 =H) or **8d** (R^1 =Ph, R^2 =Me). The involvement of **10** as the intermediate is supported by control experiments that the isolated **10a** (R^1 = Ph, R^2 = H) was reacted with H_2O (1.0 eq) in MeCN at 80 °C for 8 h giving rise to **9a** in 69% yield. Also, H/D exchange experiments showed the intervention of the alkynyliodonium intermediate instead of **10** as a minor reaction pathway of terminal alkynes in the similar to the synthesis of thiazoles from alkynyliodonium salts by Wipf's and Ochiai's groups.^{2,3}

3.2. [2+2+1] Synthesis of imidazoles

Although Debus-Radziszewski reaction using 1,2-dicarbonyl compounds, aldehydes, and ammonia (or amine) has been known as a multicomponent approach to highly substituted imidazoles since a long time ago, this conventional method has met with disadvantages such as harsh conditions, excessive amounts of nitrogen sources, and low selectivities.⁴⁶ Consequently, as one of alternative methods, a metal-catalyzed [2+2+1] annulation of alkynes, nitriles and N-atoms from azides has been developed.^{47,48} This method, however, can stand further improvement due to high reaction temperature, tedious procedures, and the limitation of the substrate generality (*terminal alkynes only*). Therefore, we have extended the abovementioned [2+2+1] cycloaddition-type method (Section 3.1)¹¹ to the synthesis of imidazole from alkynes, nitriles and N-atoms from *N*-tosyliminophenyliodane (PhINTs) (Scheme 15).¹² On the PhINTs-mediated [2+2+1] annulations, $BF_3 \cdot \text{nitrile}$ complexes are more effective than TfOH and Tf_2NH as acid additives. Thus, in the presence of the corresponding $BF_3 \cdot \text{nitrile}$ complexes, both terminal and internal alkynes successfully reacted with PhINTs in various nitriles at rt to give the desired 2,4-disubstituted and 2,4,5-trisubstituted *N*-tosylimidazole **11** with complete regioselectivities. Since the similar regiochemistry of products were observed in the iodane-mediated [2+2+1] synthesis of oxazoles, the present imidazole synthesis would proceed via the similar mechanism to Scheme 14. By the detosylation with trifluoroacetic anhydride and pyridine, **11af** can be easily converted to Catharsitoxin E, which was isolated from the Chinese remedy giung laug.⁴⁹



Scheme 15. Iodane-mediated [2+2+1] cycloaddition-type synthesis of *N*-tosylimidazoles.

4. Conclusions

On the basis of aryl- λ^3 -iodane ArI(X)Y acting as a donor of heteroatomic functional groups and as an activator of carbon-carbon triple bonds, we have demonstrated the metal-free cycloisomerization/functionalization reactions of propargyl compounds for oxazoles and furans bearing oxygen functional groups and/or fluorine at their side chains. Also, this methodology could be extended to metal-free [2+2+1] cycloaddition-type formation of oxazoles and imidazoles. Since transition metal catalysis is the mainstream in such transformations, our findings not only provide novel and attractive procedures for the access to these heterocycles but also open a new possibility for the use of λ^3 -iodane catalyst in organic synthesis. Further studies on metal-free and catalytic cycloisomerization/functionalization reactions and cycloaddition-type reactions are under way.

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References

- Recent review: Yoshimura, A.; Zhdankin, V. V. *Chem. Rev.* **2016**, *116*, 3328. <https://doi.org/10.1021/acs.chemrev.5b00547>

2. Wipf, P.; Venkataraman, S. *J. Org. Chem.* **1996**, *61*, 8004.
<https://doi.org/10.1021/jo961681c>
3. Miyamoto, K.; Nishi, Y.; Ochiai, M. *Angew. Chem. Int. Ed.* **2005**, *44*, 6896.
<https://doi.org/10.e.2005024381002/ani>
4. Tellitu, I.; Serna, S.; Herrero, M. T.; Moreno, I.; Domínguez, E.; SanMartin, R. *J. Org. Chem.* **2007**, *72*, 1526.
<https://doi.org/10.1021/jo062320s>
5. Du, X.; Chen, H.; Liu, Y. *Chem. Eur. J.* **2008**, *14*, 9495.
<https://doi.org/10.1002/chem.200801561>
6. Saito, A.; Imura, K.; Hanzawa, Y. *Tetrahedron. Lett.* **2010**, *51*, 1471.
<https://doi.org/10.1016/j.tetlet.2010.01.018>
7. Saito, A.; Imura, K.; Hanzawa, Y. *Tetrahedron. Lett.* **2011**, *52*, 4299.
<https://doi.org/10.1016/j.tetlet.2011.06.037>
8. Saito, A.; Matsumoto, A.; Hanzawa, Y. *Tetrahedron Lett.* **2010**, *51*, 2247.
<https://doi.org/10.1016/j.tetlet.2010.02.096>
9. Saito, A.; Anzai, T.; Matsumoto, A.; Hanzawa, Y. *Tetrahedron Lett.* **2011**, *52*, 4658.
<https://doi.org/10.1016/j.tetlet.2011.06.117>
10. Asari, N.; Takemoto, Y.; Shinomoto, Y.; Yagyu, T.; Yoshimura, A.; Zhdankin, V. V.; Saito, A. *Asian J. Org. Chem.* **2016**, *5*, 1314.
<https://doi.org/10.1002/ajoc.201600383>
11. Saito, A.; Taniguchi, A.; Kambara, Y.; Hanzawa, Y. *Org. Lett.* **2013**, *15*, 2672.
<https://doi.org/10.1021/ol4009816>
12. Saito, A.; Kambara, Y.; Yagyu, T.; Noguchi, K.; Yoshimura, A.; Zhdankin, V. V. *Adv. Synth. Catal.* **2015**, *357*, 667.
<https://doi.org/10.1002/adsc.201500032>
13. Recent review: Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Chem. Rev.* **2013**, *113*, 3084.
<https://doi.org/10.1021/cr300333u>
14. Recent review: Ibrar, A.; Khan, I.; Abbas, N.; Farooq, U.; Khan, A. *RSC Adv.* **2016**, *6*, 93016.
<https://doi.org/10.1039/C6RA19324B>
15. Digest paper: Y. Hu, X. Xin, B. Wan, *Tetrahedron Lett.* **2015**, *56*, 32.
<https://doi.org/10.1016/j.tetlet.2014.11.061>
16. Arcadi, A.; Cacchi, S.; Cascia, L.; Fabrizi, G.; Marinelli, F. *Org. Lett.* **2001**, *3*, 2501.
<https://doi.org/10.1021/ol016133m>
17. Beccalli, E. M.; Borsini, E.; Broggin, G.; Palmisano, G.; Sottocornola, S. *J. Org. Chem.* **2008**, *73*, 4746.
<https://doi.org/10.1021/jo800621n>
18. Hashmi, A. S. K.; Weyrauch, J. P.; Schuster, A.; Hengst, T.; Schetter, A.; Littmann, A.; Rudolph, M.; Hamzic, M.; Visus, J.; Rominger, F.; Frey, W.; Bats, J. W. *Chem. Eur. J.* **2010**, *16*, 956.
<https://doi.org/10.1002/chem.200902472>
19. Hashmi, A. S. K.; Rudolph, M.; Scymura, S.; Visus, J.; Frey, W. *Eur. J. Org. Chem.* **2006**, 4905.
<https://doi.org/10.1002/ejoc.200600572>
20. Hashmi, A. S. K.; Littmann, D.-C. A. *Chem. Asian J.* **2012**, *7*, 1435.
<https://doi.org/10.1002/asia.201200046>
21. Wang, B.; Chen, Y.; Zhou, L.; Wang, J.; Tung, C.-H.; Xu, Z. *J. Org. Chem.* **2015**, *80*, 12718.

- <https://doi.org/10.1021/acs.joc.5b02382>
22. Hu, Y.; Yi, R.; Wang, C.; Xin, X.; Wu, F.; Wan, B. *J. Org. Chem.* **2014**, *79*, 3052.
<https://doi.org/10.1021/jo5001719>
23. Mo, D.-L.; Dai, L.-X.; Hou, X.-L. *Tetrahedron Lett.* **2009**, *50*, 5578.
<https://doi.org/10.1016/j.tetlet.2009.07.081>
24. Wachenfeldt, H. V.; Paulsen, F.; Sundin, A.; Strand, D. *Eur. J. Org. Chem.* **2013**, 4578.
<https://doi.org/10.1002/ejoc.201300285>
25. Ochiai, M. In *Hypervalent Iodine Chemistry: Modern Developments in Organic Synthesis*; Wirth T. Ed.; Springer Verlag: Berlin, 2003; Vol. 224, p 5.
https://doi.org/10.1007/3-540-46114-0_2
26. Grushin, V. V. *Chem. Soc. Rev.* **2000**, *29*, 315.
<https://doi.org/10.1039/a909041j>
27. Cao, H.; Jiang, H.; Yuan, G.; Chen, Z.; Qi, C.; Huang, H. *Chem. Eur. J.* **2010**, *16*, 10553.
<https://doi.org/10.1002/chem.201000807>
28. Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Wiley-VCH: Weinheim, 2013.
<https://doi.org/10.1002/9783527651351>
29. Sawaguchi, M.; Hara, S.; Fukuhara, T.; Yoneda, Y. *J. Fluorine Chem.* **2000**, *104*, 277.
[https://doi.org/10.1016/S0022-1139\(00\)00241-4](https://doi.org/10.1016/S0022-1139(00)00241-4)
30. Kitamura, T.; Muta, K.; Kuriki, S. *Tetrahedron Lett.* **2013**, *54*, 6118.
<https://doi.org/10.1016/j.tetlet.2013.08.129>
31. Banik, S. M.; Medley, J. W.; Jacobsen, E. N. *Science* **2016**, *353*, 51.
<https://doi.org/10.1126/science.aaf8078>
32. Suzuki, S.; Kamo, T.; Fukushi, K.; Hiramatsu, T.; Tokunaga, E.; Dohi, T.; Kita, Y.; Shibata, N. *Chem. Sci.* **2014**, *5*, 2754.
<https://doi.org/10.1039/c3sc53107d>
33. Ye, C.; Twamley, B.; Shreeve, J. M. *Org. Lett.* **2005**, *7*, 3961.
<https://doi.org/10.1021/ol051446t>
34. Alhalib, A.; Kamouka, S.; Moran, W. J. *Org. Lett.* **2015**, *17*, 1453.
<https://doi.org/10.1021/acs.orglett.5b00333>
35. Molnár, I. G.; Gilmour, R. J. *Am. Chem. Soc.* **2016**, *138*, 5004.
<https://doi.org/10.1021/jacs.6b01183>
36. Hara, S.; Yoshida, M.; Fukuhara, T.; Yoneda, N. *J. Chem. Soc., Chem. Commun.* **1998**, 965.
<https://doi.org/10.1039/a801273c>
37. Ochiai, M.; Hirobe, M.; Yoshimura, A.; Nishi, Y.; Miyamoto, K.; Shiro, M. *Org. Lett.* **2007**, *9*, 3335.
<https://doi.org/10.1021/ol071345q>
38. Müller, T. J. J. Ed. *Multicomponent Reactions, Science of Synthesis*; Thieme: Stuttgart, 2014, vols. 1 and 2.
39. Ishiwata, Y.; Togo, H. *Tetrahedron* **2009**, *65*, 10720.
<https://doi.org/10.1016/j.tet.2009.09.109>
40. Saito, A.; Hyodo, N.; Hanzawa, Y. *Molecules* **2012**, *17*, 11046.
<https://doi.org/10.3390/molecules170911046>
41. Huang, H.; Ji, X.; Wu, W.; Jiang, H. *Adv. Synth. Catal.* **2013**, *355*, 170.
<https://doi.org/10.1002/adsc.201200582>

42. He, W.; Li, C.; Zhang, L. *J. Am. Chem. Soc.* **2011**, *133*, 8482.
<https://doi.org/10.1021/ja2029188>
43. Li, X.; Huang, L.; Chen, H.; Wu, W.; Huang, H.; Jiang, H. *Chem. Sci.* **2012**, *3*, 3463.
<https://doi.org/10.1039/c2sc21041j>
44. Kitamura, T.; Furuki, R.; Taniguchi, H.; Stang, P. J. *Tetrahedron* **1992**, *48*, 7149.
[https://doi.org/10.1016/S0040-4020\(01\)88255-7](https://doi.org/10.1016/S0040-4020(01)88255-7)
45. Ochiai, M.; Kitagawa, Y.; Toyonari, M.; Uemura, K.; Oshima, K.; Shiro, M. *J. Org. Chem.* **1997**, *62*, 8001.
<https://doi.org/10.1021/jo970735v>
46. Jadhav, S. D.; Kokare, N. D.; Jadhav, S. D. *J. Heterocycl. Chem.* **2008**, *45*, 1461.
<https://doi.org/10.1002/jhet.5570450533>
47. Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 14972.
<https://doi.org/10.1021/ja805079v>
48. Bimolecular reaction: Xiao, Y.; Zhang, L. *Org. Lett.* **2012**, *14*, 4662.
<https://doi.org/10.1021/ol302102h>
49. Suenaga, K.; Shimogawa, H.; Nakagawa, S.; Uemura, D. *Tetrahedron Lett.* **2001**, *42*, 7079.
[https://doi.org/10.1016/S0040-4039\(01\)01468-X](https://doi.org/10.1016/S0040-4039(01)01468-X)

Author's Biography



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