

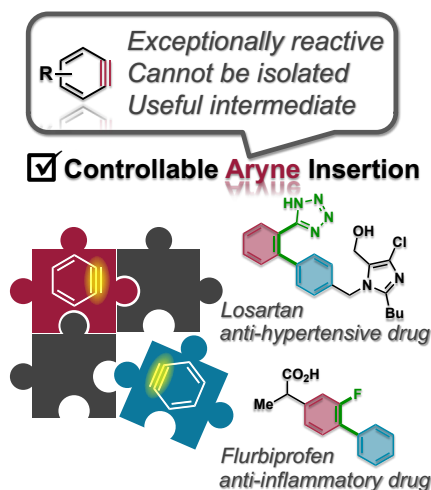
## 2E1a

## Copper-Catalyzed Arylstannylation of Arynes in a Sequence

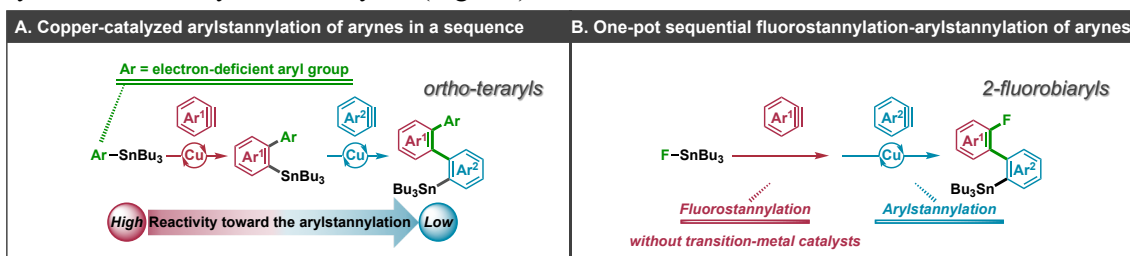
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Arynes are exceptionally reactive and transient species because of their highly strained carbon–carbon triple bond, and therefore they must be generated in situ from suitable precursors. Since a wide range of such pharmaceutically important molecules as Losartan and Flurbiprofen consist of *ortho*-teraryl and *ortho*-substituted biaryl frameworks, and insertion reactions of arynes into  $\sigma$ -bonds provide convenient and powerful way of synthesizing these important molecular frameworks, considerable attention has been paid to developing the insertion reactions of arynes. In particular, the key issue we have to address in this chemistry is controlling the number of arynes to be inserted, and sequential insertion of different arynes (Fig. 1).

Arylmatalation of arynes is an attractive option because it enables synchronous construction of C(aryl)–C(aryl) and C(aryl)–metal bonds, thus being utilizable for further  $\pi$ -extension and functionalization. Although the sequential arylmetalation of arynes should have potential for synthesizing various *ortho*-teraryls and *ortho*-substituted biaryls of structural complexity, attention has hitherto been mostly paid to the synthesis of biaryls via single insertion of arynes,<sup>[1]</sup> and sequential insertion of different arynes has not been yet reported, to the best our knowledge. We report herein a unique catalysis of a Cu(I) salt for the arylstannylation of arynes (Fig. 2A).<sup>[2]</sup> Because the aryne insertion leads to a decrease in the reactivity of arylstannanes toward the arylstannylation, the single or dual insertion of arynes into arylstannanes is precisely controllable by simply changing the equivalence of the aryne precursors employed. Therefore, the sequential insertion of different arynes into the C(aryl)–metal bonds has first become feasible under the copper catalysis. Since the smooth conversion was observed especially by use of fluorine-substituted arylstannanes, we have also achieved one-pot sequential fluorostannylation–arylstannylation, which provide various 2-fluorobiaryl motifs, based on our previous result that 2-fluoroarylstannanes are readily available by the fluorostannylation of arynes (Fig. 2B).<sup>[3]</sup>



**Fig. 1** Synthetic potential of aryne insertion



**Fig. 2** Sequential insertion of different arynes into the C(aryl)–Sn bonds or F–Sn bonds

## References

- [1] J.-A. García-López, M. F. Greaney, *Chem. Soc. Rev.* **2016**, *45*, 6766–6798.
- [2] H. Tanaka, H. Kuriki, T. Kubo, I. Osaka, H. Yoshida, *Chem. Commun.* **2019**, *55*, 6503–6506.
- [3] H. Tanaka, I. Osaka, H. Yoshida, *Chem. Lett.* **2019**, *48*, 1032–1034.