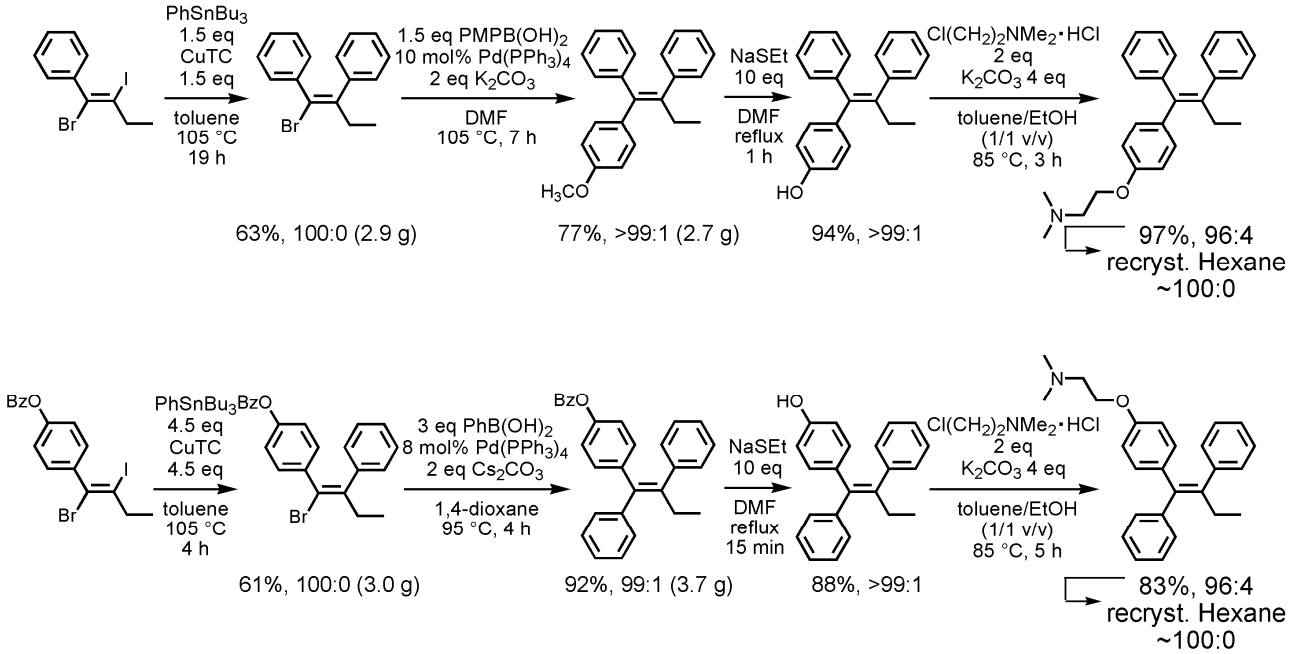
Stereo-Defined Scaffold Strategy for Tamoxifens from (*E*)-1-Bromo-2-iodoalkenes.

Yoshino Fujii*, Yuka Tamura, Nako Hashimoto, Naoki Endo, Tetsuo Iwasawa
Department of Materials Chemistry, Ryukoku University
Seta, Otsu 520-2194, Japan
iwasawa@rins.ryukoku.ac.jp

Efficient regio- and stereoselective synthesis of biological active Tamoxifen analogues still remains a grand challenge, because the tetra-substituted olefins have inherently steric hindrance of eclipsing geometries around the carbon-carbon double bonds[1, 2]. Herein we present chemo-selective activation reactions of (*E*)-1-bromo-2-iodoalkenes: the iodine atom of the scaffold selectively undertook CuTC-mediated cross-coupling reactions with tributylphenyltin, suppressing side-production of alkynes which are terribly caused by *β*-halogen elimination reactions in (*E*)-1-bromo-2-iodoalkenes. The stereochemistry of the double bond is fully retained in the activation of the vinylic bromine, deprotection, and alkylation steps: thus it enables us to singly construct (*E*)- and (*Z*)-Tamoxifen (**Scheme 1**), and the template strategy would provide a general entry of Tamoxifen analogues syntheses[3].



Scheme 1. Stereo-defined template-syntheses of (*E*)- and (*Z*)-Tamoxifens.

References

1. Flynn, A. B.; Ogilvie, W. W. *Chem. Rev.* **2007**, *107*, 4698-4745.
2. Endo, N.; Iwasawa, T. *Tetrahedron.* **2017**, *73*, 5833-5840.
3. Fujii, Y.; Tamura, Y.; Hashimoto, N.; Endo, N.; Iwasawa, T. *ChemistrySelect* **2019**, *4*, 2721-2725.