

Iodine-mediated Cyclization of *o*-(Arylethynyl)phenylthiazoles with Substituents on Aryl Ring to Form Thiazoloisoquinolium Salts

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We have reported iodine-mediated cyclization of *o*-(phenylethynyl)phenylthiazole derivatives to form thiazoloisoquinolium salts.¹⁾ In the case of the thiazole and benzothiazole analogues, the salts with mixture of iodide and triiodide as a counter anion were obtained. Herein we examined the introduction of substituent on the phenyl ring at the end of triple bond.

When we prepared **3a** by Sonogashira coupling, the transformation of thiazole ring to cyano group was observed to give **4** (Scheme 1). When thiazole ring was exchanged into benzothiazole ring, Sonogashira coupling proceeded to give **3b**.

The iodine-mediated cyclization reaction of **3b-e** with methoxy carbonyl and carboxylic acid was examined with 1 mol-equiv.

of iodine in CHCl_3 . During the reaction progress, the precipitate was obtained. As the results, we found that the thiazoloisoquinolium salts with triiodide anion were mainly obtained (Table 1, Entries 1 and 3). It was clear difference of the reaction with **3f** (Entry 5). To prevent the effect of the precipitate formation, we examined the reaction in DMF. The clear solution was kept after the reaction progress. And the majority of triiodide anion was not changed (Entries 2 and 4). Thus, the ratio of counter anion was influenced by the substituents on phenyl ring.

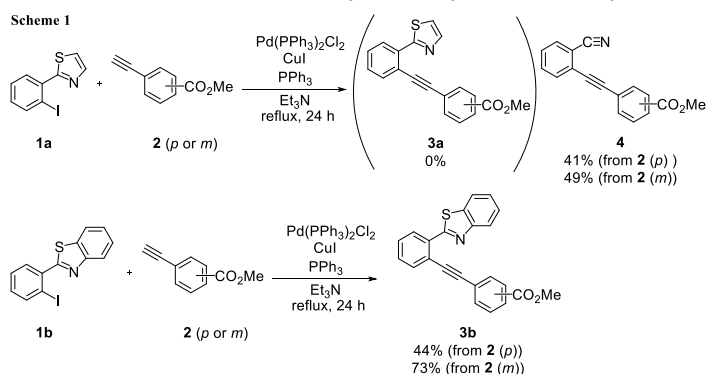


Table 1. Reaction of **3** with I_2

Entry	Substrate	Solvent	% Yield ($\text{I}^- : \text{I}_3^-$) ^{a)}
1	3b ($\text{R}^1 = \text{CO}_2\text{Me}$, $\text{R}^2 = \text{H}$)	CHCl_3	53 (10 : 90)
2	3c ($\text{R}^1 = \text{CO}_2\text{H}$, $\text{R}^2 = \text{H}$)	DMF	49 (22 : 78)
3	3d ($\text{R}^1 = \text{H}$, $\text{R}^2 = \text{CO}_2\text{Me}$)	CHCl_3	50 (0 : 100)
4	3e ($\text{R}^1 = \text{H}$, $\text{R}^2 = \text{CO}_2\text{H}$)	DMF	53 (20 : 80)
5	3f ($\text{R}^1 = \text{H}$, $\text{R}^2 = \text{H}$)	CHCl_3	67 (42 : 58)

a) Yield and ratio were determined by the estimation with weight of the precipitate and the elemental analysis.

1) Matsumoto, S.; Sumida, R.; Tan, S. E.; Akazome, M. *Heterocycles*, **2018**, *93*, 755.