

Convergent synthesis of 2-iminothiazoles containing α -diazo carbonyl groups from 4-haloacetoacetates and thioureas

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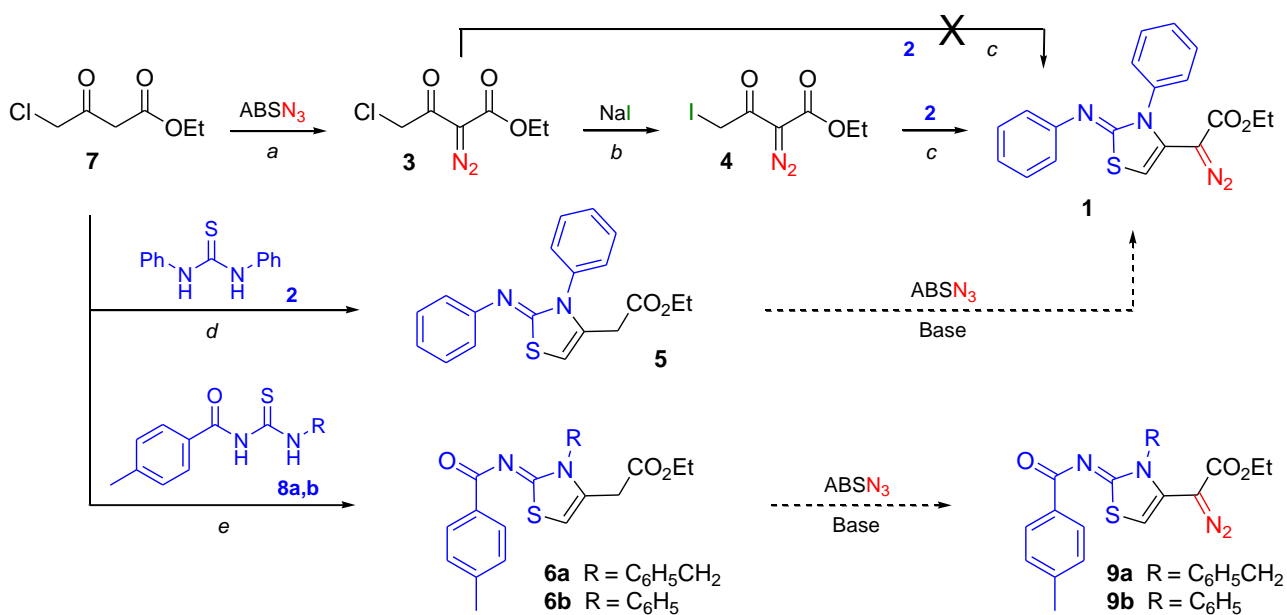
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ABSTRACT

2-Aminothiazoles are known for their diverse biological activities,¹ while α -diazo carbonyl compounds are valued as versatile building blocks.² However, research on the synthesis and reactivity of thiazoles containing α -diazo carbonyl groups remains limited.³ This study presents the successful synthesis of α -diazothiazolyl ester **1** from *N,N*-diphenylthiourea (**2**) and functionalized α -diazo esters **3** or **4**, as well as the synthesis of 2-iminothiazole-4-acetates **5** and **6** as substrates for the diazo transfer reaction (Scheme). Initially, the synthesis involved the reaction between *N,N*-diphenylthiourea (**2**) and γ -chloro- α -diazo- β -keto ester **3**, which was readily obtained from ethyl 4-chloroacetoacetate (**7**) through a method developed by us⁴ (Scheme 1). However, the expected product **1** was not obtained. Therefore, the chlorine atom in **3** was first replaced with iodine to give the γ -iodo- α -diazo- β -keto ester **4**, which reacted with thiourea **2** to provide 2-iminothiazole **1** with 22% yield. In parallel, 2-iminothiazoles **5** and **6a,b** were synthesized from chloroacetoacetate **7** and the corresponding thioureas **2** and **8** in ethanol under reflux. These molecules are suitable precursors of α -diazothiazolyl esters **1** and **9a,b** through the base-catalyzed diazo transfer reaction, which is currently under investigation.



Scheme. Synthesis of α -diazothiazolyl ester **1** and suitable thiazole precursors for the diazo transfer reaction.

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CNPq, CAPES, FAPESC, INCT-Catálise

REFERENCES

- [1] Pathania, S.; Narang, R. K.; Rawal, R. K. *Eur. J. Med. Chem.* **2019**, *180*, 486-508.
 [2] Wang, J. *Tetrahedron Lett.* **2022**, *108*, 154135.
 [3] Padwa, A.; Sá, M. M.; Weingarten, M. D. *Tetrahedron* **1997**, *53*, 2371-2386.
 [4] Costin, T. A.; Dutra, L. G.; Bortoluzzi, A. J.; Sá, M. M. *Tetrahedron* **2017**, *73*, 4549-4559.