Electrophilic Cyclization of (*Z*)-Thiobutenynes: Synthesis of 3-Iodothiophenes

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INTRODUCTION

Heteroaromatic organic compounds containing the thiophenic structural unit has been isolated from natural sources like animals and plants. They are also found in synthetic compounds such as agrochemicals, pharmaceuticals, photographic and electronics products.[1] This heterocycle is also widely used in Medicinal Chemistry in design of new drugs, due it is considered a classic bioisoster of the benzenic and furanic rings.[2]

RESULTS AND DISCUSSION

For the synthesis of the 3-iodothiophenes type **4**, iodocyclization reactions were performed using I_2 as electrophilic source in CH_2Cl_2 and (Z)-thiobutenynes **1a-g**. This methodology applies well to the synthesis of trisubstituted 3-iodothiophenes (compounds **4a-d**, Table 1), but it is not efficient for the synthesis of disubstituted 3-iodothiophenes **4e-g**. In this case, the unwanted olefins **5e-g** were formed (route b, Scheme 1). After an exhaustive investigation of reaction conditions with different solvents (THF, CH_3CN, $CHCl_3$, EtOH) and different temperatures, the best condition found to prepare thiophenes **4e-g** is one that employs I_2 (1,1 equiv), and 1,2-dichloroethane as solvent at 70 °C (route a, Scheme 1, Table 1).

Scheme 1. Proposed mechanism for the reaction of iodocyclization

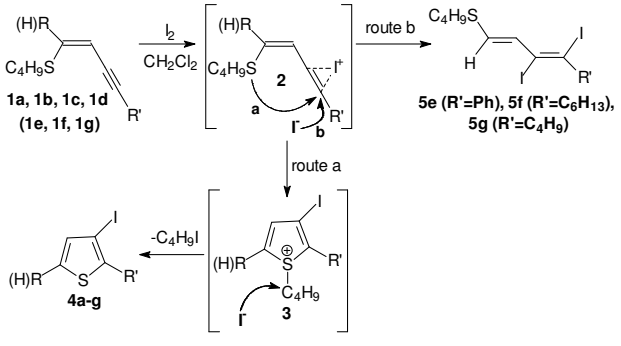
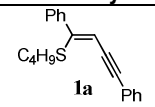
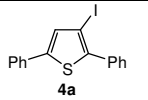
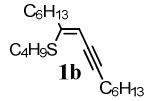
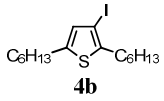
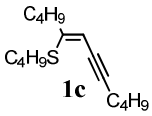
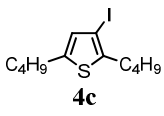
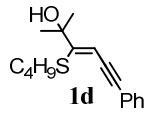
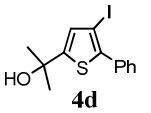
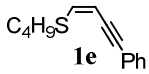
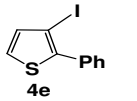
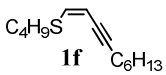
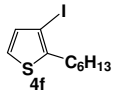
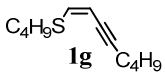
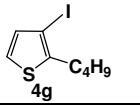


Table 1. Products obtained

(Z)-thiobutenynes	Products	Time (min) / Yield(%)[a]
		5 min. / 80%
		20min. / 61%
		20min. / 65%
		30min. / 84%
		60min. / 81%
		120min. / 70%
		120min. / 65%

[a]product isolated after purification by chromatographic column.

CONCLUSION

The methodologies developed are efficient to prepare di and trisubstituted 3-iodothiophenes in good yields. Studies are being conducted to demonstrate the generality of the methodologies.

ACKNOWLEDGEMENTS

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