



# 3*H*-1,2-dithiole-3-thione to (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole transformation: theoretical and experimental studies

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## INTRODUCTION

During the development of hybrid chemopreventive agents containing chalcone framework and 3*H*-1,2-dithiole-3-thione moiety an unexpected product was observed. When ADT-OH (Table 1) was subjected to classical alkylation conditions<sup>1</sup>, working in an excess of KI and K<sub>2</sub>CO<sub>3</sub>, we have obtained the resulting product of the electrophile character of the thiocarbonyl moiety on the 3-position of the 1,2-dithiole, instead of the expected nucleophilic-reaction product. The aim of this work was rationalized this observed reactivity from an experimental and theoretical point of view.

## RESULTS AND DISCUSSION

Different conditions were assayed to test the formation of (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole. Experiments consisted on studying the relevance of the reactants, i.e. KI, enolates, and 3*H*-1,2-dithiole-3-thiones combined with microwave assisted synthesis. Firstly, we analysed the generation of product **2** (Table 1), from ADT-OH, in absence of KI and the reactivity of 3*H*-1,2-dithiole-3-thiones with other enolates different of α-chloroacetone to explore the 3-thiocarbonyl electrophile. The results (Table 1) showed that the incorporation of acetyl-moieties in product **2** appeared when was used α-chloroacetone as enolate and in the presence of KI.

**Table 1.** Reaction conditions to generate **1** and **2**.

Run	KI	Base	methylketone	Products <sup>a</sup>	
				2	1
1	17eq <sup>b</sup>	K <sub>2</sub> CO <sub>3</sub> (17eq)	α-cac <sup>c</sup> (1eq)	(+)	(-)
2	17eq	K <sub>2</sub> CO <sub>3</sub> (17eq)	ac <sup>d</sup> (solvent)	-	-
3	-	NaH (1eq)	acp <sup>e</sup> (1eq)	-	-
4	-	K <sub>2</sub> CO <sub>3</sub> (1eq)	α-cac(0.91eq)	(-)	(+)

<sup>a</sup> (+) denotes formation of the product, (-) denotes absence of the product, and "-" denotes product not expected. <sup>b</sup> Respect to ADT-OH. <sup>c</sup> α-cac: α-chloroacetone. <sup>d</sup> ac: acetone. <sup>e</sup> acp: acetophenone

Secondly other enolate, phenacyl bromide, and other 3*H*-1,2-dithiole-3-thione were studied (Table 2). The 3*H*-1,2-dithiole-3-thione transformation to the corresponding (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole occurred in all the cases. Thirdly, microwave-irradiation heating was studied as alternative experimental conditions (Table 2).

**Table 2.** Scope of the transformation 3*H*-1,2-dithiole-3-thione to (*E*)-3-[1-(alkylthio)alkylidene]-3*H*-1,2-dithiole.

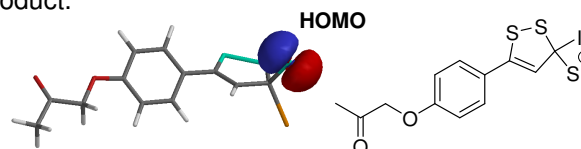
-R	-X	-R'	Product	-R''	Yield <sup>a</sup> (%)	Yield <sup>a</sup> (%) μW
H	Cl	CH <sub>3</sub>	<b>2</b>	CH <sub>2</sub> COCH <sub>3</sub>	54	82
H	Br	Ph	<b>3</b>	H	27	60
CH <sub>3</sub>	Cl	CH <sub>3</sub>	<b>4</b>	CH <sub>3</sub>	13	76
CH <sub>3</sub>	Br	Ph	<b>5</b>	CH <sub>3</sub>	22	22

<sup>a</sup> Refers to purified yield, which is >95% pure as determined by <sup>1</sup>H NMR spectroscopy.

Additionally, we carried out a theoretical study explaining the unexpected reactivity in terms of Pearson hard and soft acid base (HSAB) theory.

## CONCLUSION

The nucleophile of the following intermediate, result of the addition of iodine, could explain the observed product.



## ACKNOWLEDGEMENTS

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## REFERENCES

<sup>1</sup> Félix, S.; Ascenso, J.R.; Lamartine, R.; Pereira, J.L.C. Tetrahedron, **1999**, 55, 8539-8546