



# Benzo[*b*]thiophene dimerization: A promising experimental finding directed to the C-3 functionalization with aryl alcohols.

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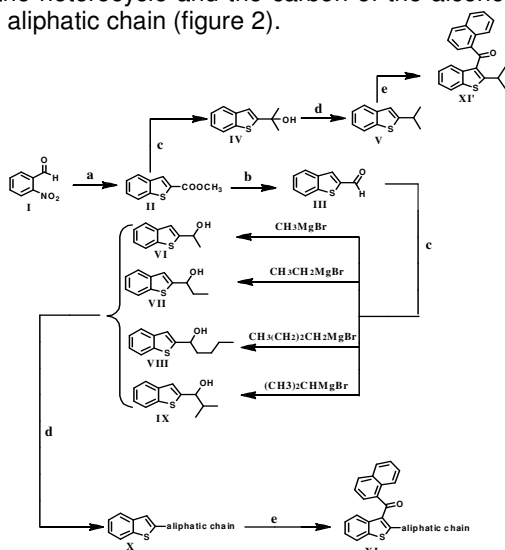
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## INTRODUCTION

The benzo[*b*]thiophene functionalization with benzyl groups at **C-3** has been a synthetic challenge. Indeed, up to the date, few efforts have been successful in the achievement of this goal, and all of them involving drastic experimental conditions<sup>1,2</sup>. In this opportunity, trying to synthesize new benzo[*b*]thiophene frameworks, we inform the non-expectable obtaining of benzo[*b*]thiophene dimers linked by a **C-3** bond. In this sense, we think that this interesting experimental finding could lead to develop a new method to synthesize 3- substituted benzo[*b*]thiophene with different kinds of benzyl alcohols.

## RESULTS AND DISCUSSION

As a part of our efforts directed to the obtaining of new series with affinity by human endocannabinoid receptor CB1, we designed a synthetic strategy resumed on scheme 1. Unexpectedly, during the alcohol reduction (step **d**) along with the alkyl derivatives (**V** for example) we obtained benzo[*b*]thiophenes dimers linked between the **C-3** of the heterocycle and the carbon of the alcohols in the aliphatic chain (figure 2).



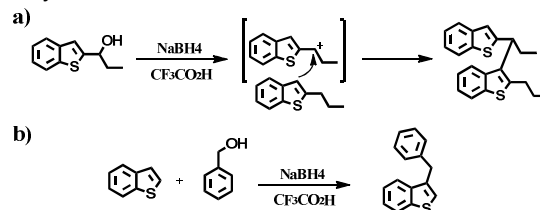
**Scheme 1:** SHCH<sub>2</sub>COOCH<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>, DMF. **b)** DIBAL, N<sub>2</sub>, THF, -78°C. **c)** Corresponding Grignards, THF, N<sub>2</sub> **d)** NaBH<sub>4</sub>, TFA, CH<sub>2</sub>Cl<sub>2</sub>. **e)** 1-Naphthoyl chloride, AlCl<sub>3</sub>, ClCH<sub>2</sub>CH<sub>2</sub>Cl.

Structure				
Number	VI'	VII'	VII'	IX'
Yield (%)	30	35	37	32

**Figure 2:** Dimers of benzo[*b*]thiophenes formed on the alcohol reduction (step **d**) and their respective yields.

The dimerization mechanism probably involves the carbocation intermediate which is produced during the alcohol reduction. Subsequently this carbocation is attacked by the C-3 atom of another benzo[*b*]thiophene molecule (scheme 2a).

This result could give an interesting light in the search of an efficient strategy directed to get C-3 substituted benzo[*b*]thiophene. An example with benzyl alcohol is shown on scheme 2b.



**Scheme 2:** a) Mechanism of carbocation production and subsequently nucleophilic attack of 3-C benzo[*b*]thiophene. b) Example of a useful reaction among the heterocycle and vinyl alcohols.

## CONCLUSION

We report a novel class of benzo[*b*]thiophene dimers formed through the generation of a carbocation intermediate and the C-3 benzo[*b*]thiophene. This result represents a probable new strategy directed to the obtaining of 3- substituted benzo[*b*]thiophene. New experimental examples of this reaction are currently ongoing in order to define the scope of this strategy.

## ACKNOWLEDGEMENTS

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## REFERENCES

- Peter, D.C.; Andrew, K.; Shaun, T.M.; James, G.K.Y. Alkylation of Thiophenes and Preparation on Benzothiophenes Using Modified Montmorillonite Clay Catalyst. *Phosphorus, Sulfur, Silicon Rel. Elem.* **1994**, 95, 441-443.
- Peter, D.C.; Shaun, T.M. Benzoylation of Benzo[*b*]thiophene using ZnCl<sub>2</sub>- Modified Montmorillonite Clay. *Phosphorus, Sulfur, Silicon Rel. Elem.* **1995**, 105, 157-62.