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SYNTHESIS OF 3,4-DIHYDROXYXANTHONE DERIVATIVES: HIT OPTIMIZATION

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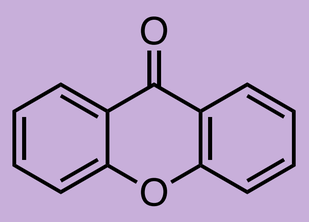
1. INTRODUCTION

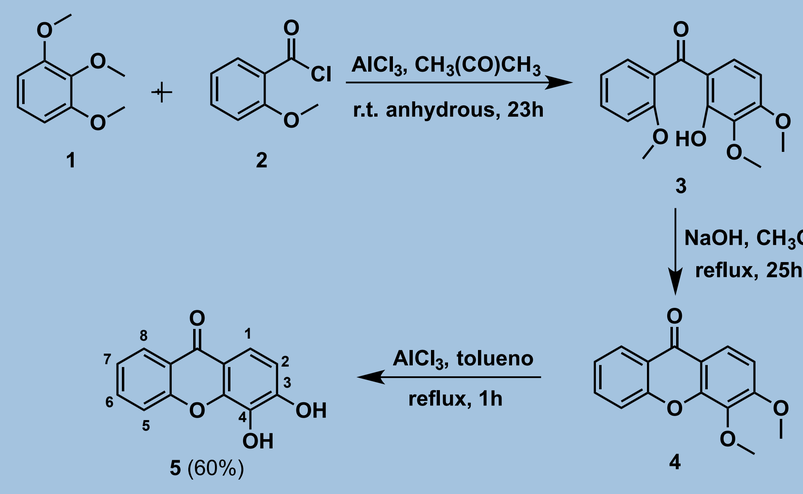
Xanthones (9*H*-xanthen-9-ones) belong to a class of *O*-heterocycles and correspond chemically to the structure of the dibenzo-γ-pyrone [1]. Xanthone scaffold can be considered as a privileged structure and the growing interest in this class of compounds has been associated to the diverse pharmacological activities that can display [2-3].



The hit compound 3,4-dihydroxyxanthone (**5**) [4] is a versatile building block that exhibited good antifouling activity. Herein, the synthesis of three new derivatives is reported and their structure elucidation was performed by NMR and IR techniques.

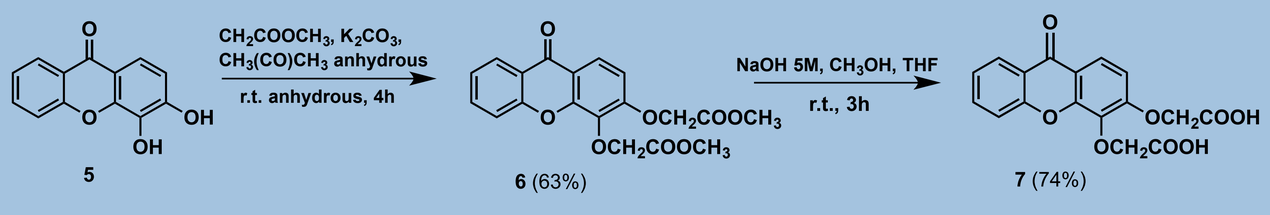
2. SYNTHESIS

3,4-Dihydroxyxanthone (**5**) was synthesized *via* benzophenone (Scheme 1), one of the most used pathways in synthesis of xanthones [4].

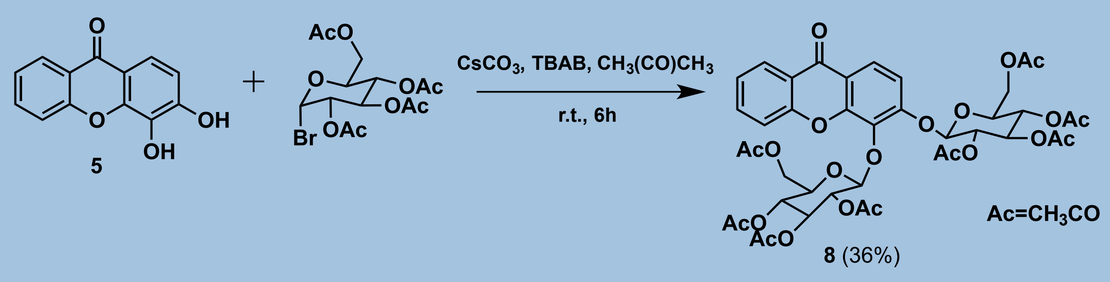


Scheme 1 – Synthesis of 3,4-dihydroxyxanthone (**5**).

Three new derivatives, namely 3,4-diacetomethoxy (**6**), 3,4-dicarboxymethoxyxanthone (**7**) and 3,4-*O*-β-D-acetoglucoxanthone (**8**) were synthesized by different methods (Schemes 2 and 3).



Scheme 2 – Synthesis of 3,4-diacetomethoxyxanthone (**6**) and 3,4-dicarboxymethoxyxanthone (**7**).



Scheme 3 – Synthesis of 3,4-*O*-β-D-acetoglucoxanthone (**8**).

3. STRUCTURE ELUCIDATION

Structure elucidation of 3,4-dihydroxyxanthone (**5**) and derivatives **7 and 8**, was performed by IR, ^{1}H, and ^{13}C NMR.

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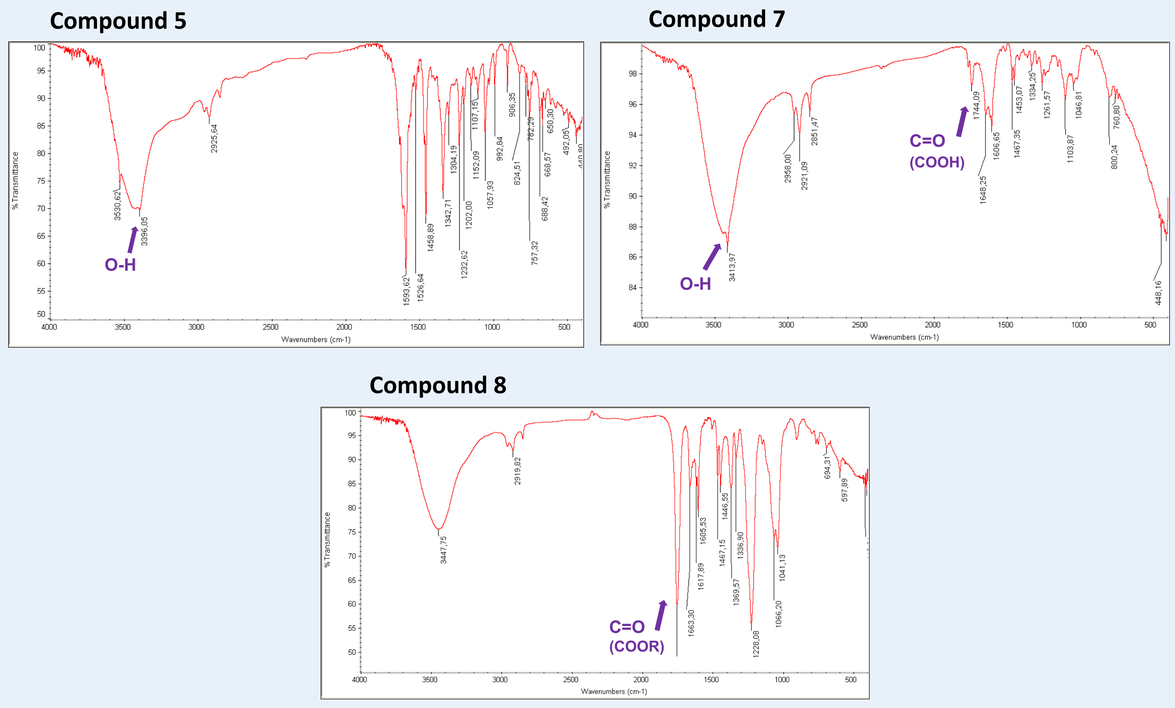

Figure 1 – IR spectra of compounds **5**, **7**, and **8** (KBr).

NMR

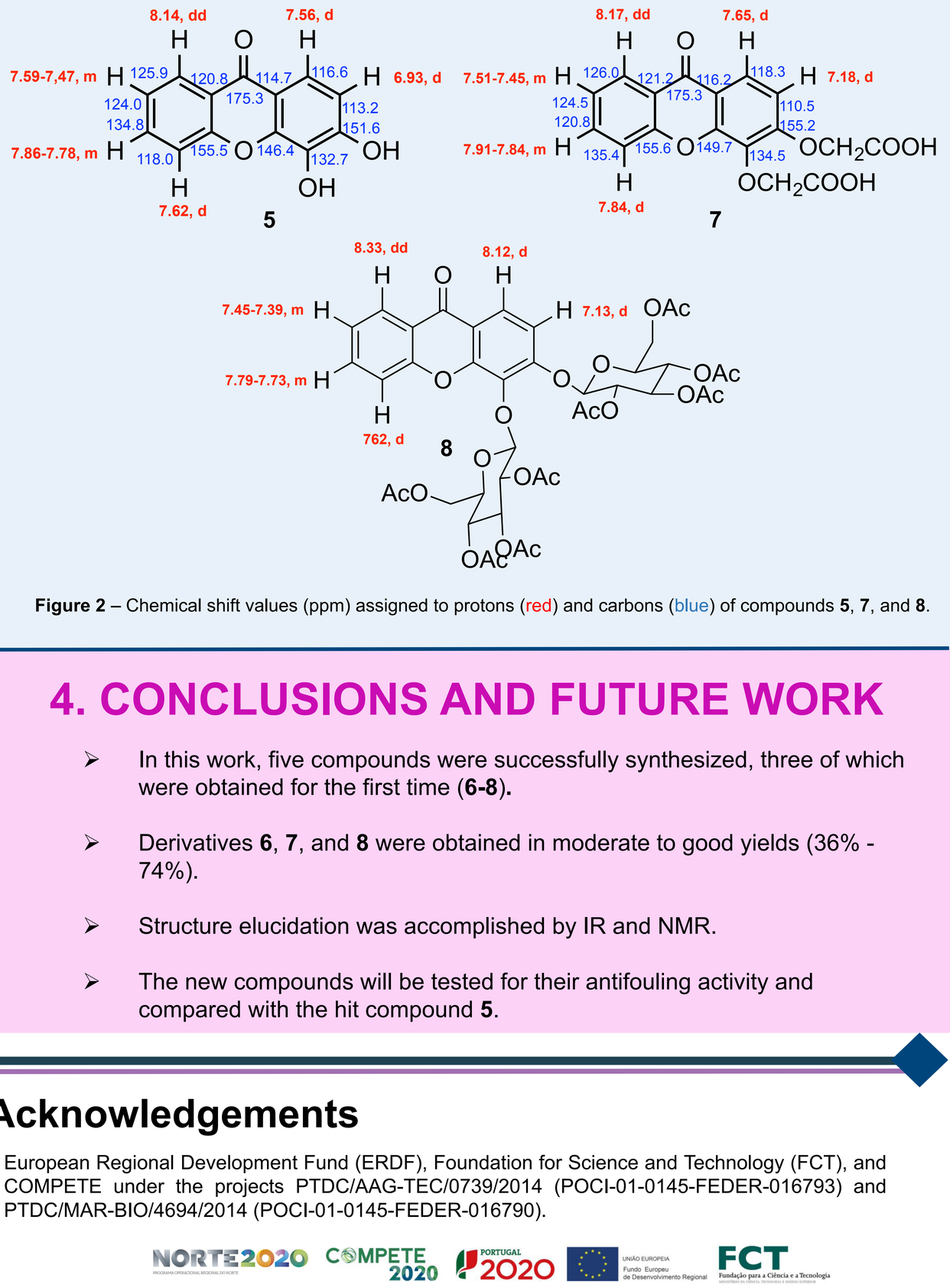

Figure 2 – Chemical shift values (ppm) assigned to protons (red) and carbons (blue) of compounds **5**, **7**, and **8**.

4. CONCLUSIONS AND FUTURE WORK

- In this work, five compounds were successfully synthesized, three of which were obtained for the first time (**6-8**).
- Derivatives **6**, **7**, and **8** were obtained in moderate to good yields (36% - 74%).
- Structure elucidation was accomplished by IR and NMR.
- The new compounds will be tested for their antifouling activity and compared with the hit compound **5**.

References

[1] Sousa, M. E.; Pinto, M. M. *Current medicinal chemistry* **2005,** *12* (21), 2447-79.
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[3] Azevedo, C.; Afonso, C.; Pinto, M. *Current Organic Chemistry* **2012,** *16* (23), 2818-2867.
[4] Pedro, M.; Cerqueira, F.; Sousa, M. E.; Nascimento, M. S.; Pinto, M. *Bioorganic & medicinal chemistry* **2002,** *10* (12), 3725-30.

Acknowledgements

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