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Synthesis and chemical reactivity of novel polyhydroxylated bis-chalcones

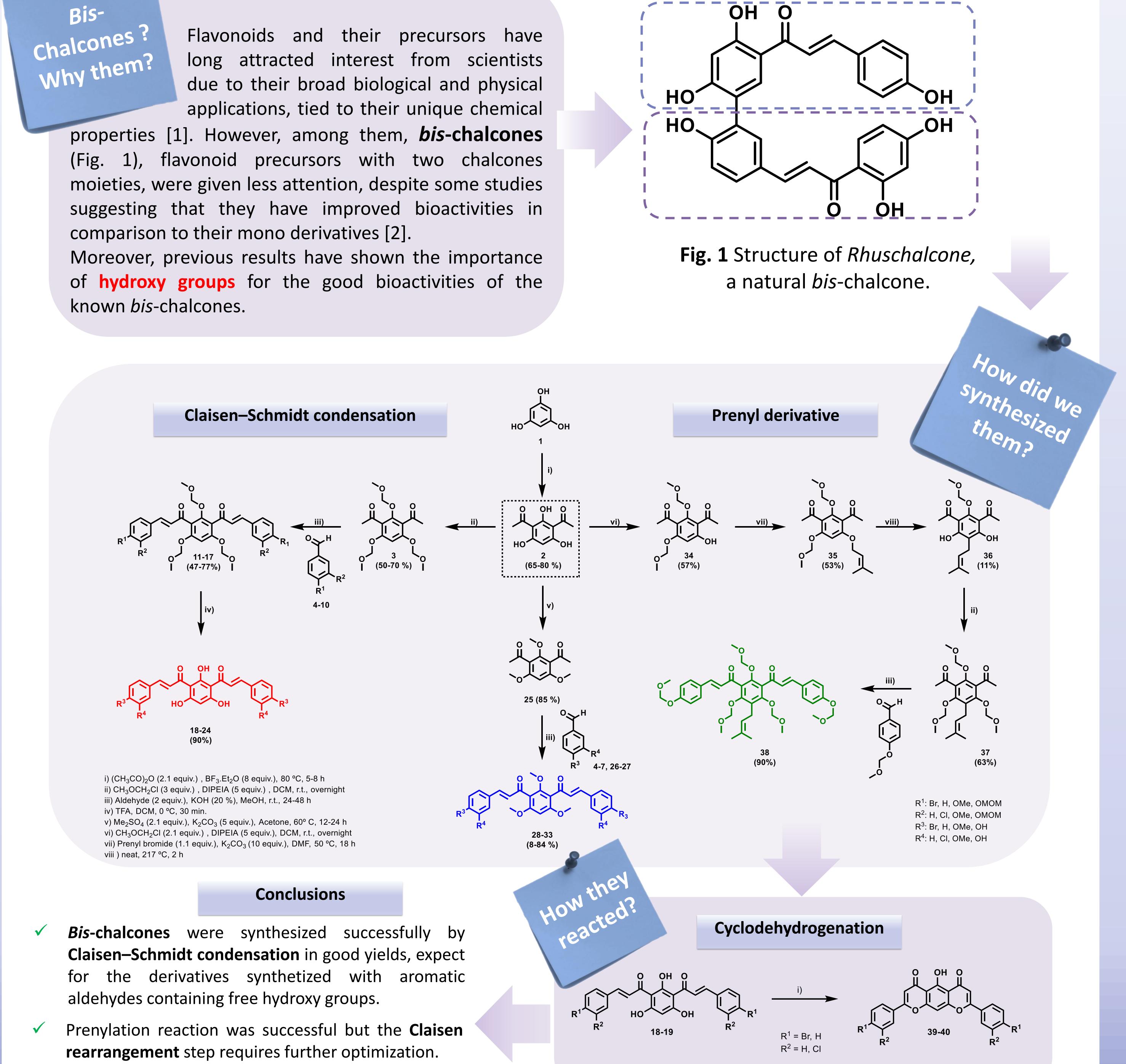


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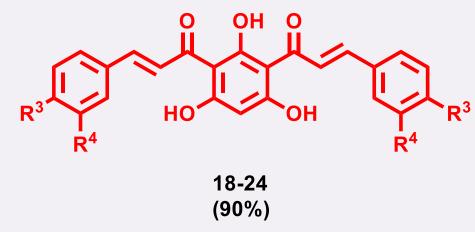
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Flavonoids and their precursors have long attracted interest from scientists due to their broad biological and physical applications, tied to their unique chemical



moieties, were given less attention, despite some studies suggesting that they have improved bioactivities in comparison to their mono derivatives [2]. Moreover, previous results have shown the importance of hydroxy groups for the good bioactivities of the known *bis*-chalcones.



i) (CH₃CO)₂O (2.1 equiv.) , BF₃.Et₂O (8 equiv.), 80 °C, 5-8 h ii) CH₃OCH₂CI (3 equiv.), DIPEIA (5 equiv.), DCM, r.t., overnight iii) Aldehyde (2 equiv.), KOH (20 %), MeOH, r.t., 24-48 h iv) TFA, DCM, 0 °C, 30 min. v) Me₂SO₄ (2.1 equiv.), K₂CO₃ (5 equiv.), Acetone, 60° C, 12-24 h vi) CH₃OCH₂CI (2.1 equiv.) , DIPEIA (5 equiv.), DCM, r.t., overnight vii) Prenyl bromide (1.1 equiv.), K₂CO₃ (10 equiv.), DMF, 50 °C, 18 h viii) neat, 217 °C, 2 h



Bis-chalcones were synthesized successfully by **Claisen–Schmidt condensation** in good yields, expect for the derivatives synthetized with aromatic aldehydes containing free hydroxy groups.

- Prenylation reaction was successful but the **Claisen rearrangement** step requires further optimization.
- Cyclization of *bis-chalcones* was successful yet difficult to purify. The presence of a free hydroxy group during the reaction may have caused unwanted degradation.
- The next step will be the evaluation of the anti**inflammatory activity** of all *bis*-chalcones obtained.

i) DMSO, I₂, 190 °C, 30 min.

References

[1] A. Sousa, M. Lucas, D. Ribeiro, C. Correia, V. L. M. Silva, A. M. S. Silva, E. Fernandes, M. Freitas, J. Nat. Prod., 83 (2020), 3131–3140. [2] C. Zhuang, W. Zhang, C. Sheng, W. Zhang, C. Xing, Z. Miao, Chem. Rev., 117 (2017), 7762-7810

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