Synthesis of (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones

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Introduction

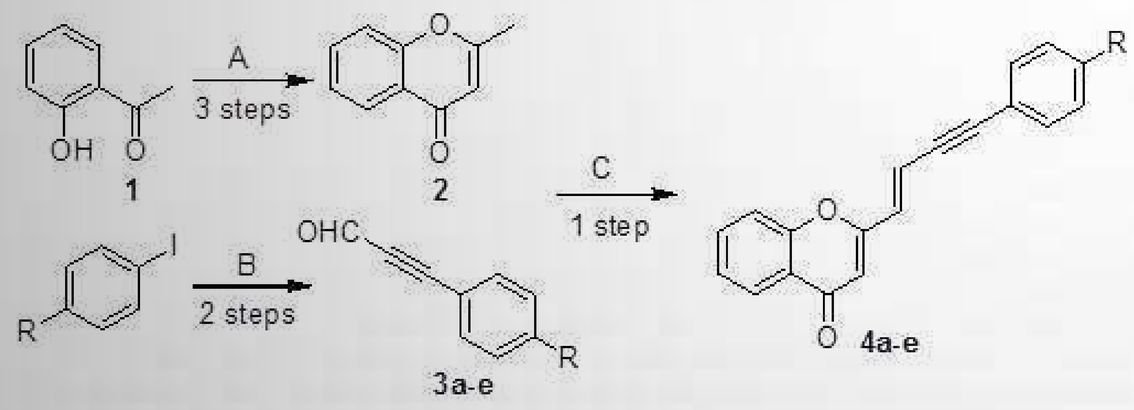
Chromones are a well-known class of naturally occurring oxygen-containing heterocyclic compounds; many of them playing important biological functions in nature [1]. Although 2-methylchromones are one of the scarcest classes of natural chromones, their synthesis and reactivity is well studied. They can participate in several chemical transformations such as oxidation, thiation, hydrogenation, photolysis, cycloaddition and condensation reactions, being useful targets in the synthesis of novel heterocyclic compounds [2]. The acidity of the 2-methyl group, due to the low electron density at C-2 caused by oxygen atom and the α,β-unsaturated ketone system, led us to explore the condensation of 2-methylchromones [3] with propargyl aldehydes [4].

Experimental section and results

The synthetic strategy for the preparation of (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones involved:

- The synthesis of 2-methylchromone **2** by a three step sequence starting from 2'-hydroxyacetophenone **1**.
- The synthesis of propargyl aldehydes **3** reacting the appropriated iodobenzene with propargyl alcohol and subsequent oxidation.
- The condensation of 2-methylchromone **2** with propargyl aldehydes **3a-e** leading to the desired (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones **4a-e**.

General procedure



Reaction Conditions:
A: (i) MeCOCl, dry pyridine, r.t., 12 h; (ii) NaH, dry THF, reflux, 2 h; (iii) *p*-TSA, DMSO, 100°C, 2 h.
B: (i) $Pd(PPh_3)Cl_2$, PPy, CuI, propargyl alcohol, toluene, 60 °C, 2h; (ii) activated MnO_2, ethyl acetate, reflux, 2h.
C: Sodium, dry EtOH, r.t., 4 h.

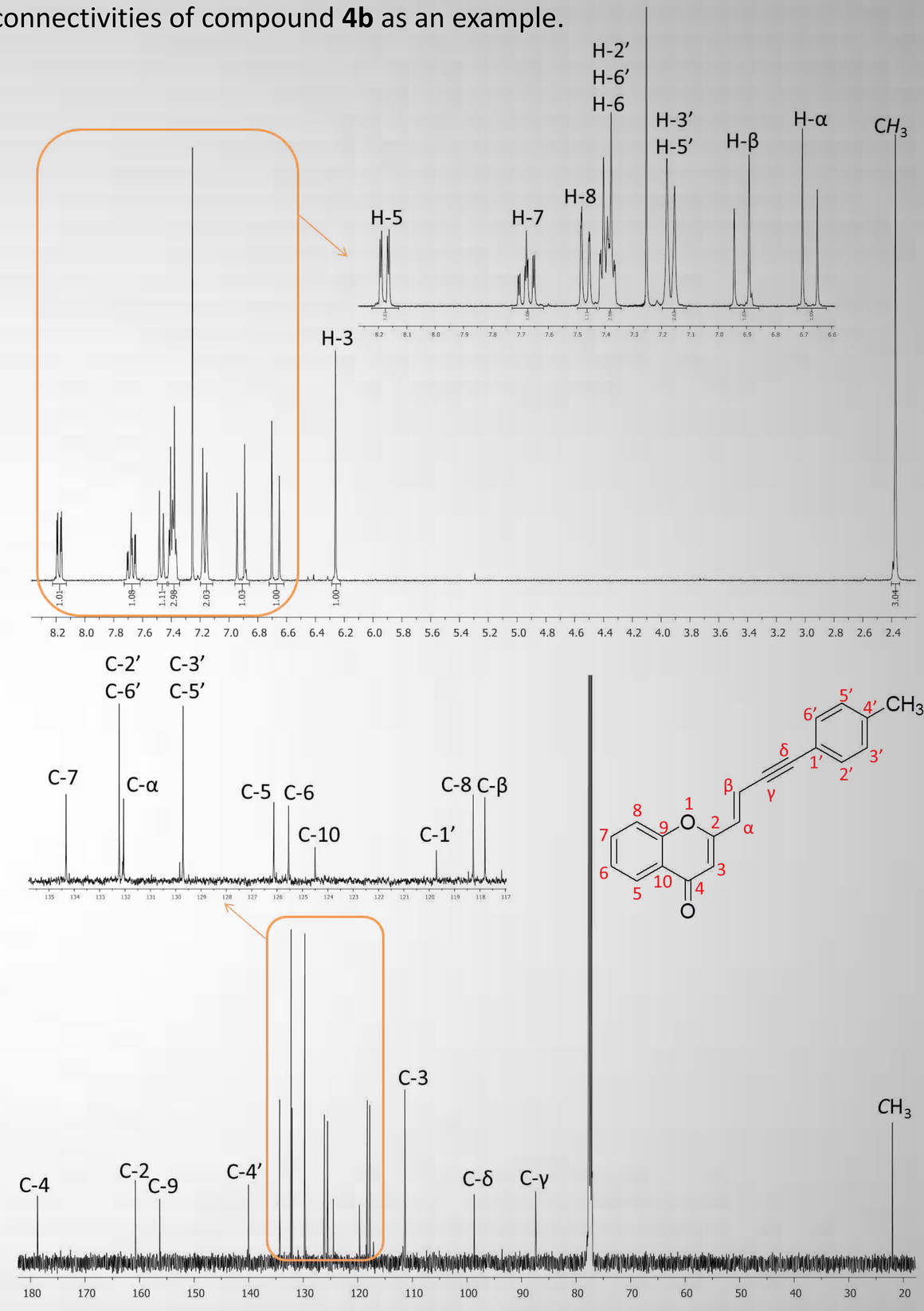
Results

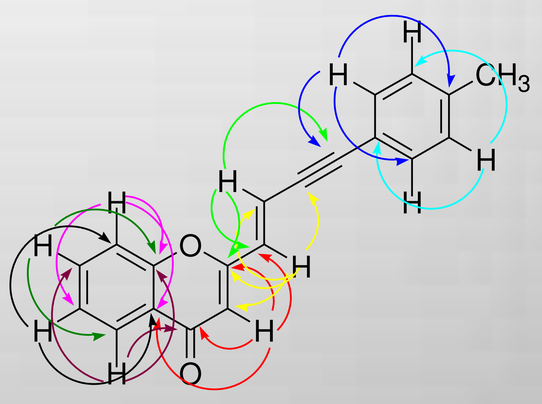
Compound	R	Yield (%)
4a	H	52
4b	CH_3	80
4c	OCH_3	80
4d	Br	59
4e	NO_2	30

[1] Sharma S. K., Kumar S., Chand K., Kathuria A., Gupta A., Jain R. *Curr. Med. Chem.* **2011**, *18*, 3825.
[2] Ibrahim, M. A.; Ali, T. E.; Alnamer, Y. A.; Gabr, Y. A. *Arkivoc* **2010**, (i), 98.
[3] Hirao, I.; Yamaguchi, M.; Hamada, M. *Synthesis*, **1984**, 1076.
[4] a) Tretyakov, E. V.; Tkachev, A. V.; Rybalova, T. V.; Gatilov, Y. V.; Knight, D. W.; Vasilevsky, S. F.; *Tetrahedron*, **2000**, *56*, 10075. b) Wadsworth, D. H.; Gecr, S. M.; Detty, M. R. *J. Org. Chem.* **1987**, *52*, 3662. c) Bumagin, N. A.; Ponomaryov, A. B.; Beletskaya, I. P. *Synthesis*, **1984**, 728.

Structural elucidation

The structural characterization of compounds **4a-e** was obtained by 1D and 2D-NMR studies. We present below the ^{1}H-NMR, ^{13}C-NMR and HMBC connectivities of compound **4b** as an example.





Most important HMBC connectivities of compound **4b**.

Conclusions

The (*E*)-2-(4-arylbut-1-en-3-ynyl)-4*H*-chromen-4-ones **4a-d** were synthesized *via* aldol condensation of 2-methylchromone **2** (obtained *via* Baker-Venkataraman methodology) with propargyl aldehydes **3a-d** in moderate to good yields. Compound **4e** was obtained in low yield due to the degradation of the corresponding propargyl aldehyde during the condensation reaction.

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