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Convenient synthesis of linear pyrano[3,2-*g*]-, [2,3-*g*]- and angular pyrano[3,2-*f*]coumarins from 4[(1,1-dimethyl-2-propynyl)oxy]phenol☆

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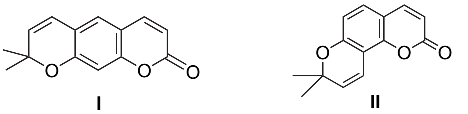
Abstract—An easy preparation of new 4-alkoxycarbonyl angular and linear pyranocoumarins starting from 4-[(1,1-dimethyl-2-propynyl)-oxy]phenol and their transformation to the known coumarins xanthyletin, 8,8-dimethylpyrano[3,2-*f*]chromen-3(8*H*)-one and 7,7-dimethyl-pyrano[2,3-*g*]chromen-2(7*H*)-one is described.

1. Introduction

Several linear and angular pyranocoumarins, like xanthyletin (**I**) and seselin (**II**) have been isolated from natural sources.[1–5] These compounds are known to possess useful biological activities.[3–6] Thus, xanthyletin shows[4] antifungal, insecticidal, anticancer, and anti-HIV activities, while seselin is used as a photoactive drug for skin disorders.[5] For the syntheses of these compounds various methods have been developed.[4–11]



I **II**

Thus, the 7-(1,1-dimethyl-prop-2-ynyl)ethers of coumarins, when heated, at reflux in *N*,*N*-dimethylaniline, gave the angular pyranocoumarins with cyclization taking place at the more reactive 8-position. If the 8-position is substituted however, the corresponding 8-substituted linear pyranocoumarins are obtained.[6–8] Thermal [3,3]-sigmatropic rearrangement of 6-prop-2-ynyloxycoumarins also resulted in the efficient synthesis of angular pyrano[3,2-*f*]chromen-2(7*H*)-ones.[9] Angular pyranocoumarins were also obtained from both 5- and 7-hydroxycoumarins and 1,1-diethoxy-3-methyl-2-butene,[10] while seselin and seselin derivatives were conveniently prepared in a two-step approach from 2,4-dihydroxybenzaldehyde and 2,4-dihydroxyacetophenone, using Claisen rearrangement and Wittig reaction.[5] 6-Hydroxy-2,2-dimethyl-2*H*-chromen-7-carbaldehyde and 7-hydroxy-2,2-dimethyl-2*H*-chromen-6-carbaldehyde, prepared earlier by the formylation of the corresponding 6-methoxy- and 7-methoxy-chromene derivatives and subsequent demethylation, were effectively converted into the corresponding linear pyranocoumarins by refluxing with *N*,*N*-dimethylacetamide dimethylacetal.[11]

4-Alkoxycarbonylcoumarins have been prepared earlier,[12,13] mainly by our group, from the reaction of *o*-quinones with alkoxycarbonylmethylene(triphenyl)phosphoranes ($Ph_3P{=}CHCOOR$) via an initial Wittig monoolefination to the corresponding *o*-quinonemethide, which by further Michael addition of a second ylide species followed by Hofmann elimination of Ph_3P, and finally by δ-lactonization gives rise to the corresponding coumarins. Recently Yavari and co-workers reported[14] that reactions of phenols with DMAD in the presence of Ph_3P lead to the corresponding 4-methoxycarbonylcoumarins via an initial addition of Ph_3P to the acetylenic ester and a concominant protonation of the reactive 1:1 adduct, followed by electrophilic attack of the vinyltriphenylphosphonium cation formed to the aromatic ring, in the *ortho* position relative to the strongly activating PhO-group.

Brown and co-workers in 1990 reported[15] the synthesis of 4-[(1,1-dimethyl-2-propynyl)oxy]phenol **1** from hydroquinone, which by refluxing in *o*-xylene afforded 2,2-dimethylchromen-6-ol **2**. Oxidation of **2** with Fremy's salt gave 2,2-dimethyl-2*H*-chromene-6,7-dione (**3**).

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Keywords: Pyranocoumarins; Xanthyletin; Phenols; DMAD; Ph_3P; Wittig reaction; δ-Lactonization; Dealkoxycarbonylation.

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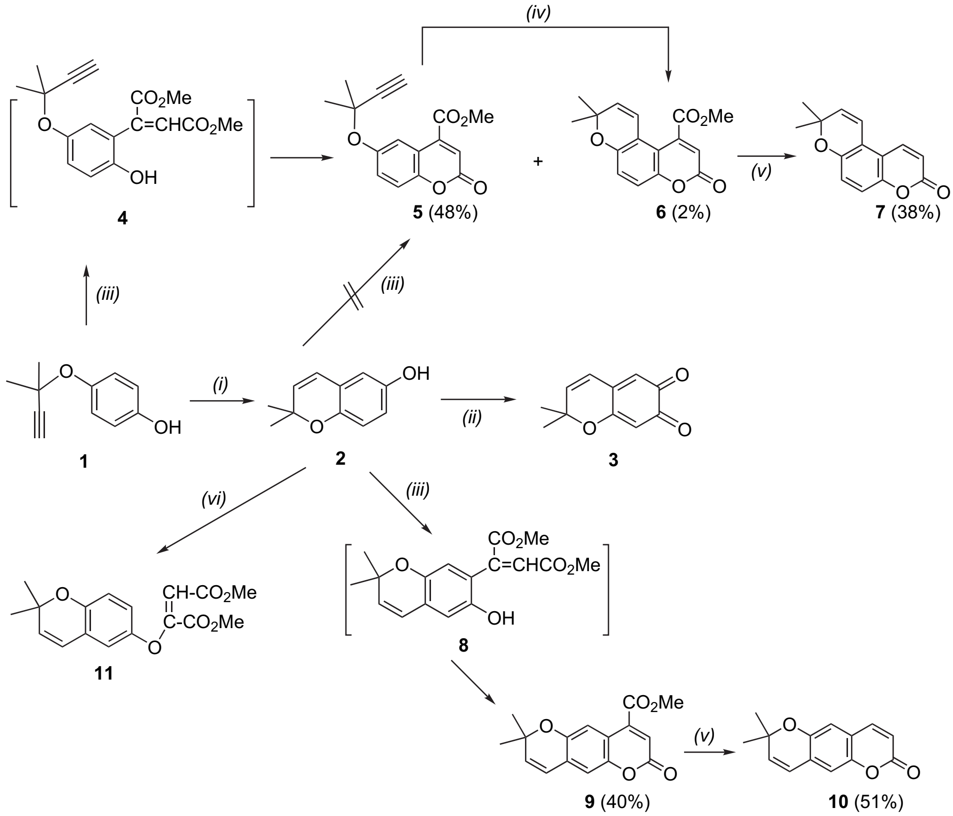
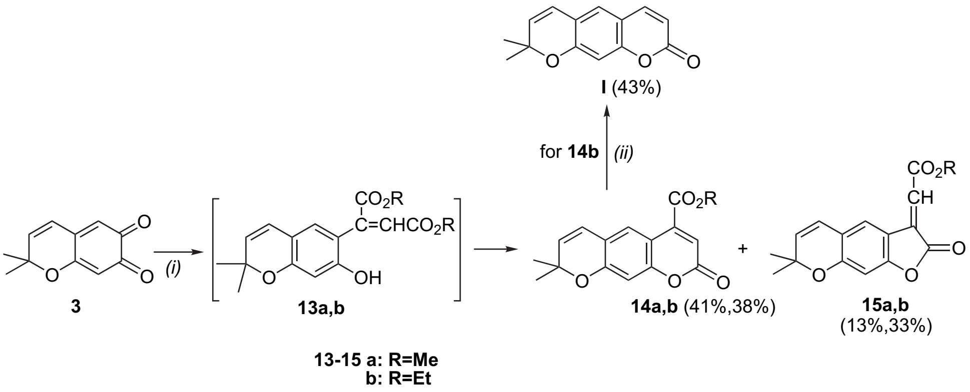


Scheme 1. Reagents and conditions: (i) Ref. 15, *o*-xylene, reflux, N_2 (91%); (ii) Ref. 15, Fremy's salt (68%); (iii) Ph_3P, DCM, DMAD (at −5 °C), reflux; (iv) *o*-xylene, reflux (77%); (v) Cu, quinoline, N_2, 175–180 °C, 19 h and (vi) DMAD, $ZnCl_2$, N_2, 100 °C, 1.5 h (23%).



Scheme 2. Reagents and conditions: (i) $Ph_3P{=}CHCOOR$ (**12a**: R=Me, **b**: R=Et), DCM, rt, N_2, 30 min and (ii) Cu, quinoline, N_2, 175–180 °C, 19 h.

As a continuation of our investigation on the syntheses of coumarin derivatives,[13] we now report the easy preparation of the new coumarin derivatives **6**, **9**, and **14a**,**b** from the compounds **1**, **2**, and **3**, respectively. The reactions studied and the products obtained are depicted in Schemes 1–2.

2. Results and discussion

Treatment of phenol **1** with DMAD in the presence of Ph_3P in refluxing DCM for two days, and separation of the reaction mixture by column chromatography afforded methyl 6-[(1,1-dimethyl-2-propynyl)oxy]-2-oxo-2*H*-chromene-4-carboxylate (**5**) and methyl 8,8-dimethyl-3-oxo-3,8-dihydropyrano[3,2-*f*]chromene-1-carboxylate (**6**) in 48% and 2% yields, respectively. Compound **5** by refluxing in *o*-xylene for 20 h gave coumarin **6** in 77% yield (Scheme 1). Obviously product **5** was obtained by δ-lactonization of the intermediate **4** and gave the angular coumarin **6** by further cyclization.[9]

When compound **1** was previously cyclized to phenol **2** according to the lit. 15 and the latter was then subjected to a similar treatment with Ph_3P and DMAD in refluxing DCM for five days, ethyl 7,7-dimethyl-2-oxo-2,7-dihydropyrano[2,3-*g*]chromene-4-carboxylate (**9**) was obtained in 40% yield. The linear coumarin **9** was obviously produced by further δ-lactonization of the intermediate **8**. Both key intermediates **4** and **8** are formed via an electrophilic attack of the vinyltriphenylphosphonium cation[14] on the aromatic