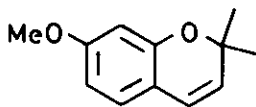


SYNTHESIS OF 2,2-DIMETHYL-2H-CHROMENES

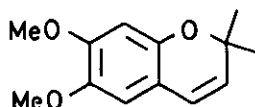
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Abstract — The antijuvenile hormones precocenes I and II (1,2), and related 2,2-dimethyl-2H-chromenes (12,13) were synthesized by oxidative cyclization of *o*-isoprenylphenols with *m*-chloroperbenzoic acid, followed by dehydration of the corresponding 3-chromanols with methyltriphenoxyposphonium iodide.

Precocene I (7-methoxy-2,2-dimethyl-2H-chromene, 1) and precocene II (6,7-dimethoxy-2,2-dimethyl-2H-chromene, 2) isolated from the plant *Ageratum houstonianum*¹ are potentially useful insect antijuvenile hormone. Owing to this attractive biological property, several synthetic methods have been reported².



1



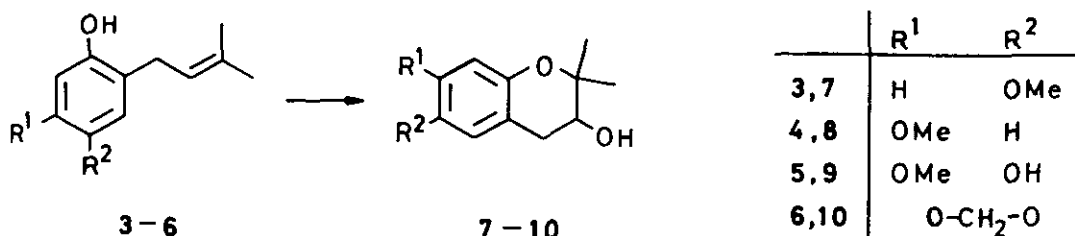
2

In continuation of our studies on the synthesis of biologically active natural products^{3,4}, we wish to report an alternative method for the synthesis of precocenes and related chromenes by oxidative cyclization⁵ of *o*-isoprenylphenols and subsequent dehydration.

The *o*-isoprenylphenols 3,4,5 and 6 were prepared according to Yamada's method⁶.

Compound 5 was more conveniently obtained by isoprenylation of methoxyhydroquinone with 2-methylbut-3-en-2-ol in aqueous formic acid⁷.

The oxidative cyclization of substrates 3-6 were performed with *m*-chloroperbenzoic acid in methylene chloride solution at 0°C. Catalytic amounts of concentrated hydrochloric acid were added in order to avoid the formation of 2,3-dihydrobenzofurans⁸ and maximize the production of 2,2-dimethyl-3-chromanols 7-10 (Scheme 1).



Scheme 1

Yields and spectral properties of chromanols 7-10 prepared under these conditions are described in Table 1.

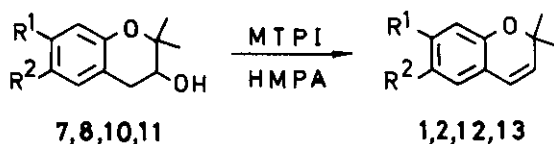
Table 1. Chromanols obtained by oxidative cyclization of *o*-prenylphenols 3 + 6.

Substance	Yield(%)	I.r.spectra(ν cm ⁻¹) ^a	¹ H-nmr spectra(δ ppm) ^b	M.spectra;m/z(%)
7	40	3310, 1490, 1370, 1360	1.32(s, 3H), 1.36(s, 3H), 2.09(br s, 1H), 2.72(dd, 1H, J=17; 5Hz), 3.06(dd, 1H, J=17; 5Hz), 3.66-3.92(m, 1H), 3.78(s, 3H), 6.5-6.9(m, 3H).	M ⁺ 208(100), 175(49), 137(96)
8	81	3450, 1620, 1580, 1500, 1445, 1380, 1365	1.34(s, 3H), 1.38(s, 3H), 1.83(br s, 1H), 2.69(dd, 1H, J=16; 5Hz), 3.03(dd, 1H, J=17; 5Hz), 3.7-3.9(m, 1H), 3.79(s, 3H), 6.44(s, 1H, J=13Hz), 6.53(dd, 1H, J=8; 3Hz), 6.98(d, 1H, J=8Hz).	M ⁺ 208(29), 175(5), 137(100)
9	32	3450, 1510, 1375br	1.32(s, 3H), 1.38(s, 3H), 1.74(br s, 1H), 2.66(dd, 1H, J=17; 5Hz), 3.01(dd, 1H, J=17; 5Hz), 3.6-4.0(m, 1H), 3.88(s, 3H), 5.26(br s, 1H), 6.44(s, 1H), 6.64(s, 1H)	M ⁺ 224(34), 191(7), 154(14), 153(100)
10	90	3515, 1630, 1480, 1390, 1380	1.31(s, 3H), 1.37(s, 3H), 1.82(br s, 1H), 2.66(dd, 1H, J=17; 5Hz), 3.01(dd, 1H, J=17; 5Hz), 3.76(t, 1H, J=5Hz), 5.91(s, 2H), 6.43(s, 1H), 6.54(s, 1H)	M ⁺ 222(29), 189(6), 152(12), 151(100)

a. Obtained in KBr (7,9,10) and neat (8); b. Performed in CDCl₃ solution using TMS as internal standard.

Attempted dehydration of chromanol **7** by means of a variety of reagents (POCl_3/Py ; TsCl/Py and DMF ; MsCl/Py and DMF) gave only low conversions (10-45%). Better results were obtained by reaction of **7** with methyltriphenoxyposphonium iodide⁹ in dry HMPA solution, to afford the chromene **12** in 80% yield. In view of this, dehydration of chromanol **8**, **10** and **11** were carried out using this procedure. The results obtained are summarized in Table 2.

Table 2. 2,2-Dimethyl-2H-chromenes prepared by dehydration of chromanols.



Substrate	Chromene ¹⁰	R ¹	R ²	Yield (%)
7	12	H	OMe	80
8	1	OMe	H	81
10	13	O-CH ₂ O		45 ^b
11^a	2	OMe	OMe	55 ^b

a. Compound **11** was obtained by methylation of **9** with $\text{Me}_2\text{SO}_4\text{-KOH}$;

b. No attempts were made to improve yields.

Experimental details of this chromene synthesis will be reported in a forthcoming paper.

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