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DIRECT PREPARATION OF 3,4-DICHLORO-2,2-DIMETHYL-3-CHROMENES FROM 2,2-DIMETHYL-4-CHROMANONES

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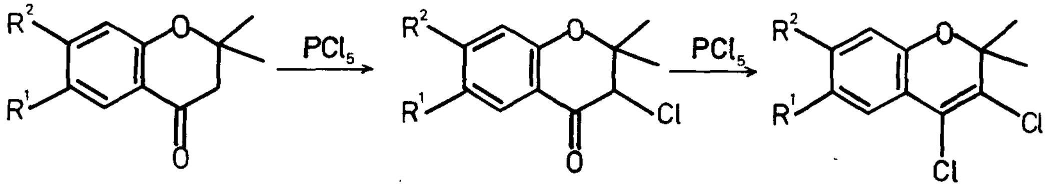
Summary: Reaction of 2,2-dimethyl-4-chromanones(1) with two equivalents of phosphorus pentachloride affords 3,4-dichloro-2,2-dimethyl-3-chromenes(2) in variable yields depending on the substituents of the aromatic ring. A plausible pathway for this reaction is given.

In a research program of this laboratory devoted to the preparation of insect antijuvenile hormone[1] analogues for structure-activity relationship studies, the synthesis of 6-and/or 7-alkoxy-2,2-dimethyl-3-and/or 4-halogenochromenes was required.

By analogy with previous results reported in the literature on the reaction of acetophenones with PCl_5[2], one might expect that treatment of 2,2-dimethyl-4-chromanones(1) with this reagent would easily afford the corresponding 2,2-dimethyl-4-chloro-3-chromenes. However, when equimolecular amounts of 7-methoxy-2,2-dimethyl-4-chromanone(1c) and PCl_5 were allowed to react about 50% of starting compound remained unchanged and the only product isolated from the reaction mixture exhibited the spectral and analytical features expected for 7-methoxy-2,2-dimethyl-3,4-dichloro-3-chromene(2c).

This unforeseeable result suggested the participation of PCl_5 in two consecutive processes, in which the intermediate formed in the first reaction step should be more reactive towards that reagent than the starting 1. Accordingly, as shown in Table 1, when the reaction was carried out on several 6-and/or 7-alkoxy-4-chromanones using a 1:2 1:PCl_5 molar ratio, in CCl_4, 8 h at room temperature, followed by evaporation of the solvent and purification of the residue by SiO_2 column chromatography (4:1 hexane:diethyl ether), bulb to bulb distillation at reduced pressure or crystallization, high yields of the corresponding 3,4-dichloro-2,2-dimethyl-3-chromenes 2 were obtained.

A plausible pathway for this reaction is as follows:



1 3 2

Whereas the transformation implied in the second step has been known for many years[3], we could not find previous evidence for the α-chlorination of such carbonyl compounds with PCl_5. However, in the reaction of 2,2-dimethyl-4-chromanone(1a) a 54% yield of 3-chloro-2,2-dimethyl-4-chromanone(3a) was isolated together with 15% of 2a, in all the other cases where the aromatic ring bears electron-donor substituents, the intermediate 3 or any of its possible precursors could not be detected and the reaction proceeded towards completion.

Table 1

Preparation of 3,4-dichloro-2,2-dimethyl-3-chromenes(2)

Compound	R^1	R^2	Yield[a] (%)	m.p. or b.p.(°/torr)[b]	IR(CCl_4) ν(cm^{-1})	^1H NMR (ppm)
a	H	H	15[c]	—	1615	1.53(s,6H);6.50-7.40 (m,4H)
b[d]	OCH_3	H	82	115°/0.3	1655,1615,1575	1.50(s,6H);3.71(s,3H); 6.60-6.90(m,3H)
c	H	OCH_3	81	112°/0.3	1625,1615	1.51(s,6H);3.70(s,3H); 6.20-6.50(m,2H);7.20 (d,J=9Hz,1H)
d	OCH_3	OCH_3	78	69.5-70.5	1612	1.50(s,6H);3.75(s,6H); 6.28(s,1H);6.83(s,1H)
e	$-OCH_2O-$		78	72-73	1632,1625	1.50(s,6H);5.87(s,2H); 6.29(s,1H);6.86(s,1H)

a)All new compounds gave satisfactory elemental microanalyses. b) m.p. determined on a Kofler hot stage apparatus are uncorrected; b.p. measured in bulb to bulb distillation. c)Yellowish oil purified by column chromatography(SiO_2, 4:1 hexane:diethyl ether); in this way 54% of 3a was also isolated. d) Reaction carried out under reflux.

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