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A CONVENIENT SYNTHESIS OF 4-METHYL-2H-1-BENZOTHIOPYRAN-2-ONES (4-METHYLTHIOCOUMARINS)

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4-Methyl-2H-1-benzothiopyran-2-ones (4-methylthiocoumarins) were conveniently prepared by the reaction of S-phenyl 3-oxobutanethioates with aluminium chloride. The spectral characteristics of these compounds were summarized.

It is well known that 2H-1-benzothiopyran-2-ones (thiocoumarins) can not be obtained by the Pechmann reaction of benzenethiols.$^{1)}$ Thiocoumarins are generally prepared from the unstable 2-mercaptobenzaldehydes which require multistage processes from benzenethiol derivatives.$^{2)}$ Recently, it has been reported that thiocoumarins are prepared from 2-t-butylthiobenzaldehyde by two steps.$^{3)}$ The spectral characteristics of 4-methylthiocoumarins are very little known. In a previous paper,$^{4)}$ we reported a method to prepare the thiocoumarin by the cyclization of S-phenyl 3-oxobutanethioates 1, which were obtained by the reaction of benzenethiols and diketene, with polyphosphoric acid (PPA). But in most those cases, isomeric 2-methylthiochromone derivatives 3 were exclusively obtained. We studied the reaction of 1 with various condensing agents to prepare 4-methylthiocoumarins 2.

We now found that some of 4-methylthiocoumarins 2 were conveniently obtained when aluminium chloride was used as a condensing agent in the cyclization of S-phenyl 3-oxobutanethioates 1. 4-Methylthiocoumarin 2a was prepared from compound 1 as follows: Compound 1(X=H) was added to the suspension of $AlCl_3$ in CS_2 or to $AlCl_3$. After stirring for 2 h or 5 h at reaction temperature shown in Table 1, the mixture was poured into cold water. The resulting solid was separated and recrystallized from EtOH. In any cases in Table 1, no 2-methylthiochromone 3a was obtained.

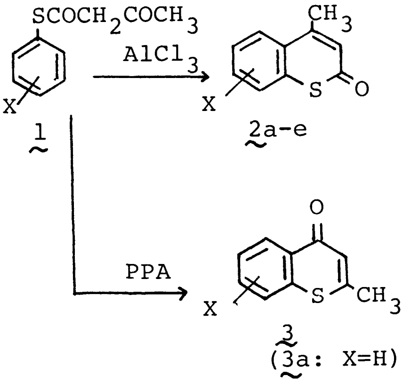
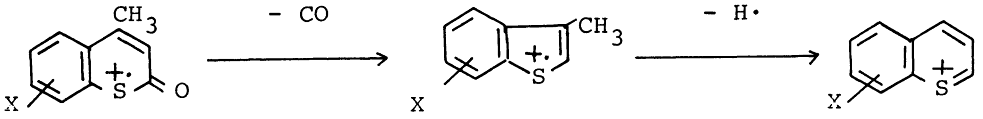


Table 1. The reaction of S-phenyl 3-oxobutanethioate 1 (X=H) with $AlCl_3$

Entry	Solvent	Tempt (°C)	Reaction time (h)	$AlCl_3$ (mole ratio)	Yield of 2a (%)
1	CS_2	46	2	10	29
2	CS_2	46	5	2	trace
3	CS_2	46	5	10	38
4	-	80-90	2	10	48
5	-	140-150	2	10	24

Other 4-methylthiocoumarin derivatives 2b-2e could be prepared by the same method for 2a (Entry 4) (2b: 42%, 2c: 31%, 2d: 16%, 2e: 22%). However, the reaction of methoxyl derivatives of S-phenyl 3-oxobutanethioates 1 (X=2,5-dimethoxy and p- or m- methoxy) with $AlCl_3$ gave only an oily undetermined material, and any of thiocoumarins were not isolated. When $ZnCl_2$ was used as a condensing agent for 1 (X=H), thianthrene was obtained in 11% yield. In the cases of other condensing agents such as PCl_5, P_2O_5, and Ac_2O, oily undetermined materials were obtained. The spectral data and mp of new compounds 2d and 2e were as follows: 2d; mp 167-169°C, νco 1650 and 1630 cm^{-1}, NMR($CDCl_3$) δ=2.65(3H,s), 6.68 (1H,s), and 7.48-8.37 (6H,m), λmax (EtOH) 275nm (ε 2.6×10^4) and 286nm (ε 2.5×10^4), 2e; mp 157-158°C, νco 1645 cm^{-1}, NMR($CDCl_3$)δ=2.54 (3H,s), 6.57 (1H,s), 7.50 (2H,m), and 7.80 (1H,m), λmax (EtOH) 233nm (ε 2.8×10^4), 241nm (ε 2.9×10^4), 290nm (ε 1.2×10^4), and 301nm (ε 1.0×10^4). The spectral characteristics of 4-methylthiocoumarins were as follows: Mass spectra; The major fragmentation was initial loss of carbon monoxide from the molecular ion, followed by the loss of a hydrogen atom leading to the formation of the ring-expanded thianaphthalenium ion (M→[M-28]→[M-29]) (Scheme 1 and Table 2). NMR spectra; The benzenoid proton in 5-position of 4-methylthiocoumarins 2 showed the chemical shift in the range 7.78 - 7.90 ppm. The difference between this proton and other aromatic protons was 0.34 - 0.53 ppm. IR spectra; The carbonyl bands of 2 were found in the range 1635 - 1650 cm^{-1}.



M M-28 M-29

Scheme 1.

Table 2. The Mass and NMR (aromatic protons) spectra of 4-methylthiocoumarins 2

No.	Compounds	m/e (rel. intensity)	NMR ($CDCl_3$) ppm 5-position	NMR ($CDCl_3$) ppm other
2a[5)]	X=H	176 (M,46), 148 (M-28,76), 147 (M-29,100)	7.95	7.56 (3H,m)
2b[5)]	X=7-CH_3	190 (M,45), 162 (M-28,100), 161 (M-29,100)	7.78	7.20-7.30 (2H,m)
2c[5)]	X=6-CH_3	190 (M,48), 162 (M-28,95), 161 (M-29,100)	7.78	7.44 (2H,s)
2d	X=7,8-Benzo	226 (M,46), 198 (M-28,100), 197 (M-29,79)	7.48-8.37 (6H,m)	
2e	X=7-Cl	212 (M+2,9), 210 (M,24), 184 (40), 183 (47) 182 (M-28, 100), 181 (M-29,90)	7.80	7.50 (2H,m)

All products gave satisfactory microanalyses (C± 0.25%, H± 0.08%).

References and Notes

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3) O. Meth-Cohn and B. Tarnowski, Synthesis, 1978, 56.
4) H. Nakazumi and T. Kitao, Chem. Lett., 1978, 929.
5) 2a; mp 126-127 °C(lit,[2)] 124°C), 2b; mp 108-109°C (lit,[2)] 110°C), 2c; mp 114-115°C (lit,[2)] 120°C).

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