BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 50 (6), 1643—1644 (1977)

Synthesis of 3-(Alkoxycarbonylmethylthio)coumarins from Thiocyanatoacetic Esters and Salicylaldehydes

Satoshi KAMBE, Tokiharu TAKAJO, Toshio HAYASHI,* and Hiroshi MIDORIKAWA**

Oyama Technical College, Oyama-shi, Tochigi 323

**The Institute of Physical and Chemical Research, Wako-shi Saitama 351*

***Department of Domestic Science, Showa Women's University, Tokyo 154*

(Received December 8, 1976)

Synopsis. A number of 3-(alkoxycarbonylmethylthio)-coumarins (**3**) were prepared by reactions of thiocyanatoacetic esters (**1**) with salicylaldehydes in the presence of potassium carbonate.

In previous papers,[1-5] it has been shown that thiocyanatoacetic ester (**1**) is available for the synthesis of sulfur-containing heterocycles. Here, the direct synthesis of the hitherto unknown coumarin derivatives from **1** and salicylaldehydes are reported. The reaction of **1b** with salicylaldehyde was carried out in the presence of potassium carbonate at room temperature giving 3-(methoxycarbonylmethylthio)coumarin (**3b**) as the major product and 3,3′-thiodicoumarin (**4**) as a minor product. The structural elucidation of the products are based on elemental analysis and spectral studies. Further confirmation of the structure (**3b**) was made by a comparison with an authentic sample prepared from 2-mercapto-3-(*o*-hydroxyphenyl)acrylic acid (**5**) and **1b** or ethyl chloroacetate (**6**). On the other hand, **4** was also obtained by the reaction of **3** with **2** in the presence of potassium carbonate. In this reaction, **1** and substituted salicylaldehydes also gave similar coumarin derivatives (**3**), but the product corresponding to **4** could not be found.

Although an investigation of the reaction mechanism was not undertaken, the reaction is considered to proceed

TABLE 1. COMPOUNDS **3a—f**, **4**, AND **5**

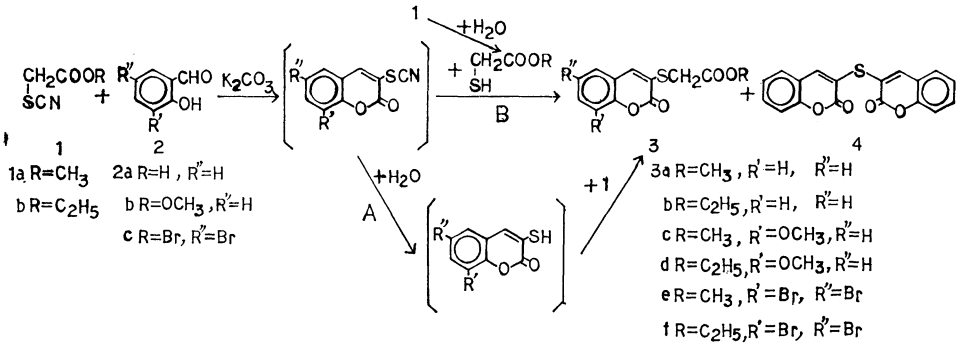
Compound	Yield (%)	Mp (°C)	Formula	Found %			Calcd %		
				C	H	S	C	H	S
3a	29	143—144	$C_{12}H_{10}O_4S$	57.22	3.92	12.79	57.60	4.03	12.81
3b	36	113—114	$C_{13}H_{12}O_4S$	59.19	4.64	12.13	59.08	4.58	12.13
3c	17	118—119	$C_{13}H_{12}O_5S$	55.72	4.32	11.40	55.72	4.53	11.42
3d	20	129—130	$C_{14}H_{14}O_5S$	57.27	4.55	10.64	57.14	4.80	10.87
3e	7	158—159	$C_{12}H_8O_4SBr_2$	35.15	2.01	7.78	35.29	1.96	7.84
3f	12	155—156	$C_{13}H_{10}O_4SBr_2$	37.11	2.39	7.60	36.96	2.36	7.58
4	4[a], 6[b]	271—273	$C_{18}H_{10}O_4S$	66.98	2.98	9.95	67.08	3.13	9.92
5	81	134—135	$C_9H_8O_3S$	54.75	4.11	16.50	55.10	4.11	16.31

a) From **1a** and **2a**. b) From **1d** and **2a**.

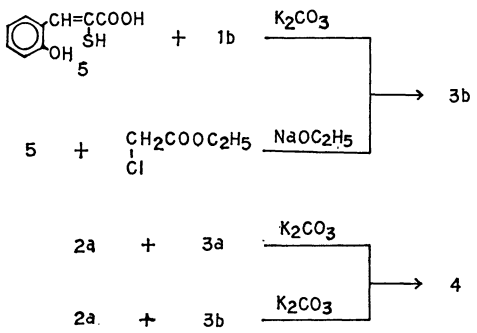
TABLE 2. IR AND NMR DATA FOR THE COMPOUNDS **3a—f**, **4**, AND **5**

Compound	IR[a] (ν_{max}, cm^{-1})	NMR[b] δ, (ppm)
3a	1745, 1706, 1600	7.90 (s, 1H, -C<u>H</u>=C=), 7.15—7.75 (m, $4H_{arom}$), 4.30 (s, 2H, -S-C<u>H_2</u>-), 3.69 (s, 3H, -COOC<u>H_3</u>)
3b	1734, 1706, 1610	7.90 (s, 1H, -C<u>H</u>=CH=), 7.26—7.66 (m, $4H_{arom}$), 3.81—4.31 (m, 4H, -COOC<u>H_2</u>-CH_3, -S-C<u>H_2</u>-), 1.20 (t, 3H, -COOCH_2-C<u>H_3</u>)
3c	1740, 1705, 1610	7.86 (s, 1H, -C<u>H</u>=C=), 7.00—7.47 (m, $3H_{arom}$), 4.02 (s, 2H, -S-C<u>H_2</u>-), 3.90 (s, 3H, -OC<u>H_3</u>), 3.67 (s, 3H, -COOC<u>H_3</u>)
3d	1728, 1698, 1610	7.86 (s, 1H, -C<u>H</u>=C=), 7.15—7.35 (m, $3H_{arom}$), 3.80—4.30 (m, 7H, -COOC<u>H_2</u>-CH_3, -S-C<u>H_2</u>-, -OC<u>H_3</u>)
3e	1728, 1698, 1610	8.00 (s, 1H, -C<u>H</u>=C=), 7.65—7.95 (m, $2H_{arom}$), 4.00 (s, 2H, -S-C<u>H_2</u>-), 3.68 (s, 3H, -COOC<u>H_3</u>)
3f	1760, 1730, 1600	8.06 (s, 1H, -C<u>H</u>=C=), 7.70—7.96 (m, $2H_{arom}$), 4.00—4.17 (m, 4H, -COOC<u>H_2</u>-CH_3, -S-C<u>H_2</u>-), 1.20 (t, 3H, -COOCH_2-C<u>H_3</u>)
4	1697, 1605	8.33 (s, 2H, 2×-C<u>H</u>=C=), 7.35—7.75 (m, $8H_{arom}$)
5	3400, 3150, 2570, 1680, 1615	9.10 (b, 3H, -S<u>H</u>, -O<u>H</u>, -COO<u>H</u>), 8.10 (s, 1H, -C<u>H</u>=C=), 7.70 (q, 1H, aromatic H relative to the OH group), 6.70—7.30 (m, $3H_{arom}$)

a) The IR spectra were recorded for Nujol mulls. b) The NMR spectra were determined in DMSO-d_6 for **3a—3f**, CF_3COOH for **4**, solution of $CDCl_3$:DMSO-d_6=3:1 for **5** with tetramthylsilane as internal reference; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broad.



Scheme 1.



Scheme 2.

via route A or B. Product **4** may form upon further condensation of **3** with **2** as depicted above.

Experimental

Preparation of 3 and 4. A mixture of **1** (0.02 mol), salicylaldehyde (0.01 mol) and potassium carbonate (0.01 mol) was stirred in 10 ml of acetone at room temperature for 6—7 h. Upon cooling to room temperature, crystals precipitated; the precipitate was washed with water, dried, and then washed with hot ethanol. The residue was recrystallized from dioxane to give **4**. To the ethanolic washing was added a small amount of water, and then the solution, when allowed to stand overnight at room temperature, gave pale yellow crystals (**3**) which were recrystallized from alcohol. Substituted coumarines (**3c—f**) are also obtained similarly, but no compound of type **4** could be found.

Preparation of 2-Mercapto-3-(o-hydroxyphenyl)acrylic Acid (5). The title acid was prepared by a modification of the reported method.[6] 5-(*o*-Hydroxybenzylidene)-2-thioxothiazolidin-4-one (0.01 mol) was hydrolyzed with 8% sodium hydroxide (20 ml) by heating to 50—60 °C. The mixture was well stirred until a clear solution was obtained. After cooling with an ice-salt mixture, the solution was acidified with 3M-hydrochloric acid, and the stirring was continued for 30 min. The resulting acid was washed with water, dried in air, and recrystallized from dichloromethane.

Preparation of an Authentic Sample from 2-Mercapto-3-(o-hydroxyphenyl)acrylic Acid (5) and Ethyl Chloroacetate. To a solution of sodium 2-mercapto-3-(*o*-hydroxyphenyl)acrylate (0.005 mol) in absolute ethanol (10 ml) was added ethyl chloroacetate (0.005 mol). The solution was stirred for 4 h and then allowed to stand overnight in a refrigerator. The resulting crystals were collected on a filter, washed with water, and dried. Recrystallization from ethanol gave **3b**; yield: 0.6 g (45%); mp 113—114 °C.

Preparation of an Authentic Sample from 2-Mercapto-3-(o-hydroxyphenyl)acrylic Acid and 1b. A mixture of 2-mercapto-3-(*o*-hydroxyphenyl)acrylic acid (0.005 mol), **1b** (0.005 mol) and potassium carbonate (0.005 mol) in acetone (10 ml) was stirred at room temperature for 5 h. After the mixture was allowed to stand overnight in a refrigerator, crystalline matter separated out. Recrystallization from ethanol gave **3b**; yield: 0.5 g (38%); mp 113—114 °C.

Preparation of 4 from 3 and Salicylaldehyde. A mixture of **3** (0.005 mol), salicylaldehyde (0.005 mol), and potassium carbonate (0.005 mol) in acetone (10 ml) was stirred for 1 h. Crystalline matter precipitated out during the reaction; this was recrystallized from dioxane affording **4**; yield 0.9 g (56%) from **3a** and salicylaldehyde; 1.1 g (69%) from **3b** and salicylaldehyde: mp 271—272 °C.

References

1) S. Kambe, T. Hayashi, H. Yasuda, and H. Midorikawa, *Bull. Chem. Soc. Jpn.*, **44**, 1357 (1971).
2) S. Kambe, T. Hayashi, H. Yasuda, and A. Sakurai, *Nippon Kagaku Zasshi*, **92**, 867 (1971).
3) S. Kambe and T. Hayashi, *Bull. Chem. Soc. Jpn.*, **45**, 952 (1972).
4) S. Kambe and T. Hayashi, *Bull. Chem. Soc. Jpn.*, **45**, 3192 (1972).
5) S. Kambe, *Bull. Chem. Soc. Jpn.*, **46**, 2926 (1973).
6) N. Campbell and J. E. McKall, *J. Chem. Soc.*, **1948**, 1251.