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Rapid Communication

Photohalogenation of 3-acetylcoumarins: Facile synthesis of 3-(2-amino-4-thiazolyl)coumarins and their conversion into 3-[2,5-dimethylpyrrol-1-yl) thiazol-4-yl]-coumarins

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3-Acetylcoumarins react with thiourea in the presence of N-bromosuccinimide using benzoyl peroxide as radical initiator to furnish 3-(2-amino-4-thiazolyl)coumarins **1**. Compounds **1** can also be obtained by reacting 3-acetylcoumarin with bromine in the presence of trichloro-(N,N-ethylene-bis-aminobenzamide)-lanthanum (III) or samarium ((III) as catalyst followed by treatment with thiourea. These compounds (**1**) have been converted into pyrrole derivatives **2** by reacting with acetonylacetone.

Thiazoles are generally synthesized by Hantzsch thiazole synthesis from α-halogenoketones and thioureas or thioamides[1,2]. Later, King *et.al.*[2,4] and other workers[5] synthesized aminothiazoles by replacing α-halogenoketones with ketone and halogen. Despite this modification, the method still remains cumbersome and time consuming (24-25 hr).

We report herein a facile synthesis of 3-(2-amino-4-thiazolyl)coumarins **1** by reacting 3-acetylcoumarins with thiourea in the presence of N-bromosuccinimide and benzoyl peroxide in a single step. Compounds **1** were also prepared by a photohalogenation process involving ketones (3-acetylcoumarins) with bromine in the presence of lanthanum (III) and samarium (III) catalysts[6]. The photohalogenation was carried out on a 300 watt tungston lamp. Reaction of 3-acetylcoumarins using NBS and benzoyl peroxide or bromine in the presence of catalyst is known to proceed through a free radical mechanism. The bromine free radical formed abstracts the hydrogen atom from the acetyl group of 3-acetylcoumarin to give 3-coumarinacyl free radical. Both the radicals combine to yield 3-(ω-bromoacetyl)coumarin which in turn reacts with thiourea in *in situ* to give 3-(2-amino-4-thiazolyl)coumarins **1**. In contrast to King's method, the present methods are less time consuming, involve simple work-up procedures and are of general applicability. The yields of the products are better to those of previous method[7]. The structures of aminothiazoles **1** were supported by their elemental analyses (cf. Table I) and mixed melting point determination.

A number of 3-(2-aminothiazolyl) coumarins with open chain functionalities and heterocyclic systems at 2-position of thiazole ring have been studied exhaustively[8]. In continuation of our studies in this area[9], we thought it would be of interest to incorporate a heterocyclic moiety like pyrrole. 3-(2-Amino-4-thaizolyl)coumarins **1** were chosen as starting materials owing to high reactivity of the amino group of these compounds towards

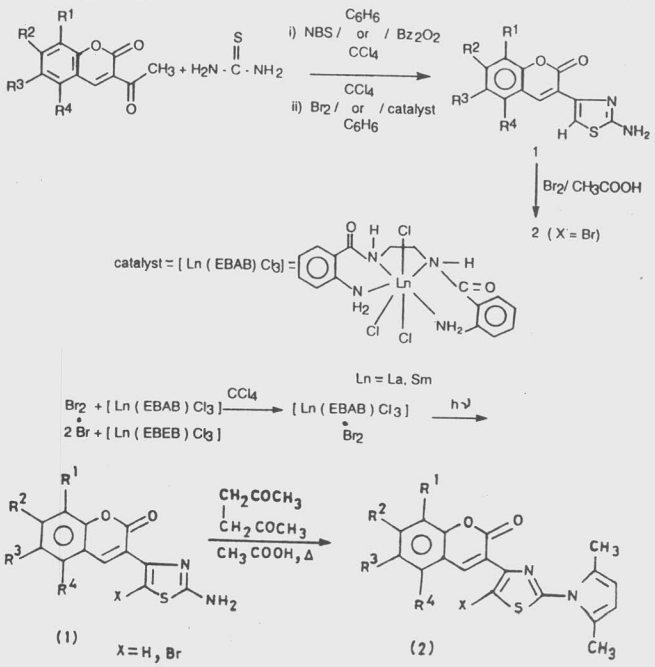

Table I — Physical data of compounds **1** and **2**

Compd*	R^1 R^2	R^3 R^4	X	m.p Found (reported)[10] °C	Recrystallized from	Mol. formula	Found (Calcd) (%) C	H	N	S
1a	H H	H H	H	222-25 (225-27)	Alcohol	$C_{12}H_8N_2O_2S$	--	--	--	--
1b	OCH_3 H	H H	H	235-37	MeOH	$C_{13}H_{10}N_2O_3S$	56.90 (56.93	3.62 3.64	10.00 10.20	11.63 11.69)
1c	H H	Br H	H	204-6 (204-6)	MeOH	$C_{12}H_7BrN_2O_2S$	--	--	--	--
1d	Br H	Br H	H	220-22 (220-22)	MeOH	$C_{12}H_6Br_2N_2O_2S$	--	--	--	--
1e	H H	Cl H	H	176-78 (176-78)	MeOH	$C_{12}H_7ClN_2O_2S$	--	--	--	--
1f	Cl H	Cl H	H	190-92 (192)	MeOH	$C_{12}H_6Cl_2N_2O_2S$	--	---	--	--
2a	H H	H H	H	148-50	MeOH	$C_{18}H_{14}N_2O_2S$	67.00 (67.08	4.31 4.34	8.61 8.69	9.90 9.93)
2b	H H	H H	Br	>300	DMF+MeOH	$C_{18}H_{13}BrN_2O_2S$	53.81 (53.86	3.21 3.24	6.92 6.98	7.93 7.98)
2c	H H	CH_3 H	H	282-84	Aq.DMF	$C_{19}H_{16}N_2O_2S$	67.81 (67.85	4.71 4.76	8.30 8.33	9.48 9.52)
2d	H H	CH_3 H	Br	247-49	Aq.DMF	$C_{19}H_{15}BrN_2O_2S$	54.90 (54.93	3.60 3.61	6.70 6.74	7.68 7.71)
2e	OCH_3 H	H H	H	259-61	Aq.DMF	$C_{19}H_{18}N_2O_3S$	64.71 (64.77	4.50 4.54	7.92 7.95	9.00 9.09)
2f	OCH_3 H	H H	Br	234-36	DMF+MeOH	$C_{19}H_{17}BrN_2O_3S$	52.88 (52.90	3.43 3.48	6.46 6.49	7.40 7.42)
2g	H H	5,6- Benzo	H	163-64	AcOH	$C_{22}H_{16}N_2O_2S$	70.92 (70.96	4.28 4.30	7.49 7.52	8.57 8.60)
2h	H H	5,6- Benzo	Br	215-17	DMF+alcohol	$C_{22}H_{15}BrN_2O_2S$	58.51 (58.53	3.30 3.32	6.00 6.20	7.00 7.09)
2i	H H	Br H	H	170-71	MeOH+C_6H_6	$C_{18}H_{13}Br_2N_2O_2S$	53.83 (53.86	3.21 3.24	6.92 6.98	7.94 7.98)
2j	H H	Br H	Br	233-35	Aq.DMF	$C_{18}H_{12}Br_2N_2O_2S$	44.95 (45.00	2.48 2.50	5.80 5.83	6.61 6.66)
2k	Br H	Br H	-	>300	Aq.DMF	$C_{18}H_{12}Br_2N_2O_2S$	44.96 (45.00	2.48 2.50	5.81 5.83	6.62 6.66)
2l	Br H	Br H	Br	257-59	Aq.DMF	$C_{18}H_{11}Br_3N_2O_2S$	38.61 (38.64	1.93 1.96	4.97 5.00	5.70 5.72)
2m	H H	Cl H	-	215-17	MeOH+$CHCl_3$	$C_{18}H_{13}ClN_2O_2S$	60.53 (60.58	3.61 3.64	7.81 7.85	8.95 8.97)
2n	H H	Cl H	Br	283-85	Aq.DMF	$C_{18}H_{13}ClBrN_2O_2S$	49.56 (49.59	2.71 2.75	6.40 6.42	7.30 7.34)
2o	H OH	H H	H	>300	Aq.DMF	$C_{18}H_{14}N_2O_3S$	63.87 (63.90	4.10 4.14	8.25 8.28	9.44 9.46)

Table I — *Contd*

Table I — Physical data of compounds **1** and **2** —*Contd*

Compd*	R^1 R^2	R^3 R^4	X	m.p Found (reported)[10] °C	Recrystallized from	Mol. formula	Found (Calcd) (%) C	H	N	S
2p	H OH	H H	Br	261-63	Aq.DMF	$C_{18}H_{13}BrN_2O_3S$	51.76 (51.79	3.10 3.11	6.67 6.71	7.64 7.67)

* All the compounds were obtained in 80-90% yields.

electrophilic reagents. 3-(2-Amino-4-thiazolyl)-coumarins on reaction with bromine in acetic acid gave the corresponding 3-(2-amino-5-bromo-4-thiazolyl)coumarins. The 5th position of the thiazole is highly reactive towards electrophilic substitution reaction. Condensation of **1** with acetonylacetone in the presence of acetic acid yielded the pyrrole derivatives **2**.

Experimental Section

Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 282 instrument, ^1H NMR spectra on a Varian 90-MHZ spectrometer using TMS as internal standard, and mass spectra on a Jeol-JMS-D300 (Japan) mass spectrometer at 70 eV.

3-(2-Amino-4-thiazolyl)coumarins 1: Method-a. A mixture of 3-acetylcoumarin (0.02 mole), thiourea (0.02 mole), N-bromosuccinimide (0.02 mole) and a small amount of benzoyl peroxide in dry benzene (30-40 mL) or in dry carbon tetrachloride was heated under reflux on a 300 watt tungsten lamp for 6 hr, the solvent distilled off and the resultant hydrobromide treated with water. The solid separated was filtered and neutralized with 10% Na_2CO_3 solution to yield the free base **1** which was recrystallized from a suitable solvent using charcoal.

The aminothiazoles **1a-1f**, thus prepared, are recorded in Table I. The yields are 60-70%.

***La*$^{3+}$ *and* Sm^{3+} *catalysed bromination of 3-acetylcoumarins followed by in situ* cyclization to thiazolylcoumarins 1: Method-b.** A mixture of appropriate 3-acetylcoumarin (0.01 mole), bromine (0.01 mole) and lanthanum or samarium catalyst (2 mg) either in dry carbon tetrachloride (40 mL) or in dry C_6H_6 was refluxed on a 300 watt tungston bulb for 5 min. whereupon the red colour of bromine had disappeared. To this thiourea (0.01 mole) was added and the mixture refluxed further for 5 min. The yellow solid, thus obtained, was filtered and washed with methanol and then with dilute solution of ammonia to liberate the free base **1**. The yields of the products were 80-90% (cf. Table I).

5-Bromo-3-(2-amino-4-thiazolyl)coumarins (1; X= Br) were prepared according to our earlier procedure[10].

3-[2-(2,5-Dimethylpyrrol-l-yl)thiazol-4-yl] coumarins 2: A mixture of 3-(2-amino-4-thiazolyl)coumarin (0.01 mole), acetonylacetone (0.005 mole) and acetic acid (10 mL) was refluxed for 6 hr and the reaction mixture placed in an ice-cold water. The solid thus separated was filtered and recrystallized from a suitable solvent to give **2** (Table I) in 80-90% yields.

2a: m.p. 148-50°, yield 80%; IR (KBr): 1605 (C=N) and 1725 cm^{-1} (lactone carbonyl); ^1H NMR ($CDCl_3$: δ 2.3 (s, 6H, 2xCH_3), 5.9 (s, 2H, pyrrole-H), 8.5(1H,s, C_5-H of thiazole) 8.7(s,1H,C_4-H of coumarin) and 7.2-7.6 (m,4H, Ar-H); MS:m/z 322 (100%) 309(4.2), 307(57.0), 280(5.1), 229(8.2), 177(6.2), 175(3.1), 174(6.0), 173(5.5), 172(5.7), 171(21.4) and 94(50).

2e: IR(KBr): 1605(-C=N-), 1720 cm^{-1} (lactonic carbonyl); ^1H NMR (DMSO-d_6 +$CDCl_3$): δ 2.1 (s,6H, 2xCH_3), 4.0(s,3H,OCH_3), 6.3(s,2H, pyrrole-H), 7.05-7.4 (m,3H, Ar-H), 7.6(s,1H, thiazole-H) and 8.5 (s,1H, C_4-H of coumarin); MS: m/z 352 (12.5%), 337(111), 275(12.5), 274(100), 246(10.0), 241(10), 203(15.7) and 133(10).

2i: IR(KBr): 1600 (-C=N-),1720 cm^{-1} (lactonic carbonyl); ^1H NMR ($CDCl_3$): δ 2.2 (s,6H, 2×CH_3), 6.0(s,2H, pyrrole-H), 7.2-7.4 and 7.7-7.8 (m, 3H, Ar-H and 1H-thiazole) 8.5(s,1H, C_4-H of coumarin); MS: m/z 402(45%), 388(30), 387(30), 324(80), 322(70), 269(50), 268(48), 253(90), 251(100), 223(15), 198(10), 167(10) and 145(10).

2h: IR(KBr): 1610(-C=N-), 1720 cm^{-1} (lactonic carbonyl); ^1H NMR ($CDCl_3$): δ 2.3(s,6H, 2×CH_3), 6.0(s,2H, pyrrole-H), 7.3(s,1H, thiazole-H), 7.5-8.1 (m, 5H, Ar-H) and 9.6 (s,1H, C_4-H of coumarin); MS: m/z 374(26%), 372(95), 357(50), 294(62), 266(20), 221(20), 195(20), 152(20) and 139(10).

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