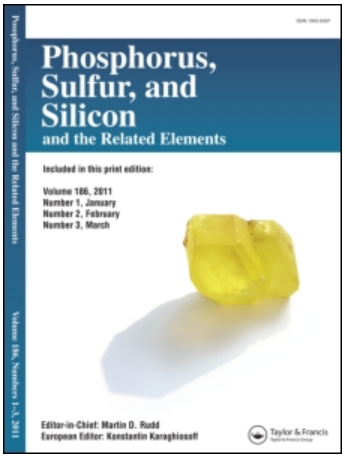

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The Synthesis of Some New Fused and Substituted Chromenes

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The Synthesis of Some New Fused and Substituted Chromenes

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Some new chromeno[2,3-b]pyrimidines, chromeno[3,2-c]pyridines, chromeno[2,3-b]pyridines and 3-chromenyl-1,3-thiazines were synthesized via the synthetic studies of the reaction of 2-imino-2H-chromen-3-thiocarboxamide with some aromatic aldehydes, active nitriles, and their ylidene derivatives.

Keywords Chromenopyridines; chromenothiazines; malononitrile; ylidenenitriles

INTRODUCTION

Fused coumarins comprise a very interesting class of compounds for their significant antibacterial[1–7] and novobiocin[8,9] activities. For these reasons we continue our previous work,[6,7] which deals with the synthesis of chromenopyrazoles, chromenopyridines, and chromenoazepines. We report here the synthesis of some new chromenopyrimidines, chromenopyridines, and 3-chromenyl-1,3-thiazines.

RESULTS AND DISCUSSION

The treatment of 2-imino-2H-chromene-3-thiocarboxamide **1**[10] with different aromatic aldehydes, namely benzaldehyde, p-anisaldehyde, p-nitrobenz-aldehyde, and 2-naphthaldehyde, in a 1:1 molar ratio in refluxing tetra-hydrofuran containing a catalytic amount of piperidine gave the cyclized products 2-phenyl-2,3-dihydro-4H-chromeno[2,3-d]-pyrimidine-4-thione, 2-(4-methoxyphenyl)-2,3-dihydro-4H-chromeno-[2,3-d]pyrimidine-4-thione, 2-(4-nitrophenyl)-2,3-dihydro-4H-chromeno[2,3-d]pyrimidine-4-thione, and 2-(2-naphthyl)-2,3-dihydro-4H-chromenomeno[2,3-d]pyrimidine-4-thiones **2a–d**. The effect of a cyclic ketone on compound **2b** was tested via its reaction with cyclohexanone in refluxing dioxan in the presence of triethylamine as a catalyst where

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TABLE I Analytical and Spectral Data of the Prepared Compounds

Compound No.	M.P. (°C)[a] Crys. Solv.	Yield %	M.F. (M.wt)	Analytical Data[b] Calc. (Found) % C	H	N	S	I.R. (Kbr)[c] (cm^{-1})	^{1}H-NMR (DMSO-d_6)[d] (δ ppm)
2$_a$	274–276	68	$C_{17}H_{12}N_2OS$	69.84	4.14	9.58	10.97	3146(NH); 1188	8.12(s, 1H, C_5-H); 8.00–7.12 (m, 11H, arom. + NH + C_2-H)
	THF		(292.35)	(70.10)	(4.07)	(9.75)	(10.86)	(C═S)	
2$_b$	197–198	54	$C_{18}H_{14}N_2O_2S$	67.06	4.38	8.69	9.95	3139 (NH); 1173	8.42(s, 1H, C_5-H); 8.13–6.94 (m, 9H, arom. + C_2-H); 6.21 (s,
	methanol		(322.38)	(67.22)	(4.30)	(8.88)	(10.12)	(C═S)	1H, NH); 3.94 (s, 3H, OCH_3)
2$_c$	184–186	91	$C_{17}H_{11}N_3O_3S$	60.52	3.29	12.46	9.51	3183 (NH); 1177	8.64 (s, 1H, C_5-H); 8.41–7.10 (m, 10H, arom. + C_2-H + NH)
	EtOH/dioxane		(337.35)	(60.70)	(3.35)	(12.60)	(9.36)	(C═S)	
2$_d$	252–254	56	$C_{21}H_{14}N_2OS$	73.66	4.12	8.18	9.36	3153 (NH); 1199 (C═S)	8.81 (s, 1H, C_5-H); 8.20–7.12 (m, 13H, arom. + C_2-H + NH)
	dioxane		(342.41)	(73.80)	(4.08)	(8.38)	(9.14)		
3$_b$	261–263	73	$C_{24}H_{22}N_2O_2S$	71.61	5.51	6.96	7.97	3140 (NH)	9.80(s, 1H, NH); 8.22–6.75 (m, 9H, arom. + $CH_{pyrim.}$);
	EtOH/dioxane		(402.51)	(71.89)	(5.60)	(6.75)	(8.14)		3.82 (s, 3H,OCH_3); 3.69(s, 1H, CH_{pyran}); 2.31–1.20 (m, 8H, $4CH_{2\ Cyclohex}$)
4	238–239	85	$C_{12}H_{10}N_2O_2S$	58.52	4.09	11.37	13.02	3288, 3146 (2NH);	9.40 (s, 1H, NH_{acetyl}); 8.32 (s,
	AcOH/EtOH		(246.29)	(58.69)	(4.15)	(11.554)	(12.82)	1697(C═O); 1143 (C═S)	1H, C_4-H); 7.83–7.13(m, 5H, arom.+NH); 2.40(s, 3H, $COCH_3$)
5[*]	267–269 DMSO	79	$C_{12}H_8N_2OS$	63.14	3.53	12.27	14.05	1150 (C═S)	8.50 (s, 1H, C_5-H); 7.65–7.05 (m, 4H, arom.); 2.30 (s, 1H,
			(228.27)	(63.02)	(3.60)	(12.48)	(13.94)		CH_3)
6	243 EtOH/dioxane	68	$C_{11}H_8N_2O_2S$	56.88	3.47	12.06	13.81	3289, 3146 (2NH); 1697 (C═O); 1143	11.80 (s, 1H, NH_{formyl}); 8.71(s, 1H, C_4-H); 8.24 (s, 1H,
			(232.26)	(56.72)	(3.41)	(12.26)	(13.65)	(C═S)	CHO); 7.70–7.10(m, 5H, arom. + NH)

7	203–205 EtOH	53	$C_{11}H_6N_2OS$	61.67	2.82	13.08	14.97	1170 (C═S)	8.85(s, 1H, C_5-H); 8.30 (s, 1H, C_2-H); 7.85–7.27(m,4H, arom.)
			(214.24)	(61.46)	(2.90)	(13.28)	(14.78)		
8	>300 EtOH/dioxane	64	$C_{13}H_7N_3OS$	61.65	2.79	16.59	12.66	3344, 3210(2NH); 2202(CN); 1237 (C═S)	10.00 (s, 1H, C_5-H); 8.92 (s, 1H, NH); 861(s, 1H, NH); 7.90–6.82 (m, 4H, arom)
			(253.28)	(61.46)	(2.84)	(16.82)	(12.54)		
9	>300 EtOH	75	$C_{13}H_9N_3O_2$ S	57.55	3.34	15.49	11.82	3320, 3195 (2NH) ; 2211 (CN); 1690 (C═O)	12.84 (s, 1H, NHCO); 9.61(s, 1H, C_4-H); 8.90 (s, 1H, = NH); 7.85–7.00(m, 4H, arom.); 4.80 (s, 2H, CH_2).
			(271.29)	(57.82)	(3.39)	(15.69)	(11.70)		
10	>300 EtOH/dioxane	84	$C_{13}H_9N_3OS_2$	54.34	3.16	14.62	22.32	3176 (NH); 2650 (SH); 2171 (CN); 1213(C═S)	9.93 (s, 1H, NH); 8.70 (s, 1H, C_4- . H); 7.44–6.60(m, 4H, arom.); 3.11 (s, 2H, CH_2); 1.60 (s, 1H, SH)
			(287.36)	(54.61)	(3.20)	(14.44)	(22.41)		
11	296–298 EtOH/dioxane	71	$C_{13}H_7N_3OS$	61.65	2.79	16.59	12.66	2211 (CN); 1157 (C═S)	8.90(s, 1H, C_5-H); 7.86–7.10 (m, 4H, arom.); 4.82–4.09 (d, 2H, CH_2)
			(253.28)	(61.74)	(2.89)	(16.70)	(12.48)		
12	>300 (dec.) EtOH/THF	51	$C_{13}H_8N_4O$	66.10	3.41	23.72	— — — —	3431, 3348, 3181 (NH, NH_2); 2205 (CN)	8.80 (s, 1H, C_5-H); 8.60(s, 1H, NH); 7.84–6.90 (m, 4H, arom.); 6.73 (s, 2H, NH_2)
			(236.23)	(66.31)	(3.48)	(23.54)			
13	134–135 EtOH	24	$C_{15}H_{13}N_3O_3$	63.60	4.63	14.83	— — —	3398, 3183 (2NH); 2202(CN); 1737 (C═O)	11.72–11.50 (br, 2H, 2NH); 8.70 (s, 1H, C_4-H); 8.12–7.24 (m, 4H, arom.); 4.60 (s,1H, CH); 4.73 — 4.20 (q, 2H, CH_2); 1.60–1.30 (t, 3H, CH_3)
			(283.28)	(63.44)	(4.57)	(14.71)			
14	>300 EtOH/dioxane	62	$C_{13}H_7N_3O_2$	65.82	2.97	17.71	— —	3450 (OH); 3173 (NH); 2214 (CN)	12.90 (s, 1H, NH); 12.73 (s, 1H, OH); 8.90 (s, 1H, C_5–H); 7.88–7.40 (m, 4H, arom.)
			(237.21)	(65.68)	(3.03)	(17.58)			
15	>300 (sub.) EtOH	63	$C_{13}H_7N_3OS$	61.65	2.79	16.59	12.66	3164 (NH); 2600 (SH); 2209 (CN)	8.73(s,1H,NH) 7.80(s,1H,C_5–H); 7.63–6.80 (m, 4H, arom.); 3.40 (s, 1H, SH)
			(253.28)	(61.90)	(2.71)	(16.75)	(12.48)		

(*Continued on next page*)

Table I Analytical and Spectral Data of the Prepared Compounds (*Continued*)

Compound No.	M.P. (°C)[a] Crys. Solv.	Yield %	M.F. (M.wt)	Analytical data[b] Calc. (Found) % C	H	N	S	I.R. (Kbr)[c] (cm^{-1})	^{1}H-NMR (DMSO-d_6)[d] (δ ppm)
16$_a$	190–192 EtOH	54	$C_{20}H_{14}N_4OS$ (358.42)	67.02 (67.30)	3.94 (3.89)	15.63 (15.49)	8.95 (8.76)	3437, 3353, 3244 (NH, NH_2); 2213 (CN)	9.90(s, 1H, NH); 8.14(s, 1H, C_4-H); 7.82–6.94 (m, 9H, arom.); 6.67 (s, 2H, NH_2); 6.10 (s, 1H, CH)
16$_b$	199 EtOH	86	$C_{20}H_{13}N_5O_3S$ (403.41)	59.55 (59.38)	3.25 (3.33)	17.36 (17.20)	7.95 (8.15)	3452, 3361, 3242 (NH, NH_2); 2197 (CN)	10.11 (s, 1H, NH); 8.65–7.13 (m, 10H, C_4-H + arom.); 6.80 (s, 2H, NH_2); 5.78 (s, 1H, CH)
16$_c$	270–273 EtOH/pet. ether 60–80	73	$C_{21}H_{16}N_4O_2S$ (388.44)	64.93 (64.78)	4.15 (4.25)	14.42 (14.61)	8.25 (8.04)	3437, 3351, 3241 (NH, NH_2); 2209 (CN)	9.80 (s, 1H, NH); 7.65–6.80 (m, 9H, arom + C_4-H); 6.53 (s, 2H, NH_2); 5.81 (s, 1H, CH); 3.72 (s, 3H, OCH_3)
16$_d$	218–219 EtOH	81	$C_{22}H_{18}N_4O_5S$ (450.47)	58.66 (58.86)	4.03 (4.10)	12.44 (12.61)	7.12 (6.90)	3416, 3341, 3237 (NH, NH_2); 1744 (C═O)	10.60 (s, 1H, NH); 8.77–6.83(m, 9H, arom. + C_4-H); 6.62 (s, 2H, NH_2); 6.00(s, 1H, CH); 4.89–4.40 (q, 2H, CH_2); 1.38–1.10(t, 3H, CH_3)
16$_e$	192–194 EtOH/($CHCl_3$)	28	$C_{24}H_{15}N_3O_2S$ (409.46)	70.40 (70.61)	3.69 (3.58)	10.26 (10.37)	7.83 (7.68)	3437 (OH); 3320 (NH); 2213 (CN)	11.22 (s, 1H, NH); 10.53(s, 1H, OH); 8.53–7.40 (m, 12H, arom. + C_4-H); 6.10 (s, 1H, CH)
16$_f$	159–161 Et. Acetate/pet. ether 60–80	45	$C_{26}H_{21}N_3O_3S$ (455.53)	68.55 (68.4 0)	4.65 (4.50)	9.22 (9.31)	7.04 (7.20)	3440, 3380, 3260 (NH, NH_2); 1730 (C═O)	10.30 (s, 1H, NH); 8.35–7.23 (m, 12H, arom. + C_4-H); 6.76(s, 2H, NH_2); 6.30(s, 1H, CH); 4.74–4.25 (q, 2H, CH_2); 1.40–1.00 (t, 3H, CH_3)

17	280–283 (char.) EtOH/($CHCl_3$)	20	$C_{14}H_8N_4OS$ (280.31)	59.99 (60.15)	2.88 (2.79)	19.99 (19.80)	11.44 (11.63)	3339 (NH); 2640 (SH); 2198 (CN)	9.00 (s, 1H, NH); 8.92(s, 1H, ═CH); 7.75–6.94(m, 5H, C_4-H + arom.); 3.50 (s, 1H, SH)
18	187–189 EtOH/pet.0 ether 60–8	48	$C_{14}H_8N_4OS$ (280.31)	59.99 (60.14)	2.88 (2.77)	19.99 (2083)	11.44 (11.61)	3319; 3202 (2NH); 2196 (CN)	11.70 (s, 1H, NH); 10.40(s, 1H, NH); 8.74 (s, 1H, $CH_{thiazyl}$); 8.32(s, 1H, C_4-H); 7.75–6.83(m, 4H, arom.)
19	>300 EtOH	26	$C_{15}H_{10}N_4OS$ (294.33)	61.21 (61.05)	3.42 (3.50)	19.04 (19.20)	10.89 (10.65)	3178 (NH); 2630 (SH); 2201 (CN)	10.60 (s, 1H, NH); 7.86–7.16(m, 4H, arom.); 6.82(s, 1H, C_4-H); 4.00(s, 1H, SH); 2.80(s, 3H, CH_3)
20	234–236 EtOH/pet. ether 60–80	51	$C_{15}H_{10}N_4OS$ (294.33)	61.21 (61.08)	3.42 (3.50)	19.04 (19.23)	10.89 (10.68)	3281, 3174 (2NH); 2204 (CN)	12.64(s, 1H, NH); 11.60(s, 1H, NH); 8.20(s, 1H, C_4-H); 7.55–6.84 (m, 4H, arom.); 2.82(s, 3H, CH_3)
21	195–196 EtOH/pet. ether 60–80	35	$C_{16}H_{13}N_3O_3S$ (327.36)	58.70 (58.55)	4.00 (4.18)	12.84 (12.98)	9.80 (9.62)	3169 (NH); 2645 (SH); 2206 (CN); 1734 (C═O)	10.30 (s, 1H, NH); 8.95(s, 1H, = CH); 7.86–6. 94 (m, 5H, C_4-H + arom.); 5.21–4.82 (q, 2H, CH_2); 4.20 (s, 1H, SH); 1.82–1.34 (t, 3H, CH_3)
22	198–199 EtOH	48	$C_{14}H_7N_3O_2S$ (281.29)	59.78 (59.59)	2.51 (2.59)	14.94 (14.72)	11.40 (11.59)	3291 (NH); 2202 (CN); 1697 (C═O)	10.40 (s, 1H, NH); 8.94 (s, 1H, $CH_{thiazyl}$); 8.45(s, 1H, C_4-H); 7.90–7.14 (m, 4H, arom.)

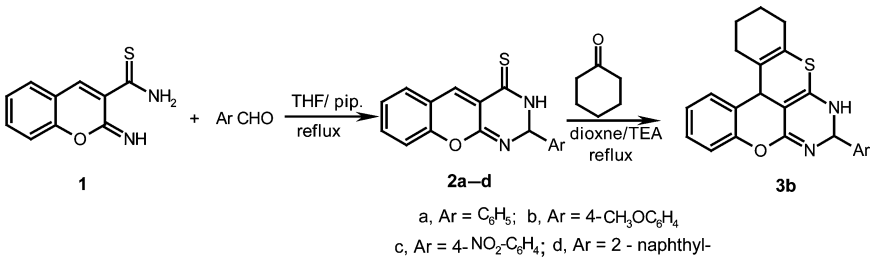
[a]Uncorrected.

[b]Satisfactory microanalyses, obtained: (C ± 0.30%; H ± 0.11%; N ± 0.35%; S ± 0.20%).

[c]Measured on Nicolet 710 FTIR spectrophotometer.

[d]Measured with Varian EM 360 L spectrometer at 400 MHz using TMS as internal standard.

*TFA used as a solvent for ^{1}H-NMR measurement.

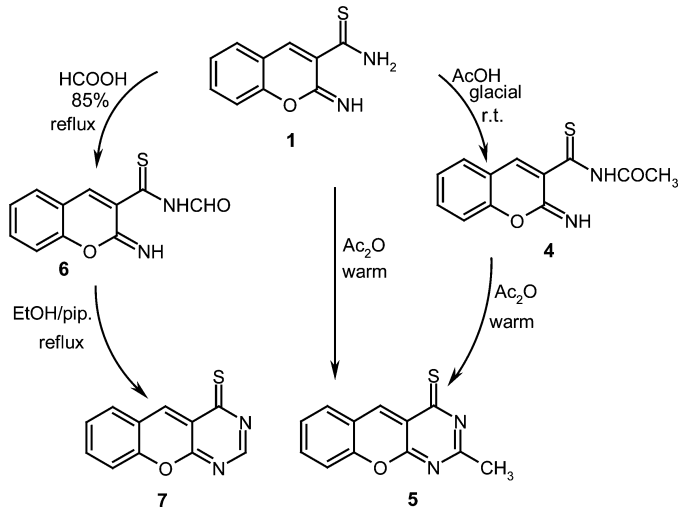


SCHEME 1

4-(8,8a,10,11,12,13-hexahydro-7H-5-oxa-9-thia-6,8-diazanaphtho [2,-3,4-de]anthracen-7-yl)phenyl methyl ether **3b** was obtained (Scheme 1, Table I).

The formation of compound **3b** is assumed to proceed through the addition of the active methylene group of cyclohexanone on $C_3 = C_4$ of the chromene moiety followed by the elimination of a water molecule from the interaction of the tautomeric SH group and the carbonyl group.

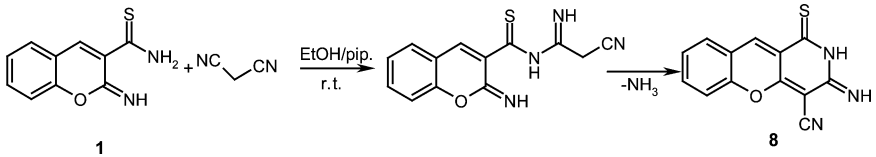
The acetylation of compound **1** was achieved by treating compound **1** with glacial acetic acid at r.t. to give N-[(2-imino-2H-chromen-3-yl)carbonothioyl]acetamide **4**, which in turn cyclized to 2-methyl-4H-chromeno[2,3-d] pyrimidine-4-thione **5** in an 81% yield on heating with acetic anhydride. The same compound **5** was obtained directly by warming compound **1** with an excess amount of acetic anhydride in 79% (Scheme 2, Table I). Also, N-formyl-2-imino-2H-chromene-3-thiocarboxamide **6** was formed through the reaction of our starting



SCHEME 2

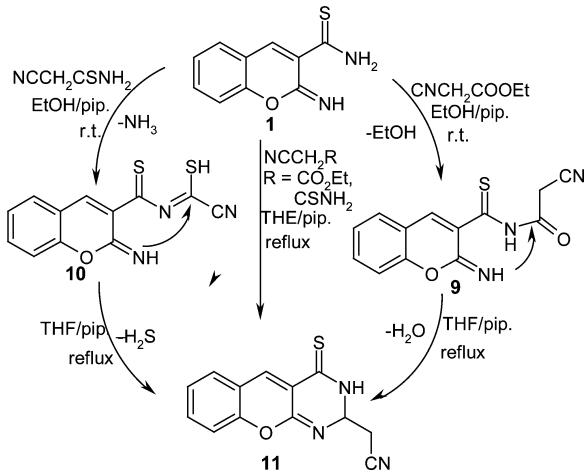
material with warmed formic acid, which underwent intramolecular cyclization into benzo[g]quinazoline-4(10H)-thione **7** in refluxing ethanol containing piperidine as a catalyst (Scheme 2, Table I).

The action of active nitriles on our starting material was studied. So, on treating compound **1** with malononitrile at r.t. in ethanol using piperidine as a catalyst, 3-imino-1-thioxo-2,3-dihydro-1H-chromeno-[3,2-c] pyridine-4-carbonitrile **8** was yielded (Scheme 3, Table I).

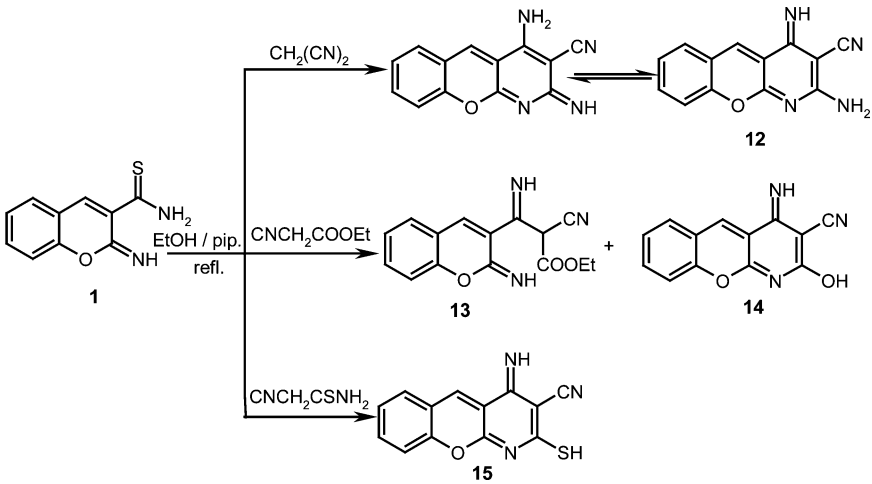


SCHEME 3

Also, the treatment of compound **1** with ethyl cyanoacetate or cyanothio-acetamide in ethanol containing a few drops of piperidine at r.t. afforded 2-cyano-N-[(2-imino-2H-chromen-3-yl)carbonothioyl]acetamide **9** or 2-cyano-N-[(2-imino-2H-chromen-3-yl)carbono-thioyl]ethanimidothioic acid **10**. Both compounds **9** and **10** gave the same cyclized product (4-thioxo-4H-chromeno[2,3-d]pyrimidin-2-yl)-acetonitrile **11** in 83% and 80% yields in refluxing tetrahydrofuran along with few drops of piperidine. Compound **11** was obtained directly in a 71% yield by refluxing compound **1** with ethyl cyanoacetate or cyanothioacetamide in tetrahydrofura along with piperidine as a catalyst (Scheme 4, Table I).



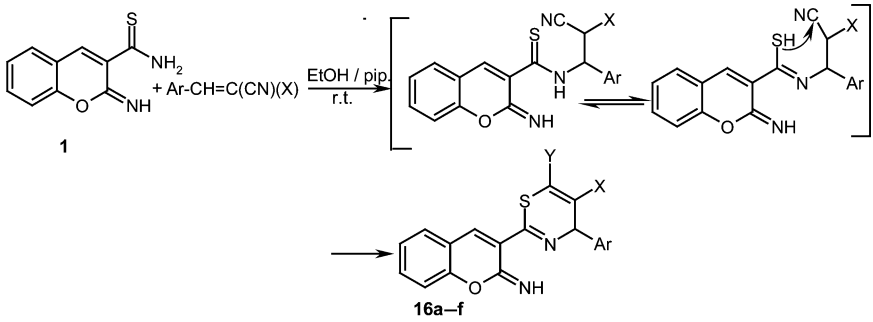
SCHEME 4



SCHEME 5

It has been reported[11] that the reaction of compound **1** with malononitrile or ethyl cyanoacetate along with ammonium acetate in a 1:1:1.5 molar ratio, respectively, in refluxing ethanol afforded the corresponding benzopyrano[3,4-c]pyridine-4H-thiones. Herein we report that the reaction of compound **1** with malononitrile, ethyl cyanoacetate, or cyanothioacetamide in refluxing ethanol using piperidine as a catalyst afforded 2-amino-4-imino-2H-chromeno[2,3-b]pyridine-3-carbonitrile **12**, ethyl 2-cyano-3-imino-3-(2-imino-2H-chromen-3-yl)propanoate **13**, 2-hydroxy-4-imino-4H-chromeno[2,3-d]pyridine-3-carbonitrile **14**, or 4-imino-2-mercapto-4H-chromeno[2,3-b]pyridine-3-cabonitrile **15**, respectively (Scheme 5, Table I). The reaction pathway is believed to be a nucleophilic attack of the methylene anion at the thione group with elimination of H_2S molecule to give the condensation product (this was confirmed by isolating the intermediate **13**) followed by intramolecular cyclization through the nucleophilic attack of the imino group at the cyano, carbonyl or thione group respectively.

The reaction of compound **1** with arylidene(benzylidene, p-nitrobenzylidene, p-methoxybenzylidene)malononitrile, ethyl p-nitrobezylidenecyano-acetate, and ethyl 2-naphthylidenecyanoacetate at r.t. in the presence of piperidine as a catalyst afforded 6-amino-2-(2-imino-2H-chromen-3-yl)-4-phenyl-4H-1,3-thiazine-5-carbonitrile **16a**, 6-amino-2-(2-imino-2H-chromen-3-yl)-4-(4-nitrophenyl-4H-1,3-thiazine-5-carbonitrile **16b**, 6-amino-2-(2-imino-2H-chromen-3-yl)-4-(4-methoxyphenyl-4H-1,3-thiazine-5-carbonitrile **16c**, ethyl 6-amino-2-(2-imino-2H-chromen-3-yl)-4-(4-nitophenyl)-4H-1,3-thiazine-5-carboxylate **16d**,

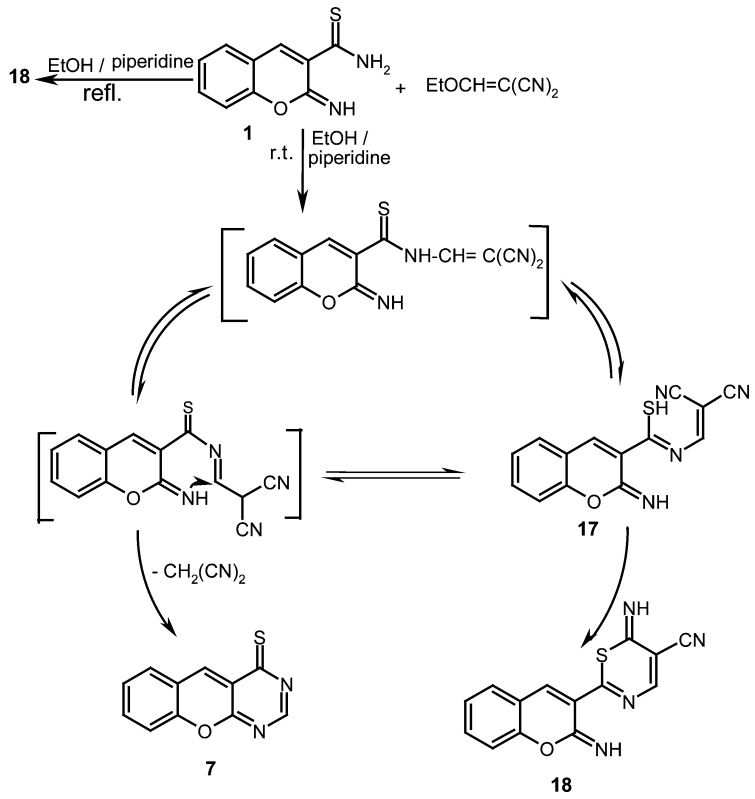


SCHEME 6

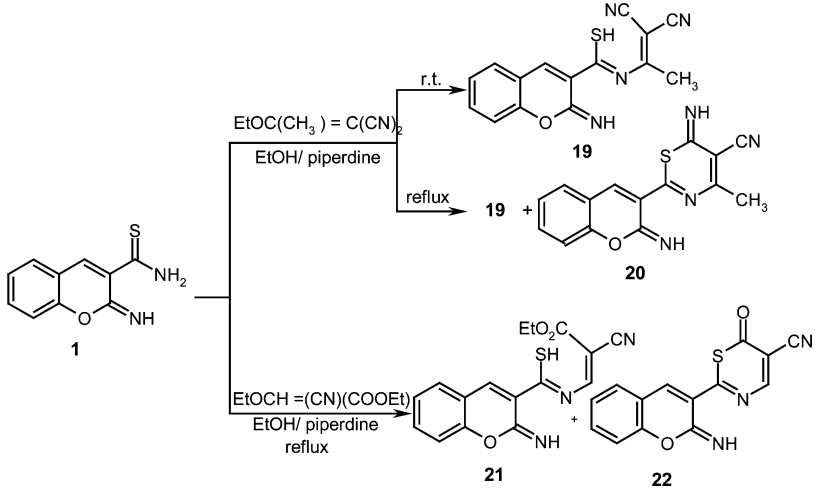
6-hydroxy-2-(2-imino-2H-chromen-3-yl)-4-(2-naphthyl)-4H-1,3-thiazine-5-carbonitrile **16e**, and ethyl 6-amino-2-(2-imino-2H-chromen-3-yl)-4-(2-naphthyl)-4H-1,3-thiazine-5-carboxylate **16f** (Scheme 6, Table I).

Moreover, compound **1** was subjected to react with ethoxymethylenemalononitrile in ethanol using piepridine as a catalyst at r.t. in which a mixture of N- (2,2-dicyanovinyl)-2-imino-2H-chromene-3-carbimidothioic acid **17**, benzo[g]quinazoline-4(10H)-thione **7**, and 6-imino-2-(2-imino-2H-chromen-3-yl)-6H-1,3-thiazine-5-carbonitrile **18** were isolated in 20%, 28%, and 48% yields, respectively. Carrying out the same reaction in refluxing ethanol afforded compound **18** only in an 80% yield. (Scheme 7, Table I).

Similarly, the reaction of compound **1** with(1-ethoxyethylidene)-malononitrile in ethanol in the presence of piperidine as a catalyst at r.t. gave the open structure **19** in a 26% yield. But the reaction of the same reagents in refluxing ethanol afforded a mixture of N-(2,2-dicyano-1-methylvinyl)-2-imino-2H-chromene-3-carbimidothioic acid **19** and 6-imino-2-(2-imino-2H-chromen-3-yl)-4-methyl-6H-1,3-thiazine-5-carbonitrile **20** in 30% and 51% yields, respectively. Also, the treatment of compound **1** with ethyl ethoxymethylenecyanoacetate in refluxing ethanol using a piperidine catalyst afforded N-[2-cyano-3-ethoxy-3-oxoprop-1-enyl]-2-imino-2H-chromene-3-carbimidothioi acid **21** and 2-(2-imino-2H-chromen-3-yl)-6-oxo-6H-1,3-thiazine-5-carbonitrile **22** (Scheme 8, Table I).



SCHEME 7



SCHEME 8

CONCLUSION

This synthetic study reveals that the reaction of the starting material 2-imino-2H-chromene-3-thiocarboxamide with the active nitriles and their ylidene derivatives depends on reaction conditions (temperature and time).

EXPERIMENTAL

The synthesis of 2-phenyl-2,3-dihydro-4H-chromeno[2,3-d]pyrimidine-4-thione,2-(4-methoxyphenyl)-2,3-dihydro-4H- chromeno[2,3-d]pyrimi–dine-4-thione, 2-(4-nitrophenyl)-2,3-dihydro-4H-chromeno[2,3-d]pyri–midine-4-thione and 2-(2-naphthyl)-2,3-dihydro-4H-chromeno[2,3-d]pyrimidine-4-thione 2a–d

General Procedure

To a solution of compound **1** (1.02 g, 0.005 mole) and benzaldehyde (0.50 mL), p-anisaldehyde (0.57 mL), p-nitrobenzaldehyde (0.75 g) or 2-naphthaldehyde (0.79 g) in tetrahydrofuran (50 mL), and 3 drops of piperidine were added. The reaction mixture was refluxed for 4 h. Compound **2d** was precipitated on heating, collected by filtration, and crystallized. The reaction mixture was left to cool where compounds **2a** and **2b** were separated, collected by filtration, and crystallized. The reaction mixture was evaporated, and the solid residue was washed with a water/ethanol mixture and crystallized where compound **2c** was obtained (Table I).

The Synthesis of 4-(8,8a,10,11,12,13-Hexahydro-7H-5-oxa-9-thia-6,8-diazanaphtho[2,3,4-de]anthracen-7-yl)phenyl Methyl Ether 3b

A mixture of compound **2b** (0.80 g, 0.0025 mole), cyclohexanone (0.26 mL, 0.0025 mole), and 2 drops of triethylamine and dioxane (20 mL) was stirred at r.t. for 1 h and then refluxed for 2 h. The reaction mixture was evaporated, and the residual solid was washed with a water/ethanol mixture and crystallized (Table I).

The Synthesis of N-[(2-imino-2H-chromen3-yl)-carbonothioyl]acetamide 4

Compound **1** (1.02 g, 0.005 mole) was dissolved in glacial acetic acid (20 mL) and stirred for 2 h at r.t. The separated solid was collected by filtration, washed with ethanol, and crystallized (Table I).

The Synthesis of 2-Methyl-4H-chromeno[2,3-d]-pyrimidine-4-thione 5

Compound **4** (0.615 g, 0.0025 mole) or compound **1** (1.02 g, 0.005 mole) was refluxed in acetic anhydride (10 mL) for 10 min. The reaction mixture was poured into an ice-water mixture, and the separated solid was filtered off, washed with water, and crystallized (Table I).

The Synthesis of N-formyl 2-Imino-2H-chromene-3-thiocarboxamide 6

A solution of compound **1** (1.02 g, 0.005 mole) in 10 mL of formic acid (85%) was heated (60–65°C) for 10 min. The reaction mixture was evaporated in vacuo. The residual solid was washed with water and crystallized (Table I).

The Synthesis of Benzo[g]quinazoline-4(10H)-thione 7

A mixture of compound 6 (0.697 g, 0.003 mole) and 2 drops of piperidine and 15 mL of ethanol was refluxed for 2 h. The reaction mixture was evaporated. The residual solid was washed with water and crystallized (Table I).

The Synthesis of 3-Imino-1-thioxo-2,3-dihydro-1H-chromeno[3,2-c]pyridine-4-carbonitrile 8,2-Cyano-N-[(2-imino-2H-chromen-3-yl)carbonothioyl]acetamide 9, and 2-Cyano-N-[(2-imino-2H-chromen-3-yl)carbonothioyl]-ethanimidothioic Acid 10: General Procedure

A solution of compound **1** (1.02 g, 0.005 mole) and malononitrile, (0.33 g, 0.005 mole), ethyl cyanoacetate (0.503 mL, 0.005 mole), or cyanothioacetamide (0.50 g, 0.005 mole) in ethanol (50 mL) was treated with 2 drops of piperidine. The reaction mixture was stirred for 15 min and left for 72 h. The precipitate was collected by filtration and crystallized from the proper solvent (Table I).

The Synthesis of (4-Thioxo-4H-chromeno[2,3-d]pyrimidin-2-yl)-acetonitrile 11

A mixture of compound **1, 9**, or **10** (0.002 mole), tetrahydrofuran (40 mL), and 2 drops of piperidine was refluxed for 3 h. The solvent was evaporated in vacuo. The solid residue was washed with water

followed by ethanol and crystallized from an ethanol/dioxane mixture (Table I).

The Synthesis of 4-Amino-2-imino-2H-chromeno[2,3-b]-pyridine-3-carbonitrile 12, Ethyl 2-Cyano-3-imino-3-(2-imino-2H-chromen-3-yl)propanoate 13, 2-Hydroxy-4-imino-4H-chromeno[2,3-d]pyridine-3-carbonitrile 14, and 4-Imino-2-mercapto-4H-chromeno[2,3-b]pyridine-3-cabonitrile 15: General Procedure

To a mixture of compound **1** (1.02 g, 0.005 mole), ethanol(50 mL), 2 drops of piperidine, malononitrile, and ethyl cyanoacetate or cyanothioacetamide (0.005 mole) was added. The reaction mixture was refluxed until the evolution of H_2S gas ceased (5 h). Compound **13** was precipitated on heating, which was collected by filtration and crystallized. Compounds **12** and **15** were precipitated after cooling, collected by filtration, and crystallized. Compound **14** was isolated via the evaporation of the filtrate of compound **13** and washing the solid residue with water followed by crystallization (Table I).

The Synthesis of Compounds 16a–f: General Procedure

A mixture of compound **1** (0.51 g, 0.0025 mole) and ethanol (40 mL) containing 3 drops of piperidine was treated with benzylidenemalononitrile (0.39 g), p-nitrobenzylidenemalononitrile, (0.59 g), p-methoxybenz-ylidenemalononitrile (0.42 g), ethyl p-nitrobenzylidenecyanoacetate (0.555 g), or ethyl 2-naphthylidenecyanoacetate (0.527 g). The reaction mixture was stirred for 15 min and left for 48 h at r.t. The reaction mixture was evaporated in vacuo. The solid residue was washed with water and ethanol followed by crystallization to give compounds **16a, 16b**, and **16d**. In the case of compounds **16c** and **16e**, the solid residue was treated with a $CHCl_3$/pet. ether (40–60°C) mixture, and the precipitate was collected by filtration and crystallized. The filtrate of **16e** was evaporated, and the solid residue was crystallized to give **16f** (Table I).

The Synthesis of N-(2,2-dicyanovinyl)-2-imino-2H-chromene-3-carbimidothioic Acid 17 and 6-Imino-2-(2-imino-2H-chromen-3-yl)-6H-1,3-thiazine-5-carbonitrile 18

A mixture of compound **1** (2.04 g, 0.01 mole), ethoxymethylenemalononitrile (1.22 g, 0.01 mole), ethanol (50 mL), and 3 drops of piperidine was stirred for 30 min and left for 4 h at r.t. The precipitate was collected

by filtration, washed with ethanol, and crystallized to give compound **7**. The filtrate was left for 6 h, and the separated solid was filtered off, washed with ethanol, and crystallized to give compound **18**. The second filtrate was evaporated in vacuo, and the solid residue was washed with water, and pet. ether (60–80°C) and crystallized to give compound **17** (Table I).

Synthesis of Compound 18: Direct Method

To a solution of compound **1** (0.005 mole) and ethoxymethylenemalononitrile (0.005 mole) in ethanol (30 mL), 3 drops of piperidine was added. The reaction mixture was refluxed for 2 h and left to cool. The precipitate was filtered off, washed with ethanol, and crystallized.

The Synthesis of N-(2,2-dicyano-1-methylvinyl)-2-imino-2H-chromene-3-carbimidothioic Acid 19

A solution of compound **1** (0.51 g, 0.0025 mole) and 1-ethoxyethylidenemalononitrile (0.33 g, 0.0025 mole) in ethanol (30 mL) was treated with two drops of piperidine. The reaction mixture was stirred for 6 h at r.t. and left for 24 h. The precipitate was collected by filtration, washed with ethanol, and crystallized.

The Synthesis of and 6-Imino-2-(2-imino-2H-chromen-3-yl)-4-methyl-6H-1,3-thiazine-5-carbonitrile 20

A mixture of compound **1** and 1-ethoxyethylidenemalononitrile (0.0025 mole), ethanol (40 mL), and 2 drops of piperdine was refluxed for 3 h and left to cool. The precipitate was filtered off, washed with ethanol, and crystallized to give compound **19**. The filtrate was evaporated, and the solid residue was washed with water and pet. (60–80°C) and crystallized to give compound **20**.

The Synthesis of N[2-cyano-3-ethoxy-3-oxoprop-1-enyl]-2-imino-2H-chromene-3-carbimidothioic Acid 21 and 2-(2-Imino-2H-3-chromen-3-yl)-6-oxo-6H-1,3-thiazine-5-carbonitrile 22

A solution of compound **1** (0.51 g, 0.005 mole) and ethyl ethoxymethylenecyanoacetate (0.42 g, 0.005 mole) in ethanol (40 mL) was treated with 2 drops of piperidine. The reaction mixture was refluxed for 5 h. The reaction mixture was concentrated to half its volume and left to cool. The precipitate was collected by filtration and crystallized to give compound **22**. The filtrate was evaporated. The residual

solid was washed with pet. ether (60–80°C) and crystallized to give compound **21**.

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