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REACTION OF 3-IODOCHROMONE WITH NUCLEOPHILES 2. REACTION WITH MERCAPTOAZOLES

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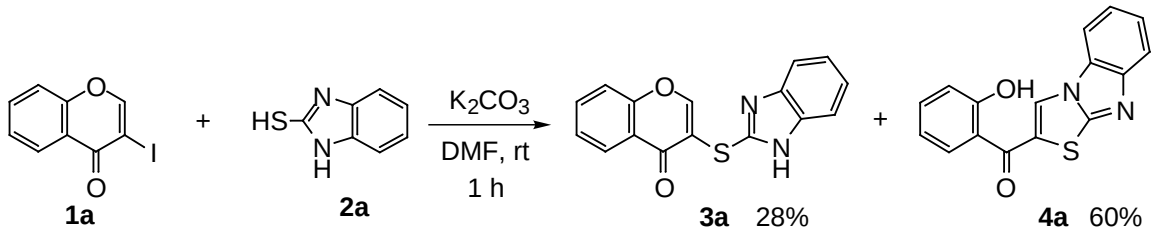
Abstract – 3-Iodochromone (**1a**) easily reacted with mercaptoazoles in the presence of potassium carbonate to give 3-azolylthiochromones in good yields. In the case of 2-mercaptobenzimidazole (**2a**) as a nucleophile, the benzimidazo[2,1-*b*]thiazole derivative (**4a**) was obtained as the major product along with 3-(1*H*-benzimidazol-2-ylthio)chromone (**3a**). The ratio of the two products was found to be affected by the electron density on the nitrogen atom in the benzimidazole ring.

Because 3-iodochromone (**1a**)[1] has an α,β-unsaturated carbonyl moiety and a good leaving group at the 3-position of the pyrone ring, the conjugate addition reaction is expected to occur at the 2-position of the chromone skeleton with a nucleophile.[2] In our previous paper, we reported the Michael type reactions of 3-iodochromone (**1a**) with azoles such as imidazole, pyrazole, indazole in the presence of potassium carbonate as the base to produce the 2-(1-azolyl)chromones in high yields.[3] Interestingly, the treatment of **1a** with indole as a nucleophile afforded 2-(1-indolyl)chromone and its rearrangement product. In the course of our study to find further applications of 3-iodochromone, we expanded the investigation to the reactions of **1a** with mercaptoazoles based on the expectation of the formation of new heterocyclic compounds.

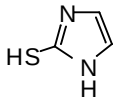
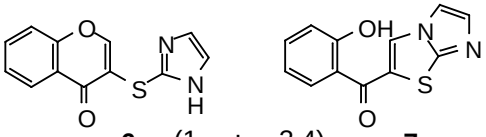
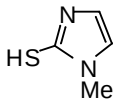
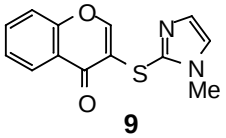
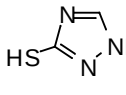
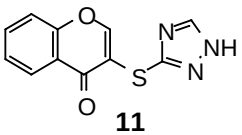
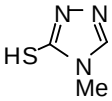
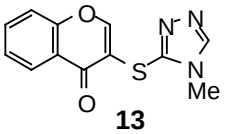
Thetreatment of 3-iodochromone (**1a**) with 2-mercaptobenzimidazole (**2a**) in the presence of potassium carbonate in DMF at room temperature, interestingly, gave 3-(1*H*-benzimidazol-2-ylthio)chromone (**3a**) and the benzimidazo[2,1-*b*]thiazole derivative (**4a**) in 28% and 60% yields, respectively, and no 2-substituted chromone was detected (Scheme 1). The two obtained products were found to have the same molecular formula, $C_{16}H_{10}N_2O_2S$, based on the elemental analytical data and the MS spectra [m/z 294 (M^+)]. The ^{1}H-NMR spectrum of the compound (**3a**) showed a signal for the 2-position of the chromone ring at 8.56 ppm and a broad signal at 11.70 ppm corresponding to a proton from the NH group along with eight aromatic proton signals. In addition, four aromatic protons on the benzimidazole ring showed as broad signal due to the tautomer-like behavior of the imidazole ring.[4] The ^{1}H-NMR spectrum of the compound (**4a**) showed a proton signal of the new thiazole ring at 8.38 ppm and a signal at 11.08 ppm corresponding to a chelated OH group.



Scheme 1

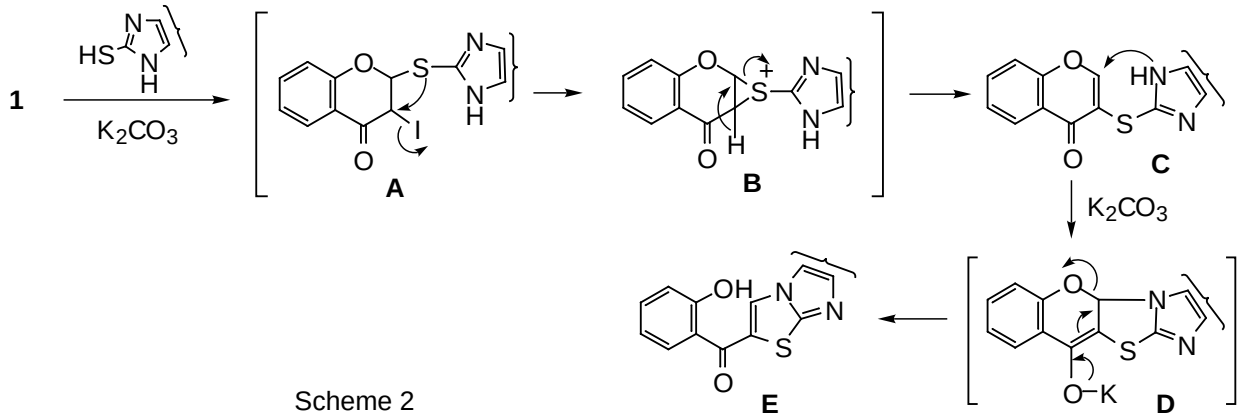
The reactions of **1a** with other mercaptoazoles were then examined and these results are summarized in Table 1. As for the mercaptoazoles, 2-mercaptoimidazole (**5**) as well as 2-mercaptobenzimidazole (**2a**) effectively reacted to give the 3-(1*H*-imidazol-2-ylthio)chromone (**6**) and imidazo[2,1-*b*]thiazole (**7**) in 18% and 62% yields, respectively (Entry 1). The reactions of **1a** with 2-mercapto-1-methylimidazole (**8**), 3-mercapto-1,2,4-triazole (**10**), and 3-mercapto-4-methyl-4*H*-1,2,4-triazole (**12**) gave the corresponding 3-azolylthiochromones as the sole products in good yields (Entries 2-4).

Table 1. Reaction of 3-iodochromone (**1a**) with mercaptoazoles

Entry	Azole	Product (ratio)	Yield/%[a]
1	 **5**	 **6** (1 : 3.4) **7**	80
2	 **8**	 **9**	88
3	 **10**	 **11**	72
4	 **12**	 **13**	70

[a] Isolated yields.

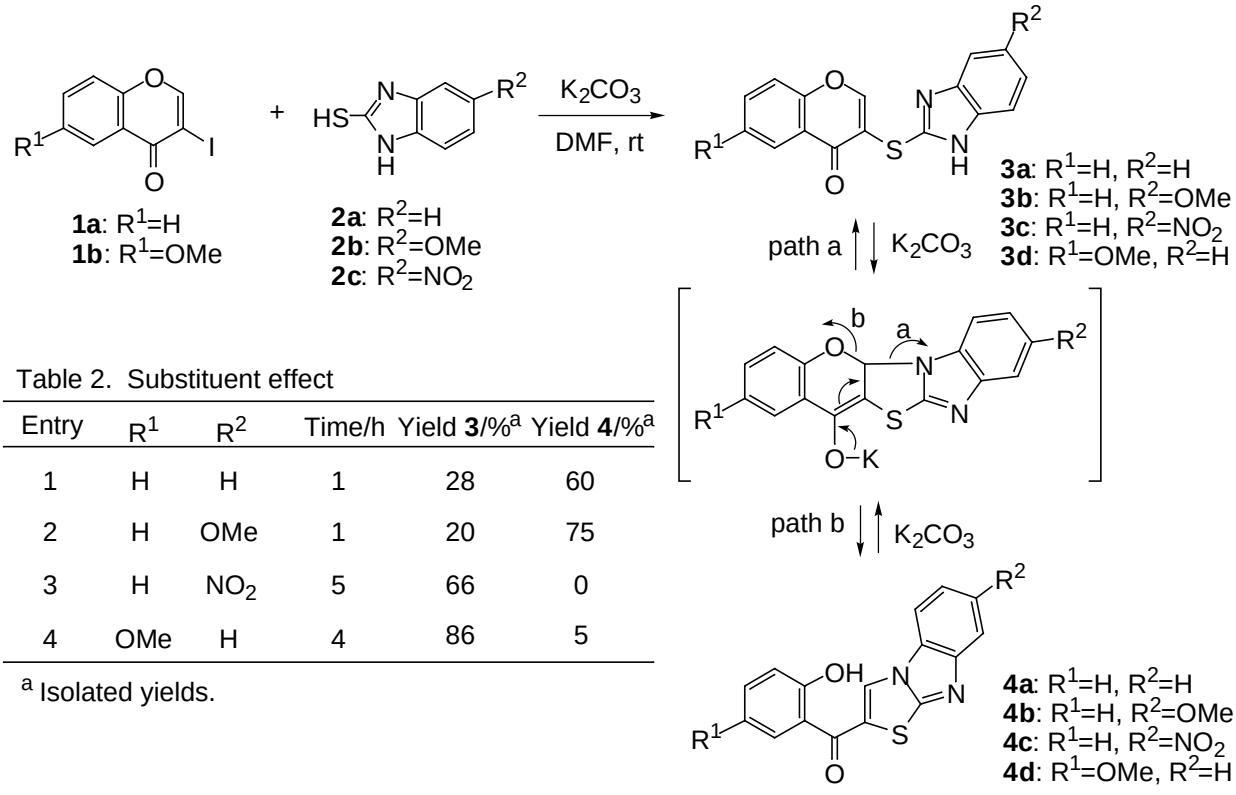
A plausible reaction mechanism of 3-iodochromone (**1a**) with the mercaptoazoles is illustrated in Scheme 2. The conjugate addition of the thiol to the activated site (2-position of the chromone ring) would form the intermediate (**A**). The displacement of iodine by sulfur in the intermediate (**A**) would generate the three-membered ring episulfonium ion (**B**).[5] The subsequent cleavage of the carbon-sulfur bond of the episulfonium ion (**B**) due to deprotonation would give the 3-azolylthiochromone (**C**). The formation of the compound (**E**) possibly involves the intramolecular nucleophilic attack of the azole moiety in the formed **C** on the enone of the chromone ring followed by cleavage of the carbon-oxygen bond in the resulting intermediate (**D**).



Scheme 2

It was found that two compounds derived from **1a** and **2a** are equilibrated with each other under the appropriate reaction conditions. Thus, the pure compound (**3a**) was refluxed in MeOH for 8 h to attain an equilibrium with the compound (**4a**) (**3a** : **4a** = 6 : 1). The same result was also obtained when the compound (**4a**) was used as the substrate. On the contrary, under basic conditions (K_2CO_3 / DMF, rt), the isomeric reaction attained equilibrium with a **3a** : **4a** mixture of 1 : 2.2.

The substituent effect on the benzimidazole ring was then investigated (Table 2, Entries 1-3). As the results, the ratio of **3** and **4** was found to be affected by the electron density on the nitrogen atom in the benzimidazole ring. Namely, benzimidazole bearing an electron-donating group produced an increased ratio of benzimidazo[2,1-*b*]thiazole (**4**) (Entry 2). On the contrary,3-(1*H*-benzimidazol-2-ylthio)-chromone (**3c**) was obtained in 66% yield as the sole product when the reaction of **1a** with benzimidazole having a nitro group was carried out (Entry 3). Furthermore, a substituent on the chromone ring also exerted a profound effect on the ratio of products. Namely, the reaction of 3-iodo-6-



1a: R^1=H
1b: R^1=OMe

2a: R^2=H
2b: R^2=OMe
2c: R^2=NO_2

3a: R^1=H, R^2=H
3b: R^1=H, R^2=OMe
3c: R^1=H, R^2=NO_2
3d: R^1=OMe, R^2=H

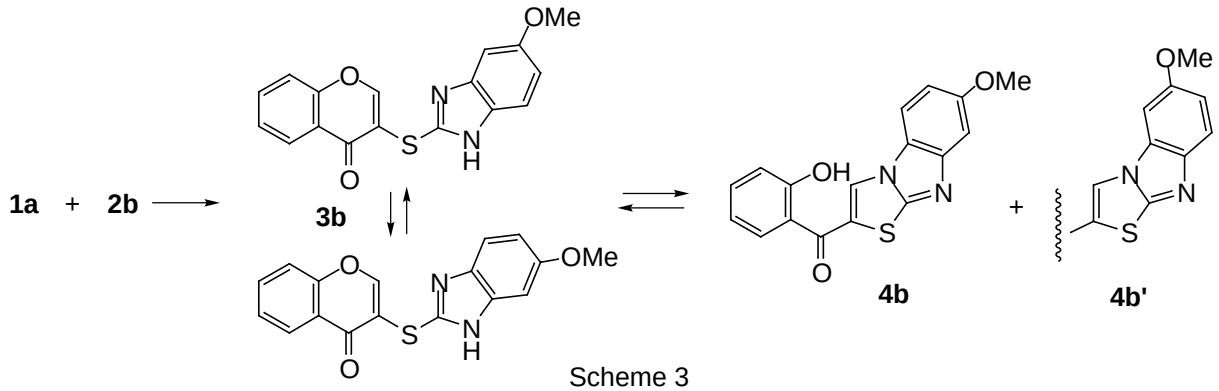
4a: R^1=H, R^2=H
4b: R^1=H, R^2=OMe
4c: R^1=H, R^2=NO_2
4d: R^1=OMe, R^2=H

Table 2. Substituent effect

Entry	R^1	R^2	Time/h	Yield **3**/%[a]	Yield **4**/%[a]
1	H	H	1	28	60
2	H	OMe	1	20	75
3	H	NO_2	5	66	0
4	OMe	H	4	86	5

[a] Isolated yields.

methoxychromone (**1b**) with 2-mercaptobenzimidazole (**2a**) decreased the yield of the benzimidazo[2,1-*b*]thiazole derivative and the yield of the 3-(1*H*-benzimidazol-2-ylthio)chromone derivative was increased (Entry 4). It was found that the reaction of **1a** with 2-mercapto-5-methoxybenzimidazole (**2b**) formed the two benzimidazo[2,1-*b*]thiazole derivatives, the 7- and 6-methoxybenzimidazo[2,1-*b*]thiazoles (**4b**, **4b'**), due to tautomer behavior of the 3-(1*H*-benzimidazol-2-ylthio)chromone (**3b**) as shown in Scheme 3.



Scheme 3

The structure of **4b** was confirmed by analysis of its NOE experiments (Figure 1).

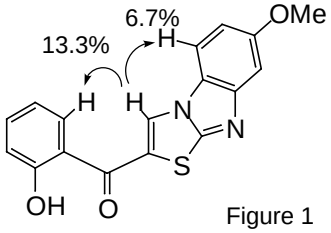
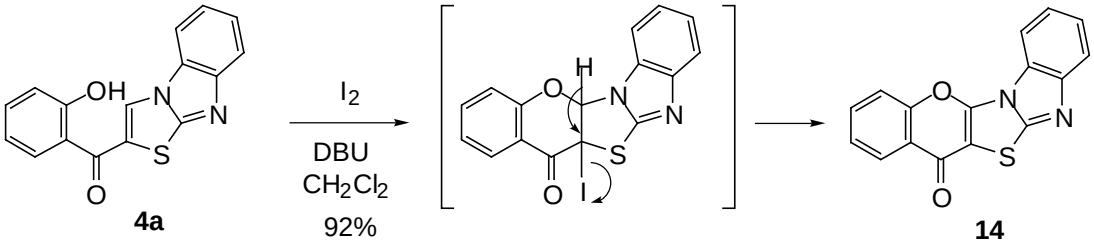


Figure 1

Interestingly, compound (**4a**) was readily converted to the condensed-ring compound (**14**). Thus the treatment of **4a** with iodine in the presence of DBU smoothly promoted the cyclization, and the corresponding benzimidazothiazolobenzopyran derivative (**14**) was obtained in excellent yield (Scheme 4).



Scheme 4

EXPERIMENTAL

All melting points were determined using a Yanagimoto micro-hot stage and are uncorrected. IR spectra were recorded using a JASCO FT/IR-5300 spectrophotometer and NMR spectra were measured using a

JEOL JNM-A500 with tetramethylsilane as the internal standard. MS spectra were recorded using a JEOL JMS-700 spectrometer. Column chromatography was done on a BW-820 MH (Fuji silysia).

General Procedure for the Reaction of 3-Iodochromone with Mercaptoazoles. A mixture of 3-iodochromone (**1a**, 136 mg, 0.5 mmol), mercaptoazoles (0.5 mmol), and K_2CO_3 (276 mg, 2 mmol) in DMF (5 mL) was stirred for 1-5 h at rt. After removal of the K_2CO_3, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane –AcOEt).

Reaction of 3-Iodochromone (1a) with 2-Mercaptobenzimidazole (2a). According to the general procedure, **1a** (136 mg, 0.5 mmol) and **2a** (75 mg, 0.5 mmol) were treated with K_2CO_3 at 1 h to give **3a** (41 mg, 28%) and **4a** (88 mg, 60%), respectively.

3-(1*H*-Benzimidazol-2-ylthio)-4*H*-1-benzopyran-4-one (3a): colorless needles (from AcOEt-MeOH), mp 228-229 °C; IR (KBr) 3244, 3055, 1647, 1622, 1599, 1460 cm^{-1}; ^{1}H-NMR [$CDCl_3$ (DMSO-d_6 1 drop)] δ 7.15-7.19 (2H, m, Ar), 7.20-7.70 (2H, m, Ar), 7.47 (1H, ddd, *J* = 8.2, 7.0, 0.9 Hz, H-6), 7.51 (1H, dd, *J* = 8.5, 0.9 Hz, H-8), 7.74 (1H, ddd, *J* = 8.2, 7.0, 1.0 Hz, H-7), 8.24 (1H, dd, *J* = 8.2, 1.5 Hz, H-5), 8.56 (1H, s, H-2), 11.70 (1H, s, NH); ^{13}C-NMR [$CDCl_3$ (DMSO-d_6 1 drop)] δ 110.91, 116.22, 118.35, 118.78, 122.50, 123.68, 126.07, 126.18, 134.46, 146.52, 156.38, 159.10, 175.83; MS m/z 294 (M^+). *Anal*. Calcd for $C_{16}H_{10}N_2O_2S$: C, 65.29; H, 3.42; N, 9.52. Found: C, 65.32; H, 3.30; N, 9.51.

2-(2-Hydroxybenzoyl)benzimidazo[2,1-*b*]thiazole (4a): pale yellow solid (from AcOEt-hexane), mp 220-223 °C; IR (KBr) 3435, 1630, 1564, 1459, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.07 (1H, ddd, *J* = 8.2, 7.3, 1.2 Hz, H-5'), 7.14 (1H, dd, *J* = 8.5, 1.2 Hz, H-3'), 7.35 (1H, ddd, *J* = 8.2, 7.3, 1.0 Hz, H-6 or -7), 7.46 (1H, ddd, *J* = 8.2, 7.3, 1.0 Hz, H-6 or -7), 7.60 (1H, ddd, *J* = 8.5, 7.3, 1.8 Hz, H-4'), 7.74 (1H, dd, *J* = 8.2, 1.0 Hz, H-5 or -8), 7.83 (1H, dd, *J* = 8.2, 1.0 Hz, H-5 or -8), 7.95 (1H, dd, *J* = 8.2, 1.8 Hz, H-6'), 8.38 (1H, s, H-3), 11.08 (1H, s, OH); ^{13}C-NMR ($CDCl_3$) δ 110.77, 118.98, 119.04, 119.58, 119.77, 122.09, 124.82, 125.20, 128.46, 129.40, 130.14, 136.60, 148.55, 156.21, 161.93, 189.03; MS *m/z* 294 (M^+). *Anal*. Calcd for $C_{16}H_{10}N_2O_2S$: C, 65.29; H, 3.42; N, 9.52. Found: C, 65.29; H, 3.27; N, 9.35.

Reaction of 3-Iodochromone (1a) with 2-Mercaptoimidazole (5). According to the general procedure, **1a** (136 mg, 0.5 mmol) and **5** (50 mg, 0.5 mmol) were treated with K_2CO_3 at 1 h to give **6** (22 mg, 18%) and **7** (76 mg, 62%), respectively.

3-(1*H*-Imidazol-2-ylthio)-4*H*-1-benzopyran-4-one (6): colorless prisms (from AcOEt-hexane), mp 162-164 °C; IR (KBr) 3314, 3036, 1633, 1611, 1557, 1508, 1462 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.07 (2H, s, H-4' and –5'), 7.48 (1H, ddd, *J* = 8.2, 7.3, 0.9 Hz, H-6), 7.49 (1H, dd, *J* = 8.5, 0.9 Hz, H-8), 7.73 (1H, ddd, *J* = 8.5, 7.3, 1.8 Hz, H-7), 8.26 (1H, dd, *J* = 8.2, 1.8 Hz, H-5), 8.48 (1H, s, H-2), 10.76 (1H, br s, NH); ^{13}C-NMR ($CDCl_3$) δ 117.77, 118.33, 123.52, 126.06, 126.10, 134.50, 136.73, 156.36, 158.29, 176.87; MS *m/z* 244 (M^+). *Anal*. Calcd for $C_{12}H_8N_2O_2S$: C, 59.01; H, 3.30; N, 11.47. Found: C, 59.01; H, 3.08; N, 11.42.

2-(2-Hydroxybenzoyl)imidazo[2,1-*b*]thiazole (7): pale yellow needles (from AcOEt-hexane), mp 146-147 °C; IR (KBr) 3445, 3152, 1628, 1607, 1568, 1476, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.01 (1H, ddd, *J* = 8.2, 7.3, 1.2 Hz, H-5'), 7.11 (1H, dd, *J* = 8.5, 1.2 Hz, H-3'), 7.45 (1H, d, *J* = 1.5 Hz, H-5 or -6), 7.54

(1H, d, *J* = 1.5 Hz, H-5 or 6), 7.58 (1H, ddd, *J* = 8.5, 7.3, 1.8 Hz, H-4'), 7.89 (1H, dd, *J* = 8.2, 1.8 Hz, H-6'), 8.14 (1H, s, H-3), 11.12 (1H, s, OH); ^{13}C-NMR ($CDCl_3$) δ 113.02, 118.93, 118.97, 119.48, 125.24, 130.34, 130.52, 136.66, 136.85, 150.38, 162.04, 189.54; MS *m/z* 244 (M^+). *Anal.* Calcd for $C_{12}H_8N_2O_2S$: C, 59.01; H, 3.30; N, 11.47. Found: C, 58.99; H, 3.21; N, 11.34.

Reaction of 3-Iodochromone (1a) with 2-Mercapto-1-methylimidazole (8). According to the general procedure, **1a** (136 mg, 0.5 mmol) and **8** (57 mg, 0.5 mmol) were treated with K_2CO_3 at 1 h to give **9** (114 mg, 88%).

3-(1*H*-1-Methylmidazol-2-ylthio)-4*H*-1-benzopyran-4-one (9): colorless needles (from AcOEt-hexane), mp 198-199 °C; IR (KBr) 3096, 1644, 1611, 1558, 1466, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.95 (3H, s, NMe), 7.00 (1H, d, *J* = 1.2 Hz, H-4' or –5'), 7.07 (1H, d, *J* = 1.2 Hz, H-4' or –5'), 7.40 (1H, ddd, *J* = 8.2, 7.0, 0.9 Hz, H-6), 7.44 (1H, dd, *J* = 8.5, 0.9 Hz, H-8), 7.67 (1H, ddd, *J* = 8.5, 7.0, 1.5 Hz, H-7), 8.17 (1H, dd, *J* = 8.2, 1.5 Hz, H-5), 8.32 (1H, s, H-2); ^{13}C-NMR ($CDCl_3$) δ 34.29, 118.17, 119.12, 123.39, 123.52, 125.65, 126.00, 130.10, 133.99, 137.53, 156.25, 156.99, 174.89; MS *m/z* 258 (M^+). *Anal.* Calcd for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85. Found: C, 60.50; H, 3.91; N, 10.93.

Reaction of 3-Iodochromone (1a) with 2-Mercapto-1,2,4-triazole (10). According to the general procedure, **1a** (136 mg, 0.5 mmol) and **10** (51 mg, 0.5 mmol) were treated with K_2CO_3 at 2 h to give **11** (88 mg, 72%).

3-(1*H*-1,2,4-triazol-3-ylthio)-4*H*-1-benzopyran-4-one (11): pale brown prisms (from MeOH), mp 234-236 °C; IR (KBr) 3452, 3127, 2938, 1624, 1557, 1495, 1460 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 7.54 (1H, ddd, *J* = 8.2, 7.3, 0.9 Hz, H-6), 7.71 (1H, dd, *J* = 8.5, 0.9 Hz, H-8), 7.86 (1H, ddd, *J* = 8.5, 7.3, 1.8 Hz, H-7), 8.05 (1H, dd, *J* = 8.2, 1.8 Hz, H-5), 8.36 (1H, br s, H-5'), 8.83 (1H, s, H-2), 12.5-13.5 (1H, br s, NH); ^{13}C-NMR (DMSO-d_6) δ 115.11, 118.58, 123.08, 125.40, 126.21, 134.74, 146.48, 155.85, 159.96, 173.69; MS *m/z* 245 (M^+). *Anal.* Calcd for $C_{11}H_7N_3O_2S$: C, 53.87; H, 2.88; N, 17.13. Found: C, 53.87; H, 2.65; N, 17.10.

Reaction of 3-Iodochromone (1a) with 3-Mercapto-4-methyl-4*H*-1,2,4-triazole (12). According to the general procedure, **1a** (136 mg, 0.5 mmol) and **12** (58 mg, 0.5 mmol) were treated with K_2CO_3 at 2 h to give **13** (91 mg, 70%).

3-(4-Methyl-4*H*-1,2,4-triazol-3-ylthio)-4*H*-1-benzopyran-4-one (13): pale brown prisms (from AcOEt-MeOH), mp 213-214 °C; IR (KBr) 3103, 1626, 1612, 1466 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 3.78 (3H, s, NMe), 7.52 (1H, ddd, *J* = 7.9, 7.0, 0.8 Hz, H-6), 7.69 (1H, dd, *J* = 8.5, 0.8 Hz, H-8), 7.84 (1H, ddd, *J* = 8.5, 7.0, 1.5 Hz, H-7), 8.01 (1H, dd, *J* = 7.9, 1.5 Hz, H-5), 8.60 (1H, s, H-2 or –5'), 8.78 (1H, s, H-2 or –5'); ^{13}C-NMR (DMSO-d_6) δ 31.52, 116.38, 118.63, 122.77, 125.27, 126.30, 126.31, 134.92, 146.56, 155.81, 158.74, 173.59; MS *m/z* 259 (M^+). *Anal.* Calcd for $C_{12}H_9N_3O_2S$: C, 55.59; H, 3.50; N, 16.21. Found: C, 55.86; H, 3.02; N, 16.19.

Reaction of 3-Iodochromone (1a) with 2-Mercapto-5-methoxybenzimidazole (2b). According to the general procedure, **1a** (136 mg, 0.5 mmol) and **2b** (90 mg, 0.5 mmol) were treated with K_2CO_3 at 1 h to give **3b** (32 mg, 20%), **4b** (73 mg, 45%) and **4b'** (49 mg, 30%).

3-(5-Methoxy-1*H*-benzimidazol-2-ylthio)-4*H*-1-benzopyran-4-one (3b): colorless solid (from AcOEt-hexane), mp 149-150 °C; IR (KBr) 3468, 3057, 1653, 1615, 1560, 1460 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.79

(3H, s, OMe), 6.81 (1H, dd, *J* = 8.8, 2.4 Hz, H-6'), 6.92 (1H, br s, H-4' or –7'), 7.40 (1H, br s, H-4' or –7'), 7.46 (1H, dd, *J* = 8.5, 0.8 Hz, H-8), 7.47 (1H, ddd, *J* = 8.2, 7.0, 0.8 Hz, H-6), 7.71 (1H, ddd, *J* = 8.5, 7.0, 1.8 Hz, H-7), 8.25 (1H, dd, *J* = 8.2, 1.8 Hz, H-5), 8.54 (1H, s, H-2), 11.00 (1H, br s, NH); ^{13}C-NMR ($CDCl_3$) δ 55.73, 112.54, 116.43, 118.37, 119.62, 123.58, 126.20, 126.26, 134.69, 144.92, 156.39, 156.67, 159.45, 176.92; MS *m/z* 324 (M^+). *Anal*. Calcd for $C_{17}H_{12}N_2O_3S$: C, 62.95; H, 3.73; N, 8.64. Found: C, 62.75; H, 3.86; N, 8.53.

2-(2-Hydroxybenzoyl)-7-methoxybenzimidazo[2,1-*b*]thiazole (4b): yellow solid (from AcOEt-hexane), mp 200-202 °C; IR (KBr) 3459, 3084, 2996, 1630, 1607, 1591, 1566, 1489, 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.90 (3H, s, OMe), 6.95 (1H, dd, *J* = 8.8, 2.4 Hz, H-6), 7.06 (1H, ddd, *J* = 7.9, 7.0, 1.0 Hz, H-5'), 7.13 (1H, dd, *J* = 8.5, 1.0 Hz, H-3'), 7.28 (1H, d, *J* = 2.4 Hz, H-8), 7.59 (1H, ddd, *J* = 8.5, 7.0, 1.5 Hz, H-4'), 7.60 (1H, d, *J* = 8.8 Hz, H-5), 7.94 (1H, dd, *J* = 7.9, 1.5 Hz, H-6'), 8.32 (1H, s, H-3), 11.08 (1H, br s, OH); MS *m/z* 324 (M^+). *Anal*. Calcd for $C_{17}H_{12}N_2O_3S$: C, 62.95; H, 3.73; N, 8.64. Found: C, 62.87; H, 3.75; N, 8.59.

2-(2-Hydroxybenzoyl)-6-methoxybenzimidazo[2,1-*b*]thiazole (4b'): yellow needles (from AcOEt-hexane), mp 145-148 °C; IR (KBr) 3443, 3082, 1622, 1588, 1558, 1480 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.90 (3H, s, OMe), 7.07 (1H, ddd, *J* = 7.9, 7.0, 1.0 Hz, H-5'), 7.08 (1H, dd, *J* = 8.8, 2.4 Hz, H-7), 7.13 (1H, dd, *J* = 8.5, 1.0 Hz, H-3), 7.21 (1H, d, *J* = 2.4 Hz, H-5), 7.60 (1H, ddd, *J* = 8.5, 7.0, 1.5 Hz, H-4'), 7.70 (1H, d, *J* = 8.8 Hz, H-8), 7.95 (1H, dd, *J* = 7.9, 1.5 Hz, H-6'), 8.31 (1H, s, H-3), 11.08 (1H, br s, OH); MS *m/z* 324 (M^+). *Anal*. Calcd for $C_{17}H_{12}N_2O_3S$: C, 62.95; H, 3.73; N, 8.64. Found: C, 62.96; H, 3.59; N, 8.54.

Reaction of 3-Iodochromone (1a) with 2-Mercapto-5-nitrobenzimidazole (2c). According to the general procedure, **1a** (136 mg, 0.5 mmol) and **2c** (98 mg, 0.5 mmol) were treated with K_2CO_3 at 5 h to give **3c** (112 mg, 66%).

3-(5-Nitro-1*H*-benzimidazol-2-ylthio)-4*H*-1-benzopyran-4-one (3c): pale yellow powder (from MeOH), mp 260-262 °C; IR (KBr) 3458, 1616, 1520, 1462, 1343 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 7.52-7.58 (1H, m, H-4' or –7'), 7.57 (1H, ddd, *J* = 8.2, 7.0, 1.0 Hz, H-6), 7.78 (1H, dd, *J* = 8.5, 1.0 Hz, H-8), 7.90 (1H, ddd, *J* = 8.5, 7.0, 1.8 Hz, H-7), 8.03 (1H, dd, *J* = 8.8, 2.4 Hz, H-6'), 8.07 (1H, dd, *J* = 8.2, 1.8 Hz, H-5), 8.25 (1H, br s, H-4'or –7'), 9.06 (1H, s, H-2), 13.08 (1H, br s, NH); High-resolution MS *m/z* Calcd for $C_{16}H_9N_3O_4S$ (M^+); 339.0314, Found: 339.0303.

Reaction of 3-Iodo-6-methoxychromone (1b) with 2-Mercaptobenzimidazole (2a). According to the general procedure, **1b** (151 mg, 0.5 mmol) and **2a** (75 mg, 0.5 mmol) were treated with K_2CO_3 at 4 h to give **3d** (139 mg, 86%) and **4d** (8 mg, 5%), respectively.

3-(1*H*-Benzimidazol-2-ylthio)-6-methoxy-4*H*-1-benzopyran-4-one (3d): colorless solid (from AcOEt-hexane), mp 234-236 °C; IR (KBr) 3263, 3056, 1649, 1615, 1562, 1485 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 3.85 (3H, s, OMe), 7.07-7.12 (2H, m, Ar), 7.26-7.44 (2H, m, Ar), 7.43 (1H, d, *J* = 3.1 Hz, H-5), 7.47 (1H, dd, *J* = 9.2, 3.1 Hz, H-7), 7.74 (1H, d, *J* = 9.2 Hz, H-8), 8.98 (1H, s, H-2), 12.37 (1H, br s, NH); MS *m/z* 324 (M^+). *Anal*. Calcd for $C_{17}H_{12}N_2O_3S$: C, 62.95; H, 3.73; N, 8.64. Found: C, 62.93; H, 3.58; N, 8.59.

2-(2-Hydroxy-5-methoxybenzoyl)benzimidazo[2,1-*b*]thiazole (4d): pale yellow needles (from AcOEt-hexane), mp 229-231 °C; IR (KBr) 3447, 3086, 2949, 1634, 1570, 1487, 1447 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.86 (3H, s, OMe), 7.08 (1H, dd, *J* = 9.2 Hz, H-3'), 7.23 (1H, dd, *J* = 9.2. 3.1 Hz, H-4'), 7.35 (1H, ddd, *J* = 8.2, 7.3, 1.2 Hz, H-6 or -7), 7.41 (1H, d, *J* = 3.1 Hz, H-6'), 7.46 (1H, ddd, *J* = 8.2, 7.3, 1.2 Hz, H-6 or -7), 7.75 (1H, dd, *J* = 8.5, 1.2 Hz, H-5 or -8), 7.83 (1H, dd, *J* = 8.5, 1.2 Hz, H-5 or -8), 8.42 (1H, s, H-3), 10.58 (1H, s, OH); High-resolution MS *m/z* Calcd for $C_{17}H_{12}N_2O_3S$ (M^+); 324.0569, Found: 324.0575.

Isomeric reaction of 3a and 4a in MeOH. The compound (**3a**, 15 mg) was refluxed in MeOH (3 mL). After 8 h, the solvent was evaporated under reduced pressure to give a 6 : 1 mixture of **3a** and **4a**. The ratio of the two compounds was determined by ^{1}H-NMR analysis of the crude reaction mixture. When the compound (**4a**) was used as the substrate, the same result was obtained.

Isomeric reaction of 3a and 4a under basic conditions. A solution of **3a** (10 mg) and K_2CO_3 (10 mg) in DMF (2 mL) was stirred at rt. After being stirred for 1 h, water (10 mL) was added to the mixture and then extracted with ether (20 ml x 3). The ethereal layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give a 1 : 2.2 mixture of **3a** and **4a**. The ratio of the two compounds was determined by ^{1}H-NMR analysis of the crude reaction mixture. When the compound (**4a**) was used as the substrate, the same result was obtained.

5*H*-Benzimidazo[2',1':2,3]thiazolo[4,5-*b*]benzopyran-5-one (14): To a stirred solution of benzimidazo[2,1-*b*]thiazole (**4a**) (88 mg, 0.3 mmol) and DBU (182 mg, 1.2 mmol) in CH_2Cl_2 (3 mL) a solution of iodine (84 mg, 0.33 mmol) in CH_2Cl_2 (2 mL) was dropwise added over a 20 min period at 0 °C. After being stirred for 10 min, the reaction was quenched at the same temperature by adding saturated aqueous $Na_2S_2O_3$ (2 mL). The mixture was vigorously stirred for 5 min and allowed to warm to rt. The mixture was extracted with CH_2Cl_2 (20 mL x 3), the combined organic layers were dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (eluent: hexane-AcOEt = 3 : 1) to give **14** (81 mg, 92%), mp 280-282 °C (from AcOEt-hexane). IR (KBr) 3032, 1649, 1616, 1557, 1510, 1481, 1462 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.41 (1H, ddd, *J* = 7.9, 7.3, 1.0 Hz), 7.47 (1H, ddd, *J* = 7.9, 7.3, 1.0 Hz), 7.57 (1H, ddd, *J* = 7.9, 7.3, 1.0 Hz), 7.72 (1H, dd, *J* = 8.5, 1.0 Hz), 7.81 (1H, dd, *J* = 7.9, 1.0 Hz), 7.82 (1H, ddd, *J* = 8.5, 7.3, 1.5 Hz), 8.07 (1H, dd, *J* = 7.9, 1.0 Hz), 8.36 (1H, dd, *J* = 7.9, 1.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 104.78, 111.75, 117.67, 119.82, 122.76, 122.78, 125.57, 126.21, 126.55, 128.77, 134.04, 147.00, 148.35, 152.58, 153.61, 171.18; MS *m/z* 292 (M^+). *Anal*. Calcd for $C_{16}H_8N_2O_2S$: C, 65.74; H, 2.76; N, 9.58. Found: C, 65.68; H, 2.53; N, 9.47.

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