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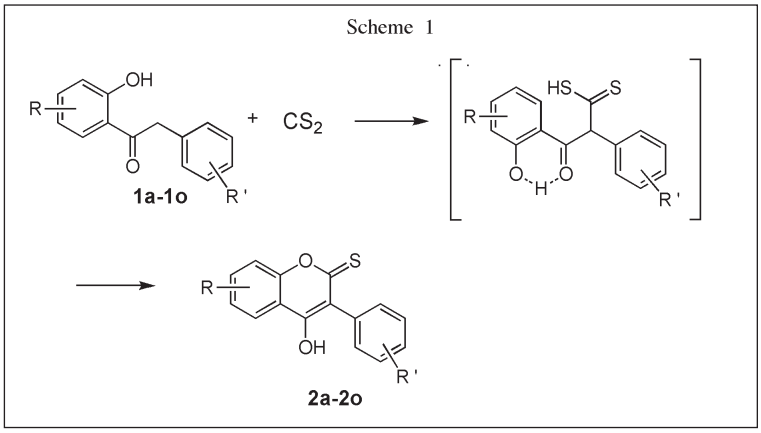
Scheme 1



A convenient and efficient method for the preparation of 3-aryl-chromene-2-thiones was reported. These compounds **2a-2o** with various functional groups were synthesized in high yield by a KF/Al_2O_3 meditated reaction of deoxybenzoins with CS_2 under mild conditions.

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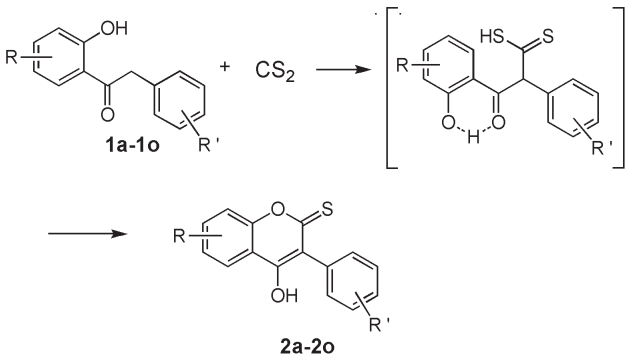
Isoflavones are widely found in a number of natural products. These natural products have demonstrated numerous biological activities such as antioxidant [1], anti-inflammatory [2], anticardiovascular, anticarcinogenic activities [3]. Aromatase inhibitory activities of isoflavone derivatives containing sulfur recently have been reported [4]. 3-Arylchromene-2-thiones are important intermediates which can be easily transformed to isoflavones. Pat *et al* reported the synthesis of chromene-2-thiones analogs by using KHMDS as a base [5]. However, this method requires skillful handling of the base, low temperature, and anhydrous reaction conditions. Recently, a high yielding one-pot synthesis of 2-(alkylthio)isoflavone has been reported using NaOH as a base and Bu_4NHSO_4 as a phase-transfer catalyst [6]. However the hydroxy group on the benzene ring needs to be protected first during the reactions.

In recent years, heterogeneous catalysts have been preferred for carrying out various chemical transformations due to environmental considerations. KF/Al_2O_3, taking the advantage of its strongly basic nature, has now replaced organic bases in a number of reactions [7]. We reported herein that KF/Al_2O_3 efficiently catalyzed the conversion of deoxybenzoins bearing unprotected hydroxy group on the benzene ring into 3-aryl-chromene-2-thiones.

The synthesis of 3-aryl-chromene-2-thiones is illustrated in Scheme 1.

In the presence of KF/Al_2O_3, the reactions of various deoxybenzoins **1a-1o** with CS_2 were carried out respectively to afford the corresponding products **2a-2o**

Scheme 1



Reagents and conditions:CS_2,KF/Al_2O_3,DMF,120 ^oC,3-5 h

(Table 1). The reactions were completed within 3-5 h and the yields of the products were high. The hydroxy group on the benzene ring did not need to be protected for these reactions. The catalyst was easily prepared [8] from the readily available KF and Al_2O_3. Because the reaction worked under heterogeneous conditions, the catalyst could be easily handled and removed from the reaction mixture by simple filtration, avoiding the complicated isolation and separation procedure. The target products could be obtained without further chromatography. When only KF was used as a catalyst, no products were obtained. It was found that when the deoxybenzoins bearing 2'-Cl substituted group (**2d**, **2j**), the reaction was somewhat sluggish

and incomplete. There was no product obtained when the 2' and 5' positions were substituted by methoxy groups.

Table 1

Yields and Melting Points of Compounds **2a-2o**

No.	R	R'	Yield (%)[a]	Mp(°C)
2a	4-OH	H	90 (0)[b]	142-144
2b	4-OH	4'-CH_3	86	133-135
2c	4-OH	4'-Cl	91	136-138
2d	4-OH	2'-Cl	66	128-130
2e	4-OH	4'-OCH_3	85	177-179
2f	4-OH	3'-OCH_3	86	77-78
2g	4-OH	3',4'-2OCH_3	87	229-231
2h	4-OCH_3	H	95	213-215
2i	4-OCH_3	4'-Cl	93	216-218
2j	4-OCH_3	2'-Cl	68	154-155
2k	2,4-2OCH_3	H	82	217-219
2l	2,4-2OCH_3	4'-Cl	89	165-166
2m	2,4-2OCH_3	4'-OCH_3	83	216-218
2n	2,4-2OCH_3	3',4'-2OCH_3	80	203-205
2o	2,4-2OCH_3	4'-CH_3	87	213-215

[a] Isolated yield; [b] without KF/Al_2O_3.

In conclusion, we have developed a simple and novel method for efficient conversion of deoxybenzoins into 3-aryl-chromene-2-thiones by using KF/Al_2O_3 as a heterogeneous catalyst. Based on our studies, this method offers several advantages including cheap starting materials, excellent yield, very facile purification and simple experimental procedure.

EXPERIMENTAL

Melting points are uncorrected. ^{1}HNMR spectra were recorded on a Brucker ADVANCE-400 MHz spectrometer with $SiMe_4$ as the internal standard. IR spectra were recorded on a Bruck Vector 200 spectrophotometer and microanalyses were performed on a MOD-1106 elemental analyzer.

General Procedure.

The mixture of deoxybenzoin (1.0 mmol), carbon disulfide (0.6 ml, 10 mmol), and KF/Al_2O_3 (2.0 mmol) was stirred in DMF (3.0 ml) at 120 °C for 3-5 hr. After cooling to room temperature, the reaction mixture was filtered with suction and the filtrate was poured into water (10 ml), and then extracted with ethyl acetate (10 ml). The aqueous layer was separated and acidified with hydrochloric acid until no further precipitate forms. The precipitated product was filtered with suction, washed thoroughly with water and dried.

4,6-Dihydro-3-phenylchromene-2-thione (**2a**).

Compound **2a**: IR (KBr, cm^{-1}): 3253, 1630, 1227, 1083; ^{1}H-NMR (400 MHz, DMSO, ppm) δ: 10.85 (s, 1H, -OH), 7.90 (d, J=9.2Hz, 1H, Ar-H), 7.22-7.40 (m, 5H, Ar-H), 6.90 (d, J=9.2Hz, 1H, Ar-H), 6.24 (s, 1H, Ar-H), 4.27 (brs, 1H, -OH).

Anal. Calcd. for $C_{15}H_{10}O_3S$: C 66.65, H 3.73; found: C 66.63, H 3.71.

4,6-Dihydro-3-*p*-tolylchromene-2-thione (**2b**).

Compound **2b**: IR (KBr, cm^{-1}): 3215, 1620, 1357, 1227, 1083, 847; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 10.99 (s, 1H, -OH), 7.97-7.99 (m, 1H, Ar-H), 7.19 (d, J=8Hz, 2H, Ar-H), 7.14 (d, J=8.0Hz, 2H, Ar-H), 6.94 (d, J=8.0Hz, 1H, Ar-H), 6.89 (s, 1H, Ar-H), 4.23 (brs, 1H, -OH), 2.35 (s, 3H, -CH_3).

Anal. Calcd. for $C_{16}H_{13}O_3S$: C 67.35, H 4.59; found: C 67.34, H 4.60.

3-(4-Chlorophenyl)-4,6-dihydroxychromene-2-thione (**2c**).

Compound **2c**: IR (KBr, cm^{-1}): 3209, 1621, 1217, 1064; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 10.92 (s, 1H, -OH), 7.91 (d, J=8.8Hz, 1H, Ar-H), 7.44 (d, J=8.4Hz, 2H, Ar-H), 7.30 (d, J=8.0Hz, 2H, Ar-H), 6.93 (dd, J=8.8Hz, 2.0Hz, 1H Ar-H), 6.84 (s, 1H, Ar-H), 4.22 (brs, 1H, -OH).

Anal. Calcd. for $C_{15}H_9ClO_3S$: C 59.12, H 2.98; found: C 59.10, H 2.97.

3-(2-Chlorophenyl)-4,6-dihydroxychromene-2-thione (**2d**).

Compound **2d**: IR (KBr, cm^{-1}): 3135, 1635, 1358, 1098, 835; ^{1}H-NMR (400 MHz, DMSO, ppm) δ: 10.93 (s, 1H, -OH), 7.94 (d, J=8.8Hz, 1H, Ar-H), 7.51-7.53 (m, 1H, Ar-H), 7.37-7.40 (m, 2H, Ar-H), 7.29-7.31 (m, 1H, Ar-H), 6.91-6.95 (m, 2H, Ar-H).

Anal. Calcd. for $C_{15}H_{10}ClO_3S$: C 58.92, H 3.30; found: C 58.90, H 3.32.

4,6-Dihydroxy-3-(4-methoxyphenyl)chromene-2-thione (**2e**).

Compound **2e**: IR (KBr, cm^{-1}): 3136, 1623, 1505, 1225, 842; ^{1}H-NMR (400 MHz, DMSO, ppm) δ: 10.81 (s, 1H, -OH), 7.87 (d, J=8.8Hz, 1H, Ar-H), 7.16 (d, J=8.0Hz, 2H, Ar-H), 6.93 (d, J=8.0Hz, 2H, Ar-H), 6.89 (dd, J=8.8Hz, 2.0Hz, 1H, Ar-H), 6.81 (s, 1H, Ar-H), 4.22 (brs, 1H, -OH), 3.78 (s, 3H, -OCH_3).

Anal. Calcd. for $C_{16}H_{12}O_4S$: C 63.99, H 4.03; found: C 63.96, H 4.01.

4,6-Dihydroxy-3-(3-methoxyphenyl)chromene-2-thione (**2f**).

Compound **2f**: IR (KBr, cm^{-1}): 3143, 1602, 1362, 1263, 1093, 761; ^{1}H-NMR (400 MHz, DMSO, ppm) δ: 10.88 (s, 1H, -OH), 7.89 (d, J=8.8Hz, 1H, Ar-H), 7.32 (t, J=4.0Hz, 1H, Ar-H), 6.91-6.93 (m, 2H, Ar-H), 6.74-6.75 (m, 3H, Ar-H), 3.74 (s, 3H, -OCH_3).

Anal. Calcd. for $C_{16}H_{12}O_4S$: C 63.99, H 4.03. found: C 63.97, H 4.02.

4,6-Dihydroxy-3-(3,4-dimethoxyphenyl)chromene-2-thione (**2g**).

Compound **2g**: IR (KBr, cm^{-1}): 3226, 1629, 1517, 1251, 1081, 843; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 10.82 (s, 1H, -OH), 7.85 (d, J=8.8Hz, 1H, Ar-H), 6.96 (d, J=8.8Hz, 1H, Ar-H), 6.89 (dd, J=8.8Hz, 2.0Hz, 1H, Ar-H), 6.84 (s, 1H, Ar-H), 6.82 (s, 1H, Ar-H), 4.46 (brs, 1H, -OH), 3.77 (s, 3H, -OCH_3), 3.70 (s, 3H, -OCH_3).

Anal. Calcd. for $C_{17}H_{14}O_5S$: C 61.81, H 4.27; found: C 61.79, H 4.26.

4-Hydroxy-6-methoxy-3-phenylchromene-2-thione (**2h**).

Compound **2h**: IR (KBr, cm^{-1}): 3164, 1628, 1380, 1298, 971, 845; ^{1}H-NMR (400 MHz, DMSO, ppm) δ: 7.46-7.48 (m, 2H, Ar-H), 7.36-7.40 (m, 3H, Ar-H), 6.73 (d, J=2.0Hz, 1H, Ar-H), 6.43 (d, J=2.0Hz, 1H, Ar-H), 4.32 (brs, 1H, -OH), 3.87(s, 3H, -OCH_3).

Anal. Calcd. for $C_{17}H_{14}O_3S$: C 68.44, H 4.73; found: C 68.41, H 4.70.

4-Hydroxy-6-methoxy-3-(4-chlorophenyl)chromene-2-thione (**2i**).

Compound **2i**: IR (KBr, cm^{-1}): 3101, 1626, 1341, 1270, 1090, 821; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 7.94 (d, J=8.8Hz, 1H, Ar-H), 7.39 (d, J=8.8Hz, 2H, Ar-H), 7.26 (d, J=8.4Hz, 2H, Ar-H), 7.08 (d, J=2.4Hz, 1H, Ar-H), 7.03 (dd, J=8.8Hz, 2.0Hz, 1H, Ar-H), 5.23 (brs, 1H, -OH), 3.87 (s, 3H, $-OCH_3$).

Anal. Calcd. for $C_{16}H_{11}ClO_3S$: C 60.28, H 3.48; found: C 60.26, H 3.45.

4-Hydroxy-6-methoxy-3-(2-chlorophenyl)chromene-2-thione (**2j**).

Compound **2j**: IR (KBr, cm^{-1}): 3146, 1632, 1227, 1073, 854; ^{1}H-NMR (400 MHz, DMSO, ppm) δ: 7.98 (d, J=8.8Hz, 1H, -OH), 7.50-7.52 (m, 1H, Ar-H), 7.37-7.39 (m, 2H, Ar-H), 7.29-7.32 (m, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 7.07 (dd, J=8.8Hz, 2.0Hz, 1H, Ar-H), 3.91 (s, 3H, $-OCH_3$).

Anal. Calcd. for $C_{16}H_{11}ClO_3S$: C 60.28, H 3.48; found: C 60.27, H 3.46.

4-Hydroxy-6,8-dimethoxy-3-phenylchromene-2-thione (**2k**).

Compound **2k**: IR (KBr, cm^{-1}): 3264, 1628, 1380, 1298, 1157, 971; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 9.65 (s, 1H, -OH), 7.44-7.48 (m, 2H, Ar-H), 7.38-7.40 (m, 3H, Ar-H), 6.74 (s, 1H, Ar-H), 6.44 (s, 1H, Ar-H), 4.04 (s, 3H, $-OCH_3$), 3.91 (s, 3H, $-OCH_3$).

Anal. Calcd. for $C_{17}H_{14}O_4S$: C 64.95, H 4.49; found: C 64.93, H 4.47.

4-Hydroxy-6,8-dimethoxy-3-(4-chlorophenyl)chromene-2-thione (**2l**).

Compound **2l**: IR (KBr, cm^{-1}): 3289, 1610, 1291, 1097, 826; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 9.69 (s, 1H, -OH), 7.41-7.45 (m, 2H, Ar-H), 7.31-7.35 (m, 2H, Ar-H), 6.73 (s, 1H, Ar-H), 6.44 (s, 1H, Ar-H), 4.06 (s, 3H, $-OCH_3$), 3.92 (s, 3H, $-OCH_3$).

Anal. Calcd. for $C_{17}H_{13}ClO_4S$: C 58.54, H 3.76; found: C 58.52, H 3.78.

4-Hydroxy-6,8-dimethoxy-3-(4-methoxyphenyl)chromene-2-thione (**2m**).

Compound **2m**: IR (KBr, cm^{-1}): 3287, 1608, 1287, 1041, 818 ; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 10.1 (s, 1H, -OH), 7.05-7.08 (m, 2H, Ar-H), 6.80-6.82 (m, 2H, Ar-H), 6.74 (d, J=2.0Hz, 1H, Ar-H), 6.54 (d, J=1.6Hz, 1H, Ar-H), 3.85(s, 3H, $-OCH_3$), 3.79(s, 3H, $-OCH_3$), 3.67(s, 3H, $-OCH_3$).

Anal. Calcd. for $C_{18}H_{16}O_5S$: C 62.78, H 4.68; found: C 62.75, H 4.66.

4-Hydroxy-6,8-dimethoxy-3-(3,4-dimethoxyphenyl)chromene-2-thione (**2n**).

Compound **2n**: IR (KBr, cm^{-1}): 3282, 1630, 1294, 1121, 1051; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 10.38 (s, 1H, -OH), 6.98 (d, J=8.4Hz, 1H, Ar-H), 6.90 (d, J=2.4Hz, 2H, Ar-H), 6.83 (dd, J=8Hz, 1.6Hz, 1H, Ar-H), 6.7(d, J=2.0Hz, 1H, Ar-H), 4.02 (s, 3H, $-OCH_3$), 3.96 (s, 3H, $-OCH_3$), 3.82 (s, 3H, $-OCH_3$), 3.74 (s, 3H, $-OCH_3$).

Anal. Calcd. for $C_{19}H_{18}O_6S$: C 60.95, H 4.85; found: C 60.93, H 4.84.

4-Hydroxy-6,8-dimethoxy-3-*p*-tolylchromene-2-thione (**2o**).

Compound **2o**: IR (KBr, cm^{-1}): 3272, 1611, 1293, 1131, 824; ^{1}H-NMR (400MHz, DMSO, ppm) δ: 10.3 (s, 1H, -OH), 7.11-7.17 (m, 4H, Ar-H), 6.84 (s, 1H, Ar-H), 6.63 (s, 1H, Ar-H), 3.96 (s, 3H, $-OCH_3$), 3.89 (s, 3H, $-OCH_3$), 2.31 (s, 3H, Ar-CH_3).

Anal. Calcd. for $C_{18}H_{16}O_4S$: C 65.84, H 4.91; found: C 65.82, H 4.90.

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