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ONE-POT SYNTHESIS OF 3-ARYL-3*H*,4*H*-[1,2]-DI-THIOLO[3,4-*b*]BENZOTHIOPYRAN-4-ONES AND 1-(*o*-BROMO-PHENYL)-3-ARYL-2-PROP-2-EN-1-ONES

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Abstract – 3-Aryl-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-ones were prepared by the reaction of 1 equiv. of 2'-bromoacetophenone with 3.5 equiv. of potassium *O*-ethyl xanthate and 1 equiv. of an appropriate aromatic or heteroaromatic aldehyde. The yields of the thiopyran-4-ones are high. The key step of the reaction appears to be the conversion of the aldehyde to the corresponding thioaldehyde by the xanthate. The thioaldehyde is subsequently trapped by the anion of 2-thioxothiochroman-4-one intermediate. The intermediacy of thioaldehydes was confirmed by treating aldehydes with potassium ethyl xanthate in the absence of 2'-bromo ketones. Additionally, chalcones were readily prepared by the condensation of 2'-bromo ketones with appropriate aldehydes in the presence of potassium *O*-ethyl xanthate.

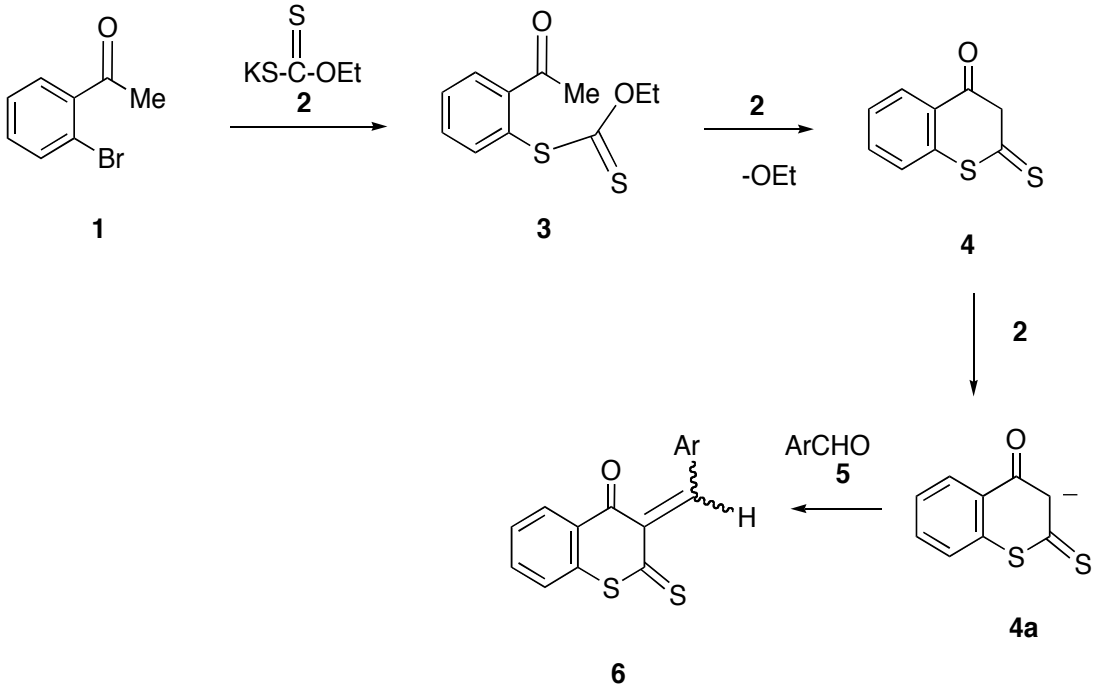
INTRODUCTION

In the family of heterocyclic compounds, sulfur heterocycles are next in importance to nitrogen heterocycles for their manifold biological and pharmacological activities.[1-3] As a result of this general and efficient methods for their preparation are continually being developed.[4,5] For the past several years our group has been concerned in preparing new heterocycles *via* benzyne either by benzyne ring closure reaction[6] or Diels-Alder cycloaddition of benzyne with different dienes viz. thiones,[7] selenoureas,[8] furans,[9] etc. With this in mind, we initiated a research program with the goal of preparing sulfur containing heterocycles. From this study we have developed a facile, high-yield synthesis of 4*H*-1,3-thiones,[7] 1,2-isothiazoles,[8] benzothiopyrano[2,3-*b*]indoles,[8] 4*H*-naphtho[2,3-*e*] derivatives of 1,3-thiazines[8] by a [4+2] cycloaddition reaction in which alkylidin-1-yl-3-benzo[*b*]thiazine-2-ones, alkylidin-1-yl-3-benzo[*b*]indole-2-thiones and thiaazadienes serve as dienes and benzynes or acetylenes behave as

dienophiles. As an extension of our previous work, we became interested preparing a series of new dienes containing a thiochromone moiety, *i.e.,* 2-arylidene-2-thioxothiochroman-4-ones. During this study, we unexpectedly uncovered a hitherto unreported one-pot synthesis of novel heterocycle 3-aryl-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-ones. This work has provided a new method for the regiospecific construction of heteroaromatic building blocks containing a thiochromone moiety, which is found in a large number of molecules of medicinal significance.[10,11]

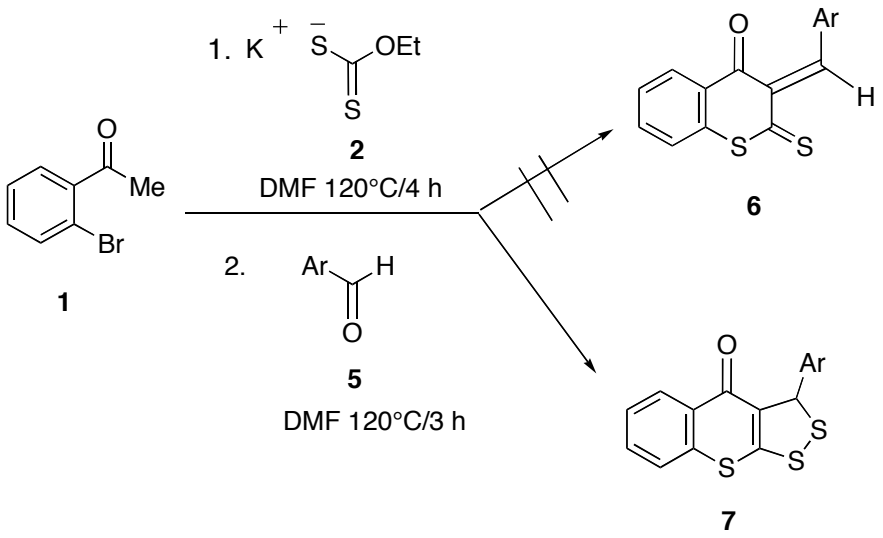
RESULTS AND DISCUSSION

Until recently, potassium ethyl xanthate has not been used extensively in anionic sulfur nucleophilic substitution reactions.[12,13] Thus, we were intrigued by a recent report[14] on *ortho*-selective nucleophilic substitution of 2-haloanilines with potassium/sodium *O*-ethyl xanthate. In that study, 2-haloanilines underwent smooth nucleophilic substitution reactions with *O*-ethyl xanthate. The resulting adduct then underwent facile cyclization by the addition of the1-amino group onto the C=S moiety with the concomitant lose of ethyl alcohol to give 2-(3*H*)-benzothiazolethiones. It occurred to us that the reaction of 2'-bromoacetophenone (**1**) with potassium *O*-ethyl xanthate (**2**) might proceed similarly. We postulated, as shown in Scheme 1, that the xanthate (**2**) would displace the 2'-bromo group of **1** by the usual aromatic nucleophilic substitution pathway yielding adduct (**3**). Deprotonation of the COMe hydrogen by **2** would then afford an enolate by adding to the C=S group would yield 2-thioxothio- chromen-4-one (**4**). By using an excess of **2**, **4** might be deprotonated to give the anion (**4a**) which would subsequently condense with an aldehyde (**5**) to give the desired product (**6**).



Scheme 1 Original postulate for the course of the reaction of **1**, **2**, and **5** to give **6**.

However, as shown in Scheme 2, when we carried out the reaction of **1** with 3.5 equiv. of **2** at 120 °C for



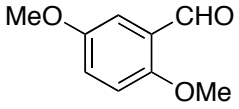
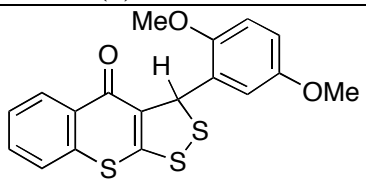
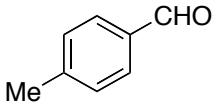
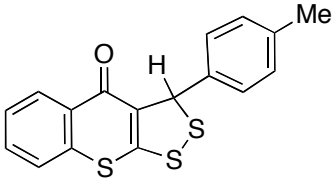
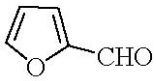
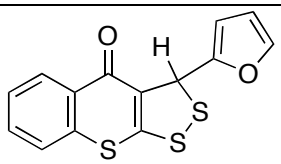
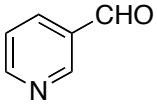
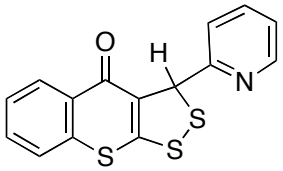
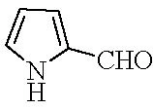
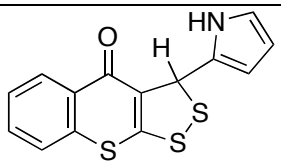
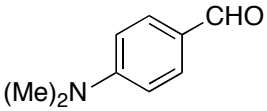
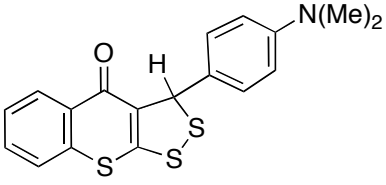
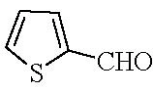
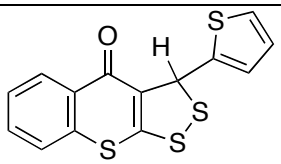
Scheme 2

4 h followed by dropwise addition of aldehyde (**5**) and additional stirring for 3 h, the hitherto unreported products, *i.e*. 3-aryl-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-ones (**7a–g**) were obtained in 42-94% yields; the expected products (**6**) were not observed. The results are listed in Table 1. The compounds (**7a–g**) were identified on the basis of ^{1}H NMR, ^{13}C NMR spectrum, and elemental analysis. Apparently, the aldehydes (**5a–g**) are converted to the corresponding thioaldehydes (**8a–g**) under the basic condition of these reactions. To confirm this, 1.5 equiv. of both the aldehydes (**5**) and **2** were subjected to similar reaction conditions and found, indeed, to give the thioaldehydes (**8**) as determined by GC/MS spectroscopy. Unfortunately, the thioaldehydes could not be fully characterized due to their instability. Such behavior has been fully documented in the chemical literature, and in fact, the characterization of thioaldehydes is usually indirectly accomplished by trapping them with typical Diels-Alder dienophiles, such as cyclopentadiene,[15] or by preparing α,β-unsaturated thioaldehydes, *in situ*, which undergo [4+2] self-dimerization to various dithiin products.[16] From the nature of the dithiolo products formed in this study it is likely that thioaldehydes (**8**) were formed *in situ* and subsequently trapped by the anionic intermediate (**4a**). Thioaldehydes have been recently prepared by the reaction of aldehydes formed *in situ* with bis(dimethylaluminum) disulfide[16] or bis(trimethylsilyl) disulfide in the presence of a catalytic amount of BuLi.[15] However, the use of potassium *O*-ethyl xanthate (**2**) in the synthesis of thioaldehydes in this study is unprecedented.

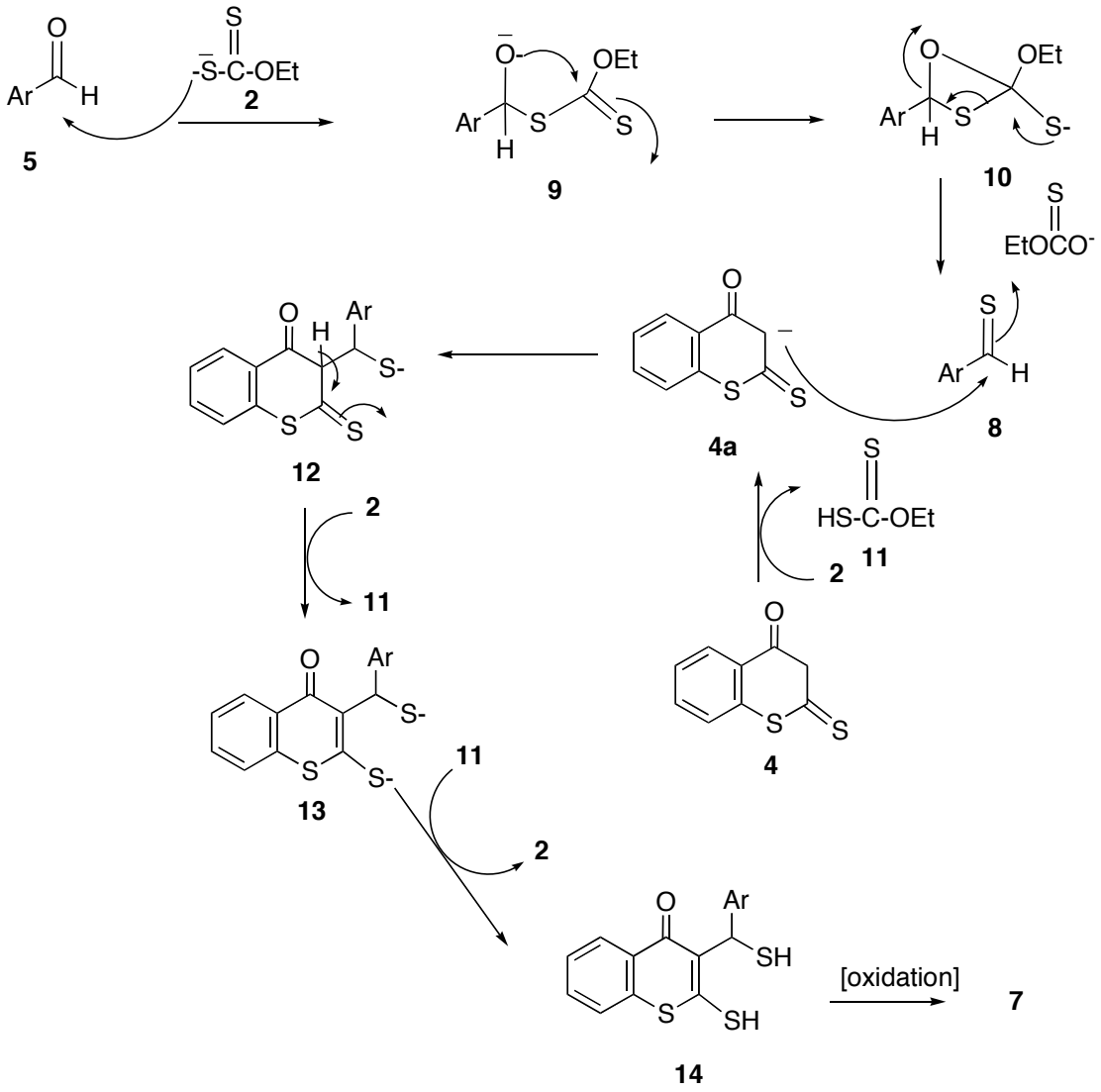
Scheme 3 presents a possible reaction path for the synthesis of titled compounds (**7a–g**). Before the addition of the aldehyde (**5**), the anionic intermediate (**4a**) is probably synthesized according to Scheme 1. Upon the addition of the aldehyde, the adduct (**9**) is obtained which undergoes intramolecular addition of the oxygen anion onto the C=S group to give the cyclic compound (**10**) from which $EtOC(=S)O^{-}$ is

eliminated to give the thioaldehyde (**8**). The anionic species (**4a**) is then formed by the reaction of **2** and **4** with the liberation of xanthic acid (**11**), which condenses with **8** to give adduct (**12**). Adduct (**12**) then

Table 1 Yields of Products (7a–g)

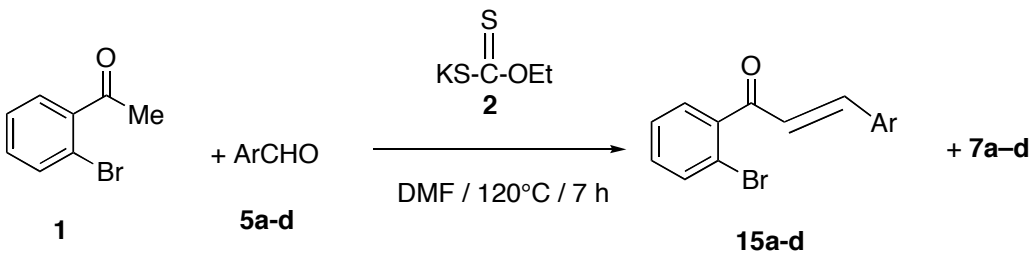
Entry	Aldehyde (**5**)	Product (**7**)	Yield, %
1	 **5a**	 **7a**	94
2	 **5b**	 **7b**	88
3	 **5c**	 **7c**	84
4	 **5d**	 **7d**	42
5	 **5e**	 **7e**	51
6	 **5f**	 **7f**	60
7	 **5g**	 **7g**	78

is converted to the thiolate dianion (**13**) by **2**. Diprotonated of **13** by **11** then gives the 1,3-dithiol (**14**) species, which under the basic conditions of the reaction oxidizes to the observed product (**7**). 1,3-Dithiols are known to form disulfide bonds under basic condition.[17]



Scheme 3

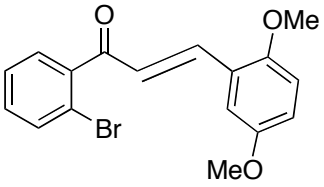
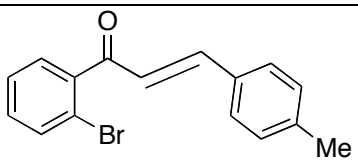
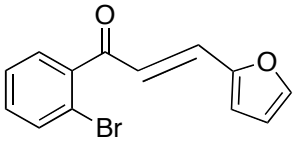
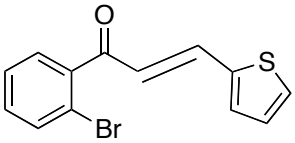
In a separate reaction, shown in Scheme 4, the three reagents, *i.e*. 2'-bromoacetophenone (**1**), potassium *O*-ethyl xanthate (**2**), and an aldehyde (**5**) were mixed together at room temperature then heated to 120 °C



Scheme 4

and stirred an additional 7 h. As shown in Table 2, simple aldol-type condensation products (**15a-d**) with the

Table 2

Entry	Aldehyde	Products	Yields, % **15:7**
1	**5a**	 + **7a** **15a**	91:8
2	**5b**	 + **7b** **15b**	95:5
3	**5c**	 + **7c** **15c**	91:5
4	**5d**	 + **7d** **15d**	91:5

(*E*) configuration were predominantly formed (91–95%) with only minor amounts (5–8%) of **7** were detected. The structures were confirmed by ^{1}H NMR (J = 13-15Hz, *trans*), ^{13}C NMR spectrum, and elemental analysis.

Under these conditions, thioaldehydes (**8**) were formed in very low yields. It is conceivable that in presence of potassium *O*-ethyl xanthate (**2**), the keto methyl group of 2'-bromoacetophenone (**1**) is converted to a enolate carbanion which attacks the highly active aldehyde already present in the medium at a much faster rate than the aromatic nucleophilic substitution reaction. Nonetheless, this reaction provides a new route to these types of α,β–unsaturated ketones (**15**), commonly known as chalcones, which may have biological significance.[18,19]

CONCLUSION

We have presented a hitherto unreported one-pot synthesis of novel 3-aryl-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]-benzothiopyran-4-ones which should provide new opportunities for regiospecific construction of aromatic building blocks from readily available starting materials. Furthermore, we have found a new way of preparing thioaldehydes by treatment with the corresponding aldehydes with potassium xanthate.

EXPERIMENTAL

General Data: Melting points were taken on a Mel-Temp capillary apparatus and are uncorrected with respect to stem correction. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz Bruker ADVANCE DRX-400 Multinuclear NMR spectrometer. Chemical shifts are reported in reference to TMS as internal standard. Elemental analysis were obtained from SMU Analytical Service Laboratories

Preparation of 3-Aryl-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-ones.

General procedure: 2'-Bromoacetophenone (**1**) (2 g, 10.1 mmol) and potassium *O*-ethyl xanthate (**2**) (4.8 g, 29.9 mmol) were taken in a two neck round bottom flask and refluxed in anhydrous DMF (20 mL) at 120 °C for 4 h under argon atmosphere. Next 2,5-dimethoxybenzaldehyde (**5a**) (2.5 g, 15.0 mmol) in anhydrous DMF (7 mL) was added slowly to the reaction mixture through dropping funnel over 45 min. After complete addition of the aldehyde, the reaction mixture stirred at 120 °C for another 3 h. After cooling, it was diluted with ice-cold water and neutralized with 1N HCl solution. Then the reaction mixture was extracted with ethyl acetate, washed thoroughly with water and dried over anhydrous Na_2SO_4. Purification was done through column chromatography over silica gel using 5% ethyl acetate-hexane as eluant.

3-(2,5-Dimethoxyphenyl)-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-one (**7a**).

Separated as a crystalline yellowish solid, mp 172–174 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 3.65 (s, 3H, -OMe), 3.91 (s, 3H, -OMe), 6.50 (s, 1H, aliphatic proton), 6.59 (d, *J*=1.9 Hz, 1H, aromatic), 6.77 (d, *J* = 8.0 Hz, 1H, aromatic), 6.87 (dd, *J* = 1.9 Hz, 8.0 Hz, 1H, aromatic), 7.50–7.59 (m, 3H, aromatic), 8.42 (dd, *J* = 2.2 Hz, 7.4 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$): δ 55.6, 55.9, 56.5, 111.89, 112.5, 114.3, 126.1, 128.3, 128.6, 129.6, 130.8, 132.1, 133.0, 136.0, 150.5, 153.7, 155.7, 175.4. Anal. Calcd for $C_{18}H_{14}O_3S_3$: C, 57.73; H, 3.77. Found: C, 57.58; H, 3.73.

3-(*p*-Methylphenyl)-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-one (**7b**).

Separated as a light yellow crystalline solid, mp 161–163 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 2.32 (s, 3H, $-CH_3$), 6.30 (s, 1H, aliphatic proton), 7.13 (d, *J* = 8.0 Hz, 2H, aromatic), 7.35 (d, *J* = 8.0 Hz, 2H, aromatic), 7.49–7.62 (m, 3H, aromatic), 8.43 (d, *J* = 8.0 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$): δ 21.6, 62.5, 126.1, 127.0, 128.3, 129.6, 129.9, 130.9, 132.0, 134.5, 135.9, 137.7, 138.6, 153.8, 175.6. Anal Calcd for $C_{17}H_{12}OS_3$: C, 62.16; H, 3.68. Found: C, 62.27; H, 3.64.

3-(Furan-2-yl)-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-one (7c).

Separated as yellow needles, mp 180–182 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 6.17 (d, *J*=4.0 Hz, 1H, aromatic), 6.30 (s, 1H, aliphatic proton), 6.38 (d, J = 4.0 Hz, 1H, aromatic), 7.41 (s, 1H, aromatic), 7.53–7.65 (m, 3H, aromatic), 8.48 (d, 1H, *J* = 8.0 Hz, aromatic). ^{13}C NMR ($CDCl_3$): δ 55.35, 108.15, 111.19, 126.18, 128.44, 129.71, 130.9, 131.8, 132.2, 135.8, 143.3, 151.1, 155.2, 175.5. Anal. Calcd for $C_{14}H_8O_2S_3$: C, 55.24; H, 2.65. Found: C, 55.27; H, 2.65.

3-(Pyridin-2-yl)-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-one (7d).

Separated as yellow crystals, mp 173–175 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 6.58 (s, 1H, aliphatic proton), 6.92 (d, *J* = 4.8 Hz, 1H, aromatic), 7.14 (s, 1H, aromatic), 7.21(d, *J* = 4.8 Hz, 1H, aromatic), 7.51–7.63 (m, 3H, aromatic), 8.47 (dd, *J* = 2.5 Hz, 8.0 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$): δ 57.5, 125.8, 126.2, 127.2, 127.3, 128.4, 129.7, 130.9, 132.1, 134.7, 135.8, 142.9, 153.8, 175.3. Anal. Calcd for $C_{15}H_9NOS_3$: C, 57.12; H, 2.88. Found: C, 57.18; H, 2.76.

3-(1*H*-Pyrrol-2-yl)-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-one (7e).

Separated as a brown solid, mp 178–180 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 6.05 (s, 1H, aliphatic proton), 6.13 (d, *J* = 6.5 Hz, 1H, aromatic), 6.31 (s, 1H, aromatic), 7.12–7.37 (m, 4H, aromatic). 8.01 (d, *J* = 8.0 Hz, 1H, aromatic), 8.5 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$): δ 46.3, 106.9, 107.4, 117.5, 125.8, 126.0, 129.8, 130.3, 130.5, 133.6, 134.5. 178.1 Anal. Calcd for $C_{14}H_9NOS_3$: C, 55.42; H, 2.99. Found: C, 55.48; H, 2.95.

3-(4-*N*,*N*-Dimethylaminophenyl)-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-one (7f).

Separated as a red solid, mp 182–183 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$) δ 2.99 (s, 6H, Me_2N), 4.56 (s, 1H, aliphatic proton), 6.59 (d, *J* =8.0 Hz, 2H, aromatic), 6.71 (d, *J* = 8.0 Hz, 2H, aromatic), 7.20-–7.30 (m, 3H, aromatic), 8.15 (dd, *J* = 8.0 Hz, 2.3 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$) δ 43.0, 46.2, 114.0, 114.1, 126.0, 126.3, 128.7, 128.9, 129.5, 130.5, 131.0, 133.5, 134.6, 137.3, 138.8, 141.9, 175.3. Anal. Calcd for $C_{18}H_{15}NOS_3$: C, 60.47; H, 4.23. Found: C, 60.50; H, 4.35.

3-(Thiophene-2-yl)-3*H*,4*H*-[1,2]dithiolo[3,4-*b*]benzothiopyran-4-one (7g).

Separated as a light yellow solid material, mp 230–232 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 5.62 (s, 1H, aliphatic proton), 7.21–7.30 (m, 2H, aromatic), 7.54–7.60 (m, 4H, aromatic), 7.68 (d, *J* =7.0 Hz, 1H, Aromatic), 8.26 (dd, *J* = 7.7 Hz, 2.1 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$): δ 46.9, 121.9, 125.3, 126.0, 129.0, 130.0, 132.5, 133.8, 134.2, 135.3, 137.2, 139.2, 146.2, 151.2, 178.0. Anal. Calcd for $C_{14}H_8OS_4$: C, 52.47; H, 2.52. Found: C, 52.50; H, 2.47.

General Procedure For The Preparation of 3-Aryl-1-(*o*-bromophenyl)prop-2-en-1-ones (15a-d)

2'-Bromoacetophenone (**1**) (1 g, 5.02 mmol), potassium *O*-ethyl xanthate (**2**) (2.4 g, 15.1 mmol) and appropriate aldehyde (**5a-d**) (1.2 equiv, 6.02 mmol) were dissolved in dry DMF (10 mL) and the resulting

mixture was heated at 120 °C for 7 h under argon atmosphere. Upon cooling, the reaction mixture was diluted with ice-cold water and neutralized with 1N HCl. The diluted reaction mixture was extracted with ethyl acetate, washed thoroughly with water for several times, then dried over anhydrous Na_2SO_4. After the removal of solvent (in *vacuo*), the remaining residue was purified by column chromatography over silica gel using ethyl acetate-hexane (2:98,v/v) as eluent. The physical and spectral properties of **15a–d** are given below.

(*E*)-1-(*o*-Bromophenyl)-3-(2, 5-dimethoxyphenyl)prop-2-en-1-one (**15a**).

Separated as yellow needles, mp 106–107 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 3.80 (s, 3H, -OMe), 3.81 (s, 3H, -OMe), 6.85 (d, *J*=8.0 Hz, 1H, aromatic), 6.95 (dd, *J* = 2.8, 8.0 Hz, 1H, aromatic), 7.10 (d, *J* = 2.8 Hz, 1H, aromatic), 7.17 (d, *J* = 16.2 Hz, 1H, -CH), 7.41–7.43 (m, 3H, aromatic), 7.65 (d, *J* = 7.7 Hz, 1H, aromatic), 7.76 (d, *J* = 16.2 Hz, 1H, -CH). ^{13}C NMR ($CDCl_3$): δ 56.2, 56.5, 112.9, 113.7, 118.48, 119.9, 124.3, 127.1, 127.6, 129.6, 131.6, 133.8, 141.7, 142.2, 153.6, 153.9, 195.5. Anal. Calcd for $C_{17}H_{15}O_3Br$: C, 58.78; H, 4.32. Found: C, 58.84; H, 4.38 %.

(*E*)-1-(*o*-Bromophenyl)-3-(4-methylphenyl)prop-2-en-1-one (15b).

Separated as a thick viscous oil. ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 3H, -Me), 7.07 (d, *J* = 16.0 Hz, 1H, -CH), 7.22 (d, *J*=8.0 Hz, 1H, aromatic), 7.40-7.48 (m, 7H, aromatic, -CH), 7.66 (d, *J* = 8.0 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$): δ 21.9, 119.9, 120.0, 125.6, 127.7, 129.0, 129.5, 130.1, 131.0, 131.6, 132.0, 133.8,141.6, 142.0, 147.2, 195.2. Anal. Calcd for $C_{16}H_{13}OBr$: C, 63.81; H, 4.35. Found: C, 63.88 ; H, 4.40 .

(*E*)-1-(*o*-Bromophenyl)-3-(furan-2-yl)prop-2-en-1-one (15c).

Separated as a yellow oil. ^{1}H NMR ($CDCl_3$): δ 6.71 (s, 1H, aromatic), 6.99 (d, *J* = 16.0 Hz, 1H, -CH), 7.13 (s, 1H, aromatic), 7.20 (s, 1H, aromatic), 7.35-7.41 (m, 3H, aromatic), 7.52 (d, *J* = 16.0 Hz, 1H, -CH), 7.65 (d, *J* = 8.0, 1H, aromatic). ^{13}C NMR ($CDCl_3$): δ 109.3, 113.2, 123.9, 127.7, 129.4, 131.7, 132.6, 133.8, 141.5, 144.4, 145.3, 151.4, 194.5. Anal. Calcd for $C_{13}H_9O_2Br$: C, 56.34; H, 3.27. Found: C, 56.36 ; H, 3.37.

(*E*)-1-(*o*-Bromophenyl)-3-(thiophene-2-yl)prop-2-en-1-one (15d).

Separated as a red solid, mp 30–31 °C (ethyl acetate-hexane). ^{1}H NMR ($CDCl_3$): δ 6.90 (d, *J* = 15.8 Hz, 1H, -CH), 7.08 (s, 1H, aromatic), 7.30–7.35 (m, 2H, aromatic), 7.42–7.46 (m, 3H, aromatic), 7.56 (d, *J* = 15.8 Hz, -CH), 7.65 (d, *J* = 7.9 Hz, 1H, aromatic). ^{13}C NMR ($CDCl_3$): δ 119.9, 125.3, 127.7, 128.8, 129.5, 130.2, 131.8, 132.7, 133.8, 139.2, 140.2, 141.4, 194.4. Anal. Calcd for $C_{13}H_9OBrS$: C, 53.24; H, 3.07. Found: C, 53.29; H, 3.11.

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REFERENCES

1. S. Kamila, C. Mukerjee, and A. De, *Tetrahedron Lett*., 2001, **42**, 5955.
2. S. Kamila, C. Mukherjee, S. Mondal, and A. De, *Tetrahedron*, 2003, **59**, 13393.
3. T. Misra, S. Kamila, C. Basu, T. Ganguly, and A. De, *Spectrochimica Acta Part A*, 2001, **57**, 2795.
4. C. Mukherjee and A. De, *Synlett*, 2002, **2**, 325.
5. C. Mukherjee, S. Kamila, and A. De, *Synth. Lett*., 2003, **10**, 1474.
6. C. Mukherjee and E. R. Biehl, *Heterocycles,* 2004, **63**, 2309.
7. S. Kamila and E. R. Biehl, *Heterocycles*, 2004, **63**, 2785.
8. U. N. Rao, R. Sathunuru, and E, Biehl, *Heterocycles*, 2004, **63**, 1067.
9. U. N. Rao, J. Maguire, and E. Biehl, *Arkivoc*, 2004, 88.
10. P. M. Dewick, '*The Flavanoids Advances in Research Since 1986',* ed. by J. B. Harborne, Chapmann Hall , New York, 1994.
11. A. E. Jakobs and Christiaens, *J. Org. Chem*., 1996, **61**, 4842.
12. F. E. Scully, Jr. and T. J. Ortega, *J. Org. Chem.,* 1989, **54**, 2978.
13. X. Creary, *Tetrahedron Lett.,* 1999, **40**, 29.
14. L. Zhu and M. Zhang, *J. Org. Chem.,* 2004, **69**, 7371.
15. S. Murai, T. Nakajima, and S. Suga, *J. Am. Chem. Soc.,* 1988, **110**, 197.
16. M. Li, S. Niu, M. Segi, K. Tanaka, T. Nakajima, R. A. Zingaro, J. H. Reibenspies, and M. B. Hall, *J. Org. Chem*., 2000, **65**, 6601.
17. A. Cihan and S. Uysal, *Synth. React. Inorg. Met.-Org. Chem*., 2004, **34**, 1825.
18. A. R. Jeffrey, R. B. Sulsky, and D. R. Magnin, '*Heterocyclylbiphenyl aP2 inhibitors'***,** PCT Int. Appl. 2000.
19. R. Goodman, D. G. Jones, J. S. Kerr, L. R. Mantegna, C. McAllister, R. C. Newton, S. Nurnberg, P. K. Welch, and M. B. Covington, *J. Med. Chem.,* 1993, **36**, 1434.