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CuI-catalyzed thioarylation of active methylene compounds with in situ generated benzenethiols: Preparation of α -thioaryl- β -dicarbonyls and 4-thioaryl-5-pyrazolones

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ABSTRACT

In this paper, a one-step copper-catalyzed procedure for oxidative coupling of active methylene compounds including cyclic β -diketones, cyclic β -ketoesters and 5-pyrazolone with benzenethiols is described. Benzenethiols are in situ generated in the reaction mixture from aryl halides and thiourea as sulfur transfer reagent. α -Thioaryl compounds are obtained in excellent yields and in short reaction time via the process which is free from the foul smell of thiols.

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1. Introduction

Sulfur functionalities are important building blocks in organic synthesis. They are important industrial compounds used in the agrochemicals, pharmaceutical and cosmetic industries as well as in the manufacture of polymers [1]. Among them, α -thioaryl- β -dicarbonyl compounds are extremely useful intermediates for the synthesis of heterocyclic compounds and pharmaceutical products [2]. For the formation of C–S bond between ketones and thiophenols, one of them need to be transformed to the corresponding electrophiles. Thus, traditional synthetic routes for preparation of these compounds can be divided into two categories: the nucleophilic substitution of α -halogenated ketones with thiophenols or disulfides [3] and the reaction of enolates with various sulfonylating reagents, such as sulfenamides [4], thiosulfonates [5], sulfuryl chloride [6], sulphenyl halides [7] and disulfides [8]. Since most electrophiles are directly or indirectly prepared from their corresponding nucleophiles, recently, efforts have been devoted toward the oxidative coupling between two nucleophiles. In this way, Tan et al. reported a new route to thioethers by reacting the sulfur

nucleophiles with active methylene compounds in the presence of carbon tetrabromide [9]. Also, the iodine-catalyzed oxidative coupling between 1,3-diketones and thiophenols to afford β -dicarbonyl thioethers was recently described by Hu and co-workers [10].

Despite extensive efforts in the sulfonylation of indole [11] and imidazole [12] derivatives, less attention to date has been paid to the sulfonylation of dicarbonyl compounds.

In continuation of our research on C–S coupling reactions [13], herein, we report a novel method for odourless thioarylation of β -diketones and pyrazolones from aryl halides in the presence of sulfur transfer reagent. To our knowledge, there are no report describing the sulfonylation of active methylene compounds using aryl halides.

2. Results and discussion

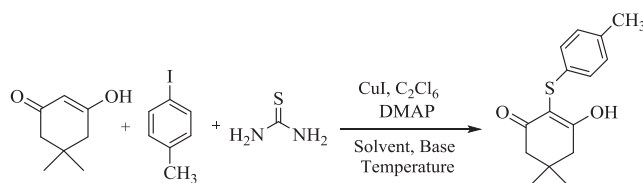
The initial screening of the reaction conditions was conducted using 5,5-dimethylcyclohexane-1,3-dione (dimedone) (1.0 mmol) and 4-iodotoluene (2.0 mmol) in the presence of thiourea (2.6 mmol), C_2Cl_6 (1.5 mmol), CuI (20 mol%), DMAP (20 mol%) and Na_2CO_3 (2.0 mmol) at 120 °C. The reaction in DMSO afforded the desired product in 70% yield after 24 h (Table 1, entry 1). No better

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Table 1

Optimization of oxidative coupling reaction between dimedone (1.0 mmol) and 4-iodotoluene (2.0 mmol) under different conditions.



Entry	Catalyst (mol%)	Solvent	Base (2.0 mmol)	T (°C)	Time (h)	Yield (%) ^a
1	CuI (20)	DMSO	Na ₂ CO ₃	120	24	70
2	CuI (20)	PEG-200	Na ₂ CO ₃	120	24	45
3	CuI (20)	H ₂ O	Na ₂ CO ₃	100	24	—
4	CuI (20)	Toluene	Na ₂ CO ₃	reflux	24	—
5	CuI (30)	DMSO	Na ₂ CO ₃	120	24	70
6	CuI (15)	DMSO	Na ₂ CO ₃	120	24	41
7	CuI (10)	DMSO	Na ₂ CO ₃	120	24	25
8	—	DMSO	Na ₂ CO ₃	120	24	—
9	CuCl (20)	DMSO	Na ₂ CO ₃	120	24	trace
10	CuCl ₂ (20)	DMSO	Na ₂ CO ₃	120	24	—
11	Cu(OAc) ₂ (20)	DMSO	Na ₂ CO ₃	120	24	—
12	Cu(PPh ₃) ₃ I (20)	DMSO	Na ₂ CO ₃	120	24	55
13	CuI (20)	DMSO	K ₂ CO ₃	120	24	75
14	CuI (20)	DMSO	Bu ₃ N	120	24	40
15	CuI (20)	DMSO	KOH	120	5	90
16	CuI (20)	DMSO	KOH (4.0)	120	15 min	93
17	CuI (20)	DMSO	KOH (4.0)	100	24	64
18	CuI (20)	DMSO	KOH (4.0)	130	15 min	93
19 ^b	CuI (20)	DMSO	KOH (4.0)	120	24	—

^a Isolated yield.^b The reaction was carried out in the absence of C₂Cl₆.

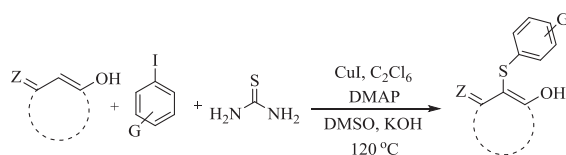
results were obtained, when the reaction was carried out in polyethylene glycol (PEG-200, 120 °C), H₂O (100 °C) or in refluxing toluene (Table 1, entries 2–4). Therefore, the subsequent reactions were performed in DMSO. No further yield improvement is achieved using higher concentration of ligand or/and substrates or increasing the catalyst loading. On the other hand, reducing the amount of CuI, greatly reduced the reaction yield (Table 1, entries 6 and 7). As expected, in the absence of catalyst, no product was formed (Table 1, entry 8). Performing the reaction in the presence of other Cu-catalysts such as CuCl, CuCl₂, Cu(OAc)₂ and Cu(PPh₃)₃I showed that the appropriate choice of catalyst was CuI (Table 1, entries 9–12). Next, alternative bases such as K₂CO₃, Bu₃N, KOH were screened, however in these cases, KOH is the best, providing product in 93% isolated yield within 15 min (Table 1, entries 13–16). A temperature of 120 °C was found to be the optimal reaction temperature. Decreasing the temperature, resulted the product in lower yield (Table 1, entry 17) and higher temperature (Table 1, entry 18) did not have any significant effect on the conversion; The sulfenylation carried out at 100 and 130 °C, afforded 64% and 93% yields respectively. Finally, we observed that no sulfenylation product was detected in the absence of C₂Cl₆ (Table 1, entry 19).

We then applied the obtained optimized conditions (dicarbonyl compound (1.0 mmol), aryl halide (2.0 mmol), thiourea (2.6 mmol), C₂Cl₆ (1.5 mmol), CuI (20 mol%), DMAP (20 mol%) and KOH (4.0 mmol) in DMSO at 120 °C), for the reaction of different aryl iodides with active methylene compounds in the presence of sulfur transfer reagent. The results are summarized in Table 2.

The reactions of cyclic β -diketones (5,5-dimethylcyclohexane-1,3-dione and cyclohexane-1,3-dione), cyclic β -ketoesters (chromane-2,4-dione and 6-methyl-2H-pyran-2,4(3H)-dione) and 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one with iodo-benzene proceeded smoothly in accordance with the optimized reaction conditions, affording the corresponding products in

excellent yields. Electronically different aryl iodides were also proved to be very efficient and in these cases, the corresponding sulfenylated products were obtained in excellent yields (Table 2, entries 1–18). The aryl iodides functionalized with *ortho* substituents demonstrated viable reactivity, suggesting that steric factors on the arene group of halides do not apply a limitation for the product formation.

To further extend the substrate scope, various active methylene compounds such as malononitrile, methyl 2-cyanoacetate, ethyl 2-cyanoacetate, ethyl 3-oxobutanoate (Table 2, entries 19–22) were treated with *p*-iodoanisole under the optimized reaction conditions. However, with this substrate combination, the expected C–S bond formation did not occur and in all cases, the corresponding disulfide was formed as the sole product in the reaction mixture. Unexpectedly, when linear β -diketone such as pentane-2,4-dione was used as the coupling partners, no product was formed (Table 2, entry 23). The only difference between these structures (linear and circle) after the reaction with copper iodide is the formation of a six-membered chelate ring in linear structures that cannot be formed in the circles. But, it is not clear to us whether this difference is involved in the formation of cyclic products. As shown in entry 24 of Table 2, simple ketone enolates are not sufficiently reactive toward thioarylation by the use of our catalytic system; when acetophenone was allowed to react with *p*-iodoanisole under the optimized reaction conditions, no product was detected even after prolonged reaction time. After the successful application of this methodology for different aryl iodides, we studied the applicability of this catalytic system for the reaction of aryl bromides under the obtained optimized reaction conditions. As summarized in Table 3, couplings of different aryl bromides with cyclic β -diketones, cyclic β -ketoesters and pyrazolones for the preparation of desired products, found to be facile, generating high yields (Table 3, entries 1–13).

Table 2The scope of thioarylation of active methylene compounds with aryl iodides.^a

Entry	Active methylene compound	ArI	Time (min)	Yield (%) ^b
1			18	91 [14]
2			15	93 [14]
3			17	95
4			26	91
5			25	86
6			20	89
7			23	86
8			24	91
9			21	94 [15]
10			18	92 [15]
11			19	85

(continued on next page)

Table 2 (continued)

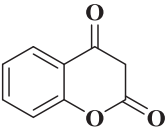
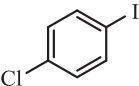
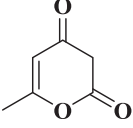
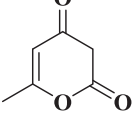
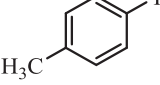
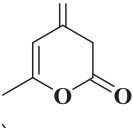
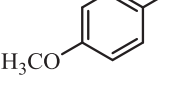
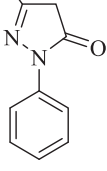
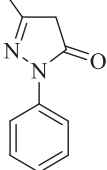
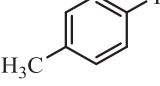
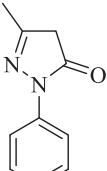
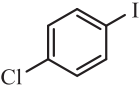
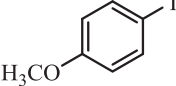
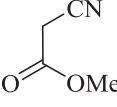
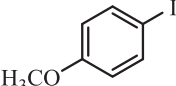
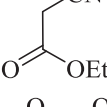
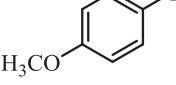
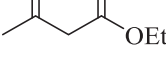
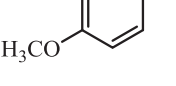
Entry	Active methylene compound	ArI	Time (min)	Yield (%) ^b
12			20	88 [15]
13			17	92 [16]
14			14	98
15			12	90
16			27	80 [17]
17			24	87 [17]
18			26	90 [17]
19			24 h	–
20			24 h	–
21			24 h	–
22			24 h	–

Table 2 (continued)

Entry	Active methylene compound	Arl	Time (min)	Yield (%) ^b
23			24 h	–
24			24 h	–

^a Reaction conditions: aryl iodides (2.0 mmol), active methylene compound (1.0 mmol), thiourea (2.6 mmol), C₂Cl₆ (1.5 mmol), CuI (20 mol%), DMAP (20 mol%), KOH (4.0 mmol) in 2 mL DMSO at 120 °C.

^b Isolated yield.

Further examination with chlorobenzene, using the above established conditions, did not afford any sulfenylated product. Thus, this catalytic system is not efficient for chloro arenes.

Based on these experiments, a proposed mechanism for sulfenylation of active methylene compounds (1,3-diketone) is shown in Scheme 1.

In the first step, CuI undergoes oxidative addition by insertion into the aryl C–X bond to produce Cu(III) species. The formed Cu(III) species is then converted to intermediate (I) by replacement of halide by thiourea. Reductive-elimination step, gives intermediate (II) along with regeneration of CuI catalyst. Hydrolysis of intermediates (II) in alkaline media generates the corresponding thiolate which undergo oxidation with C₂Cl₆ to generate the corresponding arylsulfenyl chloride or diaryl disulfide.¹³ On the other hand, a metal enolate species is formed in the reaction mixture by deprotonation of 1,3-diketone in the presence of CuI and KOH as base. The nucleophilic attack of the enolate on the reactive arylsulfenyl chloride or diaryl disulfide, yields the desired sulfenylated product.

To support the reaction mechanism, we decided to use diaryl disulfide in place of ArI/thiourea/C₂Cl₆. In this way, diphenyl disulfide has been prepared and its reaction with dimedone in the presence of KOH in DMSO was carried out at 120 °C. In this case, the sulfenylated product was obtained in 89% yield after several minutes.

In summary, we have developed a thiol-free route for the preparation of α -thioaryl- β -dicarbonyls and 4-thioaryl-5-pyrazolones via a copper-catalyzed oxidative coupling reaction between aryl halides and cyclic β -diketones, cyclic β -ketoesters and 5-pyrazolone. Carbon-Sulfur bond was formed in one-step process

using thiourea as odourless and stable source of sulfur. A variety of aromatic halides were used efficiently and the organic sulfide products were obtained in good to excellent yields. Inexpensive catalyst, one-step procedure, normal atmospheric conditions, easily available and odourless reagents are the other advantages of the present catalytic system.

3. Experimental section

3.1. General procedure for thioarylation of active methylene compounds

Thiourea (2.6 mmol, 0.204 g), C₂Cl₆ (1.5 mmol, 0.355 g), DMAP (20 mol%, 0.024 g), aryl halide (2.0 mmol), active methylene compound (1.0 mmol), CuI (20 mol%, 0.038 g) and KOH (4.0 mmol, 0.224 g) were added to a flask containing 2 mL of DMSO. The mixture was heated in an oil bath at 120 °C with stirring and the reaction was followed by TLC analysis. When the reaction was completed, the solution was let to cool, 1 mL of 1.0 M HCl was added and stirring is continued for 2 min. Next, the product was extracted with ethylacetate (3 $\times$ 3 mL). The solvent was removed and the crude product was purified by chromatography over silica gel using *n*-hexane/ethyl acetate as eluent to afford the pure product (Tables 2 and 3).

3.2. 3-Hydroxy-5,5-dimethyl-2-phenylsulfanyl-cyclohex-2-en-1-one (Table 2, entry 1)

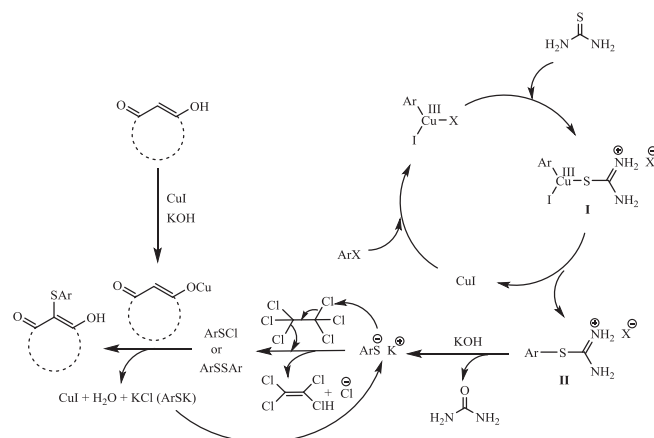
δ_H (400 MHz, CDCl₃) 1.16 (s, 6H, CH₃), 2.46 (s, 2H, CH₂), 2.62 (s, 2H, CH₂), 7.18–7.28 (m, 5H, Ar), 8.04 (s, 1H, OH). δ_C (100 MHz, CDCl₃) 28.2, 28.3, 31.6, 42.2, 51.0, 106.1, 126.3, 127.5, 129.1, 134.7, 178.3, 194.1.

3.3. 3-Hydroxy-5,5-dimethyl-2-(*p*-tolylthio)cyclohex-2-en-1-one (Table 2, entry 2)

δ_H (400 MHz, DMSO-*d*₆) 1.06 (s, 6H, CH₃), 2.24 (s, 3H, CH₃), 2.37 (s, 2H, CH₂), 2.39 (s, 2H, CH₂), 6.96 (d, 2H, *J* = 8.0 Hz, Ar), 7.05 (d, 2H, *J* = 8.0 Hz, Ar), 11.55 (s, 1H, OH). δ_C (100 MHz, DMSO-*d*₆) 20.9, 28.3, 29.5, 31.7, 45.1, 50.8, 103.8, 126.4, 129.7, 134.2, 137.9, 172.2, 180.3.

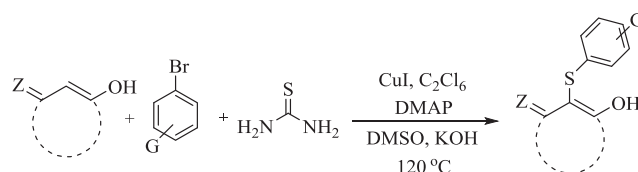
3.4. 3-Hydroxy-5,5-dimethyl-2-(*o*-tolylthio)cyclohex-2-en-1-one (Table 2, entry 3)

δ_H (400 MHz, DMSO-*d*₆) 1.08 (s, 6H, CH₃), 2.32 (s, 3H, CH₃), 2.49 (s, 4H, CH₂), 6.75 (d, 1H, *J* = 7.2 Hz, Ar), 6.98 (t, 1H, *J* = 7.2 Hz, Ar), 7.04 (t, 1H, *J* = 7.0 Hz, Ar), 7.14 (d, 1H, *J* = 7.2 Hz, Ar), 11.56 (s, 1H, OH). δ_C (100 MHz, DMSO-*d*₆) 20.0, 28.3, 31.5, 31.7, 47.5, 60.2, 102.5, 124.4, 124.7, 126.5, 130.2, 134.4, 137.4, 171.6, 189.0. Anal. Calcd for



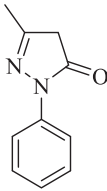
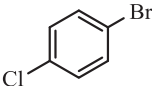
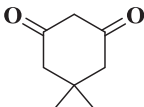
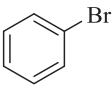
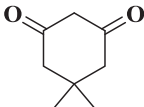
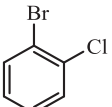
Scheme 1. A proposed mechanism for thioarylation of active methylene compounds.

Table 3
Sulfonylation of active methylene compounds with aryl bromides.^a



Entry	Active methylene compound	ArBr	Time (min)	Yield (%) ^b
1			27	89 [15]
2			34	83
3			23	94 [16]
4			19	95
5			22	92 [15]
6			30	85
7			23	87
8			25	89 [15]
9			16	91
10			27	86 [17]

Table 3 (continued)

Entry	Active methylene compound	ArBr	Time (min)	Yield (%) ^b
11			31	85 [17]
12			25	92 [14]
13			22	87

^a Reaction conditions: aryl bromides (2.0 mmol), diketone (1.0 mmol), thiourea (2.6 mmol), C₂Cl₆ (1.5 mmol), CuI (20 mol%), DMAP (20 mol%), KOH (4.0 mmol) in 2 mL DMSO at 120 °C.

^b Isolated yield.

(C₁₅H₁₈O₂S): C, 68.67; H, 6.92; S, 12.22. Found: C, 68.58; H, 6.86; S, 12.33.

3.5. 2-((2-Chlorophenyl)thio)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one (Table 2, entry 4)

δ_{H} (400 MHz, DMSO-*d*₆) 1.09 (s, 6H, CH₃), 2.51 (s, 2H, CH₂), 2.52 (s, 2H, CH₂), 6.77–6.79 (dd, 1H, *J*₁ = 8.0 Hz, *J*₂ = 1.6 Hz, Ar), 7.06–7.11 (dt, 1H, *J*₁ = 7.8 Hz, *J*₂ = 1.6 Hz, Ar), 7.16–7.21 (dt, 1H, *J*₁ = 7.6 Hz, *J*₂ = 1.2 Hz, Ar), 7.39–7.41 (dd, 1H, *J*₁ = 8.0 Hz, *J*₂ = 1.2 Hz, Ar), 8.13 (s, 1H, OH). δ_{C} (100 MHz, DMSO-*d*₆) 28.3, 31.7, 34.8, 47.3, 51.1, 101.1, 125.7, 125.8, 127.7, 128.1, 129.7, 137.4, 174.2, 189.4. Anal. Calcd for (C₁₄H₁₅ClO₂S): C, 59.46; H, 5.35; S, 11.34. Found: C, 59.52; H, 5.30; S, 11.27.

3.6. 3-Hydroxy-2-(phenylthio)cyclohex-2-en-1-one (Table 2, entry 5)

δ_{H} (400 MHz, DMSO-*d*₆) 1.94–2.00 (m, 2H, CH₂), 2.52–2.57 (m, 4H, CH₂), 7.01–7.08 (m, 3H, Ar), 7.22 (t, 2H, *J* = 7.8 Hz, Ar), 11.65 (s, 1H, OH). δ_{C} (100 MHz, DMSO-*d*₆) 20.4, 35.7, 36.7, 103.9, 124.6, 125.6, 129.0, 138.4, 187.3, 193.8. Anal. Calcd for (C₁₂H₁₂O₂S): C, 65.43; H, 5.49; S, 14.55. Found: C, 65.52; H, 5.39; S, 14.47.

3.7. 3-Hydroxy-2-(*p*-tolylthio)cyclohex-2-en-1-one (Table 2, entry 6)

δ_{H} (400 MHz, DMSO-*d*₆) 1.91–1.97 (m, 2H, CH₂), 2.23 (s, 3H, CH₃), 2.52–2.55 (m, 4H, CH₂), 6.93 (d, 2H, *J* = 8.4 Hz, Ar), 7.03 (d, 2H, *J* = 8.0 Hz, Ar), 11.53 (s, 1H, OH). δ_{C} (100 MHz, DMSO-*d*₆) 20.4, 20.9, 34.1, 34.2, 104.6, 126.1, 129.7, 133.9, 134.8, 187.9, 194.3. Anal. Calcd for (C₁₃H₁₄O₂S): C, 66.64; H, 6.02; S, 13.68. Found: C, 66.55; H, 6.11; S, 13.58.

3.8. 3-Hydroxy-2-(*o*-tolylthio)cyclohex-2-en-1-one (Table 2, entry 7)

δ_{H} (400 MHz, DMSO-*d*₆) 1.94–2.00 (m, 2H, CH₂), 2.30 (s, 3H, CH₃), 2.57 (t, 4H, *J* = 5.8 Hz, CH₂), 6.73 (d, 1H, *J* = 7.6 Hz, Ar), 6.97 (t, 1H, *J* = 7.2 Hz, Ar), 7.03 (t, 1H, *J* = 7.4 Hz, Ar), 7.12 (d, 1H, *J* = 6.8 Hz, Ar), 11.57 (s, 1H, OH). δ_{C} (100 MHz, DMSO-*d*₆) 19.3, 19.8, 28.9, 31.1,

102.6, 123.6, 123.7, 125.9, 129.5, 133.5, 136.7, 177.6, 191.8. Anal. Calcd for (C₁₃H₁₄O₂S): C, 66.64; H, 6.02; S, 13.68. Found: C, 66.55; H, 6.13; S, 13.60.

3.9. 2-((4-Chlorophenyl)thio)-3-hydroxycyclohex-2-en-1-one (Table 2, entry 8)

δ_{H} (400 MHz, DMSO-*d*₆) 2.05–2.12 (m, 2H, CH₂), 2.65–2.67 (m, 4H, CH₂), 7.07 (d, 2H, *J* = 8.4 Hz, Ar), 7.17 (d, 2H, *J* = 8.0 Hz, Ar), 11.69 (s, 1H, OH). δ_{C} (100 MHz, DMSO-*d*₆) 20.6, 34.3, 34.4, 104.8, 126.3, 129.9, 134.2, 135.0, 188.6, 193.7. Anal. Calcd for (C₁₂H₁₁ClO₂S): C, 56.58; H, 4.35; S, 12.59. Found: C, 56.67; H, 4.43; S, 12.46.

3.10. 2-Hydroxy-3-phenylsulfanyl-chromen-4-one (Table 2, entry 9)

δ_{H} (400 MHz, DMSO-*d*₆) 6.96–7.40 (m, 7H, Ar), 7.70 (d, 1H, *J* = 6.4 Hz, Ar), 7.99 (d, 1H, *J* = 5.6 Hz, Ar). δ_{C} (100 MHz, DMSO-*d*₆) 116.2, 118.0, 118.1, 123.4, 124.5, 124.6, 125.5, 128.7, 132.6, 137.8, 153.2, 161.9, 170.5.

3.11. 4-Hydroxy-3-(*p*-tolylthio)-2H-chromen-2-one (Table 2, entry 10)

δ_{H} (400 MHz, DMSO-*d*₆) 2.16 (s, 3H, CH₃), 6.92 (d, 2H, *J* = 7.6 Hz, Ar), 7.08–7.13 (m, 4H, Ar), 7.41 (t, 1H, *J* = 7.8 Hz, Ar), 7.73 (d, 1H, *J* = 6.4 Hz, Ar). δ_{C} (100 MHz, DMSO-*d*₆) 20.9, 89.1, 116.3, 119.3, 123.3, 125.0, 127.2, 128.6, 130.2, 132.4, 138.2, 153.6, 162.6, 171.9.

3.12. 2-Hydroxy-3-(*o*-tolylthio)-4H-chromen-4-one (Table 2, entry 11)

δ_{H} (400 MHz, DMSO-*d*₆) 2.54 (s, 3H, CH₃), 7.23–7.28 (m, 4H, Ar), 7.48–7.52 (m, 1H, Ar), 7.62 (d, 2H, *J* = 7.6 Hz, Ar), 7.86–7.89 (m, 1H, Ar). δ_{C} (100 MHz, DMSO-*d*₆) 21.2, 102.2, 115.9, 119.8, 120.7, 123.3, 123.4, 124.2, 126.1, 131.1, 132.9, 138.2, 153.0, 163.8, 168.0, 179.3. Anal. Calcd for (C₁₆H₁₂O₃S): C, 67.59; H, 4.25; S, 11.28. Found: C, 67.70; H, 4.17; S, 11.18.

3.13. 3-(4-Chlorophenylthio)-2-hydroxy-4H-chromen-4-one (Table 2, entry 12)

δ_{H} (400 MHz, DMSO- d_6) 7.11 (d, 2H, $J = 7.6$ Hz, Ar), 7.26–7.31 (m, 4H, Ar), 7.59 (t, 1H, $J = 6.4$ Hz, Ar), 7.92 (d, 1H, $J = 6.4$ Hz, Ar). δ_{C} (100 MHz, DMSO- d_6) 89.4, 116.6, 119.6, 123.6, 125.3, 127.5, 128.9, 129.1, 132.7, 138.5, 153.9, 162.9, 172.2.

3.14. 4-Hydroxy-6-methyl-3-(phenylthio)-2H-pyran-2-one (Table 2, entry 13)

δ_{H} (400 MHz, DMSO- d_6) 2.24 (s, 3H, CH₃), 6.18 (s, 1H, =CH), 6.99 (t, 3H, $J = 4.2$ Hz, Ar), 7.08 (d, 2H, $J = 8.0$ Hz, Ar), 12.31 (s, 1H, OH). δ_{C} (100 MHz, DMSO- d_6) 20.9, 91.5, 100.4, 126.6, 129.9, 133.6, 134.9, 163.5, 164.5, 173.1.

3.15. 4-Hydroxy-6-methyl-3-p-tolylsulfanyl-pyran-2-one (Table 2, entry 14)

δ_{H} (400 MHz, CDCl₃) 2.21 (s, 3H, CH₃), 2.22 (s, 3H, CH₃), 5.99 (s, 1H, =C–H), 7.00 (d, 2H, $J = 8.4$ Hz, Ar), 7.13 (d, 2H, $J = 8.4$ Hz, Ar), 7.74 (s, 1H, OH). δ_{C} (100 MHz, CDCl₃) 20.3, 21.0, 94.5, 98.8, 128.5, 129.8, 130.0, 137.2, 162.9, 165.3, 170.9. Anal. Calcd for (C₁₃H₁₂O₃S): C, 62.89; H, 4.87; S, 12.91. Found: C, 63.01; H, 4.75; S, 12.82.

3.16. 2-Hydroxy-3-(4-methoxyphenylthio)-6-methyl-4H-pyran-4-one (Table 2, entry 15)

δ_{H} (400 MHz, CDCl₃) 2.28 (s, 3H, CH₃), 3.80 (s, 3H, OCH₃), 6.06 (s, 1H, =CH), 6.84 (d, 2H, $J = 8.4$ Hz, Ar), 7.37 (d, 2H, $J = 8.4$ Hz, Ar). δ_{C} (100 MHz, CDCl₃) 20.2, 55.3, 95.6, 98.8, 114.8, 123.8, 131.5, 158.1, 159.1, 159.4, 170.3. Anal. Calcd for (C₁₃H₁₂O₄S): C, 59.08; H, 4.58; S, 12.13. Found: C, 59.19; H, 4.69; S, 12.00.

3.17. 3-Methyl-1-phenyl-4-(phenylthio)-1H-pyrazol-5-ol (Table 2, entry 16)

δ_{H} (400 MHz, DMSO- d_6) 2.13 (s, 3H, CH₃), 7.09 (d, 2H, $J = 7.2$ Hz, Ar), 7.13 (t, 1H, $J = 7.4$ Hz, Ar), 7.29 (t, 3H, $J = 7.6$ Hz, Ar), 7.48 (t, 2H, $J = 8.0$ Hz, Ar), 7.75 (d, 2H, $J = 8.0$ Hz, Ar), 12.22 (s, 1H, OH). δ_{C} (100 MHz, DMSO- d_6) 12.8, 87.2, 121.3, 125.3, 125.4, 126.2, 127.9, 129.4, 129.5, 138.8, 156.7, 166.2.

3.18. 5-Methyl-2-phenyl-4-p-tolylsulfanyl-3,4-dihydro-2H-pyrazol-3-ol (Table 2, entry 17)

δ_{H} (400 MHz, DMSO- d_6) 2.38 (s, 3H, CH₃), 2.65 (s, 3H, CH₃), 7.13 (d, 2H, $J = 7.6$ Hz, Ar), 7.25 (d, 2H, $J = 7.6$ Hz, Ar), 7.43 (t, 1H, $J = 7.0$ Hz, Ar), 7.62 (t, 2H, $J = 7.8$ Hz, Ar), 7.88 (d, 2H, $J = 8.0$ Hz, Ar), 12.30 (s, 1H, OH). δ_{C} (100 MHz, DMSO- d_6) 12.1, 22.7, 85.4, 120.8, 125.5, 125.6, 126.2, 128.7, 128.8, 129.2, 137.2, 151.0, 155.4.

3.19. 4-(4-Chlorophenylthio)-3-methyl-1-phenyl-1H-pyrazol-5-ol (Table 2, entry 18)

δ_{H} (400 MHz, DMSO- d_6) 2.11 (s, 3H, CH₃), 7.11 (d, 2H, $J = 8.4$ Hz, Ar), 7.31 (t, 1H, $J = 7.4$ Hz, Ar), 7.35–7.39 (m, 2H, Ar), 7.48–7.52 (m, 2H, Ar), 7.75–7.77 (m, 2H, Ar), 12.26 (s, 1H, OH). δ_{C} (100 MHz, DMSO- d_6) 12.8, 86.1, 126.3, 127.0, 129.4, 130.0, 130.3, 131.0, 132.3, 138.0, 151.7, 156.2.

3.20. 2-Hydroxy-3-phenylsulfanyl-chromen-4-one (Table 3, entry 1)

δ_{H} (400 MHz, DMSO- d_6) 7.03–7.09 (m, 3H, Ar), 7.18–7.22 (m, 2H,

Ar), 7.27–7.31 (m, 2H, Ar), 7.60 (t, 1H, $J = 7.8$ Hz, Ar), 7.88 (d, 1H, $J = 8.0$ Hz, Ar). δ_{C} (100 MHz, DMSO- d_6) 116.1, 117.9, 118.0, 123.3, 124.5, 124.6, 125.4, 128.6, 132.6, 137.7, 153.2, 161.8, 170.4.

3.21. 3-Hydroxy-2-(phenylthio)cyclohex-2-en-1-one (Table 3, entry 2)

δ_{H} (400 MHz, DMSO- d_6) 1.92–1.99 (m, 2H, CH₂), 2.50–2.56 (m, 4H, CH₂), 7.00–7.07 (m, 3H, Ar), 7.21 (t, 2H, $J = 7.6$ Hz, Ar), 11.64 (s, 1H, OH). δ_{C} (100 MHz, DMSO- d_6) 20.3, 29.4, 35.6, 103.8, 124.5, 125.5, 128.9, 138.3, 180.1, 193.7.

3.22. 4-Hydroxy-6-methyl-3-(phenylthio)-2H-pyran-2-one (Table 3, entry 3)

δ_{H} (400 MHz, DMSO- d_6) 2.16 (s, 3H, CH₃), 6.10 (s, 1H, =C–H), 6.96–6.99 (m, 3H, Ar), 7.09 (t, 2H, $J = 7.6$ Hz, Ar), 12.22 (s, 1H, OH). δ_{C} (100 MHz, DMSO- d_6) 21.0, 91.6, 100.5, 126.7, 130.0, 133.7, 135.0, 163.6, 164.6, 173.2.

3.23. 4-Hydroxy-6-methyl-3-p-tolylsulfanyl-pyran-2-one (Table 3, entry 4)

δ_{H} (400 MHz, CDCl₃) 2.22 (s, 3H, CH₃), 2.23 (s, 3H, CH₃), 6.00 (s, 1H, =C–H), 7.02 (d, 2H, $J = 8.4$ Hz, Ar), 7.14 (d, 2H, $J = 8.4$ Hz, Ar), 7.75 (s, 1H, OH). δ_{C} (100 MHz, CDCl₃) 20.0, 20.7, 94.1, 98.5, 128.2, 129.5, 129.7, 136.9, 162.5, 164.9, 170.5.

3.24. 4-Hydroxy-3-(p-tolylthio)-2H-chromen-2-one (Table 3, entry 5)

δ_{H} (400 MHz, DMSO- d_6) 2.49 (s, 3H, CH₃), 7.08 (d, 2H, $J = 7.6$ Hz, Ar), 7.23–7.28 (m, 4H, Ar), 7.56 (t, 1H, $J = 7.8$ Hz, Ar), 7.88 (d, 1H, $J = 6.4$ Hz, Ar). δ_{C} (100 MHz, DMSO- d_6) 20.8, 89.0, 116.2, 119.2, 123.2, 124.9, 127.1, 128.5, 130.1, 132.4, 138.1, 153.5, 162.5, 171.8.

3.25. 3-Hydroxy-2-(p-tolylthio)cyclohex-2-en-1-one (Table 3, entry 6)

δ_{H} (400 MHz, DMSO- d_6) 1.85–1.91 (m, 2H, CH₂), 2.16 (s, 3H, CH₃), 2.45–2.46 (m, 4H, CH₂), 6.87 (d, 2H, $J = 8.4$ Hz, Ar), 6.97 (d, 2H, $J = 8.0$ Hz, Ar), 11.47 (s, 1H, OH). δ_{C} (100 MHz, DMSO- d_6) 20.4, 20.9, 34.0, 34.1, 104.6, 126.1, 129.7, 133.9, 134.8, 185.7, 190.6.

3.26. 2-Hydroxy-3-(o-tolylthio)-4H-chromen-4-one (Table 3, entry 7)

δ_{H} (400 MHz, DMSO- d_6) 2.49 (s, 3H, CH₃), 7.18–7.27 (m, 4H, Ar), 7.43–7.47 (m, 1H, Ar), 7.58 (d, 2H, $J = 6.4$ Hz, Ar), 7.82–7.84 (m, 1H, Ar). δ_{C} (100 MHz, DMSO- d_6) 21.1, 102.1, 115.9, 119.7, 120.6, 123.2, 123.4, 124.1, 126.0, 131.0, 132.8, 138.1, 152.9, 163.7, 167.9, 179.2.

3.27. 3-(4-Chlorophenylthio)-2-hydroxy-4H-chromen-4-one (Table 3, entry 8)

δ_{H} (400 MHz, DMSO- d_6) 7.03 (d, 2H, $J = 7.6$ Hz, Ar), 7.19–7.24 (m, 4H, Ar), 7.52 (t, 1H, $J = 7.6$ Hz, Ar), 7.85 (d, 1H, $J = 6.4$ Hz, Ar). δ_{C} (100 MHz, DMSO- d_6) 89.3, 116.5, 119.6, 123.5, 125.3, 127.4, 128.8, 130.5, 132.7, 138.5, 153.9, 162.8, 172.1.

3.28. 2-Hydroxy-3-(4-methoxyphenylthio)-6-methyl-4H-pyran-4-one (Table 3, entry 9)

δ_{H} (400 MHz, CDCl₃) 2.26 (s, 3H, CH₃), 3.77 (s, 3H, OCH₃), 6.04 (s, 1H, =CH), 6.82 (d, 2H, $J = 8.8$ Hz, Ar), 7.34 (d, 2H, $J = 8.4$ Hz, Ar). δ_{C}

(100 MHz, CDCl₃) 20.3, 55.4, 95.8, 98.9, 115.0, 123.9, 131.7, 159.5, 159.6, 159.7, 170.4.

3.29. 5-Methyl-2-phenyl-4-p-tolylsulfanyl-3,4-dihydro-2H-pyrazol-3-ol (Table 3, entry 10)

δ_{H} (400 MHz, DMSO-*d*₆) 1.90 (s, 3H, CH₃), 3.15 (s, 3H, CH₃), 7.16 (d, 2H, *J* = 8.4 Hz, Ar), 7.36 (t, 1H, *J* = 7.4 Hz, Ar), 7.41–7.43 (m, 2H, Ar), 7.55 (t, 2H, *J* = 8.0 Hz, Ar), 7.80–7.82 (m, 2H, Ar). δ_{C} (100 MHz, DMSO-*d*₆) 12.4, 23.1, 85.7, 121.1, 125.9, 126.6, 129.0, 129.5, 129.9, 130.6, 137.6, 151.3, 155.7.

3.30. 4-(4-Chlorophenylthio)-3-methyl-1-phenyl-1H-pyrazol-5-ol (Table 3, entry 11)

δ_{H} (400 MHz, DMSO-*d*₆) 2.04 (s, 3H, CH₃), 7.04 (d, 2H, *J* = 8.8 Hz, Ar), 7.24 (t, 1H, *J* = 7.4 Hz, Ar), 7.29–7.31 (m, 2H, Ar), 7.43 (t, 2H, *J* = 8.0 Hz, Ar), 7.68–7.70 (m, 2H, Ar), 12.19 (s, 1H, OH). δ_{C} (100 MHz, DMSO-*d*₆) 12.7, 86.0, 121.5, 126.2, 126.9, 129.3, 129.9, 130.2, 130.9, 137.9, 151.7, 156.1.

3.31. 3-Hydroxy-5,5-dimethyl-2-phenylsulfanyl-cyclohex-2-enone (Table 3, entry 12)

δ_{H} (400 MHz, CDCl₃) 1.12 (s, 6H, CH₃), 2.41 (s, 2H, CH₂), 2.58 (s, 2H, CH₂), 7.11–7.26 (m, 5H, Ar), 8.13 (s, 1H, OH). δ_{C} (100 MHz, CDCl₃) 28.1, 28.3, 31.5, 42.1, 51.0, 106.1, 126.3, 127.4, 129.0, 134.7, 178.3, 194.0.

3.32. 2-((2-Chlorophenyl)thio)-3-hydroxy-5,5-dimethylcyclohex-2-en-1-one (Table 3, entry 13)

δ_{H} (400 MHz, DMSO-*d*₆) 1.06 (s, 6H, CH₃), 2.48 (s, 2H, CH₂), 2.49 (s, 2H, CH₂), 6.73–6.76 (dd, 1H, *J*₁ = 8.0 Hz, *J*₂ = 1.6 Hz, Ar), 7.03–7.07 (m, 1H, Ar), 7.13–7.17 (m, 1H, Ar), 7.36 (t, 1H, *J* = 6.8 Hz, Ar), 8.10 (s, 1H, OH). δ_{C} (100 MHz, DMSO-*d*₆) 28.0, 31.4, 34.4, 47.0, 50.8, 100.7, 125.4, 125.5, 127.3, 127.7, 129.3, 137.0, 173.8, 189.0.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.tet.2018.07.049>.

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