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VIP *Very Important Paper*

I_2-Promoted Direct C–H Sulfenylation of Isoquinolin-1(2*H*)-ones with Sulfonyl Chlorides

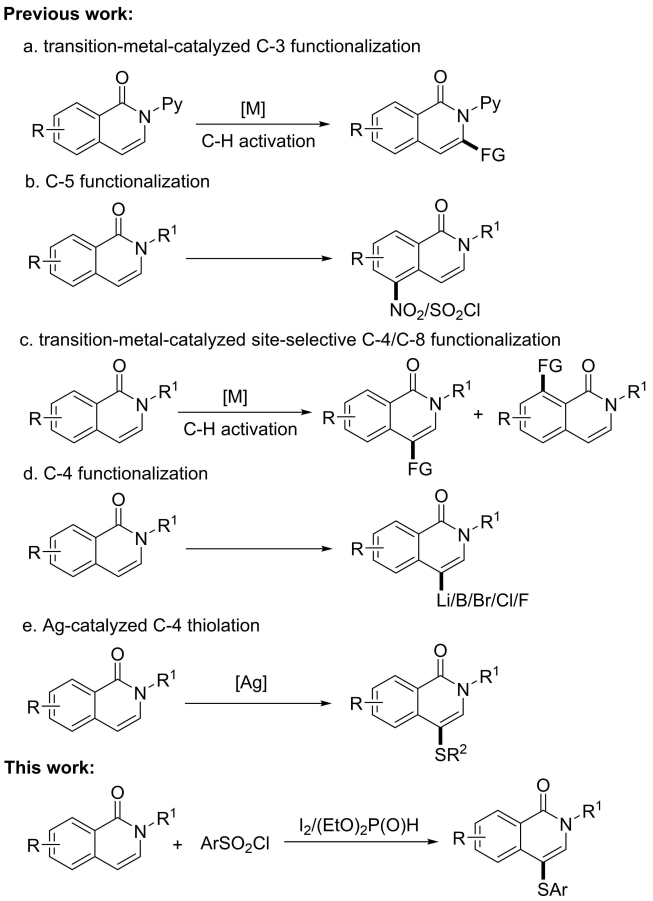
Cai-Yun Yang,[a] Xia Li,[b] Bo Liu,[a] and Guo-Li Huang*[a]

A simple, efficient, and green method for the iodine-promoted regioselective C-4 sulfenylation of isoquinolin-1(2*H*)-ones using commercially available aryl sulfonyl chlorides as the sulfur source was described under metal- and solvent-free conditions. The reaction proceeded smoothly under simple conditions to obtain 4-arylthioisoquinolin-1(2*H*)-ones in moderate to good yields, and showed high regioselectivity, broad substrate scope, and good functional group tolerance. A radical reaction mechanism involving ArS$^{\bullet}$ radicals as key intermediates is proposed for the present transformation.

Introduction

The isoquinolone scaffold as a privileged structural motif have been widely found in natural products and bioactive molecules,[1] and show a wide range of biological activities.[1b,2] Accordingly, an increasing number of attentions has focused on the development of straightforward access to functionalized isoquinolin-1(2*H*)-one, and different functional groups have been introduced into the scaffold using various catalytic systems. With the aid of directing group 2-pyridinyl (2-Py), different functional groups have been introduced into the C3 position of isoquinolin-1(2*H*)-one by transition-metal-catalyzed C–H functionalization (Scheme 1a).[3] Recently, Rode[4] and Lai[5] reported the nitration and chlorosulfonylation reaction at the C5 position of isoquinolin-1(2*H*)-one (Scheme 1b). Meanwhile, Hong[6] and Patil[7] developed the catalyst-controlled site-selective mothed for arylation and alkynylation reaction at the C4/C8 position of this scaffold (Scheme 1c). In addition, some approaches for the construction of C–X (X=Li, B, Br, Cl, F) bonds at the C4 position have also been reported, such as lithiation,[8] borylation,[1b] bromination,[9] chlorination,[10] and fluorination[11] (Scheme 1d). Although great progress has been achieved in this field, most of these transformations suffer from expensive transition-metal, multiple steps and relatively hash reaction conditions.

Significant progress has been made in the formation of C–S bonds through the direct functionalization of C–H under different conditions.[12] In this transformation, various sulfenylating or thiolating reagents have been used, such as thiols,[13] disulfides,[12c,14] sodium sulfinates,[15] sulfonyl hydrazides,[16] and sulfonyl chlorides.[17] Among them, sulfonyl chloride is easily available and inexpensive, does not have the unpleasant odor of thiols or disulfides, and usually used as a sulfonylation reagent to build C–S bonds. In 1988, Nagarajan[18] and co-workers first reported the reaction of isoquinolin-1(2*H*)-one derivative and *p*-nitrobenzenesulfonyl chloride in the presence of Et_3N to give the sulfenylated product in very low yield (10%), and specu-



Scheme 1. Strategies for the synthesis of functionalized isoquinolin-1(2*H*)-one derivatives.

[a] C.-Y. Yang, Dr. B. Liu, Dr. G.-L. Huang
School of Chemistry and Chemical Engineering
Yunnan Normal University
Kunming 650500, China
E-mail: hgli2005@126.com
[b] X. Li
Department of Library
Yunnan Normal University
Kunming 650500, China

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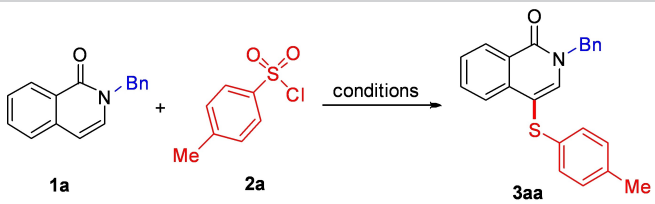
lated that the reaction involved an intermolecular reduction/oxidation process. Very recently, Zhu[19] developed a new $AgSbF_6$-mediated regioselective deoxygenative C–H thiolation of isoquinolin-1(2*H*)-ones with diphenyl disulfides (Scheme 1e). Despite this progress, metal-free-catalyzed direct C-4 sulfenylation of isoquinolin-1(2*H*)-ones has not yet been documented. Based on our continued interest in direct functionalization of C–H bonds,[20] herein, we report a new I_2-promoted reaction for the synthesis of C-4 sulfonylated isoquinolin-1(2*H*)-ones with aryl sulfonyl chlorides under metal- and solvent-free conditions.

Results and Discussion

We selected 2-benzylisoquinolin-1(2*H*)-one (**1a**) and *p*-toluenesulfonyl chloride (**2a**) as the reaction substrates for optimized conditions. The results were summarized in Table 1. Initially C-4 sulfenylation took place in the presence of tetrabutylammonium iodide (TBAI, 0.5 equiv.) and diethyl phosphite ($(EtO)_2P(O)H$, 2.0 equiv.) in CH_3CN at 80 °C under an air atmosphere for 24 hours, affording product **3aa** in 21% yield (entry 1, Table 1). Inspired by this result, various additives such as I_2, KI, *N*-iodosuccinimide (NIS) and NH_4I were screened (entries 2–5, Table 1). To our delight, the use of I_2 as a additive significantly improved the catalytic efficiency and gave a good yield (88%). We investigated the effect of the amount of I_2 on the reaction, reducing the catalyst loading from 50 to 30 mol% clearly lowered the conversion of product from 88 to 47% (entry 6). It is evident that the amount of catalyst has remarkable effect on this reaction. The effect of reaction time has also been investigated. However, we have tried to shorten the reaction time from 24 to 18 h, the conversion was obviously lowered from 88 to 72% (entries 7, Table 1). Then, different phosphorus reagents failed the reaction, using tributyl phosphine (Bu_3P), triphenylphosphane (Ph_3P), triethyl phosphite ($(EtO)_3P$) as the additives gave very poor yield (entries 8–10, Table 1), di-*iso*-propyl phosphite ($(i\text{-}PrO)_2P(OH)$), diphenylphosphine oxide ($Ph_2P{=}O$), and triphenyl phosphite ($(PhO)_3P$), which were less efficient (entries 11–13, Table 1). Finally, in order to investigate the solvent effect on the reaction, the model reaction was carried out in various solvents at 80 °C (entries 14–20, Table 1), gratifyingly, the best result (94% yield) was obtained under solvent-free. However, when the reaction was carried out in N_2 atmosphere, the desired product **3aa** was not detected (entry 21). Based on the detailed investigations, the optimised conditions were 0.5 equiv. of I_2 and 2 equiv. of diethyl phosphite as the additive at 80 °C under solvent-free and air atmosphere for 24 h.

With the optimised conditions in hand, we subsequently focused on examining the scope and generality of this protocol (Table 2). Firstly, a wide range of substituted aryl sulfonyl chlorides was subjected to the reaction with 2-benzylisoquinolin-1(2*H*)-one (**1a**) to produce the corre-

Table 1. Optimization of the reaction conditions.[a]

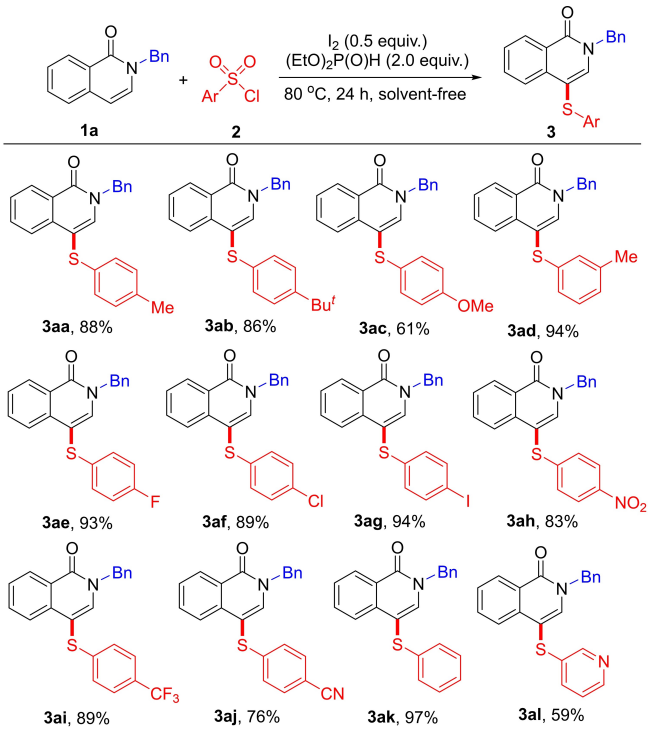


1a **2a** **3aa**

Entry	Additive **1**	Additive **2**	Solvent	Yield [%][b]
1	TBAI	$(EtO)_2P(O)H$	CH_3CN	21
2	I_2	$(EtO)_2P(O)H$	CH_3CN	88
3	KI	$(EtO)_2P(O)H$	CH_3CN	22
4	NIS	$(EtO)_2P(O)H$	CH_3CN	53
5	NH_4I	$(EtO)_2P(O)H$	CH_3CN	28
6[c]	I_2	$(EtO)_2P(O)H$	CH_3CN	47
7[d]	I_2	$(EtO)_2P(O)H$	CH_3CN	72
8	I_2	Bu_3P	CH_3CN	30
9	I_2	Ph_3P	CH_3CN	43
10	I_2	$(EtO)_3P$	CH_3CN	64
11	I_2	$(i\text{-}PrO)_2P(OH)$	CH_3CN	81
12	I_2	$Ph_2P{=}O$	CH_3CN	85
13	I_2	$(PhO)_3P$	CH_3CN	85
14	I_2	$(EtO)_2P(O)H$	DCE	81
15	I_2	$(EtO)_2P(O)H$	DMSO	56
16	I_2	$(EtO)_2P(O)H$	Toluene	86
17	I_2	$(EtO)_2P(O)H$	1,4-Dioxane	77
18	I_2	$(EtO)_2P(O)H$	THF	85
19	I_2	$(EtO)_2P(O)H$	DMF	-
20	I_2	$(EtO)_2P(O)H$	–	94
21[e]	I_2	$(EtO)_2P(O)H$	–	N.D.[f]

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), additive **1** (0.1 mmol), additive **2** (0.4 mmol), 80 °C, 24 h, under air. [b] NMR yield based on **1a** using dibromomethane as the internal standard. [c] I_2 (0.06 mmol). [d] Run for 18 h. [e] Reaction in N_2 atmosphere. [f] N.D. = no detection.

Table 2. Substrate scope of sulfonyl chlorides for the sulfenylation reactions.[a,b]



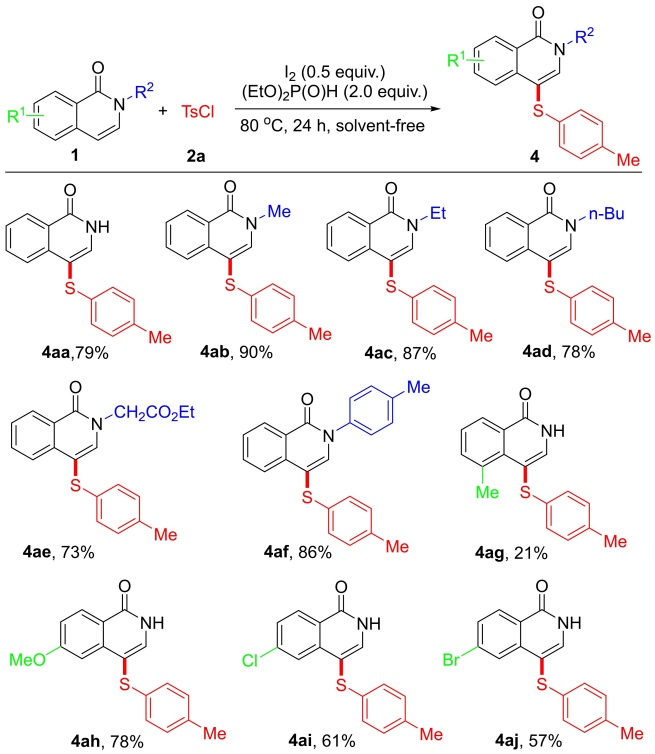
[a] Reaction conditions: **1a** (0.20 mmol), **2** (0.40 mmol), I_2 (0.10 mmol), $(EtO)_2P(O)H$ (0.40 mmol), 80 °C, 24 h, under air. [b] Isolated yields.

sponding product **3aa**–**3al** in moderate to good yields (59-97%). Notably, benzenesulfonyl chlorides bearing with electron-donating alkyl and alkoxy groups (Me, *t*-Bu, OMe) have proven to be suitable substrates for the reaction to provide the corresponding products (**3aa**–**3ad**) in synthetic acceptable yields (61–94%). In addition, Halides such as F, Cl and I were also found compatible for this reaction, and afforded the desired products in 89–94% yields (**3ae**–**3ag**). Even stronger electron withdrawing substituents such as $-NO_2$, $-CF_3$, or –CN on the phenyl ring could proceed well, and gave the corresponding products (**3ah**, **3ai**, **3aj**) in good yields, which provided the facile generation of a variety of 4-arylthio-substituted isoquinolin-1(2*H*)-ones. It is noteworthy that pyridine-3-sulfonyl chloride reacted smoothly to afford the corresponding C-4 sulfenylated product (**3al**) in moderate yield.

After studying the scope of aryl sulfonyl chlorides in C-4 sulfenylation of 2-benzylisoquinolin-1(2*H*)-one (**1a**), we turned our attention to investigate the scope of substituted isoquinolin-1(2*H*)-ones, and the results were summarized in Table 3. We were pleased to observe that a wide range of N^2-alkylated isoquinolin-1(2*H*)-ones undergo the reaction successfully, affording the desired products (**4ab**–**4ae**) in good to excellent yields. To further investigate the functional group tolerance, arylated substituted substrates on N^2-positions of isoquinolin-1(2*H*)-one reacted smoothly to give the corresponding C-4 sulfenylated compounds (**4af**) in good yields. Additionally, the reaction of substrate **2a** with several substituted *N*-unprotected isoquinolin-1(2*H*)-ones furnished the corresponding products (**4aa**, **4ag**–**4aj**) in moderate yields. It is noteworthy that although relatively low yields were obtained when the *N*-unprotected isoquinolin-1(2*H*)-ones were subjected to the reaction, it may provide a significant opportunity for their further transformation on nitrogen atom, especially in pharmacological demand.

To examine the practicality of the reaction system, the I_2-promoted C-4 sulfenylated reaction was conducted on a gram scale, and the desired product **3aa** was obtained in a good yield of 84%, thus highlighting the synthetic utility of this methodology (Scheme 2a). To gain insight into the reaction mechanism, several control experiments were carried out. When the model reaction took place in the absence of I_2 (Scheme 2b), the desired product (**3aa**) was not detected, and the same result was obtained without $(EtO)_2P(O)H$ (Scheme 2c). Notably, *p*-toluenesulfonyl chloride (**2a**) was replaced with sodium 4-methylbenzenesulfinate (**3a**) for this reaction, affording the desired products in relatively low yield (17%, Scheme 2d). However, when 2-benzylisoquinolin-1(2*H*)-one (**1a**) reacted with *p*-toluenethiol (**4a**) or *p*-toluene disulfide (**5a**) under standard conditions, respectively, the sulfenylated product also did not obtained (Scheme 2e). In addition, when a radical-trapping reagent (TEMPO) was employed in the model reaction, the direct sulfenylation was suppressed (Scheme 2f), suggesting that the reaction possibly involves a radical process.

Table 3. Substrate scope of isoquinolin-1(2*H*)-ones for the sulfenylation reactions.[a,b]



[a] Reaction conditions: **1** (0.20 mmol), **2a** (0.40 mmol), I_2 (0.10 mmol), $(EtO)_2P(O)H$ (0.40 mmol), 80 °C, 24 h, under air. [b] Isolated yields.

Based on these preliminary mechanistic studies and relevant reports,[17a,c,f] a plausible reaction mechanism is proposed, as shown in Scheme 3. Firstly, the reaction was initiated by the reduction of aryl sulfonyl chlorides (**2**) with the assistance of iodine and diethyl phosphite to generate the electrophilic ArSI species. Subsequently, the homolysis of ArSI possibly would yield an ArS• radical intermediate under heating. Next, the reactive ArS• radical intermediates could couple with isoquinolin-1(2*H*)-one substrate leading to a formation of an arene-SAr radical intermediate, in which the radical could be stabilized by the adjacent nitrogen atom. Finally, a subsequent loss of proton from the latter was coupled with ArSI to afford the desired sulfenylated product, and accompanied by the formation of the ArS• radical and HI.

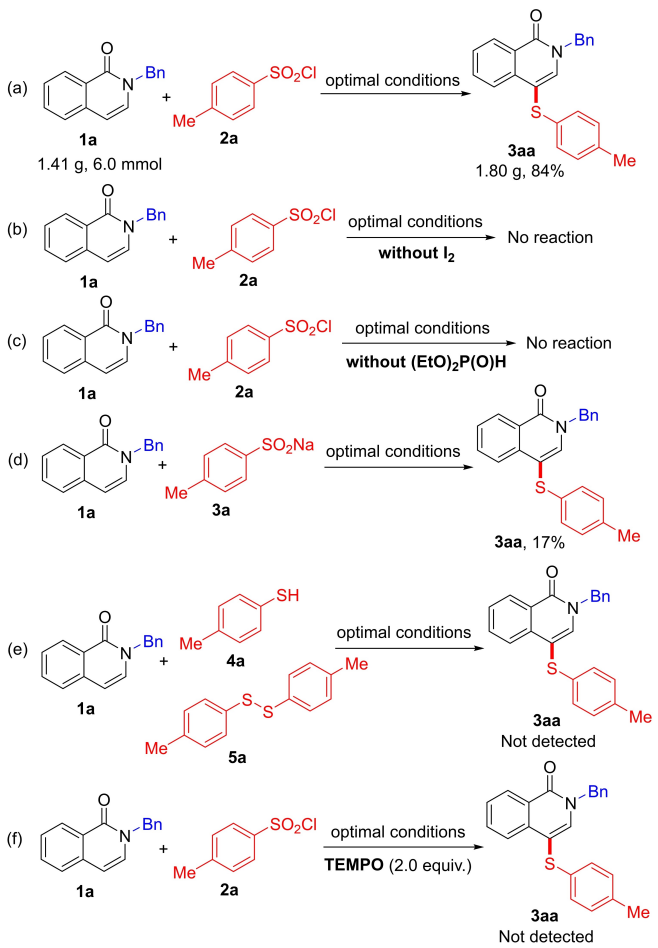
Conclusion

In summary, we have successfully described an iodine-promoted direct C–S bond coupling of the C(sp^2)–H bond of isoquinolinones with aryl sulfonyl chlorides under metal- and solvent-free conditions. C-4 sulfenylation employ inexpensive and easily available arylsulfonyl chloride as sulfur source, and are applicable to a broad range of substrates, affording the products in moderate to excellent yields. Preliminary mechanistic studies indicate that this procedure is likely to proceed via radical processes. These methods provide an alternative and facile synthetic route to access a series of 4-arylthio-substituted isoquinolin-1(2*H*)-one derivatives, which might have potential applications in organic, material and pharmaceutical areas.

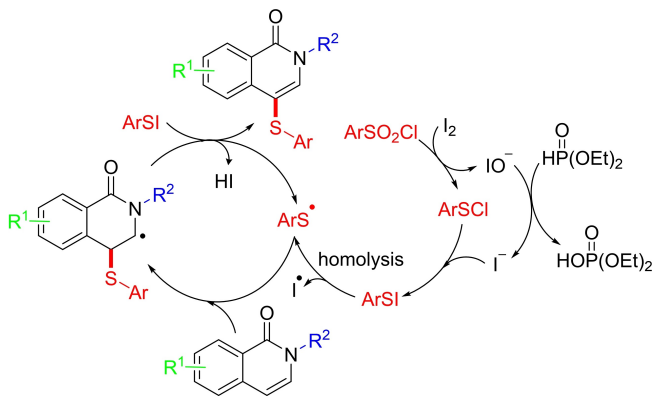
Experimental Section

General Information: All chemicals were purchased from the Wencai New Material Technology and Merck in high purity and were used directly without any purification. Solvents were freshly distilled prior to use. All reactions were carried out under air atmosphere unless noted. ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance III 500 MHz spectrometer in $CDCl_3$ or DMSO-d_6 solution. High resolution mass (HRMS) spectra were measured with a VG Auto Spec-3000 spectrometer. Melting points (mp) were determined with a digital electrothermal apparatus without further correction. TLC analyses were performed on commercial glass plates bearing a 0.25 mm layer of Merck silica gel 60 F254. Silica gel (200–300 mesh) was used for column chromatography.

General experimental procedure for sulfenylation of isoquinolin-1(2*H*)-ones with aryl sulfonyl chlorides: A 10 mL round bottom flask equipped with a magnetic stir bar was charged with a mixture of isoquinolinones (0.2 mmol), aryl sulfonyl chlorides (0.4 mmol, 2.0 equiv.), molecular iodine (I_2) (0.1 mmol, 0.5 equiv), and diethyl phosphite (0.4 mmol, 2 equiv). The vial was capped, and the reaction mixture was stirred at 80 °C for 24 h. Upon completion, saturated $NaHSO_3$ (5 mL) and distilled deionized H_2O (10 mL) was added, and the mixture was extracted with ethyl acetate (3 × 15 mL). The combined organic



Scheme 2. Control experiments.



Scheme 3. Proposed mechanism.

layer was washed with saturated NaCl, dried over anhydrous $MgSO_4$, and concentrated in vacuo. The crude product was purified by SiO_2 column chromatography to afford the desired products.

2-Benzyl-4-(*p*-tolylthio)isoquinolin-1(*2H*)-one (3 aa): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.6. White solid, yield: 88 %, m.p. 99–101 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.48 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.64–7.60 (m, 2H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 4.4 Hz, 4H), 7.32–7.30 (m, 1H), 7.00 (s, 4H), 5.25 (s, 2H), 2.26 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.2, 139.0, 137.2, 136.4, 135.7, 133.5, 132.9, 129.8, 129.0, 128.5, 128.1, 128.1, 127.5, 126.7, 126.6, 125.3, 107.9, 51.9, 20.9 ppm. HRMS (ESI): Calcd for $C_{23}H_{20}NOS$ [M + H$^+$]: 358.1260, Found 358.1264.

2-Benzyl-4-((4-(tert-butyl)phenyl)thio)isoquinolin-1(*2H*)-one (3 ab): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.5. Yellow solid, yield: 86 %, m.p. 140–142 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.49 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.67–7.62 (m, 2H), 7.54–7.50 (m, 1H), 7.35 (d, *J* = 4.4 Hz, 4H), 7.33–7.30 (m, 1H), 7.23–7.19 (m, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 5.25 (s, 2H), 1.25 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.2, 148.8, 139.1, 137.3, 136.3, 133.7, 132.9, 128.9, 128.5, 128.1, 128.1, 127.5, 126.5, 126.1, 126.1, 125.4, 107.7, 51.9, 34.4, 31.2 ppm. HRMS (ESI): Calcd for $C_{26}H_{26}NOS$ [M + H$^+$]: 400.1730, Found 400.1735.

2-Benzyl-4-((4-methoxyphenyl)thio)isoquinolin-1(*2H*)-one (3 ac): Chromatography (EtOAc/dichloromethane = 1 : 100), R_f = 0.3. White solid, yield: 61 %, m.p. 76–78 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.50–8.44 (m, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.65–7.57 (m, 2H), 7.52–7.46 (m, 1H), 7.34 (d, *J* = 4.4 Hz, 4H), 7.31–7.26 (m, 1H), 7.13–7.08 (m, 2H), 6.78–6.72 (m, 2H), 5.23 (s, 2H), 3.72 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.1, 158.3, 138.4, 137.1, 136.4, 132.8, 129.1, 128.9, 128.4, 128.0, 128.0, 127.4, 127.2, 126.5, 125.2, 114.7, 109.0, 55.3, 51.8 ppm.HRMS (ESI): Calcd for $C_{23}H_{20}NO_2S$ [M + H$^+$]: 374.1209, Found 374.1206.

2-Benzyl-4-(*m*-tolylthio)isoquinolin-1(*2H*)-one (3 ad): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.4. Colorless oil, yield: 94 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 8.9 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.66–7.59 (m, 2H), 7.55–7.49 (m, 1H), 7.38–7.33 (m, 4H), 7.31 (dd, *J* = 6.1, 2.6 Hz, 1H), 7.07 (t, *J* = 7.7 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.86 (d, *J* = 7.8 Hz, 1H), 5.26 (s, 2H), 2.23 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.2, 139.2, 138.9, 137.2, 136.9, 136.3, 132.9, 128.9, 128.8, 128.4, 128.0, 128.0, 127.5, 126.7, 126.5, 126.5, 125.3, 123.3, 107.3, 51.8, 21.3 ppm. HRMS (ESI): Calcd for $C_{23}H_{20}NOS$ [M + H$^+$]: 358.1260, Found 358.1263.

2-Benzyl-4-((4-fluorophenyl)thio)isoquinolin-1(*2H*)-one (3 ae): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.4. White solid, yield: 93 %, m.p. 105–107 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.49 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.63 (d, *J* = 5.5 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 4.3 Hz, 4H), 7.32 (dd, *J* = 8.8, 4.6 Hz, 1H), 7.08 (ddt, *J* = 8.2, 5.1, 2.5 Hz, 2H), 6.93–6.88 (m, 2H), 5.26 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.1, 161.3 (d, J_{CF} = 122.8 Hz), 139.1, 136.9, 136.3, 133.0, 132.1 (d, J_{CF} = 12.6 Hz), 129.0, 128.5 (d, J_{CF} = 15.8 Hz), 128.4, 128.1, 127.9 (d, J_{CF} = 30.8 Hz), 126.6, 125.1, 116.3, 116.1, 107.7, 51.9. ppm. HRMS (ESI): Calcd for $C_{22}H_{17}FNOS$ [M + H$^+$]: 362.1009, Found 362.1012.

Benzyl-4-((4-chlorophenyl)thio)isoquinolin-1(*2H*)-one (3 af): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.4. White solid, yield: 89 %, m.p. 124–126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 9.0 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.66–7.61 (m, 2H), 7.56–7.51 (m, 1H), 7.36 (d, *J* = 4.4 Hz, 4H), 7.34–7.30 (m, 1H), 7.17–7.13 (m, 2H), 7.02–6.98 (m, 2H), 5.26 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.2, 139.5, 136.8, 136.2, 135.9, 133.1, 131.5, 129.1, 129.0, 128.6, 128.2, 128.1, 127.8, 127.4, 126.6, 125.1, 106.7, 51.9 ppm. HRMS (ESI): Calcd for $C_{22}H_{17}ClNOS$ [M + H$^+$]: 378.0714, Found 378.0720.

2-Benzyl-4-((4-iodophenyl)thio)isoquinolin-1(*2H*)-one (3 ag): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.4. White solid, yield: 94 %, m.p. 157–159 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.66–7.61 (m, 2H),

7.56–7.51 (m, 1H), 7.50–7.46 (m, 2H), 7.36 (d, J = 4.0 Hz, 4H), 7.34–7.30 (m, 1H), 6.83–6.78 (m, 2H), 5.25 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.2, 139.5, 137.9, 137.6, 136.8, 136.2, 133.1, 129.0, 128.6, 128.2, 128.1, 127.9, 127.8, 126.6, 125.1, 106.4, 90.0, 51.9 ppm. HRMS (ESI): Calcd for $C_{22}H_{17}INOS$ [M + H$^+$]: 470.0070, Found 470.0072.

2-Benzyl-4-((4-nitrophenyl)thio)isoquinolin-1(*2H*)-one (3 ah): Chromatography (EtOAc/dichloromethane = 1 : 100), R_f = 0.3. Yellow solid, yield: 83 %, m.p. 174–176 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.56–8.52 (m, 1H), 8.06–8.01 (m, 2H), 7.74 (d, J = 7.9 Hz, 1H), 7.69–7.63 (m, 2H), 7.60–7.55 (m, 1H), 7.37 (d, J = 4.4 Hz, 4H), 7.35–7.31 (m, 1H), 7.15–7.10 (m, 2H), 5.28 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.1, 147.5, 145.4, 140.2, 136.4, 136.0, 133.4, 129.1, 128.9, 128.3, 128.1, 126.6, 125.4, 124.6, 124.2, 104.6, 52.0 ppm. HRMS (ESI): Calcd for $C_{22}H_{17}N_2O_3S$ [M + H$^+$]: 389.0954, Found 389.0960.

2-Benzyl-4-((4-(trifluoromethyl)phenyl)thio)isoquinolin-1(*2H*)-one (3 ai): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.4. White solid, yield: 89 %, m.p. 145–147 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.52 (dd, J = 8.1, 1.0 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.68–7.63 (m, 2H), 7.58–7.53 (m, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 4.4 Hz, 4H), 7.35–7.30 (m, 1H), 7.12 (d, J = 8.3 Hz, 2H), 5.27 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.1, 142.7, 139.9, 136.4 (d, J_{CF} = 35.9 Hz), 133.2, 129.0, 128.7, 128.3, 128.2, 128.1, 127.9, 126.6, 125.8 (q, J_{CF} = 3.8 Hz), 125.5, 124.9, 105.5, 52.0. ppm. HRMS (ESI): Calcd for $C_{23}H_{17}F_3NOS$ [M + H$^+$]: 412.0977, Found 412.0981.

4-((2-Benzyl-1-oxo-1,2-dihydroisoquinolin-4-yl)thio)benzonitrile (3 aj): Chromatography (EtOAc/petroleum ether = 1 : 6), R_f = 0.3. Yellow solid, yield: 76 %, m.p. 128–130 °C. ^{1}H NMR(500 MHz, DMSO-d_6) δ = 8.36–8.31 (m, 2H), 7.76 (ddd, J = 8.3, 7.1, 1.2 Hz, 1H), 7.73–7.67 (m, 3H), 7.63–7.58 (m, 1H), 7.41–7.33 (m, 5H), 7.32–7.25 (m, 3H), 5.27 (s, 2H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ = 161.5, 145.3, 142.8, 137.6, 136.8, 133.9, 133.3, 132.6, 129.1, 128.5, 128.3, 128.1, 128.1, 126.9, 126.5, 126.3, 124.7, 119.2, 108.1, 103.0, 51.8 ppm. HRMS (ESI): Calcd for $C_{23}H_{17}N_2OS$ [M + H$^+$]: 369.1056, Found 369.1050.

2-Benzyl-4-(phenylthio)isoquinolin-1(*2H*)-one (3 ak): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.5. White solid, yield: 97 %, m.p. 97–99 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.50 (d, J = 8.6 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.66–7.60 (m, 2H), 7.52 (t, J = 7.5 Hz, 1H), 7.36 (d, J = 4.7 Hz, 4H), 7.33–7.30 (m, 1H), 7.19 (t, J = 7.6 Hz, 2H), 7.12–7.06 (m, 3H), 5.26 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.4, 139.5, 137.5, 137.3, 136.5, 133.1, 129.4, 129.2, 129.1, 128.7, 128.3, 128.2, 128.0, 127.8, 126.7, 126.3, 125.7, 125.5, 107.3, 52.1 ppm. HRMS (ESI): Calcd for $C_{22}H_{18}NOS$ [M + H$^+$]: 344.1104, Found 344.1106.

2-Benzyl-4-(pyridin3-ylthio)isoquinolin-1(*2H*)-one (3 al): Chromatography (EtOAc/petroleum ether = 1 : 2), R_f = 0.3. Yellow oil, yield: 59 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.50 (d, J = 9.0 Hz, 1H), 8.40 (s, 1H), 8.34 (d, J = 3.9 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.69–7.61 (m, 2H), 7.56–7.50 (m, 1H), 7.36 (d, J = 4.4 Hz, 4H), 7.34–7.30 (m, 2H), 7.09 (dd, J = 8.0, 4.7 Hz, 1H), 5.26 (s, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.1, 147.3, 146.8, 139.7, 136.6, 136.1, 134.5, 133.7, 133.2, 129.0, 128.7, 128.2, 128.0, 127.8, 126.6, 124.9, 123.7, 105.7, 51.9 ppm. HRMS (ESI): Calcd for $C_{21}H_{17}N_2OS$ [M + H$^+$]: 345.1056, Found 345.1053.

4-(*p*-Tolylthio)isoquinolin-1(*2H*)-one (4 aa):[14d,19] Chromatography (EtOAc/petroleum ether = 1 : 2), R_f = 0.3. Pink solid, yield: 79 %, m.p. 165–167 °C.^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.00 (s, 1H), 8.47–8.42 (m, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.71–7.63 (m, 2H), 7.57–7.51 (m, 1H), 7.10–6.99 (m, 4H), 2.27 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 163.9, 138.2, 135.7, 135.3, 133.4, 133.4, 129.8, 127.8, 127.5, 126.9, 126.4, 125.6, 108.5, 20.9 ppm. HRMS (ESI): Calcd for $C_{16}H_{14}NOS$ [M + H$^+$]: 268.0791, Found 268.0794.

2-Methyl-4-(*p*-tolylthio)isoquinolin-1(*2H*)-one (4 ab): Chromatography (EtOAc/petroleum ether = 1 : 4), R_f = 0.2. Yellow solid, yield: 90 %, m.p. 145–147 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.49–8.43 (m, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.65–7.59 (m, 2H), 7.53–7.48 (m, 1H), 7.03 (t, J = 2.7 Hz, 4H), 3.65 (s, 3H), 2.26 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.6, 140.1, 137.4, 135.6, 133.7, 132.7, 129.8, 128.1, 127.4, 126.6, 126.3, 125.3, 107.3, 37.1, 20.9 ppm. HRMS (ESI): Calcd for $C_{17}H_{16}NOS$ [M + H$^+$]: 282.0947, Found 282.0954.

2-Ethyl-4-(*p*-tolylthio)isoquinolin-1(*2H*)-one (4 ac): Chromatography (EtOAc/petroleum ether = 1 : 6), R_f = 0.4.Yellow oil, yield: 87 %. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.46 (d, J = 7.3 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.64–7.58 (m, 2H), 7.53–7.47 (m, 1H), 7.03 (s, 4H), 4.10 (q, J = 7.2 Hz, 2H), 2.26 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 161.9, 139.0, 137.3, 135.6, 133.8, 132.7, 129.8, 128.2, 127.4, 126.6, 126.5, 125.2, 107.4, 44.6, 20.9, 14.7 ppm. HRMS (ESI): Calcd for $C_{18}H_{18}NOS$ [M + H$^+$]: 296.1104, Found 296.1110.

2-Butyl-4-(*p*-tolylthio)isoquinolin-1(*2H*)-one (4 ad): Chromatography (EtOAc/petroleum ether = 1 : 8), R_f = 0.5. Yellow solid, yield: 78 %, m.p. 104–106 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.46 (d, J = 8.9 Hz, 1H), 7.90 (d, J = 7.9 Hz, 1H), 7.64–7.58 (m, 2H), 7.52–7.47 (m, 1H), 7.02 (s, 4H), 4.07–4.01 (m, 2H), 2.26 (s, 3H), 1.80 (p, J = 7.6 Hz, 2H), 1.42 (dq, J = 14.8, 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.1, 139.5, 137.2, 135.5, 133.8, 132.7, 129.8, 128.2, 127.3, 126.5, 126.5, 125.2, 107.0, 49.3, 31.4, 20.9, 20.0, 13.8 ppm. HRMS (ESI): Calcd for $C_{20}H_{22}NOS$ [M + H$^+$]: 324.1417, Found 324.1421.

Ethyl-2-(1-oxo-4-(*p*-tolythio)isoquinolin-2(1H)-yl)acetate (4 ae): Chromatography (EtOAc/petroleum ether = 1 : 4), R_f = 0.4. White solid, yield: 73 %, m.p. 132–134 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.44 (d, J = 8.9 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.55 (s, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.06 (d, J = 8.3 Hz, 2H), 7.02 (d, J = 8.3 Hz, 2H), 4.74 (s, 2H), 4.26 (q, J = 7.1 Hz, 2H), 2.26 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 167.8, 162.2, 139.4, 137.4, 135.7, 133.4, 133.1, 129.8, 128.3, 127.6, 126.7, 126.1, 125.4, 107.9, 62.0, 50.1, 20.9, 14.1 ppm. HRMS (ESI): Calcd for $C_{20}H_{20}NO_3S$ [M + H$^+$]: 354.1158, Found 354.1161.

2-(*p*-Tolyl)-4-(*p*-tolylthio)isoquinolin-1(*2H*)-one (4 af): Chromatography (EtOAc/petroleum ether = 1 : 10), R_f = 0.4. White solid, yield: 86 %, m.p. 124–126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.52–8.48 (m, 1H), 7.95 (d, J = 7.9 Hz, 1H), 7.72 (s, 1H), 7.66 (td, J = 8.3, 7.8, 1.3 Hz, 1H), 7.56–7.50 (m, 1H), 7.33 (q, J = 8.3 Hz, 4H), 7.09 (d, J = 8.3 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 2.42 (s, 3H), 2.27 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 162.0, 139.7, 138.4, 138.0, 137.3, 135.7, 133.5, 133.1, 130.0, 129.8, 128.7, 127.7, 126.7, 126.5, 125.4, 107.7, 21.2, 20.9 ppm.

5-Methyl-4-(*p*-tolylthio)isoquinolin-1(*2H*)-one (4 ag):[19] Chromatography (EtOAc/petroleum ether = 1 : 2), R_f = 0.3. Pink solid, yield: 21 %. ^{1}H NMR (500 MHz, CDCl3) δ = 11.09 (s, 1H), 8.43 (d, J = 7.7 Hz, 1H), 7.61 (s, 1H), 7.47 (d, J = 6.8 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.04 (d, J = 8.1 Hz, 2H), 6.95 (d, J = 8.2 Hz, 2H), 2.86 (s, 3H), 2.27 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 164.4, 138.0, 137.5, 137.0, 136.7, 135.8, 135.1, 129.9, 127.6, 127.1, 126.7, 125.4, 107.2, 23.4, 20.9 ppm.

6-Methoxy-4-(*p*-tolylthio)isoquinolin-1(*2H*)-one (4 ah): Chromatography (EtOAc/petroleum ether = 1 : 1), R_f = 0.2. Pink solid, yield: 78 %, m.p. 237–239 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.08 (s, 1H), 8.34 (d, J = 8.9 Hz, 1H), 7.65 (s, 1H), 7.36 (d, J = 2.5 Hz,

1H), 7.12–7.06 (m, 3H), 7.03 (d, J = 8.1 Hz, 2H), 3.79 (s, 3H), 2.27 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ = 163.6, 163.6, 140.6, 136.0, 135.9, 133.3, 129.9, 129.8, 127.2, 119.9, 116.9, 108.3, 106.7, 55.5, 20.9 ppm. HRMS (ESI): Calcd for $C_{17}H_{16}NO_2S$ [$M+H^+$]: 298.0896, Found 298.0900.

6-Chloro-4-(*p*-tolylthio)isoquinolin-1(2*H*)-one (4 ai):[19] Chromatography (EtOAc/petroleum ether = 1:1), R_f = 0.2. Pink solid, yield: 61 %. ^{1}H NMR (500 MHz, DMSO-d_6) δ = 11.91 (d, J = 5.5 Hz, 1H), 8.24 (d, J = 8.5 Hz, 1H), 7.77 (d, J = 6.0 Hz, 1H), 7.73 (d, J = 2.0 Hz, 1H), 7.57 (dd, J = 8.5, 2.1 Hz, 1H), 7.09 (s, 4H), 2.22 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ = 161.6, 139.7, 139.7, 138.7, 135.9, 133.4, 130.5, 130.4, 127.8, 127.0, 125.6, 124.1, 104.0, 20.9 ppm.

6-Bromo-4-(*p*-tolylthio)isoquinolin-1(2*H*)-one (4 aj):[19] Chromatography (EtOAc/petroleum ether = 1:1), R_f = 0.2. Pink solid, yield: 57 %. ^{1}H NMR (500 MHz, DMSO-d_6) δ = 11.91 (d, J = 5.4 Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.90 (d, J = 1.9 Hz, 1H), 7.76 (d, J = 6.0 Hz, 1H), 7.70 (dd, J = 8.5, 1.9 Hz, 1H), 7.09 (s, 4H), 2.22 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ = 161.7, 139.8, 139.6, 135.9, 133.4, 130.6, 130.5, 130.4, 127.9, 127.2, 127.0, 125.9, 103.8, 20.9 ppm.

Supporting Information

(See footnote on the first page of this article): Full experimental details, ^{1}H and ^{13}C NMR spectra can be found in the supplementary content section of this article's web page.

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Conflict of Interest

The authors declare no conflict of interest.

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[1] a) Z. Jin, *Nat. Prod. Rep.* **2013**, *30*, 849–868; b) N. Kaila, B. Follows, L. Leung, J. Thomason, A. Huang, A. Moretto, K. Janz, M. Lowe, T. S. Mansour, C. Hubeau, K. Page, P. Morgan, S. Fish, X. Xu, C. Williams, E. Saiah, *J. Med. Chem.* **2014**, *57*, 1299–1322; c) G. R. Pettit, S. Ducki, S. A. Eastham, N. Melody, *J. Nat. Prod.* **2009**, *72*, 1279–1282; d) A. Cappelli, G. I. Pericot Mohr, G. Giuliani, S. Galeazzi, M. Anzini, L. Mennuni, F. Ferrari, F. Makovec, E. M. Kleinrath, T. Langer, M. Valoti, G. Giorgi, S. Vomero, *J. Med. Chem.* **2006**, *49*, 6451–6464; e) A. L. Ruchelman, P. J. Houghton, N. Zhou, A. Liu, L. F. Liu, E. J. LaVoie, *J. Med. Chem.* **2005**, *48*, 792–804; f) M. Nagarajan, A. Morrell, B. C. Fort, M. R. Meckley, S. Antony, G. Kohlhagen, Y. Pommier, M. Cushman, *J. Med. Chem.* **2004**, *47*, 5651–5661; g) M. C. González, C. Zafra-Polo, M. A. Blázquez, A. Serrano, D. Cortes, *J. Nat. Prod.* **1997**, *60*, 108–110.

[2] a) K. R. Fales, F. G. Njoroge, H. B. Brooks, S. Thibodeaux, A. Torrado, C. Si, J. L. Toth, J. R. Mc Cowan, K. D. Roth, K. J. Thrasher, K. Frimpong, M. R. Lee, R. D. Dally, T. A. Shepherd, T. B. Durham, B. J. Margolis, Z. Wu, Y. Wang, S. Atwell, J. Wang, Y.-H. Hui, T. I. Meier, S. A. Konicek, S. Geeganage, *J. Med. Chem.* **2017**, *60*, 9599–9616; b) E. Goodfellow, Z. Senhaji Mouhri, C. Williams, B. J. Jean-Claude, *Bioorg. Med. Chem. Lett.* **2017**, *27*, 688–694; c) T. Bosanac, E. R. Hickey, J. Ginn, M. Kashem, S. Kerr, S. Kugler, X. Li, A. Olague, S. Schlyer, E. R. R. Young, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3746–3749; d) J. Roth, F. Madoux, P. Hodder, W. R. Roush, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2628–2632; e) R. M. Garbaccio, S. Huang, E. S. Tasber, M. E. Fraley, Y. Yan, S. Munshi, M. Ikuta, L. Kuo, C. Kreatsoulas, S. Stirdivant, B. Drakas, K. Rickert, E. S. Walsh, K. A. Hamilton, C. A. Buser, J. Hardwick, X. Mao, S. C. Beck, M. T. Abrams, W. Tao, R. Lobell, L. Sepp-Lorenzino, G. D. Hartman, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6280–6285.

[3] a) D. Das, P. Poddar, S. Maity, R. Samanta, *J. Org. Chem.* **2017**, *82*, 3612–3621; b) Y.-Q. Zhu, Y.-X. Niu, L.-W. Hui, J.-L. He, K. Zhu, *Adv. Synth. Catal.* **2019**, *361*, 2897–2903; c) J. A. Boerth, J. R. Hummel, J. A. Ellman, *Angew. Chem. Int. Ed.* **2016**, *55*, 12650–12654; *Angew. Chem.* **2016**, *128*, 12840–12844; d) J. Xia, L. Kong, X. Zhou, G. Zheng, X. Li, *Org. Lett.* **2017**, *19*, 5972–5975; e) D. Das, A. Biswas, U. Karmakar, S. Chand, R. Samanta, *J. Org. Chem.* **2016**, *81*, 842–848; f) P. Peng, J. Wang, H. Jiang, H. Liu, *Org. Lett.* **2016**, *18*, 5376–5379; g) S.-Y. Chen, Q. Li, H. Wang, *J. Org. Chem.* **2017**, *82*, 11173–11181; h) J. Ni, H. Zhao, A. Zhang, *Org. Lett.* **2017**, *19*, 3159–3162; i) M. Min, D. Kang, S. Jung, S. Hong, *Adv. Synth. Catal.* **2016**, *358*, 1296–1301; j) D. Das, R. Samanta, *Adv. Synth. Catal.* **2018**, *360*, 379–384; k) L. Zhang, X. Zheng, J. Chen, K. Cheng, L. Jin, X. Jiang, C. Yu, *Org. Chem. Front.* **2018**, *5*, 2969–2973; l) A. Biswas, D. Giri, D. Das, A. De, S. K. Patra, R. Samanta, *J. Org. Chem.* **2017**, *82*, 10989–10996; m) M. Tian, B. Liu, J. Sun, X. Li, *Org. Lett.* **2018**, *20*, 4946–4949; n) X. Zhou, Y. Pan, X. Li, *Angew. Chem. Int. Ed.* **2017**, *56*, 8163–8167; *Angew. Chem.* **2017**, *129*, 8275–8279; o) Y. Li, F. Xie, X. Li, *J. Org. Chem.* **2016**, *81*, 715–722.

[4] H. B. Rode, M. L. Sos, C. Grütter, S. Heynck, J. R. Simard, D. Rauh, *Bioorg. Med. Chem.* **2011**, *19*, 429–439.

[5] a) J. Y. Q. Lai, Y. Ferguson, M. Jones, *Synth. Commun.* **2003**, *33*, 3427–3433; b) J. Y. Q. Lai, S. Langston, R. Adams, R. E. Beevers, R. Boyce, S. Burckhardt, J. Cobb, Y. Ferguson, E. Figueroa, N. Grimster, A. H. Henry, N. Khan, K. Jenkins, M. W. Jones, R. Judkins, J. Major, A. Masood, J. Nally, H. Payne, L. Payne, G. Raphy, T. Raynham, J. Reader, V. Reader, A. Reid, P. Ruprah, M. Shaw, H. Sore, M. Stirling, A. Talbot, J. Taylor, S. Thompson, H. Wada, D. Walker, *Med. Res. Rev.* **2005**, *25*, 310–330.

[6] S. Lee, S. Mah, S. Hong, *Org. Lett.* **2015**, *17*, 3864–3867.

[7] A. C. Shaikh, D. R. Shinde, N. T. Patil, *Org. Lett.* **2016**, *18*, 1056–1059.

[8] A. D. Sercel, J. P. Sanchez, H. D. Hollis Showalter, *Synth. Commun.* **2007**, *37*, 4199–4208.

[9] a) A. Ansari, S. Satalkar, V. Patil, A. S. Shete, S. Kaur, A. Gupta, S. Singh, M. Raja, D. L. Severance, S. Bernales, S. Chakravarty, D. T. Hung, S. M. Pham, F. J. Herrera, R. Rai, *Bioorg. Med. Chem. Lett.* **2017**, *27*, 217–222; b) K.-H. Rimböck, A. Pöthig, T. Bach, *Synthesis* **2015**, *47*, 2869–2884; c) K. A. B. Austin, E. Herdtweck, T. Bach, *Angew. Chem. Int. Ed.* **2011**, *50*, 8416–8419; *Angew. Chem.* **2011**, *123*, 8566–8569.

[10] P. V. Fish, C. G. Barber, D. G. Brown, R. Butt, M. G. Collis, R. P. Dickinson, B. T. Henry, V. A. Horne, J. P. Huggins, E. King, M. O'Gara, D. McCleverty, F. McIntosh, C. Phillips, R. Webster, *J. Med. Chem.* **2007**, *50*, 2341–2351.

[11] D. A. Price, K. James, S. Osborne, G. W. Harbottle, *Tetrahedron Lett.* **2007**, *48*, 7371–7373.

[12] a) C. Shen, P. Zhang, Q. Sun, S. Bai, T. S. A. Hor, X. Liu, *Chem. Soc. Rev.* **2015**, *44*, 291–314; b) X. Zhu, Y. Yang, G. Xiao, J. Song, Y. Liang, G. Deng, *Chem. Commun.* **2017**, *53*, 11917–11920; c) T. Kittikool, S. Yotphan, *Eur. J. Org. Chem.* **2020**, *2020*, 961–970; d) Y.-S. Kang, P. Zhang, M.-Y. Li, Y.-K. Chen, H.-J. Xu, J. Zhao, W.-Y. Sun, J.-Q. Yu, Y. Lu, *Angew. Chem. Int. Ed.* **2019**, *58*, 9099–9103; e) T. Gensch, F. J. R. Klauck, F. Glorius, *Angew. Chem. Int. Ed.* **2016**, *55*, 11287–11291; *Angew. Chem.* **2016**, *128*, 11457–11461.

[13] a) S. Zhu, Y. Zhang, J. Luo, F. Wang, X. Cao, S. Huang, *Green Chem.* **2020**, *22*, 657–661; b) Y. Jiang, Y.-Y. Feng, J.-X. Zou, S. Lei, X.-l. Hu, G.-F. Yin, W. Tan, Z. Wang, *J. Org. Chem.* **2019**, *84*, 10490–10500; c) L.-Y. Xie, Y.-L. Chen, L. Qin, Y. Wen, J.-W. Xie, J.-X. Tan, Y. Huang, Z. Cao, W.-M. He, *Org. Chem. Front.* **2019**, *6*, 3950–3955; d) F.-L. Zeng, X.-L. Chen, S.-Q. He, K. Sun, Y. Liu, R. Fu, L.-B. Qu, Y.-F. Zhao, B. Yu, *Org. Chem. Front.* **2019**, *6*, 1476–1480; e) G. S. Sorabad, M. R. Maddani, *Asian J. Org. Chem.* **2019**, *8*, 1336–1343.

[14] a) K.-A. Green, J. M. Hoover, *ACS Catal.* **2020**, *10*, 1769–1782; b) X. Huang, J. Li, X. Li, J. Wang, Y. Peng, G. Song, *RSC Adv.* **2019**, *9*, 26419–26424; c) G. Shi, R. Khan, X. Zhang, Y. Yang, Y. Zhan, J. Li, Y. Luo, B. Fan, *Asian J. Org. Chem.* **2020**, *9*, 788–792; d) K. Phakdeeyothin, S. Yotphan, *Org. Biomol. Chem.* **2019**, *17*, 6432–6440.

[15] a) Y.-Z. Ji, H.-J. Li, J.-Y. Zhang, Y.-C. Wu, *Chem. Commun.* **2019**, *55*, 11864–11867; b) F. Zhao, Q. Tan, D. Wang, J. Chen, G.-J. Deng, *Adv. Synth. Catal.* **2019**, *361*, 4075–4081.
[16] a) F.-L. Yang, S.-K. Tian, *Angew. Chem. Int. Ed.* **2013**, *52*, 4929–4932; *Angew. Chem.* **2013**, *125*, 5029–5032; b) R. Singh, D. S. Raghuvanshi, K. N. Singh, *Org. Lett.* **2013**, *15*, 4202–4205; c) X. Kang, R. Yan, G. Yu, X. Pang, X. Liu, X. Li, L. Xiang, G. Huang, *J. Org. Chem.* **2014**, *79*, 10605–10610; d) S.-r. Guo, W.-m. He, J.-n. Xiang, Y.-q. Yuan, *Chem. Commun.* **2014**, *50*, 8578–8581.
[17] a) J. Hu, X. Ji, S. Hao, M. Zhao, M. Lai, T. Ren, G. Xi, E. Wang, J. Wang, Z. Wu, *RSC Adv.* **2020**, *10*, 31819–31823; b) Q. Wu, D. Zhao, X. Qin, J. Lan, J. You, *Chem. Commun.* **2011**, *47*, 9188–9190; c) F. Zhao, Q. Tan, D. Wang, G.-J. Deng, *Green Chem.* **2020**, *22*, 427–432; d) X. Yu, Q. Wu, H. Wan, Z. Xu, X. Xu, D. Wang, *RSC Adv.* **2016**, *6*, 62298–62301; e) W. Zhao, A. Zhou, *ChemCatChem* **2015**, *7*, 3464–3467; f) Y. Chen, F. Xiao, H. Chen, S. Liu, G.-J. Deng, *RSC Adv.* **2014**, *4*, 44621–44628.
[18] K. Nagarajan, V. R. Rao, R. K. Shah, S. J. Shenoy, H. Fritz, W. J. Richter, D. Muller, *Helv. Chim. Acta* **1988**, *71*, 77–92.
[19] Y.-Q. Zhu, J.-L. He, Y.-X. Niu, H.-Y. Kang, T.-F. Han, H.-Y. Li, *J. Org. Chem.* **2018**, *83*, 9958–9967.
[20] a) G. Huang, H. Sun, X. Qiu, C. Jin, C. Lin, Y. Shen, J. Jiang, L. Wang, *Org. Lett.* **2011**, *13*, 5224–5227; b) Y. Ma, M. Na, Y. Gu, G. Huang, X. Li, Y. Chen, *Appl. Organomet. Chem.* **2015**, *29*, 165–169; c) G. Huang, M. Teng, B. Liu, M. Rong, Y. Liu, Y. Chen, *J. Organomet. Chem.* **2016**, *818*, 163–167; d) F. Li, X.-J. Gu, C.-E. Zeng, X. Li, B. Liu, G.-L. Huang, *Eur. J. Org. Chem.* **2020**, 2923–2928.

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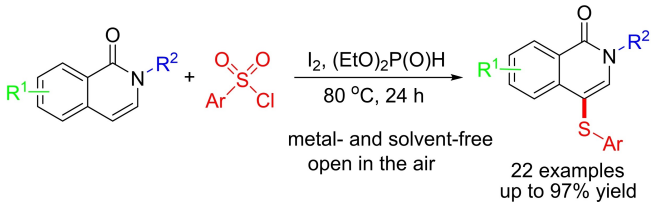

*C.-Y. Yang, X. Li, Dr. B. Liu, Dr. G.-L. Huang**

Iodine-promoted regioselective C-4 sulfenylation of isoquinolin-1(2*H*)-ones using commercially available aryl sulfonyl chlorides as the sulfur source under metal- and solvent-free conditions was described. These methods provide an alternative and facile synthetic route to access a series of 4-arylthio-substituted isoquinolin-1(2*H*)-one derivatives in moderate to good yields. This is a useful, time-efficient, and scalable procedure for the construction of C(sp^2)–S bonds.