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AN EFFICIENT SYNTHESIS OF 3-(ARYLSULFANYL)QUINOLIN-4(1*H*)-ONES *VIA* CYCLIZATION OF *N*-{2-[2-(ARYLSULFANYL)ACETYL]PHENYL}BENZAMIDES WITH *N*,*N*-DIMETHYLFORMAMIDE DIMETHYL ACETAL

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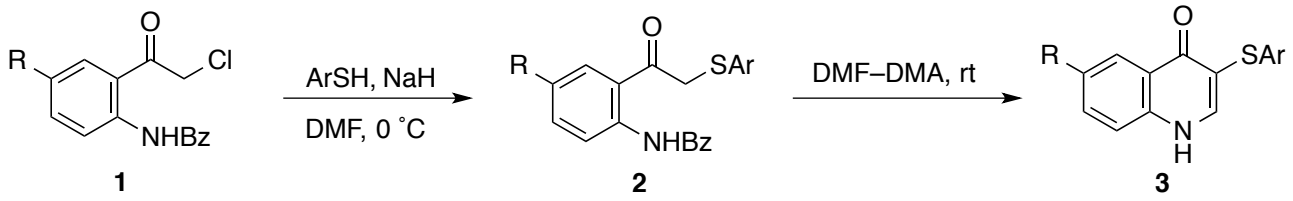
Abstract – The reaction of *N*-[2-(2-chloroacetyl)phenyl]benzamides, readily derived from 2-(2,2-dichloroethenyl)benzenamines, with sodium arenethiolates gives the corresponding *N*-{2-[2-(arylsulfanyl)acetyl]phenyl}benzamides. These are treated with *N*,*N*-dimethylformaide dimethyl acetal (DMF–DMA) to yield 3-(arylsulfanyl)quinolin-4(1*H*)-ones in generally good yields.

Compounds with the quinolin-4(1*H*)-one structure exhibit a wide variety of biological activities of pharmaceutical interest.[1] For example, a 2-(aryloxymethyl)-3-methyl derivatives is a NAD(P)H inhibitor,[1c] some 8-(3*H*-[1,2,3]triazol-4-yl) derivatives are inhibitors of phosphatidylinositol 3-kinases,[1e] and some 3-aryl derivatives have been reported to exhibit potential anticancer activity.[1f] Utilizations of quinolin-4(1*H*)-ones for the preparation of structurally more complex compounds has also been reported.[2] Therefore, in recent years effort has been directed to the development of efficient methods for the construction of this heterocyclic skeleton.[3] However, there have been only a few reports on the preparation of 2-(arylsulfanyl)quinolin-4(1*H*)-ones.[4,5] For example, Ivachtchenko *et al*. have reported the synthesis of 2-(phenylsulfanyl)quinolin-4(1*H*)-one and its transformation into 4-substituted 3-(phenylsulfonyl)quinolines as potential antagonists of serotonin 5-HT_6 receptors.[4] New general methodology is of considerable potential value for synthetic organic and medicinal chemistries. On the other hand, we have recently reported that 2-aryl-4-(2,2-dihalomethylidene)-4*H*-3,1-benzoxazines can be prepared by treating *N*-[2-(2,2-dihaloethenyl)phenyl]arenecarboxamides with sodium hydride,[6] and that these 2-aryl-4-(2,2-dichloromethylidene)-4*H*-3,1-benzoxazines are hydrolyzed under acidic conditions to give *N*-[2-(2-chloroacetyl)phenyl]arenecarboxamides, which provides, *via* cyclization with triethylamine

in the presence of di-*tert*-butyl dicarbonate, 1,2-dihydro-3*H*-indol-3-ones.[7] In this paper, we disclose, as an extensive utilization of these chloroacetyl amides, an efficient synthesis of 2-(arylsulfanyl)quinolin-4(1*H*)-ones (**3**) from *N*-[2-(2-chloroacetyl)phenyl]benzamides (**1**) by an easy two step sequence.

Our study was initiated by reacting *N*-[2-(2-chloroacetyl)phenyl]benzamide (**1a**) with sodium benzenethiolate, generated *in situ* by treating benzenethiol with sodium hydride in DMF at 0 ˚C, in order to produce *N*-{2-[2-(phenylsulfanyl)acetyl]phenyl}benzamides (**2a**). The substitution reaction proceeded rapidly and cleanly at 0 ˚C to afford the desired product in high yield. The reaction could not be monitored by TLC on silica, and was monitored by ^{1}H NMR spectroscopy using sampling specimens. Similarly, by using the other two *N*-[2-(2-chloroacetyl)phenyl]benzamides (**1b)** and **(1c**) and the other four arenethiols, the other nine *N*-{2-[2-(arylsulfanyl)acetyl]phenyl}benzamides (**2**) were produced (Scheme 1). The yields are generally good as summarized in Table 1.



1 **2** **3**

Scheme 1

Table 1. Preparation of 3-(arylsulfanyl)quinolin-4(1*H*)-ones (**3**)

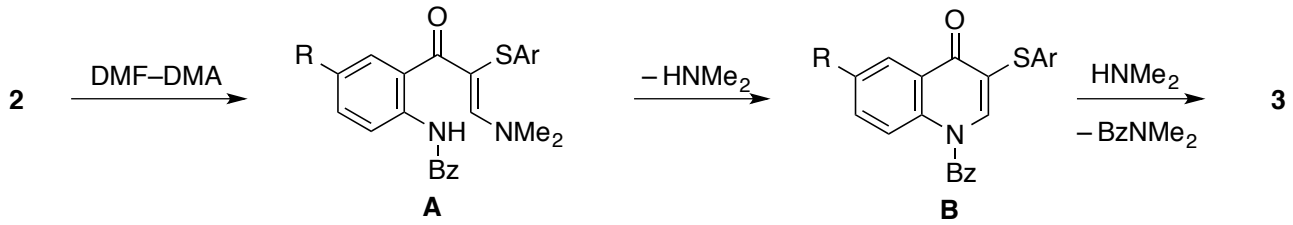
Entry	**1**	Ar in ArSH	**2**	Yield/%[a]	**3**	Yield/%[a]
1	**1a** (R = H)	Ph	**2a**	90	**3a**	77
2	**1a**	4-MeC_6H_4	**2b**	81	**3b**	89
3	**1a**	4-ClC_6H_4	**2c**	82	**3c**	78
4	**1a**	3-MeOC_6H_4	**2d**	82	**3d**	81
5	**1a**	naphthalen-2-yl	**2e**	73	**3e**	95
6	**1b** (R = Cl)	Ph	**2f**	61	**3f**	56
7	**1b**	naphthalen-2-yl	**2g**	85	**3g**	67
8	**1c** (R = OMe)	Ph	**2h**	91	**3h**	76
9	**1c**	4-ClC_6H_4	**2i**	94	**3i**	68
10	**1c**	3-MeOC_6H_4	**2j**	87	**3j**	85

[a] Yields of isolated products

The compounds (**2**), thus obtained, were allowed to react with *N*,*N*-dimethylformaide dimethyl acetal (DMF–DMA) at room temperature. The reactions were easily monitored by TLC on silica gel and were complete within 5 h to afford 3-(arylsulfanyl)quinolin-4(1*H*)-ones (**3**). The yields of the products are also compiled in Table 1 and are generally good to excellent, though those of the 6-chloro derivatives (**3f**) and (**3g**) are only moderate-to-fair as can be seen from Entries 6 and 7. The diminished yields of these products may be ascribed to the chloro substituent, which decrease nucleophilicity of the amide nitrogen.

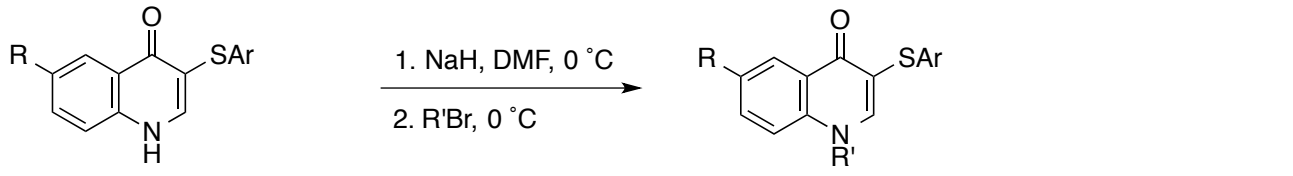
In the previous paper,[4] the authors present the structure of **3a** as 3-(phenylsulfanyl)quinolin-4-ol. However, the spectral data for **3a** obtained by us reveal that **3a** is 3-(phenylsulfanyl)quinolin-4(1*H*)-one (see Experimental).

Products (**3**) are thought to be produced from **1** *via* the intermediates (**A**) and (**B**), as illustrated in Scheme 2. Thus, the (dimethylamino)methylidene intermediates (**A**) are first formed by reacting **2** with DMF–DMA. Intramolecular conjugate addition and the subsequent elimination of dimethylamine give the 1-benzoyl-3-(arylsulfanyl)quinolin-4(1*H*)-one intermediates (**B**), of which debenzoylation with dimethylamine leads to **3**. No more than trace amount of the 1-benzoylquinolinone product could be detected in each case.



Scheme 2

When compounds (**3**) were treated successively with sodium hydride and haloalkanes in DMF at 0 ˚C, 1-alkyl-3-(arylsulfanyl)quinolin-4(1*H*)-ones (**4**) were obtained in relatively good yields,[8] as shown in Scheme 3. We assumed that the 3-arylsulfanyl group increases the nucleophilicity of the nitrogen.



4a R = H, Ar = Ph, R' = Bn 76%
4b R = MeO, Ar =Ph, R' = *c*-$PrCH_2$ 56%
4c R = MeO, Ar =4-ClC_6H_4, R' = $NCCH_2$ 68%

Scheme 3

The forgoing results have indicated that 3-(arylsulfanyl)quinolin-4(1*H*)-ones can be prepared using a two-step sequence from *N*-{2-[2-(arylsulfanyl)acetyl]phenyl}benzamides. Since the present synthesis uses readily available starting materials and is achieved by operationally very simple procedure, it represents a versatile method for the general preparation of this type of quinolin-4(1*H*)-ones, which are hard to prepare by previous methods. Further investigation on the synthesis of related heterocycles utilizing this methodology is now under way in our laboratory.

EXPERIMENTAL

All melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer Spectrum 65 FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 and 125 MHz, respectively. High-resolution MS spectra were measured by a JEOL JMS-T100GCV spectrometer (EI or FI, TOF; 70eV or 2100V, respectively) or a Thermo Scientific Exactive spectrometer (ESI, positive). Elemental analyses were performed with an Elementar Vario EL II instrument. TLC was carried out on Merck Kieselgel 60 PF_{254}. Column chromatography was performed using WAKO GEL C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

Starting Materials. *N*-[(2-Chloroacetyl)phenyl]benzamide (**1a**) and *N*-[(2-chloroacetyl)phenyl]-4-methoxybenzamide (**1c**) were prepared according to the reported procedure.[7] All other chemicals used in this study were commercially available.

***N*-[4-Chloro-(2-chloroacetyl)phenyl]benzamide (1b).** This compound were prepared from 4-chloro-2-(2,2-dichloroethenyl)benzenamines[7] according to the reported sequence,[7] *via* the corresponding benzamide and benzoxazine derivatives.

***N*-[4-Chloro-2-(2,2-dichloroethenyl)phenyl]benzamide:** yield: 87%; a white solid; mp 126–128 ˚C (hexane/CH_2Cl_2); IR (KBr) 3212, 1651, 1624, 1608 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.83 (s, 1H), 7.38 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.39 (d, *J* = 2.3 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.69 (br s, 1H), 7.87 (d, *J* = 7.4 Hz, 2H), 8.08 (d, *J* = 9.1 Hz, 1H). Anal. Calcd for $C_{15}H_{10}Cl_3NO$: C, 55.16; H, 3.09; N, 4.29. Found: C, 55.08; H, 3.13; N, 4.32.

6-Chloro-4-(*Z*)-(chloromethylidene)-2-phenyl-4*H*-3,1-benzoxazine: yield: 82%; a white solid; mp 162–164 ˚C (hexane/CH_2Cl_2); IR (KBr) 1637, 1612 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.87 (s, 1H), 7.18–7.23 (m, 3H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 8.14 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 93.83, 120.70, 121.04, 128.01, 128.23, 128.48, 130.50, 130.96, 132.20, 133.08, 136.85, 145.13, 154.17. Anal. Calcd for $C_{15}H_9Cl_2NO$: C, 62.10; H, 3.13; N, 4.83. Found: C, 61.91; H, 3.12; N, 4.76.

***N*-[4-Chloro-2-(2-chloroacetyl)phenyl]benzamide (1b):** yield: 94%; white needles; mp 121–123 ˚C (hexane/CH_2Cl_2); IR (KBr) 3240, 1671, 1605 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.80 (s, 2H), 7.53–7.64 (m, 4H), 7.84 (d, *J* = 2.3 Hz, 1H), 8.05 (d, *J* = 7.6 Hz, 2H), 9.03 (d, *J* = 9.2 Hz, 1H), 12.21 (br s, 1H). Anal. Calcd for $C_{15}H_{11}Cl_2NO_2$: C, 58.47; H, 3.60; N, 4.55. Found: C, 58.52; H, 3.68; N, 4.49.

Typical Procedure for the Preparation of *N*-{2-[2-(Arylsulfanyl)acetyl]phenyl}benzamides (2). *N*-{2-[2-(Phenylsulfanyl)acetyl]phenyl}benzamide (2a). To a stirred suspension of NaH (28 mg, 0.70 mmol) in DMF (4 mL) at 0 ˚C was added PhSH (71 mg, 0.70 mmol) dropwise. After evolution of H_2 gas had ceased, a solution of **1a** (0.19 g, 0.70 mmol) in DMF (4 mL) was added dropwise. After 30 min,

saturated aqueous NH_4Cl (30 mL) was added and the mixture was extracted with AcOEt (3 × 15 mL). The combined extracts were washed with H_2O (3 × 20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated by evaporation. The residual solid was recrystallized from hexane/CH_2Cl_2 to give **2a** (0.22 g, 90%); a white solid; mp 141–144 °C; IR (KBr) 3228, 1672, 1650, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.37 (s, 2H), 7.16 (td, *J* = 8.0, 1.1 Hz, 1H), 7.20–7.29 (m, 4H), 7.40 (dd, *J* = 8.0, 1.1 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.56 (td, *J* = 7.4, 1.1 Hz, 1H), 7.90 (dd, *J* = 8.0, 1.1 Hz, 1H), 8.00 (d, *J* = 7.4 Hz, 2H), 8.99 (d, *J* = 8.0 Hz, 1H), 12.30 (br s, 1H). HR-MS (FI). Calcd for $C_{21}H_{17}NO_2S$ (M): 347.0980. Found: *m/z* 347.0975.

***N*-(2-{2-[(4-Methylphenyl)sulfanyl]acetyl}phenyl)benzamide (2b):** a white solid; mp 88–90 °C (hexane/CH_2Cl_2); IR (KBr) 3266, 1672, 1651, 1609 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.25 (s, 3H), 4.29 (s, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.55 (dd, *J* = 7.4, 6.9 Hz, 1H), 7.64 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 6.9 Hz, 2H), 8.97 (d, *J* = 8.0 Hz, 1H), 12.24 (br s, 1H). Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.30; N, 3.88; S, 8.87. Found: C, 73.05; H, 5.15; N, 3.89; S, 8.77.

***N*-(2-{2-[(4-Chlorophenyl)sulfanyl]acetyl}phenyl)benzamide (2c):** a white solid; mp 139–141 °C (hexane/CH_2Cl_2); IR (KBr) 3267, 1672, 1646, 1609 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.33 (s, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.23–7.41 (m, 4H), 7.50–7.57 (m, 3H), 7.66 (dd, *J* = 8.0, 7.4 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 7.4 Hz, 2H), 8.99 (d, *J* = 8.0 Hz, 1H), 12.25 (br s, 1H). Anal. Calcd for $C_{21}H_{16}ClNO_2S$: C, 66.05; H, 4.22; N, 3.67. Found: C, 65.71; H, 4.00; N, 3.63.

***N*-(2-{2-[(3-Methoxyphenyl)sulfanyl]acetyl}phenyl)benzamide (2d):** a white solid; mp 112–114 °C (hexane/CH_2Cl_2); IR (KBr) 3233, 1671, 1650, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.73 (s, 3H), 4.38 (s, 2H), 6.76 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.94 (d, *J* = 2.3 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 7.14–7.20 (m, 2H), 7.50 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.56 (dd, *J* = 7.6, 6.9 Hz, 1H), 7.65 (dd, *J* = 7.6, 6.9 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 2H), 8.99 (d, *J* = 8.4 Hz, 1H), 12.31 (br s, 1H). Anal. Calcd for $C_{22}H_{19}NO_3S$: C, 70.01; H, 5.07; N, 3.71; S, 8.49. Found: C, 69.97; H, 5.03; N, 3.71; S, 8.39.

***N*-(2-{2-[(Naphthalen-2-yl)sulfanyl]acetyl}phenyl)benzamide (2e):** a pale-yellow solid; mp 117–119 °C (hexane/CH_2Cl_2); IR (KBr) 3241, 1672, 1647, 1609 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.41 (s, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.41–7.51 (m, 6H), 7.64 (dd, *J* = 8.4, 7.6 Hz, 1H), 7.69–7.76 (m, 3H), 7.85 (s, 1H), 7.91–7.94 (m, 3H), 9.00 (d, *J* = 8.4 Hz, 1H), 12.25 (br s, 1H). Anal. Calcd for $C_{25}H_{19}NO_2S$: C, 75.54; H, 4.82; N, 3.52; S, 8.07. Found: C, 75.37; H, 4.77; N, 3.53; S, 8.02.

***N*-{4-Chloro-2-[2-(phenylsulfanyl)acetyl]phenyl}benzamide (2f):** a white solid; mp 115–117 °C (hexane/CH_2Cl_2); IR (KBr) 3225, 1677, 1653, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.31 (s, 2H), 7.23–7.30 (m, 3H), 7.40 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.79 (d, *J* = 2.3 Hz, 1H), 7.97 (dd, *J* = 6.9, 1.5 Hz, 2H), 8.98 (d, *J* = 9.2 Hz, 1H), 12.16 (br s, 1H). Anal. Calcd for $C_{21}H_{16}ClNO_2S$: C, 66.05; H, 4.22; N, 3.67; S, 8.40. Found: C, 66.35; H, 4.43; N, 3.60; S, 8.48.

***N*-(4-Chloro-2-{2-[(naphthalen-2-yl)sulfanyl]acetyl}phenyl)benzamide (2g):** a white solid; mp 152–154 °C (hexane/CH_2Cl_2); IR (KBr) 3235, 1683, 1660, 1604 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.37 (s, 2H), 7.40–7.45 (m, 4H), 7.48 (d, *J* = 9.2 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.57 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.70 (dd, *J* = 9.2, 3.0 Hz, 1H), 7.76–7.78 (m, 2H), 7.81 (d, *J* = 2.3 Hz, 1H), 7.86–7.88 (m, 3H), 8.97 (d, *J* = 9.2 Hz, 1H), 12.09 (br s, 1H). Anal. Calcd for $C_{25}H_{18}ClNO_2S$: C, 69.52; H, 4.20; N, 3.24; S, 7.42. Found: C, 69.45; H, 4.14; N, 3.53; S, 7.34.

***N*-{4-Methoxy-2-[2-(phenylsulfanyl)acetyl]phenyl}benzamide (2h):** a yellow solid; mp 123–125 °C (hexane/CH_2Cl_2); IR (KBr) 3236, 1674, 1664, 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.82 (s, 3H), 4.33 (s, 2H), 7.21–7.28 (m, 4H), 7.36 (d, *J* = 2.3 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 7.6 Hz, 2H), 8.92 (d, *J* = 9.2 Hz, 1H), 11.98 (br s, 1H). Anal. Calcd for $C_{22}H_{19}NO_3S$: C, 70.01; H, 5.07; N, 3.71; S, 8.49. Found: C, 69.80; H, 5.02; N, 3.90; S, 8.56.

***N*-(2-{2-[(4-Chlorophenyl)sulfanyl]acetyl}-4-methoxyphenyl)benzamide (2i):** a yellow solid; mp 142–144 °C (hexane/CH_2Cl_2); IR (KBr) 3238, 1671, 1655, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.85 (s, 3H), 4.29 (s, 2H), 7.21–7.26 (m, 3H), 7.32–7.34 (m, 3H), 7.51 (dd, *J* = 7.6, 6.9 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 6.9 Hz, 2H), 8.91 (d, *J* = 9.2 Hz, 1H), 11.91 (br s, 1H). Anal. Calcd for $C_{22}H_{18}ClNO_3S$: C, 64.15; H, 4.40; N, 3.40; S, 7.78. Found: C, 64.02; H, 4.43; N, 3.62; S, 7.99.

***N*-(2-{4-Methoxy-2-[(3-methoxyphenyl)sulfanyl]acetyl}phenyl)benzamide (2j):** a yellow solid; mp 95–97 °C (hexane/CH_2Cl_2); IR (KBr) 3288, 1677, 1655, 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.73 (s, 3H), 3.83 (s, 3H), 4.35 (s, 2H), 6.76 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.94 (s, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 7.19 (dd, *J* = 8.4, 7.6 Hz, 1H), 7.22 (dd, *J* = 9.2, 3.1 Hz, 1H), 7.36 (d, *J* = 3.1 Hz, 1H), 7.50 (dd, *J* = 7.6, 6.9 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.98 (d, *J* = 6.9 Hz, 2H), 8.92 (d, *J* = 9.2 Hz, 1H),12.00 (br s, 1H). Anal. Calcd for $C_{23}H_{21}NO_4S$: C, 67.79; H, 5.19; N, 3.44. Found: C, 67.62; H, 5.23; N, 3.32.

Typical Procedure for the Preparation of 3-(Arylsulfanyl)quinolin-4(1*H*)-ones (3). 3-(Phenylsulfanyl)quinolin-4(1*H*)-one (3a).[4] A solution of **2a** (0.22 g, 0.63 mmol) in DMF-DMA (5 mL) was stirred for 5 h. After removal of the excess DMF-DMA and other volatile materials under reduced pressure, the residue was dissolved in CH_2Cl_2 (12 mL) and the solution was stand at rt overnight. The precipitate was collected by filtration under reduced pressure to give pure **3a** (0.12 g, 77%); a white solid; mp 244–246 °C; IR (KBr) 3207, 1626, 1608 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.08–7.11 (m, 3H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 8.38 (s, 1H), 12.1 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 109.52, 118.69, 124.19, 125.07, 125.13, 125.47, 126.20, 128.83, 132.20, 137.69, 139.83, 145.63, 174.93.

3-[(4-Methylphenyl)sulfanyl]quinolin-4(1*H*)-one (3b): a white solid; mp 254–256 °C (CH_2Cl_2); IR (KBr) 3207, 1625, 1612 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.21 (s, 3H), 7.05 (s, 4H), 7.37 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.59 (d, *J* = 8.6 Hz, 1H), 7.68 (ddd, *J* = 8.6, 6.9, 1.1 Hz, 1H), 8.10 (dd, *J* = 8.6, 1.1 Hz, 1H),

8.28 (s, 1H), 12.4 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 20.49, 110.73, 118.69, 124.07, 125.04, 125.41, 127.17, 129.51, 132.09, 133.75, 134.72, 139.81, 144.83, 174.81. HR-MS (EI). Calcd for $C_{16}H_{13}NOS$ (M): 267.0718. Found: *m/z* 267.0715. Anal. Calcd for $C_{16}H_{13}NOS$: C, 71.88; H, 4.90; N, 5.24; S, 11.99. Found: C, 71.61; H, 4.80; N, 5.34; S, 11.95.

3-[(4-Chlorophenyl)sulfanyl]quinolin-4(1*H*)-one (3c): a white solid; mp 258–260 °C (CH_2Cl_2); IR (KBr) 3201, 1629, 1610 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.11 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.39 (dd, *J* = 8.6, 7.4 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.70 (ddd, *J* = 8.6, 7.4, 1.1 Hz, 1H), 8.11 (dd, *J* = 8.6, 1.1 Hz, 1H), 8.42 (s, 1H), 12.3 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 108.86, 118.75, 124.21, 125.16, 125.41, 127.75, 128.65, 129.51, 132.20, 136.93, 139.91, 145.93, 174.73. HR-MS (EI). Calcd for $C_{15}H_{10}ClNOS$ (M): 287.0172. Found: *m/z* 287.0167. Anal. Calcd for $C_{15}H_{10}ClNOS$: C, 62.61; H, 3.50; N, 4.87. Found: C, 62.32; H, 3.62; N, 4.80.

3-[(3-Methoxyphenyl)sulfanyl]quinolin-4(1*H*)-one (3d): a white solid; mp 210–211 °C (CH_2Cl_2); IR (KBr) 3208, 1628, 1610 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.66 (s, 3H), 6.65–6.68 (m, 3H), 7.14 (dd, *J* = 8.6, 7.6 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.70 (dd, *J* = 8.6, 6.7 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 8.37 (s, 1H), 12.3 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 55.00, 109.38, 110.46, 111.89, 118.41, 118.65, 124.15, 125.10, 125.41, 129.70, 132.16, 139.11, 139.78, 145.63, 159.48, 174.84. HR-MS (EI). Calcd for $C_{16}H_{13}NO_2S$ (M): 283.0667. Found: *m/z* 283.0654. Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.94; S, 11.31. Found: C, 67.70; H, 4.59; N, 4.91; S, 11.27.

3-[(Naphthalen-2-yl)sulfanyl]quinolin-4(1*H*)-one (3e): a white solid; mp 283–285 °C (CH_2Cl_2); IR (KBr) 3212, 1627, 1607 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.11 (dd, *J* = 7.6, 6.7 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 1H), 7.32 (dd, *J* = 7.6, 6.7 Hz, 1H), 7.35–7.41 (m, 3H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 8.25 (s, 1H), 12.3 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 104.68, 121.04, 121.83, 124.39, 124.74, 124.79, 126.21, 126.37, 126.49, 127.50, 127.55, 128.33, 128.44, 130.44, 133.33, 139.30, 150.05, 156.18, 173.68. HR-MS (EI). Calcd for $C_{19}H_{13}NOS$ (M): 303.0718. Found: *m/z* 303.0722. Calcd for $C_{19}H_{13}NOS$: C, 75.22; H, 4.32; N, 4.62; S, 10.57. Found: C, 75.00; H, 4.30; N, 4.65; S, 10.57.

6-Chloro-3-(phenylsulfanyl)quinolin-4(1*H*)-one (3f): a white solid; mp 252–254 °C (CH_2Cl_2); IR (KBr) 3204, 1626, 1608 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.09–7.12 (m, 3H), 7.22 (dd, *J* = 8.6, 6.7 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.6 Hz, 1H), 8.03 (s, 1H), 8.41 (s, 1H), 12.4 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 110.15, 121.20, 124.34, 125.23, 126.05, 126.39, 128.73, 128.87, 132.26, 137.22, 138.48, 145.80, 173.76. HR-MS (EI). Calcd for $C_{15}H_{10}ClNOS$ (M): 287.0172. Found: *m/z* 287.0184. Anal. Calcd for $C_{15}H_{10}ClNOS$: C, 62.61; H, 3.50; N, 4.87; S, 11.14. Found: C, 62.45; H, 3.62; N, 4.97; S, 11.24.

6-Chloro-3-[(naphthalen-2-yl)sulfanyl]quinolin-4(1*H*)-one (3g): a white solid; mp 297–299 ˚C (CH_2Cl_2); IR (KBr) 3204, 1627, 1610 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.30 (d, *J* = 7.6 Hz, 1H), 7.39–7.44 (m, 2H), 7.60 (s, 1H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.73–7.83 (m, 4H), 8.04 (d, *J* = 1.9 Hz, 1H), 8.47 (s, 1H), 12.5 (br, 1H). HR-MS (EI). Calcd for $C_{19}H_{12}ClNOS$ (M): 337.0328. Found: *m/z* 337.0318. Anal. Calcd for $C_{19}H_{12}ClNOS$: C, 67.55; H, 3.58; N, 4.15. Found: C, 67.26; H, 3.53; N, 4.13.

6-Methoxy-3-(phenylsulfanyl)quinolin-4(1*H*)-one (3h): a white solid; mp 274–275 ˚C (CH_2Cl_2); IR (KBr) 3203, 1613 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.83 (s, 3H), 7.07–7.10 (m, 3H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.34 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.51 (d, *J* = 1.9 Hz, 1H), 7.58 (d, *J* = 9.6 Hz, 1H), 8.32 (s, 1H), 12.2 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 55.44, 104.70, 108.23, 120.55, 122.57, 124.97, 126.09, 126.31, 128.82, 134.45, 137.93, 144.64, 156.22, 174.38. HR-MS (EI). Calcd for $C_{16}H_{13}NO_2S$ (M): 283.0667. Found: *m/z* 283.0661. Anal. Calcd for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62; N, 4.94; S, 11.31. Found: C, 67.78; H, 4.65; N, 5.02; S, 11.37.

3-[(4-Chlorophenyl)sulfanyl]-6-methoxyquinolin-4(1*H*)-one (3i): a white solid; mp 315–317 ˚C (CH_2Cl_2); IR (KBr) 3197, 1614 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.82 (s, 3H), 7.09 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.34 (dd, *J* = 8.6, 2.9 Hz, 1H), 7.50 (d, *J* = 2.9 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 8.36 (s, 1H), 12.4 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 55.48, 104.70, 107.65, 120.66, 122.66, 126.38, 127.69, 128.70, 129.47, 134.57, 137.19, 144.94, 156.29, 174.26. HR-MS (EI). Calcd for $C_{16}H_{12}ClNO_2S$ (M): 317.0277. Found: *m/z* 317.0279. Anal. Calcd for $C_{16}H_{12}ClNO_2S$: C, 60.47; H, 3.81; N, 4.41; S, 10.09. Found: C, 60.17; H, 3.89; N, 4.56; S, 10.40.

6-Methoxy-3-[(3-methoxyphenyl)sulfanyl]quinolin-4(1*H*)-one (3j): a white solid; mp 235–237 ˚C (CH_2Cl_2); IR (KBr) 3197, 1615 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.65 (s, 3H), 3.83 (s, 3H), 6.61–6.67 (m, 3H), 7.13 (dd, *J* = 8.6, 7.6 Hz, 1H), 7.34 (dd, *J* = 9.6, 2.9 Hz, 1H), 7.51 (d, *J* = 2.9 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 8.33 (s, 1H), 12.3 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 55.08, 55.47, 104.69, 108.04, 110.31, 111.76, 118.27, 120.60, 122.65, 126.34, 129.80, 134.46, 139.43, 144.82, 156.27, 159.54, 174.40. HR-MS (ESI). Calcd for $C_{17}H_{16}NO_3S$ (M+H): 314.0851. Found: *m/z* 314.0837. Anal. Calcd for $C_{17}H_{15}NO_3S$: C, 65.16; H, 4.82; N, 4.47. Found: C, 65.12; H, 4.38; N, 4.38.

Typical Procedure for the Preparation of 1-Alkyl-3-(arylsulfanyl)quinolin-4(1*H*)-ones (4). 1-(Phenylmethyl)-3-(phenylsulfanyl)quinolin-4(1*H*)-one (4a). To a stirred suspension of NaH (60% in mineral oil; 12 mg, 0.29 mmol) in DMF (1.5 mL) at 0 ˚C was added a solution of **3a** (74 mg, 0.29 mmol) in DMF (1 mL) dropwise. After evolution of H_2 gas had ceased, BnBr (50 mg, 0.29 mmol) was added and stirring was continued for 4 h at the same temperature. Saturated aqueous NH_4Cl (20 mL) was added and the mixture was extracted with AcOEt (3 × 10 mL). The combined extracts were washed with H_2O (3 × 15 mL) and brine (15 mL), dried (Na_2SO_4), and concentrated by evaporation. The residual solid was recrystallized from hexane/CH_2Cl_2 to give **4a** (76 mg, 76%); colorless needles; mp 153–154 ˚C; IR (KBr)

1626, 1601 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.33 (s, 2H), 7.11–7.15 (m, 3H), 7.22 (t, *J* = 6.9 Hz, 2H), 7.29–7.39 (m, 7H), 7.55 (td, *J* = 6.9, 1.1 Hz, 1H), 8.08 (s, 1H), 8.51 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 56.69, 113.63, 116.23, 124.51, 125.93, 126.07, 126.57, 127.72, 128.04, 128.45, 128.91, 129.28, 132.41, 134.60, 136.54, 139.75, 148.21, 175.90. HR-MS (EI). Calcd for $C_{22}H_{17}NOS$ (M): 343.1031. Found: *m/z* 343.1017. Anal. Calcd for $C_{22}H_{17}NOS$: C, 76.94; H, 4.99; N, 4.08. Found: C, 76.73; H, 5.00; N, 4.06.

1-(Cyclopropylmethyl)-6-methoxy-3-(phenylsulfanyl)quinolin-4(1*H*)-one (4b): a colorless viscous oil; R_f 0.30 (AcOEt/hexane 1:1); IR (neat) 1624, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.39–0.42 (m, 2H), 0.69–0.73 (m, 2H), 1.31–1.35 (m, 1H), 3.92 (s, 3H), 3.98 (d, *J* = 6.9 Hz, 2H), 7.12 (dd, *J* = 7.4, 6.9 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 2H), 7.27–7.32 (m, 3H), 7.51 (d, *J* = 9.2 Hz, 1H), 7.92 (d, *J* = 2.9 Hz, 1H), 8.01 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 4.46, 10.21, 55.79, 57.50, 96.66, 111.50, 117.15, 122.92, 125.64, 127.71, 127.81, 128.81, 134.26, 137.00, 146.18, 156.61, 175.28. HR-MS (EI). Calcd for $C_{20}H_{19}NO_2S$ (M): 337.1136. Found: *m/z* 337.1151. Anal. Calcd for $C_{20}H_{19}NO_2S$: C, 71.19; H, 5.68; N, 4.15. Found: C, 71.12; H, 5.66; N, 4.12.

2-{3-[(4-Chlorophenyl)sulfanyl]-6-methoxy-4-oxoquinolin-1-yl}acetonitrile (4c): a beige solid; mp 97–99 °C (hexane/CH_2Cl_2); IR (KBr) 1626, 1602 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.87 (s, 3H), 5.60 (s, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.54 (dd, *J* = 9.2, 3.1 Hz, 1H), 7.63 (d, *J* = 3.1 Hz, 1H), 7.81 (d, *J* = 9.2 Hz, 1H), 8.61 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 40.36, 55.65, 106.52, 109.43, 115.70, 118.48, 122.64, 127.13, 128.12, 128.81, 129.95, 133.45, 136.12, 149.09, 156.81, 173.91. HR-MS (EI). Calcd for $C_{18}H_{13}ClN_2O_2S$ (M): 356.0386. Found: *m/z* 356.0398. Anal. Calcd for $C_{18}H_{13}ClN_2O_2S$: C, 60.59; H, 3.67; N, 7.85. Found: C, 60.42; H, 3.99; N, 7.59.

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