Beckmann Rearrangement Using Indium(III) Chloride: Synthesis of Substituted Oxazoloquinolines from the Corresponding Ketoximes of 3-Acyl-1*H*-quinolin-4-ones

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Abstract: Nitrilium ion intermediates in the Beckmann rearrangement of 3-acyl-4-quinolinone ketoximes, in the presence of $InCl_3$, were trapped by the β-hydroxy group of the tautomeric form of the ketoxime giving, predominantly, the corresponding oxazoloquinolines with isooxazoloquinolines formed as minor products.

Key words: indium(III) chloride, Beckmann rearrangement, β-hydroxy ketoxime, cyclization, oxazoloquinoline

Fused aromatic oxazolopyridine and oxazoloquinoline moieties are frequently found in biologically potent molecules such as immunomodulators with the potential for treatment of cancer and viral diseases,[1] protein kinase inhibitors for oncolytic drugs,[2] PDE4 inhibitors for antiasthmatic and anti-inflammatory agents,[3] hypolipidemia and arteriosclerosis,[4] and non-opioid analgesics.[5] In our continued effort to prepare various analogues with 4-quinolinone skeletons[6] for biological activity tests, we were in need of substituted oxazoloquinolines. In order to prepare such analogues, an attempt was made to obtain the corresponding amide from its ketoxime via the Beckmann rearrangement, so that subsequent hydrolysis of the amide, followed by cyclization of 3-amino-4-quinolinol with acetic anhydride[7a–c] or benzoic acid[7d] would provide oxazoloquinolines. In order to achieve a Beckmann rearrangement, protic or Lewis acids were employed to protonate or to form a complex with the hydroxyl group of oxime so that it would become labile as a leaving group.[8] Though polyphosphoric acid (PPA) is commonly used for Beckmann rearrangements, its viscosity presents several drawbacks, particularly during work-up and with its use in large quantities as a solvent. Recently, various Lewis acid catalysts such as $BiCl_3$,[9] $Yb(OTf)_3$,[10] $InCl_3$,[11] $FeCl_3$,[12] AlI_3,[13] Bu_4ReO_4,[14] Ga(III),[15] and Sb(V)[15] in different solvents have been used successfully to facilitate the reaction with greater efficiency. Among these catalysts, $BiCl_3$, $Yb(OTf)_3$ and $InCl_3$ have been shown to convert *o*-hydroxyacetophenone ketoximes to the corresponding anilides without cyclisation of the intermediate nitrilium ion by the β-hydroxy group.[9–11] In contrast, it was reported that cyclized products, benzoxazoles, were formed using phosphoryl chloride in dimethylacetamide (DMA),[16a] polyphosphoric acid trimethylsilyl ester (PPSE)[16b] or Zeolite.[16c] Intramolecular trapping of a nitrilium ion by the β-hydroxy group of aliphatic ketoximes has also been noticed.[17] Although synthetic methods for the preparation of benzoxazoles from *o*-hydroxyacetophenones and *o*-hydroxybenzaldehyde are known, those of the corresponding oxazolopyridines are rare.[18] Initially, 3-(1-hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (**1a**) was reacted in $POCl_3$–DMA[16a] in the hope that the oxazoloquinoline could be obtained directly. Unfortunately, only a small amount of oxazoloquinoline **2a** was obtained (11% yield), along with a large amount of intractable polar products. We then repeated the reaction using 0.1 equivalent of either $BiCl_3$, $Yb(OTf)_3$ or $InCl_3$ in refluxing acetonitrile to prepare the corresponding anilides.[9–11] Surprisingly, a mixture of 2-methyl-4-methylsulfanyloxazolo[4,5-*c*]quinoline (**2a**) and 3-methyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (**3a**) instead of the corresponding anilides were obtained (Table 1).[19]

Table 1 Product Yields of **2a** and **3a** with Different Catalysts in Refluxing Acetonitrile

Catalyst	Reaction time (h)	Product yield (%)[a]	
		2a	**3a**
None[b]	12	14	18
$POCl_3$–DMA[c]	3.0	11	trace
$BiCl_3$	5.5	3	77
$Yb(OTf)_3$[d]	6.0	24	49
$InCl_3$	2.0	73	22

[a] Isolated yields.
[b] 66% of starting material was recovered.
[c] See ref. 16a.
[d] 14% of starting material was recovered.

Among the catalysts employed, the reaction with $InCl_3$ proceeded smoothly within two hours, exhibiting higher selectivity for **2a**, while $Yb(OTf)_3$ and $BiCl_3$ both formed **3a** sluggishly (~6 hours) with the latter resulting in **3a** almost exclusively. A mixture of oxazoloquinoline **2a** and isooxazoloquinoline **3a** in a ratio of 1:0.3 was obtained with $InCl_3$, whereas employing $Yb(OTf)_3$ resulted in a ratio of 1:2, along with 14% of the unreacted starting mate-

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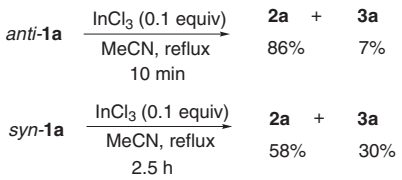
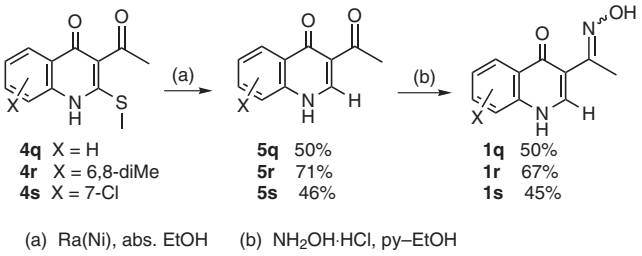
rial. The Beckmann rearrangement seemed to be severely suppressed with $BiCl_3$ resulting in a dramatic change in the product ratio to 1:26 for **2a** and **3a**. Although the reaction proceeded to some degree without a catalyst, a large amount of starting material (66%) was recovered even after 12 hours, probably due to some degree of intra- or intermolecular protonation by acidic protons of the substrate. In view of the above observations, we chose to use $InCl_3$ as a catalyst in order to optimize oxazoloquinoline formation. Various substituted quinolinone ketoximes **1** were prepared as mixtures of *syn* and *anti* forms according to known procedures[20] and reacted under the conditions described above to provide a mixture of oxazoloquinolines **2**, and isooxazoloquinolines **3** (Table 2). Regardless of substituents (X, R, R′), major products were oxazoloquinolines **2**, in yields ranging between 38–86%, while minor products were isooxazoloquinolines **3** in yields of between 1–37% except in the case of **1n** which resulted in the formation of more isooxazoloquinoline **3n** (49%) than oxazoloquinoline **2n** (37%). In the latter, exceptional case, shift of the heterocyclic moiety seems to be highly preferred to that of the phenyl moiety since the N-phenyl amide was not detected in the product. The observed reversal of selectivity compared to the other substrates might be due to phenyl participation during nitrilium ion formation.[21] In order to compare the reactivity of the *syn* and *anti* geometric isomers, *anti*-**1a** and *syn*-**1a** were separated (58% and 30% yields, respectively) and each isomer was subjected to the above reaction conditions. While *anti*-**1a** underwent cyclization within 10 minutes and exhibited higher selectivity to afford **2a** and **3a** in yields of 86% and 7% respectively, *syn*-**1a** took much longer to react (2.5 hours) and showed poor selectivity, providing **2a** and **3a** in yields of 58% and 30% respectively (Equation 1). TLC analysis did not detect anilide formation in the course of the reaction of either *anti*-**1a** or *syn*-**1a**, nor did it indicate any interconversion of *syn* to *anti* isomer.



Equation 1 Reactivities of *anti*-**1a** and *syn*-**1a**.

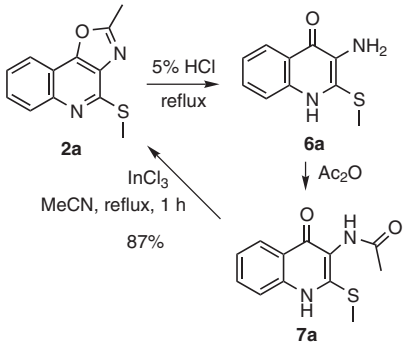
Desulfanylated oximes **1q–s** were prepared as in Scheme 1. Substrates **4q–s**[6c] were treated with Raney Ni to afford desulfanylated quinolinones **5q–s** which were subsequently converted to oximes **1q–s** as a mixture of *anti* and *syn* isomers. Each isomer, *anti*-**1q** and *syn*-**1q**, was separated in yields of 91% and 7% respectively. Both isomers exhibited similar trends to *anti*-**1a** and *syn*-**1a** in reaction rate and selectivity for cyclization, i.e. the *anti* isomer exhibited faster rate and higher selectivity than the *syn* isomer. Reaction of *anti*-**1q** provided **2q** and **3q** within 40 minutes in yields of 71% and 17% respectively,



Scheme 1 Preparation of desulfanylated oximes **1q–s**.

whereas *syn*-**1q** provided **2q** and **3q** within 2.5 hours in yields of 38% and 36% respectively.

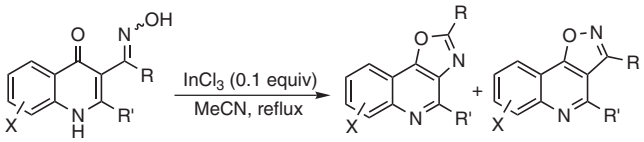
Anilide **7a**, the anticipated Beckmann rearrangement product, was prepared separately by hydrolysis of **2a** with 5% HCl to afford amine **6a**, followed by acetylation with acetic anhydride (Scheme 2). The anilide **7a** underwent cyclization under standard reaction conditions within one hour to give 87% yield of **2a**. However, reaction rate of anilide **7a** was much slower than the oxime, *anti*-**1a** (10 minutes). In contrast, it was faster than *syn*-**1a** (2.5 hours) (Equation 1). Bearing in mind that the anilide was not detected during the cyclization reaction for either of the isomers, the remarkable difference in reaction rates between oxime *anti*-**1a** and anilide **7a** strongly indicates that direct formation of oxazoloquinoline **2a** occurs without intermediate anilide formation. It should be noted that even after 28 hours under the same reaction conditions, isooxazoloquinolne **3a** was inert.



Scheme 2 Oxazoloquinoline **2a** from amide **7a**, normal Beckmann rearrangement product.

Previously, similar oxazoloquinoline formation was noticed with 2-phenyl-3-acetyl-1*H*-quinolin-4-one oxime (**1** with X = H, R = Me and R′ = Ph) to form 2-methyl-4-phenyloxazolo[4,5-*c*]quinoline (48%) employing PPA as a solvent.[22] The same substrate was also converted into isooxazoloquinoline, 3-methyl-4-phenylisooxazolo[4,5-*c*]quinoline (53%), simply by heating, neat, above its melting point. In contrast, it was reported that 1-oximinoacridine-1,9-dione, having the same quinolinone ketoxime moiety, provided only isooxazoloacridine in PPA without any rearrangement product.[23] Recently, we reported[24] that *O*-mesitylsulfonyl ketoxime derivatives of **4** cyclized to isothiazoloquinolines, instead of to thiazolo-

Table 2 Product Yields of Substituted Oxazolo[4,5-c]quinolines **2** and Isoxazolo[4,5-*c*]quinolines **3**[a]



1 **2** **3**

Substrate	X	R	R′	Ratio *anti*:*syn* **1**[b]	Reaction time (h)	Product yields (%)[c]		Mp (°C)	
						2	**3**	**2**	**3**
1a	H	Me	SMe	68:32 (58: 30)[c]	2.0	73	22	94–95	96–98
anti-**1a**	H	Me	SMe	100:0	0.17	86	7	94–95	96–98
syn-**1a**	H	Me	SMe	0:100[c]	2.5	58	30	94–95	96–98
1b	8-Ph	Me	SMe	71:29	2.0	65	17	93–94	112–114
1c	6,8-di-Me	Me	SMe	81:19	15	82	16	218–220	198–200
1d	7-MeO	Me	SMe	76:24	2.0	78	1	157–158	164–165
1e	5,7-diCl	Me	SMe	87:13	2.0	62	28	158–159	162–163
1f	7-CF_3	Me	SMe	84:16	1.5	76	12	141–142	100–102
1g	6-Cl,8-CF_3	Me	SMe	80:20	1.5	75	12	165–166	211–213
1h	6-NO_2	Me	SMe	79:21	2.0	82	5	178–180	120–122
1i	8-$PhSO_2$	Me	SMe	79:21	2.0	72	12	115–116	208–210
1j	8-F	Me	SMe	71:29	1.5	80	7	146–147	140–141
1k	6,8-diF	Me	SMe	76:24	1.5	73	1	186–189	178–179
1l	8-F	Me	SBn	69:31	2.5	71	23	154–155	135–136
1m	5-NO_2, 8-F	Me	SAll	73:27	4.0	56	37	151–152	128–131
1n	H	Ph	SMe	41:59	2.5	37	49	150–151	129–130
1o	5,8-diCl	iPr	SMe	68:32	2.5	67	27	137–138	113–115
1p	6-NO_2, 8-Cl	*c*-Pr	SMe	76:24	3.5	67	27	101–102	128–129
1q	H	Me	H	89:11 (91:7)[c]	2.5	76	12	185–187	173–175
anti-**1q**	H	Me	H	100:0	0.7	71	17	185–187	173–175
syn-**1q**	H	Me	H	0:100	2.5	38	36	185–187	173–175
1r	6,8-di-Me	Me	H	82:18	2.5	51	37	172–173	158–159
1s	7-Cl	Me	H	88:12	2.5	65	10	oil	oil

[a] 0.1 equivalent of $InCl_3$ was used at reflux in MeCN.
[b] HPLC area%.
[c] Isolated yields.

quinolines via a Beckmann rearrangement, which was known to be obtained with other *O*-mesitylenesulfonyl ketoximes.[25] In this case, isothiazoloquinoline formation presumably occurred via direct nucleophilic attack on the N-atom, replacing the *O*-mesityl sulfonyl group of the ketoxime by the S-atom of the SMe group instead of the O-atom of adjacent hydroxy group before the Beckmann rearrangement took place. However, anchimeric assistance of the thiomethyl group exerted on O-substituted oximes[26] does not seem to be preferable in the presence of β-hydroxy group here in a naked oxime. As proposed previously,[24] the isothiazoloquinoline started to be formed before the oxime, so that the isolation of the corresponding *O*-mesitylenesulfonyl ketoxime was not possible.

Even though we assumed a putative route involving an oxime intermediate to explain a concerted reaction mechanism for isothiazoloquinoline formation, we found no evidence of the corresponding *O*-mesitylenesulsulfonyl ketoxime. The relatively poor ability of the hydroxyl group to function as a leaving group may have prohibited isothiazole formation in the course of oxime preparation. In the case of 3-acetyl-4-quinolinone ketoximes **1**, the iminocarbocation, generated by coordination of $InCl_3$, was trapped by the β-hydroxy group both before and after rearrangement. It should be noted that, even though each isomer was clearly separated by TLC, the chemical shifts of the two isomeric products were so similar that 700 MHz or higher NMR spectroscopy was required to differentiate the two.

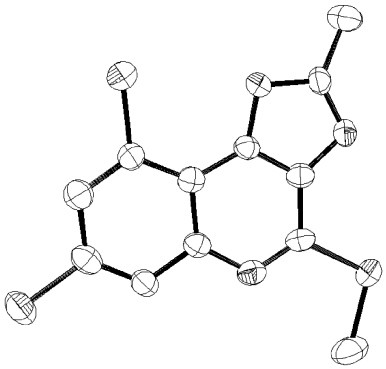


Figure 1 X-ray structure of **2e** at the 50% probability level.

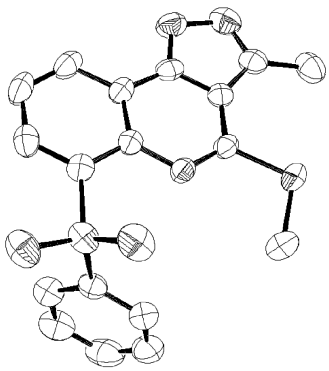


Figure 2 X-ray structure of **3i** at the 50% probability level.

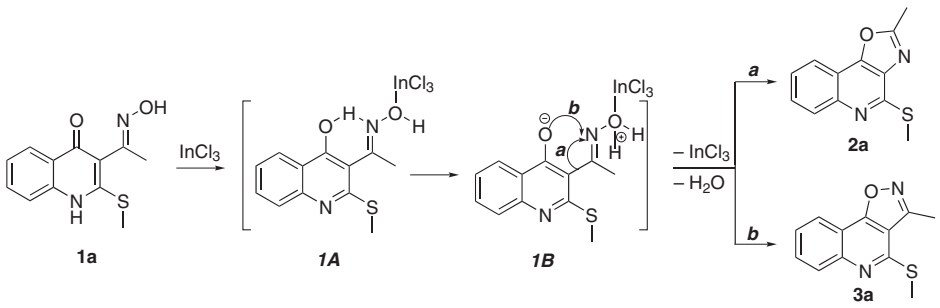
In addition to 2D NMR (700 MHz) analysis, the structures of oxazoloquinoline **2e** and isooxazoloquinoline **3i** were determined unequivocally by X-ray crystallography (Figure 1 and Figure 2).[27]

A plausible mechanism has been depicted for the *anti* isomer in Scheme **3**. Coordination of $InCl_3$ with the oxime hydroxyl group of the tautomeric form of **1a** would form a complex like ***1A***, followed by an intramolecular proton shift of the aromatic hydroxyl group to form ***1B***. Subsequently, either rearrangement could take place, generating a nitrilium ion which could then be trapped by the adjacent oxygen giving **2a** or, alternatively, direct nucleophilic attack of the oxygen anion on the nitrogen would take place to provide **3a**. Based upon the observed, slow reaction rates and the absence of detectable *anti* isomer, the *syn* isomer may proceed via an S_N1 reaction, instead of concerted *trans* migration, by coordinating the hydroxyl group with $InCl_3$ making it a better leaving group.

In conclusion, by using $InCl_3$ as a catalyst, oxazoloquinolines were selectively prepared directly from the corresponding 3-acyl-4-quinolinone ketoximes instead of via the Beckmann rearranged anilides under convenient reaction conditions.

Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Varian Gemini 300 (300 MHz), AMX 500 (500 MHz) and Bruker 700 AVANCE 700 (700 MHz) spectrometers, and ^{13}C NMR spectra were recorded on a Bruker AM-300 (75.47 MHz) spectrometer using tetramethylsilane as internal standard. Mass spectra were obtained on a Shimadzu GC/MC-QP 1000. High-resolution mass spectra were obtained on a VGQUATTRO triple quadrupole tandem Micromass Autospec Mass spectrometers (EI, 70 eV). Microanalyses were performed in KRICT with a Perkin-Elmer 240C instrument. Column chromatography was performed with Merk Kieselgel 60 silica (230–400 mesh). Analytical thin layer chromatography was performed on precoated silica gel plates (0.25mm, 60F–254E, Merck). LC/MS data were recorded on a Waters ZQ electrospray mass spectrometer (EI) equipped with PDA detection (200–600 nm) using an XTerra MS column ($C_{18,}$ 5μm, 4.6 × 100 nm) from Waters (U.K.). Typical gradients were 5–95% MeCN–H_2O containing 0.1% TFA.

Reagent grade chemicals were purchased from commercial sources and used without further purification. Organic solvents were obtained from Oreintal, Duksan, and Samchun Chemical Co. THF and Et_2O were refluxed over sodium in the presence of benzophenone



Scheme 3 Plausible mechanism for the formation of oxazolo- and isooxazoloquinoline.

and distilled prior to use under N_2. MeCN was distilled after reflux over P_2O_5. DMF was distilled from powdered BaO.

X-ray Structure Determination

Reflection data were collected on a Bruker 1K SMART CCD-based diffractometer with graphite-monochromated Mo–K_α radiation (λ = 0.7107 Å). The hemisphere of reflection data were collected as ω scan frames with 0.3°/frame and exposure times of 5 s/frame. Cell parameters were determined and refined using the SMART program (SMART, version 5.0, Data collection software, Bruker AXS, Inc., Madison, WI, 1998). Among 7331 collected reflections 2834 were unique (R_{int} = 0.1338). Data reductions were performed using SAINT software (SAINT, version 5.0, Data integration software, Bruker AXS Inc., Madison, WI, 1998).The data were corrected for Lorentz and polarization effects. A semi-empirical absorption correction was applied with the SADABS program (G. M. Sheldrick, SADABS, Program for absorption correction with the Bruker SMART system, Universität Göttingen, Germany, 1996). The structures of the compounds were solved by direct methods and refined by full matrix least-squares methods using the SHELXTL program package with anisotropic thermal parameters for all non-hydrogen atoms; all hydrogen atoms were placed in calculated positions within the isotropic thermal parameters.

7,9-Dichloro-2-methyl-4-methylsulfanyloxazolo[4,5-*c*]quinoline (2e)

Crystal Data: $C_{12}H_8Cl_2N_2OS$, FW = 299.16, monoclinic, $P2_1/c$, a = 7.308(3) Å, b = 19.897(7) Å, c = 8.752(3) Å, β = 101.587(7)°, V = 1246.6(8) Å^3, D = 1.594 Mg/m^3, $R1$ = 0.0651, $wR2$ = 0.1746, goodness-of-fit = 1.096, 1996).

6-Benzenesulfonyl-3-methyl-4-methylsulfanylisooxazolo[4,5-*c*]quinoline (3i)

Crystal Data: $C_{18}H_{14}N_2O_3S_2$, FW = 370.43, orthorhombic, Pbcn, a = 23.26(5) Å, b = 9.43(2) Å, c = 14.88(3) Å, V = 3265(12) Å^3, D = 1.507 Mg/m^3, $R1$ = 0.0554, $wR2$ = 0.1131, goodness-of-fit = 1.014.

3-(1-Hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (1a); Typical Procedure

A solution of 3-acetyl-2-methylsulfanyl-1*H*-quinolin-4-one (**4a**) (1.18 g, 5.1 mmol) and hydroxylamine hydrochloride (0.71 g, 10.1 mmol) in EtOH (20 mL) and pyridine (10 mL) was stirred at r.t. for 12 h. The solvent was then removed by rotary evaporation at 40 °C and the resulting oil was dissolved in CH_2Cl_2 (30 mL) and washed successively with aq HCl (5%, 10 mL), H_2O (20 mL), and brine (20 mL). The solution was dried over $MgSO_4$, filtered, and concentrated under vacuum to afford a mixture of *anti* and *syn* forms of **1a** as a colorless solid (0.97g, 75%). The isomeric ratio was determined by HPLC as 68:32 *syn*:*anti*. Of the two spots visible in TLC, the spot with the higher R_f value was assigned as the *anti* isomer while the spot with the lower R_f value was assigned as the *syn* isomer. The residue was used without further purification for the next step.

Yield: 75%; colorless solid; R_f = 0.12 and 0.10 (hexane–EtOAc, 3:1); mp 162–163 °C (dec.).

IR (KBr): 3199, 3064, 2897, 1623, 1603 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.14 (s, 1 H), 10.75 (s, 1 H), 7.89–7.93 (m, 2 H), 7.47–7.62 (m, 4 H), 7.18–7.29 (m, 2 H), 2.39–2.40 (d, J = 2 Hz, 6 H), 1.85 (s, 6 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 173.8, 172.5, 152.2, 149.8, 148.8, 146.0, 140.3, 131.7, 124.8, 124.0, 123.3, 119.5, 117.8, 19.7, 15.7.

MS (EI, 70 eV): m/z (%) = 248 (30) [M$^+$], 230 (45), 216 (100), 202 (25), 114 (15), 76 (13).

HRMS (EI): m/z calcd for $C_{12}H_{12}N_2O_2S$: 248.0619; found: 248.0619.

The spot with the higher R_f value was designated as *anti* isomer while that with the lower value was designated as *syn* isomer for all the oxime mixtures **1**.

The above isomeric mixture was separated by silica gel column chromatography (hexane–EtOAc, 1:1).

3-(1-Hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (*anti*-1a)

Yield: 58%; colorless solid; R_f = 0.15 (hexane–EtOAc, 1:1); mp 194–196 °C.

IR (KBr): 3175, 3062, 2923, 2854, 1743, 1619, 1602 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.21 (s, 1 H), 10.89 (s, 1 H), 8.04 (d, J = 7.4 Hz, 1 H), 7.60–7.73 (m, 2 H), 7.28–7.35 (m, 1 H), 2.62 (s, 3 H), 1.98 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 173.8, 152.2, 148.8, 140.3, 131.7, 124.8, 124.0, 123.3, 119.5, 117.8, 14.7, 14.1.

MS (EI, 70 eV): m/z (%) = 248 (30) [M$^+$], 230 (45), 216 (100), 202 (25), 114 (15), 76 (13).

HRMS (EI): m/z calcd for $C_{12}H_{12}N_2O_2S$: 248.0619; found: 248.0619.

3-(1-Hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (*syn*-1a)

Yield: 30%; colorless solid; R_f = 0.13 (hexane–EtOAc, 1:1); mp 184–186 °C.

IR (KBr): 3452, 2974, 2866, 2253, 2127, 1620, 1607 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.47 (s, 1 H), 10.31 (s, 1 H), 8.03 (d, J = 8.0 Hz, 1 H), 7.64–7.66 (m, 2 H), 7.25–7.32 (m, 1 H), 2.61 (s, 3 H), 1.99 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.5, 152.3, 149.8, 146.0, 140.4, 131.7, 124.8, 123.9, 123.3, 117.7, 19.76, 15.7.

MS (EI, 70 eV): m/z (%) = 248 (30) [M$^+$], 230 (45), 216 (100), 202 (25), 114 (15), 76 (13).

IR (KBr): 3452, 2974, 2866, 2253, 2127, 1620, 1607 cm^{-1}.

HRMS (EI): m/z calcd for $C_{12}H_{12}N_2O_2S$: 248.0619; found: 248.0619.

3-(1-Hydroxyiminoethyl)-2-methylsulfanyl-8-phenyl-1*H*-quinolin-4-one (1b)

Yield: 58%; colorless solid; R_f = 0.13 and 0.11 (hexane–EtOAc, 3:1); mp 75–76 °C (dec.).

IR (KBr): 3191, 3095, 1623, 1606 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 8.64–8.66 (d, J = 4 Hz, 1 H), 8.32–8.36 (t, J = 7.8 Hz, 1 H), 7.28–7.39 (m, 6 H), 2.23–2.36 (m, 6 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 173.0, 165.3, 163.9, 148.4, 138.0, 134.4, 130.5, 129.5, 128.9, 128.1, 127.4, 124.1, 122.9, 100.1, 19.7, 15.2, 11.7, 11.3.

MS (EI, 70 eV): m/z (%) = 324 (25) [M$^+$], 306 (70), 292 (100), 278 (30), 190 (15), 139 (10).

HRMS (EI): m/z calcd for $C_{18}H_{16}N_2O_2S$: 324.0932; found: 324.0931.

3-(1-Hydroxyiminoethyl)-5,8-dimethyl-2-methylsulfanyl-1*H*-quinolin-4-one (1c)

Yield: 80%; yellow solid; R_f = 0.10 and 0.09 (hexane–EtOAc, 3:1); mp 217–218 °C.

IR (KBr): 3189, 3092, 1624, 1601 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 7.23–7.34 (m, 2 H), 6.91–7.02 (m, 2 H), 2.83 (s, 3 H), 2.80 (s, 3 H), 2.66 (s, 3 H), 2.63 (s, 3 H), 2.59 (s, 3 H), 2.47 (s, 3 H), 2.49 (s, 3 H), 2.15 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 188.3, 178.3, 171.4, 166.1, 156.7, 156.2, 148.0, 131.1, 126.6, 125.6, 124.9, 24.6, 20.7, 19.7, 12.5, 12.3.

MS (EI, 70 eV): *m*/*z* (%) = 276 (35) [M$^+$], 258 (30), 244 (100), 230 (15), 213 (5), 122 (10), 77 (5).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{16}N_2O_2S$: 276.0932; found: 276.0932.

3-(1-Hydroxyiminoethyl)-7-methoxy-2-methylsulfanyl-1*H*-quinolin-4-one (1d)

Yield: 68%; colorless solid; R_f = 0.16 and 0.14 (hexane–EtOAc, 3:1); mp 178–180 °C.

IR (KBr): 3195, 3078, 1628, 1602 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 9.01 (s, 1 H), 7.50–7.53 (m, 1 H), 7.03 (s, 1 H), 6.73–6.82 (m, 1 H), 3.51 (s, 3 H), 2.73 (s, 3 H), 2.37 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.3, 172.1, 161.7, 152.1, 149.1, 145.8, 141.5, 126.4, 114.5, 113.6, 19.8, 15.3, 14.8.

MS (EI, 70 eV): *m*/*z* (%) = 278 (25) [M$^+$], 200 (100), 142 (35), 77 (13).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{14}N_2O_3S$: 278.0725; found: 278.0730.

5,7-Dichloro-3-(1-hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (1e)

Yield: 62%; yellow solid; R_f = 0.12 and 0.11 (hexane–EtOAc, 3:1); mp 190–191 °C.

IR (KBr): 3350, 3167, 3075, 2987, 1604, 1590 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.51 (s, 1 H), 8.57–8.58 (m, 1 H), 7.38–7.40 (m, 1 H), 2.51 (s, 3 H), 2.11 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 174.3, 171.7, 170.2, 151.3, 150.5, 131.1, 127.0, 126.3, 124.8, 122.7, 119.1, 19.4, 14.5.

MS (EI, 70 eV): *m*/*z* (%) = 317 (35) [M$^+$], 284 (75), 212 (15), 141 (25).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}Cl_2N_2O_2S$: 315.9840; found: 315.9847.

3-(1-Hydroxyiminoethyl)-2-methylsulfanyl-7-trifluoromethyl-1*H*-quinolin-4-one (1f)

Yield: 90%; colorless solid; R_f = 0.16 and 0.15 (hexane–EtOAc, 1:1); mp 172–173 °C.

IR (KBr): 3347, 3073, 2912, 1637, 1609 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.34 (d, *J* = 8.6 Hz, 1 H), 8.07 (d, *J* = 7.0 Hz, 1 H), 7.54 (t, *J* = 11.4 Hz, 1 H), 2.64 (s, 3 H), 2.18 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.9, 151.8, 150.8, 139.7, 127.0, 126.7, 124.8, 122.6, 119.9, 119.0, 115.5, 19.4, 15.1, 14.5.

MS (EI, 70 eV): *m*/*z* (%) = 316 (45) [M$^+$], 301 (23), 284 (100), 264 (40), 170 (5).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{11}F_3N_2O_2S$: 316.0493; found: 316.0490.

6-Chloro-3-(1-hydroxyiminoethyl)-2-methylsulfanyl-8-trifluoromethyl-1*H*-quinolin-4-one (1g)

Yield: 53%; yellow solid; R_f = 0.12 and 0.11 (hexane–EtOAc, 1:1); mp 205–207 °C.

IR (KBr): 3167, 3006, 1624, 1607 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.91 (s, 1 H), 8.34 (d, *J* = 11.8 Hz, 1 H), 7.86 (t, *J* = 9.4 Hz, 1 H), 2.64 (s, 3 H), 2.10 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 161.2, 156.8, 149.4, 143.8, 128.45, 128.41, 127.5, 125.3, 124.2, 124.0, 123.2, 123.1, 120.0, 115.7, 15.0, 12.9.

MS (EI, 70 eV): *m*/*z* (%) = 350 (15) [M$^+$], 293 (10), 275 (100), 262 (70), 201 (10), 75 (12).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{10}ClF_3N_2O_2S$: 350.0103; found: 350.0105.

3-(1-Hydroxyiminoethyl)-2-methylsulfanyl-6-nitro-1*H*-quinolin-4-one (1h)

Yield: 56%; yellow solid; R_f = 0.16 and 0.15 (hexane–EtOAc, 1:1); mp 188–190 °C.

IR (KBr): 3444, 3006, 2989, 1610 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.61 (s, 1 H), 10.91 (s, 1 H), 9.00 (s, 1 H), 8.35 (d, *J* = 9.4 Hz, 1 H), 7.82–7.90 (m, 1 H), 2.65 (s, 3 H), 2.12 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 181.3, 171.4, 164.6, 151.4, 141.6, 141.5, 138.7, 130.1, 126.5, 124.2, 116.5, 95.4, 15.7, 13.1, 12.3.

MS (EI, 70 eV): *m*/*z* (%) = 293 (13) [M$^+$], 275 (100), 261 (65), 229 (35), 215 (15), 75 (15).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{11}N_3O_4S$: 293.0470; found: 293.0466.

8-Benzenesulfonyl-3-(1-hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (1i)

Yield: 84%; yellow solid; R_f = 0.10 and 0.09 (hexane–EtOAc, 1:1); mp 115–117 °C (dec.).

IR (KBr): 3306, 3005, 2989, 1614 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.59–8.66 (m, 3 H), 8.18 (s, 1 H), 7.90–7.96 (m, 2 H), 7.40–7.75 (m, 2 H), 2.70 (s, 3 H), 2.21 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 156.7, 149.5, 149.3, 147.2, 143.3, 142.0, 136.2, 133.9, 132.9, 129.9, 129.0, 126.3, 123.9, 123.2, 120.6, 115.8, 13.2, 12.7.

MS (EI, 70 eV): *m*/*z* (%) = 388 (10) [M$^+$], 370 (80), 340 (50), 305 (100), 275 (15), 77 (25).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{16}N_2O_4S_2$: 388.0551; found: 388.0557.

8-Fluoro-3-(1-hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (1j)

Yield: 72%; colorless solid; R_f = 0.10 and 0.08 (hexane–EtOAc, 1:1); mp 191–193 °C.

IR (KBr): 3246, 3006, 2989, 1637, 1602 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.31–8.38 (m, 1 H), 7.89–7.44 (m, 2 H), 2.72 (s, 3 H), 2.51 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 149.5, 142.0, 136.1, 132.9, 129.0, 126.4, 126.3, 123.8, 123.2, 123.1, 14.9, 13.2.

MS (EI, 70 eV): *m*/*z* (%) = 266 (15) [M$^+$], 215 (30), 229 (35), 215 (15), 175 (10), 77 (15).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{11}FN_2O_2S$: 266.0525; found: 266.0521.

6,8-Difluoro-3-(1-hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (1k)
Yield: 77%; colorless solid; R_f = 0.10 and 0.09 (hexane–EtOAc, 1:1); mp 202–204 °C.

IR (KBr): 3234, 3006, 2989, 1567 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 11.42 (s, 1 H), 7.66–7.70 (m, 2 H), 2.54 (s, 3 H), 2.07 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 165.0, 163.4, 163.3, 162.7, 161.5, 161.4, 161.3, 154.8, 140.3, 126.1, 121.9, 110.9, 107.7, 24.7, 20.2, 18.3.

MS (EI, 70 eV): *m*/*z* (%) = 284 (20) [M^+], 267 (20), 252 (100), 238 (20), 150 (10), 112 (10).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{10}F_2N_2O_2S$: 284.0431; found: 284.0480.

2-Benzylsulfanyl-8-fluoro-3-(1-hydroxyiminoethyl)-1*H*-quinolin-4-one (1l)
Yield: 79%; colorless solid; R_f = 0.13 and 0.12 (hexane–EtOAc, 1:1); mp 102–105 °C.

IR (KBr): 3219, 3076, 2369, 1627, 1602 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 10.5 (s, 1 H), 7.60–7.68 (m, 1 H), 7.53–7.55 (m, 1 H), 7.17–7.35 (m, 5 H), 6.86–6.92 (m, 1 H), 4.02 (s, 2 H), 2.73 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 164.6, 162.9, 162.5, 162.2, 160.5, 160.3, 154.8, 143.8, 142.8, 134.5, 134.4, 133.6, 133.4, 132.1, 129.3, 126.5, 123.6, 120.8, 119.8, 38.8, 30.3, 20.3, 16.1.

MS (EI, 70 eV): *m*/*z* (%) = 342 (100) [M^+], 265 (35), 142 (13), 117 (10).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{15}FN_2O_2S$: 342.0838; found: 342.0831.

2-Allylsulfanyl-8-fluoro-3-(1-hydroxyiminoethyl)-5-nitro-1*H*-quinolin-4-one (1m)
Yield: 72%; colorless solid; R_f = 0.15 and 0.14 (hexane–EtOAc, 1:1); mp 182–185 °C (dec.).

IR (KBr): 3434, 3016, 1632, 1607 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 7.93–8.01 (m, 1 H), 7.74–7.83 (m, 1 H), 5.73–5.81 (m, 2 H), 4.92–4.97 (m, 1 H), 4.71–4.80 (m, 2 H), 2.35 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 180.1, 172.3, 167.2, 159.3, 149.2, 141.3, 132.7, 123.7, 121.2, 120.3, 118.2, 117.9, 37.2, 13.2.

MS (EI, 70 eV): *m*/*z* (%) = 337 (25) [M^+], 291 (100), 141 (25), 77 (15).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}FN_3O_4S$: 357.0532; found: 357.0529.

3-(Hydroxyiminophenylmethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (1n)
Yield: 47%; yellow solid; R_f = 0.10 and 0.09 (hexane–EtOAc, 1:1); mp 101–105 °C.

IR (KBr): 3236, 3006, 2989, 1607, 1567 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 11.77 (s, 1 H), 8.93 (d, *J* = 7.4 Hz, 1 H), 7.73–7.83 (m, 4 H), 7.34–7.52 (m, 3 H), 2.60 (s, 3 H).

^{13}C NMR (175 MHz, DMSO-d_6): δ = 166.0, 158.5, 154.9, 147.4, 131.3, 130.3, 129.9, 128.3, 128.0, 127.6, 127.4, 126.0, 121.5, 113.4, 112.5, 29.6, 12.6.

MS (EI, 70 eV): *m*/*z* (%) = 310 (100) [M^+], 278 (20), 143 (15), 112 (13).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{14}N_2O_2S$: 310.0776; found: 310.0771

5,8-Dichloro-3-(1-hydroxyimino-3-methylbutyl)-2-methylsulfanyl-1*H*-quinolin-4-one (1o)
Yield: 84%; brown solid; R_f = 0.11 and 0.10 (hexane–EtOAc, 1:1); mp 145–148 °C (dec.).

IR (KBr): 3397, 2976, 2929, 1647, 1606 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 10.11 (s, 1 H), 8.90 (d, *J* = 4.5 Hz, 1 H), 7.60 (d, *J* = 7.5 Hz, 1 H), 2.79 (s, 3 H), 1.76 (s, 3 H), 1.73 (s, 3 H), 1.21–1.16 (m, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 159.4, 155.0, 138.5, 129.1, 127.2, 126.8, 124.0, 121.2, 118.3, 114.5, 66.9, 58.1, 33.5, 25.0, 15.1.

MS (EI, 70 eV): *m*/*z* (%) = 359 (40) [M^+], 298 (100), 221 (20), 150 (15), 112 (13).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{16}Cl_2N_2O_2S$: 358.0309; found: 358.0308.

8-Chloro-3-(cyclopropylhydroxyiminomethyl)-2-methylsulfanyl-6-nitro-1*H*-quinolin-4-one (1p)
Yield: 57%; colorless solid; R_f = 0.11 and 0.10 (hexane–EtOAc, 1:1); mp 111–113 °C.

IR (KBr): 3474, 3346, 2919, 1609 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 12.44 (s, 1 H), 12.09 (s, 1 H), 8.77–8.78 (m, 1 H), 7.76–7.79 (m, 1 H), 5.75 (m, 1 H), 4.80–5.21 (m, 2 H), 2.09 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 167.1, 157.6, 147.1, 143.2, 137.0, 131.7, 123.9, 123.7, 122.4, 121.8, 21.2, 17.7, 12.6.

MS (EI, 70 eV): *m*/*z* (%) = 353 (35) [M^+], 260 (100), 188 (15), 141 (13).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}ClN_3O_4S$: 353.0237; found: 353.0229.

3-(1-Hydroxyiminoethyl)-1*H*-quinolin-4-one (1q)
Yield: 50%; colorless solid; R_f = 0.25 and 0.18 (CH_2Cl_2–MeOH, 20:1); mp 201–204 °C (dec.).

IR (KBr): 3215, 3072, 2924, 1758, 1735, 1616. 1615, 1585 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 10.79 (s, 1 H), 9.09 (s, 1 H), 8.13–8.16 (m, 1 H), 7.94 (s, 1 H), 7.54–7.70 (m, 2 H), 7.36 (d, *J* = 7.8 Hz, 1 H), 2.11 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 188.3, 175.3, 174.8, 174.3, 169.1, 149.4, 138.9, 138.6, 123.5, 118.1, 115.4, 16.5, 13.3.

MS (EI, 70 eV): *m*/*z* (%) = 202 (100) [M^+], 184 (35), 157 (25), 40 (10).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}NO_2$: 202.0742; found: 202.0741.

3-(1-Hydroxyiminoethyl)-1*H*-quinolin-4-one (*syn*-1q)
Yield: 7%; colorless solid; R_f = 0.25 (CH_2Cl_2–MeOH, 20:1); mp 173–175 °C.

IR (KBr): 3362, 2925, 2854, 1737, 1463, 1264 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 9.09 (s, 1 H), 8.13 (d, *J* = 7.6 Hz, 1 H), 7.94 (s, 1 H), 7.54–7.70 (m, 2 H), 7.36 (d, *J* = 7.8 Hz, 1 H), 2.11 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 188.3, 175.2, 174.9, 174.3, 169.2, 149.2, 138.9, 123.4, 118.3, 115.4, 13.5.

MS (EI, 70 eV): *m*/*z* (%) = 202 (100) [M^+], 184 (20), 157 (15), 57 (20), 40 (10).

3-(1-Hydroxyiminoethyl)-1*H*-quinolin-4-one (*anti*-1q)
Yield: 91%; colorless solid; R_f = 0.18 (CH_2Cl_2–MeOH, 20:1); mp 210–212 °C.

IR (KBr): 3336, 3039, 2575, 1831, 1752 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 10.79 (s, 1 H), 8.14 (d, J = 7.6 Hz, 1 H), 7.95 (s, 1 H), 7.54–7.70 (m, 2 H), 7.36 (d, J = 7.8 Hz, 1 H), 2.11 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 188.3, 175.4, 174.9, 174.2, 169.2, 149.2, 138.7, 123.4, 118.3, 115.4, 16.5.

MS (EI, 70 eV): m/z (%) = 202 (100) [M$^+$], 184 (20), 157 (15), 57 (20), 40 (10).

3-(1-Hydroxyiminoethyl)-6,8-dimethyl-1*H*-quinolin-4-one (1r)
Yield: 76%; colorless solid; R_f = 0.18 and 0.16 (hexane–EtOAc, 3:1); mp 123–126 °C.

IR (KBr): 3156, 3047, 2923, 2852, 1875, 1613 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.15 (s, 1 H), 8.62 (s, 1 H), 7.59 (s, 1 H), 7.34 (s, 1 H), 7.08 (s, 1 H), 2.46 (s, 3 H), 2.36 (s, 3 H), 2.13 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 175.2, 153.5, 149.4, 136.4, 136.2, 134.4, 133.8, 133.3, 127.5, 126.7, 126.7, 126.3, 125.4, 125.0, 122.2, 122.0, 20.6, 17.3, 17.09, 17.05, 14.0.

MS (EI, 70 eV): m/z (%) = 230 (100) [M$^+$], 200 (15), 199 (50), 173 (20).

HRMS (EI): m/z calcd for $C_{13}H_{14}N_2O_2$: 230.10553; found: 230.10538

7-Chloro-3-(1-hydroxyiminoethyl)-1*H*-quinolin-4-one (1s)
Yield: 45%; oil; R_f = 0.27 and 0.25 (hexane–EtOAc, 3:1).

IR (KBr): 3358, 2975, 1719, 1685, 1611 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 11.69 (s, 1 H), 10.94 (s, 1 H), 8.24–8.72 (m, 1 H), 8.11–8.15 (m, 2 H), 7.89–7.94 (m, 1 H), 2.67 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 181.3, 165.1, 153.9, 149.6, 142.4, 131.7, 121.6, 119.8, 115.6, 112.7, 28.9.

MS (EI, 70 eV): m/z (%) = 236 (100) [M$^+$], 215 (15), 170 (25), 127 (10), 117 (15).

HRMS (EI): m/z calcd for $C_{11}H_9ClN_2O_2$: 236.03526; found: 236.03545.

Oxazoloquinoline 2e and Isooxazoloquinoline 3e; Typical Procedure
To a stirred solution of 5,7-dichloro-3-(1-hydroxyiminoethyl)-2-methylsulfanyl-1*H*-quinolin-4-one (**1e**) (500 mg, 1.58 mmol) in dry MeCN (20 mL), a catalytic amount of anhydrous indium(III) chloride (0.16 mmol, 35 mg) was added and the resulting mixture was refluxed for 0.5 h. The solvent was distilled off, and the residue was partitioned between EtOAc (3 × 200 mL) and H_2O (20 mL). The organic layer was separated, washed with brine (15 mL), and dried over $MgSO_4$. Filtration and evaporation of the solvent under vacuum gave a crude product (454 mg) which was separated by silica gel column chromatography (hexane–EtOAc, 5:1) to afford oxazoloquinoline **2e** (293 mg, 62%) and isoxazoloquinoline **3e** (132 mg, 28%).

2-Methyl-4-methylsulfanyloxazolo[4,5-c]quinoline (2a)
Yield: 73%; colorless solid; R_f = 0.34 (hexane–EtOAc, 5:1); mp 94–95 °C.

IR (KBr): 3725, 3646, 2925, 2360, 1637 cm^{-1}.

^{1}H NMR (700 MHz, $CDCl_3$): δ = 8.24 (d, J = 8.1 Hz, 1 H), 8.05 (d, J = 8.7 Hz, 1 H), 7.75 (t, J = 16.8 Hz, 1 H), 7.55 (t, J = 15.0 Hz, 1 H), 2.79 (s, 3 H), 2.80 (s, 3 H).

^{13}C NMR (175 MHz, $CDCl_3$): δ = 163.2, 152.8, 146.0, 133.0, 128.7, 128.5, 125.7, 120.1, 114.7, 29.7, 14.5, 12.0.

MS (EI, 70 eV): m/z (%) = 230 (100) [M$^+$], 197 (15), 184 (17), 115 (10), 76 (5).

IR (KBr): 3725, 3646, 2925, 2360, 1637 cm^{-1}.

HRMS (EI): m/z calcd for $C_{12}H_{10}N_2OS$: 230.0507; found: 230.0513.

3-Methyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3a)
Yield: 22%; colorless solid; R_f = 0.48 (hexane–EtOAc, 5:1); mp 96–98 °C.

IR (KBr): 3691, 2927, 2358, 1633, 1590 cm^{-1}.

^{1}H NMR (700 MHz, $CDCl_3$): δ = 8.23 (d, J = 8.0 Hz, 1 H), 8.04 (d, J = 8.0 Hz, 1 H), 7.67–7.78 (m, 1 H), 7.49–7.58 (m, 1 H), 2.79 (s, 3 H), 2.75 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9, 155.0, 154.9, 147.6, 131.0, 128.0, 125.9, 121.6, 113.7, 112.7, 12.2, 12.1.

MS (EI, 70 eV): m/z (%) = 230 (100) [M$^+$], 197 (30), 184 (20), 142 (5), 130 (10), 102 (15).

HRMS (EI): m/z calcd for $C_{12}H_{10}N_2OS$: 230.0507; found: 230.0506.

2-Methyl-4-methylsulfanyl-6-phenyloxazolo[4,5-c]quinoline (2b)
Yield: 65%; colorless solid; R_f = 0.24 (hexane–EtOAc, 5:1); mp 93–94 °C.

IR (KBr): 2958, 2928, 2870, 1840, 1608, 1589 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.06 (d, J = 9.8 Hz, 1 H), 7.76–7.81 (m, 3 H), 7.42–7.75 (m, 4 H), 2.78 (s, 3 H), 2.58 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.2, 152.0, 150.8, 142.9, 139.8, 139.6, 132.7, 130.7, 129.5, 127.4, 125.5, 119.5, 115.0, 29.6, 14.5, 11.9.

MS (EI, 70 eV): m/z (%) = 306 (100) [M$^+$], 273 (15), 260 (5), 190 (5), 146 (5).

HRMS (EI): m/z calcd for $C_{18}H_{14}N_2OS$: 306.0826; found: 306.0849.

3-Methyl-4-methylsulfanyl-6-phenylisoxazolo[4,5-c]quinoline (3b)
Yield: 17%; yellow solid; R_f = 0.52 (hexane–EtOAc, 5:1); mp 112–114 °C.

IR (KBr): 3059, 3029, 2927, 2898, 1901, 1736, 1627 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.27 (d, J = 8.2 Hz, 1 H), 7.63–7.85 (m, 4 H), 7.44–7.51 (m, 3 H), 2.78 (s, 3 H), 2.56 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.8, 155.1, 154.8, 143.9, 138.5, 136.4, 131.7, 130.2, 127.5, 125.4, 124.5, 120.5, 118.5, 29.6, 14.3, 11.7.

MS (EI, 70 eV): m/z (%) = 306 (100) [M$^+$], 278 (25), 260 (10), 190 (10), 149 (10), 91 (10), 58 (10).

HRMS (EI): m/z calcd for $C_{18}H_{14}N_2OS$: 306.0826; found: 306.0825.

2,6,8-Trimethyl-4-methylsulfanyloxazolo[4,5-c]quinoline (2c)
Yield: 85%; yellow solid; R_f = 0.21 (hexane–EtOAc, 5:1); mp 218–220 °C.

IR (KBr): 2921, 2389, 2285, 1598 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 (s, 1 H), 7.30 (s, 1 H), 2.79 (s, 3 H), 2.77 (s, 3 H), 2.74 (s, 3 H), 2.50 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.9, 150.7, 149.8, 143.3, 136.4, 135.2, 132.8, 131.1, 116.9, 114.3, 21.6, 18.4, 14.5, 12.0.

MS (EI, 70 eV): *m*/*z* (%) = 258 [M$^+$] (100), 225 (15), 213 (10), 156 (10), 115 (5).

Anal. Calcd for $C_{14}H_{14}N_2OS$: C, 65.09; H, 5.46; N, 10.84; S, 12.41. Found: C, 65.04; H, 5.32; N, 10.70; S, 12.08.

3,6,8-Trimethyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3c)
Yield: 16%; yellow solid; R_f = 0.51 (hexane–EtOAc, 5:1); mp 198–200 °C.

IR (KBr): 2923, 2397, 1641, 1604, 1502 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59 (s, 1 H), 7.18 (s, 1 H), 2.60 (s, 3 H), 2.56 (s, 3 H), 2.49 (s, 3 H), 2.38 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.3, 154.5, 151.4, 144.2, 135.6, 135.1, 134.8, 132.8, 117.9, 112.7, 21.3, 18.1, 11.9, 11.8.

MS (EI, 70 eV): *m*/*z* (%) = 258 (100) [M$^+$], 243 (10), 230 (30), 225 (25), 156 (5), 115 (5), 103 (4), 77 (4).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{14}N_2OS$: 258.0826; found: 258.0830.

7-Methoxy-2-methyl-4-methylsulfanyloxazolo[4,5-c]quinoline (2d)
Yield: 78%; colorless solid; R_f = 0.23 (hexane–EtOAc, 5:1); mp 157–158 °C.

IR (KBr): 2993, 2931, 2853, 1878, 1741 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 9.0 Hz, 1 H), 7.44 (s, 1 H), 7.18 (d, *J* = 11.5 Hz, 1 H), 3.97 (s, 3 H), 2.80 (s, 3 H), 2.73 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.4, 160.3, 152.9, 150.9, 147.8, 131.7, 121.1, 117.9, 109.0, 107.8, 55.5, 14.5, 12.0.

MS (EI, 70 eV): *m*/*z* (%) = 260 (100) [M$^+$], 227 (10), 214 (10), 160 (5), 130 (5).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{12}N_2OS$: 260.0619; found: 260.0624.

7-Methoxy-3-methyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3d)
Yield: 1%; colorless solid; R_f = 0.49 (hexane–EtOAc, 5:1); mp 164–165 °C.

IR (KBr): 2968, 2921, 2845, 1626, 1602 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.0 Hz, 1 H), 7.34 (s, 1 H), 7.12 (d, 1 H, *J* = 8.0 Hz), 3.94 (s, 3 H), 2.74 (s, 3 H), 2.71 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.6, 162.0, 155.4, 154.9, 149.7, 130.8, 122.7, 117.6, 112.3, 107.9, 55.5, 12.2, 12.1.

MS (EI, 70 eV): *m*/*z* (%) = 260 (100) [M$^+$] , 232 (35), 214 (15), 199 (9), 171 (7), 144 (8), 63 (10).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{12}N_2O_2S$: 260.0619; found: 260.0625.

7,9-Dichloro-2-methyl-4-methylsulfanyloxazolo[4,5-c]quinoline (2e)
Yield: 62%; colorless solid; R_f = 0.25 (hexane–EtOAc, 5:1); mp 158–159 °C.

IR (KBr): 3070, 2924, 1742, 1697, 1619 cm^{-1}.

^{1}H NMR (700 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 2.1 Hz, 1 H), 7.56 (d, *J* = 2.1 Hz, 1 H), 2.79 (s, 3 H), 2.76 (s, 3 H).

^{13}C NMR (175 MHz, $CDCl_3$): δ = 164.3, 155.7, 148.9, 146.6, 134.4, 133.7, 127.5, 126.9, 126.6, 112.8, 14.6, 12.0.

MS (EI, 70 eV): *m*/*z* (%) = 298 (100) [M$^+$ – 1], 265 (10), 253 (15), 210 (5), 198 (10).

HRMS (EI): *m*/*z* calcd for $C_{12}H_8Cl_2N_2OS$: 297.9734; found: 297.9731.

7,9-Dichloro-3-methyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3e)
Yield: 28%; yellow solid; R_f = 0.45 (hexane–EtOAc, 5:1); mp 100–102 °C.

IR (KBr): 3080, 2934, 1735, 1680, 1608 cm^{-1}.

^{1}H NMR (700 MHz, $CDCl_3$): δ = 7.994 (d, *J* = 2.1 Hz, 1 H), 7.527 (d, *J* = 2.1 Hz, 1 H), 2.79 (s, 3 H), 2.77 (s, 3 H).

^{13}C NMR (175 MHz, $CDCl_3$): δ = 164.5, 157.9, 154.6, 148.7, 136.2, 129.9, 127.4, 126.3, 115.0, 112.2, 12.3, 12.2.

MS (EI, 70 eV): *m*/*z* (%) = 298 (100) [M + H]$^+$, 270 (30), 252 (15), 198 (5), 173 (5), 148 (7), 109 (5), 74 (5).

HRMS (EI): *m*/*z* calcd for $C_{12}H_8Cl_2N_2OS$: 297.9734; found: 297.9740.

2-Methyl-4-methylsulfanyl-7-trifluoromethyloxazolo[4,5-c]-quinoline (2f)
Yield: 76%; colorless solid; R_f = 0.27 (hexane–EtOAc, 5:1); mp 141–142 °C.

IR (KBr): 3748, 2360, 1602 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.35 (s, 1 H), 8.13 (d, *J* = 8.5 Hz, 1 H), 7.71 (d, *J* = 8.5 Hz, 1 H), 2.80 (s, 3 H), 2.79 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.2, 155.0, 149.8, 144.8, 134.3, 130.3, 126.1, 125.1, 122.9, 121.3, 116.4, 14.6, 12.0.

MS (EI, 70 eV): *m*/*z* (%) = 298 (100) [M$^+$], 279 (10), 265 (25), 252 (20).

HRMS (EI): *m*/*z* calcd for $C_{13}H_9F_3N_2OS$: 298.0387; found: 298.0395.

3-Methyl-4-methylsulfanyl-7-trifluoromethylisoxazolo[4,5-c]-quinoline (3f)
Yield: 12%; colorless solid; R_f = 0.42 (hexane–EtOAc, 5:1); mp 100–102 °C.

IR (KBr): 2933, 1610, 1351 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.27–8.28 (m, 2 H), 7.71 (d, *J* = 9.5 Hz, 1 H), 2.77 (s, 3 H), 2.76 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.9, 157.1, 155.2, 146.7, 132.8, 132.5, 125.6, 122.7, 121.6, 115.4, 114.6, 12.3, 12.2.

MS (EI, 70 eV): *m*/*z* (%) = 298 (100) [M$^+$], 279 (5), 270 (40), 198 (7), 170 (10).

HRMS (EI): *m*/*z* calcd for $C_{13}H_9F_3N_2OS$: 298.0387; found: 298.0385.

8-Chloro-2-methyl-4-methylsulfanyl-6-trifluoromethyloxazolo[4,5-c]quinoline (2g)
Yield: 82%; colorless solid; R_f = 0.28 (hexane–EtOAc, 5:1); mp 178–180 °C.

IR (KBr): 3058, 2927, 2387, 2360, 2285, 1633, 1515 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.43 (d, *J* = 10 Hz, 1 H), 8.17 (d, *J* = 10 Hz, 1 H), 2.83 (s, 3 H), 2.81 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.4, 158.0, 150.5, 147.6, 144.3, 134.2, 129.8, 122.4, 117.2, 113.7, 29.7, 14.5, 12.1.

MS (EI, 70 eV): *m*/*z* (%) = 332 (100) [M$^+$], 297 (25), 222 (15), 181 (10), 124 (15).

HRMS (EI): *m*/*z* calcd for $C_{13}H_8ClF_3N_2OS$: 331.9997; found: 331.9996.

8-Chloro-3-methyl-4-methylsulfanyl-6-trifluoromethylisoxazolo[4,5-c]quinoline (3g)
Yield: 12%; yellow solid; R_f = 0.56 (hexane–EtOAc, 5:1); mp 211–213 °C.

IR (KBr): 3482, 3372, 2923, 2389, 1635 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.51–8.54 (m, 1 H), 8.14–8.15 (m, 1 H), 2.83 (s, 3 H), 2.82 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.4, 158.0, 150.5, 147.6, 144.3, 134.2, 129.8, 122.4, 117.2, 113.7, 29.7, 14.5, 12.1.

MS (EI, 70 eV): *m*/*z* (%) = 332 (100) [M^+], 297 (10), 181 (15), 124 (10), 71 (5).

HRMS (EI): *m*/*z* calcd for $C_{13}H_8ClF_3N_2OS$: 331.9997; found: 331.9994.

2-Methyl-4-methylsulfanyl-8-nitrooxazolo[4,5-c]quinoline (2h)
Yield: 75%; yellow solid; R_f = 0.24 (hexane–EtOAc, 5:1); mp 165–166 °C.

IR (KBr): 3058, 2927, 2387, 2399, 1635, 1515 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 9.18 (s, 1 H), 8.52–8.55 (m, 1 H), 8.12–8.14 (m, 1 H), 2.78 (s, 3 H), 2.74 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.4, 158.1, 150.6, 147.7, 144.4, 143.5, 129.8, 122.4, 117.3, 113.8, 14.6, 12.2.

MS (EI, 70 eV): *m*/*z* (%) = 275 (100) [M^+], 242 (5), 229 (30), 184 (5), 114 (10), 75 (15).

Anal. Calcd for $C_{12}H_9N_3O_3S$: C, 52.36; H, 3.30; N, 15.26; S, 11.65. Found: C, 52.18; H, 3.33; N, 15.14; S, 11.98.

3-Methyl-4-methylsulfanyl-8-nitroisoxazolo[4,5-c]quinoline (3h)
Yield: 5%; yellow solid; R_f = 0.39 (hexane–EtOAc, 5:1); mp 120–122 °C.

IR (KBr): 3093, 3004, 2923, 1673, 1635 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 9.08–9.09 (m, 1 H), 8.44–8.47 (m, 1 H), 8.06–8.08 (m, 1 H), 2.76 (s, 3 H), 2.73 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.7, 160.3, 155.3, 149.7, 144.5, 129.5, 124.8, 118.7, 114.3, 113.0, 12.4, 12.2.

MS (EI, 70 eV): *m*/*z* (%) = 275 (100) [M^+], 242 (5), 229 (55), 196 (5), 183 (10), 145 (10), 75 (13).

Anal. Calcd for $C_{12}H_9N_3O_3S$: C, 52.36; H, 3.30; N, 15.26; S, 11.65. Found: C, 52.26; H, 3.23; N, 15.24; S, 11.68.

6-Benzenesulfonyl-2-methyl-4-methylsulfanyl-oxazolo[4,5-c]-quinoline (2i)
Yield: 72%; crystal; R_f = 0.32 (hexane–EtOAc, 1:1); mp 115–116 °C.

IR (KBr): 3064, 2927, 1629, 1373, 1307, 1155, 1012, 773, 732, 688, 590 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.70–8.71 (d, *J* = 9.0 Hz, 1 H), 8.34–8.36 (d, *J* = 13.0 Hz, 1 H), 7.92–7.93 (m, 2 H), 7.69–7.72 (t, *J* = 15.5 Hz, 1 H), 7.51 (m, 1 H), 7.42–7.45 (m, 2 H), 2.75 (s, 3 H), 2.60 (s, 3 H).

^{13} C NMR (125 MHz, $CDCl_3$): δ = 164.11, 155.93, 142.34, 141.20, 135.23, 133.57, 132.64, 131.76, 128.64, 126.92, 124.49, 116.01, 14.54, 12.90.

MS (EI, 70 eV): *m*/*z* (%) = 370 (100) [M^+], 342, 305, 291, 273, 228, 77.

HRMS (EI): *m*/*z* calcd for $C_{18}H_{14}N_2O_3S_2$: 370.0446; found: 370.0445.

6-Benzenesulfonyl-3-methyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3i)
Yield: 12%; yellow solid; R_f = 0.48 (hexane–EtOAc, 5:1); mp 208–210 °C.

IR (KBr): 2389, 2281, 1635, 1500 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 9.0 Hz, 1 H), 8.54 (d, *J* = 9.0 Hz, 1 H), 7.90–7.92 (m, 2 H), 7.75 (t, *J* = 15.5 Hz, 1 H), 7.53 (m, 1 H), 7.45–7.47 (m, 2 H), 2.72 (s, 3 H), 2.60 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.8, 158.4, 155.3, 143.3, 142.2, 135.0, 133.8, 132.7, 128.7, 128.2, 126.8, 124.8, 115.1, 114.2, 12.8, 12.2.

MS (EI, 70 eV): *m*/*z* (%) = 370 (50) [M^+], 305 (100), 291 (10), 273 (13),145 (5), 77 (10).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{14}N_2O_3S_2$: 370.0446; found: 370.0440.

6-Fluoro-2-methyl-4-methylsulfanyloxazolo[4,5-c]quinoline (2j)
Yield: 80%; yellow solid; R_f = 0.27 (hexane–EtOAc, 5:1); mp 146–147 °C.

IR (KBr): 3849, 3731, 2381, 2362, 2285, 1594, 1502 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.0 Hz, 1 H), 7.36–7.39 (m, 1 H), 7.31–7.33 (m, 1 H), 2.81 (s, 3 H), 2.74 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.3, 156.3, 156.0, 155.2, 137.3, 125.9, 117.3, 116.0, 115.9, 115.5, 114.2, 12.2.

MS (EI, 70 eV): *m*/*z* (%) = 248 (100) [M^+], 215 (30), 202 (20), 148 (10), 120 (10), 94 (5).

HRMS (EI): *m*/*z* calcd for $C_{12}H_9FN_2OS$: 248.0419; found: 248.0423.

6-Fluoro-3-methyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3j)
Yield: 7%; yellow solid; R_f = 0.45 (hexane–EtOAc, 5:1); mp 140–141 °C.

IR (KBr): 3866, 3748, 2389, 1604, 1511 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.02–8.04 (m, 1 H), 7.48–7.52 (m, 2 H), 2.85 (s, 3 H), 2.81 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.2, 158.3, 156.3, 155.3, 137.4, 125.9, 117.3, 116.0, 115.9, 114.2, 12.5, 12.2.

MS (EI, 70 eV): *m*/*z* (%) = 248 (100) [M^+], 220 (50), 202 (15), 148 (15), 120 (20), 94 (35).

HRMS (EI): *m*/*z* calcd for $C_{12}H_9FN_2OS$: 248.0419; found: 248.0419.

6,8-Difluoro-2-methyl-4-methylsulfanyloxazolo[4,5-c]quinoline (2k)
Yield: 73%; yellow solid; R_f = 0.23 (hexane–EtOAc, 5:1); mp 186–189 °C.

IR (KBr): 3759, 3525, 2457, 2179, 1598, 1511 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.41–7.48 (m, 1 H), 7.13–7.28 (m, 1 H), 2.82 (s, 3 H), 2.79 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.0, 159.0, 156.9, 152.9, 149.8, 134.3, 132.9, 115.9, 104.3, 100.1, 14.4, 11.9.

MS (EI, 70 eV): *m*/*z* (%) = 266 (100) [M^+], 233 (30), 220 (15), 166 (10), 151 (9), 138 (7).

HRMS (EI): *m*/*z* calcd for $C_{12}H_8F_2N_2OS$: 266.0325; found: 266.0324.

6,8-Difluoro-3-methyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3k)
Yield: 1%; yellow solid; R_f = 0.39 (hexane–EtOAc, 5:1); mp 178–179 °C.

IR (KBr): 3536, 3245, 2184, 1751, 1596 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.70–7.72 (m, 1 H), 7.28–7.35 (m, 1 H), 2.84 (s, 3 H), 2.82 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.0, 159.0, 156.9, 152.9, 149.8, 134.3, 132.9, 115.9, 104.3, 100.1, 14.4, 11.9.

MS (EI, 70 eV): *m*/*z* (%) = 266 (100) [M^+], 238 (30), 220 (10), 165 (10), 150 (15).

HRMS (EI): *m*/*z* calcd for $C_{12}H_8F_2N_2OS$: 266.0325; found: 266.0325.

4-Benzylsulfanyl-6-fluoro-2-methyloxazolo[4,5-c]quinoline (2l)
Yield: 71%; yellow solid; R_f = 0.30 (hexane–EtOAc, 5:1); mp 154–155 °C.

IR (KBr): 3063, 2926, 2850, 1920, 1646 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.74–7.79 (m, 1 H), 7.61–7.65 (m, 2 H), 7.22–7.45 (m, 5 H), 4.76 (s, 2 H), 2.76 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 163.7, 160.3, 155.2, 152.6, 150.3, 138.2, 129.6, 128.4, 127.1, 125.9, 125.7, 116.7, 115.9, 115.8, 113.7, 113.4, 33.2, 14.5.

MS (EI): *m*/*z* (%) = 324 (100) [M^+], 309 (5), 291 (65), 247 (18), 202 (10), 91 (40).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{13}FN_2OS$: 324.0732; found: 324.0735.

4-Benzylsulfanyl-6-fluoro-3-methylisoxazolo[4,5-c]quinoline (3l)
Yield: 23%; yellow solid; R_f = 0.37 (hexane–EtOAc, 5:1); mp 135–136 °C.

IR (KBr): 3062, 2924, 1725 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.01–7.99 (m, 1 H), 7.48–7.62 (m, 3 H), 7.28–7.38 (m, 4 H), 4.77 (s, 2 H), 2.77 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 193.2, 160.1, 155.3, 154.9, 137.6, 129.6, 129.5, 128.6, 127.4, 126.2, 126.0, 117.4, 117.3, 116.3, 115.9, 97.2, 33.5, 12.3.

MS (EI, 70 eV): *m*/*z* (%) = 324 (100) [M^+], 291 (60), 247 (20), 215 (30), 202 (7), 91 (70).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{13}FN_2OS$: 324.0732; found: 324.0730.

4-Allylsulfanyl-6-fluoro-2-methyl-9-nitrooxazolo[4,5-c]quinoline (2m)
Yield: 56%; colorless solid; R_f = 0.28 (hexane–EtOAc, 5:1); mp 151–152 °C.

IR (KBr): 2958, 2929, 2871, 1840, 1685, 1660 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.43–8.46 (m, 1 H), 7.47–7.52 (m, 1 H), 5.70–5.81 (m, 1 H), 4.89–5.06 (m, 2 H), 3.29 (m, 2 H), 2.57 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.6, 161.1, 150.6, 142.1, 137.9, 131.6, 130.7, 124.3, 123.1, 116.8, 114.7, 101.5, 29.3, 12.0.

MS (EI, 70 eV): *m*/*z* (%) = 319 (100) [M^+], 254 (15), 181 (20), 124 (5), 71 (5).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{10}FN_3O_3S$: 319.0426; found: 319.0426.

4-Allylsulfanyl-6-fluoro-3-methyl-9-nitroisoxazolo[4,5-c]quinoline (3m)
Yield: 37%; brown solid; R_f = 0.35 (hexane–EtOAc, 5:1); mp 128–131 °C.

IR (KBr): 3014, 2619, 1810, 1655, 1594 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.41–8.46 (m, 1 H), 7.44–7.49 (m, 1 H), 5.67–5.78 (m, 1 H), 4.84–5.01 (m, 2 H), 3.41–3.45 (m, 2 H), 2.54 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.6, 162.1, 150.6, 142.3, 138.9, 135.0, 131.7, 124.0, 119.1, 117.8, 114.3, 111.5, 39.1, 11.9.

MS (EI, 70 eV): *m*/*z* (%) = 319 (100) [M^+], 254 (15), 181 (200), 144 (8), 63 (10).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{10}FN_3O_3S$: 319.0426; found: 319.0427.

4-Methylsulfanyl-2-phenyloxazolo[4,5-c]quinoline (2n)
Yield: 37%; yellow solid; R_f = 0.29 (hexane–EtOAc, 5:1); mp 150–151 °C.

IR (KBr): 3064, 2926, 1633 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.33–8.38 (m, 1 H), 8.09–8.21 (m, 2 H), 7.52–7.72 (m, 6 H), 2.85 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.5, 153.4, 150.3, 146.2, 133.9, 131.7, 131.3, 130.4, 130.0, 128.9, 128.6, 128.4, 127.7, 126.6, 125.7, 120.3, 14.1.

MS (EI, 70 eV): *m*/*z* (%) = 292 (100) [M^+], 245 (50), 168 (30), 145 (9), 77 (13).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{12}N_2OS$: 292.0670; found: 292.0673.

4-Methylsulfanyl-3-phenylisoxazolo[4,5-c]quinoline (3n)
Yield: 49%; yellow solid; R_f = 0.35 (hexane–EtOAc, 5:1); mp 129–130 °C.

IR (KBr): 3789, 2955, 1630 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.1 Hz, 1 H), 8.08 (d, *J* = 8.0 Hz, 1 H), 7.75–7.83 (m, 2 H), 7.56–7.63 (m, 5 H), 2.68 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 158.6, 155.0, 147.5, 134.2, 131.3, 130.4, 130.0, 128.9, 128.4, 128.1, 127.7, 127.5, 126.1, 121.6, 113.6, 14.1.

MS (EI, 70 eV): *m*/*z* (%) = 292 (100) [M^+], 168 (30), 114 (13), 75 (7).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{12}N_2OS$: 292.0670; found: 292.0665.

6,9-Dichloro-2-isopropyl-4-methylsulfanyloxazolo[4,5-c]quinoline (2o)
Yield: 67%; yellow solid; R_f = 0.38 (hexane–EtOAc, 10:1); mp 137–138 °C.

IR (KBr): 3091, 2872, 1841, 1618, 1573 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.64–7.66 (m, 1 H), 7.33–7.39 (m, 1 H), 2.90–2.91 (m, 2 H), 2.77 (s, 3 H), 2.29–2.32 (m, 1 H), 1.01–1.02 (d, *J* = 2.5 Hz, 3 H), 1.00 (d, *J* = 2.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.6 155.3, 142.0, 134.9, 131.9, 130.5, 129.7, 128.3, 126.8, 126.1, 115.3, 37.5, 22.7, 22.4, 12.1.

MS (EI, 70 eV): *m*/*z* (%) = 340 (100) [M – 1]$^+$, 325 (10), 307 (5), 297 (20), 265 (5), 198 (5).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}Cl_2N_2OS$: 340.0203; found: 340.0203.

6,9-Dichloro-3-isopropyl-4-methylsulfanylisoxazolo[4,5-c]quinoline (3o)
Yield: 27%; yellow solid; R_f = 0.39 (hexane–EtOAc, 5:1); mp 113–115 °C.

IR (KBr): 2976, 2930, 2872, 1712, 1618, 1606 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.54 (d, *J* = 2.4 Hz, 1 H), 7.38 (d, *J* = 2.4 Hz, 1 H), 2.98–3.01 (m, 2 H), 2.81 (s, 3 H), 2.36–2.39 (m, 1 H), 1.09 (d, *J* = 6.5 Hz, 3 H), 1.01 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.5, 157.1, 143.72, 134.84, 131.5, 130.4, 129.7, 128.2, 126.6, 126.0, 114.2, 37.3, 27.7, 22.4, 12.1.

MS (EI, 70 eV): *m*/*z* (%) = 340 (100) [M$^+$], 325 (15), 307 (5), 297 (15), 285 (10), 270 (5).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}Cl_2N_2OS$: 340.0203; found: 340.0201.

6-Chloro-2-cyclopropyl-4-methylsulfanyl-8-nitrooxazolo[4,5-c]quinoline (2p)
Yield: 67%; colorless solid; R_f = 0.31 (hexane–EtOAc, 5:1); mp 101–102 °C.

IR (KBr): 2923, 2397, 1641, 1604, 1502 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 10.0 Hz, 1 H), 7.29 (d, *J* = 10.0 Hz, 1 H), 2.74 (s, 3 H), 2.01–2.07 (m, 1 H), 0.96–0.99 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.1, 151.6, 147.8, 143.7, 138.0, 132.7, 123.9, 123.4, 121.4, 120.5, 20.7, 15.7, 11.6.

MS (EI, 70 eV): *m*/*z* (%) = 335 (100) [M$^+$], 289 (35), 207 (5), 166 (15), 77 (5).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{10}ClN_3O_3S$: 335.0131; found: 335.0136.

6-Chloro-3-cyclopropyl-4-methylsulfanyl-8-nitroisoxazolo[4,5-c]quinoline (3p)
Yield: 27%; colorless solid; R_f = 0.39 (hexane–EtOAc, 5:1); mp 128–129 °C.

IR (KBr): 2923, 2397, 1641, 1604, 1502 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 10.0 Hz, 1 H), 7.22 (d, *J* = 10.0 Hz, 1 H), 2.62 (s, 3 H), 2.02–2.09 (m, 1 H), 0.86–0.89 (m, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.1, 150.4, 146.8, 140.4, 137.9, 132.7, 121.9, 120.4, 118.4, 110.5, 18.7, 10.7, 8.6.

MS (EI, 70 eV): *m*/*z* (%) = 335 [M$^+$] (100), 207 (50), 166 (15), 148 (7), 109 (5), 74 (5).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{10}ClN_3O_3S$: 335.0131; found: 335.0134.

2-Methyloxazolo[4,5-c]quinoline (2q)
Yield: 76%; colorless solid; R_f = 0.21 (hexane–EtOAc, 5:1); mp 185–187 °C.

IR (KBr): 3075, 2917, 2853, 1926, 1850 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.15 (s, 1 H), 8.39–8.43 (m, 1 H), 8.26 (d, *J* = 4.4 Hz, 1 H), 7.73 (d, *J* = 6.8 Hz, 2 H), 7.45 (t, *J* = 7.4Hz, 1 H), 2.77 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): = 194.2, 189.2, 184.9, 176.6, 144.6, 129.9, 127.9, 124.5, 123.7, 121.8, 29.8.

MS (EI, 70 eV): *m*/*z* (%) = 184 (35) [M$^+$], 149 (55), 111 (30), 97 (55), 57 (100).

HRMS (EI): *m*/*z* calcd for $C_{11}H_8N_2O$: 184.0636; found: 184.0636.

3-Methylisoxazolo[4,5-c]quinoline (3q)
Yield: 12%; colorless solid; R_f = 0.27 (hexane–EtOAc, 5:1); mp 173–175 °C.

IR (KBr): 3027, 2977, 1850, 1643 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.13 (s, 1 H), 8.07 (t, *J* = 5.2 Hz, 1 H), 7.52–7.59 (m, 2 H), 7.21–7.28 (m, 2 H), 2.83 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): = 194.5, 189.7, 185.8, 176.7, 144.8, 129.9, 128.6, 125.1, 124.1, 123.6, 25.5.

MS (EI, 70 eV): *m*/*z* (%) = 184 (45) [M$^+$], 154 (15), 125 (15), 91 (20), 83 (65), 57 (100).

HRMS (EI): *m*/*z* calcd for $C_{11}H_8N_2O$: 184.0636; found: 184.0636.

2, 6,8-Trimethyloxazolo[4,5-c]quinoline (2r)
Yield: 71%; colorless solid; R_f = 0.35 (hexane–EtOAc, 10:1); mp 172–173 °C.

IR (KBr): 2924, 1898, 1638, 1603 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.07 (s, 1 H), 8.02 (s, 1 H), 7.57 (s, 1 H), 2.86 (s, 3 H), 2.74 (s, 3 H), 2.60 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): = 153.7, 147.7, 145.6, 142.1, 138.7, 135.6, 133.8, 130.9, 118.6, 115.9, 21.8, 19.1, 10.4.

MS (EI, 70 eV): *m*/*z* (%) = 212 (35) [M$^+$], 198 (10), 156 (100), 103 (25), 96 (15).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{12}N_2O$: 212.0949; found: 212.0953.

3,6,8-Trimethylisoxazolo[4,5-c]quinoline (3r)
Yield: 17%; colorless solid; R_f = 0.41 (hexane–EtOAc, 10:1); mp 158–159 °C.

IR (KBr): 2956, 2853, 1782, 1607, 1580, 1502 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.08 (s, 1 H), 8.02 (s, 1 H), 7.57 (s, 1 H), 2.87 (s, 3 H), 2.75 (s, 3 H), 2.60 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): = 155.6, 148.4, 145.8, 143.0, 137.9, 136.0, 133.9, 130.9, 119.1, 116.2, 21.5, 18.9, 10.3.

MS (EI, 70 eV): *m*/*z* (%) = 212 (25) [M$^+$], 156 (100), 103 (18), 96 (20), 77 (24).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{12}N_2O$: 212.0949; found: 212.0949.

7-Chloro-2-methyloxazolo[4,5-c]quinoline (2s)
Yield: 65%; oil; R_f = 0.38 (hexane–EtOAc, 10:1).

IR (KBr): 3054, 2814, 1745, 1677, 1599 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.10–8.14 (m, 1 H), 7.64–7.69 (m, 2 H), 7.01 (s, 1 H), 2.79 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 176.5, 160.8, 159.7, 150.5, 149.0, 139.7, 137.6, 129.8, 109.3, 100.6, 34.3.

MS (EI, 70 eV): *m*/*z* (%) = 218 (100) [M$^+$], 198 (10), 183 (25), 126 (30), 77 (10).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{17}ClN_2O$: 218.0246; found: 218.0244.

7-Chloro-3-methylisoxazolo[4,5-c]quinoline (3s)
Yield: 10%; oil; R_f = 0.42 (hexane–EtOAc, 10:1).

IR (KBr): 3060, 2834, 1711, 1681, 1612 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.06–8.09 (m, 1 H), 7.20–7.29 (m, 2 H), 7.02 (s, 1 H), 2.79 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): = 176.7, 161.3, 159.9, 151.2, 149.7, 139.8, 137.7, 130.5, 111.3, 101.8, 32.7.

MS (EI, 70 eV): *m*/*z* (%) = 218 (100) [M$^+$], 177 (15), 126 (25), 109 (5), 77 (15).

HRMS (EI): *m/z* calcd for $C_{11}H_{17}ClN_2O$: 218.0246; found: 218.0255.

Desufanylation: 3-Acetyl-1*H*-quinolin-4-one (5q); Typical Procedure

To a solution of 3-acetyl-2-methylsulfanyl-1*H*-quinolin-4-one (**4q**) (1 g, 4.3 mmol) in abs EtOH (30 mL), Raney Ni was added and the suspension was shaken for 12 h under a hydrogen atmosphere in a Parr reactor. The reaction mixture was filtered through a sintered funnel and the residue was washed with ethanol. The filtrate was taken and the solvent was evaporated under vacuum to give a residue that was separated by silica gel column chromatography (hexane–EtOAc, 5:1) to afford **5q** (0.40 g, 50%) as a brown solid.

R_f = 0.12 (hexane–EtOAc, 3:1); mp 201–202 °C.

IR (KBr): 3051, 2922, 2279, 2122, 1621 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 8.10 (d, *J* = 7.8 Hz, 1 H), 7.29 (m, 2 H), 7.02–7.08 (m, 2 H), 2.31 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 197.1, 176.1, 162.5, 148.6, 129.7, 127.4, 125.0, 122.5, 120.8, 116.4, 13.9.

MS (EI, 70 eV): *m/z* (%) = 187 (100) [M^+], 171 (15), 145 (20), 118 (10), 100 (35), 82 (65).

HRMS (EI): *m/z* calcd for $C_{11}H_9NO_2$: 187.0633; found: 187.0655.

3-Acetyl-6,8-dimethyl-1*H*-quinolin-4-one (5r)

Yield: 71%; colorless solid; R_f = 0.10 (hexane–EtOAc, 3:1); mp 181–182 °C.

IR (KBr): 3242, 2919, 1612, 1550, 1514 cm^{-1}.

^1H NMR (200 MHz, DMSO-d_6): δ = 7.85 (s, 1 H), 7.78 (s, 1 H), 7.27 (s, 1 H), 3.18 (s, 3 H), 2.45 (s, 3 H), 2.34 (s, 3 H).

^{13}C NMR (125 MHz, DMSO-d_6): = 175.2, 136.8, 135.1, 133.3, 131.3, 130.3, 126.4, 125.3, 124.9, 122.0, 23.9, 20.7, 17.1.

MS (EI, 70 eV): *m/z* (%) = 216 (70) [M + H]$^+$, 199 (100), 173 (15).

HRMS (EI): *m/z* calcd for $C_{13}H_{13}NO_2$: 215.0946; found: 215.0919.

3-Acetyl-7-chloro-1*H*-quinolin-4-one (5s)

Yield: 46%; yellow solid; R_f = 0.15 (hexane–EtOAc, 3:1); mp 165–167 °C.

IR (KBr): 3346, 3253, 3078, 2989, 1646, 1553 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.6 Hz, 1 H), 7.86 (s, 1 H), 7.35–7.39 (m, 2 H), 2.61 (s, 3 H).

^{13}C NMR (175 MHz, $CDCl_3$): δ = 198.3, 174.6, 157.9, 144.8, 136.6, 127.9, 127.6, 124.4, 123.6, 118.1, 14.7.

MS (EI, 70 eV): *m/z* (%) = 221 (100) [M^+], 187 (10), 171 (5), 77 (15), 41 (20).

HRMS (EI): *m/z* calcd for $C_{11}H_8ClNO_2$: 221.0243; found: 221.0212.

3-Amino-2-methylsulfanyl-1*H*-quinolin-4-one (6a)

A solution of oxazoloquinoline **2a** (0.1 g, 0.43 mmol) in THF (20 mL) containing aq HCl (5%, 5 mL) was refluxed for 3 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL), and the organic phase was separated and washed with sat aq Na_2CO_3 (3 × 50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under vacuum. The solid was chromatographed on a silica gel column (hexane–EtOAc, 1:1) to give 3-aminoquinoline **6a**.

Yield: 78%; yellow solid; R_f = 0.12 (hexane–EtOAc, 1:1); mp 170–172 °C.

IR (KBr): 3418, 3318, 3053, 2897, 2845, 1635, 1563 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 8.12 (d, *J* = 8.0 Hz, 1 H), 8.02 (d, *J* = 8.0 Hz, 1 H), 7.73 (t, *J* = 15.5 Hz, 1 H), 7.41 (t, *J* = 15.0 Hz, 1 H), 2.81 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.3, 144.3, 140.5, 132.7, 125.0, 124.7, 123.1, 119.1, 116.5, 17.8.

MS (EI): *m/z* (%) = 206 (100) [M^+] , 190 (40), 143 (25), 77 (13).

HRMS (EI): *m/z* calcd for $C_{10}H_{10}N_2OS$: 206.0513; found: 206.0517.

3-(*N*-Acetyl)amino-2-methylsulfanyl-1*H*-quinolin-4-one (7a)

A mixture of 3-aminoquinoline **6a** (50 mg, 0.24 mmol) and Ac_2O (10 mL), was stirred at r.t. for 1 h. The resulting oil was diluted with CH_2Cl_2 (20 mL), and washed with H_2O (3 × 20 mL). The organic layer was dried ($MgSO_4$), filtered, and the solvent was evaporated under vacuum to give a crude mixture (mass balance 43 mg), which was separated by silica gel column chromatography (hexane–EtOAc, 5:1) to afford the acetylated product **7a** (28 mg, 46%) as a white solid along with diacetylated product, *N*-acetyl-*N*-(2-methylsulfanyl-4-oxo-1,4-dihydroquinolin-3-yl)acetamide (16 mg, 23%).

R_f = 0.13 (hexane–EtOAc, 3:1); mp 180–181 °C.

IR (KBr): 3242, 3197, 2923, 1763, 1674 cm^{-1}.

^1H NMR (500 MHz, DMSO-d_6): δ = 7.99 (d, *J* = 7.2 Hz, 1 H), 7.82 (d, 1 H, *J* = 8.2 Hz), 7.70 (t, *J* = 10.0 Hz, 1 H), 7.50 (d, *J* = 7.2 Hz, 1 H), 2.70 (s, 3 H), 2.47 (s, 3 H).

^{13}C NMR (175 MHz, $CDCl_3$): δ = 189.7, 165.4, 146.9, 138.7, 134.9, 131.7, 127.7, 126.1, 125.1, 118.7, 19.7, 14.3.

MS (EI): *m/z* (%) = 248 (100) [M^+], 206 (30), 191 (15), 173 (5), 160 (25), 146 (10), 102.

HRMS (EI): *m/z* calcd for $C_{12}H_{12}N_2O_2S$: 248.0619; found: 248.0613.

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(27) X-ray crystal structure analysis of **2e** and **3i**: atomic coordinates, bond lengths [Å] and angles [deg], anisotropic displacement parameters, hydrogen coordinates, torsion angles [deg] have been deposited at Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, under deposition number CCDC 273870 for **2e**, CCDC 273871 for **3i** [fax: +44(1223)336033], E-mail: deposit@ccdc.cam.ac.uk).