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Regioselective Sulfonylation and *N*- to *O*-Sulfonyl Migration of Quinazolin-4(3*H*)-ones and Analogous Thienopyrimidin-4(3*H*)-ones

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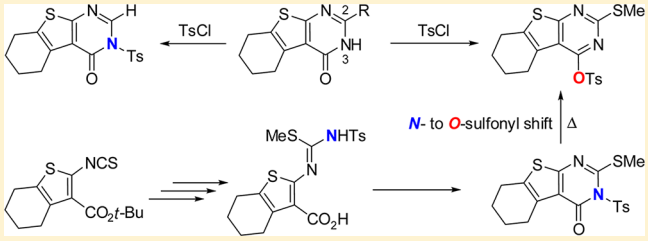
Supporting Information

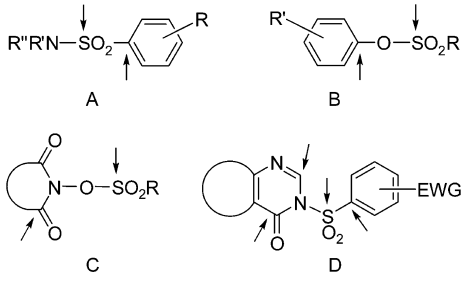
ABSTRACT: The sulfonylation of quinazolin-4(3*H*)-ones and related tetrahydrobenzothieno[2,3-*d*]pyrimidin-4(3*H*)-ones with mesyl, tosyl, and *p*-cyanobenzenesulfonyl chloride was studied. A hydrogen substituent at 2-position directed the sulfonyl group to the N-3 position, while alkylsulfanyl or amino substituents led to sulfonylation of the carbonyl oxygen. The latter effect was attributed to steric influence and the positive mesomeric effect of the 2-substituent. An access to *N*-sulfonylated 2-substituted regioisomers was established. An unexpected 1,3-sulfonyl migration was observed and further analyzed. This process occurred as an intramolecular *N*- to *O*-shift as verified by kinetic and crossover experiments.



INTRODUCTION

Nucleophilic displacement reactions of sulfonamides and sulfonates are characterized by competitive reaction pathways and have been the subject of numerous mechanistic studies and synthetic applications. The underlying mechanistic variations are known to depend on the nucleophile, the solvent, and explicitly, the substrate, i.e., the structure of the parent sulfonic acid and the amine or alcohol/phenol portion, respectively.[1] Sulfonamides composed of basic amines are notably stable to alkaline hydrolysis and other conditions, whereas sulfonamides of less basic amines are easier to cleave due to their improved nucleofugality. Alternatively, arenesulfonamides can undergo a nucleophilic aromatic substitution at the *ipso*-carbon of the electron-poor aromatic ring (Chart 1, A; nucleophilic attacks are indicated by arrows) as utilized in nosyl protecting groups.[2] In common nucleophilic substitutions of alkyl sulfonates, the sulfonate anion serves as leaving group. In aryl sulfonates (Chart 1, B), nucleophilic displacement reactions take place at the SO_2 center by S−O bond scission,[3,4] and a competing C−O bond cleavage occurs to release the sulfonate anion from a Meisenheimer-type intermediate.[1]

Chart 1. Possible Sites for Nucleophilic Attack at Arenesulfonamides, Aryl Sulfonates, *N*-(Sulfonyloxy)imides, and Fused 3-(Arylsulfonyl)pyrimidin-4(3*H*)-ones



N-Unsubstituted *O*-sulfonyl hydroxamic acids are substrates for the Lossen rearrangement, whereas *N*-substituted derivates behave differently in the presence of nucleophiles. By concomitant loss of the sulfonyl group, amides or lactams with the newly introduced substituent in α-position are formed.[5] In *N*-(sulfonyloxy)imides (Chart 1, C), the typical reaction is initiated by the nucleophilic attack at the carbonyl carbon followed by the expulsion of the sulfonate,[6,7] but a nucleophilic displacement at the sulfonate sulfur is also possible.[8] Moreover, α-sulfonyl carbanions of alkanesulfonates or -sulfonamides can attack electrophilic sites to undergo intramolecular or intermolecular coupling reactions.[9] Thus, in heterocyclic chemistry, different sulfonyl transfer reactions may have to be considered, for example, for the targeted preparation of *N*- or *O*-sulfonylated lactams and their utilization for subsequent chemical transformations.

In this study, we examined sulfonylation reactions of quinazolin-4(3*H*)-ones and related thieno[2,3-*d*]pyrimidin-4(3*H*)-ones. While the regioselectivity of alkylation of such systems has been investigated,[10,11] corresponding reports on sulfonylation of fused pyrimidinones are lacking. The products, i.e., *N*- or *O*-sulfonylated heterocycles, possess biological activities and represent attractive intermediates for diverse transformations. Fused pyrimidin-4(3*H*)-ones, e.g., unsubstituted in the 2-position and bearing an arylsulfonyl substituent at N-3, are susceptible to nucleophilic attack at four positions (Chart 1, D).[12]

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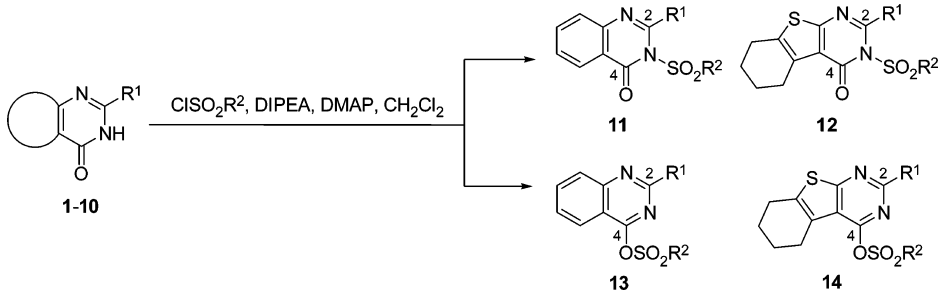
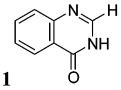
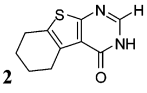
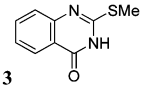
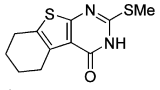
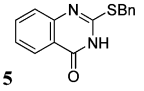
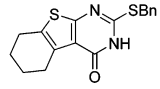
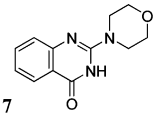
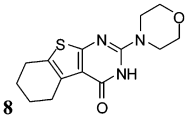
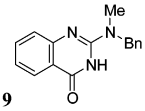
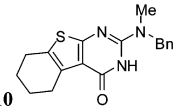
Table 1. Preparation of *N*- and *O*-Sulfonylated Fused Pyrimidines 11−14



Entry	Substrate	SO_2R^2	Yield (%)
1	 **1**	Ts	73 (**11a**)
2	**1**	$SO_2C_6H_4$-4-CN	55 (**11b**)
3	**1**	Ms	58 (**11c**)
4	**1**	$SO_2C_6H_2$-2,4,6-*i*-Pr	52 (**11d**)
5	 **2**	Ts	74 (**12a**)
6	**2**	$SO_2C_6H_4$-4-CN	72 (**12b**)
7	**2**	Ms	40 (**12c**)
8	**2**	$SO_2C_6H_2$-2,4,6-*i*-Pr	61 (**14d**)
9	 **3**	Ts	83 (**13e**)
10	**3**	$SO_2C_6H_4$-4-CN	71 (**13f**)
11	 **4**	Ts	69 (**14e**)
12	**4**	$SO_2C_6H_4$-4-CN	76 (**14f**)
13	**4**	Ms	56 (**14g**)
14	 **5**	Ts	64 (**13h**)
15	**5**	$SO_2C_6H_4$-4-CN	34 (**13i**)
16	 **6**	Ts	30 (**14h**)
17	**6**	$SO_2C_6H_4$-4-CN	31 (**14i**)
18	**6**	Ms	47 (**14j**)
19	 **7**	Ts	41 (**13k**)
20	**7**	$SO_2C_6H_4$-4-CN	50 (**13l**)
21	 **8**	Ts	66 (**14k**)
22	**8**	$SO_2C_6H_4$-4-CN	79 (**14l**)
23	**8**	Ms	68 (**14m**)
24	 **9**	Ts	67 (**13n**)
25	**9**	$SO_2C_6H_4$-4-CN	51 (**13o**)
26	 **10**	Ts	68 (**14n**)
27	**10**	$SO_2C_6H_4$-4-CN	74 (**14o**)
28	**10**	Ms	56 (**14p**)

Quinazoline-2,4-diones with aromatic sulfonyl groups at position N-3 were identified as inhibitors of the serine protease chymase. Their interaction with the target enzyme was assumed to involve a nucleophilic attack of the active-site serine at the C-4 carbonyl followed by ring-opening.[13] In addition, related compounds are useful in heterocyclic syntheses. For example, N-3 tosyl-substituted quinazolin-4(3*H*)-one undergoes a ring-opening−recyclization reaction with primary alkylamines to afford 3-alkylquinazolin-4(3*H*)-ones upon loss of tosyl amide.[14] Inosines bearing aromatic sulfonyl groups at position N-1 (corresponding to N-3 in pyrimidin-4(3*H*)-ones) have been studied in detail with respect to their reactivity toward primary aliphatic amines. An initial attack at C-2 and alternate ring closure reactions of the ring-open intermediates yield various types of products.[15]

O-Sulfonylated fused pyrimidin-4(3*H*)-ones have attracted attention as versatile electrophilic intermediates. For example, activation of quinazolin-4(3*H*)-ones with tosyl chloride generates a sulfonate structure, which is subsequently replaced with thiols or amines.[16] Arylsulfonyloxy groups were

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introduced at C-6 of purines (corresponding to position C-4 in pyrimidines) and successfully used for the preparation of corresponding amines, *O*-alkyl or *O*-aryl ethers.[17,18] Furthermore, 6-arylsulfonyloxy purines are valuable building blocks for Pd-catalyzed cross-couplings. Such derivatives of 2′-deoxyguanosine or guanosine were shown to undergo Suzuki-Miyaura reactions with arylboronic acids,[19] and were employed as halogen surrogates in Stille-type reactions with vinyltributylstannane.[20] Similarly, 4-arylsulfonyloxy derivatives of uridines and thymidines were successfully utilized in C−C coupling reactions.[21,22]

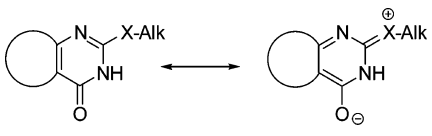
RESULTS AND DISCUSSION

As initial part of this study, we investigated the regioselectivity of the sulfonylation of a series of representative fused pyrimidin-4-ones (**1**−**10**). Three sulfonyl chlorides, i.e., mesyl, tosyl, and *p*-cyanobenzenesulfonyl chloride, were reacted with **1**−**10** in dichloromethane in the presence of DIPEA (*N*,*N*-diisopropylethylamine) and DMAP (4-dimethylaminopyridine) at room temperature (Table 1, all entries except of entries 4 and 8), and the main products of these transformations were isolated. On the one hand, *N*-sulfonylated compounds (**11a**−**c** and **12a**−**c**) were obtained in good yields from quinazoline **1** and thienopyrimidine **2**, bearing no substitutent at position 2 (R^1 = H). On the other hand, starting materials **3**−**10** with various substituents R^1 in position 2 gave exclusively the corresponding *O*-sulfonylated products.

A steric influence of the sulfonylating reagent was studied by treating **1** and **2** with the sterically demanding 2,4,6-triisopropylbenzenesulfonyl chloride (Table 1, entries 4 and 8). This reagent has frequently been used for *O*-sulfonylations of related lactams.[4,22−24] The reaction of the quinazolinone **1** afforded the *N*-sulfonylated product **11d**, whereas the thienopyrimidinone **2** gave the *O*-sulfonylated product **14d**.

A strong impact of the substituent at position 2 on the outcome of the sulfonylation was observed. A hydrogen substituent with the lowest steric hindrance for an electrophilic attack at the adjacent N-3 position allowed for the sulfonylation of the lactam nitrogen. The only exception (entry 8) was the formation of **14d** from 2,4,6-triisopropylbenzenesulfonyl chloride and the thienopyrimidinone **2**. The quinazolinone **1** gave exclusively 3-sulfonylated products, even with 2,4,6-triisopropylbenzenesulfonyl chloride (entry 4). The different behavior of **1** and **2** might be attributed to an increased electron density of the carbonyl oxygen in **2** due to the anellated thiophene ring.[25] The larger 2-substituents (i.e., methylsulfanyl, benzylsulfanyl, morpholino, *N*-benzyl-*N*-methylamino) directed the sulfonyl group to the carbonyl oxygen. In addition to the steric influence, the positive mesomeric effect of these substituents, connected to carbon C-2 via S or N atoms, is expected to contribute to *O*-sulfonylation. Such substituents can donate their lone pair for resonance, which leads to an increased electron density at the oxygen (Chart 2).[10]

Chart 2. Mesomeric Effect of the 2-Substituent (X = N-Alk, S) in Fused Pyrimidin-4(3*H*)-ones



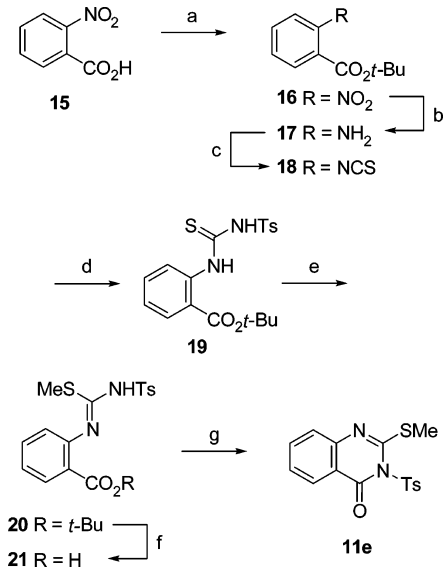
With the exception of 2,4,6-triisopropylbenzenesulfonyl chloride, the nature of the reagent, i.e., aliphatic (mesyl), electron-rich aromatic (tosyl), or electron-deficient aromatic (*p*-cyanobenzenesulfonyl chloride), did not influence the regioselectivity of the reaction.

The structures of the two types of products were elucidated on the basis of ^{1}H and ^{13}C NMR spectra and confirmed by X-ray diffraction analyses, both for two representative *N*-sulfonylated derivatives (**11d** and **12b**; see the Supporting Information, Figures S1 and S2) and for seven *O*-sulfonylated derivatives **14d**, **13e**, **14e**, **14f**, **14g**, **14k**, and **14o** (see the Supporting Information, Figures S3−9). Comparison of the ^{13}C NMR resonances of the *N*- and *O*-isomers revealed diagnostic differences (see below).

Our results are in accordance with the reported *N*-sulfonylation of quinazolin-4(3*H*)-one **1**.[14,26] Analogously, reaction of inosine derivatives with 2,4-dinitrobenzenesulfonyl chloride or *ortho*-nosyl chloride only gave *N*-sulfonylated products.[12,15] Mixtures of *N*- and *O*-sulfonylated products were formed in reactions of hypoxanthine nucleosides with 2,4,6-triisopropylbenzenesulfonyl chloride,[18] whereas 2-isobutyrylamino and 2-(dimethylamino)methyleneamino hypoxanthines and as well as 2-amino, 2-tritylamino, acetylamino and 2-benzoylamino guanosines furnished *O*-sulfonylated compounds when reacted with aromatic sulfonyl chlorides.[4,23] Reactions of thymidines and uridines with aromatic sulfonyl chlorides resulted in 4-sulfonyloxy products.[21,22,24]

For the exemplary preparation of the 2-substituted *N*-sulfonyl compounds, which were not accessible via direct sulfonylation of pyrimidinones **3**−**10**, we followed another synthetic strategy. It includes, similar to the preparation of 3-arylsulfonylquinazoline-2,4-diones,[13] the attachment of the sulfonyl group to the terminal nitrogen of an isothiourea moiety prior to cyclization (Scheme 1). Starting from 2-nitrobenzoic acid (**15**), the corresponding *tert*-butyl ester was

Scheme 1. Synthesis of the *N*-Sulfonylated Quinazoline 11e[a]



[a]Reagents and conditions: (a) (i) $(COCl)_2$, cat. DMF, CH_2Cl_2, 2 h; (ii) *t*-BuOH, cat. $ZnCl_2$, pyridine, 12 h; (b) H_2, Pd/C (10%), EtOH, 3 days; (c) $CSCl_2$, Et_3N, EtOAc, −78 °C to rt, 12 h; (d) $TsNH_2$, K_2CO_3, acetone, reflux, 20 h; (e) MeI, EtOH, $NaOH_{(aq)}$, 2 h; (f) TFA, 2 h; (g) CDI, THF, 1 h.

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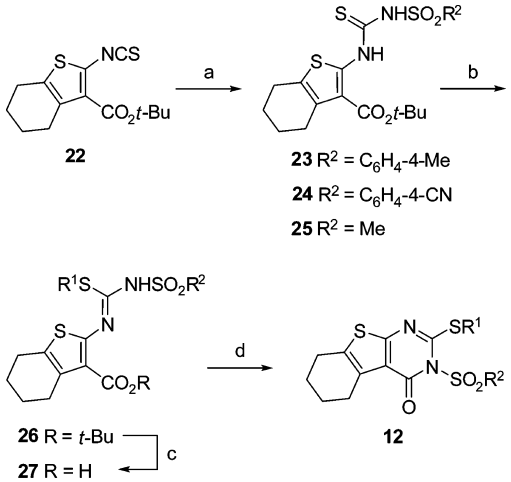
prepared with oxalyl chloride and a catalytic amount of DMF, followed by the treatment with *tert*-butyl alcohol in the presence of pyridine and $ZnCl_2$. The resulting ester **16** was hydrogenated using Pd/C to give the *tert*-butyl ester of anthranilic acid (**17**). Upon treatment with thiophosgene, **17** was converted to the isothiocyanate **18**. Reaction with *p*-toluenesulfonamide in the presence of potassium carbonate yielded the corresponding sulfonylthiourea **19**, which was *S*-methylated to give **20**. Cleavage of the ester group with trifluoroacetic acid produced the benzoic acid derivative **21**. While 2-thioureidobenzoic acids are readily accessible in their open-chain structure, in particular if an electron withdrawing group is placed at the terminal nitrogen,[27] benzoic acids with an adjacent isothioureido group have not been described so far. Compound **21** was cyclized by activating the carboxylic acid with CDI to yield the desired *N*-tosylated product **11e**.

In order to receive further pairs of isomeric *N*- and *O*-sulfonated compounds, in addition to the quinazolines **11e** and **13e**, a subseries of *N*-sulfonylated tetrahydrobenzothienopyrimidines was prepared. For this purpose, the established synthetic route was transferred to the thiophene scaffold (Scheme 2). Isothiocyanate **22** was synthesized[28] and

Scheme 2. Synthesis of *N*-Sulfonylated Thieno[2,3-*d*]pyrimidines 12e−h,j[a]



26, 27, 12	R^1	SO_2R^2
e	Me	Ts
f	Me	$SO_2C_6H_4$-4-CN
g	Me	Ms
h	Bn	Ts
j	Bn	Ms

[a]Reagents and conditions: (a) $R^2SO_2NH_2$, K_2CO_3, acetone, reflux, 20 h (R^2 = C_6H_4-4-Me or C_6H_4-4-CN) or NaH, DMF, 60 °C, 1 h (R^2 = Me); (b) R^1I/Br, EtOH, $NaOH_{(aq)}$, 2 h; (c) TFA, 2 h; (d) $(COCl)_2$, cat. DMF, CH_2Cl_2, 1 h.

subsequently reacted with different sulfonamides. In the case of the less acidic methanesulfonamide, sodium hydride was applied as base according to a literature report.[29] *S*-Alkylation yielded compounds **26**, whose *tert*-butyl esters were cleaved.[30] The resulting 2-isothioureidothiophene-3-carboxylic acids **27** underwent cyclocondensation with oxalyl chloride to give the final *N*-sulfonyl compounds **12e**, **12f**, **12g**, **12h**, and **12j**. The molecular structure of **12e** is shown in the Supporting Information (Figure S10).

Oxalyl chloride was not applicable for the cyclization of the benzoic acid derivative **21** (Scheme 1) as, instead of **11e**, the corresponding desulfonylated quinazolinone **3** (for structure, see Table 1) and tosyl chloride were isolated. These products originate from the nucleophilic attack of chloride at the sulfur atom of **11e**. The different behavior reflects the decreased electron density of the quinazolinone in comparison to the thienopyrimidinone scaffold. This finding indicates the ability of N-3 sulfonylated fused pyrimidines to act as sulfonyl donors.

In their ^{13}C NMR spectra, the three downfield signals were found to be indicative to distinguish between the substrates of the sulfonylation reaction, the *N*-sulfonylated products **11** and **12** and the isomeric *O*-sulfonylated products **13** and **14**. For example, in the case of the *N*-sulfonyl quinazoline **11e**, the three downfield carbon shifts (146.1, 154.2, 161.2 ppm for C-2, C-4 and C-8a) appeared at higher field than in **3** (149.2, 155.2, 163.1 ppm for C-2, C-4 and C-8a). On the contrary, the signals for the *O*-sulfonylated quinazoline **13e** were shifted downfield (153.3, 160.9, 166.9 ppm for C-2, C-4 and C-8a) in comparison to the substrate **3**. For the thienopyrimidine series, similar shift differences were noticed. The *N*-sulfonylated thienopyrimidines **12e**, **12f**, **12g**, **12h**, and **12j** showed resonances (~155, ~157, ~160 ppm for C-2, C-4, C-9a) similar to or at higher field than the unsulfonylated compounds **4** and **6** (~155, ~158, ~163 ppm for C-2, C-4, C-9a). A notable downfield shift occurred for two of the three downfield carbon signals as a result of the *O*-sulfonylation of **4** and **6** to **14e**, **14f**, **14g**, **14h**, and **14j** (~156, ~165, ~171 ppm for C-2, C-4, and C-9a). The corresponding signals for 2-unsubstituted, *O*-sulfonylated **14d** appeared at 151.2, 157.8, and 170.1 ppm.

When inspecting different cyclization conditions, **27e** (Scheme 2) was also treated with boiling acetic anhydride. Instead of **12e**, we obtained the isomeric *O*-sulfonylated product **14e** (for structure, see Table 1) suggesting that an unexpected migration of the sulfonyl group from the nitrogen atom to the carbonyl oxygen might have occurred.[33] To proof this hypothesis, compound **12e** was heated in acetonitrile and the course of the reaction was monitored by HPLC (Figure 1, see also the Supporting Information, Figure S11). The separation of both regioisomers was accomplished using an isocratic elution. Indeed, **12e** was completely converted to **14e** and side products were only formed to minor extent. The reaction followed a first-order kinetics and the analysis of the migration process by nonlinear regression using the equation for exponential decay gave a first-order rate constant of 0.0041 ± 0.0001 min^{-1}. These data confirm the postulated sulfonyl transfer to the thermodynamically more stable *O*-sulfonylated isomer and are also in agreement with the results of the direct sulfonylation as outlined in Table 1. However, the educts which are unsubstituted at 2-position, i.e., **1** and **2**, behaved differently and were predominately sulfonylated at the nitrogen N-3. When **12a** was heated in acetonitrile over 24 h, it remained unchanged. Thus, an *N*- to *O*-transfer did not occur, which indicates that in this case the *N*-sulfonylated products represent the thermodynamically favored isomers.

Further kinetic experiments were performed to shed light on the observed *N*- to *O*-sulfonyl migration. We repeated the experiment in the presence of 0.2 equiv of the unsulfonylated thienopyrimidine **4**. Under the assumption of an intermolecular sulfonyl shift,[34] **4** might act as sulfonyl acceptor and **12e** as donor. The additive **4** would then lead to an accelerated sulfonyl transfer. However, we obtained the same first-order rate constant as before (see the Supporting Information, Figure

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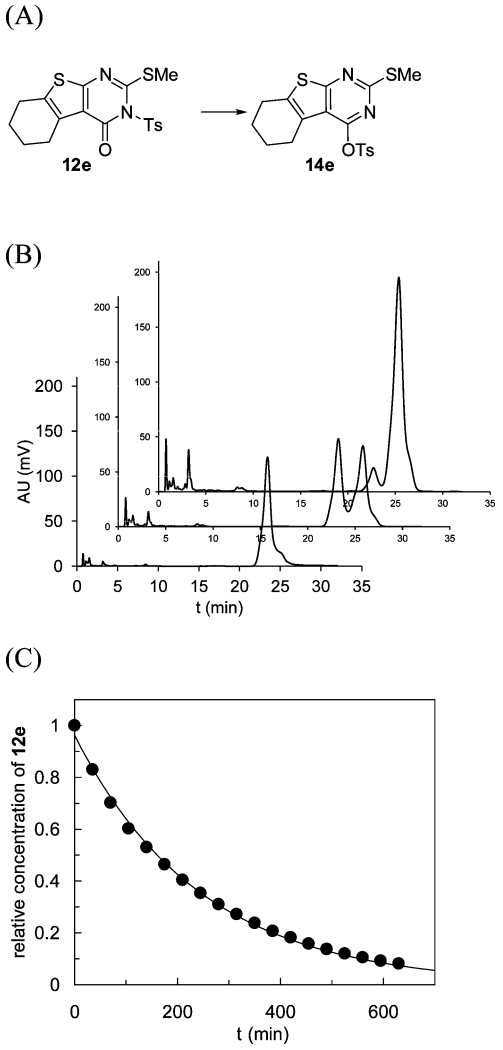

Figure 1. (A) *N*- to *O*-sulfonyl migration to convert **12e** into **14e**. Compound **12e** (1 mM) was heated in acetonitrile at 81 °C, and the reaction mixture was subjected to HPLC analysis. (B) Chromatograms after 0 min (bottom), 175 min (middle), and 630 min (top). Retention times of **12e** and **14e** were 22.7 and 25.4 min, respectively. (C) Relative concentrations of **12e**, determined as the ratio of the AUC of the substrate to the sum of the AUCs of substrate and product, were plotted versus reaction time. Nonlinear regression using the equation for exponential decay gave a first-order rate constant of 0.0041 ± 0.0001 min^{-1}.

S12). The kinetic analysis of the crossover migration reaction in the presence of 0.2 equiv of the unsulfonylated quinazoline **3** as additive is illustrated in Figure 2. This time, a sulfonyl transfer from the thienopyrimidine **12e** to **3** would lead to the formation of the crossover product, i.e., the *O*-sulfonylated quinazoline **13e**. This possible product, available by direct sulfonylation (Table 1), was employed as reference for the HPLC analysis. However, no additional product peak was observed and **13e** was not formed. Again, the depletion of **12e** was only accompanied by the formation of **14e** and the rate constant was similar to the previous experiments. It could be concluded from these findings that the unsulfonylated heterocycles do not function as intermediates in the sulfonyl transfer. We therefore postulate an intramolecular 1,3-sulfonyl migration as the underlying mechanism.

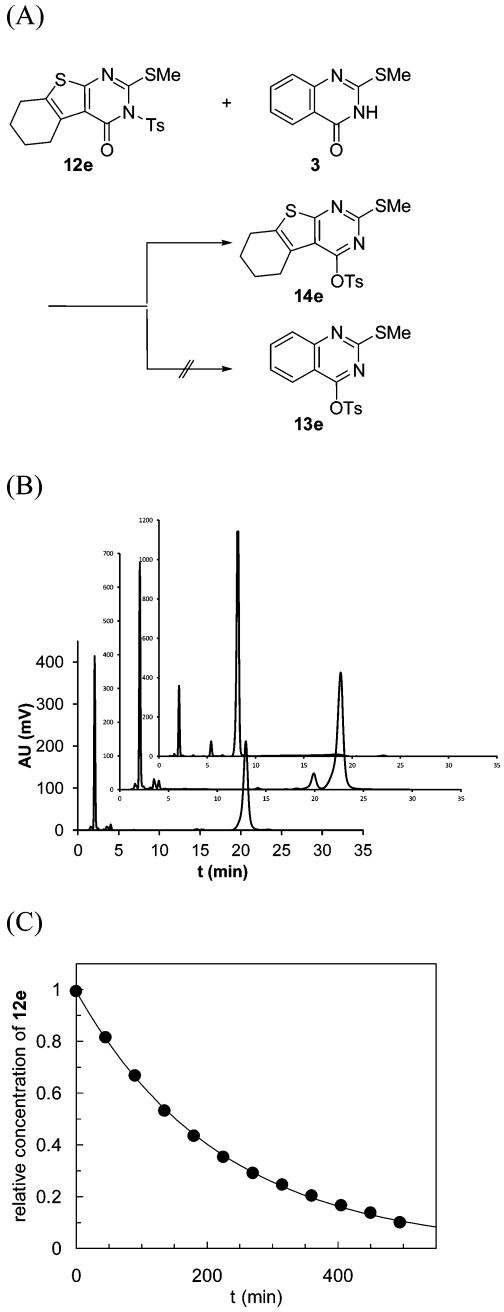

Figure 2. (A) Sulfonyl migration in the presence of a potential sulfonyl acceptor. Compounds **12e** (1 mM) and **3** (0.2 mM) were heated in acetonitrile at 81 °C and the reaction mixture was subjected to HPLC analysis. The *O*-sulfonylated product **14e** was exclusively formed. An intermolecular sulfonyl migration, i.e., the conversion of **3** into **13e**, did not occur. (B) Chromatograms of the reaction mixture after 0 min (bottom) and 495 min (middle), chromatogram of **13e** (top). Retention times were as follows: 20.6 min (**12e**), 2.07 min (**3**), 22.3 min (**14e**), and 8.22 min (**13e**). (C) Relative concentrations of **12e** were plotted versus reaction time and the first-order rate constant of 0.0045 ± 0.0001 min^{-1} was obtained as described in Figure 1.

There are several literature reports on sulfonyl shifts.[35,36] For example, similar *N*- to *O*-sulfonyl shifts in pyridinones have been observed (Chart 3, A).[37] In addition to such 1,3-migrations, the aromatization of 6-hydroxy-1-tosyl-1,6-dihydro-2*H*-pyrid-3-ones and a subsequent tosyl transfer gave 3-pyridyl tosylates (Chart 3, B). This 1,4-sulfonyl migration was assumed to proceed as intramolecular reaction.[38]

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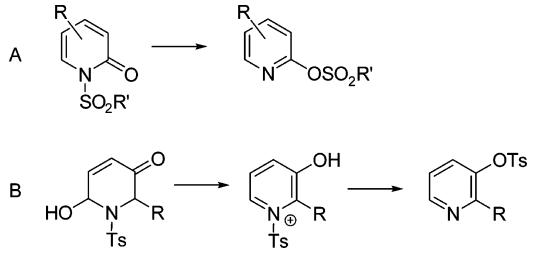
Chart 3. 1,3- and 1,4-Sulfonyl Migrations in Pyridinones



Further 1,3-sulfonyl shifts have been described which occur as *N*- to *C*-migrations. 3-Tosyl-4-vinylidene-2-oxazolidinones undergo an intramolecular migration of the sulfonyl group from N to Cα that can be promoted by enol ethers or silanes. The reactions are proposed to pass through intermediate four-membered sulfurane oxides.[39] Such cyclic intermediates resemble the 1,2-oxathietan-4-one-type transition states in the intramolecular carboxyl-catalyzed hydrolysis of sulfonamides.[40] An aza-Claisen-1,3-sulfonyl shift was reported when *N*-allyl-*N*-sulfonyl ynamides were heated in toluene for several hours and α-sulfonyl carbonitriles were formed.[41] *N*-Alkynyl-*N*-sulfonyl hydroxylamines are precursors for 3-pyrrolidinones whereby the Au^{I}-catalyzed cyclization is accompanied by a *N*- to *C*-transfer.[42] $AuBr_3$-catalyzed syntheses of 3- and 6-sulfonylindoles were reported, with the former reactions being intramolecular 1,3-sulfonyl migrations.[43] However, recently published $AlCl_3$-assisted transformations of *N*-sulfonyl to 7-sulfonyl indoles were found to be nonconcerted processes involving N–S cleavage and subsequent C-7 sulfonylation as could be demonstrated by a crossover experiment.[44]

In summary, the regioselectivity of sulfonylation reactions of quinazolin-4(3*H*)-ones and tetrahydrobenzothieno[2,3-*d*]-pyrimidin-4(3*H*)-ones was found to depend on the respective 2-substituent. 2-Unsubstituted substrates afforded predominately *N*-sulfonylated products, whereas methylsulfanyl, benzylsulfanyl, morpholino and *N*-benzyl-*N*-methylamino substituents directed the sulfonyl group to the carbonyl oxygen. A synthetic access to the corresponding *N*-sulfonylated isomers was demonstrated, which relies on the attachment of the sulfonyl group to the nitrogen atom prior to the ring closure. We observed an *N*- to *O*-sulfonyl migration which was, although unexpected to occur, in agreement with the regioselectivity of the direct sulfonylations. Most likely, this sulfonyl shift proceeded as an intramolecular event.

EXPERIMENTAL SECTION

General Experimental Methods. Thin-layer chromatography was carried out on aluminum sheets, silica gel 60 F_{254}. Detection was performed with UV light at 254 nm. Preparative column chromatography was performed on silica gel 60 (70–230 mesh). Petroleum ether used was a mixture of alkanes boiling between 40 and 60 °C, according to the supplier's declaration. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 500 and 125 MHz, unless stated otherwise. NMR spectra were recorded in $CDCl_3$ or DMSO-d_6, and chemical shifts δ are given in ppm referring to the signal center using the solvent peaks for reference: $CDCl_3$ 7.26/77.0 ppm and DMSO-d_6 2.49/39.7 ppm. In addition, HSQC and HMBC spectra of representative compounds were measured. HRMS (EI or ESI) spectra were recorded on a micrOTOF-Q spectrometer. LC-DAD chromatograms and ESI-MS spectra were recorded on an HPLC system with mass spectrometer. Elemental analyses were performed for C, H, and N. HPLC was carried out with a UV detector (λ = 220 nm) on a 5 μ C18 column, 110A, 250 × 4.60 mm, 5 μm. Elution was performed with an isocratic mixture of H_2O and acetonitrile (45:55). A flow rate of 2.0 mL/min was applied. Compounds **1**,[45] **2**,[46] **3**,[47] **4**,[31] and **5**[47] were prepared as described.

*Quinazolin-4(3H)-one (**1**).* A mixture of 2-aminobenzoic acid (10.0 g, 73 mmol) and formamide (15 mL) was refluxed for 4 h. After the mixture was cooled to room temperature, water (200 mL) was added and the precipitate was filtered off. The crude product was recrystallized from acetonitrile (100 mL) to yield **1** as a white solid (8.44 g, 79%): mp 213–214 °C (lit.[45] mp 215 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 (ddd, 1H, ^3J = 7.6 Hz, ^3J = 7.6 Hz, ^4J = 1.3 Hz), 7.65 (d, 1H, ^3J = 7.9 Hz), 7.80 (ddd, 1H, ^3J = 7.1 Hz, ^3J = 8.4 Hz, ^4J = 1.6 Hz), 8.08 (s, 1H), 8.11 (dd, 1H, ^3J = 7.9 Hz, ^4J = 1.3 Hz), 12.20 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 122.8, 126.0, 126.9, 127.3, 134.4, 145.5, 148.9, 160.9. The material's identity was confirmed by comparison with ^{1}H NMR and ^{13}C NMR literature data.[48]

*5,6,7,8-Tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4(3H)-one (**2**).* A mixture of ethyl 2-amino-5,6,7,8-tetrahydrobenzo[*b*]thiophene-3-carboxylate (2.25 g, 10 mmol) and formamide (60 mL) was refluxed for 2 h, then left to cool to room temperature overnight. The precipitated solid was filtered off, washed with water (50 mL), dried, and recrystallized from EtOH (60 mL) to yield **2** as brown crystals (1.32 g, 64%): mp 269–270 °C (lit.[46] mp 259 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.71–1.81 (m, 4H), 2.71–2.73 (m, 2H), 2.84–2.87 (m, 2H), 7.97 (s, 1H), 12.23 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.9, 22.6, 24.6, 25.5, 122.8, 131.0, 132.2, 145.0, 157.8, 162.6. Anal. Calcd for $C_{10}H_{10}N_2OS$: C, 58.23; H, 4.89; N, 13.58. Found: C, 58.23; H, 4.86; N, 13.72.

*2-(Methylsulfanyl)quinazolin-4(3H)-one (**3**).* 2-Thioxo-2,3-dihydroquinazolin-4(1*H*)-one (2.23 g, 12.5 mmol) and NaOH (0.55 g, 13.75 mmol) were dissolved in water (62.5 mL). Methyl iodide (0.86 mL, 13.75 mmol) was added dropwise, and the solution was stirred for 3 h at room temperature. The resulting precipitate was filtered off and washed with water (20 mL) to yield **3** as a pale brown solid (1.66 g, 69%): mp 209–210 °C (lit.[47] mp 210–211 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.68 (s, 3H), 7.38 (ddd, 1H, ^3J = 7.4 Hz, ^3J = 7.5 Hz, ^4J = 0.9 Hz), 7.60 (d, 1H, ^3J = 7.9 Hz), 7.70 (ddd, 1H, ^3J = 7.1 Hz, ^3J = 8.4 Hz, ^4J = 1.6 Hz), 8.24 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.3 Hz), 11.05 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.4, 119.8, 125.8, 126.4, 126.7, 134.9, 149.2, 155.2, 163.1. Anal. Calcd for $C_9H_8N_2OS{\cdot}0.2H_2O$ C, 55.20; H, 4.32; N, 14.30. Found: C, 55.17, H, 4.07; N, 14.28.

*2-(Methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4(3H)-one (**4**).* Ethyl 2-(3-benzoylthioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (18.0 g, 46.2 mmol) was heated under reflux for 2 h in a mixture of EtOH (230 mL) and 1 N NaOH (115 mL). After being cooled to room temperature, the solution was filtered and diluted with EtOH (30 mL) and 1 N NaOH (230 mL). Methyl iodide (4.8 mL, 77 mmol) was added dropwise, and the mixture was stirred for an additional 2 h. A solid was obtained, filtered off, and washed with water (80 mL) to yield 3-methyl-2-(methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (0.64 g, 5%). The filtrate was acidified with 2 N HCl to precipitate **4** as a white solid (10.9 g, 90%): mp 255–257 °C (lit.[31] mp 251–255 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.67–1.82 (br m, 4H), 2.49 (s, 3H), 2.66–2.68 (m, 2H), 2.79–2.81 (m, 2H), 12.50 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.0, 21.9, 22.6, 24.4, 25.3, 119.0, 130.2, 130.7, 156.5, 158.2, 162.8. The material's identity was confirmed by comparison with ^{1}H NMR literature data.[49]

*2-(Benzylsulfanyl)quinazolin-4(3H)-one (**5**).* 2-Thioxo-2,3-dihydroquinazolin-4(1*H*)-one (1.78 g, 10 mmol) was dissolved in EtOH (75 mL) and 1 N NaOH (20 mL). Benzyl bromide (1.31 mL, 11 mmol) was added dropwise, and the solution was stirred for 3 h at room temperature. The mixture was diluted with water (70 mL) and acidified with 2 N HCl to pH ~3. The resulting precipitate was filtered off and washed with water (20 mL) to yield **5** as a white solid (2.14 g, 80%): mp 213-215 °C (lit.[47] mp 212–213 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.54 (s, 2H), 7.25–7.32 (m, 3H), 7.39 (ddd, 1H, ^3J = 7.4 Hz, ^3J = 7.6 Hz, ^4J = 1.0 Hz), 7.44 (m, 2H), 7.62 (d, 1H, ^3J = 8.2 Hz), 7.72 (ddd, 1H, ^3J = 7.7 Hz, ^3J = 7.8 Hz, ^4J = 1.6 Hz), 8.20 (dd, 1H, ^3J = 7.9 Hz, ^4J = 1.6 Hz), 9.95 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.0, 120.0, 125.9, 126.4, 126.8, 127.7, 128.6, 129.2, 134.9, 136.5,

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149.0, 154.1, 162.9. Anal. Calcd for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.51; N, 10.44. Found: C, 67.12; H, 4.46; N, 10.22.

2-(Benzylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4(3H)-one (**6**). Ethyl 2-(3-benzoylthioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (2.33 g, 6.0 mmol) was heated under reflux for 2 h in EtOH (30 mL) and 1 N NaOH (15 mL). After being cooled to room temperature, the solution was filtered and diluted with EtOH (10 mL) and 1 N NaOH (30 mL). Benzyl bromide (1.2 mL, 10 mmol) was added dropwise, and the mixture was stirred for 2 h. The solution was filtered off, and the filtrate was acidified with 2 N HCl to precipitate **6** as a white solid (2.33 g, 93%): mp 225−228 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.70−1.81 (m, 4H), 2.68−2.82 (m, 4H), 4.41 (s, 2H), 7.23−7.26 (m, 1H), 7.28−7.41 (m, 4H), 12.53 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.9, 22.6, 24.5, 25.3, 33.9, 119.3, 127.5, 128.6, 129.2, 130.5, 130.8, 137.0, 155.3, 158.2, 162.6. Anal. Calcd for $C_{17}H_{16}N_2OS_2$: C, 62.16; H, 4,91; N, 8.53. Found: C, 61.97; H, 5.07; N, 8.34.

2-(Morpholin-4-yl)quinazolin-4(3H)-one (**7**). 2-(Methylsulfanyl)-quinazolin-4(3*H*)-one (**3**) (0.96 g, 5.0 mmol) was heated in morpholine (20 g, 20 mL, 230 mmol) in a sealed glass reactor at 160 °C overnight. After being cooled to room temperature, the solution was diluted with water (80 mL) and acidified with 2 N HCl to pH ∼2. The aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine (50 mL) and dried with anhydrous Na_2SO_4. After evaporation, the residue was recrystallized from EtOH/EtOAc (50 mL, 1:1) to yield **7** as white needles (0.61 g, 53%): mp 247−250 °C (lit.[50] mp 245−248.5 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.59 (m, 4H), 3.65−3.67 (m, 4H), 7.14−7.17 (m, 1H), 7.28−7.29 (m, 1H), 7.57−7.60 (m, 1H), 7.90−7.91 (m, 1H), 11.34 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 45.4, 65.8, 117.4, 122.5, 125.1, 126.0, 134.5, 150.4, 151.1, 163.1. Anal. Calcd for $C_{12}H_{13}N_3O_2$: C, 62.33; H, 5.67; N, 18.17. Found: C, 62.31; H, 5.56; N, 18.18.

2-(Morpholin-4-yl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4(3H)-one (**8**). 2-(Methylsulfonyl)-5,6,7,8-tetrahydrobenzo-[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**28**) (0.20 g, 0.7 mmol) was heated in morpholine (5.0 g, 5 mL, 57 mmol) in a sealed glass reactor at 160 °C for 18.5 h. After the mixture was cooled to room temperature, the resulting precipitate was filtered off and washed with water (10 mL) to yield **8** as a pale gray solid (0.14 g, 69%): mp >350 °C (lit.[51] mp 330 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.68−1.80 (m, 4H), 2.59−2.62 (m, 2H), 2.75−2.78 (m, 2H), 3.51−3.53 (m, 4H), 3.61−3.64 (m, 4H), 10.95 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.0, 22.9, 24.4, 25.4, 45.4, 65.7, 114.2, 126.1, 130.1, 152.0, 159.3, 165.8. Anal. Calcd for $C_{14}H_{17}N_3O_2S{\cdot}0.5H_2O$: C, 55.98; H, 6.04; N, 13.99. Found: C, 56.03; H, 5.76; N, 13.89.

2-(N-Benzyl-N-methylamino)quinazolin-4(3H)-one (**9**). 2-(Methylsulfanyl)quinazolin-4(3*H*)-one (**3**) (0.96 g, 5.0 mmol) was heated in *N*-benzyl-*N*-methylamine (18.8 g, 20 mL, 155 mmol) in a sealed glass reactor at 180 °C overnight. After the mixture was cooled to room temperature, the precipitated solid was filtered off and recrystallized from EtOH (60 mL) to yield **9** as white needles (0.53 g, 40%): mp 199−200 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.20 (s, 3H), 4.91 (s, 2H), 7.07−7.10 (m, 1H), 7.24−7.31 (m, 5H), 7.38 (d, 1H, ^3J = 8.2 Hz), 7.54−7.57 (m, 1H), 7.95 (d, 1H, ^3J = 7.0 Hz), 10.83 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 35.3, 52.9, 116.4, 122.1, 124.9, 126.3, 127.46, 127.52, 128.7, 134.8, 137.0, 150.6, 151.2, 165.0; HRMS-ESI *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{15}N_3ONa$ 288.1107, found 288.1106.

2-(N-Benzyl-N-methylamino)-5,6,7,8-tetrahydrobenzo[4,5]-thieno[2,3-d]pyrimidin-4(3H)-one (**10**). 2-(Methylsulfonyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**28**) (0.20 g, 0.7 mmol) was heated in *N*-benzyl-*N*-methylamine (6.6 g, 7 mL, 54 mmol) in a sealed glass reactor at 200 °C for 52 h. After being cooled to room temperature, the mixture was poured on ice−water (150 mL) and neutralized with 8 N HCl. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The organic layer was washed with 2 N CH_3COOH (50 mL) and brine (100 mL) and dried with anhydrous Na_2SO_4. After evaporation, the residue was suspended in MeOH (30 mL) and filtered off to yield **5a** as white needles (0.12 g, 53%): mp 250−253 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.68−1.79 (m, 4H), 2.58−2.60 (m, 2H), 2.75−2.78 (m, 2H), 3.01 (s, 3H), 4.77 (s, 2H), 7.19−7.34 (m, 5H), 10.93 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.17, 22.9, 24.3, 25.5, 35.8, 52.2, 113.4, 125.1, 127.2, 127.3, 128.7, 130.1, 137.5, 152.0, 159.2, 166.4; HRMS-EI *m*/*z* [M]$^+$ calcd for $C_{18}H_{19}N_3OS$ 325.1243, found 325.1245.

2-(Methylsulfonyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4(3H)-one (**28**). Method A: 2-(Methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**4**) (0.51 g, 2.0 mmol) was stirred for 5 h at 45 °C in AcOH/H_2O_2 (10 mL/8 mL, 30%). The precipitate was filtered off and washed with water (60 mL) to yield the product as a white solid (0.20 g, 35%). Method B: 2-(Methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**4**) (1.26 g, 5.0 mmol) was suspended in acetone (50 mL) and cooled to 0 °C. *m*-CPBA (70%, 2.70 g, 11 mmol) was added over 30 min. The mixture was stirred for 24 h at room temperature. After evaporation in vacuo, the residue was dissolved in H_2O (70 mL) and 2 N NaOH (15 mL). The solution was acidified with 2 N HCl to pH ∼5. The precipitate was filtered off and washed with water (25 mL) to yield **28** as a white solid (0.45 g, 32%): mp 246−249 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.82−1.91 (m, 4H), 2.80−2.83 (m, 2H), 3.01−3.04 (m, 2H), 3.32 (s, 3H), 10.38 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.0, 22.7, 25.3, 25.5, 40.4, 124.7, 132.5, 138.8, 149.0, 156.7, 160.1. Anal. Calcd for $C_{11}H_{12}N_2O_3S_2 \times 0.2\ H_2O$: C, 45.88; H, 4.34; N, 9.73. Found: C, 45.92; H, 4.42; N, 9.81.

General Prodecure for Sulfonylation. DIPEA (*N*,*N*-diisopropylethylamine, 1.2 equiv) and the sulfonyl chloride (1.2 equiv, unless stated otherwise) were added to a suspension of the appropriate substrate (**1**−**10**) and a catalytic amount of DMAP (4-dimethylaminopyridine) in CH_2Cl_2. The mixture was stirred at room temperature, and a solution was obtained. After evaporation in vacuo, the residue was recrystallized from MeOH or purified by column chromatography to yield compounds **11**−**14**. The compounds are listed in the order of their appearance in Table 1.

3-(4-Methylbenzenesulfonyl)quinazolin-4(3H)-one (**11a**). Compound **1** (0.29 g, 2.0 mmol), DMAP (20 mg), DIPEA (0.31 g, 2.4 mmol), and 4-methylbenzenesulfonyl chloride (0.46 g, 2.4 mmol) were reacted in CH_2Cl_2 (10 mL) for 2 h. The crude product was recrystallized from MeOH to yield **11a** as white crystals (0.51 g, 73%): mp 184−187° (lit.[26] mp 185−188 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.37 (d, 2H, ^3J = 8.2 Hz), 7.46 (ddd, 1H, ^3J = 7.1 Hz, ^3J = 8.0 Hz, ^4J = 1.3 Hz), 7.70 (dd, 1H, ^3J = 8.2 Hz, ^4J = 0.6 Hz), 7.74−7.77 (m, 1H), 8.04−8.06 (d, 2H, ^3J = 8.5 Hz), 8.15−8.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 122.0, 127.2, 128.0, 128.3, 129.8, 133.4, 135.6, 140.4, 146.7, 146.7, 158.6. Anal. Calcd for $C_{15}H_{12}N_2O_3S$ C, 59.99; H, 4.03; N, 9.33. Found: C, 59.97; H, 4.14; N, 9.15.

4-((4-Oxoquinazolin-3(4H)-yl)sulfonyl)benzonitrile (**11b**). Compound **1** (0.15 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-cyanobenzenesulfonyl chloride (0.24 g, 1.2 mmol) were reacted in CH_2Cl_2 (10 mL) for 1 h. The crude product was recrystallized from MeOH to yield **11b** as a white solid (0.17 g, 55%): mp 200−202 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (ddd, 1H, ^3J = 7.6 Hz, ^3J = 7.6 Hz, ^4J = 1.3 Hz), 7.72 (d, 1H, ^3J = 7.6 Hz), 7.80 (ddd, 1H, ^3J = 8.0 Hz, ^3J = 7.6 Hz, ^4J = 1.3 Hz), 7.86−7.88 (d, 2H, ^3J = 8.8 Hz), 8.13−8.15 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.3 Hz), 8.29−8.31 (d, 2H, ^3J = 8.8 Hz), 8.72 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 116.7, 118.8, 121.6, 127.2, 128.2, 128.8, 130.4, 132.8, 136.1, 139.5, 140.5, 146.5, 158.5. Anal. Calcd for $C_{15}H_9N_3O_3S$: C, 57.87; H, 2.91; N, 13.50. Found: C, 57.90; H, 2.96; N, 13.16.

3-(Methylsulfonyl)quinazolin-4(3H)-one (**11c**). Compound **1** (0.73 g, 5.0 mmol), DMAP (40 mg), DIPEA (0.78 g, 6.0 mmol), and methanesulfonyl chloride (0.69 g, 6.0 mmol) were reacted in CH_2Cl_2 (30 mL) for 7 h. The product was purified by column chromatography using petroleum ether/EtOAc (1:1) to yield **11c** as a white powder (0.65 g, 58%): mp 146−149 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.65 (s, 3H), 7.54−7.58 (m, 1H), 7.73−7.75 (m, 1H), 7.81−7.85 (m, 1H), 8.29−8.31 (m, 1H), 8.55 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 42.6, 121.7, 127.3, 128.2, 128.6, 136.0, 139.7, 146.8, 159.7. Anal. Calcd for $C_9H_8N_2O_3S$: C, 48.21; H, 3.60; N, 12.49. Found: C, 48.33; H, 3.73; N, 12.28.

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*3-(2,4,6-Triisopropylbenzenesulfonyl)quinazolin-4(3H)-one (**11d**).* Compound **1** (0.15 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 2,4,6-triisopropylbenzenesulfonyl chloride (0.36 g, 1.2 mmol) were reacted in CH_2Cl_2 (10 mL) for 1 h. The crude product was recrystallized from MeOH to yield **11d** as colorless crystals (0.22 g, 52%): mp 157−159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (d, 12H, ^3J = 6.7 Hz), 1.20 (d, 6H, ^3J = 6.9 Hz), 2.95 (sept, 1H), 4.03 (sept, 2H), 7.34 (s, 2H), 7.58−7.62 (m, 1H), 7.78−7.80 (m, 1H), 7.91−7.95 (m, 1H), 8.08−8.09 (m, 1H), 8.92 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.3, 24.1, 29.0, 33.6, 121.2, 124.5, 126.8, 128.0, 129.0, 130.1, 136.5, 140.3, 146.3, 151.2, 155.5, 158.6; HRMS-ESI *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{28}N_2NaO_3S$ 435.1713, found 435.1715.

*3-(4-Methylbenzenesulfonyl)-5,6,7,8-tetrahydrobenzo[4,5]-thieno[2,3-d]pyrimidin-4(3H)-one (**12a**).* Compound **2** (0.21 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-methylbenzenesulfonyl chloride (0.23 g, 1.2 mmol) were reacted in CH_2Cl_2 (7.5 mL) for 3 h. The crude product was recrystallized from MeOH to yield **12a** as white crystals (0.27 g, 74%): mp 166−167 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.66−1.76 (m, 4H), 2.41 (s, 3H), 2.70−2.73 (m, 4H), 7.49 (d, 2H, ^3J = 7.9 Hz), 8.03 (d, 2H, ^3J = 8.5 Hz), 8.75 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.4, 21.6, 22.3, 24.6, 25.2, 122.0, 129.5, 130.0, 131.7, 133.3, 135.5, 141.6, 146.7, 154.3, 160.9. Anal. Calcd for $C_{17}H_{16}N_2O_3S_2$: C, 56.65; H, 4.47; N, 7.77. Found: C,56.44; H, 4.57; N, 7.72.

*4-((4-Oxo-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-3(4H)-yl)sulfonyl)benzonitrile (**12b**).* Compound **2** (0.41 g, 2.0 mmol), DMAP (20 mg), DIPEA (0.31 g, 2.4 mmol), and 4-cyanobenzenesulfonyl chloride (0.48 g, 2.4 mmol) were reacted in CH_2Cl_2 (7.5 mL) for 30 min. A solid precipitated, which was filtered off and washed with CH_2Cl_2 (5 mL). The filtrate was evaporated in vacuo, and the combined material was recrystallized from MeOH/CH_2Cl_2 (9:1) to yield **12b** as pale yellow crystals (0.53 g, 72%): mp 206−211 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.66−1.77 (m, 4H), 2.69−2.75 (m, 4H), 8.18 (d, 2H, ^3J = 8.8 Hz), 8.34 (d, 2H, ^3J = 8.8 Hz), 8.73 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.6, 22.3, 24.6, 25.2, 117.4, 117.6, 121.9, 130.1, 131.7, 133.6, 135.7, 140.3, 141.5, 154.3, 161.0. Anal. Calcd for $C_{17}H_{13}N_3O_3S_2$: C, 54.97; H, 3.53; N, 11.31. Found: C, 54.71; H, 3.70; N, 11.20.

*3-(Methylsulfonyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4(3H)-one (**12c**).* Compound **2** (0.21 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.31 g, 2.4 mmol), and methanesulfonyl chloride (0.27 g, 2.4 mmol) were reacted in CH_2Cl_2 (7.5 mL) for 1 h. The crude product was recrystallized from MeOH to yield **12c** as a brown solid (0.11 g, 40%): mp 152−155 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.75−1.83 (m, 4H), 2.77−2.79 (m, 2H), 2.86−2.89 (m, 2H), 3.80 (s, 3H), 8.44 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.8, 22.4, 24.7, 25.3, 42.1, 122.1, 131.8, 135.3, 141.6, 155.5, 161.2; HRMS-EI *m*/*z* [M]$^+$ calcd for $C_{11}H_{12}N_2O_3S_2$ 284.0284, found 284.0290.

*5,6,7,8-Tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-yl 2,4,6-Triisopropylbenzenesulfonate (**14d**).* Compound **2** (0.21 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 2,4,6-triisopropylbenzenesulfonyl chloride (0.36 g, 1.2 mmol) were reacted in CH_2Cl_2 (10 mL) for 1 h. The crude product was recrystallized from MeOH to yield **14d** as colorless crystals (0.29 g, 61%): mp 135−137 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.24 (d, 18H, ^3J = 5.7 Hz), 1.89−1.92 (m, 4H), 2.84−2.86 (m, 2H), 2.92 (sept, 1H, ^3J = 7.0 Hz), 3.00−3.01 (m, 2H), 4.28 (sept, 2H, ^3J = 6.8 Hz), 7.19 (s, 2H), 8.43 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.1, 22.7, 23.5, 24.5, 25.4, 25.7, 120.3, 123.9, 126.3, 131.5, 138.4, 150.8, 151.2, 154.3, 157.8, 170.1; HRMS-ESI *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{32}N_2NaO_3S_2$ 473.1927, found 473.1932.

*2-(Methylsulfanyl)quinazolin-4-yl 4-Methylbenzenesulfonate (**13e**).* Compound **3** (0.19 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-methylbenzenesulfonyl chloride (0.23 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 30 min. The crude product was recrystallized from EtOH to yield **13e** as pale yellow crystals (0.28 g, 83%): mp 146−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.45 (s, 3H), 2.54 (s, 3H), 7.37 (d, 2H, ^3J = 7.9 Hz), 7.47 (ddd, 1H, ^3J = 6.6 Hz, ^3J = 8.4 Hz, ^4J = 1.3 Hz), 7.76−7.78 (m, 2H), 8.03−8.05 (m, 1H), 8.06−8.08 (d, 2H, ^3J = 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 21.8, 113.6, 123.5, 126.6, 129.57, 129.59, 133.5, 135.0, 146.0, 153.3, 160.9, 166.9, one signal was not detected; HRMS-ESI *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{14}N_2O_3S_2Na$ 369.0338, found 369.0330.

*2-(Methylsulfanyl)quinazolin-4-yl 4-Cyanobenzenesulfonate (**13f**).* Compound **3** (0.19 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-cyanobenzenesulfonyl chloride (0.24 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 1 h. The product was purified by column chromatography using petroleum ether/EtOAc (4:3) to yield **13f** as a white solid (0.25 g, 71%): mp 122−124 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.55 (s, 3H), 7.50−7.53 (m, 1H), 7.80−7.86 (m, 2H), 7.88−7.90 (d, 2H, ^3J = 8.9 Hz), 8.04−8.06 (m, 1H), 8.33 (d, 2H, ^3J = 8.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 113.3, 117.0, 118.3, 123.3, 126.8, 126.9, 130.3, 132.6, 135.4, 140.8, 153.5, 160.5, 166.6; HRMS-ESI *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{11}N_3O_3S_2Na$ 380.0134, found 380.0136.

*2-(Methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl 4-Methylbenzenesulfonate (**14e**).* Compound **4** (0.25 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-methylbenzenesulfonyl chloride (0.23 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 1.5 h. The crude product was recrystallized from EtOH to yield **14e** as yellow crystals (0.28 g, 69%): mp 123−124 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.83−1.91 (m, 4H), 2.40 (s, 3H), 2.45 (s, 3H), 2.75−2.79 (m, 2H), 2.91−2.94 (m, 2H) 7.36 (d, 2H, ^3J = 7.85 Hz), 7.99 (d, 2H, ^3J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 21.7, 22.1, 22.7, 25.2, 25.5, 116.9, 126.1, 129.1, 129.6, 134.2, 135.7, 145.6, 156.5, 165.2, 171.4. Anal. Calcd for $C_{18}H_{18}N_2O_3S_3$: C, 53.18; H, 4.46; N, 6.89. Found: C, 53.02; H, 4.35; N, 6.83.

*2-(Methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl 4-Cyanobenzenesulfonate (**14f**).* Compound **4** (0.51 g, 2.0 mmol), DMAP (20 mg), DIPEA (0.31 g, 2.4 mmol), and 4-cyanobenzenesulfonyl chloride (0.48 g, 2.4 mmol) were reacted in CH_2Cl_2 (10 mL) for 30 min. The crude product was recrystallized from MeOH to yield **14f** as yellow crystals (0.64 g, 76%): mp 162−165 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.81−1.86 (m, 4H), 2.31 (s, 3H), 2.81−2.85 (m, 4H), 8.22 (d, 2H, ^3J = 8.9 Hz), 8.30 (d, 2H, ^3J = 8.9 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.6, 21.6, 22.3, 24.8, 25.1, 116.5, 117.4, 117.5, 125.6, 129.4, 133.9, 136.7, 140.5, 155.8, 164.9, 171.2. Anal. Calcd for $C_{18}H_{15}N_3O_3S_3$: C, 51.78; H, 3.62; N, 10.06. Found: C, 51.61; H, 3.75; N, 9.91.

*2-(Methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl Methanesulfonate (**14g**).* Compound **4** (0.25 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and methanesulfonyl chloride (0.14 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 1.5 h. The crude product was recrystallized from MeOH to yield **14g** as brown crystals (0.11 g, 56%): mp 152−155 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.83−1.84 (m, 4H), 2.59 (s, 3H), 2.81−2.84 (m, 4H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 14.1, 21.6, 22.3, 24.9, 25.1, 41.8, 116.6, 125.8, 136.2, 156.4, 165.1, 171.0. Anal. Calcd for $C_{12}H_{14}N_2O_3S_3$: C, 43.63; H, 4.27; N, 8.48. Found: C, 43.37; H, 4.41; N, 8.38.

*2-(Benzylsulfanyl)quinazolin-4-yl 4-Methylbenzenesulfonate (**13h**).* Compound **5** (0.40 g, 1.5 mmol), DMAP (15 mg), DIPEA (0.23 g, 1.8 mmol), and 4-methylbenzenesulfonyl chloride (0.34 g, 1.8 mmol) were reacted in CH_2Cl_2 (7.5 mL) for 2 h. The product was purified by column chromatography using petroleum ether/EtOAc (6:1) to yield **13h** as a white solid (0.41 g, 64%): mp 105−107 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 4.39 (s, 2H), 7.22−7.34 (m, 5H), 7.40−7.42 (m, 2H), 7.47−7.50 (m, 1H), 7.78−7.82 (m, 2H), 8.04−8.06 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 35.4, 113.8, 123.6, 126.6, 126.7, 127.3, 128.5, 129.1, 129.5, 129.6, 133.5, 135.1, 137.2, 146.0, 153.2, 161.0, 166.0. Anal. Calcd for $C_{22}H_{18}N_2O_3S_2$: C, 62.54; H, 4.29; N, 6.63. Found: C, 62.58; H, 4.16; N, 6.41.

*2-(Benzylsulfanyl)quinazolin-4-yl 4-Cyanobenzenesulfonate (**13i**).* Compound **5** (0.27 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-cyanobenzenesulfonyl chloride (0.24 g, 1.2 mmol) were reacted in CH_2Cl_2 (16 mL) for 1 h. The crude product was recrystallized from MeOH to yield **13i** as a light green solid (0.15 g, 34%): mp 145−148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.41 (s, 2H), 7.24−7.25 (m, 1H), 7.29−7.32 (m, 2H), 7.41−7.42 (m, 2H), 7.51−7.54 (m, 1H), 7.83−7.86 (m, 4H), 8.05−8.06 (m, 1H), 8.29 (d,

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2H, ^3J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.3, 113.4, 116.9, 118.2, 123.3, 126.8, 127.0, 127.4, 128.6, 129.1, 130.2, 132.6, 135.5, 136.9, 140.7, 153.3, 160.7, 165.6. Anal. Calcd for $C_{22}H_{15}N_3O_3S_2$: C, 60.95; H, 3.49; N, 9.69. Found: C, 60.87; H, 3.56; N, 9.61.

*2-(Benzylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl 4-Methylbenzenesulfonate (**14h**).* Compound **6** (0.22 g, 0.7 mmol), DMAP (10 mg), DIPEA (0.12 g, 0.9 mmol), and 4-methylbenzenesulfonyl chloride (0.17 g, 0.9 mmol) were reacted in CH_2Cl_2 (5 mL) for 2 h. The crude product was recrystallized from MeOH to yield **14h** as pale yellow crystals (0.10 g, 30%): mp 149−153 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.85−1.91 (m, 4H), 2.37 (s, 3H), 2.77−2.79 (m, 2H), 2.93−2.95 (m, 2H), 4.19 (s, 2H), 7.21−7.32 (m, 7H), 7.97 (d, 2H, ^3J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 22.1, 22.8, 25.3, 25.6, 35.4, 117.3, 126.2, 127.3, 128.5, 129.06, 129.09, 129.64, 134.3, 136.0, 137.0, 145.7, 156.6, 164.3, 171.5. Anal. Calcd for $C_{24}H_{22}N_2O_3S_3$: C, 59.73; H, 4.59; N, 5.80. Found: C, 60.00; H, 4.59; N, 5.79.

*2-(Benzylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl 4-Cyanobenzenesulfonate (**14i**).* Compound **6** (0.31 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-cyanobenzenesulfonyl chloride (0.24 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 30 min. The crude product was recrystallized from MeOH to yield **14i** as pale yellow crystals (0.15 g, 31%): mp 174−177 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.88−1.91 (m, 4H), 2.79−2.81 (m, 2H), 2.92−2.94 (m, 2H), 4.25 (s, 2H), 7.23−7.34 (m, 5H), 7.78−7.80 (m, 2H), 8.19−8.22 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.1, 22.7, 25.2, 25.6, 35.3, 117.0, 118.0, 126.0, 127.5, 128.6, 129.0, 129.8, 132.6, 136.7, 136.8, 141.4, 156.2, 164.2, 171.8. Anal. Calcd for $C_{24}H_{19}N_3O_3S_3$: C, 58.40; H, 3.88; N, 8.51. Found: C, 58.23; H, 3.94; N, 8.20.

*2-(Benzylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl Methanesulfonate (**14j**).* Compound **6** (0.63 g, 2.0 mmol), DMAP (20 mg), DIPEA (0.31 g, 2.4 mmol), and methanesulfonyl chloride (0.27 g, 2.4 mmol) were reacted in CH_2Cl_2 (10 mL) for 1 h. The product was purified by column chromatography using CH_2Cl_2 to yield **14j** as a pale brown solid (0.38 g, 47%): mp 184−186 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.84−1.91 (m, 4H), 2.79−2.81 (m, 2H), 2.90−2.93 (m, 2H), 3.50 (s, 3H), 4.45 (s, 2H), 7.22−7.31 (m, 4H), 7.41−7.43 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.1, 22.7, 25.2, 25.6, 35.7, 41.9, 117.6, 126.2, 127.4, 128.6, 128.9, 136.5, 136.8, 156.6, 164.3, 171.9; HRMS-EI m/z $[M]^+$ calcd for $C_{18}H_{18}N_2O_3S_3$ 406.0475, found 406.0480.

*2-(Morpholin-4-yl)quinazolin-4-yl 4-Methylbenzenesulfonate (**13k**).* Compound **7** (0.23 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-methylbenzenesulfonyl chloride (0.23 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 2 h. The crude product was recrystallized from *n*-hexane/EtOAc (2:1) to yield **13k** as pale green crystals (0.16 g, 41%): mp 133−136 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.44 (s, 3H), 3.68−3.71 (m, 8H), 7.17−7.20 (m, 1H), 7.35 (d, 2H, ^3J = 8.5 Hz), 7.50 (br d, 1H, ^3J = 8.5 Hz), 7.62−7.66 (m, 1H), 7.86 (dd, 1H, ^3J = 8.2 Hz, ^4J = 1.3 Hz), 7.95 (d, 2H, ^3J = 8.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 44.5, 66.7, 110.7, 123.1, 123.5, 125.3, 128.5, 129.7, 134.3, 135.0, 145.6, 154.9, 157.1, 162.3. Anal. Calcd for $C_{19}H_{19}N_3O_4S$: C, 59.21; H, 4.97; N, 10.90. Found: C, 59.15; H, 4.82; N, 10.82.

*2-(Morpholin-4-yl)quinazolin-4-yl 4-Cyanobenzenesulfonate (**13l**).* Compound **7** (0.23 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-cyanobenzenesulfonyl chloride (0.24 g, 1.2 mmol) were reacted in CH_2Cl_2 (10 mL) for 2 h. The crude product was recrystallized from MeOH (60 mL) to yield **13l** as green crystals (0.20 g, 50%): mp 143−146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68−3.69 (m, 8H), 7.21−7.24 (m, 1H), 7.52 (d, 1H, ^3J = 8.6 Hz), 7.66−7.69 (m, 1H), 7.82−7.84 (m, 1H), 7.88 (d, 2H, ^3J = 8.5 Hz), 8.20 (d, 2H, ^3J = 8.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.5, 66.6, 110.4, 116.7, 118.0, 123.2, 123.5, 125.6, 129.0, 132.9, 135.4, 141.5, 155.2, 157.0, 162.1; HRMS-EI m/z $[M]^+$ calcd for $C_{19}H_{16}N_4O_4S$ 396.0887, found 396.0892.

*2-(Morpholin-4-yl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl 4-Methylbenzenesulfonate (**14k**).* Compound **8** (0.15 g, 0.5 mmol), DMAP (5 mg), DIPEA (0.08 g, 0.6 mmol), and 4-methylbenzenesulfonyl chloride (0.12 g, 0.6 mmol) were reacted in CH_2Cl_2 (5 mL) for 3 h. The crude product was recrystallized from MeOH to yield **14k** as white crystals (0.15 g, 66%): mp 207−211 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.77−1.83 (m, 4H), 2.43 (s, 3H), 2.68−2.71 (m, 2H), 2.75−2.79 (m, 2H), 3.41 (m, 4H), 3.53−3.55 (m, 4H), 7.50 (d, 2H, ^3J = 8.2 Hz), 7.92 (d, 2H, ^3J = 8.6 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.3, 21.8, 22.6, 24.8, 24.9, 44.4, 65.8, 111.4, 125.3, 128.4, 130.2, 130.9, 134.0, 145.9, 157.0, 157.2, 172.7. Anal. Calcd for $C_{21}H_{23}N_3O_4S_2$: C, 56.61; H, 5.20; N, 9.43. Found: C, 56.44; H, 5.38; N, 9.34.

*2-(Morpholin-4-yl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl 4-Cyanobenzenesulfonate (**14l**).* Compound **8** (0.15 g, 0.5 mmol), DMAP (5 mg), DIPEA (0.08 g, 0.6 mmol), and 4-cyanobenzenesulfonyl chloride (0.12 g, 0.6 mmol) were reacted in CH_2Cl_2 (6 mL) for 1 h. The crude product was recrystallized from MeOH to yield **14l** as white crystals (0.18 g, 79%): mp 231−232 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.80−1.92 (m, 4H), 2.69−2.71 (m, 2H), 2.81−2.83 (m, 2H), 3.50 (m, 4H), 3.63−3.65 (m, 4H), 7.86 (d, 2H, ^3J = 8.6 Hz), 8.15 (d, 2H, ^3J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.2, 22.9, 25.2, 25.3, 44.6, 66.5, 112.1, 116.8, 117.7, 125.4, 129.0, 132.0, 132.7, 142.1, 157.0, 157.1, 173.4. Anal. Calcd for $C_{21}H_{20}N_4O_4S_2$: C, 55.25; H, 4.42; N, 12.27. Found: C, 55.15; H, 4.42; N, 12.31.

*2-(Morpholin-4-yl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4-yl Methanesulfonate (**14m**).* Compound **8** (0.15 g, 0.5 mmol), DMAP (5 mg), DIPEA (0.16 g, 1.2 mmol), and methanesulfonyl chloride (0.14 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 4 h. The crude product was recrystallized from MeOH to yield **14m** as white solid (0.16 g, 68%): mp 178−180 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.77−1.83 (m, 4H), 2.69−2.75 (m, 4H), 3.68 (s, 8H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.8, 22.6, 24.8, 24.9, 41.6, 44.6, 65.9, 111.5, 125.4, 130.9, 157.3, 157.6, 172.6; HRMS-EI m/z $[M]^+$ calcd for $C_{15}H_{19}N_3O_4S_2$ 369.0812, found 369.0818.

*2-(N-Benzyl-N-methylamino)quinazolin-4-yl 4-Methylbenzenesulfonate (**13n**).* Compound **9** (0.27 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-methylbenzenesulfonyl chloride (0.23 g, 1.2 mmol) were reacted in CH_2Cl_2 (10 mL) for 2 h. The crude product was recrystallized from MeOH to yield **13n** as pale green crystals (0.28 g, 67%): mp 80−82 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.29 (br s, 3H), 3.06 (br s, 3H), 4.76 (br s, 2H), 7.12−7.20 (m, 5H), 7.25−7.30 (m, 3H), 7.52 (d, 1H, ^3J = 8.2 Hz), 7.64 (ddd, 1H, ^3J = 8.4 Hz, ^3J = 7.1 Hz, ^4J = 1.3 Hz), 7.85−7.93 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 34.8, 52.5, 110.5, 122.6, 123.6, 125.3, 127.1, 127.4, 128.3, 128.5, 129.6, 134.3, 134.8, 138.0, 145.2, 155.1, 157.9, 162.3; HRMS-ESI m/z $[M + H]^+$ calcd for $C_{23}H_{22}N_3O_3S$ 420.1376, found 420.1370.

*2-(N-Benzyl-N-methylamino)quinazolin-4-yl 4-Cyanobenzenesulfonate (**13o**).* Compound **9** (0.27 g, 1.0 mmol), DMAP (10 mg), DIPEA (0.16 g, 1.2 mmol), and 4-cyanobenzenesulfonyl chloride (0.24 g, 1.2 mmol) were reacted in CH_2Cl_2 (10 mL) for 1 h. The crude product was recrystallized from MeOH to yield **13o** as light green crystals (0.22 g, 51%): mp 122−127 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.09 (br s, 3H), 4.64 (br s, 2H), 7.03 (m, 2H), 7.21−7.49 (m, 6H), 7.56 (d, 1H, ^3J = 8.6 Hz), 7.68 (ddd, 1H, ^3J = 7.7 Hz, ^3J = 7.9 Hz, ^4J = 1.3 Hz), 7.91−7.99 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.0, 52.5, 110.2, 116.8, 117.5, 123.0, 123.3, 125.5, 126.7, 127.6, 128.6, 128.8, 132.7, 135.3, 137.6, 141.5, 155.4, 157.7, 162.2. Anal. Calcd for $C_{23}H_{18}N_4O_3S$: C, 64.17; H, 4.21; N, 13.01. Found: C, 63.85; H, 4.27; 12.92.

*2-(N-Benzyl-N-methylamino)-5,6,7,8-tetrahydrobenzo[4,5]-thieno[2,3-d]pyrimidin-4-yl 4-Methylbenzenesulfonate (**14n**).* Compound **10** (0.16 g, 0.5 mmol), DMAP (5 mg), DIPEA (0.08 g, 0.6 mmol), and 4-methylbenzenesulfonyl chloride (0.12 g, 0.6 mmol) were reacted in CH_2Cl_2 (5 mL) for 3 h. The crude product was recrystallized from MeOH to yield **14n** as white crystals (0.17 g, 68%): mp 87−90 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.83−1.88 (m, 4H), 2.28 (s, 3H), 2.68−2.71 (m, 2H), 2.88−2.90 (m, 2H), 2.94 (s, 3H), 4.61 (br s, 2H), 7.07−7.08 (m, 4H), 7.23−7.27 (m, 3H), 7.80−7.82 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 22.3, 23.0, 25.3, 25.4,

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34.8, 52.6, 111.5, 125.8, 127.1, 127.3, 128.3, 128.5, 129.5, 130.3, 135.1, 138.0, 144.9, 157.5, 158.3, 173.3. Anal. Calcd for $C_{25}H_{25}N_3O_3S_2$: C, 62.61; H, 5.25; 8.76. Found: C, 62.30; H, 5.47; N, 8.61.

*2-(N-Benzyl-N-methylamino)-5,6,7,8-tetrahydrobenzo[4,5]-thieno[2,3-d]pyrimidin-4-yl 4-Cyanobenzenesulfonate (**14o**).* Compound **10** (0.16 g, 0.5 mmol), DMAP (5 mg), DIPEA (0.08 g, 0.6 mmol), and 4-cyanobenzenesulfonyl chloride (0.12 g, 0.6 mmol) were reacted in CH_2Cl_2 (7 mL) for 1 h. The crude product was recrystallized from MeOH to yield **14o** as white crystals (0.17 g, 74%): mp 167−170 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.83−1.91 (m, 4H), 2.71−2.73 (m, 2H), 2.88−2.89 (m, 2H), 2.99 (br s, 3H), 4.52 (br s, 2H), 7.01 (m, 2H), 7.30−7.45 (m, 5H), 7.96 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.3, 23.0, 25.3, 25.3, 35.1, 52.6, 111.6, 116.9, 117.3, 125.5, 126.7, 127.5, 128.6, 128.8, 131.4, 132.6, 137.4, 142.0, 157.2, 157.8, 173.4. Anal. Calcd for $C_{25}H_{22}N_4O_3S_2$: C, 61.20; H, 4.52; N, 11.42. Found: C, 60.86; H, 4.58; N, 11.11.

*2-(N-Benzyl-N-methylamino)-5,6,7,8-tetrahydrobenzo[4,5]-thieno[2,3-d]pyrimidin-4-yl Methanesulfonate (**14p**).* Compound **10** (0.16 g, 0.5 mmol), DMAP (5 mg), DIPEA (0.16 g, 1.2 mmol), and methanesulfonyl chloride (0.14 g, 1.2 mmol) were reacted in CH_2Cl_2 (5 mL) for 3 h. The crude product was recrystallized from MeOH to yield **14p** as white crystals (0.12 g, 56%): mp 149−150 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.76−1.83 (m, 4H), 2.69−2.75 (m, 4H), 3.12 (s, 3H), 3.62 (br s, 3H), 4.86 (s, 2H), 7.24−7.33 (m, 5H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.8, 22.6, 24.8, 25.0, 35.4, 41.5, 52.3, 110.9, 125.4, 127.2, 127.2, 128.7, 130.3, 137.9, 157.3, 158.0, 172.8; HRMS-EI m/z $[M]^+$ calcd for $C_{19}H_{21}N_3O_3S_2$ 403.1019, found 403.1020.

*tert-Butyl 2-Nitrobenzoate (**16**).* 2-Nitrobenzoic acid (**15**) (11.7 g, 70 mmol) was suspended in CH_2Cl_2 (105 mL) and oxalyl chloride (7.0 mL, 70 mmol), and four drops of DMF were added. The suspension was stirred until a solution was obtained, and after evaporation, *tert*-butyl alcohol (52.5 mL), pyridine (52.5 mL), and a catalytic amount of $ZnCl_2$ (50 mg) were added to the residue. The mixture was stirred for 12 h and cold 1N HCl solution (250 mL) was added. The product was extracted with EtOAc (3 × 200 mL), and the organic layer was dried with anhydrous Na_2SO_4 and evaporated to obtain **16**[52] as a pale green oil (13.8 g, 88%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (s, 9H), 7.56 (ddd, 1H, ^3J = 7.9 Hz, ^3J = 7.6 Hz, ^4J = 1.6 Hz), 7.61 (ddd, 1H, ^3J = 7.2 Hz, ^3J = 7.6 Hz, ^4J = 1.3 Hz), 7.70 (dd, 1H, ^3J = 7.7 Hz, ^4J = 1.6 Hz), 7.81 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7, 83.7, 123.5, 128.9, 129.8, 131.2, 132.6, 148.4, 164.2. The material's identity was confirmed by comparison with ^{1}H NMR and ^{13}C NMR literature data.[53]

*tert-Butyl 2-Aminobenzoate (**17**).* A suspension of *tert*-butyl 2-nitrobenzoate (**16**) (12.4 g, 55.5 mmol) and Pd/C (1.2 g) in EtOH (100 mL) was hydrogenated using hydrogen gas at approximately 2 atm. Upon completion, the catalyst was filtered off and the filtrate evaporated in vacuo. Compound **17**[54] was obtained as a colorless oil (9.05 g, 84%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.57 (s, 9H), 5.67 (br s, 2H), 6.59−6.62 (m, 2H), 7.20−7.23 (m, 1H), 7.79−7.80 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.3, 80.5, 112.5, 116.1, 116.6, 131.4, 133.5, 150.3, 167.6. ($C_{11}H_{15}NO_2$); LC-MS (ESI) (90% H_2O to 100% MeOH in 10 min, then 100% MeOH to 20 min, DAD 220−400 nm), 100% purity, m/z = 194.26 ($[M + H]^+$).

*tert-Butyl 2-Isothiocyanatobenzoate (**18**).* Thiophosgene (2.7 g, 23.0 mmol) was dissolved in EtOAc (90 mL) and cooled to −78 °C. Triethylamine (4.6 g, 46.0 mmol) dissolved in EtOAc (60 mL) was added dropwise over 30 min. The resulting suspension was stirred vigorously for 15 min, and *tert*-butyl 2-aminobenzoate (**17**) (4.0 g, 21 mmol) in EtOAc (70 mL) was added over 30 min. The obtained solution was stirred for 20 h at room temperature, subsequently diluted with EtOAc (200 mL), and washed sequentially with water (2 × 200 mL) and brine (200 mL). The organic layer was dried with anhydrous Na_2SO_4 and evaporated in vacuo to yield **18** as a brown oil, which solidified upon cooling to −20 °C (4.47 g, 83%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.61 (s, 9H) 7.27−7.30 (m, 2H) 7.43−7.46 (m, 1H), 7.86−7.88 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.2, 82.5, 126.8, 128.0, 128.4, 129.7, 131.4, 132.5, 134.2, 163.2; HRMS-EI m/z $[M]^+$ calcd for $C_{12}H_{13}NO_2S$ 235.0662, found 235.0668. ($C_{12}H_{13}NO_2S$).

*tert-Butyl 2-(3-(4-Methylbenzenesulfonyl)thioureido)benzoate (**19**).* 4-Methylbenzenesulfonamide (1.71 g, 10 mmol) and potassium carbonate (1.80 g, 10 mmol) were added to a solution of *tert*-butyl 2-isothiocyanatobenzoate (**18**) (2.35 g, 10 mmol) in anhydrous acetone (100 mL), and the mixture was refluxed for 20 h. After evaporation, the residue was dissolved in a mixture of water (70 mL) and EtOH (35 mL) and acidified with 2 N HCl. A precipitate was filtered off and washed with water (20 mL) to afford **19** (0.90 g, 24%) as a pale brown solid: mp 134−136 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.61 (s, 9H), 2.42 (s, 3H), 7.19−7.22 (m, 1H), 7.31 (d, 2H, ^3J = 8.2 Hz), 7.42−7.45 (m, 1H), 7.88 (d, 2H, ^3J = 8.5 Hz), 7.92−7.94 (m, 1H), 8.14−8.16 (m, 1H), 11.60 (br s, 1H), one signal (NH) was not detected; ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 28.2, 82.9, 122.8, 124.9, 125.5, 127.6, 130.0, 130.8, 132.2, 135.6, 139.1, 145.3, 166.0, 177.1. Anal. Calcd for $C_{19}H_{22}N_2O_4S_2$: C, 56.14; H, 5.45; N, 6.89. Found: C, 55.75; H, 5.46; N, 6.50.

*(Z)-tert-Butyl 2-((4-Methylbenzenesulfonamido)(methylsulfanyl)-methyleneamino)benzoate (**20**).* *tert*-Butyl 2-(3-(4-methylbenzenesulfonyl)thioureido)benzoate (**19**) (1.27 g, 3.15 mmol) was dissolved in EtOH (30 mL), and 1 N NaOH (6 mL) and methyl iodide (0.64 mL, 4.5 mmol) were added dropwise. The mixture was stirred for 2 h at room temperature. After acidification with 2 N HCl to pH ∼3, the mixture was stored at −20 °C for 2 h to obtain **20** as white needles (0.83 g, 55%): mp 85−87 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.58 (s, 9H), 2.39 (s, 3H), 2.51 (s, 3H), 7.17−7.20 (m, 1H), 7.26 (d, 2H, ^3J = 7.9 Hz), 7.43−7.47 (m, 1H), 7.89 (d, 2H, ^3J = 8.2 Hz), 7.91−7.92 (m, 1H), 8.09−8.10 (m, 1H), 11.06 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 21.5, 28.1, 83.1, 121.8, 124.4, 125.2, 126.8, 129.2, 131.1, 133.2, 138.8, 139.4, 142.7, 165.1, 166.8. Anal. Calcd for $C_{20}H_{24}N_2O_4S_2{\cdot}0.2H_2O$: C, 56.63; H, 5.80; N, 6.60. Found: C, 56.52; H, 5.78; N, 6.72..

*(Z)-2-((4-Methylbenzenesulfonamido)(methylsulfanyl)-methyleneamino)benzoic Acid (**21**).* (*Z*)-*tert*-Butyl 2-((4-methylbenzenesulfonamido)(methylsulfanyl)methyleneamino)-benzoate (**20**) (0.50 g, 1.2 mmol) was dissolved in a mixture of CH_2Cl_2 (14 mL) and trifluoroacetic acid (7 mL), and the solution was stirred for 2 h at room temperature. After evaporation in vacuo, the residue was suspended in EtOAc (10 mL) and the insoluble material was filtered off to yield **21** (0.42 g, 96%) as a white solid: mp 174−176 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.37 (s, 3H), 2.56 (s, 3H), 7.31 (ddd, 1H, ^3J = 7.9 Hz, ^3J = 7.5 Hz, ^3J = 1.3 Hz), 7.37 (d, 2H, ^3J = 7.9 Hz), 7.61 (ddd, 1H, ^3J = 8.5 Hz, ^3J = 7.1 Hz, ^4J = 1.6 Hz), 7.76 (d, 2H, ^3J = 8.2 Hz), 8.00 (dd, 1H, ^3J = 7.9 Hz, ^4J = 1.6 Hz), 8.10 (d, 1H, ^3J = 8.2 Hz), 11.09 (s, 1H), 13.79 (br s, 1H); ^{13}C NMR: (125 MHz, DMSO-d_6) δ 14.7, 21.1, 120.9, 123.9, 125.5, 126.5, 129.5, 131.3, 133.7, 138.9, 139.5, 142.7, 164.8, 168.9. Anal. Calcd for $C_{16}H_{16}N_2O_4S_2$: C, 52.73; H, 4.43; N, 7.69. Found: C, 52.52; H, 4.40; N, 7.60.

*3-(4-Methylbenzenesulfonyl)-2-(methylsulfanyl)quinazolin-4(3H)-one (**11e**).* (*Z*)-2-((4-Methylbenzenesulfonamido)-(methylsulfanyl)methyleneamino)benzoic acid (**21**) (0.18 g, 0.5 mmol) was dissolved in THF (10 mL) and 1,1′-carbonyldiimidazole (0.1 g, 0.6 mmol) was added. The mixture was stirred for 1 h at room temperature. After evaporation in vacuo, the residue was purified by flash column chromatography using petroleum ether/EtOAc (2:1) to yield **11e** as a white solid (0.13 g, 78%): mp 122−127 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.43 (s, 3H), 2.57 (s, 3H), 7.30 (ddd, 1H, ^3J = 7.7 Hz, ^3J = 7.6 Hz, ^4J = 1.0 Hz), 7.35 (d, 2H, ^3J = 8.5 Hz), 7.48 (d, 1H, ^3J = 8.2 Hz), 7.66 (ddd, 1H, ^3J = 7.6 Hz, ^3J = 7.4 Hz, ^4J = 1.6 Hz), 8.02 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.6 Hz), 8.16 (d, 2H, ^3J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.8, 21.8, 119.6, 126,2, 126.5, 127.2, 129.3, 129.5, 135.5, 135.6, 145.4, 146.1, 154.2, 161.2; HRMS-ESI m/z $[M + Na]^+$ calcd for $C_{16}H_{14}N_2O_3S_2Na$ 369.0338, found 369.0336.

*tert-Butyl 2-Isothiocyanato-4,5,6,7-tetrahydrobenzo[b]-thiophene-3-carboxylate (**22**).* A mixture prepared from thiophosgene (8.0 g, 70 mmol), $CaCO_3$ (7.0 g, 70 mmol), CH_2Cl_2 (35 mL), and H_2O (70 mL) was stirred at 0 °C, and a solution of *tert*-butyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate[27] (17.7 g, 70 mmol) in CH_2Cl_2 (120 mL) was added dropwise over a period of 40 min. The mixture was stirred overnight at room temperature. The organic layer was washed with water, dried using anhydrous

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Na_2SO_4, and evaporated in vacuo. The residue was purified by column chromatography using petroleum ether/EtOAc (9:1) to obtain **22** as a yellow solid (15.6 g, 75%): mp 89 °C (lit.[28] mp 79−80 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.52 (s, 9H), 1.67−1.76 (m, 4H), 2.62−2.66 (m, 4H). Anal. Calcd for $C_{14}H_{17}NO_2S_2$: C, 56.92; H, 5.80; N, 4.74. Found: C, 56.64; H, 5.58; N; 4.71.

*tert-Butyl 2-(3-(4-Methylbenzenesulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**23**).* 4-Methylbenzenesulfonamide (1.71 g, 10 mmol) and potassium carbonate (1.80 g, 10 mmol) were added to a solution of *tert*-butyl 2-isothiocyanato-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**22**) (2.95 g, 10 mmol) in anhydrous acetone (140 mL), and the reaction mixture was refluxed for 20 h. After evaporation, the residue was dissolved in a mixture of water (140 mL) and EtOH (100 mL) and acidified with 2 N HCl. A precipitate was filtered off and washed with water (20 mL) to yield **23** (4.42 g, 95%) as a pale yellow solid: mp 176−180 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.62 (s, 9H), 1.73−1.77 (m, 4H), 2.39 (s, 3H), 2.59−2.61 (m, 2H), 2.73−2.75 (m, 2H), 7.26−7.28 (m, 2H), 7.91−7.93 (m, 2H), 8.10 (s, 1H), 13.15 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 22.8, 22.9, 24.3, 26.5, 28.4, 82.5, 117.3, 127.8, 128.2, 130.0, 131.4, 135.2, 145.4, 146.9, 165.6, 171.8. Anal. Calcd for $C_{21}H_{26}N_2O_4S_3$: C, 54.05; H, 5.62; N, 6.00. Found: C, 54.37; H, 5.56; N, 6.12.

*tert-Butyl 2-(3-(4-Cyanobenzenesulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**24**).* 4-Cyanobenzenesulfonamide (0.64 g, 3.5 mmol) and potassium carbonate (0.46 g, 3.5 mmol) were added to a solution of *tert*-butyl 2-isothiocyanato-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**22**) (1.03 g, 3.5 mmol) in anhydrous acetone (40 mL), and the mixture was refluxed for 20 h. After evaporation, the residue was dissolved in a mixture of water (60 mL) and EtOH (90 mL) and acidified with 2 N HCl. A precipitate was filtered off and washed with water (20 mL) to provide **24** (1.27 g, 76%) as a yellow solid: mp 164−167 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.61 (s, 9H), 1.74−1.77 (m, 4H), 2.60−2.62 (m, 2H), 2.72−2.74 (m, 2H), 7.78−7.80 (m, 2H), 8.17−8.19 (m, 2H), 8.31 (br s, 1H), 13.18 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.79, 22.79, 24.4, 26.5, 28.4, 82.8, 116.9, 117.3, 117.8, 128.5, 128.6, 131.6, 133.1, 142.3, 146.6, 165.9, 170.7. Anal. Calcd for $C_{21}H_{23}N_3O_4S_3$: C, 52.81; H, 4.85; N, 8.80. Found: C, 52.45; H, 4.87; N, 8.57.

*tert-Butyl 2-(3-(Methylsulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**25**).* Methanesulfonamide (0.52 g, 5.5 mmol) and sodium hydride (0.22 g, 5.5 mmol, 70% oil dispersion) were dissolved in anhydrous DMF (15 mL) and stirred for 15 min. *tert*-Butyl 2-isothiocyanato-4,5,6,7-tetrahydrobenzo[*b*]-thiophene-3-carboxylate (**22**) (1.47 g, 5.0 mmol) was added, and the mixture was stirred at 60 °C for 1 h. After evaporation in vacuo, the residue was dissolved in water (20 mL) and EtOH (10 mL) and acidified with 6 N HCl to provide a precipitate that was collected by suction filtration to yield **25** (1.93 g, 99%) as a white solid: mp 159−162 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (s, 9H), 1.73−1.79(m, 4H), 2.63−2.65 (m, 2H), 2.72−2.75 (m, 2H), 3.33 (s, 3H), 8.09 (s, 1H), 13.02 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.84, 22.84, 24.4, 26.5, 28.3, 41.5, 82.7, 117.3, 128.3, 131.5, 146.7, 166.0, 171.8. Anal. Calcd for $C_{15}H_{22}N_2O_4S_3$: C, 46.13; H, 5.68; N, 7.17. Found: C, 46.22; H, 5.97; N, 6.96.

*(Z)-tert-Butyl 2-((4-Methylbenzenesulfonamido)(methylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**26e**).* *tert*-Butyl 2-(3-(4-methylbenzenesulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**23**) (1.45 g, 3.0 mmol) was dissolved in a mixture of EtOH (30 mL) and 1 N NaOH (6 mL). Methyl iodide (0.64 g, 4.5 mmol) was added dropwise, and the mixture was stirred for 2 h at room temperature. After acidification with 2 N HCl to pH ∼3, a precipitate was filtered off to obtain **26e** as a white solid (1.31 g, 91%): mp 209−213 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (s, 9H), 1.71−1.77 (m, 4H), 2.38 (s, 3H), 2.59−2.61 (m, 5H), 2.68−2.70 (m, 2H), 7.24−7.25 (m, 2H), 7.88−7.89 (m, 2H), 12.05 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.0, 21.5, 22.81, 22.84, 24.4, 26.5, 28.3, 82.5, 114.3, 127.2, 129.1, 129.1, 131.0, 139.0, 142.7, 146.5, 159.8, 166.8. Anal. Calcd for $C_{22}H_{28}N_2O_4S_3 \times 0.1\ H_2O$: C, 54.77; H, 5.89; N, 5.81. Found: C, 54.42; H, 5.92; N, 5.76.

*(Z)-tert-Butyl 2-((4-Cyanobenzenesulfonamido)(methylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**26f**).* *tert*-Butyl 2-(3-(4-cyanobenzenesulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**24**) (1.05 g, 2.2 mmol) was dissolved in a mixture of EtOH (20 mL) and 2 N NaOH (2.2 mL). Methyl iodide (0.47 g, 3.3 mmol) was added dropwise, and the mixture was stirred for 2 h at room temperature. After acidification with 2 N HCl to pH ∼3, a precipitate was filtered off to obtain **26f** as a pale yellow solid (1.00 g, 92%): mp 194−196 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (s, 9H), 1.73−1.77 (m, 4H), 2.58−2.60 (m, 2H), 2.65 (s, 3H), 2.68−2.71 (m, 2H), 7.75−7.76 (m, 2H), 8.10−8.12 (m, 2H), 12.26 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 22.73, 22.77, 24.4, 26.5, 28.3, 82.9, 114.9, 115.7, 117.7, 127.8, 129.6, 131.3, 132.4, 145.8, 146.0, 160.7, 166.8. Anal. Calcd for $C_{22}H_{25}N_3O_4S_3$: C, 53.74; H, 5.13; N, 8.55. Found: C, 53.59; H, 5.15; N, 8.43.

*(Z)-tert-Butyl 2-((Methylsulfonyl)(methylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**26g**).* *tert*-Butyl 2-(3-(methylsulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**25**) (1.56 g, 4.0 mmol) was dissolved in a mixture of EtOH (30 mL) and 2 N NaOH (4 mL). Methyl iodide (0.85 g, 6 mmol) was added dropwise, and the mixture was stirred for 2 h at room temperature. After acidification with 2 N HCl to pH ∼3, a precipitate was filtered off to obtain **26g** as a white solid (1.27 g, 78%): mp 135−138 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56 (s, 9H), 1.73−1.79 (m, 4H), 2.61−2.63 (m, 2H), 2.67 (s, 3H), 2.71−2.73 (m, 2H), 3.14 (s, 3H), 12.07 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 22.79, 22.84, 24.4, 26.5, 28.3, 42.4, 82.6, 114.3, 128.7, 131.1, 146.3, 159.2, 166.8; HRMS-EI *m*/*z* $[M]^+$ calcd for $C_{16}H_{24}N_2O_4S_3$: 404.0893, found: 404.0898.

*(Z)-tert-Butyl 2-((4-Methylbenzenesulfonamido)(benzylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**26h**).* *tert*-Butyl 2-(3-(4-methylbenzenesulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**23**) (0.7 g, 1.5 mmol) was dissolved in a mixture of EtOH (20 mL) and 1 N NaOH (3 mL). Benzyl bromide (0.38 g, 2.25 mmol) was added dropwise, and the mixture was stirred for 2 h at room temperature. After acidification with 2 N HCl to pH ∼ 3, a precipitate was filtered off to obtain **26h** as a white solid (0.58 g, 70%): mp 152−155 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (s, 9H), 1.71−1.77 (m, 4H), 2.40 (s, 3H), 2.58−2.60 (m, 2H), 2.68−2.70 (m, 2H), 4.34 (s, 2H), 7.23−7.32 (m, 7H), 7.87 (d, 2H, ^3J = 8.2 Hz), 12.08 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.5, 22.79, 22.82, 24.4, 26.5, 28.3, 36.6, 82.5, 127.3, 128.1, 128.8, 129.1, 129.3, 131.1, 133.2, 138.9, 142.7, 146.2, 158.6, 158.8, 166.5. Anal. Calcd for $C_{28}H_{32}N_2O_4S_3 \times 1.0\ H_2O$: C, 58.51; H, 5.96; N, 4.87. Found: C, 58.69; H, 5.63; N, 4.90.

*(Z)-tert-Butyl 2-((Methylsulfonamido(benzylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**26j**).* *tert*-Butyl 2-(3-(methylsulfonyl)thioureido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**25**) (0.39 g, 1 mmol) was dissolved in a mixture of EtOH (10 mL) and 1 N NaOH (2 mL). Benzyl bromide (0.26 g, 1.5 mmol) was added dropwise, and the mixture was stirred for 2 h at room temperature. After acidification with 2 N HCl to pH ∼3, a precipitate was filtered off to afford **26j** as a white solid (0.38 g, 80%): mp 178−181 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.55 (s, 9H, 1.73−1.79 (m, 4H), 2.61−2.63 (m, 2H), 2.70−2.73 (m, 2H), 3.12 (s, 3H), 4.42 (s, 2H), 7.26−7.33 (m, 3H), 7.42−7.44 (m, 2H), 12.09 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.78, 22.83, 24.4, 26.5, 28.3, 36.8, 42.4, 82.6, 128.3, 128.9, 129.0, 129.4, 131.3, 133.0, 146.1, 158.1, 166.6, one carbon signal was not observed; HRMS-EI *m*/*z* $[M]^+$ calcd for $C_{22}H_{28}N_2O_4S_3$ 480.1206, found 480.1215.

*(Z)-2-((4-Methylbenzenesulfonamido)(methylsulfanyl)-methyleneamino)-4,5,6,7-tetra-hydrobenzo[b]thiophene-3-carboxylic Acid (**27e**).* (*Z*)-*tert*-Butyl 2-((4-methylbenzene-sulfonamido)-(methylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]-thiophene-3-carboxylate (**26e**) (0.30 g, 0.62 mmol) was dissolved in CH_2Cl_2 (7 mL) and trifluoroacetic acid (3.5 mL), and the mixture was stirred for 2 h at room temperature. After evaporation in vacuo, the residue was suspended in EtOAc (10 mL) and filtered off to yield **27e** as a light-brown solid (0.22 g, 84%): mp 225−226 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.67−1.73 (m, 4H), 2.36 (s, 3H), 2.58−2.61 (m,

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2H), 2.65 (s, 3H), 2.69−2.71 (m, 2H), 7.37 (d, 2H, ^3J = 8.2 Hz), 7.75 (d, 2H, ^3J = 8.2 Hz), 12.12 (s, 1H), one signal (CO_2H) was not detected; ^{13}C NMR: (125 MHz, DMSO-d_6) δ 14.4, 21.1, 22.3, 22.6, 23.8, 25.8, 113.9, 126.7, 128.4, 129.5, 131.4, 139.0, 142.9, 145.7, 160.5, 167.9; LC-MS (ESI) (90% H_2O to 100% MeOH in 10 min, then 100% MeOH to 20 min, DAD 220−400 nm), 98% purity, m/z = 425.18 ($[M + H]^+$). Anal. Calcd for $C_{18}H_{20}N_2O_4S_3 \cdot 0.3H_2O$: C, 50.28; H, 4.83; N, 6.52. Found: C, 50.08; H, 4.88; N, 6.23.

*(Z)-2-((4-Cyanobenzenesulfonamido)(methylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic Acid (**27f**).* (*Z*)-*tert*-Butyl 2-((4-cyanobenzene-sulfonamido)-(methylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]-thiophene-3-carboxylate (**26f**) (0.73 g, 1.5 mmol) was dissolved in CH_2Cl_2 (15 mL) and trifluoroacetic acid (7.5 mL), and the mixture was stirred for 2 h at room temperature. After evaporation in vacuo, the residue was suspended in EtOAc (10 mL) and filtered off to yield **27f** as a light-brown solid (0.56 g, 85%): mp 211−214 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.65−1.73 (m, 4H), 2.58−2.61 (m, 2H), 2.67 (s, 3H) 2.69−2.71 (m, 2H), 8.01−8.03 (m, 2H), 8.05−8.06 (m, 2H), 12.31 (s, 1H), one signal (CO_2H) was not detected; ^{13}C NMR (125 MHz, DMSO-d_6) δ 14.5, 22.2, 22.5, 23.8, 25.8, 114.4, 115.0, 117.9, 127.4, 128.8, 131.6, 133.3, 145.4, 145.8, 161.6, 167.8; HRMS-ESI m/z $[M - H]^-$ calcd for $C_{18}H_{16}N_3O_4S_3$ 434.0308, found 434.0314.

*(Z)-2-(Methylsulfonamido(methylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic Acid (**27g**).* (*Z*)-*tert*-Butyl 2-((methylsulfonyl)(methylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**26g**) (0.81 g, 2.0 mmol) was dissolved in CH_2Cl_2 (20 mL) and trifluoroacetic acid (10 mL), and the mixture was stirred for 2 h at room temperature. After evaporation in vacuo, the residue was suspended in EtOAc (10 mL) and filtered off to obtain **27g** as a white solid (0.67 g, 96%): mp 213-215 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.68−1.75 (m, 4H), 2.61−2.63 (m, 2H), 2.70 (s, 3H), 2.71−2.73 (m, 2H), 3.08 (s, 3H), 12.03 (s, 1H), one signal (CO_2H) was not detected; ^{13}C NMR: (125 MHz, DMSO-d_6) δ 14.4, 22.3, 22.6, 23.8, 25.9, 42.2, 113.5, 128.1, 131.4, 146.0, 159.5, 168.0. Anal. Calcd for $C_{12}H_{16}N_2O_4S_3$: C, 41.36; H, 4.63; N, 8.04. Found: C, 41.61; H, 4.80; N, 7.72.

*(Z)-2-((4-Methylbenzenesulfonamido)(benzylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic Acid (**27h**).* (*Z*)-*tert*-Butyl 2-((4-methylbenzenesulfonamido)-(benzylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]-thiophene-3-carboxylate (**26h**) (0.45 g, 0.8 mmol) was dissolved in CH_2Cl_2 (8 mL) and trifluoroacetic acid (4 mL), and the mixture was stirred for 2 h at room temperature. After evaporation in vacuo, the residue was suspended in EtOAc (10 mL) and filtered off to yield **27h** as a white solid (0.29 g, 59%): mp 204−207 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.69−1.72 (m, 4H), 2.38 (s, 3H), 2.58−2.59 (m, 2H), 2.70−2.71 (m, 2H), 4.50 (s, 2H), 7.28−7.30 (m, 5H), 7.37 (d, 2H, ^3J = 7.9 Hz), 7.73 (d, 2H, ^3J = 8.2 Hz), 12.26 (br s, 1H), one signal (CO_2H) was not detected; ^{13}C NMR (125 MHz, DMSO-d_6) δ 21.1, 22.3, 22.6, 23.8, 25.8, 35.6, 114.1, 126.8, 128.1, 128.7, 128.9, 129.2, 129.5, 131.6, 133.9, 138.8, 142.9, 145.5, 158.8, 167.9. Anal. Calcd for $C_{24}H_{24}N_2O_4S_3$: C, 57.58; H, 4.83; N, 5.60. Found: C, 57.42; H, 4.61; N, 5.39.

*(Z)-2-((Methylsulfonamido)(benzylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic Acid (**27j**).* (*Z*)-*tert*-Butyl 2-((methylsulfonamido)(benzyl-sulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**26j**) (0.3 g, 0.63 mmol) was dissolved in CH_2Cl_2 (6 mL) and trifluoroacetic acid (3 mL), and the mixture was stirred for 2 h at room temperature. After evaporation in vacuo, the residue was recrystallized from EtOAc (30 mL) to obtain **27j** as white crystals (0.24 g, 90%): mp 202−204 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.69−1.75 (m, 4H), 2.62−2.64 (m, 2H), 2.72−2.74 (m, 2H), 3.08 (s, 3H), 4.56 (s, 2H), 7.30−7.39 (m, 3H), 7.47−7.48 (m, 2H), 12.17 (br s, 1H), one signal (CO_2H) was not detected; ^{13}C NMR (125 MHz, DMSO-d_6) δ 22.3, 22.6, 23.9, 25.9, 35.7, 42.2, 113.9, 128.2, 128.4, 129.0, 129.4, 131.6, 133.9, 145.8, 157.9, 167.9; HRMS-EI m/z $[M - H_2O]^+$ calcd for $C_{18}H_{18}N_2O_3S_3$ 406.0474, found 406.0483; LC-MS (ESI) (90% H_2O to 100% MeOH in 10 min, then 100% MeOH to 20 min, DAD 220−400 nm), 97% purity, m/z = 425.17 ($[M + H]^+$).

*3-(4-Methylbenzenesulfonyl)-2-(methylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4(3H)-one (**12e**).* To a suspension of (*Z*)-2-((4-methylbenzenesulfonamido)-(methylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]-thiophene-3-carboxylic acid (**27e**) (0.21 g, 0.5 mmol) in CH_2Cl_2 (5 mL) were added three drops of DMF and oxalyl chloride (0.05 mL, 0.5 mmol). The mixture was stirred for 45 min at room temperature. After evaporation in vacuo, the residue was purified by flash column chromatography using petroleum ether/EtOAc (2:1) to yield **12e** as a white solid (0.15 g, 74%): mp 195−197 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70−1.75 (m, 2H), 1.77−1.82 (m, 2H), 2.43 (s, 3H), 2.51 (s, 3H), 2.65−2.68 (m, 2H), 2.78−2.80 (m, 2H), 7.32−7.34 (m, 2H), 8.11−8.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.1, 21.8, 22.0, 22.8, 25.0, 25.3, 118.9, 129.2, 129.4, 131.9, 132.9, 135.8, 145.9, 155.3, 157.4, 160.5; HRMS-EI m/z $[M]^+$ calcd for $C_{18}H_{18}N_2O_3S_3$ 406.0475, found 406.0482.

*4-((2-(Methylsulfanyl)-4-oxo-5,6,7,8-tetrahydrobenzo[4,5]thieno-[2,3-d]pyrimidin-3(4H)-yl)sulfonyl)benzonitrile (**12f**).* To a suspension of (*Z*)-2-((4-cyanobenzenesulfonamido)(methylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (**27f**) (0.22 g, 0.5 mmol) in CH_2Cl_2 (5 mL) were added three drops of DMF and oxalyl chloride (0.05 mL, 0.5 mmol). A solution was obtained and the mixture was stirred for 45 min at room temperature. After evaporation in vacuo, the residue was purified by flash column chromatography using petroleum ether/EtOAc (9:1) to yield **12f** as a white solid (0.12 g, 56%): mp 136−143 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.71−1.75 (m, 2H), 1.78−1.83 (m, 2H), 2.54 (s, 3H), 2.66−2.69 (m, 2H), 2.74−2.76 (m, 2H), 7.83 (d, 2H, ^3J = 8.9 Hz), 8.32 (d, 2H, ^3J = 8.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.0, 21.9, 22.7, 25.0, 25.3, 117.0, 118.0, 118.6, 129.6, 131.9, 132.5, 133.7, 142.9, 154.9, 157.1, 160.6; HRMS-EI m/z $[M]^+$ calcd for $C_{18}H_{15}N_3O_3S_3$: 417.0271, found: 417.0277.

*3-(Methylsulfonyl)-2-(methylsulfanyl)-5,6,7,8-tetrahydrobenzo-[4,5]thieno[2,3-d]-pyrimidin-4(3H)-one (**12g**).* To a suspension of (*Z*)-2-((methylsulfonamido)(methylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]-thiophene-3-carboxylic acid (**27g**) (0.21 g, 0.5 mmol) in CH_2Cl_2 (5 mL) were added three drops of DMF and oxalyl chloride (0.05 mL, 0.5 mmol). The mixture was stirred for 45 min at room temperature. After evaporation in vacuo, the residue was purified by flash column chromatography using petroleum ether/EtOAc (9:1) to yield **12g** as a white solid (0.13 g, 78%): mp 147−150 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.77−1.87 (m, 4H), 2.48 (s, 3H), 2.70−2.73 (m, 2H), 2.87−2.90 (m, 2H), 3.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.9, 22.0, 22.8, 25.0, 25.3, 44.5, 118.7, 131.95, 133.4, 155.0, 158.5, 160.8. Anal. Calcd for $C_{12}H_{14}N_2O_3S_3$: C, 43.62; H, 4.27; N, 8.48. Found: C, 43.68; H, 4.86; N, 7.91.

*3-(4-Methylbenzenesulfonyl)-2-(benzylsulfanyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]-pyrimidin-4(3H)-one (**12h**).* To a suspension of (*Z*)-2-((4-methylbenzenesulfonamido)(benzylsulfanyl)-methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (**27h**) (0.21 g, 0.5 mmol) in CH_2Cl_2 (5 mL) were added three drops of DMF and oxalyl chloride (0.05 mL, 0.5 mmol). The mixture was stirred for 45 min at room temperature. After evaporation in vacuo, the residue was purified by flash column chromatography using petroleum ether/EtOAc (2:1) to yield **12h** as a white solid (0.14 g, 59%): mp 195−197 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.70−1.75 (m, 2H), 1.77−1.82 (m, 2H), 2.42 (s, 3H), 2.66−2.69 (m, 2H), 2.77−2.79 (m, 2H), 4.33 (s, 2H), 7.22−7.35 (m, 5H), 7.41 (d, 2H, ^3J = 8,5 Hz), 8.08 (d, 2H, ^3J = 8,5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.8, 22.0, 22.8, 25.0, 25.3, 38.5, 119.1, 127.48, 127.48, 128.5, 129.2, 129.4, 129.6, 132.0, 133.1, 135.6, 145.9, 154.0, 157.3, 160.2; HRMS-ESI m/z $[M + Na]^+$ calcd for $C_{24}H_{22}N_2O_3S_3Na$ 505.0685, found 505.0678.

*2-(Benzylsulfanyl)-3-(methylsulfonyl)-5,6,7,8-tetrahydrobenzo-[4,5]thieno[2,3-d]pyrimidin-4(3H)-one (**12j**).* To a suspension of (*Z*)-2-((methylsulfonamido)(benzylsulfanyl)methyleneamino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (**27j**) (0.20 g, 0.47 mmol) in CH_2Cl_2 (5 mL) were added three drops of DMF and oxalyl chloride (0.05 mL, 0.5 mmol). The mixture was stirred for 30 min at

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room temperature. After evaporation in vacuo, the residue was purified by flash column chromatography using petroleum ether/EtOAc (4:1 to 2:1) to yield **12j** as a white solid (0.15 g, 78%): mp 148−151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.77−1.88 (m, 4H), 2.71−2.74 (m, 2H), 2.87−2.90 (m, 2H), 3.62 (s, 3H), 4.30 (s, 2H), 7.23−7.25 (m, 1H), 7.27−7.30 (m, 2H), 7.37−7.38 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.1, 22.8, 25.1, 25.3, 38.3, 44.5, 119.0, 127.6, 128.5, 129.7, 132.0, 133.6, 135.7, 153.6, 158.4, 160.5. Anal. Calcd for $C_{18}H_{18}N_2O_3S_3$: C, 53.18; H, 4.46; N, 6.89. Found: C, 52.78; H, 4.80; N, 6.52.

HPLC Analysis of the Sulfonyl Migration. A mixture of compound **12e** (13.2 mg, 0.032 mmol) and anhydrous acetonitrile (32 mL) was refluxed under argon atmosphere. Without interrupting the heating, aliquots of 200 μL were collected via a syringe through a rubber septum. After 2 min, these aliquots were directly subjected to the HPLC. The chromatograms were analyzed to determine relative concentrations under the assumption of equal extinction coefficients for **12e** and **14e** at 220 nm. The first-order rate constant of the exponential decay was determined by nonlinear regression using the program GraFit v5.0 (Erithacus Software, Horley, U.K.). Similarly, the reaction of compound **12e** (13.2 mg, 0.032 mmol) in acetonitrile (32 mL) in the presence of compound **3** (1.23 mg, 0.0064 mmol) and the reaction of **12e** (13.2 mg, 0.032 mmol) in acetonitrile (32 mL) in the presence of compound **4** (1.64 mg, 0.0064 mmol) were analyzed.

■ ASSOCIATED CONTENT

Supporting Information

X-ray crystal structures (CIF), additional analytical data to sulfonyl migration, and ^{1}H NMR, ^{13}C NMR, HSQC, and HMBC spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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