JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b03115 • Publication Date (Web): 03 Jan 2020

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Direct Sulfenylation of the Purines C_8-H Bond with Thiophenols

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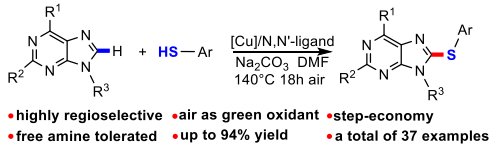
Supporting Information

ABSTRACT: The one-step copper-mediated regioselective formation of the C_8-S bond for purine derivatives with arylthiols was achieved using air as the green oxidant in the presence of 1.0 equivalent of Na_2CO_3 and stoichiometric CuCl and 1,10-phenanthroline monohydrate. This method provides an economical, easy-to-handle and effective method for the synthesis of 8-sulfenylpurine derivatives in moderate to excellent yields. The reaction is selective for C8 over C2 and C6. It also tolerates a free amine on the purine, and it has a wide substrate scope.



INTRODUCTION

The purine heterocyclic framework, an important pharmaceutical intermediate with a broad range of functions, is widely used in the field of biological and medicinal chemistry.[1] The derivatives with the arylthio group on the purine's C8 atom have attracted the interest of synthetic chemists due to their important roles in antitumor and anticancer efforts.[2] PU-H71, MPC-3100 and CUDC-305 (**Figure 1**) are effective Hsp90 inhibitors[3] which can lead to cell- specific growth arrest or apoptosis in cancer cells, as well as inhibition or regression of tumor growth. Therefore, the synthesis of such compounds by the direct sulfenylation of purine's C8 with various sulphur sources is of great interest.

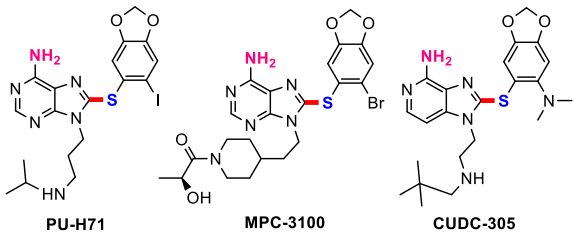
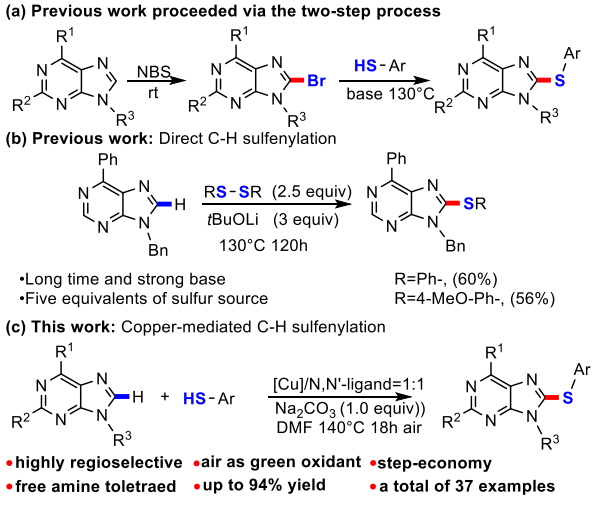


Figure 1. Examples of purine analogues possessing biological activities.

The C-S bond is an important structural unit found in a large number of biologically active molecules and functional materials.[4] The direct sulfenylation of purines C_8-H bond to synthesize a series of 8-sulfenylpurine derivatives is difficult due to the low activity of C_8-H bond. Therefore, the conventional method for synthesizing 8-sulfenylpurine derivatives was by the nucleophilic substitution reaction of arylthiols with 8-bromopurines, and the 8-bromopurines were formed by bromination of the purines' C_8-H bond. The total yield of this method was less than 70% (**Scheme 1a**).[5] In the past few decades, many efforts have been made in the C(sp^2)-H bonds direct functionalization which enabled the efficient construction of carbon-heteroatom bonds as a highly atom-economy. In 2013, Hocek's group[6] firstly reported the direct C_8-H sulfenylation reaction of 6-phenyl-9-benzyl purine with diphenyl disulfide in the presence of *t*BuOLi (**Scheme 1b**). However, this reaction required 2.5 equiv of disulfide together with a long reaction time (120 h), and two products were obtained with yields of 60% and 56%. Thus, further development for direct sulfenylation of purines C_8-H bond is strongly desired.

The formation of a C-S bond through metal-catalyzed/mediated nitrogen heterocyclic compound C-H bond has been a subject of particular interest.[7] Pd,[8] Ru,[9] Ag[10] and other transition metals-catalyzed[11] the C-H to intramolecular or intermolecular C-S bond transformation. This usually required other metal additives or other special requirements. Moreover, on the basis of the literature[12] and our previous work, these methods have no significant effect on purine and its derivatives. The failure may be due to the four N atoms of the purine being easily chelated or coordinated with these metals causing catalyst poisoning. In recent years, due to their low cost and as alternative catalysts for C-H bond functionalization, copper salts were used in a large number of studies for the direct functionalization the C-H bond of heterocyclic compounds (benzothiazole, benzoxazole, etc.).[13] In 2013, Zhu and co-workers described copper-catalyzed direct thiolation of xanthines and related heterocycles with disulfides using $Cu(OAc)_2 \cdot H_2O$ as the catalyst under oxygen atmosphere.[14] But it also required AgOAc as an additive and there was no mention that purines could be applied into this catalytic system. Therefore, it is necessary to develop a highly efficient and novel method for synthesizing 8-sulfenylpurine derivatives. Herein, we report the first one-step air-oxidized copper-mediated C_8-H thiolation protocol for the coupling of purine derivatives with thiophenols in the presence of base (**Scheme 1c**).

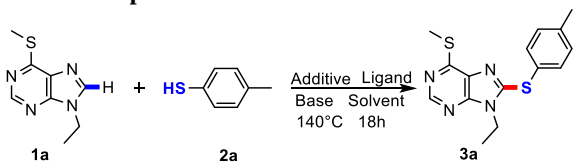
Scheme 1. Synthesis Routes of 8-Arylsulfanyl Purines



RESULTS AND DISCUSSION

In our preliminary experiments, the coupling of 6-methylthio-9-ethylpurine (**1a**) with *p*-toluenethiol (**2a**) was chosen as the model to determine the optimal reaction conditions, and the results are summarized in **Table 1**. Initially, in the absence of a metal salt or ligand, only trace amounts of desired products were obtained (entries 1 and 2). However, to our surprise, upon adding 2,2'-bipyridine ligand, the desired product **3a** was obtained in 58% yield (entry 3). Then, the nitrogen-based bidentate ligands were examined to explore the ligand effect on the C_8-S cross-coupling reaction, which revealed that 1,10-phenanthroline monohydrate was the best ligand (entries 4 and 5). Subsequently, several additives including CuBr, CuCl, $CuCl_2$, $Cu(OAc)_2$ and $CuSO_4$ were tested, and CuCl exhibited the highest reactivity (entries 6-10). Among them, the reason that Cu(II) promoted the reaction to proceed successfully may be that Cu(I) was oxidized to Cu(II) in the presence of air during the reaction. Next we investigated a series of bases including K_2CO_3, KO*t*Bu, Na_3PO_4, NaOAc and K_3PO_4, but the desired product **3a** was obtained in moderate to low yields (entries 11-15). And no product **3a** was detected when Cs_2CO_3 and NaOH were used as bases (entries 16 and 17). It is worth noting that the reaction did not occur in the absence of base (entry 18). In the subsequent screening of various solvents, we found that this C_8-S cross-coupling reaction was effective in a range of polar aprotic solvents such as DMF, NMP, DMSO, and DMA (entries 19-21). In sharp contrast, lower yields of **3a** were obtained when a polar protic solvents (EG, PEG-400, PEG-200, HFIP) or a nonpolar solvent (dioxane) were used as solvents (entries 22-26). In addition, studies on the temperature and the amount of CuCl or *p*-toluenethiol indicated that before the optimum conditions was reached, the product yield was significantly improved with an increased reaction temperature or an increased amount of CuCl or *p*-toluenethiol (entries 27-32). Remarkably, no product **3a** was obtained when the reaction was conducted under N_2 (entry 33), but a large amount of di-*p*-tolylsulfane was obtained. Finally, when the reaction was performed under a pure oxygen atmosphere, the yield was lowered to 67% (entry 34). The reduction in yield may be due to the facile formation of the di(4-methylphenyl)thioether from the oxidation of *p*-toluenethiol at high oxygen concentrations.

Table 1. Optimization of the Reaction Conditions [a]



1a 2a 3a

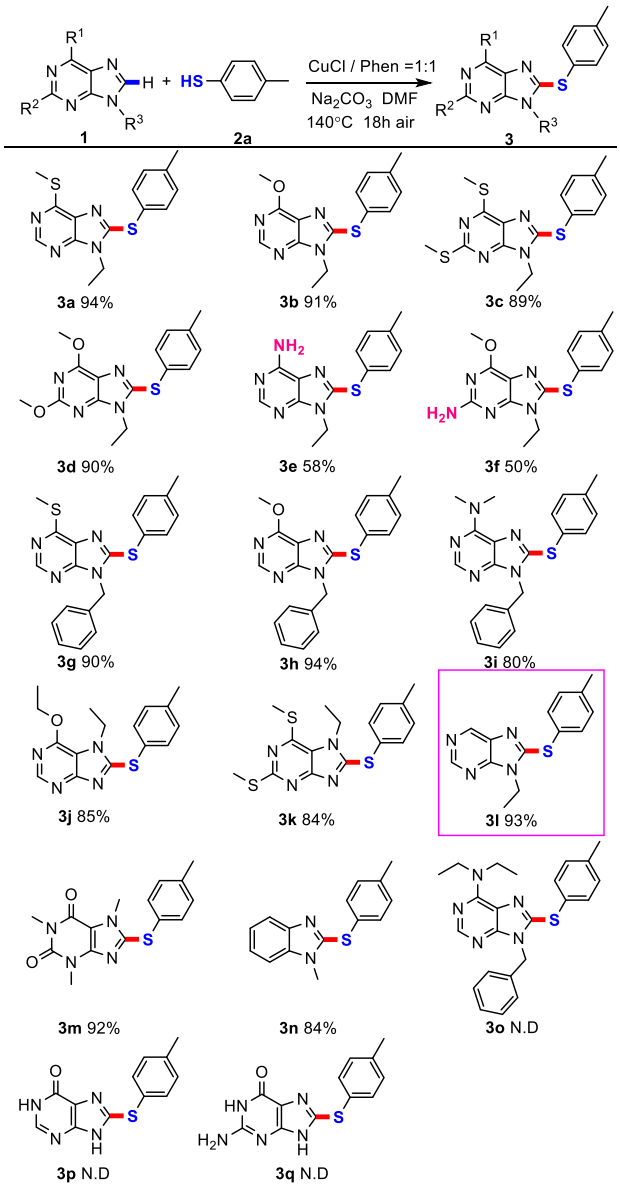
entry	additive	ligand	base	solvent	yield (%) [b]
1			Na_2CO_3	DMF	3
2	CuI		Na_2CO_3	DMF	5
3	CuI	Bpy	Na_2CO_3	DMF	58
4	CuI	Phen	Na_2CO_3	DMF	65
5	CuI	TMEDA	Na_2CO_3	DMF	44
6	CuBr	Phen	Na_2CO_3	DMF	88
7	**CuCl**	**Phen**	**Na_2CO_3**	**DMF**	**99(94)**
8	$CuCl_2$	Phen	Na_2CO_3	DMF	71
9	$Cu(OAc)_2$	Phen	Na_2CO_3	DMF	85
10	$CuSO_4$	Phen	Na_2CO_3	DMF	73
11	CuCl	Phen	K_2CO_3	DMF	62
12	CuCl	Phen	KO^{t}Bu	DMF	5
13	CuCl	Phen	Na_3PO_4	DMF	57
14	CuCl	Phen	NaOAc	DMF	49
15	CuCl	Phen	K_3PO_4	DMF	45

16	CuCl	Phen	Cs_2CO_3	DMF	N.D.
17	CuCl	Phen	NaOH	DMF	N.D.
18	CuCl	Phen		DMF	trace
19	CuCl	Phen	Na_2CO_3	NMP	56
20	CuCl	Phen	Na_2CO_3	DMSO	72
21	CuCl	Phen	Na_2CO_3	DMA	90
22	CuCl	Phen	Na_2CO_3	dioxane	5
23	CuCl	Phen	Na_2CO_3	EG	trace
24	CuCl	Phen	Na_2CO_3	PEG-400	trace
25	CuCl	Phen	Na_2CO_3	PEG-200	trace
26	CuCl	Phen	Na_2CO_3	HFIP	13
27[c]	CuCl	Phen	Na_2CO_3	DMF	87
28[d]	CuCl	Phen	Na_2CO_3	DMF	49
29[e]	CuCl	Phen	Na_2CO_3	DMF	68
30[f]	CuCl	Phen	Na_2CO_3	DMF	93
31[g]	CuCl	Phen	Na_2CO_3	DMF	78
32[h]	CuCl	Phen	Na_2CO_3	DMF	95
33[i]	CuCl	Phen	Na_2CO_3	DMF	trace
34[j]	CuCl	Phen	Na_2CO_3	DMF	67

[a]Reactions conditions: **1a** (0.20 mmol), **2a** (0.30 mmol), Additive (1.0 equiv), ligand (1.0 equiv), base (1.0 equiv), solvent (1.0 mL), under air at 140°C for 18 h. Phen: 1,10-Phenanthroline monohydrate. TMEDA: N,N,N',N'-Tetramethylethylenediamine. EG: Ethylene glycol. HFIP: 1,1,1,3,3,3-Hexafluoro-2-propanol N.D. = not determined. [b] Determined by GC using dodecane as the internal standard. [c] at 120°C. [d] at 100°C. [e] 0.5 equiv CuCl was used. [f] 1.5 equiv CuCl was used. [g] 1 equiv *p*-toluenethiol was used. [h] 2 equiv *p*-toluenethiol was used. [i] under N_2 atomosphere. [j] under O_2 atomosphere.

With the optimized reaction conditions in hand, the scope of this C_8-S cross-coupling was investigated by reacting *p*-toluenethiol (**2a**) with a series of purine derivatives. As shown in **Table 2**, many substrates with substituents at the C2, C6, N7 and N9 positions were applied to the reaction system to further synthesize a series of purine derivatives. Purine derivatives with strong electron-donating groups (−SMe, −OMe) at the C2 or C6 position formed the corresponding products with good yields (**3a-3d**, 89-94%). Gratifyingly, substrate **1e** and **1f** bearing the reactive amino group ($-NH_2$) at C2 or C6 position were an exception, and the desired products were obtained in rather modest yield (**3e-3f**, 50-58%). When the substitutent at the N9 position of the purines was the benzyl group, the products were obtained in high yields (**3g-3i**). Comparitively, the N9 alkyl-substituted substrates gave higher yields, whereas the N7 alkyl-substituted substrates gave slightly lower yields (**3b** *vs* **3j**, and **3c** *vs* **3k**). It is especially noteworthy that the coupling reaction of substrate **1l** with **2a** afforded only **3l** in 93% yield under the standard conditions. The structure of **3l** was confirmed by comparison with the ^1H and ^{13}C NMR spectra of 9-ethyl-6-(*p*-tolylthio)-9*H*-purine (**1pa**). That is to say, the C_8-S cross-coupling reaction occurred on the C8 position of the purine derivatives, not on C2, C6 or other functional groups, indicating excellent regioselectivity. Furthermore, caffeine **1m**, one of the plant alkaloids, provided product **3m** in 92% yield. Similarly, 1-methylbenzimidazole gave **3n** in 84% yield. However, no product was detected for **1o** because of the steric hinderance (**3i** *vs* **3o)**. Moreover, in the reactions of the hypoxanthine and guanine with *p*-toluenethiol under the optimized conditions, there were no corresponding products (**3p-3q**) detected.

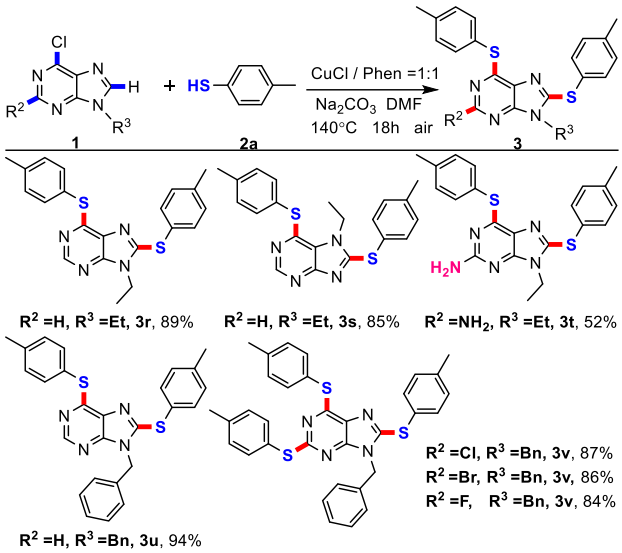
Table 2. Substrate Scope of Various Purines [a, k]



[a]Reaction conditions: **1** (0.20 mmol), **2a** (0.30 mmol), CuCl (1.0 equiv), Phen (1.0 equiv), Na_2CO_3(1.0 equiv), DMF (1.0 mL), under air at 140°C for 18 h. [k] Isolated yield.

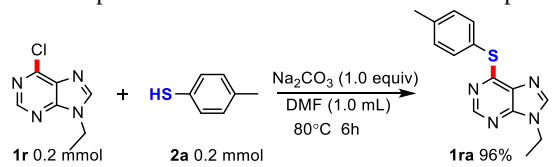
To further expand the scope of the coupling reaction, a number of 6-chloropurine derivatives with various substituents, including alkyl substituents at N7 or N9 position and halide or reactive amino substituents at C2, were examined under the further optimized reaction conditions, providing the disubstituted or trisubstituted purine derivatives in moderate to excellent isolated yields (**3r-3v**, 52-94%) (**Table 3**). The carbon-halogen bond cleavage reactions were subsequently studied. In the absence of CuCl and 1,10-phenanthroline monohydrate, 2-chloro-9-ethylpurine was reacted at 80 °C for 6 h with **2a** to form 6-(*p*-tolylthio)purine **1ra** in 96% yield (**Scheme 2**). Previous literature[15] on the reaction of 6-halogenated purine derivatives with thiophenols has shown that the reaction was carried out through a nucleophilic substitution mechanism.

Table 3. Substrate Scope of Various 6-Chloropurines [a, k]



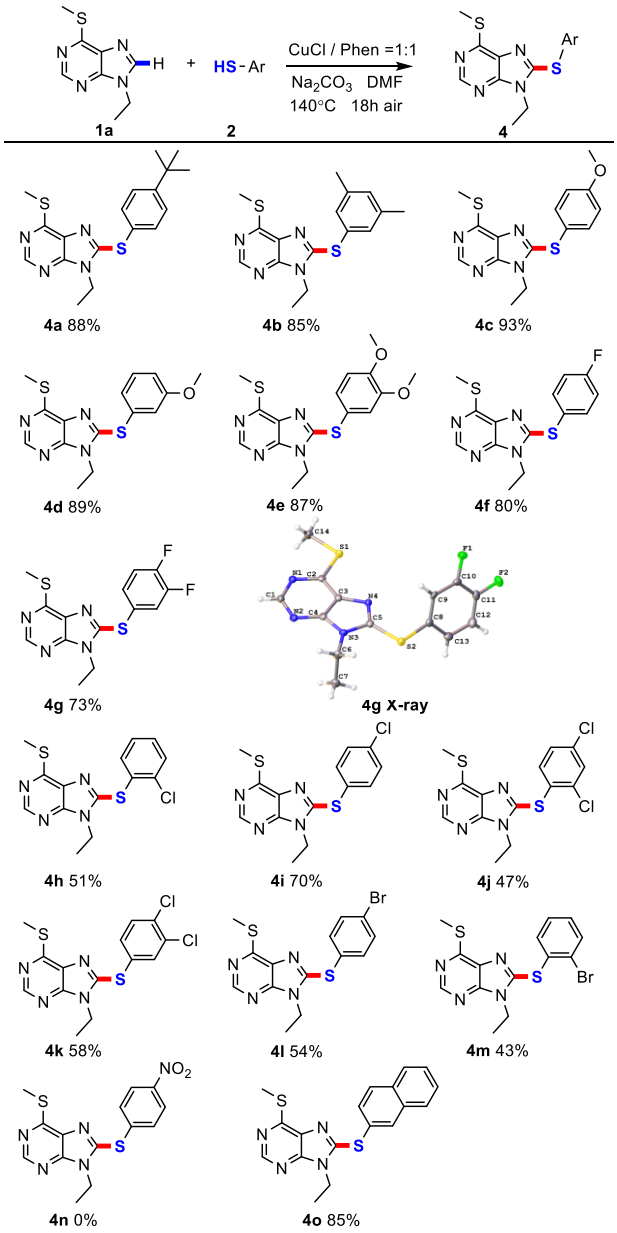
[a]Reaction conditions: **1** (0.20 mmol), **2a** (0.5 or 0.7mmol), CuCl (1.0 equiv), Phen (1.0 equiv), Na_2CO_3(2.0, 3.0 equiv), DMF (1.0 mL), under air at 140°C for 18 h. [k]Isolated yield.

Scheme 2. Nucleophilic Substitution Reaction of 6-Chloropurine with **2a**



Encouraged by the above results, the scope with respect to thiophenols was also investigated (**Table 4**). The coupling reactions proceeded smoothly and gave the products in low to good yields (**4a-4n**, 0%-93%). Thiophenols with *tert*-butyl, methyl and methoxy groups (electron withdrawing) provided better yields than those substituted with halides and nitro group (electron-withdrawing) (**4a-4e** *vs* **4f-4n**). In addition, the structure of **4g** was clearly certified by single-crystal X-ray diffraction analysis.[16] When the substituent was in the meta or ortho position of thiophenols, the yield of the products was lower compared with the substituents in the para position, and the yield was the lowest in the ortho position (**4c** *vs* **4d**, **4i** *vs* **4h and 4l** *vs* **4m**). Moreover, the coupling reaction was also successful with the substrate 2-naphthothiophenol (**4o**, 85%).

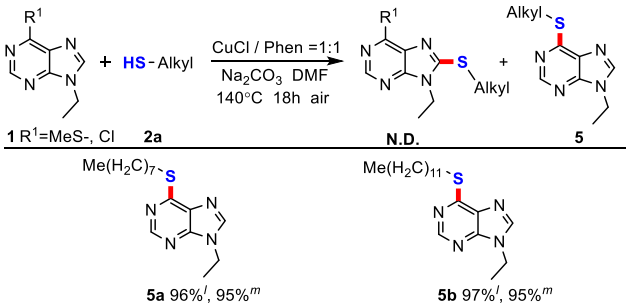
Table 4. Substrate Scope of Various Thiophenols [a, k]



[a]Reaction conditions: **1a** (0.20 mmol), **2** (0.30 mmol), CuCl (1.0 equiv), Phen (1.0 equiv), Na_2CO_3(1.0 equiv), DMF (1.0 mL), under air at 140°C for 18 h. [k]Isolated yield.

In addition to the thiophenols, the scope and generality of the approach for the direct thiolation of 6-methylthiopurine with alkylthiols under the optimized reaction conditions was examined (**Scheme 3**). The results showed that the reaction of the alkylthiols with **1a** did not occur at the C8 position, but the methylthio group at the C6 position was replaced by the alkylthio groups (**5a-5b**). The products were identical to those obtained by the reaction of 6-chloropurine with alkylthiols. Furthermore, in the absence of CuCl and ligand, this reaction was successful using the same conditions (80°C, 6 h) as the reactions of 6-chloropurines with thiophenols. The failure of the sulfenylation of the purines C_8-H bond with alkylthiols may be that alkylthiols have a lower nucleophilicity than thiophenols.

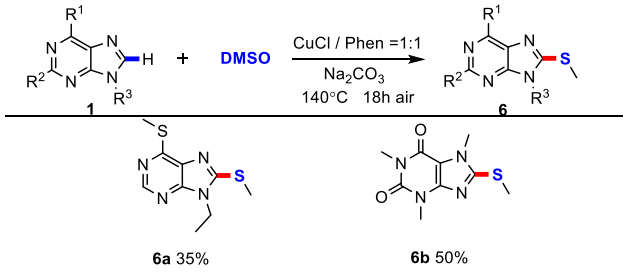
Scheme 3. Substrate Scope of Alkylthiols [a, k]



[a]Reaction conditions: **1a** (0.20 mmol), **2a** (0.30 mmol), CuCl (1.0 equiv), Phen (1.0 equiv), Na_2CO_3(1.0 equiv), DMF (1.0 mL), under air at 140°C for 18 h. [l] R^1=MeS-. [m] R^1=Cl. [k] Isolated yield.

In recent years, a Cu-mediated methylthiolation of heterocyclic compounds using DMSO as a simple, inexpensive and easy-to-handle methylthiolation reagent was reported.[17] Therefore, we explored the reaction of DMSO as the methylthiolation reagent and solvent with 6-methylthio-9-ethylpurine and obtained a low yield (35%) of **6a** under our reaction conditions (**Scheme 4**). Importantly, caffeine **1l** reacted successfully to give the products **6b** in moderate yield (50%).

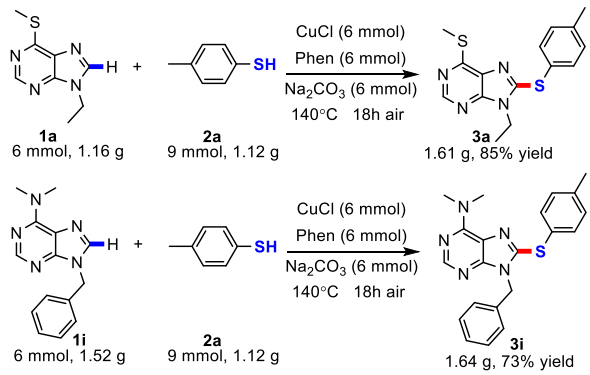
Scheme 4. Substrate Scope of Two Purines [a, k]



[a]Reaction conditions: **1a** (0.20 mmol), DMSO (1.0 mL), CuCl (1.0 equiv), Phen (1.0 equiv), Na_2CO_3(1.0 equiv), under air at 140°C for 18 h. [k] Isolated yield.

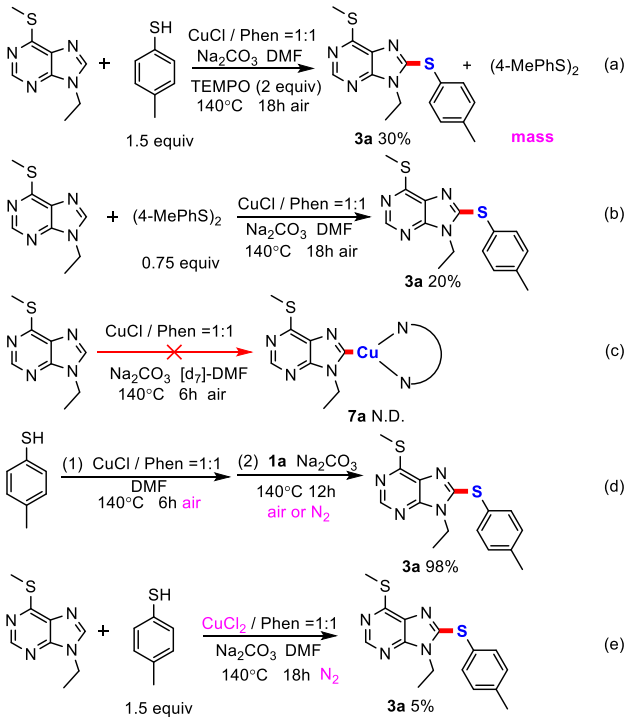
To demonstrate the practicality of the method for the synthesis of 8-sulfenylpurine derivatives in organic synthesis, we scaled up the reaction to the gram scale (**Scheme 5**). The target products 9-ethyl-6-(methylthio)-8-(*p*-tolylthio)-9*H*-purine (**3a**) and 9-benzyl-N,N-dimethyl-8-(*p*-tolylthio)-9*H*-purin-6-amine (**3i**) were successfully obtained in 85% yield and 73% yield, respectively. The results indicate that the method is applicable.

Scheme 5. Scaled-Up Version of Synthesis of 8-Sulfenylpurine Derivatives



To acquire insights into the mechanism of the reaction, control experiments were carried out (**Scheme 6**). Initially, the addition of a known radical inhibitor of TEMPO (2.0 equiv) under standard conditions resulted in a reduction in yield to 30% and the rapid production of large amounts of disulfide (Scheme 6a). Moreover, when *p*-tolyl disulfide was used instead of *p*-toluenethiol to react with 6-methylthio-9-ethylpurine, only 20% of the product was obtained (Scheme 6b), indicating that the radical mechanism is not possible and *p*-toluenethiol does not form *p*-tolyl disulfide to participate in the reaction. Subsequently, the reaction of 6-methylthio-9-ethylpurine **1a** with CuCl, Phen, and Na_2CO_3 dissolved in deuterated dimethylformamide upon heating at 140°C for 6 h based on in situ ^{1}H NMR analysis (**Figure 2**), showed no formation of the perceived C−H activated product **7a** (Scheme 6c). However, upfield shifts for the C_2-H and C_8-H protons resonances of **1a** were observed. Thus, based on the experimental result, a previous literature[18] and **3o** product were not obtained, we proposed that the coordination step of the Cu complex and the N7 of purine derivatives occurs during the reaction. For more insight, the reaction was carried out in the absence of **1a** and Na_2CO_3 under air for 6 hours, then **1a** was added and the reaction was again carried out under air or N_2 for 12 hours to give 98% of product (Scheme 6d). In addition, when CuCl was replaced by $CuCl_2$ to participate in the reaction under N_2, the product **3a** was obtained in 5% yield (Scheme 6e). The above results show the importance of the formation of Cu-SAr complex as a key intermediate, which be obtained more quickly from the reaction of the copper salt with thiophenol than from the corresponding disulfide under the optimized reaction conditions, and oxygen from the air plays a critical role in the formation phase of the Cu-SAr complex and the base participates in the elimination of hydrogen on the purine ring.

Scheme 6. Control Experiments



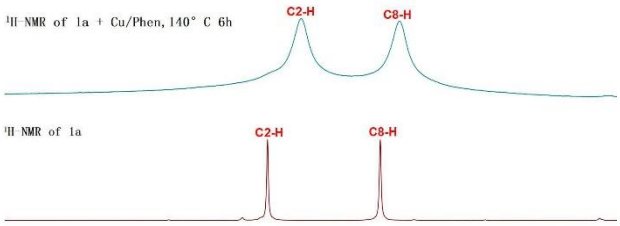
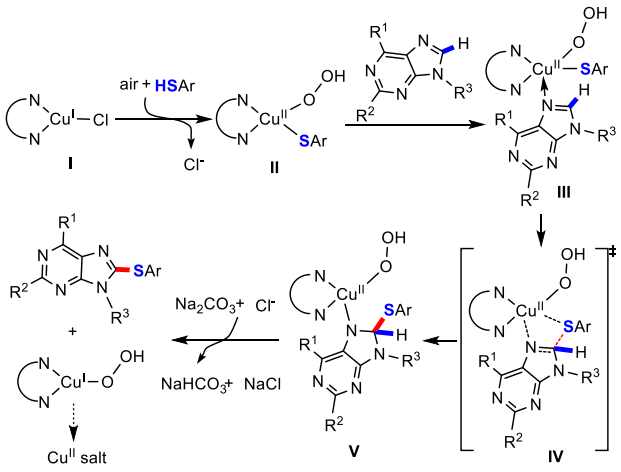


Figure 2. Interaction between **1a** and Cu/Phen

In accordance with the above evidence and some previous reports, a plausible mechanism is proposed as shown in **Scheme 7**. Starting from the Cu^{I}-Phen complex **I**, the Cu^{II}-superoxo intermediate[19] extracts the H-atom of the thiophenol in the presence of air, then complexes with ArS^{-} to form an ArS-Cu^{II}-OOH complex **II**.[20] Subsequently, the purine-coordinated intermediate **III** formed by the coordination of the ArS-Cu^{II}-OOH complex **II** with the N-atom on the five-membered ring of the purine skeleton undergoes migration of the phenylthiolate group to the electrophilic sp^2 C8 of the purine ring to create a HOO-Cu-mercaptopurine complex **V** via transition state **IV**. Finally, the complex **V** undergoes the base-assisted deprotonation and dissociation of the N-Cu coordination bond to give the desired product and Cu^{I}-hydropero complex. However, the Cu^{I}-hydropero complex is subsequently oxidized to the Cu^{II} species and can't be recycled to participate in the reaction.[21]

Scheme 7. Proposed Reaction Mechanism



CONCLUSIONS

In conclusion, we developed a general, highly regioselective and efficient protocol for the direct C-S cross-coupling between the purine heterocyclic C_8-H bond and aryl thiols along with a stoichiometric amount of copper(I) reagent and a N,N-type ligand. The high regioselectivity was confirmed by the coupling reaction of 9-ethylpurine, which contains no substituents at C2 or C6, producing **3l** as the only product. Also, the free amino group was tolerated in the reaction system (**3e**, **3f** and **3t**).

Mechanistic investigations revealed that oxygen played a critical role in the formation phase of the Cu-SAr complex, and the coordination of the Cu complex and the N7 of purine derivatives was formed during the reaction. Purine derivatives constructed by direct C-S cross-coupling have potential in medical applications. The synthetic utility of this reaction is currently being further studied.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in flame-dried sealed tubes with magnetic stirring under an air atmosphere unless otherwise noted. All reagents were purchased as analytical reagent grade and used without further purification, unless otherwise state. C2 or C6 substituted purines was synthesized from 6-chloropurine and 2,6-dichloropurine according to Huang's method.[22] C2 and C6 substituted purines were synthesized from 2-amido-6-chloropurine according to Hu's method.[23] N7 and N9 substituted purines were synthesized from N-9*H*-purines according to Kelley's method and Çelik's method.[24] Purifications of reaction products were carried out by flash chromatography using Qingdao Haiyang Chemical Co. Ltd silica gel (300-400 mesh). ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded using the Bruker DRX-400 and Bruker Ascend^{TM} 500 spectrometer using $CDCl_3$ or DMF-d_6 as solvent and TMS as an internal standard. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. Gas chromatograph mass spectra analyses were performed on SHIMADZU model GCMS-QP5000 spectrometer. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). IR spectra were recorded in KBr disks with a Bruker TENSOR 27 FTIR spectrophotometer. Melting points were determined with a Büchi Melting Point B-545 instrument. Crystal data were obtained by employing graphite monochromated Mo - Kα radiation (λ = 1.54178 Å) at 293(2) K and operating in the φ-ω scan mode. The structure was solved by direct methods SHELXS-97.

General procedure for the synthesis of starting purine derivatives 1

In a 100 mL single neck flash, the corresponding 6-chloropurine, 2,6-dichloropurine or 2-amido-6-chloropurine (10 mmol, 1.0 equiv) and 20% sodium methanethiol aqueous solution (50 mmol, 5 equiv or 100 mmol, 10 equiv) or sodium methoxide (12 mmol, 1.2 equiv or 24 mmol, 2.4 equiv) were dissolved in MT (20 mL). The mixture was stirred at 65 ℃ (oil bath) for 18 h. After completion of the reaction, the reaction mixture was cooled to room temperature, and then concentrated under reduced pressure. The solid was dissolved in water (20 mL). Then the PH value was adjusted to neutral with HCl. A large number of white solids was precipitated. The solid obtained by filtration and drying was dissolved in CH_3CN (25 mL), then K_2CO_3 (12 mmol, 1.2 equiv), and bromoethane (12 mmol, 1.2 equiv) or benzyl chloride (12 mmol, 1.2 equiv) were added. The resulting solution was stirred at 75 ℃ (oil bath) for 18 h. After completion of the reaction, the reaction mixture was cooled to room temperature, and then concentrated under reduced pressure. The solid was dissolved in ethyl acetate (30 mL), and then was filtered. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (petroleum ether : ethyl acetate = 4 : 1) to obtain the starting purine derivatives **1**.

General procedure for the synthesis of 8-sulfenylpurine derivatives

To a solution of N,N-dimethylformamide (DMF) (1.0 mL) charged with purine derivatives (**1**, 0.2 mmol, 1.0 equiv) and thiols (**2**, 0.3, 0.5 or 0.7 mmol, 1.5, 2.5 or 3.5 equiv) was added CuCl (19.8 mg, 0.2 mmol, 1.0 equiv), 1,10-Phenanthroline hydrate (36.0 mg, 0.2 mmol, 1.0 equiv), and Na_2CO_3 (0.2, 0.4 or 0.6 mmol, 1.0, 2.0 or 3.0 equiv). The reaction mixture was stirred at 140°C (oil bath) for 18 h. The mixture was cooled to room temperature and mixed with water (10.0 mL). The product was then extracted with ethylacetate (3 × 8 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The crude

product was then purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 10 : 1) to afford the desired product **3**, **4** and **5**.

General procedure for the synthesis of 8-methylthiopurine derivatives

To a solution of dimethyl sulfoxide (DMSO) (1.0 mL) charged with purine derivatives (**1**, 0.2 mmol, 1.0 equiv) was added CuCl (19.8 mg, 0.2 mmol, 1.0 equiv), 1,10-Phenanthroline hydrate (36.0 mg, 0.2 mmol, 1.0 equiv), and Na_2CO_3 (0.2 mmol, 1.0 equiv). The reaction mixture was stirred at 140 ºC (oil bath) for 18 h. The mixture was cooled to room temperature and mixed with water (10.0 mL). The product was then extracted with ethylacetate (3 × 8 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The crude product was then purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 4 : 1) to afford the desired product **6**.

General procedure for the synthesis of 9-ethyl-6-(*p*-tolylthio)-9*H*-purine

To a solution of N,N-dimethylformamide (DMF) (1.0 mL) charged with 6-chloropurine (**1r**, 0.2 mmol, 1.0 equiv) and *p*-toluenethiol (**2a**, 0.2mmol, 1.0 equiv) was added Na_2CO_3 (0.2 mmol, 1.0 equiv). The reaction mixture was stirred at 80°C (oil bath) for 6 h. The mixture was cooled to room temperature and mixed with water (10.0 mL). The product was then extracted with ethylacetate (3 × 8 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The crude product was then purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 5 : 1) to afford the desired product **1ra**.

9-ethyl-2,6-bis(methylthio)-9*H*-purine (1c): Yield: 51% (1.2 g) as yellow solid; mp = 69.4 - 69.9°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 4.23 (q, J = 7.3 Hz, 2H), 2.70 (s, 3H), 2.63 (s, 3H), 1.51 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 164.8, 160.9, 149.1, 140.9, 128.7, 38.8, 15.3, 14.6, 11.7 ppm; ν_{max}(KBr)/cm^{-1} 3043, 2973, 1564, 1448, 1340, 1212, 1143, 945, 873, 782; HR-MS (ESI) calcd for $C_9H_{13}N_4S_2$, $[M + H]^+$: 241.0576, found: 241.0579.

9-ethyl-2,6-dimethoxy-9*H*-purine (1d): Yield: 67% (1.4 g) as a white solid; mp = 118.6 - 119.2°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 4.22 (q, J = 7.3 Hz, 2H), 4.17 (s, 3H), 4.05 (s, 3H), 1.53 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.9, 161.6, 153.4, 140.2, 117.3, 54.9, 54.1, 38.7, 15.2 ppm; ν_{max}(KBr)/cm^{-1} 3095, 2960, 1736, 1600, 1524, 1476, 1358, 1073, 740, 648; HR-MS (ESI) calcd for $C_9H_{13}N_4O_2$, $[M + H]^+$: 209.1033, found: 209.1035.

6-ethoxy-7-ethyl-7*H*-purine (1j): Yield: 26% (0.5 g) as a yellow solid; mp = 119.2 - 119.7°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.96 (s, 1H), 4.55 (q, J = 6.9 Hz, 2H), 4.31 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.1 Hz, 3H), 1.41 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.8, 156.8, 152.0, 112.7, 62.8, 42.7, 16.8, 14.4 ppm; ν_{max}(KBr)/cm^{-1} 3081, 2976, 1616, 1557, 1482, 1380, 1216, 1133, 1012, 892, 789; HR-MS (ESI) calcd for $C_9H_{13}N_4O$, $[M + H]^+$: 193.1084, found: 193.1087.

7-ethyl-2,6-bis(methylthio)-7*H*-purine (1k): Yield: 34% (0.8 g) as a yellow solid; mp = 105.0 -105.6°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 4.40 (q, J = 6.6 Hz, 2H), 2.71 (s, 3H), 2.64 (s, 3H), 1.54 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 165.0, 159.5, 153.6, 145.7, 120.2, 42.8, 17.4, 14.5, 12.1 ppm; ν_{max}(KBr)/cm^{-1} 3086, 2926, 1527, 1481, 1370, 1296, 1106, 999, 868, 787; HR-MS (ESI) calcd for $C_9H_{12}N_4NaS_2$, $[M + Na]^+$: 263.0396, found: 263.0391.

9-ethyl-6-(methylthio)-8-(*p*-tolylthio)-9*H*-purine (3a): Yield: 94% (59.4 mg) as a pale yellow solid; mp = 102.1 - 103.4°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.59 (s, 3H), 2.25 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.8, 151.5, 149.9, 149.8, 139.0, 132.3, 131.8, 130.3, 125.9, 38.8, 21.2, 14.7, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3021, 2973, 2922, 1645, 1564, 1491, 1453, 1427, 1317, 1250, 1233, 1172, 1152, 952, 865, 806, 707, 575; HR-MS (ESI) calcd for $C_{15}H_{17}N_4S_2$, $[M + H]^+$: 317.0889, found: 317.0886.

9-ethyl-6-methoxy-8-(*p*-tolylthio)-9*H*-purine (3b): Yield: 91% (54.6 mg) as a white solid; mp = 122.8 - 124.3°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.41 (d, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 7.7 Hz, 2H), 4.29 (q, *J* = 7.2 Hz, 2H), 4.12 (s, 3H), 2.31 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.8, 153.3, 151.6, 149.2, 139.0, 132.5, 130.3, 126.1, 121.8, 54.1, 38.9, 21.2, 14.8 ppm; ν_{max}(KBr)/cm^{-1} 3055, 2988, 2936, 2857, 1593, 1491, 1469, 1351, 1309, 1209, 1064, 958, 889, 810, 721, 664; HR-MS (ESI) calcd for $C_{15}H_{17}N_4OS$, $[M + H]^+$: 301.1118, found: 301.1123.

9-ethyl-2,6-bis(methylthio)-8-(*p*-tolylthio)-9*H*-purine (3c): Yield: 89% (64.4 mg) as a pale yellow solid; mp = 107.8 - 109.1°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.6 Hz, 2H), 6.99 (d, *J* = 7.7 Hz, 2H), 4.06 (q, *J* = 6.8 Hz, 2H), 2.52 (s, 3H), 2.47 (s, 3H), 2.17 (s, 3H), 1.14 (t, *J* = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.7, 159.7, 150.6, 147.6, 138.6, 131.6, 130.3, 129.0, 126.8, 38.7, 21.2, 14.7, 11.8 ppm; ν_{max}(KBr)/cm^{-1} 3055, 2979, 2926, 1642, 1558, 1492, 1432, 1400, 1322, 1197, 1144, 958, 880, 805, 674, 581; HR-MS (ESI) calcd for $C_{16}H_{19}N_4S_3$, $[M + H]^+$: 363.0766, found: 363.0769.

9-ethyl-2,6-dimethoxy-8-(*p*-tolylthio)-9*H*-purine (3d): Yield: 90% (59.4 mg) as a pale yellow solid; mp = 109.2 - 110.5°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 7.5 Hz, 2H), 7.00 (d, *J* = 7.5 Hz, 2H), 4.11 (q, *J* = 6.5 Hz, 2H), 4.03 (s, 3H), 3.91 (s, 3H), 2.19 (s, 3H), 1.18 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.5, 161.0, 154.6, 146.0, 138.3, 131.4, 130.2, 127.5, 117.6, 55.0, 54.2, 38.7, 21.0, 14.7 ppm; ν_{max}(KBr)/cm^{-1} 3017, 2935, 1588, 1494, 1454, 1391, 1353, 1306, 1242, 1220, 1089, 971, 952, 804, 789, 663; HR-MS (ESI) calcd for $C_{16}H_{19}N_4O_2S$, $[M + H]^+$: 331.1223, found: 331.1221.

9-ethyl-8-(*p*-tolylthio)-9*H*-purin-6-amine (3e): Yield: 58% (33.1 mg) as a pale yellow solid; mp = 160.3 - 161.8°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.40 (s, 2H), 4.17 (q, *J* = 7.2 Hz, 2H), 2.21 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.9, 152.9, 151.2, 145.9, 138.6, 131.4, 130.3, 127.2, 120.1, 38.7, 21.1, 14.9 ppm; ν_{max}(KBr)/cm^{-1} 3338, 3162, 2967, 2929, 2359, 1658, 1597, 1568, 1489, 1465, 1309, 1205, 1016, 959, 798, 603, 569, 503; HR-MS (ESI) calcd for $C_{14}H_{16}N_5S$, $[M + H]^+$: 286.1121, found: 286.1123.

9-ethyl-6-methoxy-8-(*p*-tolylthio)-9*H*-purin-2-amine (3f): Yield: 50% (31.5 mg) as a yellow solid; mp = 111.7 - 112.2°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 5.00 (s, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 4.05 (s, 3H), 2.30 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.9, 159.3, 154.9, 143.7, 138.0, 130.8, 130.2, 128.4, 116.2, 53.9, 38.5, 21.1, 14.8 ppm; ν_{max}(KBr)/cm^{-1} 3476, 3315, 3189, 2926, 2854, 1629, 1578, 1492, 1480, 1419, 1319, 1251, 1068, 955, 808, 790, 500; HR-MS (ESI) calcd for $C_{15}H_{17}N_5NaOS$, $[M + Na]^+$: 338.1046, found: 338.1049.

9-benzyl-6-(methylthio)-8-(*p*-tolylthio)-9*H*-purine (3g): Yield: 90% (68.1 mg) as a white solid; mp = 106.5 - 107.9°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.23 - 7.15 (m, 5H), 7.02 (d, J = 8.0 Hz, 2H), 5.34 (s, 2H), 2.59 (s, 3H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.6, 151.6, 150.8, 150.2, 139.1, 135.5, 132.8, 131.7, 130.2, 128.7, 128.0, 127.7, 125.4, 46.7, 21.2, 12.0 ppm; ν_{max}(KBr)/cm^{-1} 3048, 2919, 1572, 1493, 1451, 1428, 1320, 1256, 1186, 1147, 991, 918, 866, 805, 693, 612, 549, 504; HR-MS (ESI) calcd for $C_{20}H_{19}N_4S_2$, $[M + H]^+$: 379.1046, found: 379.1049.

9-benzyl-6-methoxy-8-(*p*-tolylthio)-9*H*-purine (3h): Yield: 94% (68.1 mg) as a pale yellow solid; mp = 114.6 - 116.0°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.13 (s, 5H), 6.97 (d, J = 7.9 Hz, 2H), 5.31 (s, 2H), 4.00 (s, 3H), 2.17 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.7, 153.8, 151.8, 150.1, 139.1, 135.5, 132.8, 130.3, 128.7, 128.0, 127.7, 125.7, 121.7, 54.2, 46.9, 21.2 ppm; ν_{max}(KBr)/cm^{-1} 3032, 2933, 1574, 1492, 1419, 1402, 1304, 1240, 1180, 1068, 981, 902, 808, 728, 695, 571, 501; HR-MS (ESI) calcd for $C_{20}H_{18}N_4NaOS$, $[M + Na]^+$: 385.0586, found: 385.0585.

9-benzyl-N,N-dimethyl-8-(*p*-tolylthio)-9*H*-purin-6-amine (3i): Yield: 80% (59.4 mg) as a yellow solid; mp = 107.9 - 109.5°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.19 - 7.09 (m, 7H), 6.96 (d, J = 8.0 Hz, 2H), 5.29 (s, 2H), 3.43 (s, 6H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 154.1, 152.7, 152.3, 143.2, 137.9, 136.1, 130.7, 130.0, 128.6, 128.1, 127.6, 127.5, 120.8, 46.5, 38.6, 21.1 ppm; ν_{max}(KBr)/cm^{-1} 3027, 2923, 2853, 1589, 1560, 1492, 1454,1428, 1376, 1325, 1295, 1170, 1052, 805, 731, 697; HR-MS (ESI) calcd for $C_{21}H_{22}N_5S$, $[M + H]^+$: 376.1590, found: 376.1586.

6-ethoxy-7-ethyl-8-(*p*-tolylthio)-7*H*-purine (3j): Yield: 85% (53.4 mg) as a yellow solid; mp = 82.2 - 83.5°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.41 (d, J = 8.1 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 4.51 (q, J = 7.1 Hz, 2H), 4.30 (q, J = 7.2 Hz, 2H), 2.25 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.0, 155.4, 154.2, 151.7, 139.4, 133.5, 130.3, 124.9, 114.5, 62.7, 41.9, 21.2, 16.0, 14.5 ppm; ν_{max}(KBr)/cm^{-1} 3036, 2924, 1613, 1551, 1491, 1465, 1398, 1260, 1180, 1139, 1122, 1019, 901, 810, 663, 502; HR-MS (ESI) calcd for $C_{16}H_{19}N_4OS$, $[M + H]^+$: 315.1274, found: 315.1275.

7-ethyl-2,6-bis(methylthio)-8-(*p*-tolylthio)-7*H*-purine (3k): Yield: 84% (60.8 mg) as a yellow solid; mp = 123.4 - 124.9°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 8.1 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 2.56 (s, 3H), 2.46 (s, 3H), 2.24 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 164.6, 158.8, 156.2, 151.2, 139.8, 134.3, 130.4, 123.9, 122.2, 41.8, 21.3, 16.5, 14.4, 12.1 ppm; ν_{max}(KBr)/cm^{-1} 2980, 2932, 1563, 1529, 1465, 1374, 1284, 1206, 1094, 1014, 876, 833, 782, 503; HR-MS (ESI) calcd for $C_{16}H_{19}N_4S_3$, $[M + H]^+$: 363.0766, found: 363.0764.

9-ethyl-8-(*p*-tolylthio)-9*H*-purine (3l): Yield: 93% (50.2 mg) as a pale yellow solid; mp = 91.8 - 93.3°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.85 (s, 1H), 7.53 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 4.32 (q, J = 7.2 Hz, 2H), 2.37 (s, 3H), 1.45 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 155.1, 152.9, 151.5, 145.7, 140.1, 134.3, 130.5, 123.3, 38.2, 21.3, 14.6 ppm; ν_{max}(KBr)/cm^{-1} 3046, 2951, 1648, 1580, 1474, 1428, 1339, 1299, 1240, 1115, 956, 914, 808, 790, 679, 618; HR-MS (ESI) calcd for $C_{14}H_{15}N_4S$, $[M + H]^+$: 271.1012, found: 271.1012.

1,3,7-trimethyl-8-(*p*-tolylthio)-3,7-dihydro-1*H*-purine-2,6-dione (3m): Yield: 92% (58.2 mg) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 8.1 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 3.79 (s, 3H), 3.39 (s, 3H), 3.23 (s, 3H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.7, 151.2, 147.9, 147.1, 138.6, 131.3, 130.2, 126.7, 109.2, 33.0, 29.7, 27.8, 21.1 ppm; HR-MS (ESI) calcd for $C_{15}H_{17}N_4O_2S$, $[M + H]^+$: 317.1067, found: 317.1065.

1-methyl-2-(*p*-tolylthio)-1*H*-benzo[d]imidazole (3n): Yield: 84% (42.7 mg) as a pale yellow solid; mp = 89.4 - 90.7°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 - 7.71 (m, 1H), 7.27 (d, J = 8.2 Hz, 2H), 7.25 - 7.16 (m, 3H), 7.05 (d, J = 8.1 Hz, 2H), 3.61 (s, 3H), 2.25 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 148.5, 143.2, 138.1, 136.6, 131.1, 130.3, 128.1, 123.1, 122.3, 119.7, 109.4, 30.7, 21.2 ppm; ν_{max}(KBr)/cm^{-1} 3049, 2924, 1596, 1492, 1446, 1417, 1362, 1279, 1183, 1087, 806, 744, 565; HR-MS (ESI) calcd for $C_{15}H_{15}N_2S$, $[M + H]^+$: 255.0950, found: 255.0951.

9-ethyl-6,8-bis(*p*-tolylthio)-9*H*-purine (3r): Yield: 89% (69.8 mg) as a white solid; mp = 130.8 - 132.4°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.43 (d, J = 7.4 Hz, 2H), 7.38 (d, J = 7.6 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 7.6 Hz, 2H), 4.20 (q, J = 6.8 Hz, 2H), 2.32 (s, 3H), 2.29 (s, 3H), 1.26 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.1, 151.8, 150.7, 150.3, 139.6, 139.2, 135.5, 132.6, 131.1, 130.4, 130.1, 125.6, 123.9, 38.8, 21.4, 21.3, 14.7 ppm; ν_{max}(KBr)/cm^{-1} 3045, 2982, 2933, 2914, 1594, 1559, 1490, 1434, 1319, 1251, 1222, 1146, 1016, 949, 859, 808, 576; HR-MS (ESI) calcd for $C_{21}H_{21}N_4S_2$, $[M + H]^+$: 393.1202, found: 393.1202.

7-ethyl-6,8-bis(*p*-tolylthio)-7*H*-purine (3s): Yield: 85% (66.7 mg) as a pale yellow solid; mp = 152.3 - 153.5°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.47 (d, J = 7.9 Hz, 2H), 7.38 (d, J = 7.9 Hz, 2H), 7.15 (dd, J = 11.3, 8.1 Hz, 4H), 4.49 (q, J = 7.0 Hz, 2H), 2.31 (s, 3H), 2.28 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.7, 158.0, 152.4, 150.2, 140.1, 139.9, 135.3, 134.4, 130.4, 130.3, 124.8, 123.6, 123.5, 42.0, 21.4, 21.3, 16.6 ppm; ν_{max}(KBr)/cm^{-1} 3038, 2967, 2917, 1594, 1560, 1541, 1490, 1467, 1413, 1377, 1335, 1279, 1223, 1179, 1091, 1016, 980, 805, 762; HR-MS (ESI) calcd for $C_{21}H_{20}N_4NaS_2$, $[M + Na]^+$: 415.1022, found: 415.1025.

9-ethyl-6,8-bis(*p*-tolylthio)-9*H*-purin-2-amine (3t): Yield: 52% (42.3 mg) as a pale yellow solid; mp = 94.5 - 95.8°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 4.78 (s, 2H), 4.00 (q, J = 7.2 Hz, 2H), 2.28 (s, 3H), 2.24 (s, 3H), 1.12 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.4, 159.1, 152.2, 145.1, 139.1, 138.1, 135.5, 130.8, 130.2, 129.7, 128.1, 125.7, 124.3, 38.4, 21.4, 21.1, 14.7 ppm; ν_{max}(KBr)/cm^{-1} 3336, 3195, 2978, 2918, 1650, 1581, 1555, 1491, 1411, 1288, 1224, 1151, 1017, 914, 806, 504; HR-MS (ESI) calcd for $C_{21}H_{22}N_5S_2$, $[M + H]^+$: 408.1311, found: 408.1315.

9-benzyl-6,8-bis(*p*-tolylthio)-9*H*-purine (3u): Yield: 94% (85.4 mg) as a pale yellow solid; mp = 149.9 - 151.2°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.41 (d, J = 7.4 Hz, 2H), 7.30 (d, J = 7.5 Hz, 2H), 7.19 - 7.11 (m, 7H), 7.04 (d, J = 7.6 Hz, 2H), 5.31 (s, 2H), 2.29 (s, 3H), 2.24 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.1, 152.0, 151.5, 150.8, 139.6, 139.2, 135.6, 135.3, 132.8, 131.1, 130.3, 130.1, 128.8, 128.1, 127.7, 125.3, 123.9, 46.8, 21.5, 21.3 ppm; ν_{max}(KBr)/cm^{-1} 3038, 2922, 1594, 1556, 1492, 1449,

1430, 1317, 1255, 1189, 1147, 1006, 932, 862, 805, 731, 519; HR-MS (ESI) calcd for $C_{26}H_{23}N_4S_2$, $[M + H]^+$: 455.1359, found: 455.1361.

9-benzyl-2,6,8-tris(*p*-tolylthio)-9*H*-purine (3v): Yield: 87%, 86% and 84% (100.3 mg, 99.1 mg and 96.8 mg) as a pale yellow solid; mp = 131.8 - 133.2°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 - 7.18 (m, 6H), 7.12 - 7.08 (m, 3H), 7.04 (dd, J = 6.6, 3.1 Hz, 2H), 7.00 - 6.93 (m, 6H), 5.05 (s, 2H), 2.25 (s, 6H), 2.19 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.1, 159.4, 151.5, 149.3, 138.9, 138.9, 138.6, 135.4, 135.2, 135.1, 132.1, 130.3, 129.7, 129.6, 128.8, 128.6, 128.4, 128.1, 126.9, 126.2, 123.8, 46.9, 21.5, 21.5, 21.3 ppm; ν_{max}(KBr)/cm^{-1} 3024, 2917, 1593, 1565, 1540, 1491, 1449, 1326, 1290, 1251, 1163, 1136, 1015, 929, 874, 801, 728, 695; HR-MS (ESI) calcd for $C_{33}H_{29}N_4S_3$, $[M + H]^+$: 577.1549, found: 577.1543.

8-((4-(*tert*-butyl)phenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4a): Yield: 88% (63.0 mg) as a pale yellow solide; mp = 103.2 - 104.7°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.37 (t, J = 2.0 Hz, 1H), 7.35 (t, J = 2.0 Hz, 1H), 7.26 (t, J = 2.0 Hz, 1H), 7.25 (t, J = 1.9 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 2.56 (s, 3H), 1.20 (t, J = 7.2 Hz, 3H), 1.17 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.8, 152.0, 151.4, 149.6, 131.9, 131.7, 126.6, 126.1, 119.3, 38.8, 34.6, 31.2, 14.7, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3050, 2962, 1553, 1488, 1453, 1368, 1310, 1263, 1220, 1169, 1148, 1111, 1012, 952, 863, 820, 679, 575, 549; HR-MS (ESI) calcd for $C_{18}H_{23}N_4S_2$, $[M + H]^+$: 359.1359, found: 359.1353.

8-((3,5-dimethylphenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4b): Yield: 85% (56.1 mg) as a pale yellow solid; mp = 108.6 - 110.0°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.01 (s, 2H), 6.82 (s, 1H), 4.16 (q, J = 7.2 Hz, 2H), 2.59 (s, 3H), 2.16 (s, 6H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.1, 151.5, 149.7, 149.2, 139.2, 131.8, 130.4, 129.4, 129.3, 38.8, 21.1, 14.7, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3041, 2928, 1601, 1567, 1453, 1432, 1321, 1263, 1224, 1151, 952, 851, 797, 686, 576; HR-MS (ESI) calcd for $C_{16}H_{19}N_4S_2$, $[M + H]^+$: 331.1046, found: 331.1047.

9-ethyl-8-((4-methoxyphenyl)thio)-6-(methylthio)-9*H*-purine (4c): Yield: 93% (61.8 mg) as a white solid; mp = 152.4 - 153.9°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.52 (d, J = 7.9 Hz, 2H), 6.90 (d, J = 7.9 Hz, 2H), 4.27 (m, J = 7.0 Hz, 2H), 3.80 (s, 3H), 2.67 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 159.3, 151.2, 150.9, 149.8, 135.0, 131.8, 119.0, 115.1, 55.4, 38.6, 14.7, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3053, 2964, 2926, 1591, 1557, 1494, 1454, 1319, 1244, 1174, 1022, 951, 863, 832, 576; HR-MS (ESI) calcd for $C_{15}H_{17}N_4OS_2$, $[M + H]^+$: 333.0838, found: 333.0838.

9-ethyl-8-((3-methoxyphenyl)thio)-6-(methylthio)-9*H*-purine (4d): Yield: 89% (59.1 mg) as a white solid; mp = 105.3 - 106.9°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.23 (t, J = 8.0 Hz, 1H), 7.11 (s, 1H), 7.04 (d, J = 7.7 Hz, 1H), 6.84 (dd, J = 8.3, 2.0 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 3.77 (s, 3H), 2.69 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.2, 160.1, 151.6, 149.6, 148.6, 131.7, 131.2, 130.2, 123.4, 116.6, 114.4, 55.4, 38.9, 14.8, 11.8 ppm; ν_{max}(KBr)/cm^{-1} 3054, 2971, 2930, 1590, 1567, 1476, 1456, 1422, 1324, 1237, 1152, 1033, 950, 864, 790, 679, 549; HR-MS (ESI) calcd for $C_{15}H_{17}N_4OS_2$, $[M + H]^+$: 333.0838, found: 333.0841.

8-((3,4-dimethoxyphenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4e): Yield: 87% (63.0 mg) as a pale yellow solid; mp = 130.2 - 131.7°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.12 (s, 1H), 7.06 (d, J = 8.1 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 4.19(q, J = 7.2 Hz, 2H), 3.78 (s, 6H), 2.58 (s, 3H), 1.26 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.4, 151.3, 150.5, 150.1, 149.7, 149.5, 131.7, 126.1, 119.3, 116.3, 111.7, 56.1, 56.0, 38.6, 14.7, 11.8 ppm; ν_{max}(KBr)/cm^{-1} 3063, 2932, 2839, 1569, 1504, 1462, 1401, 1317, 1235, 1017, 953, 863, 802, 764, 616, 589; HR-MS (ESI) calcd for $C_{16}H_{19}N_4O_2S_2$, $[M + H]^+$: 363.0944, found: 363.0941.

9-ethyl-8-((4-fluorophenyl)thio)-6-(methylthio)-9*H*-purine (4f): Yield: 80% (51.3 mg) as a pale yellow solid; mp = 115.8 - 117.4°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.47 (dd, J = 8.6, 5.2 Hz, 2H), 6.98 (t, J = 8.6 Hz, 2H), 4.19 (q, J = 7.2 Hz, 2H), 2.57 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.4, 161.9, 159.7, 151.4, 149.8, 134.9, 131.8, 124.2, 116.8, 38.7, 14.8, 11.9 ppm; ^{19}F NMR (471 MHz, $CDCl_3$) δ -111.42 ppm; ν_{max}(KBr)/cm^{-1} 3063, 2972, 2922, 1586, 1568, 1489, 1434, 1319, 1223, 1168, 1087, 950, 864, 834, 679, 552; HR-MS (ESI) calcd for $C_{14}H_{14}FN_4S_2$, $[M + H]^+$: 321.0638, found: 321.0636.

8-((3,4-difluorophenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4g): Yield: 73% (49.4 mg) as a pale yellow solid; mp = 116.8 - 118.3°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.46 (ddd, J = 9.8, 7.3, 2.2 Hz, 1H), 7.32 (ddd, J = 9.0, 3.9, 1.9 Hz, 1H), 7.24 - 7.14 (m, 1H), 4.31 (q, J = 7.2 Hz, 2H), 2.69 (s, 3H), 1.39 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.1, 151.6, 149.6, 148.6, 131.7, 128.9, 125.3, 121.7, 121.6, 118.3, 118.2, 38.8, 14.9, 11.9 ppm; ^{19}F NMR (471 MHz, $CDCl_3$) δ -134.80, -135.83 ppm; ν_{max}(KBr)/cm^{-1} 3056, 2923, 2856, 1603, 1568, 1504, 1461, 1370, 1318, 1273, 1200, 1150, 1117, 952, 902, 864, 773, 586; HR-MS (ESI) calcd for $C_{14}H_{13}F_2N_4S_2$, $[M + H]^+$: 339.0544, found: 339.0547.

8-((2-chlorophenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4h): Yield: 51% (34.3 mg) as a pale yellow solid; mp = 66.8 - 68.3°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.47 - 7.43 (m, 1H), 7.34 - 7.31 (m, 1H), 7.28 - 7.24 (m, 1H), 7.23 - 7.17 (m, 1H), 4.32 (q, J = 7.2 Hz, 2H), 2.70 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.7, 151.8, 149.6, 147.4, 134.7, 132.4, 132.0, 130.4, 130.2, 129.4, 127.7, 39.1, 14.9, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3080, 2980, 2928, 1564, 1447, 1425, 1319, 1221, 1152, 1035, 950, 865, 790, 740, 572; HR-MS (ESI) calcd for $C_{14}H_{14}ClN_4S_2$, $[M + H]^+$: 337.0343, found: 337.0342.

8-((4-chlorophenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4i): Yield: 70% (47.0 mg) as a pale yellow solid; mp = 113.2 - 114.7°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.36 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 8.5 Hz, 2H), 4.16 (q, J = 7.2 Hz, 2H), 2.55 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.9, 151.5, 149.6, 148.7, 135.0, 133.3, 131.7, 129.6, 128.0, 38.7, 14.8, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3068, 2924, 1565, 1475, 1426, 1317, 1250, 1222, 1173, 1151, 1090, 1012, 952, 865, 820, 578; HR-MS (ESI) calcd for $C_{14}H_{14}ClN_4S_2$, $[M +H]^+$: 337.0343, found: 337.0345.

8-((2,4-dichlorophenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4j): Yield: 47% (34.8 mg) as a pale yellow solid; mp = 139.3 - 140.9°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.48 (d, J = 2.0 Hz, 1H), 7.37 (d, J = 8.5 Hz, 1H), 7.21 (dd, J = 8.5, 2.0 Hz, 1H), 4.33 (q, J = 7.3 Hz, 2H), 2.69 (s, 3H), 1.40 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.6, 151.8, 149.6, 147.1, 135.8, 135.1, 133.6, 131.9, 130.1, 128.5, 128.1, 39.0, 15.0, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3056, 2973, 2921, 1567, 1453, 1427, 1370, 1318, 1250, 1225, 1151, 1096, 1032, 952, 865, 813, 551; HR-MS (ESI) calcd for $C_{14}H_{13}Cl_2N_4S_2$, $[M + H]^+$: 370.9953, found: 370.9958.

8-((3,4-dichlorophenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4k): Yield: 58% (42.9 mg) as a pale yellow solid; mp = 96.2 - 97.9°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.66 (d, J = 1.8 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.37 (dd, J = 8.4, 2.0 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 2.70 (s, 3H), 1.39 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.5, 151.8, 149.6, 147.8, 133.5, 133.3, 133.1, 131.8, 131.2, 130.9, 129.6, 38.9, 15.0, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3054, 2925, 2863, 1565, 1457, 1426, 1366, 1319, 1224, 1151, 1032, 952, 864, 810, 702, 549; HR-MS (ESI) calcd for $[M + H]^+$: $C_{14}H_{13}Cl_2N_4S_2$: 370.9953, found: 370.9951.

8-((4-bromophenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4l): Yield: 54% (41.0 mg) as a yellow solid; mp = 58.8 - 60.3°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.37 - 7.34 (m, 1H), 7.32 - 7.26 (m, 1H), 7.20 (d, J = 8.1 Hz, 1H), 7.16 - 7.09 (m, 1H), 4.17 (q, J = 7.0 Hz, 2H), 2.56 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.0, 151.6, 149.6, 148.7, 135.0, 133.3, 132.5, 130.7, 129.7, 38.8, 14.9, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3054, 2988, 2926, 1565, 1473, 1434, 1321, 1251, 1223, 1152, 1089, 1010, 952, 864, 815, 502; HR-MS (ESI) calcd for $C_{14}H_{14}BrN_4S_2$, $[M + H]^+$: 380.9838, found: 380.9841.

8-((2-bromophenyl)thio)-9-ethyl-6-(methylthio)-9*H*-purine (4m): Yield: 43% (32.7 mg) as a yellow solid; mp = 193.2 - 194.5°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.36 (d, J = 7.7 Hz, 1H), 7.24 (d, J = 7.6 Hz, 1H), 7.21 - 7.08 (m, 2H), 4.24 (q, J = 7.0 Hz, 2H), 2.61 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.7, 151.8, 149.6, 147.4, 134.6, 132.3, 132.0, 130.4, 130.2, 129.4, 127.7, 39.1, 15.0, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3076, 2981, 2931, 1563, 1446, 1425, 1319, 1253, 1221, 1152, 1034, 950, 865, 790, 764, 572; HR-MS (ESI) calcd for $C_{14}H_{14}BrN_4S_2$, $[M + H]^+$: 380.9838, found: 380.9842.

9-ethyl-6-(methylthio)-8-(naphthalen-2-ylthio)-9*H*-purine (4o): Yield: 85% (55.3 mg) as a brick red solid; mp = 122.3 - 123.7°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.92 (s, 1H), 7.72 - 7.67 (m, 2H), 7.65 (dd, J = 6.1, 3.3 Hz, 1H), 7.45 - 7.41 (m, 1H), 7.38 (dd, J = 6.2, 3.2 Hz, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.2, 151.6, 149.7, 149.1, 133.6, 132.9, 131.9, 131.0, 129.3, 128.6, 127.8, 127.6, 127.1, 127.0, 126.9, 38.9, 14.8, 11.9 ppm; ν_{max}(KBr)/cm^{-1} 3051, 2978, 2925, 1691, 1560, 1498, 1452, 1427, 1319, 1252, 1218, 1151, 949, 863, 817, 757, 552; HR-MS (ESI) calcd for $C_{18}H_{17}N_4S_2$, $[M + H]^+$: 353.0889, found: 353.0892.

9-ethyl-6-(octylthio)-9*H*-purine (5a): Yield: 96% and 95% (56.0 mg and 55.51mg) as a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.03 (s, 1H), 4.32 (q, J = 7.3 Hz, 2H), 3.39 (t, J = 7.4 Hz, 2H), 1.79 (p, J = 7.5 Hz, 2H), 1.55 (t, J = 7.4 Hz, 3H), 1.49 (p, J = 7.2 Hz, 2H), 1.37 – 1.25 (m, 8H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.2, 151.5, 148.0, 142.0, 131.3, 38.8, 31.6, 29.3, 29.0, 29.0, 28.7, 28.5, 22.5, 15.3, 13.9 ppm; HR-MS (ESI) calcd for $C_{15}H_{25}N_4S$, $[M + H]^+$: 293.1794, found: 293.1790.

6-(dodecylthio)-9-ethyl-9*H*-purine (5b): Yield: 97% and 95% (67.6 mg and 66.2 mg) as a white solid; mp = 50.3 - 51.6°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.01 (s, 1H), 4.31 (q, J = 7.3 Hz, 2H), 3.39 (t, J = 7.4 Hz, 2H), 1.79 (p, J = 7.5 Hz, 2H), 1.54 (t, J = 7.3 Hz, 3H), 1.49 (p, J = 7.3 Hz, 2H), 1.37 - 1.24 (m, 16H), 0.87 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.1, 151.5, 148.1, 141.9, 131.3, 38.8, 31.8, 29.5, 29.5, 29.5, 29.4, 29.3, 29.2, 29.1, 28.7, 28.5, 22.5, 15.3, 14.0 ppm; ν_{max}(KBr)/cm^{-1} 3048, 2936, 2847, 1567, 1467, 1421, 1393, 1326, 1215, 1167, 1148, 1079, 987, 932, 858, 792, 715, 644, 576; HR-MS (ESI) calcd for $C_{19}H_{33}N_4S$, $[M + H]^+$: 349.2420, found: 349.2426.

9-ethyl-6,8-bis(methylthio)-9*H*-purine (6a): Yield: 35% (16.8mg) as a white solid; mp = 130.3 - 131.8°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 4.11 (q, J = 7.2 Hz, 2H), 2.74 (s, 3H), 2.65 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.2, 153.9, 150.6, 150.4, 131.9, 38.0, 14.4, 14.1, 11.8 ppm; ν_{max}(KBr)/cm^{-1} 3031, 2921, 2851, 1557, 1459, 1423, 1317, 1222, 1149, 951, 866, 796, 680, 553; HR-MS (ESI) calcd for $C_9H_{13}N_4S_2$, $[M + H]^+$: 241.0576, found: 241.0579.

1,3,7-trimethyl-8-(methylthio)-3,7-dihydro-1*H*-purine-2,6-dione (6b): Yield: 50% (24.0 mg) as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.48 (s, 3H), 3.30 (s, 3H), 2.64 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.5, 151.9, 151.5, 148.5, 108.6, 32.0, 29.7, 27.8, 14.7 ppm; HR-MS (ESI) calcd for $C_9H_{12}N_4NaO_2S$, $[M + Na]^+$: 263.0573, found: 263.0578.

9-ethyl-6-(*p*-tolylthio)-9*H*-purine (1ra): Yield: 96% (51.9 mg) as a white solid; mp = 113.8 - 115.1°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.93 (s, 1H), 7.46 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 4.22 (q, J = 7.3 Hz, 2H), 2.32 (s, 3H), 1.47 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.1, 152.3, 148.7, 142.5, 139.8, 135.6, 130.9, 130.2, 123.6, 39.1, 21.5, 15.5 ppm; ν_{max}(KBr)/cm^{-1} 3090, 2990, 2919, 1595, 1560, 1489, 1436, 1395, 1327, 1210, 1166, 932, 849, 817, 646, 501; HR-MS (ESI) calcd for $C_{14}H_{15}N_4S$, $[M + H]^+$: 271.1012, found: 271.1014.

ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra for all products, and crystallographic data for 4g (CIF). 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.

ACKNOWLEDGMENT

This work was supported by the financial support from the Key Laboratory Open Foundation of Functional Molecular Engineering of Guangdong Province (2018kf09)

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