

ELECTROPHILIC CYANATIONS. I. SYNTHESIS OF THIOCYANATO-HETEROARENES AND TOSYLHETEROARENES FROM MERCAPTO-HETEROARENES USING *p*-TOLUENESULFONYL CYANIDE

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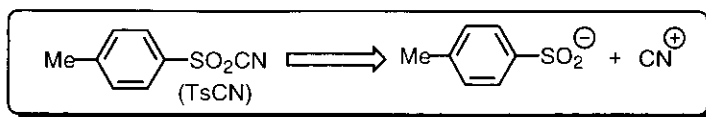
Abstract—Mercaptoheteroarenes (**1**) underwent electrophilic cyanation with *p*-toluenesulfonyl cyanide (TsCN) in THF in the presence of NaH to give the corresponding thiocyanatoheteroarenes (**2**) in moderate to good yields. In DMF, tosylheteroarenes (**4**) were formed by substitution with *p*-toluenesulfinate ion through thiocyanatoheteroarenes (**2**).

Cyanation is an important reaction in organic synthesis, because it is a carbon–chain–forming reaction, and because the cyano group can be easily converted into other functional groups, such as ketone and carboxylic acid. Nucleophilic cyanation methods employing cyanide ion (CN^-) or protected hydrogen cyanide are generally used,^{1,2} but electrophilic cyanation is also feasible. Cyanogen chloride (ClCN)³ and cyanogen (dicyane, $(\text{CN})_2$)⁴ are available for this purpose, but these compounds are not stable and are difficult to handle. Cyanogen bromide (BrCN) can be used, but may generate cyanide ion (CN^-) because of the electronegativity of bromine.

p-Toluenesulfonyl cyanide (TsCN) can also achieve electrophilic cyanation.⁵ However, despite its stability and easy handling, only a few examples of electrophilic cyanation using TsCN have been reported.⁶ We therefore decided to examine the usefulness of electrophilic cyanation with TsCN to obtain thiocyanatoheteroarenes (**2**), which are useful starting compounds for the synthesis of fused thiazoles having an amino group such as

Reagents for Electrophilic Cyanation

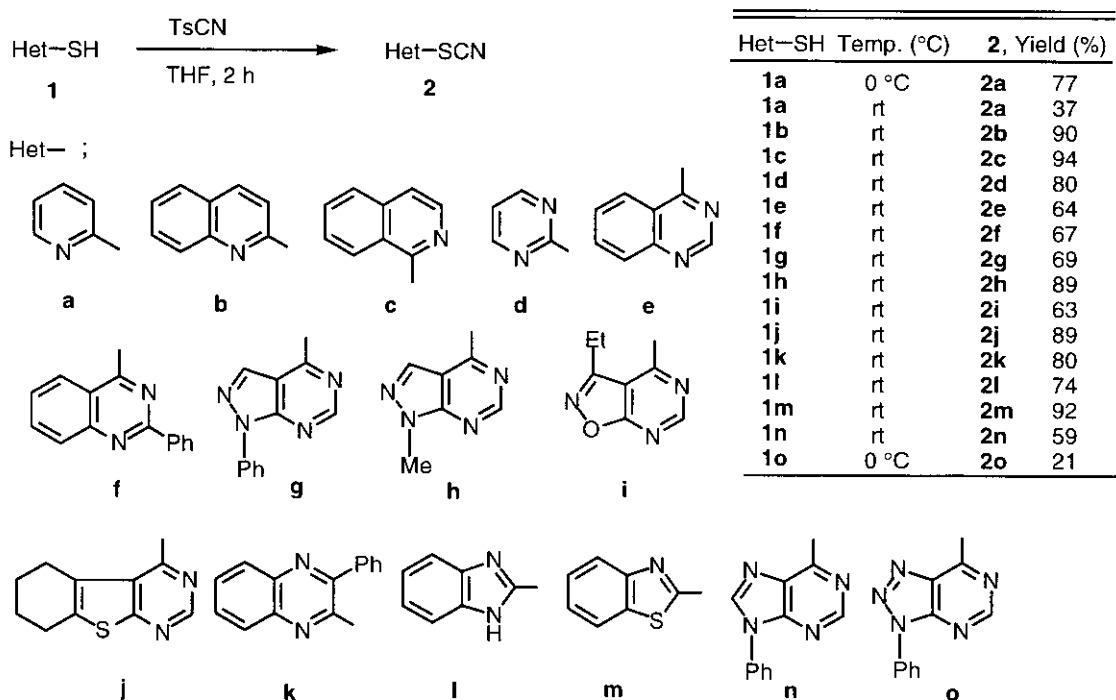
ClCN $(\text{CN})_2$ BrCN



Scheme 1

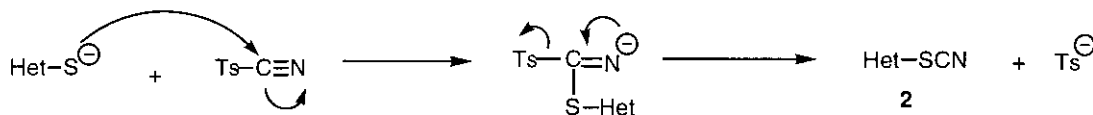
aminobenzothiazoles and aminothiazolopyrimidines,⁷ and have some biological activities.⁸ To our knowledge, thiocyanatoheteroarenes (**2**) have not previously been obtained by electrophilic cyanation of mercaptoheteroarenes (**1**) with TsCN, though a few examples of synthesis of thiocyanatoalkanes or thiocyanatoarenes using TsCN have been reported.^{6b, 9}

Treatment of 2-mercaptoquinoline (**1b**) with TsCN in THF under basic conditions gave 2-thiocyanatoquinoline (**2b**) in 90% yield, as expected. 1-Thiocyanatoisoquinoline (**2c**), 4-thiocyanatoquinazoline (**2e**), 4-thiocyanato-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2g**), 4-thiocyanato-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2h**), 4-thiocyanato-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**2j**), 2-thiocyanatobenzimidazole (**2l**), and 2-thiocyanatobenzothiazole (**2m**) were similarly obtained in good yields. In the case of the synthesis of 2-thiocyanatopyridine (**2a**), at rt, the yield was low because of the formation of di-2-pyridyl disulfide (**3a**), but at 0 °C, **2a** was formed in 77% yield. Thiocyanatophenylpurine (**2n**) was obtained in moderate yield (59%) when 6-mercaptophenylpurine (**1n**) was treated with TsCN, because hydroxyphenylpurine (**5n**) was simultaneously formed in 39% yield. Similarly, 7-thiocyanatophenyltriazolopyrimidine (**2o**) was formed in 21% yield together with hydroxyphenyltriazolopyrimidine (**5o**) in 31% yield. As the thiocyanato group of the thiocyanatoheteroarenes (**2**) seems to be active toward nucleophiles, hydroxyheteroarenes (**5**) are produced when **2** reacts with H₂O under basic conditions. These results are summarized in Scheme 2.



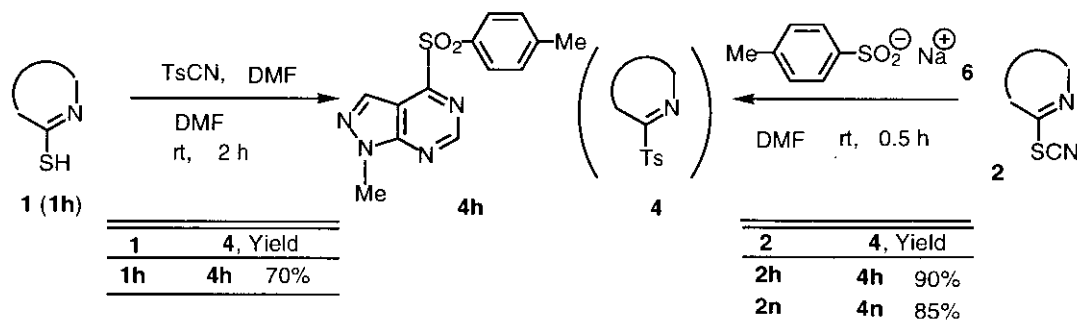
Scheme 2

The formation of thiocyanatoheteroarenes (**2**) may proceed as shown in Scheme 3. Addition of a heteroarene thiolate ion to TsCN followed by elimination of *p*-toluenesulfate ion furnishes thiocyanatoheteroarenes (**2**). This process involves electrophilic cyanation.



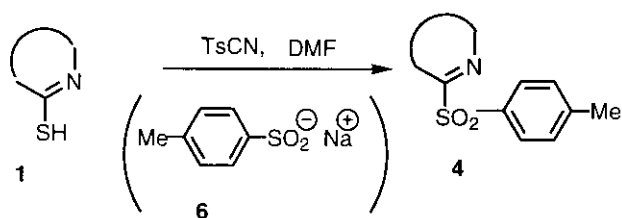
Scheme 3

In the case of **1h**, when the reaction was carried out in DMF, 4-tosyl-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**4h**) was obtained in 70% yield. The compound (**4h**) was formed by substitution of thiocyanatomethylpyrazolopyrimidine (**2h**) with *p*-toluenesulfate ion, because the treatment of **2h** with sodium *p*-toluenesulfate (**6**) resulted in the formation of **4h** in 90% yield. Similarly, 6-thiocyanatophenylpurine (**2n**) reacted with sodium *p*-toluenesulfate (**6**) to give 6-tosylphenylpurine (**4n**) in 85% yield.



Scheme 4

These results led us to synthesize tosylheteroarenes (**4**) from mercaptoheteroarenes (**1**) by electrophilic cyanation, followed by conversion of the thiocyanato group into a tosyl group (Scheme 5). We considered that the quantitative



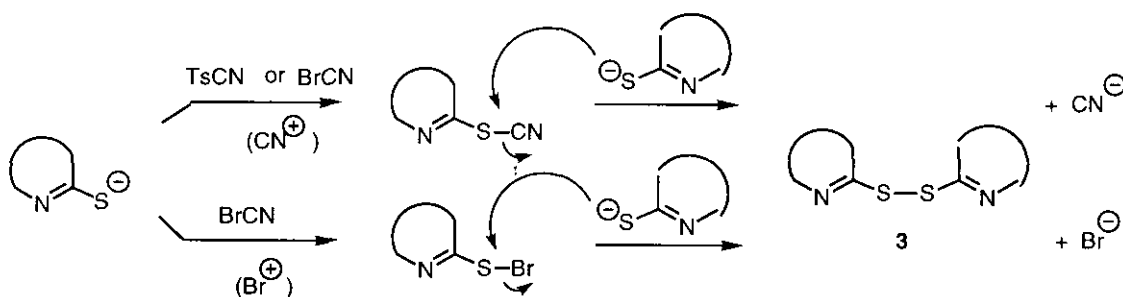
1	TsNa ^a	Temp.	Time	4, Yield (%)
1g	-	rt	2	4g 90
1j	+	rt	2	4j 23 (2j; 30%)
1j	-	rt	2	4j 35 (2j; 51%)
1j	-	50 °C	1	4j 66 (2j; 4%)
1n	-	rt	1	4n 79 (2n; 21%)

a. Method A (-) and Method B (+).

Scheme 5

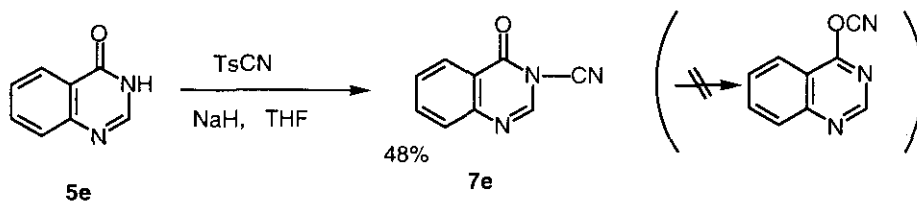
formation of tosylheteroarenes requires the presence of sufficient *p*-toluenesulfonate ion (Ts^-). In the presence (Method B) or absence (Method A) of sodium *p*-toluenesulfonate (**6**), however, the yields of **4j** obtained by the reaction of **1j** with TsCN showed no marked difference.

BrCN is often used to prepare thiocyanatoheteroarenes (**2**) by electrophilic cyanation,^{8a, 10, 11} and the preparation of thiocyanatoheteroarenes (**2**) from mercaptoheteroarene (**1**) was achieved by using BrCN in good yields. In our re-examination of the preparation of thiocyanatopyridine (**2a**) using BrCN , the desired product (**2a**, 68%) was formed together with di-2-pyridyl disulfide (**3a**) in 22% yield. Similarly, di-2-quinolyl disulfide (**3b**) was obtained in 15% yield when 2-mercaptoquinoline (**1b**) was treated with BrCN . Thus, it seems that the use of TsCN for electrophilic cyanation is more effective than that of BrCN . The two formation processes of diheteroarenyl disulfide (**3**) are considered to be as illustrated in Scheme 6, though the details are not clear.



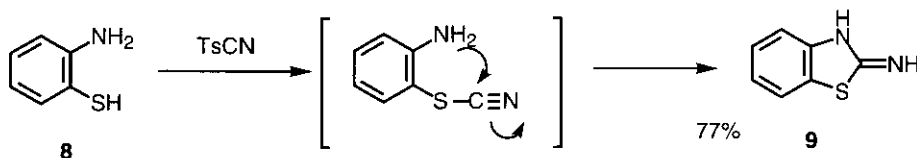
Scheme 6

An attempt to produce cyanatoheteroarenes by the electrophilic cyanation of 4(3*H*)-quinazolinone (**5e**) with TsCN resulted in the formation of 4-oxo-3,4-dihydro-3-quinazolinecarbonitrile (**7e**) in 48% yield. This result indicates that TsCN reacts preferentially with the *N*-anion rather than the *O*-anion. In the electrophilic cyanation using TsCN , the order of the reactivity is thus; $-\text{S}^- > -\text{N}^- > -\text{O}^-$.



Scheme 7

This electrophilic cyanation was applied to prepare 2-aminobenzothiazole (**9**), as shown in Scheme 8. Namely, treatment of 2-mercaptoaniline (**8**) with TsCN in THF furnished a 77% yield of 2-aminobenzothiazole (**9**) through the formation and cyclization of 2-thiocyanatoaniline.



Scheme 8

In conclusion, we have synthesized thiocyanatoheteroarenes (2) and tosylheteroarenes (4) by electrophilic cyanation from mercaptoheteroarenes (1) using TsCN. The final product (2 or 4) depends on the reaction solvent, THF or DMF. We found that TsCN is an effective reagent to achieve electrophilic cyanation.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a JASCO A-102 diffraction grating IR spectrophotometer. ¹H-NMR spectra were measured at 60 MHz on a JEOL PMX60SI NMR spectrometer, and at 270 MHz on a JEOL JNM-GSX270 FT-NMR spectrometer. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane as an internal standard, and coupling constants (*J*) are given in Hz.

Preparation of Mercaptoheteroarenes (1); General Procedure. A solution of chloroheteroarene (1.0 mmol) and thiourea (1.35 g, 2.0 mmol) in MeOH (10 mL) was refluxed for 1 h. The separated solid was collected, and recrystallized.

4-Mercaptoquinazoline (**1e**): Yield 50%, pale yellow needles (MeOH), mp > 300 °C. IR (KBr) cm⁻¹: 2930 (SH). ¹H-NMR (DMSO-*d*₆) δ: 8.59 (1H, d, *J* = 8.4, C⁸-H), 8.19 (1H, s, C²-H), 7.94–7.60 (3H, m, C^{5–7}-H).

4-Mercapto-2-phenylquinazoline (**1f**): Yield 58%, pale yellow needles (MeOH), mp 217 °C. IR (KBr) cm⁻¹: 2925 (SH). ¹H-NMR (DMSO-*d*₆) δ: 8.71 (1H, dd, *J* = 8.0, 1.0, aromatic H), 8.03–8.38 (2H, m, aromatic H), 7.43–8.03 (7H, m, aromatic H and SH).

4-Mercapto-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**1g**): Yield 82%, colorless needles (MeOH), mp 268–271 °C. IR (KBr) cm⁻¹: 3030 (SH). ¹H-NMR (DMSO-*d*₆) δ: 8.37 (1H, s, C⁶-H), 7.30–8.33 (6H, m, aromatic H).

4-Mercapto-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**1h**): Yield 78%, colorless scales (MeOH), mp 265–267 °C. IR (KBr) cm⁻¹: 3050 (SH). ¹H-NMR (DMSO-*d*₆) δ: 8.20 (1H, s, C⁶-H), 8.18 (1H, s, C³-H), 3.94 (3H, s, NMe).

4-Mercapto-5-ethylisoxazolo[5,4-*d*]pyrimidine (**1i**): Yield 82%, yellowish powder, mp 274–275 °C. IR (KBr) cm⁻¹: 2950 (SH). ¹H-NMR (DMSO-*d*₆) δ: 8.44 (1H, s, C⁶-H), 3.07 (2H, q, *J* = 7.3, CH₂CH₃), 1.32 (3H, t, *J* = 7.3, CH₂CH₃).

4-Mercapto-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**1j**): Yield 50%, yellowish needles (MeOH), mp 231–233 °C. ¹H-NMR (CDCl₃) δ: 7.89 (1H, s, C²-H), 3.15–3.48 (2H, m), 2.62–3.01 (2H, m), 1.71–2.13 (4H, m).

2-Mercapto-3-phenylquinoxaline (**1k**): A solution of 2-chloro-3-phenylquinoxaline (2.0 g, 8.3 mmol) and thioacetic acid (2.0 g, 26.3 mmol) in 10 mL of MeOH was refluxed for 20 min. The separated solid was collected and recrystallized from acetone to give **1k** in 41% yield (805 mg), orange needles, mp 242 °C. *Anal.* Calcd for $C_{14}H_{10}N_2S$: C, 70.56; H, 4.23; N, 11.76. Found: C, 70.67; H, 4.17; N, 11.84. IR (KBr) cm^{-1} : 2950 (SH). 1H -NMR (DMSO- d_6) δ : 8.05–7.25 (9H, m, aromatic H), 3.27 (1H, s, SH).

7-Mercapto-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine (**1o**): Yield 93%, yellow needles (MeOH), mp 191–193 °C. IR (KBr) cm^{-1} : 3050 (SH). 1H -NMR (DMSO- d_6) δ : 7.14–8.44 (6H, m, aromatic H).

2-Mercaptopyridine (**1a**), 2-mercaptoquinoline (**1b**), 2-mercaptopyrimidine (**2d**), 2-mercaptobenzimidazole (**1l**), and 2-mercaptobenzothiazole (**2m**) were obtained from Aldrich Co. Ltd. 2-Mercaptoisoquinoline (**1c**) and 6-mercapto-9-phenyl-9*H*-purine (**1n**) were synthesized by the reported procedures.¹²

Preparation of Thiocyanatoheteroarenes by Reaction of Mercaptoheteroarenes (2) with TsCN; General Procedure.

A mixture of a mercaptoheteroarene (**1**, 2.0 mmol) and NaH (60% in oil, 120 mg, 3.0 mmol) in 15 mL of THF was treated with TsCN (450 mg, 2.4 mmol). The reaction mixture was stirred at rt (or 0 °C) for 2 h, then poured into ice- H_2O , and extracted with $CHCl_3$. The organic layer was washed with H_2O , dried over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on SiO_2 with benzene, then $CHCl_3$. The fraction eluted with $CHCl_3$ gave the thiocyanatoheteroarene (**2**).

2-Thiocyanatopyridine (**2a**): Yellowish oil (lit.,¹¹ bp₁₀ 120–122 °C). IR (KBr) cm^{-1} : 2158 (SCN). 1H -NMR ($CDCl_3$) δ : 8.49 (1H, d, $J = 6$, C⁶-H), 7.84–7.40 (2H, m), 7.23 (1H, t, $J = 6$, C⁵-H).

2-Thiocyanatoquinoline (**2b**): Colorless needles (*n*-hexane), mp 75 °C (lit.,^{11, 15} 74–75 °C).

1-Thiocyanatoisoquinoline (**2c**): Colorless needles (*n*-hexane), mp 68 °C. *Anal.* Calcd for $C_{10}H_6N_2S$: C, 64.49; H, 3.25; N, 15.04. Found: C, 64.67; H, 3.25; N, 15.02. IR (KBr) cm^{-1} : 2183 (SCN).

2-Thiocyanatopyrimidine (**2d**): Colorless needles (*n*-hexane), mp 113 °C (lit.,¹³ 108–109 °C). *Anal.* Calcd for $C_5H_3N_3S$: C, 43.79; H, 2.21; N, 30.64. Found: C, 43.78; H, 2.13; N, 30.73. IR (KBr) cm^{-1} : 2180 (SCN). 1H -NMR ($CDCl_3$) δ : 8.66 (2H, d, $J = 6$), 7.26 (1H, t, $J = 6$).

4-Thiocyanatoquinazoline (**2e**): Colorless powder (benzene-*n*-hexane), mp 118 °C. *Anal.* Calcd for $C_9H_5N_3S$: C, 57.74; H, 2.69; N, 22.44. Found: C, 57.52; H, 2.65; N, 22.34. IR (KBr) cm^{-1} : 2160 (SCN). 1H -NMR ($CDCl_3$) δ : 9.18 (1H, s, C²-H), 7.16–8.25 (4H, m, aromatic H).

4-Thiocyanato-2-phenylquinazoline (**2f**): Colorless powder (benzene-*n*-hexane), mp 140 °C. *Anal.* Calcd for $C_{15}H_9N_3S$: C, 68.42; H, 3.45; N, 15.96. Found: C, 68.62; H, 3.33; N, 15.88. IR (KBr) cm^{-1} : 2200 (SCN). 1H -NMR ($CDCl_3$) δ : 8.47–8.80 (2H, m, aromatic H), 7.80–8.20 (2H, m, aromatic H), 7.37–7.80 (5H, m, aromatic H).

4-Thiocyanato-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2g**): Colorless needles (acetone), mp 128 °C. *Anal.* Calcd for $C_{12}H_7N_5S$: C, 56.90; H, 2.79; N, 27.65. Found: C, 56.88; H, 2.72; N, 27.80. IR (KBr) cm^{-1} : 2170 (SCN). 1H -NMR ($CDCl_3$) δ : 8.93 (1H, s, C⁶-H), 8.64 (1H, s, C³-H), 8.07–8.36 (2H, m, aromatic H), 7.23–7.79 (3H, m,

aromatic H).

4-Thiocyanato-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2h**): Colorless prisms (*n*-hexane–AcOEt), mp 152–153 °C. *Anal.* Calcd for C₇H₅N₅S: C, 43.97; H, 2.64; N, 36.63. Found: C, 43.76; H, 2.87; N, 36.35. IR (KBr) cm⁻¹: 2178 (SCN). ¹H-NMR (CDCl₃) δ: 9.04 (1H, s, C⁶-H), 8.47 (1H, s, C³-H), 4.17 (3H, s, Me).

4-Thiocyanato-3-ethylisoxazolo[5,4-*d*]pyrimidine (**2i**): Yellowish oil. *Anal.* Calcd for C₈H₆N₄OS: C, 46.60; H, 2.93; N, 27.17. Found: C, 46.40; H, 3.02; N, 27.22. IR (KBr) cm⁻¹: 2170 (SCN). ¹H-NMR (CDCl₃) δ: 9.08 (1H, s, C⁶-H), 3.06 (2H, q, *J* = 7.8, CH₂CH₃), 1.50 (3H, t, *J* = 7.8, CH₂CH₃).

4-Thiocyanato-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**2j**): Colorless powder (acetone), mp 128 °C. *Anal.* Calcd for C₁₁H₉N₃S₂: C, 53.42; H, 3.67; N, 16.99. Found: C, 53.42; H, 3.54; N, 17.04. IR (KBr) cm⁻¹: 2165 (SCN). ¹H-NMR (CDCl₃) δ: 8.81 (1H, s, C²-H), 2.68–3.12 (4H, m), 1.80–2.20 (4H, m).

2-Thiocyanato-3-phenylquinoxaline (**2k**): Colorless needles (benzene–*n*-hexane), mp 132 °C. *Anal.* Calcd for C₁₅H₉N₃S: C, 68.42; H, 3.45; N, 15.96. Found: C, 68.32; H, 3.33; N, 15.74. IR (KBr) cm⁻¹: 2160 (SCN). ¹H-NMR (CDCl₃) δ: 8.28–7.50 (9H, m, aromatic H).

2-Thiocyanatobenzimidazole (**2l**): Colorless powder (benzene), mp 169 °C (lit.,¹¹ 168–170 °C). *Anal.* Calcd for C₈H₅N₃S: C, 54.84; H, 2.88; N, 23.98. Found: C, 54.56; H, 2.64; N, 23.42. IR (KBr) cm⁻¹: 2150 (SCN). ¹H-NMR (DMSO-*d*₆) δ: 7.07–7.82 (4H, m, aromatic H), 6.84 (1H, bs, NH).

2-Thiocyanatobenzothiazole (**2m**): Colorless scales (*n*-hexane), mp 91–92 °C (lit.,¹¹ 88–91 °C). *Anal.* Calcd for C₈H₄N₂S₂: C, 49.98; H, 2.10; N, 14.57. Found: C, 49.79; H, 1.83; N, 14.44. IR (KBr) cm⁻¹: 2170 (SCN). ¹H-NMR (CDCl₃) δ: 7.70–8.15 (2H, m, aromatic H), 7.23–7.60 (2H, m, aromatic H).

6-Thiocyanato-9-phenyl-9*H*-purine (**2n**): Colorless needles (*n*-hexane–AcOEt), mp 169–170 °C. *Anal.* Calcd for C₁₂H₇N₅S: C, 56.91; H, 2.79; N, 27.65. Found: C, 56.65; H, 2.49; N, 27.51. IR (KBr) cm⁻¹: 2182 (SCN). ¹H-NMR (CDCl₃) δ: 8.97 (1H, s, C²-H), 8.41 (1H, s, C⁸-H), 7.73–7.54 (5H, m, Ph).

7-Thiocyanato-3-phenyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidine (**2o**): Colorless scales (*n*-hexane–AcOEt), mp 131–133 °C. *Anal.* Calcd for C₁₁H₆N₆S: C, 51.96; H, 2.38; N, 33.05. Found: C, 51.97; H, 2.30; N, 32.85. IR (KBr) cm⁻¹: 2168 (SCN). ¹H-NMR (CDCl₃) δ: 9.16 (1H, s, C⁵-H), 8.23 (2H, d, *J* = 7.3, Ph), 7.66–7.56 (3H, m, Ph).

In the case of the cyanation of 2-mercaptopyridine (**1a**) at rt, the second fraction eluted with CHCl₃ gave di-2-pyridyl disulfide (**3a**) in 22% yield.

In the case of **1o**, 3,7-dihydro-3-phenyl-6*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-7-one (**5o**)¹⁴ was formed in 31% yield.

Reaction of 4-Thiocyanato-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2h**) with Sodium *p*-Toluenesulfinate

(**6**). Sodium *p*-toluenesulfinate (**6**, 306 mg, 1.7 mmol) was added to a solution of 4-thiocyanato-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**2h**, 325 mg, 1.7 mmol) in 3 mL of DMF. The resulting mixture was stirred for 0.5 h at rt, then poured into ice–H₂O and extracted with AcOEt. The organic layer was washed with H₂O, dried

over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and AcOEt. The fraction eluted with *n*-hexane–AcOEt (1:1) gave 4-tosyl-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**4h**) in 90% yield (442 mg). Colorless needles (*n*-hexane), mp 168–170 °C. *Anal.* Calcd for $\text{C}_{13}\text{H}_{12}\text{N}_4\text{SO}_2$: C, 54.16; H, 4.20; N, 19.43. Found: C, 54.15; H, 3.91; N, 19.58. IR (KBr) cm^{-1} : 1329, 1143 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 9.04 (1H, s, $\text{C}^6\text{-H}$), 8.68 (1H, s, $\text{C}^3\text{-H}$), 8.01 (2H, d, $J = 8.4$), 7.37 (2H, d, $J = 8.4$), 4.18 (3H, s, NMe), 2.44 (3H, s, Me).

Reaction of 6-Thiocyanato-9-phenyl-9*H*-purine (2n) with Sodium *p*-Toluenesulfinate (6). Sodium *p*-toluenesulfinate (**6**, 180 mg, 1.0 mmol) was added to a solution of 6-thiocyanato-9-phenyl-9*H*-purine (**2n**, 253 mg, 1.0 mmol) in 3 mL of DMF. The resulting mixture was stirred for 0.5 h at rt, then poured into ice- H_2O and the separated solid was collected by filtration. The solid was dissolved in CHCl_3 and the solution was dried over Na_2SO_4 . The filtrate was extracted with AcOEt and the organic layer was dried over Na_2SO_4 . The organic layers were combined and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and AcOEt. The first fraction eluted with *n*-hexane–AcOEt (1:1) afforded recovered **2n** in 9% yield (23 mg). The second fraction gave 6-tosyl-9-phenyl-9*H*-purine (**4n**)^{1a} in 85% yield (296 mg). Colorless granules (*n*-hexane–AcOEt), mp 229–232 °C (lit.,^{1a} 230–231 °C). IR (KBr) cm^{-1} : 1337, 1142 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 9.10 (1H, s, $\text{C}^2\text{-H}$), 8.58 (1H, s, $\text{C}^8\text{-H}$), 8.19 (2H, d, $J = 8.4$), 7.70–7.53 (5H, m, N-Ph), 7.38 (2H, d, $J = 8.4$), 2.43 (3H, s, Me).

Synthesis of Tosylheteroarenes (4) from Mercaptoheteroarenes (1) Using TsCN.

Method A:

4-Tosyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (4g). Sodium hydride (60% in oil, 88 mg, 2.2 mmol) was added to a solution of 4-mercapto-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**1g**, 456 mg, 2.0 mmol) in 10 mL of DMF, and the mixture was stirred for 20 min at rt. TsCN (398 mg, 2.2 mmol) was then added, and the resulting mixture was further stirred for 2 h at rt. The reaction mixture was poured into ice- H_2O , and the separated solid was collected. The solid was dissolved in CH_2Cl_2 , and the solution was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and AcOEt. The first fraction eluted with *n*-hexane–AcOEt (1:1) gave 4-tosyl-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**4g**) in 90% yield (627 mg). Colorless granules (*n*-hexane–AcOEt), mp 195–197 °C (lit.,^{1e} 196–197 °C). IR (KBr) cm^{-1} : 1320, 1142 (SO_2). $^1\text{H-NMR}$ (CDCl_3) δ : 9.12 (1H, s, $\text{C}^6\text{-H}$), 8.77 (1H, s, $\text{C}^3\text{-H}$), 8.37–7.24 (9H, m, aromatic H), 2.44 (3H, s, Me).

4-Tosyl-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (4h). Sodium hydride (60% in oil, 88 mg, 2.2 mmol) was added to a solution of 4-mercapto-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**1h**, 332 mg, 2.0 mmol) in 10 mL of DMF, and the mixture was stirred for 20 min at rt. TsCN (398 mg, 2.2 mmol) was then added, and the resulting mixture was further stirred for 2 h at rt. The reaction mixture was poured into ice- H_2O , and extracted with AcOEt.

The organic layer was washed with H_2O , dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and AcOEt. The first fraction eluted with *n*-hexane–AcOEt (1:1) gave 4-tosyl-1-methyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**4h**) in 70% yield (406 mg).

4-Tosyl-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (4j**).** Sodium hydride (NaH, 60% in oil, 88 mg, 2.2 mmol) was added to a solution of 4-mercapto-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**1j**, 380 mg, 2.0 mmol) in DMF (10 mL), and the mixture was stirred for 20 min at rt. TsCN (398 mg, 2.2 mmol) was then added, and the resulting mixture was further stirred for 1 h at 50 °C. The reaction mixture was poured into ice– H_2O and extracted with AcOEt. The organic layer was washed with H_2O , dried over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and CH_2Cl_2 . The first fraction eluted with *n*-hexane– CH_2Cl_2 (1:1) gave 4-tosyl-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**4j**) in 66% yield (412 mg). The second fraction gave 4-thiocyanato-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**2j**) in 4% yield (17 mg).

4-Tosyl-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**4j**): Colorless prisms (*n*-hexane–AcOEt), mp 218–220 °C. *Anal.* Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_2\text{S}_2$: C, 59.28; H, 4.68; N, 8.13. Found: C, 59.07; H, 4.49; N, 8.03. IR (KBr) cm^{-1} : 1311, 1140 (SO_2). ^1H -NMR (CDCl_3) δ : 8.69 (1H, s, $\text{C}^2\text{-H}$), 7.88 (2H, d, $J = 8.4$), 7.42 (2H, d, $J = 8.4$), 3.38 (2H, m, $\text{C}^8\text{-H}$), 2.99 (2H, m, $\text{C}^5\text{-H}$), 2.51 (3H, s, Me), 1.98 (4H, m, $\text{C}^6,7\text{-H}$).

In the case of the reaction at rt for 2 h, the first fraction eluted with *n*-hexane– CH_2Cl_2 (1:1) gave **4j** in 35% yield (243 mg). The second fraction gave **2j** in 51% yield (250 mg).

6-Tosyl-9-phenyl-9*H*-purine (4n**).** A solution of 6-mercapto-9-phenyl-9*H*-purine (**1n**) in 10 mL of DMF was treated with NaH (60% in oil, 88 mg, 2.2 mmol), and the mixture was stirred for 20 min at rt. TsCN (398 mg, 2.2 mmol) was then added, and the resulting mixture was further stirred for 2 h at rt. The reaction mixture was poured into ice– H_2O and the separated solid was collected. The solid was dissolved in CH_2Cl_2 , and the solution was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and AcOEt. The first fraction eluted with *n*-hexane–AcOEt (1:1) gave 6-thiocyanato-9-phenyl-9*H*-purine (**2n**) in 21% yield (108 mg). The second fraction gave 6-tosyl-9-phenyl-9*H*-purine (**4n**) in 79% yield (554 mg).

Method B:

4-Tosyl-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (4j**).** Sodium hydride (NaH, 60% in oil, 88 mg, 2.2 mmol) was added to a solution of 4-mercapto-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**1j**, 380 mg, 2.0 mmol) and sodium *p*-toluenesulfinate (256 mg, 2.0 mmol) in DMF (10 mL), and the mixture was stirred for 20 min at rt. TsCN (398 mg, 2.2 mmol) was then added, and the resulting mixture was stirred for 2 h at rt. The reaction mixture was poured into ice– H_2O and extracted with AcOEt. The organic layer was washed with H_2O , dried over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and CH_2Cl_2 . The first fraction eluted with *n*-hexane– CH_2Cl_2 (1:1) gave 4-tosyl-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**4j**) in 23% yield (159 mg). The second fraction gave 4-thiocyanato-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**2j**) in 30% yield (149 mg).

Synthesis of Tosylheteroarenes (4) from Mercaptoheteroarenes (1) Using BrCN.

2-Thiocyanatopyridine (2a). A solution of 2-mercaptopyridine (**1a**, 222 mg, 2 mmol) and cyanogen bromide (BrCN, 254 mg, 2.4 mmol) in THF (20 mL) was treated with NaH (60% in oil, 120 mg, 3 mmol), and the mixture was stirred at rt for 2 h. The reaction mixture was poured into ice-H₂O and extracted with CHCl₃. The organic layer was dried over Na₂SO₄ and concentrated. The residue was purified by column chromatography on SiO₂. The first fraction eluted with CHCl₃ gave 2-thiocyanatopyridine (**2a**) in 68% yield (185 mg). The second fraction gave di-2-pyridyl disulfide (**3a**) in 22% yield (48 mg).

2-Thiocyanatoquinoline (2b). A solution of 2-mercaptoquinoline (**1b**, 322 mg, 2 mmol) and BrCN (254 mg, 2.4 mmol) in THF (20 mL) was treated with NaH (60% in oil, 120 mg, 3 mmol), and the mixture was stirred at rt for 2 h. The reaction mixture was poured into ice-H₂O and extracted with CHCl₃. The organic layer was washed with H₂O, dried over Na₂SO₄, and concentrated. The residue was purified by column chromatography on SiO₂. The first fraction eluted with CHCl₃ gave 2-thiocyanatoquinoline (**2b**) in 72% yield (268 mg). The second fraction gave di-2-quinolyl disulfide (**3b**) in 15% yield (48 mg).

3b; Yellowish needles (acetone-*n*-hexane), mp 137–139 °C (lit.,¹⁵ 140–142 °C). MS (m/z): 287 (M⁺-32). ¹H-NMR (CDCl₃) δ: 7.17–8.13 (m, aromatic H).

Reaction of 4(3H)-quinazolinone (5e) with TsCN. A mixture of 4(3H)-quinazolinone (**5e**, 292 mg, 2 mmol) and NaH (60% in oil, 88 mg, 2.2 mmol) in 10 mL of THF was treated with TsCN (398 mg, 2.2 mmol). The reaction mixture was stirred at 0 °C for 1 h, then poured into ice-H₂O and extracted with CHCl₃. The organic layer was washed with H₂O, dried over Na₂SO₄, and concentrated. The residue was purified by column chromatography on SiO₂ with CHCl₃. The fraction eluted with CHCl₃ gave 4-oxo-3,4-dihydro-3-quinazolinecarbonitrile (**7e**) in 48% (165 mg) yield. Colorless needles (benzene-MeOH), mp 139 °C. MS (m/z): 171 (M⁺). IR (KBr) cm⁻¹: 2254 (CN), 1720 (CO). ¹H-NMR (CDCl₃) δ: 8.58 (1H, s, C²-H), 8.35–7.58 (4H, m, aromatic H).

2-Aminobenzothiazole (9). A solution of *o*-aminothiophenol (**8**, 1250 mg, 10 mmol) in 100 mL of acetonitrile was treated with TsCN (1997 mg, 11 mmol). The reaction mixture was stirred for 1 h at rt, then concentrated under reduced pressure, and the residue was poured into ice-2*N* HCl and extracted with AcOEt. The aqueous layer was neutralized with 2*N* NaOH. The separated crystals were collected and dried to give 2-aminobenzothiazole (**9**)¹⁶ in 77% yield (1155 mg).

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