Chemoselective Arylsulfenylation of 2-Aminoimidazo[1,2-*a*]pyridines by Phenyliodine(III) Bis(trifluoroacetate) (PIFA)

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Abstract: A series of 2-(trifluoroacetamido)imidazo[1,2-*a*]-pyridines was prepared and treated with phenyliodine(III) bis(trifluoroacetate) (PIFA) in the presence of a variety of thiols leading chemoselectively to the corresponding 3-sulfides. Exposure of these adducts to silica gel in MeOH/CH_2Cl_2 provides a convenient method for the cleavage of the trifluoroacetamide group.

Key words: chemoselective sulfenylation, phenyliodine(III) bis(trifluoroacetate), imidazopyridines, trifluoroacetamide hydrolysis

Imidazopyridines and analogues,[1] structurally related to benzimidazoles, have demonstrated significant potential in the search for new drugs.[2] Their pharmacological profile is critically dependent on the nature of the substitution at the 3-position.[2] Although sulfenyl, sulfinyl and sulfonyl groups have been recognised for their distinguishing features in structure–activity relationship studies,[3] a convenient approach to their incorporation in heterocyclic systems, such as imidazopyridines and analogues, remained unknown.

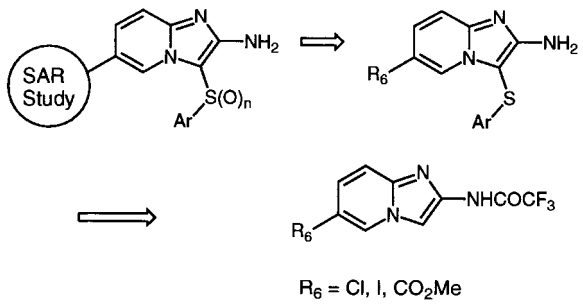
Elegant approaches involving carbanions as intermediates, such as halogen–metal exchange,[4] single electron transfer (SET) reactions mediated by aromatic anion radicals,[5] Rieke metals,[6] or the use of palladium-catalysed cross-coupling reactions,[7] suffer from the deficiency of chemoselectivity.

We found an urgent need for a general, selective and convergent approach that would allow the introduction of a large variety of sulfur groups at C-3 of imidazopyridines (Scheme 1) and be compatible with the presence of substituents, such as iodo, chloro and methoxycarbonyl groups. Benzenesulfenyl chloride has been already employed in an electrophilic sulfenylation of imidazo[1,2-*a*]pyridine.[2e] However, the reported yield was only 22% and the limited number of the commercially available sulfenyl chlorides precludes a structure–activity relationship investigation.

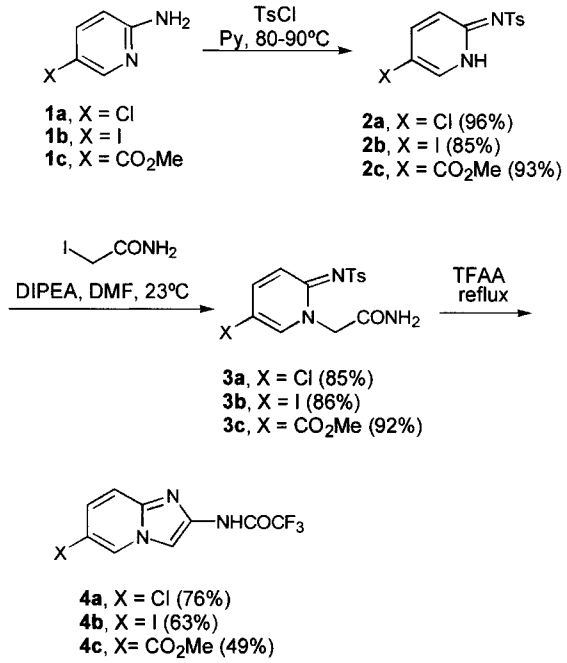
In a recent report, Kita's reagent, phenyliodine(III) bis(trifluoroacetate) (PIFA), has been described as an efficient mediator for the direct substitution of phenol ethers by various thiophenols.[8] Herein, we wish to report a new application of this reagent in the sulfenylation of functionalised imidazopyridmes.[9]

For this investigation, we have designed and synthesised the imidazopyridines **4a–c** which differ by the type of functionality at the 6-position in order to permit further transformations.

The synthesis of **4a–c** is outlined in Scheme 2. Reaction of aminopyridines **1**[10] with *p*-toluenesulfonyl chloride in pyridine using the classical procedure and subsequent treatment of the pyridin-2(1*H*)-imine **2** with iodoacetamide in the presence of Hünig's base (*i*-Pr_2NEt) in DMF provided the corresponding carboxamides **3a–c** in good yield. In our hands, the use of Hünig's base instead of the reported NaH[2e] considerably enhanced the yield of the alkylation. We were unable to detect the *exo*-alkylated isomer that was reported to be the major product when the reaction was performed in the presence of NaH.[2e] Conversion of **3a–c** to the desired 2-(trifluoroacetamido)imidazopyridines **4a–c** was accomplished by treatment with trifluoroacetic anhydride.[11]

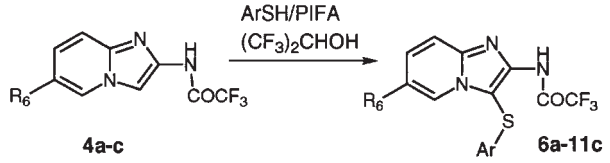


Scheme 1



Scheme 2

The sulfenylation of imidazo[1,2-*a*]pyridines **4a–c** mediated by the hypervalent iodine(III) reagent, phenyliodine(III) bis(trifluoroacetate) (PIFA), was investigated using a variety of thiols. It should be noted that when the thiol was injected into the mixture of imidazopyridine/PIFA in 1,1,1,3,3,3-hexafluoropropan-2-ol, the reaction failed to give the sulfenylated product. The PIFA should be added after dissolving or suspending the substrate and the thiol in hexafluoropropanol.



Scheme 3

As noted in Table 1, a series of sulfenylated imidazopyridine derivatives was prepared via reaction of the imidazopyridine with the appropriate and commercially available thiol in the presence of PIFA. Substrates **4a–c** were converted to the corresponding sulfides **6a–11a**, **6b–9b**, and **6c–11c** in high yield. Only *p*-nitrobenzenethiol failed to react and the starting material was recovered unchanged. It should be emphasised that neither the ester function in the substrate **4c** nor the halogen in substrates **4a** and **4b** were affected during the sulfenylation process.

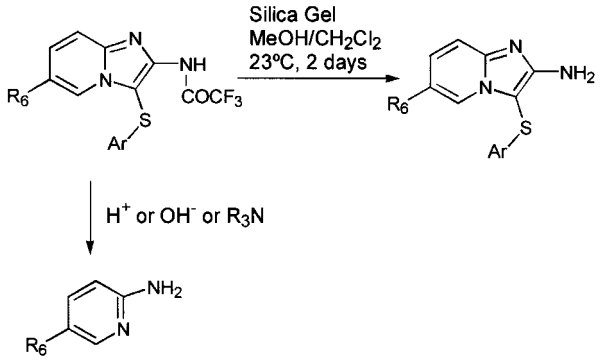
Table 1. Reaction of **4a–c** with Arenethiols in the Presence of PIFA

Substrate	Ar	Time (h)	Compound	Yield (%)
4a	Ph	4.5	**6a**	77
4a	4-ClC_6H_4	4	**7a**	72
4a	4-FC_6H_4	5	**8a**	96
4a	4-$MeOC_6H_4$	4.5	**9a**	91
4a	4-$NO_2C_6H_4$	4.5	**10a**	0
4a	3-ClC_6H_4	20	**11a**	69
4b	Ph	4.5	**6b**	84
4b	4-ClC_6H_4	4	**7b**	75
4b	4-FC_6H_4	5	**8b**	73
4b	4-$MeOC_6H_4$	4.5	**9b**	82
4b	4-$NO_2C_6H_4$	4.5	**10b**	0
4c	Ph	4.5	**6c**	83
4c	4-ClC_6H_4	4	**7c**	80
4c	4-FC_6H_4	5	**8c**	74
4c	4-$MeOC_6H_4$	4.5	**9c**	82
4c	4-$NO_2C_6H_4$	4	**10c**	0
4c	3-ClC_6H_4	4	**11c**	87

All attempts to detrifluoroacetylate compounds **7a**, **11a**, **7b**, **7c**, **11c**, and **8c** using strongly basic conditions such as NaOH or Hünig's base failed to yield the respective amines **12a**, **13a**, **12b**, **12c**, **13c**, and **14c**. Instead, the reaction led to imidazo ring opening providing the aminopyridine as the main product (Scheme 4). Surprisingly, the trifluoro-acetamide group was hydrolysed when supported on silica gel in a mixture of MeOH/CH_2Cl_2 (2:98) in good yield (Table 2).

Table 2. Hydrolysis of Trifluoroacetamides in the Presence of Silica Gel (Scheme 4)

Substrate	R_6	Ar	Compound	Yield (%)
7a	Cl	4-ClC_6H_4	**12a**	70
11a	Cl	3-ClC_6H_4	**13a**	72
7b	I	4-ClC_6H_4	**12b**	81
7c	CO_2Me	4-ClC_6H_4	**12c**	88
11c	CO_2Me	3-ClC_6H_4	**13c**	65
8c	CO_2Me	4-FC_6H_4	**14c**	55



Scheme

In conclusion, a direct and chemoselective sulfenylation of imidazopyridine at C-3 has been developed. The high yield observed in the examples reported, and the compatibility with sensitive functions present in the molecule, promise its application for the incorporation of sulfur groups into a variety of heterocyclic analogues. A convenient method for the hydrolysis of the appropriate trifluoroacetamides has also been described.

All reagents were purchased from Aldrich and used without further purification unless otherwise stated. Column chromatography was carried out on flash silica gel (Merck 230–400 mesh). TLC analysis was conducted on Whatman silica gel plates. ^1H and ^{13}C NMR spectra were recorded at 200 MHz with DMSO-d_6 or $CDCl_3$ as solvent with a Bruker AC-200 instrument. Chemicals shifts (δ values) and coupling constants (*J* values) are given in ppm and Hz respectively. C assignments were realised by DEPT and HMQC experiments. MS were recorded on a VG-Autospec mass spectrometer.

5-Chloro-*N*-tosylpyridin-2(1*H*)-imine (2a):
5-Chloropyridin-2-amine (**1a**) (10 g, 77.78 mmol) was dissolved in anhyd pyridine (60 mL). TsCl (16.31 g, 85.56 mmol) was added and the solution was heated at 80–90 °C under argon overnight. Pyridine was removed in vacuo to give a white solid. Water (1.5 L) was added and the mixture was stirred for 90 min. The white solid was collected, dried in vacuo and then crystallised (EtOAc, 200 mL) to give 21.2 g (96%) of **2a** as a white solid; mp 176 °C (EtOAc).
^1H NMR (200 MHz, $CDCl_3$): δ = 2.39 (s, 3H), 7.41 (d,1H, J_{34} = 8.6 Hz, H_3), 7.47 (AA′BB′ system, 4H, *J* = 8.4 Hz, Ar*H*), 7.62 (dd, 1H, $J_{34=}$ 8.6 Hz, J_{46} = 2.5 Hz, H_4), 8.39 (d, 1H, J_{46} = 2.5 Hz, H_6).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 21.0 (*Me*), 113.2, 125.0, 127.1, 129.6, 137.2, 138.3, 143.5, 146.2, 150.1.
MS (EI^+): *m/z* (%) = 284.04 (M^+ + 2, 2.0), 282.04 (M^+, 5.6), 217.0 (100.0).

5-Iodo-*N*-tosylpyridin-2(1*H*)-imine (2b):
Compound **2b** was prepared as described for **2a**, starting from 5-iodopyridin-2-amine[6] (**1b**). **2b** was isolated as a brown solid in 85% yield; mp 205 °C (EtOAc).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 2.34 (s, 3H), 6.92 (d, 1H, J_{34} = 8.7 Hz, H_3), 7.56 (AA′BB′ system, 4H, J = 8.1 Hz, Ar*H*), 7.98 (d, 1H, J_{34} = 8.7 Hz, J_{46} = 2.2 Hz, H_4), 8.34 (d, 1H, J_{46} = 2.2 Hz, H_6), 11.23 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 21.2 (*Me*), 85.6 (C_5), 114.3, 127.3, 129.8, 137.4, 143.6, 146.4, 150.9, 153.3.
MS (FAB$^+$): *m/z* = 374.9 (M + H)$^+$, calcd 374.2.

5-(Methoxycarbonyl)-*N*-tosylpyridin-2(1*H*)-imine (2c):
Compound **2c** was prepared as described for **2a**, starting from 5-(methoxycarbonyl)pyridin-2-amine (**1c**). **2c** was isolated as a white solid in 93% yield; mp 214 °C (EtOAc).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 2.33 (s, 3H, Ar*Me*), 3.79 (s, 3H, CO_2*Me*), 7.15 (d, 1H, J_{34} = 8.9 Hz, H_3), 7.58 (AA′BB′ system, 4H, J = 8.2 Hz, Ar*H*), 8.12 (dd, 1H, J_{46} = 2.2 Hz, J_{34} = 8.9 Hz, H_4), 8.57 (d, 1H, J_{46} = 2.2 Hz, H_6), 12.06 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 21.0 (Ar*Me*), 52.1 (CO_2*Me*), 112.0, 118.6, 127.1, 129.6, 137.5, 139.6, 143.4, 147.6, 155.1, 164.5 (*C*O_2Me).

1-(Carbamoylmethyl)-6-(methoxycarbonyl)-*N*-tosylpyridin-2(1*H*)-imine (3c):
i-Pr_2NEt (125.2 mL, 71.82 mmol) was added to a suspension of **2c** (20 g, 65.3 mmol) in anhyd DMF (120 mL) under argon. To the resulting solution was added 2-iodoacetamide (13.28 g, 71.82 mmol) and the mixture was stirred at r.t. for 24 h. The solution was poured onto water (60 mL) and stirred for 90 min. The solid was collected by filtration and washed with water (1 L) then with Et_2O (200 mL) and dried in vacuo to give **3c** as a white solid; yield: 21.76 g (92%).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 2.34 (s, 3H), 3.82 (s, 3H, CO_2*Me*), 4.89 (s, 2H), 7.39 (d, 1H, J_{34} = 9.5 Hz, H_3), 7.39 (bs, 1H, N*H*), 7.47 (AA′BB′ system, 4H, J = 8.1 Hz, Ar*H*), 7.79 (bs, 1H, N*H*), 8.07 (dd, 1H, J_{34} = 9.5 Hz, J_{46} = 2.2 Hz, H_4), 8.73 (d, 1H, J_{46} = 2.2 Hz, H_6).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 20.9 (*Me*), 52.3 (*Me*), 54.7 (CH_2), 112.6, 115.6 (CH), 125.9 (CH), 129.2 (CH), 139.6 (CH), 140.3, 141.8, 146.1 (CH), 156.1, 163.6 (*C*O_2Me), 167.2 (*C*ONH_2).
MS (FAB$^+$): *m/z* = 364.1 (M + H)$^+$, calcd 363.4.

1-(Carbamoylmethyl)-6-chloro-*N*-tosylpyridin-2(1*H*)-imine (3a):
Compound **3a** was prepared as described for **3c**, starting from **2a**. **3a** was isolated as a white solid in 85% yield.
^{1}H NMR (200 MHz, DMSO-d_6): δ = 2.32 (s, 3H), 4.78 (s, 2H), 7.32 (d, 1H, J_{34} = 9.7 Hz, H_3), 7.43 (bs, 1H, N*H*), 7.45 (AA′BB′ system, 4H, J = 8.1 Hz, Ar*H*), 7.81 (bs, 1H, N*H*), 7.82 (dd, 1H, J_{34} = 9.7 Hz, J_{46} = 2.7 Hz, H_4), 8.33 (d, 1H, J_{46} = 2.7 Hz, H_6).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 20.9 (*Me*), 54.5 (CH_2), 115.6, 116.9, 125.9, 140.1, 140.5, 141.5, 154.1, 167.1 (*C*ONH_2).
MS (EI$^+$): *m/z* (%) = 341.1 (M$^+$ + 2, 6.4), 339.1 (M$^+$, 17.4), 91 (100.0).

1-(Carbamoylmethyl)-6-iodo-*N*-tosylpyridin-2(1*H*)-imine (3b):
Compound **3b** was prepared as described for **3c**, starting from **2b**. **3b** was isolated as a brown solid in 86% yield; mp 246.7–247.5 °C.
^{1}H NMR (200 MHz, DMSO-d_6): δ = 2.32 (s, 3H), 4.75 (s, 2H), 7.15 (d, 1H, J_{34} = 9.5 Hz, H_3), 7.38 (bs, 1H, N*H*), 7.43 (AA′BB′ system, 4H, J = 8.2 Hz, Ar*H*), 7.77 (bs, 1H, N*H*), 7.90 (dd, 1H, J_{34} = 9.5 Hz, J_{46} = 2.2 Hz, H_4), 8.35 (d, 1H, J_{46} = 2.2 Hz, H_6).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 20.9 (Me), 54.2 (CH_2), 71.6 (C_5), 117.6 (CH), 125.9 (CH), 129.2 (CH), 140.6, 141.5, 146.5 (CH), 148.3, 154.2, 167.3 (*C*ONH_2).
MS (FAB$^+$): *m/z* = 432.0 (M + H)$^+$, calcd 432.2.

6-(Methoxycarbonyl)-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine (4c):
Compound **3c** (5 g, 13.76 mmol) in anhyd CH_2Cl_2 (75 mL) was dissolved in TFAA and the solution was refluxed for 3 h. Solvents were removed in vacuo and the solid was suspended in EtOAc (150 mL). After stirring for 30 min, the solid was collected and again stirred in water (50 mL) for 30 min. The solid was collected and dried in vacuo to give 1.92 g (49%) of **4c** as a white solid; mp 216.2–217.9 °C.
^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.88 (s, 3H), 7.57 (dd, 1H, J_{58} = 0.7 Hz, J_{78} = 9.5 Hz, H_8), 7.69 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.5 Hz, H_7), 8.41 (s, 1H, H_3), 9.38 (dd, 1H, J_{57} = 1.7 Hz, J_{58} = 0.7 Hz, H_5).
^{13}C NMR (75 MHz, DMSO-d_6, assigned by HMQC experiment): δ = 52.3 (Me), 103.8 (C_3), 115.2 (C_8), 115.5 (q, J_{CF} = 287.7 Hz, CO*C*F_3), 115.6, 124.3 (C_7), 131.2 (C_5), 140.6, 141.9, 154.1 (q, J_{CF} = 39.0 Hz, *C*O*C*F_3), 164.8 (*C*O_2Me).
MS (FAB$^+$): *m/z* = 288.1 (M + H)$^+$, calcd 288.0.

6-Chloro-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine (4a):
Compound **4a** was prepared as described for **4c**, starting from **3a**. After 5 h **4a** was isolated as a white solid in 76% yield (25 mL of EtOAc were required for 2.09 g of **3a** and 50 mL of water); mp 243.9–244.5 °C (EtOAc).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 7.33 (dd, 1H, J_{57} = 2.1 Hz, J_{78} = 9.5 Hz, H_7), 7.55 (d, 1H, J_{78} = 9.5 Hz, H_8), 8.24 (s, 1H, H_3), 8.88 (d, 1H, J_{57} = 2.1 Hz, H_5), 12.54 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 103.4 (C_3), 115.7 (q, J_{CF} = 287.3 Hz, CO*C*F_3), 116.6 (CH), 119.1, 125.0 (CH), 126.1 (CH), 139.8, 140.1, 154.1 (q, J_{CF} = 38.5 Hz, *C*O*C*F_3).
MS (FAB$^+$): *m/z* = 264.0 (M + H)$^+$, calcd 264.0.
Anal. Calcd for $C_9H_5ClF_3N_3O$•0.33 H_2O: C, 40.09; H, 2.12; N, 15.58. Found: C, 40.12; H, 2.13; N, 15.07.

6-Iodo-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine (4b):
Compound **4b** was prepared as described for compound **4c**, starting from **3b**. After 5 h, **4b** was isolated as a white solid in 63% yield (8 mL of EtOAc were required for 0.751 g of **3b** and 50 mL of water); mp 247 °C (EtOAc).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 7.35 (dd, 1H, J_{58} = 0.9 Hz, J_{78} = 9.3 Hz, H_8), 7.47 (dd, 1H, J_{57} = 1.6 Hz, J_{78} = 9.3 Hz, H_7), 8.19 (s, 1H, H_3), 8.96 (dd,1H, J_{58} = 0.9 Hz, J_{57} = 1.6 Hz, H_5), 12.50 (bs,1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 76.0 (C_6), 102.6 (C_3), 115.7 (q, J_{CF} = 287.3 Hz, CO*C*F_3), 117.1 (CH), 131.7 (CH), 132.9 (CH), 139.5 (C_2 or C_9), 139.9 (C_9 or C_2), 154.1 (q, J_{CF} = 37.9 Hz, *C*O*C*F_3).
MS (FAB$^+$): *m/z* = 356.0 (M + H)$^+$, calcd 355.9.
Anal. Calcd for $C_9H_5F_3IN_3O$•0.25 H_2O: C, 30.06; H, 1.54; N, 11.69. Found: C, 30.11; H, 1.65; N, 11.45.

Sulfenylation at the 3-Position; General Procedure:
PIFA (1.5 equiv) was added to a stirred solution (or suspension) of imidazo[1,2-*a*]pyridine **4a–c** (50 mg) and arenethiol (2 equiv) in 1,1,1,3,3,3-hexafluoropropan-2-ol (1 mL) at r.t. under argon. The mixture was stirred for several hours (see Table). The solvents were removed and the resulting solid was dissolved in CH_2Cl_2 (15 mL) and washed with brine. After drying (Na_2SO_4) the solvent was removed. The solid was washed with CH_2Cl_2 or CH_2Cl_2/hexane (1:1) to give the sulfenylated material as a white solid in its pure form.

*6-Chloro-3-(phenylthio)-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine* (**6a**): isolated in 77% yield after washing with CH_2Cl_2/hexane (1:1).
^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.91–6.97 (m, 2H, Ar*H*), 7.14–7.20 (m, 3H, Ar*H*), 7.30 (dd, 1H, J_{57} = 2.0 Hz, J_{78} = 9.5 Hz, H_7), 7.59 (d, 1H, J_{78} = 9.5 Hz, H_8), 8.13 (d, 1H, J_{57} = 2.0 Hz, H_5), 8.84 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 105.7 (C_3), 115.7 (q, J_{CF} = 288.6 Hz, CO*C*F_3), 118.3, (CH), 121.5 (CH), 122.5 (CH), 126.8 (CH), 128.5 (CH), 133.1 (CH), 133.1, 143.0, 144.1, 155.8 (q, J_{CF} = 37.0 Hz, *C*O*C*F_3).
MS (FAB$^+$): *m/z* = 372.1 (M + H)$^+$, calcd 371.0.

Anal. Calcd for $C_{15}H_9ClF_3N_3OS \bullet 0.2\ H_2O$: C, 48.46; H, 2.44; N, 11.3. Found: C, 48.31; H, 2.56; N, 11.03.

6-Iodo-3-(phenylthio)-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**6b**): isolated in 84% yield after washing with CH_2Cl_2/hexane (1:1).
^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.85–6.98 (m, 2H, Ar*H*), 7.12–7.26 (m, 3H, Ar*H*), 7.41 (dd, 1H, J_{58} = 0.7 Hz, J_{78} = 9.4 Hz, H_8), 7.49 (dd, 1H, J_{57} = 1.6 Hz, J_{78} = 9.4 Hz, H_7), 8.32 (m, 1H, H_5), 9.05 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 78.9 (C_6), 104.6 (C_3), 115.9 (q, J_{CF} = 286.5 Hz, CO*C*F$_3$), 118.6 (CH), 126.6 (CH), 126.7 (CH), 128.9 (CH), 129.6 (CH), 133.2, 135.3 (CH), 143.2, 143.8, 155.8 (q, J_{CF} = 35.9 Hz, *C*OCF$_3$).
MS (FAB$^+$): *m/z* = 464.0 (M + H)$^+$, calcd 463.9.
Anal. Calcd for $C_{15}H_9F_3IN_3OS$: C, 38.59; H, 2.03; N, 9.00. Found: C, 38.69; H, 2.16; N, 8.63.

6-(Methoxycarbonyl)-3-(phenylthio)-2-(trifluoracetamido)imidazo[1,2-a]pyridine (**6c**): isolated in 83% yield after washing with CH_2Cl_2/hexane (1:1).
^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.86 (s, 3H, CO_2*Me*), 6.93–6.98 (m, 2H, Ar*H*), 7.13–7.24 (m, 3H, Ar*H*), 7.66 (dd, 1H, J_{58} = 0.9 Hz, J_{78} = 9.4 Hz, H_8), 7.88 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.4 Hz, H_7), 8.80 (bs, 1H, N*H*), 8.83 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.4 Hz, H_5).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 52.7 (CO_2*Me*), 106.0 (C_3), 115.8 (q, J_{CF} = 288.6 Hz, CO*C*F$_3$), 117.2 (CH), 117.3, 126.4 (CH), 126.5 (CH), 126.8 (CH), 127.4 (CH), 129.7 (CH), 133.1, 145.2, 145.3, 155.7 (q, J_{CF} = 37.5 Hz, *C*OCF$_3$), 164.2 (*C*O$_2$Me).
MS (FAB$^+$): *m/z* = 396.1 (M + H)$^+$, calcd 396.1.
Anal. Calcd for $C_{17}H_{12}F_3N_3O_3S$: C, 51.64; H, 3.06; N, 10.63. Found: C, 51.58; H, 3.14; N, 10.70.

6-Chloro-3-(4-chlorophenylthio)-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**7a**): isolated in 72% yield after washing with CH_2Cl_2.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.03 (AA′BB′ system, 4H, *J* = 8.7 Hz, Ar*H*), 7.32 (dd, 1H, J_{57} = 2.0 Hz, J_{78} = 9.5 Hz, H_7), 7.59 (dd, 1H, J_{58} = 0.8 Hz, J_{78} = 9.5 Hz, H_8), 8.09 (dd, 1H, J_{57} = 2.0 Hz, J_{58} = 0.8 Hz, H_5), 8.79 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 105.1 (C_3), 115.8 (q, J_{CF} = 285.0 Hz, CO*C*F$_3$), 118.4, (CH), 121.6 (CH), 122.5 (CH), 128.4 (CH), 128.7 (CH), 129.4 (CH), 131.4, 132.4, 143.2, 144.3, 155.8 (q, J_{CF} = 38.3 Hz, *C*OCF$_3$).
MS (FAB$^+$): *m/z* = 406.0 (M + H)$^+$, calcd 406.0.
Anal. Calcd for $C_{15}H_8Cl_2F_3N_3OS \bullet 0.2\ H_2O$: C, 43.96; H, 2.07; N, 10.25. Found: C, 43.97; H, 2.37; N, 9.95.

3-(4-Chlorophenylthio)-6-iodo-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**7b**): isolated in 75% yield after washing with CH_2Cl_2.
^{1}H NMR (200 MHz, DMSO-d_6): δ = 7.20 (AA′BB′ system, 4H, *J* = 8.6 Hz, Ar*H*), 7.58 (dd, 1H, J_{78} = 9.4 Hz, H_8), 7.73 (dd, 1H, J_{57} = 1.6 Hz, J_{78} = 9.4 Hz, H_7), 8.47 (m, 1H, H_5), 11.93 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 79.6 (C_6), 104.0 (C_3), 115.8 (q, J_{CF} = 285.7 Hz, CO*C*F$_3$), 118.6 (CH), 128.2 (CH), 129.0 (CH), 129.5 (CH), 131.4, 132.5, 135.5 (CH),143.4, 143.7, 155.8 (q, J_{CF} = 38.1 Hz, *C*OCF$_3$).
MS (FAB$^+$): *m/z* = 497.9 (M + H)$^+$, calcd 497.9.
Anal. Calcd for $C_{15}H_8ClF_3IN_3OS \bullet 0.25\ H_2O$: C, 35.88; H, 1.71; N, 8.37. Found: C, 35.92; H, 1.72; N, 8.07.

3-(4-Chlorophenylthio)-6-(methoxycarbonyl)-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**7c**): isolated in 80% yield after washing with CH_2Cl_2.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.98 (s, 3H, CO_2*Me*), 7.04 (AA′BB′ system, 4H, *J* = 8.6 Hz, Ar*H*), 7.65 (dd, 1H, J_{58} = 1.0 Hz, J_{78} = 9.4 Hz, H_8), 7.90 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.4 Hz, H_7), 8.81 (dd, 1H, J_{57} = 1.7 Hz, J_{58} = 1.0 Hz, H_5), 10.15 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 52.7 (CO_2*Me*), 105.2 (C_3), 115.8 (q, J_{CF} = 286.0 Hz, CO*C*F$_3$), 117.3, 117.5 (CH), 126.6 (CH), 127.4 (CH), 128.0 (CH), 129.6 (CH), 131.4, 132.4, 145.4, 155.3 (q, J_{CF} = 37.5 Hz, *C*OCF$_3$), 164.2 (*C*O$_2$Me).
MS (FAB$^+$): *m/z* = 430.0 (M + H)$^+$, calcd 430.1.
Anal. Calcd for $C_{17}H_{11}ClF_3N_3O_3S \bullet 1\ H_2O$: C, 45.59; H, 2.93 ; N, 9.38. Found: C, 45.54; H, 2.56; N, 9.05.

6-Chloro-3-(4-fluorophenylthio)-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**8a**): isolated in 96% yield after washing with CH_2Cl_2/hexane (1:1).
^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.86–7.03 (m, 4H, Ar*H*), 7.30 (dd, 1H, J_{57} = 2.0 Hz, J_{78} = 9.5 Hz, H_7), 7.58 (dd, 1H, J_{58} = 0.7 Hz, J_{78} = 9.5 Hz, H_8), 8.13 (dd, 1H, J_{57} = 2.0 Hz, J_{58} = 0.7 Hz, H_5), 8.69 (bs, 1H, NH).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 106.3 (C_3), 115.8 (q, J_{CF} = 288.2 Hz, CO*C*F$_3$), 116.6 (d, CH, J_{CF} = 22.2 Hz), 118.3 (CH), 118.7, 121.6, 122.6 (CH), 128.5 (CH), 129.6 (d, CH, J_{CF} = 8.1 Hz), 143.0, 143.9, 155.9 (q, J_{CF} = 37.5 Hz, *C*OCF$_3$), 161.3 (d, J_{CF} = 244.6 Hz).
MS (FAB$^+$): *m/z* = 390.1 (M + H)$^+$, calcd 390.1.
Anal. Calcd for $C_{15}H_8ClF_4N_3OS$: C, 45.80; H, 2.15; N, 10.68. Found: C, 45.70; H, 2.17; N, 10.66.

3-(4-Fluorophenylthio)-6-iodo-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**8b**): isolated in 73% yield after washing with CH_2Cl_2.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.87–7.02 (m, 4H), 7.41 (dd, J_{58} = 0.9 Hz, J_{78} = 9.3 Hz, 1H, H_8), 7.52 (dd, J_{57} = 1.6 Hz, J_{78} = 9.3 Hz, 1H, H_7), 8.33 (dd, J_{57} = 1.6 Hz, J_{58} = 0.9 Hz, 1H, H_5), 8.71 (bs, 1H).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 79.0 (C_6), 105.1 (C_3), 115.8 (q, J_{CF} = 286.5 Hz, CO*C*F$_3$), 116.6 (d, J_{CF} = 22.3 Hz), 118.6 (CH), 128.6 (d, J_{CF} = 3.0 Hz), 128.9 (CH), 129.4 (d, J_{CF} = 8.2 Hz), 134.5 (CH), 143.2, 143.3, 155.8 (q, J_{CF} = 37.0 Hz, *C*OCF$_3$), 161.2 (d, J_{CF} = 244.1 Hz).
MS (FAB$^+$): *m/z* = 482.1 (M + H)$^+$, calcd 481.9.
Anal. Calcd for $C_{15}H_8F_4IN_3OS$: C, 37.00; H, 1.79; N, 8.62. Found: C, 36.94; H, 1.82; N, 8.44.

3-(4-Fluorophenylthio)-6-(methoxycarbonyl)-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**8c**): isolated in 74% yield after washing with CH_2Cl_2.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.87 (s, 3H, CO_2*Me*), 6.86–7.06 (m, 4H, Ar*H*), 7.64 (dd, 1H, J_{58} = 0.9 Hz, J_{78} = 9.4 Hz, H_8), 7.89 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.4 Hz, H_7), 8.85 (dd, 1H, J_{57} = 1.7 Hz, J_{58} = 0.9 Hz, H_5), 8.88 (bs,1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 52.7 (CO_2*Me*), 106.4 (C_3), 115.8 (q, J_{CF} = 288.6 Hz, CO*C*F$_3$), 116.8 (d, CH, J_{CF} = 18.3 Hz), 117.3 (CH), 117.4, 126.5 (CH), 127.4 (CH), 128.5 (d, J_{CF} = 2.2 Hz), 129.0 (d, CH, J_{CF} = 8.2 Hz), 145.0, 145.3, 155.7 (q, J_{CF} = 38.5 Hz, *C*OCF$_3$), 161.2 (d, J_{CF} = 244.2 Hz), 164.3 (*C*O$_2$Me).
MS (FAB$^+$): *m/z* = 414.1 (M + H)$^+$, calcd 414.1.
Anal. Calcd for $C_{17}H_{11}F_4N_3O_3S$: C, 48.34; H, 2.86; N, 9.90. Found: C, 48.45; H, 2.58; N, 9.89.

6-Chloro-3-(4-methoxyphenylthio)-2-(trifluoroacetamido)imidazo[1,2-a]pyridine (**9a**): isolated in 91% yield after washing with CH_2Cl_2/hexane (1:1).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 3.69 (s, 3H, O*Me*), 7.04 (AA′BB′ system, 4H, *J* = 8.8 Hz, Ar*H*), 7.54 (dd, 1H, J_{57} = 1.9 Hz, J_{78} = 9.4 Hz, H_7), 7.76 (d, 1H, J_{78} = 9.4 Hz, H_8), 8.50 (d, 1H, J_{57} = 1.9 Hz, H_5), 11.92 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 55.2 (O*Me*), 107.9 (C_3), 115.2 (CH), 115.3 (q, J_{CF} = 286.0 Hz, CO*C*F$_3$), 118.3, (CH), 121.3, 122.5 (CH), 122.8, 128.2 (CH), 130.4, (CH), 142.6, 143.4, 155.9 (q, J_{CF} = 36.8 Hz, *C*OCF$_3$), 158.9.
MS (FAB$^+$): *m/z* = 402.1 (M + H)$^+$, calcd 402.0.

*6-Iodo-3-(4-methoxyphenylthio)-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine* (**9b**): isolated in 82% yield after washing with CH_2Cl_2/hexane (1:1).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 3.69 (s, 3H, O*Me*), 7.00 (AA′BB′ system, 4H, *J* = 8.8 Hz, Ar*H*), 7.55 (d, 1H, J_{78} = 9.4 Hz, H_7), 7.69 (dd, 1H, J_{57} = 1.6 Hz, J_{78} = 9.4 Hz, H_8), 8.52 (m, 1H, H_5), 11.90 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 55.3 (O*Me*), 78.8 (C_6), 106.7 (C_3), 115.3 (CH), 115.9 (q, J_{CF} = 286.5 Hz, CO*C*F$_3$), 118.6 (CH), 122.9, 128.9 (CH), 130.2 (CH), 135.0 (CH), 142.6, 142.8, 155.7 (q, J_{CF} = 37.6 Hz, *C*OCF$_3$), 158.8.
MS (FAB$^+$): *m/z* = 494.0 (M + H)$^+$, calcd 493.9.
Anal. Calcd for $C_{16}H_{11}F_3IN_3O_2S$: C, 35.70; H, 3.00; N, 7.81. Found: C, 35.90; H, 2.20; N, 7.84.

*6-(Methoxycarbonyl)-3-(4-methoxyphenylthio)-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine* (**9c**): isolated in 82% yield after washing with CH_2Cl_2/hexane (1:1).
^{1}H NMR (200 MHz, DMSO-d_6): δ = 3.68 (s, 3H, O*Me*), 3.86 (s, 3H, CO_2*Me*), 7.01 (AA′BB′ system, 4H, *J* = 8.6 Hz, Ar*H*), 7.79 (d, 1H, J_{78} = 9.4 Hz, H_8), 7.87 (dd, 1H, J_{57} = 1.3 Hz, J_{78} = 9.4 Hz, H_7), 8.79 (m, 1H, H_5), 12.02 (bs,1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 52.7 (CO_2*Me*), 55.2 (O*Me*), 108.0 (C_3), 115.4 (CH), 115.9 (q, J_{CF} = 288.6 Hz, CO*C*F$_3$), 117.3 (CH), 122.9, 126.2 (CH), 127.5 (CH), 129.8 (CH), 144.4, 144.9, 155.8 (q, J_{CF} = 37.4 Hz, *C*OCF$_3$), 158.8, 164.3 (*C*O$_2$Me).
MS (FAB$^+$): *m/z* = 426.1 (M + H)$^+$, calcd 426.1.
Anal. Calcd for $C_{18}H_{14}F_3N_3O_4S$: C, 50.29; H, 3.40; N, 9.77. Found: C, 50.25; H, 3.17; N, 9.58.

*6-Chloro-3-(3-chlorophenylthio)-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine* (**11a**): isolated in 69% yield after washing with hexane.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.77–6.83 (m, 1H, Ar*H*), 6.92–6.94 (m, 1H, ArH), 7.10–7.14 (m, 2H, ArH), 7.33 (dd, 1H, J_{57} = 2.0 Hz, J_{78} = 9.5 Hz, H_7), 7.61 (dd, 1H, J_{58} = 0.8 Hz, J_{78} = 9.5 Hz, H_8), 8.11 (dd, 1H, J_{57} = 2.0 Hz, J_{58} = 0.8 Hz, H_5), 8.96 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 104.6 (C_3), 115.8 (q, J_{CF} = 288.1 Hz, CO*C*F$_3$), 118.4 (CH), 121.7, 122.7 (CH), 125.1 (CH), 126.0 (CH), 126.7 (CH), 128.8 (CH), 131.0 (CH), 134.1, 135.8, 143.2, 144.5, 155.8 (q, J_{CF} = 37.9 Hz, *C*OCF$_3$).
MS (FAB$^+$): *m/z* = 406.1 (M + H)$^+$, calcd 406.0.
Anal. Calcd for $C_{15}H_8Cl_2F_3N_3OS$: C, 44.07; H, 2.04; N, 10.28. Found: C, 44.08; H, 2.09; N, 10.04.

*3-(3-Chlorophenylthio)-6-(methoxycarbonyl)-2-(trifluoroacetamido)imidazo[1,2-*a*]pyridine* (**11c**): isolated in 87% yield after washing with CH_2Cl_2.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.87 (s, 3H, CO_2*Me*), 6.83–6.88 (m, 1H, Ar*H*), 6.95–6.97 (m, 1H, Ar*H*), 7.06–7.11(m, 1H, Ar*H*), 7.62 (dd, 1H, J_{58} = 0.8 Hz, J_{78} = 9.3 Hz, H_8), 7.92 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.3 Hz, H_7), 8.81 (dd, 1H, J_{57} = 1.7 Hz, J_{58} = 0.8 Hz, H_5), 10.52 (bs,1H, N*H*).
^{13}C NMR (50 MHz, $CDCl_3$): δ = 52.8 (CO_2*Me*), 103.5 (C_3), 115.7 (q, J_{CF} = 287.5 Hz, COCF$_3$), 116.8, 118.3, 124.4, 126.1, 127.2, 127.6, 127.9, 130.6, 135.3, 135.5, 145.6, 146.0, 154.9 (q, J_{CF} = 39.0 Hz, *C*OCF$_3$), 164.5 (*C*O$_2$Me).
MS (FAB$^+$): *m/z* = 430.0 (M + H)$^+$, calcd 430.0.

Hydrolysis of Trifluoroacetamides; General Procedure:
The respective imidazopyridine trifluoroacetamide derivative was dissolved in CH_2Cl_2/MeOH (98:2, 15 mL). Silica gel was added to the solution. The mixture was stirred vigorously for 1–2 d. The conversion to the amine was followed by TLC (CH_2Cl_2/MeCN 4:1). The residue was filtered and the silica gel was washed with MeCN (10 mL). Removal of the solvents gave the desired compound as a pale-yellow solid.

*2-Amino-6-chloro-3-(4-chlorophenylthio)imidazo[1,2-*a*]pyridine* (**12a**): isolated in 70% yield after column chromatography.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.43 (bs, 2H, NH_2), 7.06 (AA′BB′ system, 4H, *J* = 8.6 Hz, Ar*H*), 7.07 (dd, 1H, J_{57} = 2.0 Hz, J_{78} = 9.3 Hz, H_7), 7.34 (dd, 1H, J_{58} = 0.8 Hz, J_{78} = 9.5 Hz, H_8), 8.05 (dd, 1H, J_{57} = 2.0 Hz, J_{58} = 0.8 Hz, H_5).
^{13}C NMR (50 MHz, $CDCl_3$): δ = 89.9, 115.2 (CH), 120.2, 121.5 (CH), 126.6 (CH), 127.0 (CH), 129.4, (CH), 132.1, 133.9, 144.0, 157.0.

*2-Amino-3-(4-chlorophenylthio)-6-iodoimidazo[1,2-*a*]pyridine* (**12b**): isolated in 81% yield after washing with hexane.
^{1}H NMR (200 MHz, DMSO-d_6): δ = 4.37 (bs, 2H, NH_2), 6.99 (AA′BB′ system, 4H, *J* = 8.5 Hz, Ar*H*), 7.11 (dd, 1H, J_{58} = 0.6 Hz, J_{78} = 9.1 Hz, H_8), 7.35 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.1 Hz, H_7), 8.16 (dd, 1H, J_{57} = 1.7 Hz, J_{58} = 0.6 Hz, H_5).
^{13}C NMR (50 MHz, $CDCl_3$): δ = 74.5 (C_6), 86.7, 115.3 (CH), 126.9 (CH), 127.3 (CH), 129.3 (CH), 130.5, 133.2 (CH), 135.3, 144.1, 157.9.
MS (FAB$^+$): *m/z* = 402.0 (M + H)$^+$, calcd 401.9.
HRMS (FAB) calcd for $C_{13}H_{10}ClN_2S$ 401.932874, found 401.931500.

*2-Amino-3-(4-chlorophenylthio)-6-(methoxycarbonyl)imidazo[1,2-*a*]pyridine* (**12c**): isolated in 88% yield after washing with hexane.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.84 (s, 3H, CO_2*Me*), 4.47 (bs, 2H, NH_2), 7.00 (AA′BB′ system, 4H, *J* = 8.7 Hz, Ar*H*), 7.33 (dd, 1H, J_{58} = 0.8 Hz, J_{78} = 9.2 Hz, H_8), 7.75 (dd, 1H, J_{57} = 1.8 Hz, J_{78} = 9.2 Hz, H_7), 8.68 (dd, 1H, J_{57} = 1.8 Hz, J_{58} = 0.8 Hz, H_5), 10.15 (bs, 1H, N*H*).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 51.7 (CO_2*Me*), 87.2, 112.9 (CH), 114.4, 124.8 (CH), 125.2 (CH), 126.7 (CH), 129.0 (CH), 130.5, 134.7, 146.1, 158.8, 164.4 (*C*O$_2$Me).
MS (FAB$^+$): *m/z* = 334.1 (M + H)$^+$, calcd 334.0.
HRMS (FAB) calcd for $C_{15}H_{13}ClN_3O_2S$ 334.041701, found 334.042000.

*2-Amino-6-chloro-3-(3-chlorophenylthio)imidazo[1,2-*a*]pyridine* (**13a**): isolated in 72% yield after column chromatography.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.49 (bs, 2H, NH_2), 6.74–6.79 (m, 1H, Ar*H*), 6.87–6.89 (m, 1H, Ar*H*), 7.00–7.07 (m, 2H, Ar*H*), 7.11 (dd, 1H, J_{57} = 2.0 Hz, J_{78} = 9.3 Hz, H_7), 7.25 (dd, 1H, J_{58} = 0.8 Hz, J_{78} = 9.3 Hz, H_8), 8.07 (dd, 1H, J_{57} = 2.0 Hz, J_{58} = 0.8 Hz, H_5).
^{13}C NMR (50 MHz, $CDCl_3$): δ = 89.2, 115.1 (CH), 120.1, 121.5 (CH), 123.2 (CH), 124.9 (CH), 126.3 (CH), 127.1 (CH), 130.3, (CH), 135.3, 137.7, 144.1, 157.3.
MS (FAB$^+$): *m/z* = 310.1 (M + H)$^+$, calcd 310.0.
HRMS (FAB) calcd for $C_{13}H_{10}NCl_2N_3S$ 309.997250, found 309.996300.

*2-Amino-3-(3-chlorophenylthio)-6-(methoxycarbonyl)imidazo[1,2-*a*]pyridine* (**13c**): isolated in 65% yield after column chromatography.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.84 (s, 3H, CO_2*Me*), 4.50 (bs, 2H, NH_2), 7.00 (AA′BB′ system, 4H, *J* = 8.6 Hz, Ar*H*), 7.33 (d, 1H, J_{78} = 9.1 Hz, H_8), 7.76 (dd, 1H, J_{57} = 1.7 Hz, J_{78} = 9.1 Hz, H_7), 8.68 (d, 1H, J_{57} = 1.7 Hz, H_5).
^{13}C NMR (50 MHz, DMSO-d_6): δ = 52.7 (CO_2*Me*), 87.2, 112.9 (CH), 114.4, 124.8 (CH), 125.2 (CH), 126.7 (CH), 129.0 (CH), 130.5, 134.7, 146.1, 158.8, 164.4 (*C*O$_2$Me).
MS (FAB$^+$): *m/z* = 334.1 (M + H)$^+$, calcd 334.0.

*2-Amino-3-(4-fluorophenylthio)-6-(methoxycarbonyl)imidazo[1,2-*a*]pyridine* (**14c**): isolated in 55% yield after column chromatography.
^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.84 (s, 3H, CO_2*Me*), 4.53 (bs, 2H, NH_2), 6.82–6.96 (m, 4H, Ar*H*), 7.31 (dd, J_{58} = 0.9 Hz, J_{78} = 9.2 Hz, H_8), 7.74 (dd, J_{57} = 1.7 Hz, J_{78} = 9.2 Hz, H_7), 8.71 (dd, J_{57} = 1.7 Hz, J_{58} = 0.9 Hz, H_5).
^{13}C NMR (50 MHz, $CDCl_3$): δ = 52.3 (CO_2*Me*), 90.6, 113.9 (CH), 115.9, 116.4 (d, CH, J_{CF} = 22.3 Hz), 126.0 (CH), 126.9 (CH), 127.4

(d, CH, J_{CF} = 8.0 Hz), 130.5 (d, J_{CF} = 3.1 Hz), 146.5, 157.6, 161.5 (d, J_{CF} = 245.9 Hz), 164.4 (CO_2Me).
MS (FAB^+): *m/z* = 318.1 $(M + H)^+$, calcd 318.0.
HRMS (FAB) calcd for $C_{15}H_{13}FN_3O_2S$ 318.07125, found 318.07040.

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(1) Montgomery, J. A.; Secrist, A. A. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Pergamon: Oxford, 1984; Chapter 4.10; p 607 and references cited therein.
Minguez, L. M.; Gandásegui, T.; Vaquero, J. J.; Alvarez-Builla, J.; Garcìa-Navio, J. L.; Gago, F.; Ortiz, A. R.; Gómez-Sal, P.; Torres, R.; Rodrigo, M. M. *J. Org. Chem.* **1993**, *58*, 6030.
Gueiffer, A.; Viols, H.; Blache, Y.; Chavignon, O.; Teulade, J. C.; Aumelas, A.; Chapat, J. P. *Heterocycles* **1994**, *38*, 55.

(2) (a) Bonnet, P. A.; Michel, A.; Laurent, F.; Sablayrolles, C.; Rechencq, E.; Mani, J. C.; Boucard, M.; Chapat, J. P. *J. Med. Chem.* **1992**, *35*, 3353 and references cited therein.
(b) Bochis, R. J.; Dybas, R. A.; Eskola, P.; Kulsa, P.; Linn, B. O.; Lusi, A.; Meitzner, E. P.; Milkowski, J.; Mrozik, H.; Olen, L. E.; Peterson, A. H.; Tolman, R. L.; Wagner, A. F.; Waksmunski, F. S.; Egerton, J. R.; Ostlind, D. A. *J. Med. Chem.* **1978**, *21*, 235.
(c) Yamanaka, M.; Miyake, K.; Suda, S.; Ohhara, H.; Ogawa, T. *Chem. Pharm. Bull.* **1991**, *39*, 1556.
(d) Gudmundsson, K. S.; Drach, J. C.; Townsend, L. B. *Tetrahedron Lett.* **1996**, *37*, 6275.
(e) Bochis, R. J.; Olen, L. E.; Fisher, M. H.; Reamer, R. A.; Wilks, G.; Taylor, J. E.; Olson, G. *J. Med. Chem.* **1981**, *24*, 1483.

(3) Caldwell, C.; Mitchell, S. C. In *Comprehensive Medicinal Chemistry;* Hansch, C.; Sammes, P. G.; Taylor, J. B., Eds.; Pergamon: Oxford, 1990; Vol. 5; pp 143–162.
Sammes, P. G. In *Comprehensive Medicinal Chemistry;* Hansch, C.; Sammes, P. G.; Taylor, J. B., Eds.; Pergamon: Oxford, 1990; Vol. 2; pp 255–270.
Newall, C. E.; Hallam, D. P. In *Comprehensive Medicinal Chemistry;* Hansch, C.; Sammes, P. G.; Taylor, J. B., Eds.; Pergamon: Oxford, 1990; Vol. 2; pp 609–653.

(4) Griffen, E. J.; Roe, D. G.; Snieckus, V. *J. Org. Chem.* **1995**, *60*, 1484.

(5) Freeman, P. K.; Hutchinson, L. L. *J.Org. Chem.* **1980**, *45*, 1924.
Freeman, P. K.; Hutchinson, L. L. *J.Org. Chem.* **1983**, *48*, 4705 and references cited therein.
Cohen, T.; Bhupathy, M. *Acc. Chem. Res.* **1989**, *22*, 152.

(6) Fürstner, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 164.
Rieke, R. D. *Science* **1989**, *246*, 1260.
Ebert, G. W.; Rieke, R. D. *J. Org. Chem.* **1988**, *53*, 4482.
Wu Tse, C.; Xiong, H.; Rieke, R. D. *J. Org. Chem.* **1990**, *55*, 5045.
Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445.
Stark, D. E.; Klein, W. R.; Rieke, R. D. *Tetrahedron Lett.* **1993**, *34*, 3063.

(7) Widdowson, D. A.; Mowlem, T. J.; Gilday, J. P.; Dickens, M. J. *Tetrahedron* **1991**, *47*, 8621.

(8) Kita, Y.; Takada, T.; Mihara, S.; Whelan, B. A.; Tohma, H. *J. Org. Chem.* **1995**, *60*, 7144 and references cited therein for other sulfenylation reaction methodologies.

(9) For leading references on the use of hypervalent iodine(III) see: Varvoglis, A. *The Chemistry of Polycoordinated Iodine*; VCH: New York, 1992.
Kita, Y.; Tohma, H.; Yakura, T. *Trends Org. Chem.* **1992**, *3*, 113.
Stang, P. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 274.
Kita, Y.; Egi, M.; Ohtsubo, M.; Saiki, T.; Takada, T.; Tohma, H. *J. Chem. Soc., Chem. Commun.* **1996**, 2225.
Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Oka, S. *J. Am. Chem. Soc.* **1994**, *116*, 3684.

(10) Aminoiodopyridine **1b** was prepared following Magidson's procedure: Magidson, G.; Menshipoff, O. *Chem. Ber.* **1925**, *58*, 115.

(11) During the formation of **4c** we were able to isolate 4.8% of another regioisomer that probably is derived from the migration of the CF_3CO from the amino group to the 3-position.