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A facile and efficient method for the selective deacylation of *N*-arylacetamides and 2-chloro-*N*-arylacetamides catalyzed by $SOCl_2$

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Abstract Thionyl chloride efficiently and selectively promoted the deacylation of *N*-arylacetamides and 2-chloro-*N*-arylacetamides, under anhydrous conditions, without effecting the ester group, aminosulfonyl group, or benzyloxyamide group. This method, which has been successfully applied to a variety of substrates including different *N*-arylacetamides and 2-chloro-*N*-arylacetamides, has the attractive advantages of inexpensive reagents, satisfactory selectivity, excellent yields, short reaction time, and convenient workup. This new method can probably be used to selectively deacylate between aromatic amides and alkyl amides.

Keywords Thionyl chloride · *N*-arylacetamides · 2-chloro-*N*-arylacetamides · Deacylation

Introduction

Amino group protection is of key importance in organic synthesis. Acetylation is one of the most universal ways of protection of the amino group. The most popular reagents for acetylation of amino group are CH_3COCl and Ac_2O, and the acetylated products are usually obtained in high yields in alkaline media at ambient temperature.

Various methods have been reported for the deacetylation of aromatic amides, including:

1. Hydrolysis of the acetyl amino group under basic (NaOH [1–3], KOH [4, 5], etc.) or acidic (HCl [6, 7], HBr [8], AcOH [9], etc.) conditions;

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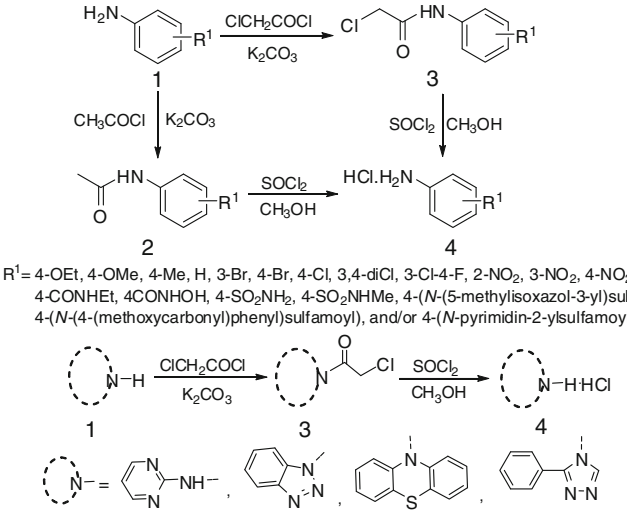
2. Alcoholysis of the acetyl amino group catalyzed by acid (HCl [10]) or alkali (CH_3ONa [11]) in alcohol.

Of the two methods, the first usually requires harsh conditions, for example high reaction temperature, excessively strong catalysts, or long time. Under such reaction conditions, the coexisting ester group is usually hydrolyzed more easily than corresponding amido group. Comparatively, the second method has the advantages of convenient operation, good yields and shorter reaction time.

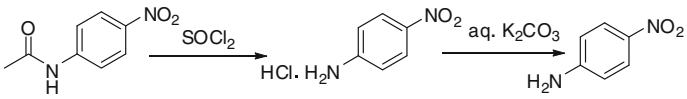
Thionyl chloride ($SOCl_2$) is a reactive chemical reagent mainly used in the industrial production of organochlorine compounds, which are often intermediates in pharmaceuticals and agrichemicals. It has not been studied as promoter in deacylation of aryl amides. We report herein a facile and efficient method for deacylation of *N*-arylacetamides and 2-chloro-*N*-arylacetamides catalyzed by $SOCl_2$. The reactions in shown in Scheme 1.

Results and discussion

To determine the optimum amount of $SOCl_2$ catalyst we initially studied the reaction of 4-nitroacetanilide (5 mmol) with different amounts of $SOCl_2$ in CH_3OH (13 mL) at room temperature (Scheme 2). It was found that use of less than 0.6 molar ratio of $SOCl_2$ to 4-nitroacetanilide gave a moderate yield of the corresponding aromatic amine and required a long time (Table 1, entries **1**–**2**), whereas use of more than 0.8 molar ratio gave an excellent yield in a short time (Table 1, entries **3**–**7**). Comprehensively taking the amount of $SOCl_2$, reaction time, and product yields into account, we chose 0.8 as the optimum molar ratio. This molar ratio is also suitable for other *N*-arylacetamides.



Scheme 1 Deacylation of *N*-arylacetamides and 2-chloro-*N*-arylacetamides



Scheme 2 Model reaction

Table 1 Catalytic effect of $SOCl_2$ on the deacetylation of 4-nitroacetanilide in CH_3OH

Entry	$SOCl_2$ (mmol)	Time (h)	Yield[a] (%)
1	1.0	16	41.1
2	2.0	14	83.2
3	3.0	5	99.1
4	4.0	2.5	99.6
5	5.0	2	99.7
6	6.0	1.1	99.8
7	7.0	0.7	99.8

Reaction conditions: 4-nitroacetanilide (5.0 mmol), CH_3OH (13.0 mL); 29 °C

[a] Isolated yield

Table 2 Deacetylation of 4-nitroacetanilide in the presence of $SOCl_2$ with different solvents

Entry	Solvent	Time (h)	Yield[a] (%)
1	CH_2Cl_2	12	Trace
2	$CHCl_3$	12	Trace
3	CH_3CN	12	Trace
4	THF	12	Trace
5	$(CH_3)_2CO$	12	Trace
6	CH_3OH	2.3	99.4
7	C_2H_5OH	7	98.7
8	*n*-C_3H_7OH	11.5	99.1

Reaction conditions: 4-nitroacetanilide (5.0 mmol), $SOCl_2$ (4.0 mmol), solvent (13.0 mL); 30 °C

[a] Isolated yield

The next work was to evaluate the solvent effect (Table 2). Different solvents, for example dichloromethane, chloroform, acetonitrile, tetrahydrofuran (THF), acetone, methanol, ethanol, and propanol, were used for transformation of 4-nitroacetanilide with $SOCl_2$ at ambient temperature. The experimental results showed that CH_3OH was the best solvent, with the highest yield and shortest reaction time (Table 2, entry **6**). It was also worthy of note that alcohols, for example CH_3OH, C_2H_5OH, and *n*-C_3H_7OH, promoted deacetylation of aromatic amides (Table 2, entries **6**–**8**), thus deacetylation of the model molecule may be a type of alcoholysis reaction.

We used a variety of catalysts to determine which was the most effective for deacetylation of 4-nitroacetanilide (5.0 mmol) at room temperature. The results obtained (Table 3) showed $SOCl_2$ was more efficient than conc. HCl, conc. H_2SO_4 and conc. HNO_3 for deacetylation of 4-nitroacetanilide under these conditions.

Finally the effect of temperature on the reaction was investigated (Table 4). Selecting the same model reaction, we examined the deacetylation of 4-nitroacetanilide (5.0 mmol) with $SOCl_2$ (4.0 mmol) at different temperatures in CH_3OH. As can be seen from Table 4, reaction rate and yield increased as the reaction

Table 3 Deacetylation of 4-nitroacetanilide in the presence of different catalysts with CH_3OH as solvent

Reaction conditions: 4-nitroacetanilide (5.0 mmol), CH_3OH (13.0 mL), 29 °C

[a] Isolated yield

Entry	Catalyst	Amount of catalyst (mmol)	Time (h)	Yield[a] (%)
1	conc. HCl	4.0	9.5	51.6
2	conc. H_2SO_4	4.0	14	45.3
3	conc. HNO_3	4.0	20	34.3
4	$SOCl_2$	4.0	2.5	99.6

Table 4 Deacetylation of 4-nitroacetanilide in the presence of $SOCl_2$ at different temperatures

Entry	Temp (°)	Time (h)	Yield[a] (%)
1	29	2.5	99.2
2	40	1.0	99.1
3	50	0.4	99.4
4	Reflux	0.1	99.6

Reaction conditions: 4-nitroacetanilide (5.0 mmol), $SOCl_2$ (4.0 mmol), CH_3OH (13.0 mL)

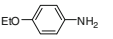
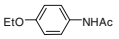
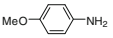
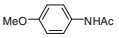
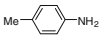
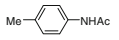
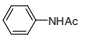
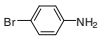
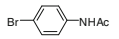
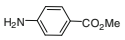
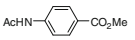
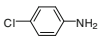
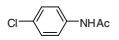
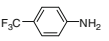
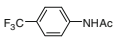
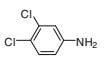
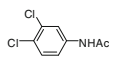
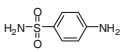
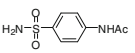
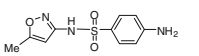
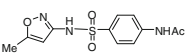
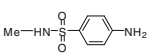
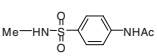
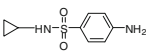
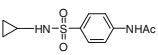
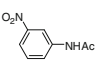
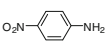
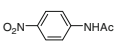
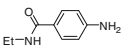
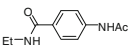
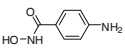
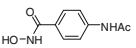
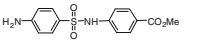
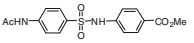
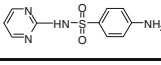
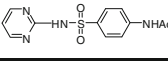
[a] Isolated yield

temperature was increased from 29 °C to reflux temperature. Hence reflux temperature was optimum because of its highest yield and shortest reaction time.

To evaluate the scope of this procedure, the deacetylation of other *N*-arylacetamides (Table 5) was also investigated under the optimum reaction conditions (Table 6). As shown, deacetylation of *N*-arylacetamides with the aid of $SOCl_2$ proceeded with excellent yields in CH_3OH solution at reflux temperature (Table 6, entries **1**–**19**). In addition, *N*-arylacetamides with electron-withdrawing groups in the aromatic ring (Table 6, entries **5**–**19**) were somewhat more reactive, with shorter reaction time (all less than 3.0 h) than those with electron-donating groups (Table 6, entries **1**–**3**, all more than 8.0 h). In particular, deacetylation of substrates with an NO_2 group in the aromatic ring required less than 0.2 h only, with excellent yields (Table 6, entry **14**–**15**), because of the strong electrophilic effect of the NO_2 group.

To expand the scope of this new method, we explored the deacylation of a variety of 2-chloro-*N*-aryl-acetamides (Table 7) in the presence of $SOCl_2$ (Table 8). It was of interest to note that deacylation of 2-chloro-*N*-arylacetamides (Table 8, entries **1**, **2**, **4**–**7**, **9**, **10**) was completed much more quickly and with much better yields than deacylation of *N*-arylacetamides with the same substituent groups in the aromatic ring (Table 6, entries **2**, **3**, **6**–**9**, **10**, **14**). Furthermore, deacylation of 2-chloro-*N*-aryl acetamides containing electron-donating groups, for example OCH_3, CH_3, in the aromatic ring (Table 8, entries **1**, **2**) was achieved within 2 h, whereas deacylation of those with electron-withdrawing groups, for example NO_2 (Table 8, entries **10**–**11**), required 0.05 h only. This difference indicated that electrophilic substituents in the aromatic ring has a fundamental effect on the rate of deacylation. Compared with 2-chloro-*N*-arylacetamides bearing a benzene ring (Table 8, entries

Table 5 Preparation of *N*-arylacetamides

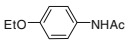
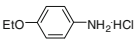
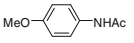
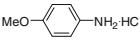
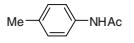
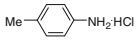
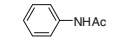
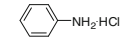
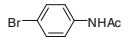
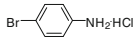
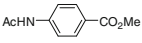
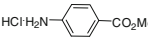
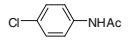
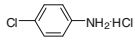
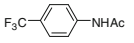
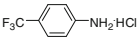
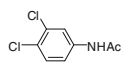
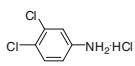
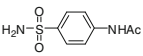
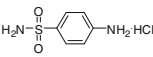
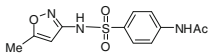
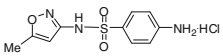
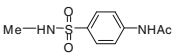
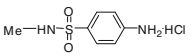
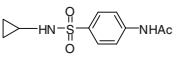
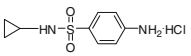
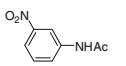
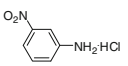
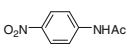
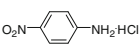
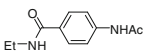
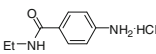
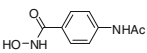
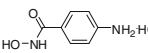
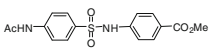
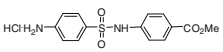
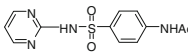
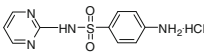
Entry	Compound **1**[a]	Product **2**[b]	Time(h)	Yield[c](%)	M.p. (°C)	Ref.
1			11	77.2	131.2-135.7 (134.4)	[12]
2			11	74.3	137.6-139.2 (130-132)	[13]
3			13	96.0	154.4-155.1 (151-154)	[14]
4			11	68.0	118.7-123.2 (114-116)	[15]
5			15	64.1	174.4-178.4 (173-174)	[16]
6			17	66.4	123.1-126.9 (127)	[17]
7			13	91.9	131.5-134.2 (172-174)	[18]
8			13	77.8	161.2-163.0 (153-155)	[19]
9			17	89.3	122.7-127.2 (121.9-123.3)	[20]
10			18	80.8	156.4-159.0 (165-166)	[21]
11			22	71.9	160.2-163.5 (220-221)	[22]
12			16	72.4	157.5-159.7 (152-153)	[23]
13			16	77.6	171.1-172.8	
14			15	67.8	144.5-145.8 (147.3-147.5)	[24]
15			15	64.2	215.1-216.5 (215-216)	[25]
16			16	78.4	184.2-186.7	
17			16	79.0	175.6-179.5	
18			16	75.4	172.4-175.8	
19			16	73.6	257.4-261.5 (257-258)	[26]

[a] The substrate(4 mmol) was treated with acetyl chloride (24 mmol) in the presence of 24 mmol K_2CO_3 in acetone at room temperature

[b] All products were identified by IR and ^{1}H NMR spectra

[c] Yields refer to pure isolated products

Table 6 $SOCl_2$-catalyzed deacylation of *N*-arylacetamides

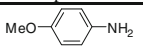
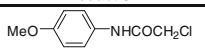
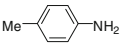
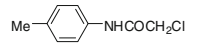
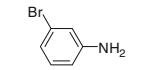
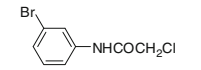
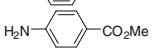
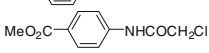
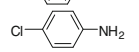
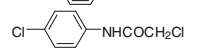
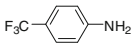
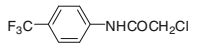
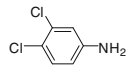
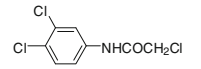
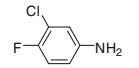
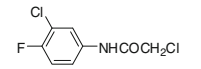
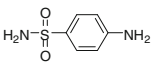
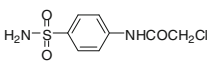
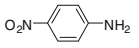
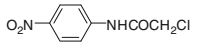
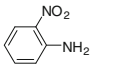
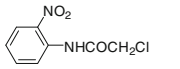
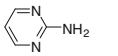
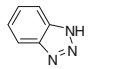
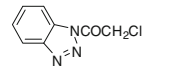
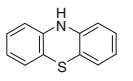
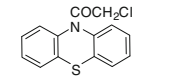
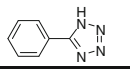
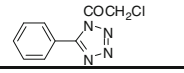
Entry	Compound **2**[a]	Product **4**[b]	Time(h)	Yield[c](%)	M.p. (°C)	Ref.
1			10.5	92.9	233.3-235.2 (233-234)	[27]
2			10.0	97.5	186.5-187.4 (185-186)	[28]
3			8.0	91.9	232.3-235.4 (232-235)	[29]
4			4.0	98.5	196.8-198.9	
5			3.0	94.7	165.2-167.0 (165.5)	[30]
6			3.0	98.8	270.1-272.5 (272)	[33]
7			2.5	93.1	249.1-251.3 (253)	[31]
8			2.5	91.6	201.2-203.8	
9			2.5	96.1	163.5-164.9 (164)	[32]
10			2.5	99. 5	263.1-265.5 (264)	[34]
11			2.0	97.6	186.4-187.8	
12			2.0	98.5	215.7-218.9	
13			2.5	98.0	205.4-206.3	
14			0.2	98.7	225.1-227.3 (225-227)	[35]
15			0.1	99.8	145.1-147.5 (145-146)	[36]
16			2.5	97.6	220.4-222.5	
17			2.6	98.0	230.1-232.3	
18			2.7	96.7	190.6-192.7	
19			2.4	95.4	215.3-217.4	

[a] The substrates (3 mmol) were treated with $SOCl_2$ (2.4 mmol) in CH_3OH at reflux temperature

[b] All products were identified by IR and ^1H NMR spectra

[c] Yields refer to pure isolated products

Table 7 Preparation of 2-chloro-*N*-arylacetamides

Entry	Compound **1**[a]	Product **3**[b]	Time(h)	Yield[c](%)	M.p. (°C)	Ref.
1			18	96.2	134.2-136.5 (125-127)	[37]
2			12	74.1	116.5-119.8 (130)	[38]
3			13	91.4	130.6-132.4 (113-114)	[39]
4			20	88.9	119.6-122.6 (144-146)	[40]
5			19	76.6	153.2-155.4 (150-155)	[41]
6			20	92.2	153.6-156.8 (158-160)	[42]
7			20	86.7	99.6-101.1 (105-106)	[43]
8			13	47.7	88.4-90.1	
9			12	78.2	236.1-239.3 (217)	[44]
10			15	84.5	193.7-196.5 (189-191)	[45]
11			20	50.4	84.4-86.0 (87-89)	[39]
12			18	66.5	116.8-118.1 (182)	[46]
13			20	52.8	79.4-81.1 (92-94)	[47]
14			20	56.5	121.1-124.2 (115-117)	[48]
15			16	81.4	184.9-187.1	

[a] The substrate(10 mmol) was treated with chloroacetyl chloride (12 mmol) in the presence of 12 mmol K_2CO_3 in acetone at 15 °C

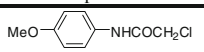
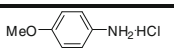
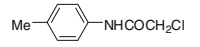
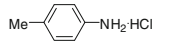
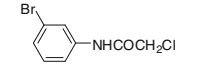
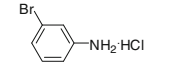
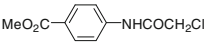
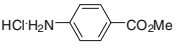
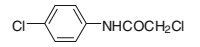
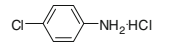
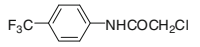
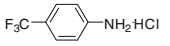
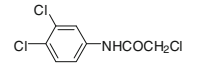
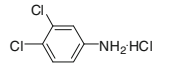
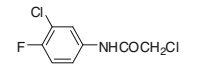
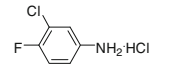
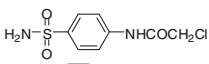
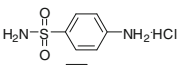
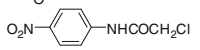
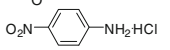
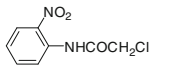
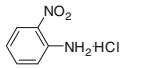
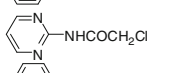
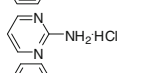
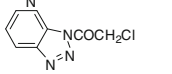
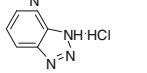
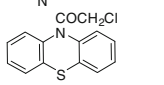
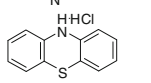
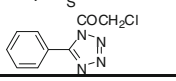
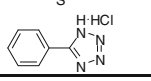
[b] All products were identified by IR and ^{1}H NMR spectra

[c] Yields refer to pure isolated products

1–**12**), those with a aromatic heterocyclic ring (Table 8, entries **12**–**15**) were, to some extent, less reactive and needed more than 3 h for completion of the reaction, but still afforded the corresponding products in excellent yields. We also found that both *N*-*p*-tolyl benzamide and *N*-benzyloxycarbonyl-benzamide could not be deacylated (not reported in this paper). Further applications of this new method to other substrates are still in progress.

The possible mechanism for this transformation is shown in Scheme 3. It is reasonable to assume that nucleophilic attack of alcohol on $SOCl_2$ produces HCl. Therefore, the mechanism proceeds through alcoholysis of *N*-arylacetamides (**1**)

Table 8 $SOCl_2$-catalyzed deacylation of 2-chloro-*N*-arylacetamides

Entry	Compound **3**[a]	Product **4**[b]	Time(h)	Yield[c](%)	M.p. (°C)	Ref.
1			2.0	99.4	185.0-186.5 (185-186)	[28]
2			2.0	99.5	232.1-234.2 (232-235)	[29]
3			2.0	99.6	230.1-231.9	
4			2.0	99.9	271.6-273.0 (272)	[33]
5			1.2	97.9	253.1-254.8 (253)	[31]
6			1.0	91.4	199.7-201.5	
7			1.0	99.5	164.1-166.0 (164)	[32]
8			1.0	99.2	193.2-195.0	
9			0.5	99.5	264.5-267.2 (264)	[34]
10			0.05	99.8	145.7-147.8 (145-146)	[36]
11			0.05	99.6	159.7-162.1	
12			4.0	99.6	204.2-206.0	
13			5.0	99.5	142.1-144.0	
14			3.5	99.4	173.5-175.0	
15			3.0	99.6	223.2-225.1	

[a] The substrates (3 mmol) were treated with $SOCl_2$ in CH_3OH (2.4 mmol) at reflux temperature

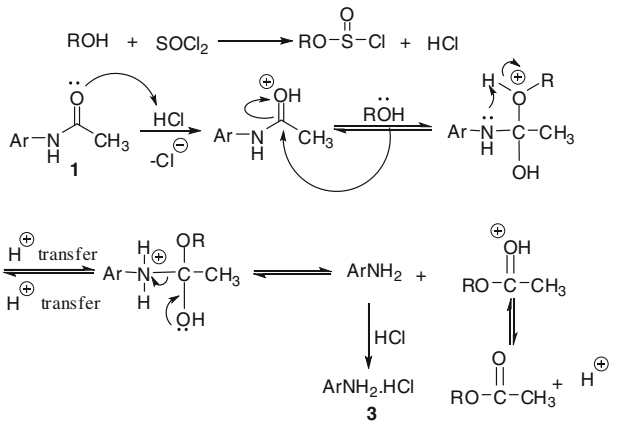
[b] All products were identified by IR and ^1H NMR spectra

[c] Yields refer to pure isolated products

leading to the formation of aromatic amides, which then furnish the corresponding aromatic amine hydrochlorides (**3**). We tried direct use of conc. HCl as the catalyst but yields were moderate only and longer reaction times were needed compared with use of $SOCl_2$ as catalyst.

Conclusion

$SOCl_2$ in alcohol is an extremely efficient reagent system for selective deacylation of aromatic amides. Facile conversion of aromatic amides to aromatic amine hydrochlorides has been achieved, with the remarkable advantages of excellent



Scheme 3 Proposed mechanism for alcoholysis of *N*-aryl-acetamides catalyzed by $SOCl_2$

yields, short reaction times, convenient workup, and satisfactory selectivity. The reaction is especially suitable when aromatic amido groups are present with ester groups, aminosulfonyl groups, or benzyloxyamide groups. We believe this reaction could be an important addition to existing methods.

Experimental

General method

Melting points were determined by use of an X-6 sophisticated micro-melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded in DMSO-d_6 or $CDCl_3$ on a Bruker AV-300 spectrometer; chemical shifts (δ) are expressed in ppm downfield from TMS, which was used as internal standard. Coupling constant (J) values are in Hz. The progress of the reactions was monitored by thin-layer chromatography (TLC) using several mobile phases of different polarity. All solvents and reagents were of chemical grade or analytical grade.

General procedure for synthesis of *N*-arylacetamides

To a solution of arylamine (6.0 mmol) and K_2CO_3 (36 mmol) in acetone (20 mL), acetyl chloride (36 mmol) was added dropwise and the reaction mixture was stirred at 0 °C for 0.25 h then left to warm to ambient temperature (approx. 30 °C). The progress of the reaction was monitored by TLC. On completion, the reaction mixture was filtered and the filtrate was evaporated with vacuum distillation to afford the crude product, which was dispersed in a mixture of petroleum ether (PE) and Et_2O to afford analytically pure product.

General procedure for synthesis of 2-chloro-*N*-arylacetamides

To a solution of arylamine (10 mmol) and K_2CO_3 (12 mmol) in acetone (20 mL), 2-chloroacetyl chloride (12 mmol) was added dropwise and the reaction mixture was stirred at 0 °C for 0.5 h then left to warm to 15 °C. The progress of the reaction was monitored by TLC. On completion, the reaction mixture was filtered and the filtrate was evaporated with vacuum distillation to afford the crude product, which was dispersed in a mixture of PE and Et_2O to afford analytically pure product.

General procedure for deacylation of *N*-arylacetamides

A mixture of *N*-arylacetamide (3 mmol) and thionyl chloride (2.4 mmol) was stirred magnetically in 6 mL methanol at reflux temperature and the progress of the reaction was monitored by TLC. The reaction mixture was evaporated with vacuum distillation to afford the crude product. Pure product was obtained by dispersion of the crude product in Et_2O.

General procedure for deacylation of 2-chloro-*N*-arylacetamides

A mixture of 2-chloro-*N*-arylacetamide (2 mmol) and thionyl chloride (1.6 mmol) was stirred magnetically in 6 mL methanol at reflux temperature and the progress of the reaction was monitored by TLC. The reaction mixture was evaporated with vacuum distillation to afford the crude product. The crude product was dispersed in Et_2O for 3 h to obtain the pure product.

Spectral data of some products

2-Chloro-N-(2-nitrophenyl)acetamide. ^{1}H NMR (300 MHz, DMSO-d_6): 10.69 (s, 1H, CONH), 8.02 (d, 1H, $J = 8.1$ Hz, Ar–H), 7.72–7.81 (m, 2H, Ar–H) 7.42 (t, 1H, $J = 7.7$ Hz, Ar–H), 4.38 (s, 2H, CH_2).

2-Chloro-N-(3-nitrophenyl)acetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.44–8.46 (m, 2H, CONH and Ar–H), 8.04 (d, 1H, $J = 8.7$ Hz, Ar–H), 7.97 (d, 1H, $J = 8.1$ Hz, Ar–H), 7.55 (t, 1H, $J = 8.0$ Hz, Ar–H), 4.25 (s, 2H, CH_2).

2-Chloro-N-(4-(trifluoromethyl)phenyl)acetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.39 (s, 1H, CONH), 7.70 (d, 2H, $J = 9.0$ Hz, Ar–H), 7.62 (d, 2H, $J = 9.0$ Hz, Ar–H), 4.22 (s, 2H, CH_2).

2-Chloro-N-(3,4-dichlorophenyl)acetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.25 (s, 1H, CONH), 7.80 (s, 1H, Ar–H), 7.37–7.44 (m, 2H, Ar–H), 4.19 (s, 2H, CH_2).

2-Chloro-N-(3-chloro-4-fluorophenyl)acetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.25 (s, 1H, CONH), 7.72–7.75 (m, 1H, Ar–H), 7.35–7.41 (m, 1H, Ar–H), 7.13 (t, 1H, $J = 9.0$ Hz, Ar–H), 4.19 (s, 2H, CH_2).

2-Chloro-N-(4-chlorophenyl)acetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.24 (s, 1H, CONH), 7.51 (d, 2H, $J = 8.7$ Hz, Ar–H), 7.33 (d, 2H, $J = 9.0$ Hz, Ar–H), 4.19 (s, 2H, CH_2).

N-(3-Bromophenyl)-2-chloroacetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.22 (s, 1H, CONH), 8.01 (s, 1H, Ar–H), 7.47 (d, 1H, $J = 8.7$ Hz, Ar–H), 7.31 (d, 1H, $J = 8.7$ Hz, Ar–H), 7.22 (t, 1H, $J = 8.1$ Hz, Ar–H), 4.19 (s, 2H, CH_2).

Ethyl 4-(2-chloroacetamido)benzoate. ^{1}H NMR (300 MHz, DMSO-d_6): 10.67 (s, 1H, CONH), 7.93 (d, 2H, $J = 9.0$ Hz, Ar–H), 7.73 (d, 2H, $J = 8.2$ Hz, Ar–H), 4.25–4.32 (m, 4H, CH_2O and CH_2Cl), 1.30 (t, 3H, $J = 7.1$ Hz, CH_3).

2-Chloro-N-(4-methoxyphenyl)acetamide. ^{1}H NMR (300 MHz, DMSO-d_6): 8.15 (s, 1H, CONH), 7.50 (d, 2H, $J = 6.3$ Hz, Ar–H), 6.90 (d, 2H, $J = 6.3$ Hz, Ar–H), 4.19 (s, 2H, CH_2), 3.81 (s, 3H, CH_3).

2-Chloro-N-(4-sulfamoylphenyl)acetamide. ^{1}H NMR (300 MHz, DMSO-d_6): 10.71 (s, 1H, CONH), 7.74–7.84 (m, 4H, Ar–H), 7.28 (s, 2H, SO_2NH_2), 4.32 (s, 2H, CH_2).

2-Chloro-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)acetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.42 (s, 1H, SO_2NH), 8.24 (s, 1H, CONH), 7.70–7.85 (m, 2H, Ar–H), 7.61 (d, 2H, $J = 8.7$ Hz, Ar–H), 6.23 (s, 1H, CH), 4.21 (s, 2H, CH_2), 2.36 (s, 3H, CH_3).

2-Chloro-N-(4-nitrophenyl)acetamide. ^{1}H NMR (300 MHz, $CDCl_3$): 8.50 (s, 1H, CONH), 8.26 (d, 2H, $J = 9.0$ Hz, Ar–H), 7.77 (d, 2H, $J = 9.0$ Hz, Ar–H), 4.24 (s, 2H, CH_2).

The following spectral data were obtained from aromatic amines (converted from the corresponding aromatic amine hydrochlorides).

4-Amino-N-methylbenzenesulfonamide. IR (KBr): 3462, 3373, 1629, 1597, 1540, 1400,1295, 1150, 1092, 828, 680, 554 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 7.40 (d, 2H, $J = 8.4$ Hz, Ar–H), 6.89–6.94 (m, 1H, SO_2NH), 6.62 (d, 2H, $J = 8.7$ Hz, Ar–H), 5.91 (s, 2H, NH_2), 2.33 (d, 2H, $J = 4.5$ Hz, CH_3)

4-Amino-N-cyclopropylbenzenesulfonamide. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 7.40–7.44 (m, 3H, SO_2NH and Ar–H), 6.61 (d, 2H, $J = 9.0$ Hz, Ar–H), 5.94 (s, 2H, NH_2), 1.99–2.05 (m, 1H, CH), 0.41 (t, 2H, $J = 5.3$ Hz, CH_2), 0.34 (t, 2H, $J = 3.6$ Hz, CH_2)

4-Amino-N-ethylbenzamide. ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 7.60 (d, 2H, $J = 8.4$ Hz, Ar–H), 6.65 (d, 2H, $J = 8.1$ Hz, Ar–H), 6.03 (s, 1H, CONH), 3.96 (s, 2H, NH_2), 3.42 $\sim$ 3.51 (m, 2H, CH_2), 1.23 (t, 3H, $J = 7.4$ Hz, CH_3)

4-Amino-N-hydroxybenzamide. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 7.62 (d, 1H, $J = 7.5$ Hz, CONH), 7.24 (d, 2H, $J = 8.1$ Hz, Ar–H), 6.46 (d, 2H, $J = 8.7$ Hz, Ar–H), 5.54 (s, 2H, NH_2), 4.13 (d, 1H, $J = 6.6$ Hz, OH)

Methyl 4-(4-aminophenylsulfonamido)benzoate. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 10.46 (s, 1H, SO_2NH), 7.80 (d, 2H, $J = 9.0$ Hz, Ar–H), 7.45 (d, 2H, $J = 8.7$ Hz, Ar–H), 7.17 (d, 2H, $J = 9.0$ Hz, Ar–H), 6.54 (d, 2H, $J = 9.0$ Hz, Ar–H), 6.05 (s, 2H, NH_2), 3.78 (s, 3H, CH_3)

4-Amino-N-(pyrimidin-2-yl)benzenesulfonamide. ^{1}H NMR (300 MHz, DMSO-d_6, ppm): 11.23 (s, 1H, SO_2NH), 8.47 (d, 2H, $J = 4.8$ Hz, Ar–H), 7.60 (d, 2H, $J = 8.7$ Hz, Ar–H), 7.01 (t, 1H, $J = 5.0$ Hz, Ar–H), 6.54 (d, 2H, $J = 8.7$ Hz, Ar–H), 5.99 (s, 2H, NH_2)

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