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Metal-free *S*-arylation of cysteine using arenediazonium salts

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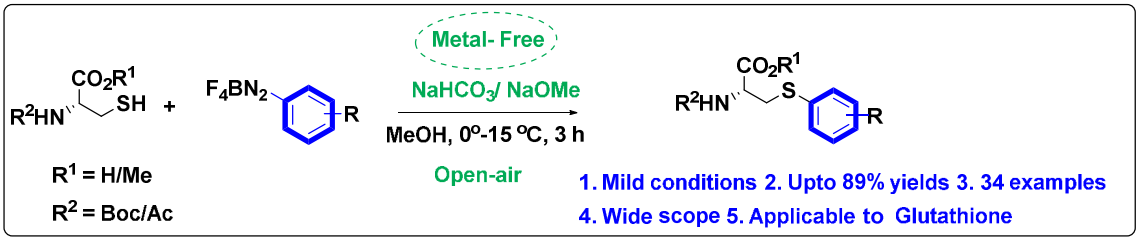
Graphical Abstract:



ABSTRACT

A mild chemoselective method for *S*-arylation of cysteine has been developed in an open-flask procedure under metal-free conditions using arenediazonium salts in methanol.

Introduction

Site-selective modification of amino acids in proteins is an active area of research in chemical biology.[1] Cysteine, by virtue of its low natural abundance (< 2%)[2] and armed with a highly nucleophilic thiol group, is an attractive target for site-selective modification of proteins. A number of methods have been developed for cysteine conjugation,[3] among which, Michael addition of cysteine is the most widely used strategy. However, the fate of these Michael adducts can widely vary depending on reaction conditions, leading to a number of side products arising out of retro-Michael reaction, thiol exchange, ring opening in case of maleimides, *etc*,[4] which necessitates exploration of new methodologies that can provide chemically robust cysteine conjugates. *S*-Arylation of cysteine appeared to be an attractive strategy towards this end, not only due to the irreversible nature of the reaction and the

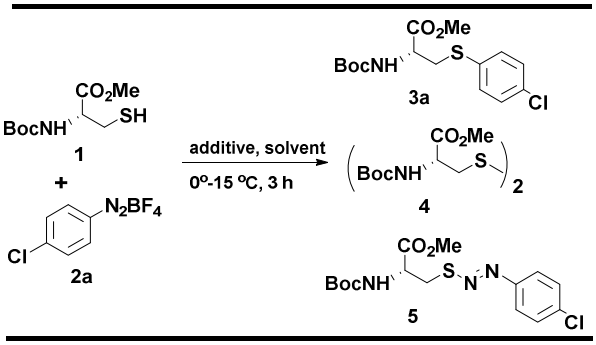
chemical stability of *S*-aryl bonds but also, for opportunities that it could provide for photolabelling of cysteine peptides and proteins using photoactive aryl payloads. Moreover, *N*-Acetyl *S*-arylcysteines (arylmercapturic acids) constitute an important class of urine biomarkers for aromatic carcinogenesis arising out of the glutathione transferase pathway,[5] whereas peptidomimetic *S*-arylcysteines are common pharmacophores that are present in a number of anti-HIV drug candidates, including the approved drug nelfinavir.[6] Taken together, these prospects provided a strong impetus to develop an efficient synthetic procedure for *S*-arylation of cysteine under mild reaction conditions. The current repertoire of *S*-arylation of cysteine is limited to SNAr displacement reactions of activated aromatics (limited substrate scope)[7] and Pd-catalyzed *S*-arylation reactions,[8] the latter being recently used by the groups of Buchwald and Davies for bio-orthogonal *S*-arylation of cysteine peptides and proteins.[9] However, Buchwald's method requires an excess of the independently prepared oxidative addition complex of aryl triflates with low-valent palladium,[9a] whereas Pd-based methods require special ligands, such as xantphos Pd-G3 precatalyst, to obtain good yields.[8c] Chan-Lam type[10] or photoredox-Ni catalyzed[11] *S*-arylation of cysteine requires harsh reaction conditions and/or are substrate specific. In view of these limitations and in continuation of our interests in the utilization of arenediazonium salts in organic synthesis[12,13] and in the synthesis of modified chalcogenide amino acids,[14] we explored the *S*-arylation of cysteine using arenediazonium salts, taking advantage of their superior reactivity over aryl halides in Pd-catalyzed[13] and radical reactions.[15] Our preliminary results that have resulted in a mild new *metal-free* synthesis of *S*-arylcysteines is reported herein. Cu_2O mediated *S*-arylation of cysteine with arenediazonium salts, known since the early 50's, have found little application due to their operational complexity and impure product formation.[16] Recently, Au-catalyzed reactions of cysteine with arenediazonium salts was reported.[17] We, while looking for metal-free conditions, were attracted to a recent report on radical aromatic substitution with

arenediazonium salts using ascorbic acid as a green radical initiator[18] and wished to apply the same for *S*-arylation of cysteine via a S_{RN} pathway. It may be noted that although $S_{RN}1$ reaction of aromatic thiols with arenediazonium salts (Stadler-Ziegler reaction) has been widely described for the synthesis of unsymmetrical diaryl sulfides,[19] similar reports with aliphatic thiols (of which cysteine is a prototype) are scarce.[20]

RESULTS AND DISCUSSION

S-Arylation of NH-Boc cysteine methyl ester (**1**) with 4-chlorobenzenediazonium tetrafluoroborate (**2a**) was studied as a model for optimization of the reaction conditions. Ascorbic acid (10%) catalyzed reactions of **1** with **2a** (1.2-1.5 equiv.) in laboratory grade MeOH at 0-15 ^{o}C gave the desired *S*-arylcysteine **3a** in 37-40% yield but was accompanied with substantial amounts of the cysteine dimer **4** (20-23%) (entries 1 & 2, Table 1). The yield of **3a** could be increased to 55% using 2 equivalents of the diazonium salt (entry 3, Table 1) but increasing the amount of ascorbic acid had no effect on the yield of **3a** (entry 4, Table 1). Reactions carried out for longer periods did not improve the yield whereas at elevated temperatures, coloured resinous impurities were formed at the expense of the desired product. While looking for conditions to improve the yield of **3a**, we came across reports that solvent MeOH itself can induce homolytic dediazoniation of diazonium salts to form aryl radicals via diazo-ether intermediates[21] and questioned the seemingly redundant role of ascorbic acid as the radical initiator. Indeed, in absence of ascorbic acid, reaction of **1** with **2a** in MeOH in presence of $NaHCO_3$ (1 equiv), gave a higher yield (73%, entry 5, Table 1) which could be further optimized using 3 equivalents of $NaHCO_3$ to give 89% yield of **3a** after chromatographic purification (entry 6, Table 1). The presence of a base was essential, since without the base, the diazo-sulfide **5** was observed as the major product (entry 7, Table1). NaOAc was ineffective as a base for this reaction. EtOH could also be used as a solvent

Table 1. Optimization of *S*-arylation of 1 with the diazonium salt 2a

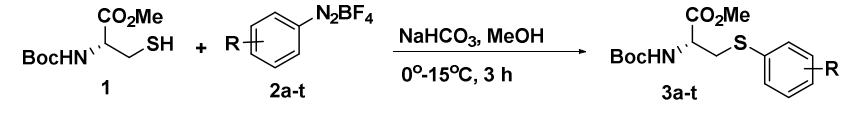


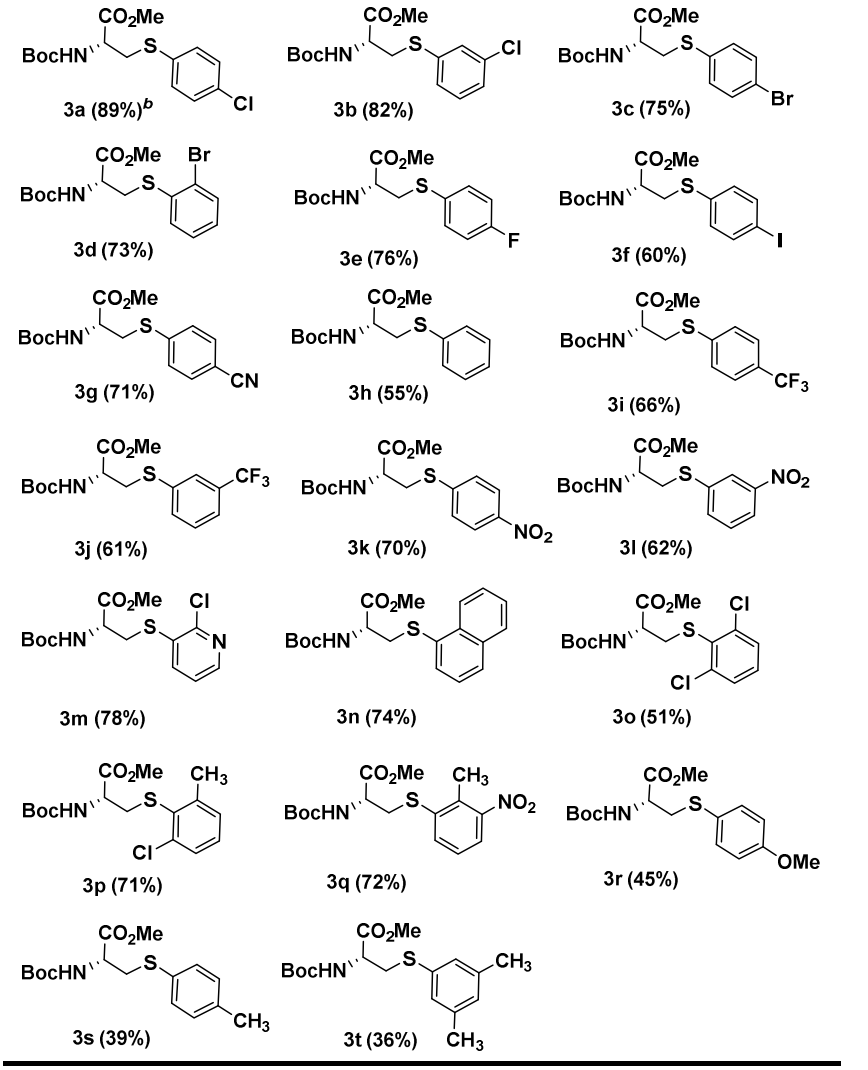
Entry	1 (equiv.)	2 (equiv.)	Additive (mol %)	Solvent	Yield %[a] 3a	4	5
1	1	1.2	Asc. Ac (10%)	MeOH	37	23	<5
2	1	1.5	Asc. Ac (10%)	MeOH	40	20	<5
3	1	2	Asc. Ac (10%)	MeOH	55	<10	<5
4	1	2	Asc. Ac (20%)	MeOH	56	<10	<5
5	1	2	$NaHCO_3$ (1)	MeOH	73	<5	<5
6	**1**	**2**	**$NaHCO_3$ (3)**	**MeOH**	**89**	**<5**	**<5**
7	1	2	-----	MeOH	10	<5	<55[b]
8	1	2	$NaHCO_3$ (3)	EtOH	73	<5	<5
9	1	2	$NaHCO_3$ (3)	THF	53	ND	ND
10	1	2	$NaHCO_3$ (3)	dioxane	60	ND	ND
11	1	2	$NaHCO_3$ (3)	DMF	36	ND	ND
12	1	2	$NaHCO_3$ (3)	CH_3CN	54	23	<5

[a]isolated yields, [b] from ^{1}H-NMR product mixture

for this reaction but non-alcoholic solvents like THF, dioxane, DMF or CH_3CN all turned out to be inferior choices (entries 8-12). The reaction was completely inhibited by TEMPO, indicative of a radical pathway.[22] A number of arenediazonium salts **2a-t** were then used for the *S*-arylation reaction of **1** under the optimized conditions (*cf.* entry 6, Table 1) and the results are shown in Table 2.

Table 2. *S*-Arylation of cysteine ester 1 with aryl diazonium salts 2a-2t





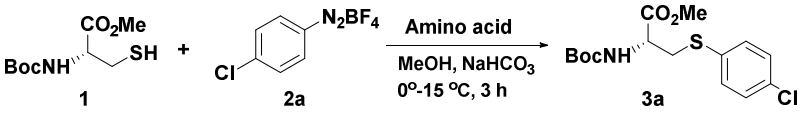
[a] **1** (1 equiv.), **2** (2 equiv.), $NaHCO_3$ (3 equiv.), MeOH, 0-15 °C. [b] isolated yields.

As expected for a radical pathway, the product yields were uniformly high irrespective of the substitution pattern on the diazonium salt used (*ortho*, *meta* or *para*). Even with sterically hindered *ortho*, *ortho'*-disubstituted diazonium salts, moderate to good yields of the *S*-arylation products **3o, 3p** could be obtained, demonstrating the superiority of this method

over the Pd-catalyzed *S*-arylation regimen. Of particular interest are the *S*-arylation products **3c, 3d, 3f** arising out of the bromo- and iodo-substituted diazonium salts, the latter (**3f**), in particular, being impossible to obtain via the Pd-catalyzed methods. These results, while attesting to the superior reactivity of the diazonium group over the halides in the radical pathway, offer further options for product diversification via various Pd-catalyzed coupling reactions. Heterocyclic (**3m**) as well as photoactive naphthyl groups (**3n**) could also be introduced on cysteine by this procedure in good yields. As expected, diazonium salts bearing electron withdrawing groups gave higher yields of the products **3a-q** vis-a-vis those with electron-donating substituents (**3r-t**).

The chemoselectivity of this *S*-arylation reaction was briefly examined in presence of other amino acids through intermolecular competition experiments (robustness screen).[23]

Table 3. Chemo-selective *S*-arylation of 1 with 2a in presence of other amino-acids



1 2a 3a

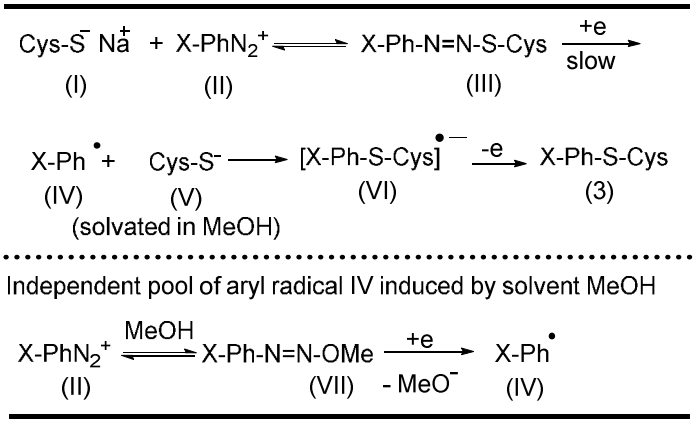
Entry	1 (equiv.)	2a (equiv.)	Amino acid (equiv.)	3a Yield %[a,b]
1	1	2	---	89
2	1	2	*L*-Serine (1)	85
3	1	2	*L*-Tyrosine (1)[c]	82
4	1	2	*L*-Alanine (1)	84
5	1	2	*L*-Tryptophan (1)	85
6	1	2	*L*-Lysine (1)	78
7	1	2	*L*-Glutamine (1)[d]	70

[a]**1** (1 equiv), **2a** (2 equiv.), amino acid (1 equiv.), $NaHCO_3$ (5 equiv), MeOH, 0-15 °C, 3h;[b]isolated yields; [c]Z-*L*-tyrosine used; [d] *L*-Glutamine sodium salt used.

Most gratifyingly, reactions of **2a** were found to be highly selective for cysteine (**1**) in presence of several amino acids (Table 3). The observed selectivities against tryptophan and tyrosine are highly significant since these amino acids are known to undergo azo-coupling reaction with diazonium salts under basic conditions. It has also been demonstrated that even in the presence of acidic hydroxyl groups of tyrosine the reaction is selective at the thiol end of cysteine.

A plausible mechanism of this reaction, drawn in analogy to the radical chain mechanism proposed for Stadler-Ziegler reactions,[24] is shown in Scheme 1.

Scheme 1. Plausible radical chain mechanism for *S*-arylation of cysteine with arenediazonium salts

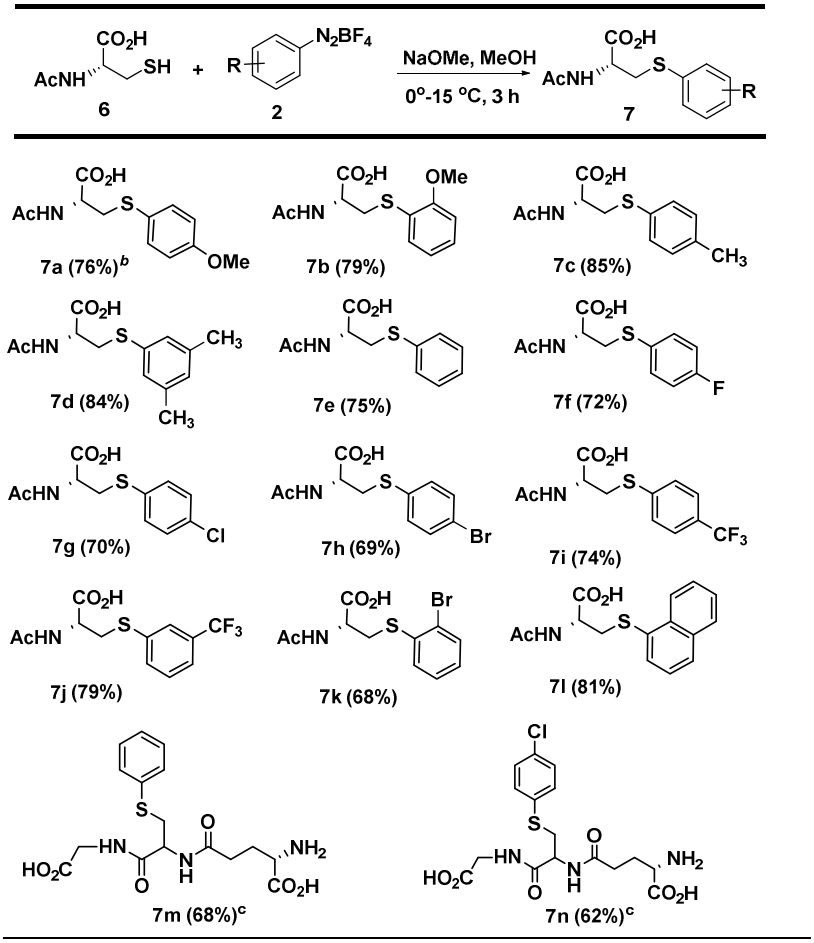


Thus, initially in the presence of base, thiolate **I** is formed which then reacts with diazosalt **II** forms azo-sulfide **III**, upon rate limiting one electron reduction, would give rise to the aryl radical **IV** and the cysteine anion **V**. Subsequent inner-cage combination between **IV** and **V** followed by electron loss would then lead to the *S*-arylcysteine **3**. Azo-sulfides derived from electron deficient diazonium salts (**III**, X = EWG) are easily reduced due to their favorable redox potentials[15a] and hence, gave higher yields of the products visa-vis their electron rich counterparts (**III**, X = EDG). MeOH could also provide an independent pool of aryl radical

IV via formation of the diazo-ether **VII**,[21b] which might compensate for unwanted side reactions of **IV**, such as H-radical capture, dimerization, etc., thereby improving the yields. MeOH might also stabilize the anion **V** through solvation, thereby facilitating the rate limiting one electron reduction of **III**.

In order to improve the yields with electron rich diazonium salts, we decided to conduct the reaction under a strongly basic medium. This, we thought, would provide a higher initial concentration of **V** through complete deprotonation of the aliphatic SH-group of cysteine which could then react with the azosulfide **III** as an electron donor[24] and/or cause a switch towards $S_{RN}2$ mechanism,[20a] rendering **III** more prone to homolytic fission.

Table 4. *S*-Arylation of NH-Ac cysteine (6) with arenediazonium salts (2)[a]



[a] 6 (1 equiv.), 2 (2 equiv.), NaOMe (4 equiv.) in MeOH at 0-15 °C. [b] isolated yields, [c] purified by HPLC.

In the event, switching to NaOMe as the base and using NH-Ac cysteine (**6**) as the substrate, electron rich diazonium salts underwent facile *S*-arylation reactions in MeOH at 0-15 °C to give the corresponding *S*-arycysteines **7a-d** in 68-85% yields (Table 4). It is likely that under these conditions, a portion of the diazonium salt would independently give rise to aryl radicals via *in-situ* formation of aryl diazotates.[25] Since the products **7a-d** are examples of arylmercapturic acids which are important urinary biomarkers for aromatic carcinogenesis,[5] we decided to extend this reaction to other diazonium salts in order to develop a facile new synthetic route to this class of compounds. Towards this end, a number of substituted diazonium salts were then used for *S*-arylation of **6** under the above conditions to provide the corresponding arylmercapturic acids **7e-7l** in good yields (Table 4). When we applied this method for the biologically important tripeptide glutathione, we were delighted to isolate the *S*-aryl glutathione derivatives **7m** and **7n** in good yields. The operational simplicity and ready availability of anilines, makes this procedure a superior alternative to the previous syntheses reported for arylmercapturic acids,[5b,7c,10b] including the recently reported xantphos Pd-G_3 pre-catalyst mediated coupling of **6** with aryl iodides.[8c]

CONCLUSION

In summary, a mild chemoselective method for *S*-arylation of cysteine has been developed in an open-flask procedure using arenediazonium salts under metal-free conditions.[28] The reaction which probably takes place under a radical chain mechanism is crucially dependent on the use of methanol as solvent.

EXPERIMENTAL SECTION

General Experimental Methods

All the reagents used in this work were obtained commercially and used without further purification unless otherwise mentioned. *N*-(tert-Butoxycarbonyl)-*L*-cysteine methyl ester (97%), *N*-Acetyl-*L*-cysteine (98%), *L*-Glutathione reduced (98%) and $NaHCO_3$ (LR grade) were purchased and used without any further purification. LR grade MeOH was used as solvent. Thin-layer chromatography (TLC) was performed using silica gel GF_{254} coated aluminum plates and the visualization of spots were done using UV illumination and charring the TLC plates sprayed with PMA solution. Column chromatography was performed on silica gel 100−200 mesh, using ethyl acetate/ pet-ether or methanol/ dichloromethane mixture as eluent. ^{1}H, ^{13}C NMR spectra of the synthesized compounds was recorded on 400 MHz NMR spectrometer using solutions in $CDCl_3$ / MeOD. Chemical shifts (^{1}H, ^{13}C) refer to using TMS as an internal standard or the central line of $CDCl_3$ (7.26 ppm, 77.16 ppm), and MeOD (3.3 ppm, 49.0 ppm) peaks. IR spectra were recorded using FT-IR spectrometer. High resolution mass spectra (HRMS) were recorded using Q-TOF Mass Spectrometer (ESI-HRMS). Melting points were determined using SMP10 melting range apparatus and are uncorrected.

The aryldiazonium salts were synthesized from their corresponding anilines using previously reported literature procedures.[26, 27] The data of new compounds are presented here and some of the compounds synthesized in this work are reported in the literature.[8c, 11a, 11b, 17]

General procedure for *S*-arylation of *N*-(tert-Butoxycarbonyl)-*L*-cysteine methyl ester:

N-(tert-Butoxycarbonyl)-*L*-cysteine methyl ester, **1** (75 mg, 0.319 mmol, 1 equiv.) was weighed in a clean round bottom flask, MeOH (3 mL) was added and reaction mixture was cooled using ice-bath. After stirring for 5 min., $NaHCO_3$ (80 mg, 0.957 mmol, 3 equiv.), and substituted aryldiazonium salt (**2a-2t**, 2 equiv.) were added. The reaction mixture was stirred (0-15 °C) for 3 h and the crude residue was directly loaded on a silica gel column and eluted with ethyl acetate/pet-ether (1/10) to get the pure products (**3a-3t)**.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-chlorophenyl)-*L*-cysteinate (3a):

Yield: 89% (98 mg), light brown solid, mp: 54-56 °C; IR (neat, cm^{-1}): 2975, 1747, 1712, 1504, 1359, 1213, 1165. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32-7.35 (m, 2H), 7.23-7.26 (m, 2H), 5.32 (d, *J* = 6.8 Hz, 1H), 4.54-4.56 (m, 1H), 3.58 (s, 3H), 3.37 (dd, *J* = 14, 4.4 Hz, 1H), 3.31 (dd, *J* = 14, 4.8 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 155, 133.5, 133.3, 132.5, 129.3, 80.3, 53.5, 52.5, 37.5, 28.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}ClNO_4SNa$ 368.0699; Found 368.0698.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(3-chlorophenyl)-*L*-cysteinate (3b):

Yield: 82% (90 mg), Dark red oily liquid; IR (neat, cm^{-1}): 3020, 1745, 1709, 1498, 1356, 1214, 1164, 1015, 743. ^1H NMR (400 MHz, $CDCl_3$): δ 7.30-7.31 (m, 1H), 7.18-7.21 (m, 1H), 7.11-7.16 (m, 2H), 5.28 (d, *J* = 7.2 Hz, 1H), 4.51- 4.53 (m, 1H), 3.53 (s, 3H), 3.31-3.35 (m, 2H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 155.1, 137.2, 134.8, 130.3, 130.2, 128.7, 127.2, 80.4, 53.4, 52.6, 37.1, 28.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}ClNO_4SNa$ 368.0699; Found 368.0677.

Methyl *S*-(4-bromophenyl)-*N*-(tert-butoxycarbonyl)-*L*-cysteinate (3c): [17]

Yield: 75% (93 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.32-7.34 (m, 2H), 7.19-7.22 (m, 2H), 5.24 (d, *J* = 7.2 Hz, 1H), 4.48-4.50 (m, 1H), 3.52 (s, 3H), 3.32-3.33 (m, 2H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 154.9, 134.3, 132.6, 132.2, 121.2, 80.3, 53.5, 52.6, 37.4, 28.4.

Methyl *S*-(2-bromophenyl)-*N*-(tert-butoxycarbonyl)-*L*-cysteinate (3d):

Yield: 73% (91 mg), Dark orange liquid; IR (neat, cm^{-1}): 2976, 1747, 1713, 1504, 1360, 1250, 1166. ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (dd, *J* = 8, 1.2 Hz, 1H), 7.41-7.43 (m, 1H), 7.26 (td, *J* = 8 Hz, 1.2 Hz, 1H), 7.05-7.23 (m, 1H), 5.37 (d, *J* = 6.4 Hz, 1H), 4.59- 4.61 (m, 1H), 3.62 (s, 3H), 3.39-3.41 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171, 136.1, 133.4, 131.3, 128.2, 127.9, 125.8, 80.3, 53.2, 52.6, 36.4, 28.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}BrNO_4SNa$ 412.0194; Found 412.0195.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-fluorophenyl)-*L*-cysteinate (3e): [17]

Yield: 76% (80 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.38-7.42 (m, 2H), 6.95-7.0 (m, 2H), 5.33 (d, *J* = 7.2 Hz, 1H), 4.51-4.53 (m, 1H), 3.55 (s, 3H), 3.24-3.34 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 165.3 (d, *J* = 245 Hz), 155 (d, *J* = 8.3 Hz), 134.1 (d, *J* = 8.3 Hz), 129.8, 116.2 (d, *J* = 21.7 Hz), 80.2, 53.4, 52.5, 38.4, 28.3.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-iodophenyl)-*L*-cysteinate (3f): [17]

Yield: 60% (84 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.58-7.60 (m, 2H), 7.12-7.14 (m, 2H), 5.30 (d, *J* = 7.2 Hz, 1H), 4.55- 4.57 (m, 1H), 3.59 (s, 3H), 3.29-3.39 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9, 154.9, 138, 132.5, 92.2, 80.3, 53.4, 52.6, 37, 28.3.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-cyanophenyl)-*L*-cysteinate (3g): [11a]

Yield: 71% (76 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8 Hz, 2H), 7.36 (d, *J* = 8 Hz, 2H), 5.37 (d, *J* = 6.4 Hz, 1H), 4.57-4.59 (m, 1H), 3.63 (s, 3H), 3.48 (dd, *J* = 14, 4.4 Hz, 1H), 3.37 (dd, *J* = 13.6, 4.4 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 154.9, 143, 132.3, 128.3, 118.6, 109.2, 80.4, 53.2, 52.7, 35.1, 28.2.

Methyl *N*-(tert-butoxycarbonyl)-*S*-phenyl-*L*-cysteinate (3h): [17]

Yield: 55% (54 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.42 (m, 2H), 7.26-7.30 (m, 2H), 7.19-7.23 (m, 1H), 5.35 (d, *J* = 6.0 Hz, 1H), 4.56-4.57 (m, 1H), 3.54 (s, 3H), 3.37-3.38 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 154.1, 133.9, 130.2, 128.2, 126.2, 76.3, 52.4, 51.4, 36.4, 27.4.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-(trifluoromethyl)phenyl)-*L*-cysteinate (3i): [17]

Yield: 66% (80 mg); ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 5.32 (d, *J* = 6.4 Hz, 1H), 4.61-4.62 (m, 1H), 3.62 (s, 3H), 3.49 (dd, *J* = 14, 4.4 Hz,

1H), 3.40 (dd, *J* = 14, 4.4 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 154, 139.8, 129.3, 128.5, 124.9 (q, *J* = 37.4 Hz), 124.5, 79.5, 52.5, 51.7, 35.1, 27.4.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(3-(trifluoromethyl)phenyl)-*L*-cysteinate (3j):

Yield: 61% (74 mg); Light orange solid, mp: 50-52 °C; IR (neat, cm^{-1}): 2973, 2926, 1746, 1711, 1592, 1505, 1322, 1218, 1166, 1129, 1016. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (s, 1H), 7.57-7.59 (m, 1H), 7.46-7.47 (m, 1H), 7.39-7.41 (m, 1H), 5.34 (m, 1H), 4.60- 4.63 (m, 1H), 3.58 (s, 3H), 3.42-3.49 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 154.9, 143.8, 136.6, 133.6, 129.4, 127, 123.6, 80.4, 53.2, 52.4, 36.9, 28.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}F_3NO_4SNa$ 402.0963; Found 402.0958.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-nitrophenyl)-*L*-cysteinate (3k):

Yield: 70% (80 mg); Dark red solid, mp: 84-86 °C; IR (neat, cm^{-1}): 3021, 1745, 1709, 1513, 1436, 1341, 1214, 1164, 1089, 849, 742.^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 5.37 (d, *J* = 6.4 Hz, 1H), 4.63-4.64 (m, 1H), 3.69 (s, 3H), 3.56 (dd, *J* = 13.6, 4.4 Hz, 1H), 3.43 (dd, *J* = 14, 4.8 Hz, 1H), 1.41(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 155.2, 145.7, 127.7, 126.3, 124.1, 80.8, 53.3, 52.9, 35.2, 28.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}N_2O_6SNa$ 379.0940; Found 379.0941.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(3-nitrophenyl)-*L*-cysteinate (3l):

Yield: 62% (70 mg); Dark red solid, mp: 99-101 °C; IR (neat, cm^{-1}): 2977, 2923, 1744, 1710, 1589, 1526, 1350, 1219, 1165, 1120, 1022. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 8.03 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 8 Hz, 1H), 5.35 (d, *J* = 6.8 Hz, 1H), 4.60- 4.62 (m, 1H), 3.65 (s, 3H), 3.51 (dd, *J* = 14, 4 Hz, 1H), 3.4 (dd, *J* = 14, 4.8 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 155.1, 148.6, 138.3, 135.6, 129.8, 124.4, 121.5, 80.6, 53.4, 52.8, 36.7, 28.3. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}N_2O_6SNa$ 379.0940; Found 379.0936.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(2-chloropyridin-3-yl)-*L*-cysteinate (3m):

Yield: 78% (86 mg); Dark red semisolid; IR (neat, cm^{-1}): 2970, 2924, 1745, 1709, 1511, 1437, 1382, 1218, 1164, 1032, 861. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, *J* = 4.8 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.18-7.21 (m, 1H), 5.35 (d, *J* = 6.8 Hz, 1H), 4.60-4.62 (m, 1H), 3.68 (s, 3H), 3.36-3.47 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 155.1, 146.6,

138.4, 132.7, 122.8, 80.5, 53.1, 52.8, 35, 28.3. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for Calcd for $C_{14}H_{19}ClN_2O_4SNa$ 369.0652; Found 369.0656.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(naphthalen-1-yl)-*L*-cysteinate (3n): [8c]

Yield: 74% (85 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H),7.69-7.72 (m, 1H), 7.59 (dt, *J* = 6.8 Hz, 1.2 Hz, 1H), 7.51-7.54 (m, 1H), 7.4 (t, *J* = 7.6 Hz, 1H), 5.35 (d, *J* = 6.8 Hz, 1H), 4.56-4.57 (m, 1H), 3.47 (s, 3H), 3.41-3.44 (m, 2H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 155, 134.2, 133.5, 131.8, 131.3, 128.8, 128.7, 126.9, 126.4, 125.6, 125.4, 80.1, 53.5, 52.3, 37.6, 28.3.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(2,6-dichlorophenyl)-*L*-cysteinate (3o):

Yield: 51% (62 mg); Orange oil; IR (neat, cm^{-1}): 2974, 1747, 1713, 1636, 1501, 1429, 1359, 1164, 1016. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8 Hz, 2H), 7.17 (t, *J* = 8 Hz, 1H), 5.52 (d, *J* = 6.8 Hz, 1H), 4.52-4.54 (m, 1H), 3.56 (s, 3H), 3.51 (dd, *J* = 14, 3.6 Hz, 1H), 3.38 (dd, *J* = 14, 4.4 Hz, 1H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 155.1, 141.2, 132.2, 130.2, 128.8, 80.2, 53.5, 52.6, 37.3, 28.4. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{19}Cl_2NO_4SNa$ 402.0310; Found 402.0311.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(2-chloro-6-methylphenyl)-*L*-cysteinate (3p):

Yield: 71% (81 mg); Light orange gummy oil; IR (neat, cm^{-1}): 2976, 1749, 1709, 1636, 1503, 1442, 1358, 1218, 1165, 1056, 855. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.30 (m, 1H), 7.12-7.14 (m, 2H), 5.40 (d, *J* = 6.8 Hz, 1H), 4.49-4.51 (m, 1H), 3.53 (s, 3H), 3.39 (dd, *J* = 14, 4.4 Hz, 1H), 3.31 (dd, *J* = 14, 4.4 Hz, 1H), 2.54 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 152.3, 145, 140.1, 129.5, 129, 128, 80.2, 53.6, 52.5, 37.2, 28.4, 22.6. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{22}ClNO_4SNa$ 382.0856; Found 382.0852.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(2-methyl-3-nitrophenyl)-*L*-cysteinate (3q):

Yield: 72% (85mg); Orange solid, mp: 71-73 °C; IR (neat, cm^{-1}): 1709, 1636, 1524, 1357, 1164, 1016. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60-7.64 (m, 2H), 7.25-7.29 (m, 1H), 5.32 (d, *J* = 6.4 Hz, 1H), 4.58-4.59 (m, 1H), 3.63 (s, 3H), 3.44 (dd, *J* = 14, 4.8 Hz, 1H), 3.34 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.54 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 155, 151.5, 138.5, 134.2, 132.8, 126.7, 122.5, 80.5, 53.3, 53.7, 36.8, 28.4, 16.7. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{22}N_2O_6SNa$ 393.1096; Found 393.1098.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(4-methoxyphenyl)-*L*-cysteinate (3r): [17]

Yield: 45% (49 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (dd, *J* = 6.8, 2 Hz, 2H), 6.76 (dd, *J* = 6.8, 2 Hz, 2H), 5.26 (d, *J* = 7.2 Hz, 1H), 4.42-4.44 (m, 1H), 3.72 (s, 3H), 3.47 (s, 3H), 3.18 (d, *J* = 4.4 Hz, 2H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 159.6, 155.2, 134.6, 124.9, 114.8, 80.2, 55.5, 53.4, 52.4, 38.9, 28.4.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(p-tolyl)-*L*-cysteinate (3s): [11b]

Yield: 39% (40 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.3 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8 Hz, 2H), 5.34 (d, *J* = 6.8 Hz, 1H), 4.52- 4.53 (m, 1H), 3.53 (m, 3H), 3.3-3.31 (m, 2H), 2.3 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 155.1, 137.4, 131.8, 129.9, 80.1, 53.4, 52.4, 37.9, 28.4, 21.1.

Methyl *N*-(tert-butoxycarbonyl)-*S*-(3,5-dimethylphenyl)-*L*-cysteinate (3t):

Yield: 36% (39 mg); Light red gummy oil; IR (neat, cm^{-1}): 2973, 1751, 1710, 1644, 1507, 1589, 1361, 1166, 1025. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01 (s, 2H), 6.83 (s, 1H), 5.36 (d, *J* = 7.6 Hz, 1H), 4.54- 4.55 (m, 1H), 3.55 (s, 3H), 3.33-3.34 (m, 2H), 2.26 (s, 6H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 155.1, 138.7, 134.2, 128.9, 128.7, 80.1, 53.3, 52.3, 37.2, 28.3, 21.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{25}NO_4SNa$ 362.1402; Found 362.1395

General procedure for *S*-arylation of *N*-acetyl-*L*-cysteine:

N-acetyl-*L*-cysteine **6** (75 mg, 0.459 mmol, 1 equiv.) was taken in a clean round bottom flask, MeOH (3 mL) was added and reaction mixture was cooled in ice-bath. After stirring for 5 min., NaOMe (4 equiv. 102 µL, 1 molar stock solution prepared by dissolving freshly cut sodium in dry methanol), substituted aryldiazonium salt (**2a-2l**, 2 equiv.) was added. The reaction mixture was stirred for 3 hours below 15 °C. The crude reaction mixture was acidified with 1N HCl at 0-5 C followed by addition of 2 mL ice-cold water. The reaction mixture was extracted with CH_2Cl_2, organic layer washed with brine and concentrated at room temperature in *vacuo*. The crude residue was loaded on a silica gel column and eluted with CH_2Cl_2/MeOH (1/10) to get the pure products (**7a-7l)**.

***N*-Acetyl-*S*-(4-methoxyphenyl)-*L*-cysteine (7a):** [8c]

Yield: 76% (94 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 4.43 (dd, *J* = 8.4, 4.0 Hz, 1H), 3.76 (s, 3H), 3.35 (dd, *J* = 14, 4.0 Hz, 1H), 3.07 (dd, *J* = 14, 8.4 Hz, 1H), 1.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 160.8, 135.2, 126.7, 115.6, 55.8, 54.6, 38.9, 22.5.

_N_-Acetyl-_S_-(2-methoxyphenyl)-_L_-cysteine (7b):

Yield: 79% (97 mg); Light pink semi solid. IR (neat, cm^{-1}): 3425, 2976, 1749, 1709, 1636, 1218, 855. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8 Hz, 1H), 6.9 (t, *J* = 7.6 Hz, 1H), 4.48 (dd, *J* = 8.4, 4 Hz, 1H), 3.86 (s, 3H), 3.43 (dd, *J* = 14, 4.4 Hz, 1H), 3.12 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 159.6, 132.9, 129.7, 123.5, 121.9, 112.2, 56.2, 53.6, 34.7, 22.3. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{15}NO_4SNa$ 292.0619; Found 292.0620.

_N_-Acetyl-_S_-(p-tolyl)-_L_-cysteine (7c): [8c]

Yield: 85% (99 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8 Hz, 2H), 7.1 (d, *J* = 8 Hz, 2H), 4.48 (dd, *J* = 7.2, 4 Hz, 1H), 3.43 (dd, *J* = 13.6, 4 Hz, 1H), 3.15 (dd, *J* = 13.6, 4 Hz, 1H), 2.27 (s, 3H),1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 137.9, 133, 132, 130.7, 54.5, 37.5, 22.4, 21.

_N_-Acetyl-_S_-(3,5-dimethylphenyl)-_L_-cysteine (7d):

Yield: 84% (103 mg); Pink solid, mp: 118-120 °C. IR (neat, cm^{-1}): 3448, 1643, 1219, 1040, 821. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99 (s, 2H), 6.82 (s, 1H), 4.46 (dd, *J* = 8, 4 Hz, 1H), 3.48 (dd, *J* = 14, 4 Hz, 1H), 3.17 (dd, *J* = 13.6, 8 Hz, 1H), 2.24 (s, 6H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.2, 172.8, 165.6, 139.6, 136.9, 128, 128.4, 55.5, 37.1, 22.7, 21.3. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{17}NO_3SNa$ 290.0827, Found 290.0829.

_N_-Acetyl-_S_-phenyl-_L_-cysteine (7e): [8c]

Yield: 75% (82 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8 Hz, 2H), 7.28 (t, *J* = 8 Hz, 2H), 7.22-7.18 (m, 1H), 4.52 (dd, *J* = 8, 4 Hz, 1H), 3.5 (dd, *J* = 14, 4 Hz, 1H), 3.20 (dd, *J* = 13.6, 8 Hz, 1H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 136.9, 131.2, 130.1, 127.6, 54.5, 36.8, 22.4.

_N_-Acetyl-_S_-(4-fluorophenyl)-_L_-cysteine (7f): [8c]

Yield: 72% (85 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.5 (m, 2H), 7.06-7.1 (m, 2H), 4.45 (dd, *J* = 8, 4 Hz, 1H), 3.50 (dd, *J* = 13.6, 4 Hz, 1H), 3.20 (dd, *J* = 13.6, 4 Hz, 1H), 1.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3 (d, *J* = 15 Hz), 172.3, 163.2 (dd, *J* = 244, 24 Hz), 134.7-134.9 (m), 131.2, 117.1, 53.6, 37.5, 22.3.

_N_-Acetyl-_S_-(4-chlorophenyl)-_L_-cysteine (7g): [8c]

Yield: 70% (88 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 4.52 (dd, *J* = 8, 4.8 Hz, 1H), 3.46 (dd, *J* = 14, 4.4 Hz, 1H), 3.19 (dd, *J* = 14, 8 Hz, 1H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 135.7, 133.7, 132.8, 130.1, 53.8, 36.8, 22.3.

_N_-Acetyl-_S_-(4-bromophenyl)-_L_-cysteine (7h): [8c]

Yield: 69% (101 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.53 (m, 1H), 3.54 (dd, *J* = 13.6, 2.8 Hz, 1H), 3.26 (dd, *J* = 13.6, 7.6 Hz, 1H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 136, 133.1, 132.9, 121.4, 53.5, 36.3, 22.3.

_N_-Acetyl-_S_-(4-(trifluoromethyl)phenyl)-_L_-cysteine (7i): [8c]

Yield: 74% (104 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56-7.5 (m, 4H), 4.52 (dd, *J* = 7.6, 4.4 Hz, 1H), 3.64 (dd, *J* = 14, 4.4 Hz, 1H), 3.27-3.34 (m, 1H), 1.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 173.1, 142.8, 129.7 (d, *J* = 35 Hz), 126.9, 126.7-126.8 (m), 124.3, 53.4, 35.2, 22.3.

_N_-Acetyl-_S_-(3-(trifluoromethyl)phenyl)-_L_-cysteine (7j):

Yield: 79% (111 mg); Yellow solid, mp: 122-124 °C. IR (neat, cm^{-1}): 3196, 1714, 1649, 1422, 1188, 880. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (m, 2H), 7.52-7.55 (m, 2H), 4.62 (dd, *J* = 7.6, 3.6 Hz, 1H), 3.58 (dd, *J* = 14,.4.4 Hz, 1H), 3.30-3.37 (m, 1H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 173.2, 138.7, 134.2, 132.3 (d, *J* = 32 Hz), 130.8, 126.9 (d, *J* = 3.6 Hz), 124.1 (d, *J* = 3.6 Hz), 53.5, 36, 22.2. HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{12}F_3NO_3SNa$ 330.0388; Found 330.0384

_N_-Acetyl-_S_-(2-bromophenyl)-_L_-cysteine (7k): [8c]

Yield: 68% (99 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8 Hz, 1H), 7.44 (d, *J* = 8 Hz, 1H), 7.3 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 4.55 (dd, *J* = 8, 4.4 Hz, 1H), 3.55 (dd, *J* = 13.6, 4 Hz, 1H), 3.26 (dd, *J* = 13.6, 4 Hz, 1H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 138.5, 134.1, 130.1, 129.1, 128.2, 124.7, 54.4, 35.8, 22.5.

_N_-Acetyl-_S_-(naphthalen-1-yl)-_L_-cysteine (7l): [8c]

Yield: 81% (107 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8 Hz, 1H), 7.85 (d, *J* = 8 Hz, 1H), 7.76 (d, *J* = 8 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.47-7.55 (m, 2H), 7.4 (t, *J* = 7.6 Hz, 1H), 4.44 (dd, *J* = 8, 4 Hz, 1H), 3.54 (dd, *J* = 13.6, 4 Hz, 1H), 3.26 (dd, *J* = 13.2, 8.4 Hz, 1H), 1.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 135.5, 134.4, 133.9, 130.8, 129.6, 128.9, 127.5, 127.3, 126.7, 125.9, 55.3, 37.7, 22.5.

General procedure for _S_-arylation of glutathione:

Glutathione (100 mg, 0.325 mmol, 1 equiv.) was taken in a clean round bottom flask, MeOH (6 mL) was added and reaction mixture was cooled in ice-bath. After stirring for 5 min., NaOMe (5 equiv. 84 µL, 1 molar stock solution prepared by dissolving freshly cut sodium in dry methanol) and aryldiazonium salt (**2a**, 5 equiv.) were added. The reaction mixture was stirred for 3 hours below 15 °C. The crude reaction mixture was dissolved in 6 mL of acetonitrile -H_2O(2:1) and was filtered through 2 micron filter paper. The clear solution was lyophilized to get a powder. It was then purified by HPLC (Phenomenex, Jupiter 4µ proteo 90 Å, 250 X 10.00 mm, 4 micron C- 18 column, flow rate 2 mL/min, concentration H_2O-CH_3CN: 95-5 to 5-95, gradient 36 minutes. Injection volume: 0.25 µL.) to get the pure products.

2-amino-5-((1-((carboxymethyl)amino)-1-oxo-3-(phenylthio)propan-2-yl)amino)-5-oxopentanoic acid (7m) [8c]

Yield: 68% (14.1 mg for 1 mL out of 6 mL reaction mixture). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 2H), 7.19-7.23 (m, 1H), 4.53 (dd, *J* = 8.8, 4.8 Hz, 1H), 3.89 (m, 1H), 3.84 (s, 2H), 3.44 (dd, *J* = 14, 4.8 Hz, 1H), 3.14 (dd, *J* = 14, 9.2 Hz, 1H), 2.48-2.49 (m, 2H), 2.12-2.14 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 171.4, 135.1, 130.1, 128.8, 126.5, 52.9, 40.5, 35.3, 31.1, 25.8.

2-amino-5-((1-((carboxymethyl)amino)-3-((4-chlorophenyl)thio)-1-oxopropan-2-yl)amino)-5-oxopentanoic acid (7n) [8c]

Yield: 62% (15 mg for 1 mL out of 6 mL reaction mixture).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 4.52 (dd, *J* = 8.8, 4.8 Hz, 1H), 3.94 (t, *J* = 6.4 Hz, 1H), 3.85(s, 2H), 3.43 (dd, *J* = 14, 5.2 Hz, 1H), 3.13 (dd, *J* = 14, 8.8 Hz, 1H), 2.51-2.54 (m, 2H), 2.11-2.18 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 172.6, 172.5, 171.5, 135.3, 133.9, 132.9, 130.2, 54.1, 53.7, 41.8, 36.8, 32.4, 27.

ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of synthesized compounds

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Notes

The authors declare no competing financial interest.

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