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Title: Synergistic Cooperative Effect of L-Arginine-[bmim]Br in Cascade Decarboxylative Knoevenagel–thia-Michael Addition Reactions: Green Approach Towards C-S Bond Formation with in-situ Generated Unactivated α,β-Unsaturated ester

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Synergistic Cooperative Effect of L-Arginine-[bmim]Br in Cascade Decarboxylative Knoevenagel–Thia-Michael Addition Reactions: Green Approach Towards C–S Bond Formation with In Situ Generated Unactivated α,β-Unsaturated Ester

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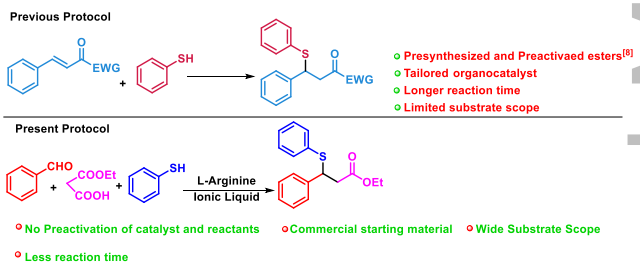
Abstract. In this report, a synergistic combination of L-arginine and [bmim]Br has been realized for the first time towards step-economical synthesis of β-aryl-β-sulfanyl esters from aromatic aldehyde, malonate and thiol via cascade thia-Michael addition reaction on in situ formed unactivated β-aryl-α,β-unsaturated esters (via decarboxylative Knoevenagel reaction) under metal-and acid/base-free conditions. Furthermore, the gram scalability and recyclability of the catalytic system (up to 5 cycles) makes our one-pot two-step protocol more economically efficient and synthetically attractive for cascade C-C and C-S bond formation than traditional two-step methods. The synergistic interaction of the catalytic system i.e. L-arginine with [bmim]Br has been probed by NMR (^{1}H and ^{13}C) studies.
Keywords: Synergistic-cooperative effect; L-Arginine; [bmim]Br; Knoevenagel-thia-Michael; Unactivated α,β-unsaturated ester

Introduction

With the introduction of the concept of green chemistry, a surge in the development of new environmentally benign processes has been observed in recent years, while on the other hand multicomponent reactions continue to facilitate the expansion of the synthetic chemist's toolbox, thus allowing the construction of complex organic motifs which were previously tedious to synthesize through traditional methods.[1-2] In this context, the search of a versatile green process for the synthesis of β-aryl-β-sulfanyl esters via thia-Michael addition reactions is of sustained interest due to the central importance of β-aryl-β-sulfanyl esters[3-5] in the modern synthetic chemistry as key intermediate for the synthesis of various drugs including thiazesim[6] as well as for their promising biological activities. However, the inherent low propensity[7] of α,β-unsaturated esters particularly β-aryl-α,β-unsaturated ester as Michael acceptor still poses a major challenge.

Conventionally, to increase the reactivity of the α,β-unsaturated esters towards thia-Michael addition reaction, various activating groups are being placed at the α or β position of the resulting alkyl cinnamates. Wang *et al*. reported the inability of their catalytic system in the thia-Michael addition reaction with ethyl cinnamate and, thus, tailored hexafluoroisopropyl cinnamate[8] was used to increase the reactivity of the substrate towards the reaction. In another report, Chu *et al*.[9] employed $FeCl_3$ for thia-Michael addition reaction on ethyl cinnamate. However the desired β- aryl-β-sulfanyl esters were obtained in low yield with very limited substrate scope. Some alternative approaches specifically utilize highly nucleophilic thiols[10,11] such as 2-(trimethylsilyl)thiophenol, 4-methoxybenzyl thiol etc. for the thia-Michael addition reaction. Despite the fact that there are some useful protocols for the synthesis of β-aryl-β-sulfanyl esters, the requirements of pre-synthesized β-aryl-α,β unsaturated esters, metal catalyst, strongly basic conditions, longer reaction time and limited substrate scopes (Scheme 1) are some of the major drawbacks of reported methods.[12-14] To date, to the best of our knowledge a fully-fledged thia-Michael addition reaction on *in situ* generated β-aryl-α,β-unsaturated esters employing multicomponent cascade reaction strategy under the influence of green cooperative catalysis is not reported in the literature.



Scheme 1. Concept of synergistic cascade decarboxylative Knoevenagel-thia-Michael addition.

Recently, a drift has been observed from the traditional mono-catalysis towards contemporary multi-catalysis particularly cooperative catalysis[15-20]

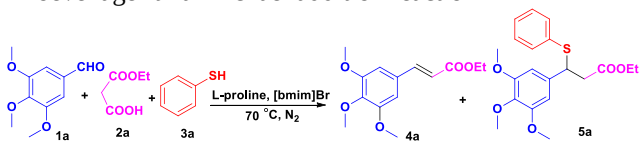
which has allowed chemists to venture into the untouched horizon of organic synthesis by improving the reactivity and selectivity of the reactions. Inspired by the robustness of the synergistic[15-17] cooperative effect, we envisaged its potential for effective cascade decarboxylative Knoevenagel condensation[21-23] and nucleophilic thia-Michael addition reaction to afford the corresponding β-aryl-β-sulfanyl esters via *in-situ* generated unactivated β-aryl-α,β-unsaturated ester.

In this report, a synergistic combination of L-arginine and [bmim]Br promoted cascade decarboxylative Knoevenagel-thia-Michael addition reaction under metal-and acid/base-free conditions is described employing aldehyde, monoethyl malonate and thiol as commercially available starting materials towards synthesis of β-aryl-β-sulfanyl ester via C-C and C-S bond formation in one pot (Scheme 1).

Results and Discussion

Initially, to test our hypothesis, we first examined the multicomponent reaction between 3,4,5-trimethoxybenzaldehyde (**1a**, 0.36 mmol), monoethyl malonate (**2a**, 1 equiv.) and thiophenol (**3a**, 1 equiv.) in presence of L-proline[24] (2 equiv.) and [bmim]Br (0.75 mL) at 70 °C (Table 1, entry 1) for 18 h under nitrogen conditions.[25] Gratifyingly, HPLC analysis of the crude reaction mixture revealed the formation of desired β-aryl-β-sulfanyl ester **5a**, albeit in 17% yield (Table 1, entry 1) along with diaryldisulfide[25] as a side product and unreacted intermediate **4a** (43%) and some unconsumed starting material **1a** (32%). Determined to improve the overall yield of **5a**, we turned our attention to optimize the reaction conditions for both steps, i.e. decarboxylative Knoevenagel reaction and thia-Michael addition. Thus, we first began investigating the effect of the amount of monoethyl malonate **2a** for decarboxylative Knoevenagel reaction with **1a**, where it was realized that increasing the amount of **2a** from 1.0 equiv. to 1.2 equiv. had only marginal effect on the reaction as some amount of starting material **1a** still remained unreacted while the desired product **5a** was obtained in 23% yield (Table 1, entry 2). Inspired by our previous reports and literature search where addition of phase transfer catalyst[26] (PTC) to the reaction mixture was reported to improve the yield of various reactions including condensation reaction, thus we decided to add tetrabutylammonium bromide (TBAB) in the above decarboxylative Knoevenagel reaction. To our satisfaction, it was observed that **1a** completely reacted with **2a** to form desired intermediate **4a**. However, there was only a slight increase in the yield of **5a** (34%) (Table 1, entry 3). After optimization of the reaction conditions for the first step i.e. decarboxylative Knoevenagel reaction, we next planned to optimize the reaction conditions for the second step, i.e. thia-Michael addition reaction between intermediate **4a** and thiophenol **3a**. It was envisioned that addition of water would enhance the nucleophilicity[27] of the thiol group towards a facile attack on intermediate **4a** besides decreasing the rate of disulfide formation during the course of reaction which might overall lead to a better product yield of **5a.** Thus varied amount of water (100-200 μL) was added to the reaction media, which led to increase in the yield of **5a** (up to 41%) with 150 μL of water (Table 1, entry 4). Towards our goal to achieve maximum yield of **5a**, varying amount of thiophenol **3a** (up to 2.0 equiv. or more) was investigated. However, the yield of **5a** could not increase beyond 47% (Table 1, entry 6) as HPLC analysis (see S.I.) of the crude reaction mixture confirms that thiophenol was still undergoing self oxidative coupling into disulfide in the presence of ionic liquid.[25] Surprisingly, it was found that addition of thiophenol in two batches (1.0 equiv. + 1.0 equiv.) improved the yield of **5a** markedly up to 67% (Table 1, entry 7) in the presence of L-proline and [bmim]Br. However, the yield of **5a** was still not to our satisfaction.

Table 1. Optimization study for cascade decarboxylative Knoevenagel-thia-Michael addition reaction[a]



S. No	Malonate (2a) [equiv.]	PhSH (3a) [equiv.]	Additive	Yield of 5a (%)[b]
1	1.0	1.2	-	17
2	1.2	1.2	-	23
3	1.2	1.2	TBAB	34
4	1.2	1.2	TBAB+ H_2O	41
5	1.2	1.5	TBAB+ H_2O	43
6	1.2	2.0	TBAB+ H_2O	47
7	**1.2**	**1.0+1.0**	**TBAB+ H_2O**	**67 (62)[c]**

[a] Reaction conditions: **1a** (0.36 mmol), **2a** (1.0-1.2 equiv.), **3a** (1.2-2.0 equiv.), L-proline (2 equiv.), [bmim]Br (0.75ml), TBAB (20 mol%), H_2O (150 μL), N_2 atm, 70 °C, 18 h; [b] yield on the basis of HPLC; [c] isolated yield.

At this point, we turned our attention towards screening of various amino acids for cascade decarboxylative Knoevenagel-thia-Michael addition reaction (Table 2, entries 1-9). Promisingly, L-arginine (Table 2, entry 8) exhibited the maximum yield of **5a** (91% HPLC yield and 88% isolated yield) followed by L-tryptophan which provided **5a** in 79% yield (Table 2, entry 6) while rest of the amino acids (Table 2, entries 2-5) provided poor yield of product **5a**. As expected, Fmoc protected L-arginine neither provided product **5a** nor intermediate **4a** (Table 2, entry 9).

Next, we screened various ionic liquids (Table 3, entries 1-6) in the presence of L-arginine for cascade

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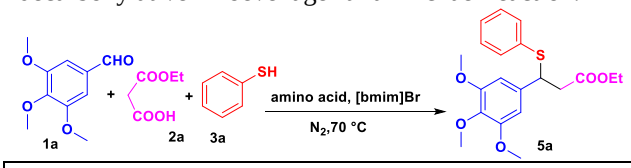
decarboxylative Knoevenagel-thia-Michael addition reaction. From the results of Table 3, it is evident that [bmim]Br[18] provided the maximum yield of **5a** (Table 3, entry 1) followed by [bmim]Cl (Table 3, entry 2) while remaining ionic liquids (Table 3,

Table 2. Screening of amino acid for cascade decarboxylative Knoevenagel-thia-Michael reaction.[a]

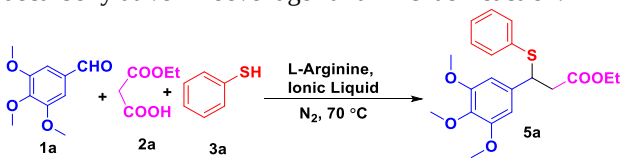


S. No	Amino acid (2 equiv)	Yield of 5a(%)[b]	S.No	Amino acid (2 equiv)	Yield of 5a(%)[b]
1	L-Proline	67 (62)[c]	6	L-Tryptophan	79
2	L-Aspartic acid	19	7	L-Lysine	67
3	L-Phenylalanine	20	8	**L-Arginine**	**91(88)**[c]
4	L-Leucine	15	9	Fmoc-L-	n.d[d]
5	L-Glutamic acid	17		Arginine	

[a] Reaction conditions: **1a** (0.36 mmol), **2a** (1.2 equiv.), **3a** (1.0 + 1.0 equiv.), amino acid (2 equiv.), [bmim]Br (0.75 ml), TBAB (20 mol%), H_2O (150 µL), N_2 atm, 70 °C, 18 h; [b] HPLC yield; [c] isolated yield; [d] n.d.= not detected.

entries 3-5) provided the desired product **5a** albeit in low yield along with unreacted intermediate **4a** and side product disulfide.[25]

Table 3. Screening of ionic liquids for cascade decarboxylative Knoevenagel-thia-Michael reaction.[a]

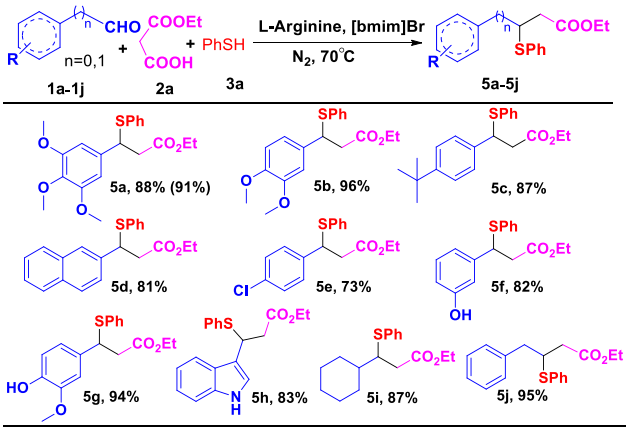


S.No.	Ionic Liquid	Yield of 5a (%)[b]
1	[bmim]Br	**88 (91)**[c]
2	[bmim]Cl	83
3	[bmim]BF_4	28
4	[bmim]PF_6	33
5	[hmim]Br	45
6	[bmmim]Br	19

[a] Reaction conditions: **1a** (0.36 mmol), **2a** (1.2 equiv.), **3a** (1.0 + 1.0 equiv.), L-arginine (2.0 equiv.), ionic liquid (0.75 ml), TBAB (20 mol%), H_2O (150 µL), N_2 atm, 70 °C, 18 h; [b] isolated yield; [c] HPLC yield.

With optimized reaction conditions in hand, the scope of the developed synergistic cooperative protocol for decarboxylative Knoevenagel-thia-Michael addition reaction with respect to the variety of structurally different aldehydes (aromatic/heteroaromatic /aliphatic) with **2a** and **3a** was investigated (Table 4, entry **5a-5j**). Both aromatic and heteroaromatic aldehydes (**5a-5g** and**5h**) provided the desired products in good to excellent yield without much influence of the electronic effect. Interestingly aliphatic aldehyde such as cyclohexane carboxaldehyde and phenylacetaldehyde underwent smooth decarboxylative Knoevenagel-thia-Michael

Table 4. Substrate scope of aldehydes for L-arginine-[bmim]Br catalyzed cascade decarboxylative Knoevenagel-thia-Michael addition reaction.[a][b]

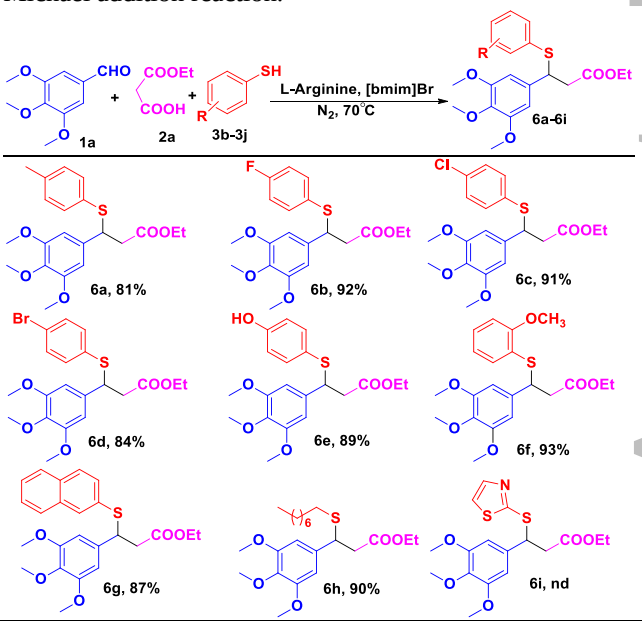


[a] Reaction conditions: **1a-1j** (0.36 mmol), **2a** (1.2 equiv.), **3a** (1.0 + 1.0 equiv.), L-arginine (2.0 equiv.), [bmim]Br (0.75 ml), TBAB (20 mol%), H_2O (150 µL), N_2 atm, 70 °C, 18 h; [b] isolated yield of **5a-5j.**

addition reaction to provide **5i-5j** in excellent yield (up to 95%).

Following investigation into the scope of the above reaction with respect to the aldehydic group (Table 4, entries **5a-5j**), variation of thiols (aromatic/ aliphatic/

Table 5. Substrate scope of thiols for L-arginine-[bmim]Br catalyzed cascade decarboxylative Knoevenagel-thia-Michael addition reaction.[a][b]

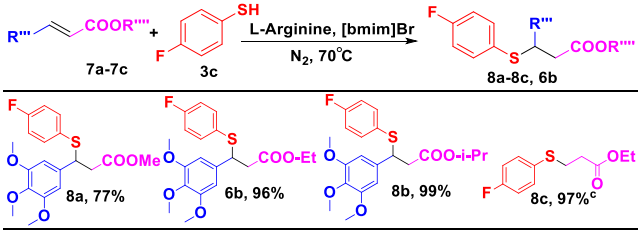


[a] Reaction conditions: **1a** (0.36 mmol), **2a** (1.2 equiv.), **3b-3j** (1.0 + 1.0 equiv.), L-arginine (2.0 equiv.), [bmim]Br (0.75 ml), TBAB (20 mol%), H_2O (150 µL), N_2 atm, 70 °C, 18 h; [b] isolated yield of **6a-6i.**

heteroaromatic) was subsequently undertaken (Table 5, entries **6a-6i**). To our satisfaction, both electron donating and withdrawing group bearing thiols provided the desired product in good to excellent yield. Less reactive aliphatic thiol also afforded the desired product (Table 5, entry **6h**) in 90% yield. Unfortunately, heteroaromatic thiol did not provide the desired product (Table 5, entry **6i**) which might be due to the formation of Arduengo-type carbene.[29]

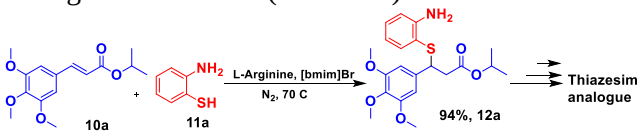
After successfully establishing the synergistic, cooperative effect of L-arginine-[bmim]Br for cascade decarboxylative Knoevenagel-thia-Michael addition (Table 4-5), we were next curious to study the reactivity of thia-Michael addition with respect to alkyl substituted α,β-unsaturated ester. Thus, pre-synthesized methyl, ethyl and isopropyl substituted β-aryl-α,β-unsaturated ester (Table 6) were subjected to thia-Michael addition reaction under developed reaction conditions. Interestingly the effect of alkyl groups were remarkable as methyl substituted β-aryl-α,β-unsaturated ester afforded 77% yield of **8a** followed by ethyl (**6b**, 96%) while *i*-propyl substituted β-aryl-α,β-unsaturated ester provided **8b** in excellent yield of 99%. Ethyl acrylate was also subjected to the developed reaction conditions, and it provided the thia-Michael addition product **8c** in 97% yield in just 4 h (Table 6, **8c**).

Table 6. Substrate scope of synthesized esters for L-arginine-[bmim]Br catalyzed cascade thia-Michael addition reaction.[a][b]

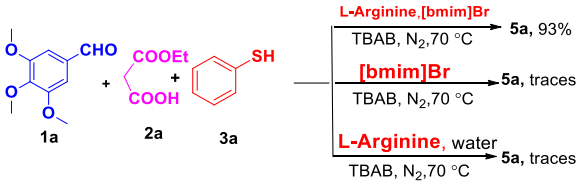


[a] Reaction conditions: **7a-7c** (0.36 mmol), **3c**(1.0 + 1.0 equiv.), L-arginine (2.0 equiv.), [bmim]Br (0.75 ml), TBAB (20 mol%), H_2O (150 µL), N_2 atm, 70 °C, 12h; [b] isolated yield of **8a-8c**, **6b**; [c] 4h.

Interestingly, the developed protocol also catalyzed the synthesis of intermediate (**12a**) of analogue of thiazesim drug which upon acidic cyclization followed by alkylation would provide an analogue of thiazesim (Scheme 2).[9]



Scheme 2. Synthesis of intermediate of analogue of thiazesim.



Scheme 3. Control experiment for synergistic study.

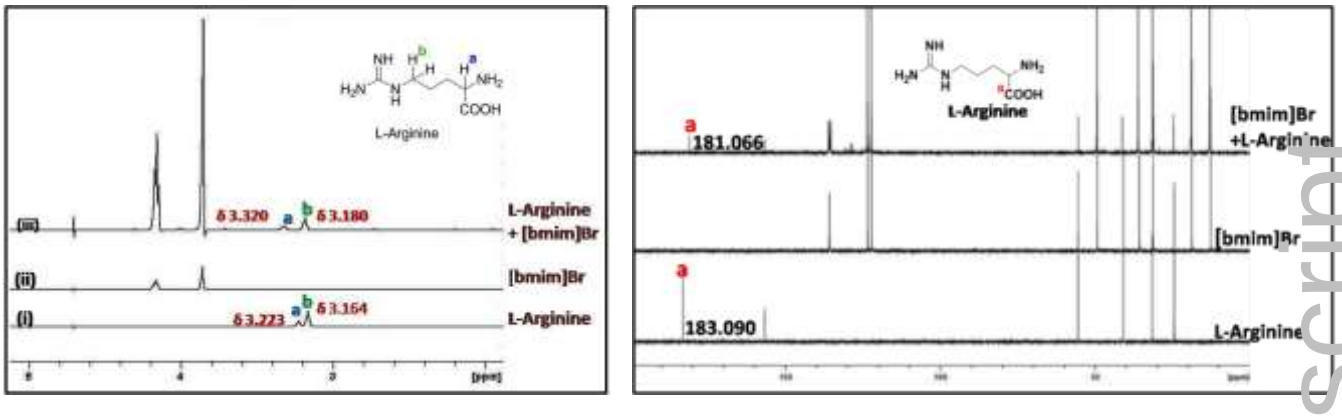
Encouraged by the above results, we next ventured to study the synergism between L-arginine and [bmim]Br for which control experiments were conducted. As illustrated in Scheme 3, the reaction between **1a**, **2a** and **3a** in presence of either L-arginine (without ionic liquid) or ionic liquid (without L-arginine) afforded the expected product **5a** in traces. The sluggish rate of decarboxylative Knoevenagel reaction between **1a** and **2a** towards formation of intermediate **4a** in the presence of individual catalyst may be attributed for the trace formation of **5a** as in the meantime thiol might be undergoing self-oxidative coupling to disulfide in the presence of either L-arginine[30] or ionic liquid[25] and thus would be not available for thia-Michael addition reaction. From these control experiments, it was clear that the presence of both the catalyst was crucial for multicomponent cascade decarboxylative Knoevenagel-thia-Michael addition reaction resulting into C-C and C-S bond formation.

On the basis of above control experiments (Scheme 3), we further initiated our effort to establish the importance of synergistic interaction between L-arginine and ionic liquid by using NMR (^1H and ^{13}C) spectroscopy. Thus, ^1H NMR spectra of a mixture of L-arginine and [bmim]Br was recorded in D_2O and compared with individual NMR spectra of L-arginine and [bmim]Br. Interestingly, the ^1H NMR spectra (Figure 1) indicated that L-arginine forms hydrogen bond with the ionic liquid resulting into the downfield shift of proton H(a) (δ 3.223) and H(b) (δ 3.164) to δ 3.320 and δ 3.180 respectively. Similarly, ^{13}C NMR spectra of a mixture of L-arginine-[bmim]Br was also recorded and it was observed that the carboxylic group of L-arginine in the presence of [bmim]Br showed an upfield shift from 183.090 ppm to 181.066 ppm when compared with ^{13}C NMR spectra of individual L-arginine. It is worth pointing out that our observations based upon NMR spectra analysis were concordant with the observation of Ren *et al.*[31] where they proposed that the head group of the amino acid along with the guanidine moiety of L-arginine interacts with the ionic liquid.

In continuation of the above synergistic interaction studies by NMR, it was visualized that the reaction could proceed via two reaction pathways viz. (i) imine formation between the aldehyde group and the arginine or (ii) by the activation of the aldehydic group by the catalytic complex, i.e. L-arginine-[bmim]Br. Thus, to probe the actual reaction pathway, ^1H NMR was recorded of a mixture of L-arginine,

[bmim]Br and vanillin (a water-soluble aromatic aldehyde) in D_2O (Figure 2). Interestingly, the ^1H NMR spectra clearly demonstrated the presence of aldehydic proton of vanillin at δ 9.296. However due to interaction with ionic liquid an upfield shift in aldehydic proton was observed, when compared with standard aldehydic proton of vanillin at δ 9.514. The result was further confirmed by ^{13}C NMR spectra where the carbonyl carbon of vanillin in the mixture appeared at 192.626 ppm while the carbonyl carbon of standard vanillin appeared at 194.591 ppm (see S.I.) The presence of aldehydic proton and carbonyl carbon in NMR spectra thus excluded the possibility of the imine pathway during the reaction pathway.

To further clarify whether the present decarboxylative Knoevenagel-thia-Michael addition reaction involves a radical pathway or not, L-arginine-[bmim]Br promoted reaction between **1a**, **2a**



(a) (b)

Figure 1. (a) ^1H NMR and; **(b)** ^{13}C NMR study for synergistic catalytic system.

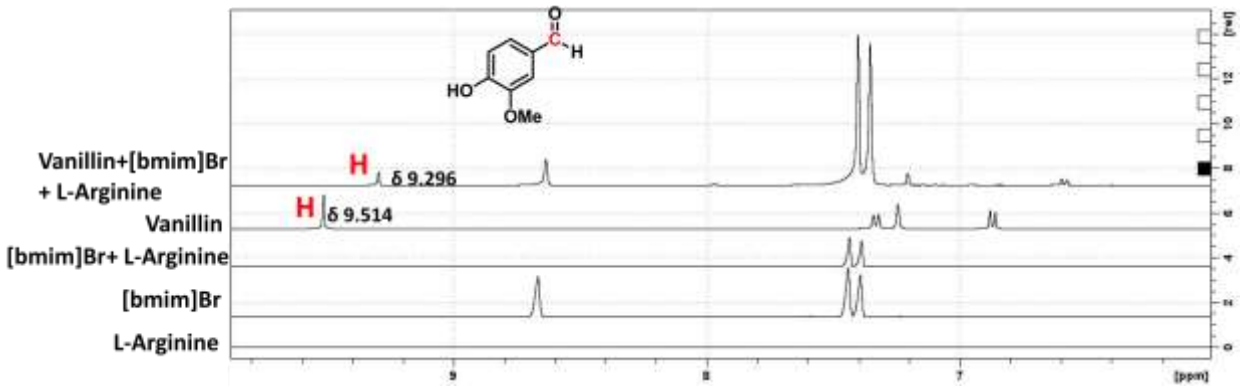
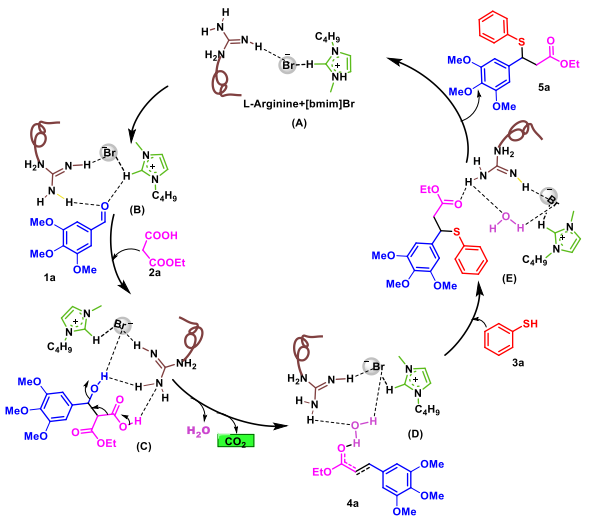


Figure 2. NMR experiment to probe the mechanism of decarboxylative Knoevenagel-thia-Michael addition reaction.

and **3a** was conducted in the presence of TEMPO (up to 4 equivalent), and the desired product **5a** was obtained in 84% yield, thus excluding the possibility of the radical mechanism during the reaction.

Based upon above mechanistic observations as well as previous studies[31, 32] including our[18] report on DFT probed synergistic interaction, we proposed a reaction mechanism for decarboxylative Knoevenagel-thia-Michael addition reaction (Scheme 4). Thus, L-arginine and [bmim]Br interact with each other via hydrogen bonding between bromide[18] anion of ionic liquid and guanidine residue of the L-arginine to generate complex A. Then the complex A interacts with the carbonyl oxygen of the aldehyde (**1a**) making it susceptible for Knoevenagel condensation reaction with monoethyl malonate (**2a**) generating intermediate C which under the influence of synergistic catalytic complex undergoes concerted decarboxylation and dehydration resulting into *in situ* generation of ethyl (E)-3-(3,4,5-trimethoxy phenyl)acrylate (**4a)** as a reactive intermediate. Subsequently, the bromide anion along with the water molecule activates the thiol (**3a**) moiety for nucleophilic thia-Michael addition on *in situ* generated intermediate **4a** resulting into generation of ethyl 3-(phenylthio)-3-(3,4,5-trimethoxyphenyl)

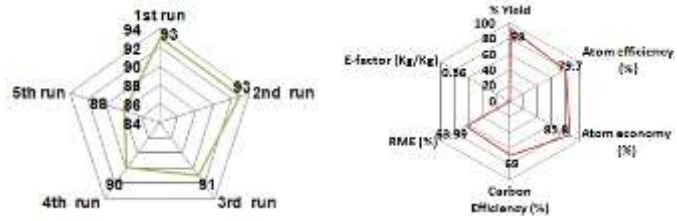


Scheme 4. Plausible reaction mechanism for decarboxylative Knoevenagel-thia-Michael addition reaction.

propanoate (**5a**) along with the release of the catalytic system, i.e. L-arginine-[bmim]Br for reuse in the next reaction cycle.

Further, from an economical point of view, recyclability of the catalytic system for the above reaction was studied and it was found that the catalytic system could be used up to 5 cycles without significant loss in the yield of **5a** (Figure 3a).

In order to assess the efficacy of the present protocol, the relevant, important green metrics and parameters (atom economy, atom efficiency, carbon efficiency, E-factor, reaction mass efficiency, etc.) were calculated and represented in a radar chart (Figure 3b).[33]



(a) **(b)**

Figure 3. (a) Recyclability study; (b) Green metrices of cascade decarboxylative Knoevenagel-thia-Michael addition reaction.

To probe the practical applicability of the developed protocol for cascade decarboxylative Knoevenagel-thia-Michael addition reaction (Table 3), preparative scale reaction was accomplished using **1a** (980 mg, 5 mmol), **2a** (1.2 equiv.) and **3a** (1.0 + 1.2 equiv.) in the presence of L-arginine-[bmim]Br under N_2 atmosphere at 70 °C which successfully afforded the desired product **5a** in 87% yield, however, it required longer reaction time of 28 h for completion of the reaction.

Conclusion

In conclusion, we have for the first time reported thia-Michael addition reaction on *in situ* generated low reactive electrophile, i.e. α,β-unsaturated esters via decarboxylative Knoevenagel reaction by harnessing the synergistic, cooperative effect of L-arginine-[bmim]Br. In fact, the crucial cooperative action of L-arginine-[bmim]Br has enabled us to synthesize a range of aromatic, heteroaromatic and aliphatic substituted β-sulfanyl esters with varied aromatic and aliphatic thiol which was not possible by use of L-arginine or [bmim]Br alone. Meritoriously, the added benefit of the recyclability of the catalytic system (up to five cycles) and gram scalable synthesis makes the protocol practical, waste-free, atom-economical and overall greener than traditional methods.

Experimental Section

General information

All the reagents/substrates were obtained from commercial sources (Sigma Aldrich or Alfa-Aesar). The solvents used for isolation/purification of the compounds were obtained from commercial sources (Merck/Sd fine) and were used without further purification. The ionic liquids used were obtained either commercially (Merck or Alfa Aesar) or synthesized according to the reported method.[34] Amino acid used in the study were purchased from Sigma-Aldrich. Column chromatography was performed using silica gel (Merck, 100-200 mesh size). The organic extracts were dried over anhydrous sodium sulfate (Merck grade). Evaporation of solvent was performed at reduced pressure using Buchi rotavapor (Switzerland).

General procedure for multicomponent decarboxylative Knoevenagel-thia-Michael addition reaction for synthesis of β-aryl-β-sulfanyl esters (Table 4 and 5).

A mixture of substituted aldehyde (0.36 mmol), monoethyl malonate (1.2 equiv.), thiophenol (1.0 equiv.), L-arginine (2.0 equiv), TBAB (20 mol%) and [bmim]Br (0.5 mL) was stirred at 70 °C under nitrogen atmosphere. After 6 h of reaction time, 1.0 equiv. of additional thiophenol was added again to the reaction mixture and the resulting reaction was maintained at 70 °C for 18 h[28] or until the completion of the reaction. After completion of reaction, the reaction was cooled and taken into diethyl ether (2 x 10 mL). The combined organic layer was washed with water and dried over anhydrous Na_2SO_4 and evaporated under vacuum. The obtained residue was purified using column chromatography (silica gel 100-200 mesh size) with EtOAc/hexane as eluent to afford the desired product **5a-5j** and **6a-6h.**

General procedure for the synthesis of β-aryl-β-sulfanyl esters utilizing presynthesized α,β-unsaturated esters (Table 6 and Scheme 2).

A mixture of substituted α,β-unsaturated esters (0.36 mmol), thiophenol (1.0 equiv.), L-arginine (2.0 equiv), TBAB (20 mol%) and [bmim]Br (0.5 mL) was stirred at 70 °C under nitrogen atmosphere. After 6 h of reaction time, 1.0 equiv. of additional thiophenol was added again to the reaction mixture and the resulting reaction mixture was maintained at 70 °C for 12 h or until the completion of the reaction. After completion of reaction, the reaction was cooled and taken into diethyl ether (2 x 10 mL). The combined organic layer was washed with water and dried over anhydrous Na_2SO_4 and evaporated in vacuo. The

obtained residue was purified using column chromatography (silica gel 100-200 mesh size) with EtOAc/Hexane as eluent to afford the desired product **8a-8c** and **6b.**

Procedure for recyclability study

A mixture of substituted aldehyde **1a** (0.36 mmol), monoethyl malonate **2a** (1.2 equiv.), thiophenol **3** (1.0 equiv.), L-arginine (2.0 equiv), TBAB (20 mol%) and [bmim]Br (0.5 mL) was stirred at 70 °C under nitrogen atmosphere. After 6 h of reaction time, 1.0 equiv. of additional thiophenol was added again to the reaction mixture and the resulting reaction mixture was maintained at 70 °C for 18h or till the completion of the reaction. After completion of the reaction, the reaction mixture was extracted by diethyl ether (2-3 times) to obtain the crude product. The catalytic system (i.e. ionic liquid-L-arginine insoluble in diethyl ether) was concentrated on rotavapor under reduced pressure to remove traces of ether and then reused for the subsequent decarboxylative Knoevenagel-thia-Michael addition reaction. The diethyl layer (2-3 times) was washed with water and dried over anhydrous Na_2SO_4 and evaporated under vacuum. The obtained residue was purified using column chromatography (silica gel 100-200 mesh size) with EtOAc/hexane as eluent to afford the desired product (**5a**). The same catalytic system could be used up to5 cycles without much loss in yield.

Ethyl 3-(phenylthio)-3-(3,4,5-trimethoxyphenyl)propanoate [5a]

91% yield (120 mg), white solid, m.p. 68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.33 (m, 2H), 7.29-7.26 (m, 3H), 6.44 (s, 2H), 4.58 (t, *J* = 7.8 Hz, 1H), 4.10-4.08 (m, 2H), 3.83 (s, 3H), 3.80(s, 6H), 3.00-2.87 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.70, 153.00, 137.24, 136.06,133.70, 133.50, 128.86 , 127.95, 104.60, 60.83, 60.76, 56.04, 49.54, 41.02, 14.13.HRMS-ESI: m/z $[M+Na]^+$ for $[C_{20}H_{24}O_5S]Na$ calculated 399.1242; observed 399.1206.

Ethyl 3-(3,4-dimethoxyphenyl)-3-(phenylthio)propanoate [5b]

96% yield (120 mg), white solid, m.p. 120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.32 (m, 2H), 7.29-7.24 (m, 3H), 6.81-6.75 (m, 3H), 4.62 (t, *J* = 8.4, 7.2 Hz, 1H), 4.09-4.07 (m, 2H), 3.87 (s, 3H), 3.84 (s, 3H), 2.99-2.88 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.74, 148.75, 148.34, 133.73, 133.48, 132.96, 128.82, 127.77, 119.77, 110.88, 110.83, 60.68, 55.84, 55.81, 48.99, 41.13, 14.12. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{19}H_{22}O_4S]Na$ calculated 369.1136; observed 369.1136.

Ethyl 3-(4-(tert-butyl)phenyl)-3-(phenylthio)propanoate [5c]

87% yield (106 mg), white solid, m.p. 52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.34 (m, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.28-7.24 (m, 3H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.67 (t, *J* = 7.7 Hz, 1H), 4.06 (qd, *J* = 7.1, 1.7 Hz, 2H), 2.99-2.91 (m, 2H), 1.31 (s, 9H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.87, 150.45, 137.32, 134.11, 133.09, 128.80, 127.59, 127.24, 125.36, 60.60, 48.74, 41.18, 34.49, 31.30, 14.04. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{21}H_{26}O_2S]Na$ calculated 365.1551; observed 365.1514.

Ethyl 3-(naphthalen-2-yl)-3-(phenylthio)propanoate [5d]

81% yield (114 mg), white solid, m.p. 52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.81-7.76 (m, 1H), 7.64-7.49 (m, 2H), 7.38 (d, *J* = 5.1 Hz, 2H), 7.30 (ddd, *J* = 6.5, 3.9, 2.0 Hz, 2H), 7.25 (ddd, *J* = 7.3, 2.8, 1.7 Hz, 3H), 5.52 (t, *J* = 7.4 Hz, 1H), 4.07 (dd, *J* = 7.1, 5.3 Hz, 2H), 3.14 (d, *J* = 7.6 Hz, 2H), 1.14 (t, *J* = 7.1 Hz, 3H)); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.91, 135.80, 134.00, 133.58, 130.85, 128.96, 128.79, 128.27, 127.86, 126.322, 125.73, 125.07, 124.63, 123.22, 60.73, 40.91, 14.05. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{21}H_{20}O_2S]Na$ calculated 359.1082; observed 359.1073.

Ethyl 3-(4-chlorophenyl)-3-(phenylthio)propanoate [5e][35]

73% yield (83 mg), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.29 (m, 2H), 7.29-7.23 (m, 5H), 7.21-7.17 (m, 2H), 4.62 (dd, *J* = 8.7, 6.9 Hz, 1H), 4.07 (dd, *J* = 7.1, 4.0 Hz, 2H), 2.92 (qd, *J* = 15.8, 7.8 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ170.43, 139.18, 133.56, 133.18, 133.15, 129.01, 128.92, 128.56, 128.03, 60.79, 48.57, 40.83, 14.07. HRMS-ESI: m/z $[M+H]^+$ for $[C_{17}H_{18}ClO_2S]$ calculated 321.0716; observed 321.0735.

Ethyl 3-(3-hydroxyphenyl)-3-(phenylthio)propanoate [5f]

82% yield (89 mg), colorless oil;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.33 (m, 2H), 7.27-7.25 (m, 3H), 7.14 (t, *J* = 7.9 Hz, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.77-6.76 (m, 1H), 6.73-6.70 (m, 1H), 5.41 (s, 1H), 4.61 (t, *J* = 7.8 Hz, 1H), 4.08 (ddq, *J* = 14.6, 7.4, 3.7 Hz, 2H), 2.99-2.88 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.08, 155.77,142.24, 133.63, 133.24, 129.66, 128.86, 127.80, 119.95, 114.67, 114.64, 60.92, 48.96, 41.10, 14.06. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{17}H_{18}O_3S]Na$ calculated 325.0874; observed 325.0858.

Ethyl 3-(4-hydroxy-3-methoxyphenyl)-3-(phenylthio) propanoate [5g]

94% yield (113 mg), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.33 (m, 2H), 7.28-7.26 (m, 3H), 6.82(d, *J* = 8.4 Hz, 1H), 6.77-6.75 (m, 2H), 5.60 (s, 1H), 4.61 (dd, *J* = 8.3, 7.2 Hz, 1H), 4.10-4.04 (m, 2H), 3.84 (s, 3H), 2.98-2.87 (m, 2H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.76, 146.33, 144.99, 133.79, 133.42, 132.32, 128.82, 127.75, 120.51, 114.16, 110.23, 60.68, 55.90, 49.07, 41.21, 14.11. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{18}H_{20}O_4S]Na$ calculated 355.0980; observed 355.0963.

Ethyl 3-(1H-indol-3-yl)-3-(phenylthio)propanoate [5h]

83% yield (97 mg), oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.37-7.15 (m, 8H), 6.95 (d, *J* = 2.3 Hz, 1H), 5.07 (t, *J* = 7.6 Hz, 1H), 4.11-4.05 (m, 2H), 3.13-3.02 (m, 2H), 1.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.43, 139.18, 133.56, 133.18, 133.14, 129.01, 128.92, 128.56, 128.03, 60.79, 48.57, 40.82, 14.07. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{19}H_{19}NO_2S]Na$ calculated 348.1034; observed 348.1041.

Ethyl 3-cyclohexyl-3-(phenylthio)propanoate [5i]

87% yield (104 mg), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.43 (m, 2H), 7.28-7.25 (m, 2H), 7.21-7.18 (m, 1H), 4.10-4.05 (m, 2H), 3.51-3.48 (m, 1H), 2.66 (dd, 5.2, 12.4 Hz, 1H), 2.54 (dd, 6.8, 12.8 Hz, 1H), 1.86-1.57 (m, 6H), 1.29-1.11 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.97, 135.83, 131.77, 128.86, 126.74, 60.52, 51.64, 42.23, 38.27, 30.21, 29.69, 26.39, 26.33, 14.15. HRMS-ESI: m/z $[M+H]^+$ for $[C_{17}H_{25}O_2S]$ 293.1575; observed 293.1572.

Ethyl 4-phenyl-3-(phenylthio)butanoate [5j]

95% yield (103 mg), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.45 (m, 2H), 7.35-7.21 (m, 8H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.82-3.74 (m, 1H), 2.96 (ddd, *J* = 21.8, 14.0, 7.2 Hz, 2H), 2.57 (dd, *J* = 7.0, 3.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.54, 153.10, 137.43, 135.80, 135.04, 134.32, 132.01, 129.02, 104.66, 60.85, 56.09, 49.84, 40.95, 14.14. HRMS-ESI: m/z $[M+H]^+$ for $[C_{18}H_{21}O_2S]$ calculated 301.1262; observed 301.1258.

Ethyl 3-(p-tolylthio)-3-(3,4,5-trimethoxyphenyl)propanoate [6a]

81% yield (114 mg), white solid, m.p. 70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 6.43

(s, 2H), 4.53 (s, 1H), 4.09 (dd, *J* = 12.8, 7.0 Hz, 2H), 3.84 (s, 3H), 3.80 (s, 6H), 2.99-2.83 (m, 2H), 2.34 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 170.78, 152.98, 138.27, 136.17, 134.27, 129.64, 104.69 , 60.83, 60.71, 56.03, 49.80, 40.95, 21.13, 14.13. HRMS-ESI: m/z $[M+H]^+$ for $[C_{21}H_{27}O_5S]$ calculated 413.1399; observed 413.1430.

Ethyl 3-((4-fluorophenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [6b]

92% yield (132 mg), white solid, m.p. 82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.28 (m, 2H), 6.99-6.95 (m, 2H), 6.39 (s, 2H), 4.49 (t, *J* = 7.8 Hz, 1H), 4.12-4.09 (m, 2H), 3.84 (s, 3H), 3.80 (s, 6H), 2.91 (dd, *J* = 7.8, 2.5 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.58, 162.94 (d, *J* = 247.0 Hz), 153.02, 137.37, 136.59 (d, *J* = 8.0 Hz), 135.93, 128.37, 115.91 (d, *J* = 22.0 Hz), 104.68, 60.83, 60.80, 56.07, 50.23, 40.76, 14.13. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{20}H_{23}FO_5S]Na$ calculated 417.1148; observed 417.1123.

Ethyl 3-((4-chlorophenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [6c]

91% yield (135 mg), white solid, m.p. 65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 4H), 6.43 (s, 2H), 4.55 (t, *J* = 7.7 Hz, 1H), 4.11 (qd, *J* = 7.1, 1.6 Hz, 2H), 3.84 (s, 3H), 3.81 (s, 6H), 2.91 (dd, *J* = 7.7, 1.9 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.53, 153.08, 137.41, 135.78, 135.02 , 134.31, 132.00, 129.00, 104.65, 60.85, 56.08, 49.84, 40.95, 14.13. HRMS-ESI: m/z $[M+H]^+$ for $[C_{20}H_{24}ClO_5S]$ calculated 428.1298; observed 428.1293.

Ethyl 3-((4-bromophenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [6d]

84% yield (137 mg), white solid, m.p. 56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.39 (m, 2H), 7.28-7.18 (m, 2H), 6.43 (s, 2H), 4.56 (s, 1H), 4.11 (qd, *J* = 7.1, 1.5 Hz, 2H), 3.84 (s, 3H), 3.81 (s, 6H), 2.91 (dd, *J* = 7.7, 1.9 Hz, 2H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.51, 153.10, 135.75, 135.14, 132.71, 131.96, 122.35, 104.65, 60.85, 56.09, 49.70, 40.96, 14.13. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{20}H_{23}ClO_5S]Na$ calculated 477.0347; observed 477.0316.

Ethyl 3-((4-hydroxyphenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [6e]

89% yield (125 mg), white solid, m.p. 118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.21 (m, 2H), 6.75-6.73 (m, 2H), 6.38 (s, 2H), 5.09 (s, 1H), 4.43 (t, *J* = 7.8 Hz, 1H), 4.11 (qd, *J* = 7.1, 1.7 Hz, 2H), 3.84 (s, 3H), 3.80 (s, 6H), 2.96-2.85 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.01, 156.52, 152.90, 137.02, 136.28, 123.42, 115.86, 104.76, 60.84, 56.05, 50.34, 40.67, 14.11. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{20}H_{24}O_6S]Na$ calculated 415.1191; observed 415.1169.

Ethyl 3-((2-methoxyphenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [6f]

93% yield (136 mg), white solid, m.p. 83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (m, 2H), 6.88 (dd, *J* = 11.8, 4.4 Hz, 2H), 6.50 (s, 2H), 4.73 (dd, *J* = 8.4, 7.0 Hz, 1H), 4.05 (qd, *J* = 7.1, 1.0 Hz, 2H), 3.87 (s, 3H), 3.81 (s, 9H), 2.94 (dd, *J* = 7.7, 2.5 Hz, 2H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.82, 159.23, 152.95 , 137.23, 136.13, 134.77, 129.51, 121.72, 120.91, 110.84, 104.71, 60.76, 60.61, 56.06, 55.79, 47.39, 41.09, 14.09. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{21}H_{26}O_6S]Na$ calculated 429.1348; observed 429.1364.

Ethyl 3-(naphthalen-2-ylthio)-3-(3,4,5-trimethoxyphenyl) propanoate [6g]

87% yield (133 mg), white solid, m.p. 92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.77 (m, 2H), 7.75 (dd, *J* = 9.0, 4.2 Hz, 2H), 7.51-7.47 (m, 2H), 7.43 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.48 (s, 2H), 4.70 (t, *J* = 7.7 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 3.75 (s, 6H), 2.99-2.93 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.71, 153.07, 136.03, 133.52, 132.84, 132.64, 130.91, 130.59, 128.38, 127.63, 127.52, 126.54, 104.72, 60.83, 60.77, 56.02, 49.51, 41.06, 14.12. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{24}H_{26}O_5S]Na$ calculated 449.1399; observed 449.1385.

Ethyl 3-(octylthio)-3-(3,4,5-trimethoxyphenyl)propanoate [6h]

90% yield (133 mg), viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (s, 2H), 4.22 (t, *J* = 7.7 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 6H), 3.83 (3H), 2.83-2.82 (m, 2H), 2.38- 2.35 (m, 2H), 1.53-1.47 (m, 2H), 1.33-1.28 (m, 5H), 1.19 (t, *J* = 7.6 Hz, 3H), 0.87 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.72, 153.10, 137.24, 137.13, 104.62, 60.76, 60.64, 56.09, 45.88, 42.02, 31.75, 31.50, 29.18, 29.12, 28.83, 22.59, 14.11, 14.03. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{22}H_{37}O_5S]$ calculated 413.2362; observed 413.2354.

Methyl 3-((4-fluorophenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [8a]

77% yield (105 mg), white solid, m.p. 101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 2H), 7.00-6.96 (m, 2H), 6.39 (s, 2H), 4.50 (t, *J* = 7.7 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 6H), 3.67 (s, 3H), 2.93 (dd, *J* = 7.7, 1.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.06, 162.27 (*J* = 290.5 Hz), 153.06, 136.57 (*J* = 8.3 Hz), 135.88, 115.93 (*J* = 21.6 Hz), 104.65, 60.84, 56.09, 51.92, 50.17, 40.56. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{19}H_{21}FO_5S]Na$ calculated 403.0991; observed 403.0992.

Isopropyl 3-((4-fluorophenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [8b]

99% yield (146 mg), white solid, m.p. 73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H), 6.99-6.95 (m, 2H), 6.38 (s, 2H), 4.98 (dt, *J* = 12.5, 6.3 Hz, 1H), 4.47 (t, *J* = 7.9 Hz, 1H), 3.83 (s, 3H), 3.80 (s, 6H), 2.88 (dd, *J* = 7.9, 3.2 Hz, 2H), 1.20 (d, *J* = 6.3 Hz, 3H), 1.15 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.07, 162.95 (d, *J* = 247.30 Hz), 152.98, 137.37, 136.62 (d, *J* = 9.0 Hz), 135.91, 128.37, 128.34, 115.89 (d, *J* = 22.0 Hz), 104.74, 68.25, 60.84, 56.06, 50.33, 40.98, 21.73, 21.70. HRMS-ESI: m/z $[M+Na]^+$ for $[C_{21}H_{25}FO_5S]Na$ calculated 431.1304; observed 431.1298.

Ethyl 3-((4-fluorophenyl)thio)propanoate [8c]

97% yield (80 mg), oil;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.39 (m, 2H), 7.05-7.01 (m, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.12 (t, *J* = 7.2 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 171.65, 162.16 (d, *J* = 245.6 Hz), 133.38 (d, *J* = 8.1 Hz), 130.05, 116.14 (d, *J* = 21.7 Hz), 60.74, 34.49, 30.44, 14.18.HRMS-ESI: m/z $[M+H]^+$ for $[C_{11}H_{14}FO_2S]$ calculated 229.0699; observed 229.0688.

Isopropyl 3-((2-aminophenyl)thio)-3-(3,4,5-trimethoxyphenyl) propanoate [12a]

94% yield (137 mg), white solid, m.p. 109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.2-7.10 (m, 2H), 6.71 (d, *J* = 7.6 Hz, 1H), 6.60 (t, *J* = 7.5 Hz, 1H), 6.32 (s, 2H), 5.02-4.96 (m, 1H), 4.42 (t, *J* = 7.9 Hz, 1H), 4.34 (s, 2H), 3.82 (s, 3H), 3.76 (s, 6H), 3.02-2.86 (m, 2H), 1.21 (d, *J* = 6.4 Hz, 3H), 1.17 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.45, 152.89, 149.62, 138.07, 137.24, 136.40, 130.76, 118.10, 115.27, 114.82, 104.42, 68.26, 60.85,

56.00, 48.34, 40.44, 21.76, 21.72. HRMS-ESI: m/z $[M+H]^+$ for $[C_{21}H_{28}NO_5S]$ calculated 406.1688; observed 406.1684.

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[28] Interestingly the progress of L-arginine-[bmim]Br catalyzed decarboxylative Knoevenagel-thia-Michael addition reaction under optimized reaction conditions was monitored at different time intervals of 3h, 6 h and 18 h by HPLC (see SI) which revealed that after 6 h of reaction time, thiol was completely oxidized into disulfide and hence it was required to add second batch of thiol after 6h. The formation of disulfide even under nitrogen conditions may be due to the thermal heating.[18]

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FULL PAPER

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