CHAPTER 2

A NOVEL SYNTHETIC APPROACH TO CINNAMIC ESTERS


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A novel synthetic approach to cinnamic esters

2.1 Introduction

Cinnamic acids and its derivatives are of high biological importance as they possess antifungal and antibacterial activities.\(^1\)\(^-\)\(^6\) Despite the great variety of well-known and tried methods, the development of new general synthetic protocols for cinnamic acids and their esters is still an active field. A wide range of approaches are available for the synthesis of cinnamic acids and their esters. Some of the most important methods are the Perkin reaction, the Claisen condensation, the Knoevenagel-Doebner condensation, and the Heck reaction. The Perkin reaction\(^7\)\(^-\)\(^{11}\) is the oldest known method of producing cinnamic acid commercially. In this reaction benzaldehyde is condensed with acetic anhydride in the presence of sodium acetate as catalyst. Other possible catalysts are potassium acetate, tertiary amines, and potassium phosphate and trimethyl borate.

The Claisen condensation\(^12\)\(^,\)\(^13\) of benzaldehyde with acetic acid esters in the presence of alkali alcoholates yields cinnamic acid esters. Cinnamic esters can be prepared from aryl halides, and esters of acrylic acid by using catalysts such as palladium.\(^14\)\(^-\)\(^{23}\) The palladium-catalyzed C-C coupling between aryl halides or vinyl halides and activated alkenes in the presence of a base is referred as the "Heck Reaction." Recent developments in the catalysts and reaction conditions have resulted in a much broader range of donors and acceptors being amenable to the Heck Reaction. One of the benefits of the Heck reaction is its outstanding \textit{trans} selectivity. But, when more than one halogen is present on the ring, it suffers with chemo selectivity. The Wittig Reaction allows the preparation of cinnamic esters by the reaction of an aldehyde or ketone with the ylide generated from phosphonium salt.\(^24\)\(^-\)\(^{27}\) Cinnamic esters can be prepared from styrene in presence of carbon monoxide by using catalysts such as platinum or palladium.\(^28\),\(^29\)

Knoevenagel has reported the synthesis of cinnamic acids from benzaldehydes and malonic esters.\(^30\)\(^-\)\(^{36}\) In this method, benzaldehyde was condensed with diethyl malonate in refluxing in benzene or toluene containing a catalytic amount of piperidine. The condensation product was further hydrolyzed to obtain the cinnamic acids. Doebner has
modified this method to obtain the cinnamic acids in a one-pot process by refluxing aromatic aldehydes benzaldehydes with malonic acid in refluxing pyridine containing catalytic amount of piperidine (Scheme 2.1) and this is the most popular method of cinnamic acid synthesis. Though the Knoevenagel-Doebner reaction has been extensively documented, substitution of the aldehyde component with an alternative functional group has not been documented. We decided to investigate on a possible alternative for the aldehyde component in the Knoevenagel-Doebner reaction for the cinnamic acid and cinnamic ester synthesis.

Scheme 2.1

\[
\text{Scheme 2.1}
\]

\[
\begin{align*}
\text{FG} & \quad \text{CHO} + \quad \text{COOH} \quad \text{COOH} \quad \xrightarrow{\text{Piperidine}} \quad \text{FG} \quad \text{CH}_2\text{CHOH} \\
\text{FG} & \quad \text{Br} \quad \text{Br} \quad \text{Br} \quad \text{Br} \quad \xrightarrow{\text{base}} \quad \text{FG} \quad \text{CHO}
\end{align*}
\]

\(a,a\)-Dibromomethyl aromatics 1 are important reagents in organic synthesis, as they are extensively used for the preparation of aromatic aldehydes. Functional group transformation of \(gem\)-dibromomethyl aromatics to aldehydes is a widely used method for the synthesis of aldehydes.\(^{37}\)

A further application of \(gem\)-dibromomethyl aromatics is described by Nicolas Weibel and co-workers.\(^{38}\) They have reported a one-pot synthesis of imines 2 starting from \(gem\)-dibromomethyl aromatics and primary amines.

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It is thus observed that, benzal bromides act as an aldehyde equivalent and participate in the reaction with an amine to produce an imine. We envisioned that, this report could be exploited further and decided to explore the application of benzal bromides as aldehyde equivalents in cinnamic acid and cinnamic ester synthesis.  

2.2 Synthesis of gem-dibromomethyl aromatics

2.2.1 Materials and methods

The methyl aromatics (respective toluenes), NBS, carbon tetrachloride and benzoyl peroxide used for the preparation of gem-dibromides were obtained from commercial sources. Preparation of gem-dibromomethyl aromatics were achieved by radical bromination (Scheme 2.2) of the corresponding methyl analogues using 2.0 equivalents of NBS. The gem-dibromomethyl aromatics 3-29 were purified by flash chromatography over silica gel (230-400 mesh) using 5% ethyl acetate in petroleum ether and stored at room temperature. $^1$H and $^{13}$C NMR spectra of the gem-dibromides were recorded on 400-MHz and 100-MHz Bruker spectrometer respectively and elemental analysis was performed on a Thermo Finnigan FLASH EA 1112 CHN analyzer. Infrared spectra were recorded on a Thermo Scientific Nicolet 6700 FT-IR spectrometer. Melting points were recorded (uncorrected) on Buchi Melting Point B-545 instrument. Coupling constants were reported wherever it was necessary in hertz (Hz). Reactions were carried out in an oven dried three-necked round-bottomed flask.

![Scheme 2.2](image)
2.2.2 Results and discussion

In the present investigation fifteen aromatic gem-dibromomethyl compounds were synthesized from the corresponding commercial methyl aromatics using NBS (2 equiv) in carbon tetrachloride containing a catalytic amount of benzoyl peroxide at reflux. The newly synthesized gem-dibromides, 3-17 are listed Table 2.1.

Table 2.1: Newly synthesized aromatic α,α-dibromomethyl compounds.
Similarly, fifteen heteroaromatic gem-dibromides are synthesized as starting materials for the current investigation. They were purified by flash chromatography using 5% ethyl acetate in hexane. The newly synthesized heteroaromatic gem-dibromides 18-32 are listed in Table 2.2. Use of 2.0 equiv of N-bromosuccinimide was found optimal to complete dibromination. The $^1$H NMR and $^{13}$C NMR spectra of selected compounds such...
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as 5, 7, 11, 20, 21, 25 and 26 are shown in figures 2.1 to 2.7 respectively. Compound characterization data for all the gem-dibromides are given in the experimental section 2.5.1 of this chapter.

2.3 Hydrolysis of gem-dibromomethyl aromatics to aldehydes

Benzalbromides were reported to produce benzaldehydes upon hydrolysis. This could be achieved by reacting them with a suitable base or acid. This transformation requiring hydrolysis of a gem-dibromomethyl group to an aldehyde often employs harsh reaction conditions such as use of H₂SO₄, aqueous sodium hydroxide and metal carbonates at high temperatures. The ready availability of starting materials prompted us to explore the hydrolysis of these benzalbromides to aldehydes. The chemistry was well established on simple benzalbromides. But when we attempted the hydrolysis of gem-dibromomethyl aromatics bearing carboxylate functionality under the above mentioned methods, the simultaneous hydrolysis of ester functionality took place. The use of mild reagent such as aqueous dimethylamine afforded mixtures of products due to the amidation of the ester group with the amine, while aqueous AgNO₃ and sodium acetate in acetic acid our hands failed to afford good yield of these aldehydes. Aqueous sodium formate, aqueous potassium oxalate and water were found to be ineffective in hydrolyzing the gem-dibromides even at high temperatures. All the above mentioned methods were invariably associated with certain limitations in terms of acid/base conditions, high temperatures, poor yields or substrate scope. An extensive search in the literature revealed the lack of rigorous methodology in this area, particularly for substrates containing carboxylate functional group. However, there are isolated examples wherein, aqueous silver nitrate is reported to effect this transformation. This prompted us to
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develop a general pathway for hydrolyzing gem-dibromomethylarenes bearing ester functionality without affecting the ester group.

As our attempts to hydrolyze selectively the gem-dibromide were futile, we looked for alternative protocols. Our attention then turned to a report by Kröhnke on the transformation of benzal bromide to a reasonably stable bis-pyridinium cation. Kröhnke has shown that the bis-pyridinium cation of benzal bromide is slowly hydrolyzed in water to benzaldehyde and pyridine. Interestingly, this method has not been exploited for the transformation of gem-dihalomethyl compounds to aldehydes and its broad scope in synthetic chemistry for the specific hydrolysis of gem-dibromomethylarenes to aldehydes has not been studied. However, Olofson and Zimmerman reported the use of bis-pyridinium cation in the synthesis of 1-deuterio aldehydes. Thus we decided to explore the synthesis of these aldehydes via their bis-pyridinium intermediate (Scheme 2.3).

Initially, we examined the hydrolysis of benzalbromide 3 (Table 2.1). Use of 2 equivalents of anhydrous pyridine did not afford complete conversion of 3 to its bis-pyridinium cation even after 20 hours at 100 °C as indicated by TLC. The reaction was then screened with varying equivalents of pyridine at 100 °C. When 5 g of 3 was exposed to excess of pyridine at reflux (16 mL, 10 equiv), the starting material was completely consumed in 30 minutes to afford a polar compound as confirmed by TLC. Further
increases in the quantity of pyridine or increase in the reaction temperature did not lower the reaction time. Once the reaction was complete as indicated by TLC, the brown reaction mass was exposed to cold water to liberate the aldehyde. The product was extracted with ether to afford benzaldehyde in 73% isolated yield.

Encouraged by this success, we decided to study the scope and generality of this reaction. As there were isolated examples of hydrolysis of a gem-dibromomethylarenes bearing a sensitive functional group to corresponding aldehyde without affecting the functional group, we decided to exploit the above methodology for the hydrolysis of gem-dibromomethylarenes bearing acid or base sensitive functional groups such as boronate or carboxylate. Aromatic gem-dibromomethyl compounds bearing ester functionality (3-9 & 11, Table 2.1) and heteroaromatic gem-dibromides bearing carboxylate group (18-25, Table 2.2) were chosen for the study from the newly synthesized gem-dibromomethylarenes. Upon subjecting these compounds to refluxing pyridine for 1-2 hours, the corresponding aldehydes (33-47, Table 2.3) were obtained in good yields. The aldehydes were isolated by extracting with diethyl ether. The $^1$H and $^{13}$C NMR spectra of selected aldehydes such as 34, 37, 39, 42, 45 and 47 are shown in figures 2.8 to 2.13 respectively. The compound characterization data ($^1$H NMR, $^{13}$C NMR, IR, MP and EA) for all the aldehydes are given in the experimental section 2.5.2 of this chapter.

In summary, a convenient and versatile method has been demonstrated for the specific hydrolytic conversion of gem-dibromomethylarenes substituted with carboxylate or boronate functionality into the corresponding aldehydes without affecting the ester group in respectable isolated yields. The method developed is mild and gave good yields of aldehydes for both aromatic and heteroaromatic substrates and can be conveniently adapted for large scale synthesis of such aldehydes.
Table 2.3: Newly synthesized aldehydes bearing acid or base labile group.

2.4 Synthesis of cinnamic acids and cinnamic esters from gem-dibromomethyl aromatics

2.4.1 Introduction

α,β-Unsaturated carboxylic acids compose a relatively large family of organic acids, which are important reagents in organic synthesis both as intermediates and final products. For example, they have been used to prepare compounds of biological relevance such as terahydroramicoid or the antibacterial reutericyclin. Also, they are present in
some natural products (e.g., the secretion of juice of honeybee queen and caffeic acid) and are versatile building blocks in organic synthesis. For their application in food industry, polymer industry, perfume industry, medicine and technical applications, they are synthesized on a commercial scale. Of the various methods, the Knoevenagel-Doebner reaction is widely recognized as the leading method to access the carbon-carbon double bond necessary to provide the \(\alpha,\beta\)-unsaturated carboxylic acid.\(^{30-36}\)

Though the Knoevenagel-Doebner reaction has been extensively documented, substitution of the aldehyde component with an alternative functional group has not been documented. Therefore, the development of a simple and stable substitute for these aromatic aldehydes using inexpensive and readily available reagents would extend the scope of the Knoevenagel-Doebner reaction in organic synthesis. We decided to investigate on a possible alternative for the aldehyde component in the Knoevenagel-Doebner reaction and explore a new synthetic strategy for the cinnamic acid and cinnamic ester synthesis.

### 2.4.2 Synthetic methodology

Nicolas Weibel and co-workers have reported a one-pot synthesis of imines starting from \(\text{gem-dibromomethylaryl}\) compounds and primary amines.\(^{38}\) A close look into this reaction reveals that, benzalbromides act as an aldehyde equivalents and participate in the reaction with an amine to produce an imine. We envisioned that, this report could be exploited further and decided to explore the application of \(\text{gem-dibromomethyl aromatics}\) as aldehyde equivalents in cinnamic acid synthesis. In the previous section, we have described the conversion of \(\text{gem-dibromomethyl aromatics}\) by aldehydes by hydrolyzing with pyridine.\(^{60}\) Similarly, pyridine is extensively used as the solvent of choice in the Knoevenagel-Doebner reaction, as it helps in the formation of cinnamic acids by tandem decarboxylation.\(^{30-36}\) Based on the above observation, it was decided to carry out the
Knoevenagel-Doebner reaction by substituting gem-dibromomethyl aromatics as aldehyde equivalents and pyridine as our preferred solvent to produce cinnamic acids. Further, Kazuyoshi Takeda and co-workers have reported the synthesis of tert-butyl cinnamates by reacting cinnamic acids with di-tert-butyl dicarbonate. We envisioned that, this report could be further exploited to synthesize the cinnamic esters from gem-dibromomethyl aromatics in a one pot synthesis (Scheme 2.4).

The synthetic approach started from the ethyl-4-(dibromomethyl)benzoate 3 (Table 2.1). Our initial trials were on converting the benzalbromides into the corresponding cinnamic acids. Thus, a mixture of 3 (1.0 equiv) and malonic acid (2.0 equiv) with anhydrous pyridine in the presence of catalytic quantity (0.01 equiv) of piperidine was stirred at reflux (Scheme 2.4). The starting material was consumed in 1.5 hours as indicated by TLC analysis. After work-up and purification by crystallization, cinnamic acid 48a was isolated in 93% yield. Use of 2 equivalents of malonic acid was found to be optimal for the complete conversion of 3 to 48a. Screening of various base catalysts such as triethylamine, N-ethyl diisopropylamine, pyrrolidine and morpholine was carried out. While pyrrolidine and morpholine catalyzed the reaction to quantitative yields in 2-3 hours, the other bases were found to be inefficient in promoting this reaction.

Next, we examined the progress of the reaction by omitting piperidine. When a mixture of benzal bromide and malonic acid was refluxed with anhydrous pyridine in the absence of piperidine, 14 hours were required for the reaction to afford 17% of 48a along with 73% of the corresponding benzaldehyde after aqueous work up. With a catalytic amount of piperidine, the reaction took barely an hour for completion. Encouraged by this success, the other gem-dibromomethylarenes such as 4-7, 11 (Table 2.1), and 18, 20, 21, 22, 25-27 and 32 (Table 2.2) were subjected to Knoevenagel-Doebner reaction with
malonic acid as described in Scheme 2.4 to yield the corresponding α,β-unsaturated carboxylic acids in excellent yields. The newly synthesized cinnamic acids are listed in Table 2.4. The $^1$H NMR and $^{13}$C NMR spectra of selected cinnamic acids are shown in figures 2.14-2.22 respectively. Compound characterization data for all the compounds described in Table 2.4 are given in the experimental section 2.5.3 of this chapter.

Our next aim was to synthesize cinnamic esters from gem-dibromomethyl aromatics in a one pot reaction. Kazuyoshi Takeda and co-workers have reported the synthesis of tert-butyl cinnamates by reacting cinnamic acids with di-tert-butyl dicarbonate. As we have already developed a novel method for the synthesis of cinnamic acids from gem-dibromomethyl aromatics, we decided to further exploit this reaction for the one-pot preparation of tert-butyl cinnamates (Scheme 2.4). Thus, a mixture of 12 (Table 2.1) (1 equiv), malonic acid (2 equiv) and BOC$_2$O (Boc-anhydride) (1.1 equiv) with anhydrous pyridine in the presence of a catalytic amount of piperidine (0.01 equiv) was stirred at
Table 2.4: Newly synthesized cinnamic acids from gem-dibromomethyl aromatics via scheme 2.4.

<table>
<thead>
<tr>
<th>No.</th>
<th>Structure</th>
<th>Name</th>
</tr>
</thead>
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<tr>
<td>48a</td>
<td><img src="image" alt="Structure 48a" /></td>
<td>EtOOC-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48b</td>
<td><img src="image" alt="Structure 48b" /></td>
<td>O-4-nitrophenyl-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48c</td>
<td><img src="image" alt="Structure 48c" /></td>
<td>MeOOC-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48d</td>
<td><img src="image" alt="Structure 48d" /></td>
<td>MeOOC-4-nitrophenyl-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48e</td>
<td><img src="image" alt="Structure 48e" /></td>
<td>Br-4-phenyl-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48f</td>
<td><img src="image" alt="Structure 48f" /></td>
<td>COOMe-4-phenyl-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48g</td>
<td><img src="image" alt="Structure 48g" /></td>
<td>Br-N-phenyl-4-phenyl-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48h</td>
<td><img src="image" alt="Structure 48h" /></td>
<td>MeOOC-N-phenyl-4-phenyl-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48i</td>
<td><img src="image" alt="Structure 48i" /></td>
<td>Br-5-pyridyl-3-phenyl-2-propenoic acid</td>
</tr>
<tr>
<td>48j</td>
<td><img src="image" alt="Structure 48j" /></td>
<td>COOBr-3-bromo-2-propenoic acid</td>
</tr>
<tr>
<td>48k</td>
<td><img src="image" alt="Structure 48k" /></td>
<td>MeOOC-S-phenyl-2-propenoic acid</td>
</tr>
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<td>MeOOC-N-phenyl-5-chloro-2-propenoic acid</td>
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<td>CN-3-phenyl-2-propenoic acid</td>
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<td><img src="image" alt="Structure 48n" /></td>
<td>O-B-phenyl-2-propenoic acid</td>
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<tr>
<td>48o</td>
<td><img src="image" alt="Structure 48o" /></td>
<td>O-B-5-thiophene-3-phenyl-2-propenoic acid</td>
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</table>
Table 2.5: Newly synthesized cinnamic esters from gem-dibromomethyl aromatics via Scheme 2.4.
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reflux. To our delight, the starting materials were consumed in 2 hours to provide the corresponding tert-butyl cinnamate 49a (Table 2.5) in 91% isolated yield. The product was extracted with diethyl ether. Use of 1.1 equivalents of BOC₂O was found optimal for the complete conversion of 12 to 49a.

Having achieved a novel methodology for the synthesis of tert-butyl cinnamates from gem-dibromomethylic aromatics in a one pot reaction, we next attempted the synthesis of various tert-butyl cinnamates from the newly synthesized gem-dibromides (Table 2.1 and Table 2.2). The new methodology was found optimal in providing good yields of cinnamates. The newly synthesized cinnamates are listed in Table 2.5. The reaction worked well on all substrates that we have tried. Substrates (gem-dibromides) possessing electron withdrawing or electron donating groups did not differ in reactivity and provided good yield of products in shorter duration. Further, aromatic and heteroaromatic gem-dibromides showed similar reactivity and the yields were comparable. The ¹H NMR and ¹³C NMR spectra of selected cinnamic esters are shown in figures 2.24-2.29. The compound characterization data of compounds described in Table 2.5 are given in the experimental section 2.5.4 of this chapter.

2.4.3 Mechanism of cinnamic acid formation

Benzal bromide is known to produce a fairly stable bis-pyridinium cation 50 on refluxing with pyridine. Krohnke has shown that the bis-pyridinium cation of benzal bromide is slowly hydrolyzed in water to benzaldehyde and pyridine. As benzaldehyde was not observed at any stage of the reaction, we speculated a reaction involving nucleophilic catalysis between the bis-cation and malonic acid to produce the intermediate 51, followed by decarboxylative elimination of pyridine to produce the cinnamic acid 48 (Scheme 2.5). It is evident from the long reaction time and poor yield of cinnamic acid in the absence of piperidine that pyridine is not basic enough to generate the carbon nucleophile from malonic acid. The formation of benzaldehyde when piperidine was
omitted is attributed to the hydrolytic cleavage of unreacted bis-pyridinium intermediate during aqueous work up.

Benzylpyridinium salts are known to condense with active methylene compounds in the presence of base. In the light of this information, it was decided to probe the reaction mechanism by isolating the bis-pyridinium cation (52, Scheme 2.6) of benzal bromide. Thus a mixture of benzal bromide (10g, 0.04mol) and pyridine (7g, 0.088mol) in anhydrous acetone (20ml) was stirred at 70°C for 12 hours under nitrogen atmosphere. The precipitated solid was carefully filtered, washed with acetone and dried under vacuum to afford 11g (67%) of the 1,1'-(phenylmethylene)bis-pyridinium dibromide 52 (Scheme 2.6) as yellow solid. This compound was analyzed and confirmed by NMR spectroscopy. The \(^1\)H NMR and \(^{13}\)C NMR spectra of 52 are shown in Fig.2.23.

When we reacted 52 with ethyl cyanoacetate in absolute ethanol containing catalytic amount of piperidine at reflux for 4 hours, ethyl-2-cyano-3-phenylacrylate (53, Scheme 2.6) was obtained in 81% yield. We could also observe the formation of benzaldehyde diethylacetal 54 as a result of reaction between ethanol and the bis-cation.
Further, with the aim of studying the reactivity of bis-pyridinium cations with alcohols, compound 52 was refluxed with ethanol. To our expectation, after 6 hours at reflux, benzaldehyde diethylacetal 54 was obtained in 73% yield (Scheme 2.7). gem-Dibromomethylarenes being a stable and readily accessible substitute for expensive, noncommercial and unstable aldehydes, this transformation would extend the scope of Knoevenagel-Doebner reaction in organic synthesis. In addition, this methodology would shorten the synthetic pathway to α,β-unsaturated carboxylic acids from gem-dibromomethylarenes, as one need not necessarily convert the gem-dibromomethylarenes into aldehydes for the synthesis of α,β-unsaturated carboxylic acids. It is worthy to note that both aromatic and heteroaromatic gem-dibromides bearing various functionalities such as carboxylate, amide, halogen, nitro, cyano, boronate and methoxy groups survived the course of reaction and provided high yields of corresponding α,β-unsaturated carboxylic acids in short time.
In conclusion, we have demonstrated a novel methodology wherein gem-dibromomethylarenes are employed as aldehyde equivalents for the first time in Knoevenagel-Doebner reaction for the efficient synthesis of \( \alpha,\beta \)-unsaturated carboxylic acids. As gem-dibromomethylarenes are stable and easily accessible from the commercial methyl analogues, this methodology would shorten the synthetic pathway to \( \alpha,\beta \)-unsaturated carboxylic acids. As the reaction provides \( \alpha,\beta \)-unsaturated carboxylic acids in a single step from gem-dibromomethylarenes, we believe that this transformation would be of appreciable use to the synthetic community.

2.5 Experimental

2.5.1 General procedure for the synthesis of gem-dibromomethyl aromatics

To a solution of Methyl aromatic compound (substituted toluene) (0.10 mol) in CCl\(_4\) (100 mL) was added NBS (0.2 mol) followed by benzoylperoxide (0.01 mol). The mixture was gradually heated to reflux for 5-8 h and cooled to room temperature. The succinimide was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (10% EtOAc/hexane) to afford the gem-dibromomethyl aromatics (3-32, Table 2.1) in good yield and purity. The characterization data of all the newly synthesized gem-dibromomethyl compounds (Table 2.1 and Table 2.2) are given below.

**Ethyl-4-dibromomethylbenzoate (3):**
White solid; 82% yield; m.p. 97-99 °C; \( \nu_{\text{max}}\text{(KBr)} \)
1704, 1287, 1133, 704, 641 cm\(^{-1}\); \(^1\)H NMR (400MHz, DMSO-\(d_6\)) 8.07-8.04 (2 H, d, \( J \) 8.4Hz, Ph), 7.65-7.63 (2 H, d, \( J \) 8.4Hz, Ph), 6.66 (1 H, s, \( \text{CHBr}_2 \)), 4.42-4.37 (2 H, q, \( \text{OCH}_2\text{Me} \)), 1.42-1.39 (3 H, t, \( \text{CH}_3\text{Me} \)); \(^{13}\)C NMR (100.6MHz, DMSO-\(d_6\)) 165.5, 145.9, 131.6, 129.9, 126.5, 61.2, 39.7, 14.3.

**Methyl-4-dibromomethyl-1-naphthoate (4):** White solid; 86% yield; mp = 90-91°C; \( R_f = 0.6 \) (petroleum ether/EtOAc, 9/1); \(^1\)H NMR (400MHz, DMSO-\(d_6\)): \( \delta \) 8.73-8.71 (d, 1H, \( J \)
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=8.2Hz), 8.50 (bs, 1H), 8.29-8.10 (m, 3H), 7.80-7.71 (m, 2H), 3.95 (s, 3H); $^{13}$C NMR (100MHz, DMSO-d6): $\delta$ 167.38, 141.08, 131.07, 129.90, 129.53, 128.69, 128.52, 127.43, 126.44, 124.69, 53.05, 40.96; Anal. Calcd for C$_{13}$H$_{16}$Br$_2$O$_2$: C, 43.61; H, 2.82%; Found: C, 43.68; H, 2.90%.

Methyl-3-bromo-4-dibromomethylbenzoate (5): Colorless liquid; 70% yield; $R_f$ = 0.65 (petroleum ether/EtOAc, 9/1); $^1$H NMR (400MHz, DMSO-d6): $\delta$ 8.09-8.06 (m, 2H), 8.03-8.00 (m, 1H), 7.32 (s, 1H), 3.86 (s, 3H); $^{13}$C NMR (100MHz, DMSO-d6): $\delta$ 164.58, 144.45, 133.77, 132.66, 131.59, 129.76, 120.15, 53.15, 40.69; Anal. Calcd for C$_9$H$_7$Br$_3$O$_2$: C, 27.94; H, 1.82%; Found: C, 27.98; H, 1.89%.

Methyl-3-dibromomethyl-4-nitrobenzoate (6): Yellow solid; 75% yield; mp = 121-123°C; $R_f$ = 0.70 (petroleum ether/EtOAc, 9/1); $^1$H NMR (400MHz, DMSO-d6): $\delta$ 8.63 (s, 1H), 8.14-8.07 (m, 2H), 7.48 (s, 1H), 3.94 (s, 3H); $^{13}$C NMR (100MHz, DMSO-d6): $\delta$ 164.45, 147.51, 135.85, 134.80, 132.66, 132.00, 125.69, 53.55, 35.8.

7-(Dibromomethyl)-2,2-dimethyl-4H-1,3-benzodioxin-4-one (7): White solid; 76% yield; mp = 84.5-86.6°C; $R_f$ = 0.75 (petroleum ether/EtOAc, 9/1); $^1$H NMR (400MHz, DMSO-d6): $\delta$ 7.95-7.93 (d, 1H, $J$ = 8.16Hz), 7.46-7.44 (dd, 1H, $J$ = 8.16Hz and 1.72Hz), 7.39 (s, 1H), 7.29-7.28 (d, 1H, $J$ = 1.84Hz), 1.68 (s, 6H); $^{13}$C NMR (100MHz, DMSO-d6): $\delta$ 159.79, 155.51, 150.55, 130.63, 121.84, 115.31, 114.17, 107.36, 40.91, 25.71; Anal. Calcd for C$_{11}$H$_{10}$Br$_2$O$_3$: C, 37.75; H, 2.88%; Found: C, 37.72; H, 2.92%.

6-(Dibromomethyl)-2,2-dimethyl-4H-1,3-benzodioxin-4-one (8): White solid; 78% yield; mp = 109-110 °C; $R_f$ (10% EtOAc/hexane) 0.75; $v_{max}$(KBr) 1726, 1432, 1303, 1153, 1047, 695 cm$^{-1}$; $^1$H NMR (400MHz, DMSO-d6) 8.08-8.07 (1 H, d, $J$ 2.3Hz, Ph), 7.97-7.95 (1 H, dd, $J$ 8.6, 2.4Hz, Ph), 7.48 (1 H, s, CHBr$_2$), 7.22-7.20 (1 H, d, $J$ 8.6Hz, Ph), 1.69 (6 H, s,
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Me$_2$C); $^{13}$C NMR (100.6MHz, DMSO-$d_6$) 159.9, 156.4, 137.4, 136.1, 127.0, 118.8, 112.7, 107.4, 41.2, 25.7; Anal. Calcd for C$_{11}$H$_{10}$Br$_2$O$_3$: C, 37.75; H, 2.88%; Found: C, 37.82; H, 2.97%.

4-Dibromomethylbenzeneboronicacidneopentylester (9): White solid; 87% yield; mp = 135-137 °C; $R_f$ (10% EtOAc/hexane) 0.75; $v_{max}$(KBr) 1475, 1442, 1318, 1135, 651 cm$^{-1}$; $^1$H NMR (400MHz, DMSO-$d_6$) 7.73-7.71 (2 H, d, $J$ 8.2Hz, Ph), 7.59-7.57 (2 H, d, $J$ 8.2Hz, Ph), 7.39 (1 H, s, CHBr$_2$), 3.75 (4 H, s, OCH$_2$), 0.94 (6 H, s, Me$_2$C); $^{13}$C NMR (100.6MHz, DMSO-$d_6$) 144.7, 140.8, 134.3, 128.9, 126.1, 71.8, 43.4, 31.9, 21.7; Anal. Calcd for C$_{12}$H$_{15}$BBr$_2$O$_2$: C, 39.83; H, 4.18%; Found: C, 39.95; H, 4.25%.

4-Dibromomethyl-3-nitrobenzeneboronicacid pinacol ester (10): Colourless liquid; 82% yield; $R_f$ = 0.70 (petroleum ether/EtOAc, 9/1); $^1$H NMR (400MHz, DMSO-$d_6$): $\delta$ 8.21-8.19 (d, 1H, $J$ = 7.88Hz), 8.09-8.05 (m, 2H), 7.49 (s, 1H), 1.30 (s, 12H); $^{13}$C NMR (100MHz, DMSO-$d_6$): $\delta$ 144.2, 139.6, 137.5, 131.6, 129.3, 84.6, 36.0, 24.5.

3-Dibromomethyl-4-fluorobenzeneboronicacid pinacol ester (11): Colourless liquid; 82% yield; $R_f$ = 0.65 (petroleum ether/EtOAc, 9/1); $^1$H NMR (400MHz, DMSO-$d_6$): $\delta$ 8.01-7.99 (dd, 1H, $J$=8.16Hz and 1.48Hz), 7.73-7.69 (m, 1H), 7.46 (s, 1H), 7.29-7.24 (dd, 1H, $J$ = 10.96Hz and 8.28Hz), 1.27 (s, 12H); $^{13}$C NMR (100MHz, DMSO-$d_6$): $\delta$ 161.90, 159.35, 138.91, 138.82, 135.50, 135.48, 129.26, 129.15, 116.51, 116.31, 84.54, 34.77, 34.73, 25.09; Anal. Calcd for C$_{13}$H$_{16}$BBr$_2$FO$_2$: C, 39.64; H, 4.09%; Found: C, 39.69; H, 4.13%.

1-(Dibromomethyl)-4-methoxy-2-nitrobenzene (12): Brown solid; $^1$H NMR (400MHz, CDCl$_3$) $\delta$ 8.15-8.13 (d, 1H, $J$ = 8.92Hz), 7.43 (s, 1H), 7.38-7.37 (d, 1H, $J$ = 2.68Hz), 7.27-7.24 (dd, 1H, $J_1$ = 8.76Hz, $J_2$ = 2.56Hz), 3.91 (s, 3H); $^{13}$C NMR (100MHz, CDCl$_3$) $\delta$
160.56, 144.85, 133.80, 128.21, 120.79, 108.49, 56.17, 34.36; Anal.Calc’d for 
C₈H₇Br₂N0₃: C, 29.57; H, 2.17; N, 4.31. Found: C, 29.73; H, 2.28; N, 4.11%.

*Methyl-4-dibromomethyl-3-iodobenzoate* (13): Yellow solid; 79% yield; mp = 98.5-
97.1°C; Rf = 0.70 (petroleum ether/EtOAc, 9/1); ¹H NMR (400MHz, DMSO-d6): δ 8.40-
8.39 (d, 1H, J 1.56Hz), 8.12-8.05 (m, 2H), 7.07 (s, 1H), 3.93 (s, 3H); ¹³C NMR (100MHz, 
DMSO-d6): δ 165.8, 149.1, 141.3, 133.5, 131.4, 131.1, 95.1, 53.1, 45.7.

*Methyl-2-dibromomethyl-4-fluorobenzoate* (14): Yellow solid; 79% yield; mp = 66.7-
69.4°C; Rf = 0.75 (petroleum ether/EtOAc, 9/1); ¹H NMR (400MHz, DMSO-d6): δ 7.92-
7.89 (m, 1H), 7.86-7.83 (m, 2H), 7.41-7.36 (m, 1H), 3.47 (s, 3H); ¹³C NMR (100MHz, 
DMSO-d6): δ 165.4, 165.2, 162.9, 145.0, 145.0, 133.0, 132.9, 121.8, 121.8, 117.7, 117.5, 
117.4, 117.2, 52.7, 37.4.

*l-(Dibromomethyl)-2-cyano-5-bromobenzene* (16): Brown solid; ¹H NMR (400MHz, 
CDCl₃) δ 8.03 (s, 1H), 7.92-7.90 (d, 1H, J = 8.24Hz), 7.83-7.80 (dd, 1H, J = 8.2, 1.84Hz), 
7.38 (s, 1H); ¹³C NMR (100MHz, CDCl₃) δ 145.4, 137.0, 134.1, 130.9, 127.6, 115.9, 109.6, 
36.7.

*Methyl-6-dibromomethylpyridine-3-carboxylate* (18): Colourless liquid; 75% yield; 
νmax(liquid film) 1733, 1436, 1114, 650 cm⁻¹; ¹H NMR (400MHz, CDCl₃) 9.12 (1 H, s, Ph), 
8.40-8.37 (1 H, dd, J 8.2, 2.0Hz, Ph), 7.89-7.87 (1 H, d, J 8.2Hz, Ph), 6.68 (1 H, s, CHBr₂), 
3.97 (3 H, s, COOMe); ¹³C NMR (100.6MHz, CDCl₃) 164.7, 162.3, 149.7, 138.8, 126.2, 
121.5, 52.6, 40.4.

*Ethyl-6-dibromomethylpyridine-2-carboxylate* (19): Colourless liquid; 71% yield; Rf (10% 
EtOAc/hexane) 0.70; νmax(liquid film) 1737, 1310, 1227, 1139, 662 cm⁻¹; ¹H NMR
(400MHz, CDCl₃) 8.14-8.12 (1 H, dd, J 7.8, 1.0Hz, Ph), 8.07-8.05 (1 H, dd, J 7.7, 1.0Hz, Ph), 7.98-7.95 (1H, m, Ph), 6.77 (1 H, s, CHBr₂), 4.50-4.45 (2 H, q, OCH₂Me), 1.45-1.41 (3 H, t, CH₂Me); ¹³C NMR (100.6MHz, CDCl₃) 164.3, 159.8, 146.1, 138.9, 126.2, 125.4, 62.2, 40.6, 14.2; Anal. Calcd for C₉H₉Br₂N₂O₂: C, 33.47; H, 2.81; N, 4.34%; Found: C, 33.65; H, 2.96; N, 4.23%.

**Methyl-2-chloro-6-dibromomethylpyridine-4-carboxylate (20):** Colorless liquid; 81% yield: $R_f = 0.70$ (petroleum ether/EtOAc, 9/1); $¹^1$H NMR (400MHz, DMSO-d₆): $\delta$ 8.07 (s, 1H), 7.88 (s, 1H), 7.46 (s, 1H), 3.91 (s, 3H); ¹³C NMR (100MHz, DMSO-d₆): $\delta$ 163.61, 159.80, 151.48, 142.22, 125.06, 118.83, 53.73, 41.14; Anal. Calcd for C₉H₆Br₂ClNO₂: C, 27.98; H, 1.76%; N, 4.08; Found: C, 27.91; H, 1.72; N, 4.01%.

**Methyl-5-bromo-2-dibromomethylfuran-3-carboxylate (21):** White solid; 72% yield; mp = 147-149°C; $R_f = 0.55$ (petroleum ether/EtOAc, 9/1); $¹^1$H NMR (400MHz, DMSO-d₆): $\delta$ 7.43 (s, 1H), 6.99 (s, 1H), 3.81 (s, 3H); ¹³C NMR (100MHz, DMSO-d₆): $\delta$ 160.96, 155.70, 125.49, 114.51, 112.81, 52.59, 25.23.

**Methyl-5-dibromomethylthiophene-2-carboxylate (22):** Brown solid; 82% yield; mp = 68-69.5°C; $R_f = 0.7$ (petroleum ether/EtOAc, 9/1); $¹^1$H NMR (400MHz, CDCl₃): $\delta$ 7.64-7.63 (d, 1H, $J = 4.0$Hz), 7.24-7.23 (dd, 1H, $J = 4.0$Hz and 0.44Hz), 6.86 (s, 1H), 3.89 (s, 3H); ¹³C NMR (100MHz, CDCl₃): $\delta$ 162.10, 151.93, 134.83, 132.68, 127.13, 52.47, 31.10.

**Methyl-3-dibromomethylthiophene-2-carboxylate (23):** Light brown solid; 76% yield; mp = 44.5-47.5 °C; $R_f$ (10% EtOAc/hexane) 0.65; $\nu_{\text{max}}$ (KBr) 1705, 1437, 1277, 1080, 693 cm⁻¹; $¹^1$H NMR (400MHz, DMSO-d₆) 7.98-7.96 (1 H, d, $J = 5.2$Hz, Ph), 7.68 (1 H, s, CHBr₂), 7.63-7.62 (1 H, d, $J = 5.2$Hz, Ph), 3.85 (3 H, s, COOMe); ¹³C NMR (100.6MHz, DMSO-d₆)
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161.3, 147.1, 133.4, 130.5, 124.6, 52.7, 32.3; Anal. Calcd for C$_7$H$_6$Br$_2$O$_2$S: C, 26.78; H, 1.93%; Found: C, 26.82; H, 1.97%.

*Methyl-5-dibromomethylisoxazole-3-carboxylate (24):* White solid; 73% yield; mp = 59-60°C; R$_f$ (10% EtOAc/hexane) 0.55; $v_{\text{max}}$(KBr) 1741, 1471, 1413, 1234, 1014, 718, 624 cm$^{-1}$; $^1$H NMR (400MHz, DMSO-$d_6$) 7.55 (1 H, s, Ph), 7.05 (1 H, s, CHBr$_2$), 3.89 (3 H, s, COOMe); $^{13}$C NMR (100.6MHz, DMSO-$d_6$) 170.6, 159.5, 156.7, 103.3, 53.5, 25.0; Anal. Calcd for C$_8$H$_5$Br$_2$NO$_2$: C, 24.11; H, 1.69; N, 4.69%; Found: C, 24.20; H, 1.72; N, 4.60%.

*5-Dibromomethylbenzo[b]thiophene-2-boronic acid pinacol ester (25):* White solid; 81% yield; mp = 178-179.9°C; R$_f$ = 0.70 (petroleum ether/ EtOAc, 9/1); $^1$H NMR (400MHz, DMSO-$d_6$): $\delta$ 8.16-8.15 (d, 1H, $J = 1.52$Hz), 8.10-8.08 (d, 1H, $J =8.56$Hz), 7.97 (s, 1H), 7.71-7.68 (dd, 1H, $J =8.56$Hz and $J =1.84$Hz), 7.55 (s, 1H), 1.31 (s, 12H); $^{13}$C NMR (100MHz, DMSO-$d_6$): $\delta$ 144.17, 139.96, 139.22, 135.29, 125.01, 123.76, 122.21, 85.02, 43.52, 25.06; Anal. Calcd for C$_{15}$H$_{17}$Br$_2$O$_2$S: C, 41.71; H, 3.97%; Found: C, 41.76; H, 3.93%.

*N-[5-Bromo-4-(dibromomethyl)-1,3-thiazol-2-yl]acetamide (26):* Brown solid; $^1$H NMR (400MHz, DMSO-$d_6$) $\delta$ 12.83 (bs, 1H), 7.20 (s, 1H), 2.15 (s, 3H); $^{13}$C NMR (100MHz, DMSO-$d_6$) $\delta$ 169.5, 158.0, 146.2, 97.6, 33.6, 22.2.

*2-Bromo-5-(dibromomethyl)pyridine (27):* White solid; mp = 90-91.5°C; $^1$H NMR (400MHz, DMSO-$d_6$) $\delta$ 8.58-8.57 (d, 1H, $J = 2.48$Hz), 8.04-8.01 (dd, 1H, $J_1 = 8.4$Hz, $J_2 = 2.68$Hz), 7.77-7.75 (d, 1H, $J = 8.36$Hz), 7.43 (s, 1H); $^{13}$C NMR (100MHz, DMSO-$d_6$) $\delta$ 150.7, 145.8, 141.9, 141.7, 132.2, 41.3.
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3-Bromo-5-(dibromomethyl)pyridine (28): White solid; mp = 101.3-102.5°C; $^1$H NMR (400MHz, DMSO-$d_6$) $\delta$ 8.65-8.64 (t, 2H), 8.16 (s, 1H), 6.61 (s, 1H); $^{13}$C NMR (100MHz, DMSO-$d_6$) $\delta$ 150.9, 145.9, 142.2, 141.8, 131.3, 39.5.

2-Bromo-4-(dibromomethyl)pyridine (29): $^1$H NMR (400MHz, DMSO-$d_6$) $\delta$ 8.49-8.47 (d, 1H, $J = 5.16$Hz), 7.79-7.78 (d, 1H, $J = 1.24$Hz), 7.67-7.66 (dd, 1H, $J_1 = 5.16$Hz, $J_2 = 1.8$Hz), 7.30 (s, 1H); $^{13}$C NMR (100MHz, DMSO-$d_6$) $\delta$ 152.81, 151.60, 141.43, 124.66, 121.17, 38.04.

8-Chloro-2-(dibromomethyl)quinoline (30): $^1$H NMR (400MHz, DMSO-$d_6$) $\delta$ 8.62-8.60 (d, 1H, $J = 8.6$Hz), 8.04-8.01 (m, 3H), 7.67-7.63 (t, 1H), 7.41 (s, 1H); $^{13}$C NMR (100MHz, DMSO-$d_6$) $\delta$ 159.2, 141.9, 139.7, 132.7, 131.2, 129.4, 128.6, 127.8, 120.7, 44.1.

Methyl-2-chloro-6-dibromomethylpyridine-3-carboxylate (31): White solid; 77% yield; mp = 54.5-57.1°C; $R_f$ (10% EtOAc/hexane) 0.65; $^1$H NMR (400MHz, DMSO-$d_6$) 8.32-8.30 (1H, d, $J = 7.96$Hz), 7.83-7.81 (1H, d, $J = 7.96$Hz), 6.97 (s, 1H), 3.95 (3H, s, COOMe); $^{13}$C NMR (100.6MHz, DMSO-$d_6$) 165.6, 162.3, 149.6, 143.2, 128.7, 121.0, 112.8, 53.5, 40.0.

2-Cyano-3-(dibromomethyl)pyridine (32): White solid; mp = 103.5-104.9°C; $^1$H NMR (400MHz, DMSO-$d_6$) $\delta$ 8.74-8.73 (dd, 1H, $J_1 = 4.72$Hz, $J_2 = 1.44$Hz), 8.37-8.35 (dd, 1H, $J_1 = 8.24$Hz, $J_2 = 1.36$Hz), 7.86-7.83 (dd, 1H, $J_1 = 8.2$Hz, $J_2 = 4.72$Hz), 7.46 (s, 1H); $^{13}$C NMR (100MHz, DMSO-$d_6$) $\delta$ 152.30, 141.72, 137.30, 130.01, 128.81, 115.47, 35.98; Anal.Calc’d for C$_7$H$_4$Br$_2$N$_2$: C, 30.47; H, 1.46; N, 10.15. Found: C, 30.54; H, 1.53; N, 10.03%.
Figure 2.1 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (5)
Figure 2.2 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (7)
Figure 2.3 \(^1\)H NMR and \(^{13}\)C NMR in DMSO-\(d_6\) (11)
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Figure 2.4 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (20)
Figure 2.5 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (21)
Figure 2.6 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (25)
Figure 2.7 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (26)
2.5.2 General procedure for the hydrolysis of gem-dibromomethyl aromatics to aldehydes

In a typical procedure, a mixture of gem-dibromomethylarene (0.10 mol) and anhydrous pyridine (1.0 mol) was refluxed at 100 °C for 1-2 hours. Once the substrate was completely consumed as monitored by TLC, the brown reaction mixture was cooled and poured into ice-cold water (100 mL). The product was extracted with diethyl ether (2 x 50 mL) and the combined organic phase was washed with water, brine solution and dried over anhydrous sodium sulfate. The solvent was removed under vacuum and the brown residue was passed through a small plug of silica gel using petroleum ether/ethyl acetate (9/1) to afford the corresponding aldehyde in good yield and purity. The characterization data of newly synthesized aldehydes (33-47) are given below.

*Methyl-3-bromo-4-formylbenzoate (33):* White solid; 89% yield; mp.= 76.8-77.6 °C; Rf (10% EtOAc/hexane) 0.55; H NMR (400MHz, DMSO-d6) 10.25 (1 H, s, CHO), 8.22-8.21 (1 H, d, J1.5Hz, Ph), 8.08-8.06 (1 H, m, Ph), 7.96-7.94 (1 H, d, J8.0Hz, Ph), 3.89 (3 H, s, COOMe); C NMR (100.6MHz, DMSO-d6) 191.3, 164.3, 136.2, 135.4, 134.2, 130.4, 128.7, 125.3, 52.9.

*Methyl-4-formyl-1-naphthoate (34):* White solid; 90% yield; mp.= 95.8-97.5 °C; H NMR (400MHz, DMSO-d6) 10.50 (1 H, s, CHO), 9.19-9.17 (1 H, d, J8.4Hz, Ph), 8.63-8.61 (1 H, d, J8.2Hz, Ph), 8.25-8.19 (2 H, m, Ph), 7.82-7.73 (2 H, m, Ph), 3.98 (3 H, s, COOMe); C NMR (100.6MHz, DMSO-d6) 194.5, 167.4, 134.5, 133.8, 133.8, 130.7, 130.7, 129.5, 128.6, 128.3, 126.1, 124.8, 53.2.

*Methyl-3-formyl-4-nitrobenzoate (35):* White solid; 90% yield; m.p. 71.5-73 °C, H NMR (400MHz, DMSO-d6) 10.23 (1 H, s, CHO), 8.39-8.38 (1 H, d, J1.5Hz, Ph), 8.38-
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8.35 (1 H, dd, J 8.2, 1.9Hz, Ph), 8.25-8.23 (1 H, d, J 8.2Hz, Ph), 3.93 (3 H, s, COOME); \(^{13}\text{C}\) NMR (100.6MHz, DMSO-d6) 189.5, 164.5, 151.7, 135.0, 134.4, 131.0, 130.7, 125.5, 53.4.

Methyl-6-formylpyridine-3-carboxylate (36): White solid; 72% yield; mp. = 115-116.7 \(^{0}\text{C}\); \(^{1}\text{H}\) NMR (400MHz, DMSO-d6) 10.16 (1 H, s, CHO), 9.38-9.37 (1 H, d, J 1.2Hz, Ph), 8.50-8.47 (1 H, dd, J 8.0, 1.2Hz, Ph), 8.06-8.03 (1 H, dd, J 8.0, 0.5Hz, Ph), 4.01 (3 H, s, COOME); \(^{13}\text{C}\) NMR (100.6MHz, DMSO-d6) 192.5, 164.8, 154.9, 151.1, 138.3, 129.2, 121.1, 52.8.

2,2-Dimethyl-4-oxo-4H-1,3-benzodioxine-6-carbaldehyde (37): White solid; 79% yield; mp. = 113-114 \(^{0}\text{C}\); \(R_f\) (10% EtOAc/hexane) 0.55; \(v_{\text{max}}\) (KBr) 1740, 1687, 1614, 1268, 1197 cm\(^{-1}\); \(^{1}\text{H}\) NMR (400MHz, DMSO-d6) 9.98 (1 H, s, CHO), 8.42 (1 H, s, Ph), 8.17-8.15 (1 H, dd, J 8.5, 1.8Hz, Ph), 7.32-7.30 (1 H, d, J 8.5Hz, Ph), 1.73 (6 H, s, CMe\(_2\)); \(^{13}\text{C}\) NMR (100.6MHz, DMSO-d6) 191.2, 159.6, 159.4, 136.5, 132.1, 131.3, 118.5, 113.1, 107.3, 25.3; Anal. Calcd for C\(_{11}\)H\(_{10}\)O\(_4\): C, 64.08; H, 4.89%; Found: C, 64.21; H, 4.95%.

2,2-Dimethyl-4-oxo-4H-1,3-benzodioxine-7-carbaldehyde (38): White solid; 87% yield; mp. = 109-111 \(^{0}\text{C}\); \(R_f\) (10% EtOAc/hexane) 0.55; \(v_{\text{max}}\) (KBr) 1738, 1701, 1444, 1389, 1298 cm\(^{-1}\); \(^{1}\text{H}\) NMR (400MHz, DMSO-d6) 10.05 (1 H, s, CHO), 8.08-8.06 (1 H, d, J 7.8Hz, Ph), 7.70-7.68 (1 H, dd, J 7.9, 1.4Hz, Ph), 7.60 (1 H, s, Ph), 1.72 (6 H, s, CMe\(_2\)); \(^{13}\text{C}\) NMR (100.6MHz, DMSO-d6) 192.7, 160.0, 156.2, 142.6, 130.7, 123.1, 118.6, 117.7, 107.4, 25.6; Anal. Calcd for C\(_{11}\)H\(_{10}\)O\(_4\): C, 64.08; H, 4.89%; Found: C, 64.16; H, 4.87%.

Ethyl-6-formylpyridine-2-carboxylate (39): White solid; 77% yield; mp. = 37.5-39.6 \(^{0}\text{C}\); \(R_f\) (10% EtOAc/hexane) 0.30; \(v_{\text{max}}\) (KBr) 1735, 1709, 1292, 1216, 1165 cm\(^{-1}\); \(^{1}\text{H}\) NMR (400MHz, DMSO-d6) 10.01 (1 H, s, CHO), 8.14-8.11 (1 H, dd, J 7.6, 1.2Hz), 4.42-4.37 (2 H, q, OCH\(_2\)Me), 1.36-
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1.33 (3 H, t, CH₂Me); ¹³C NMR (100.6MHz, DMSO-d₆) 193.0, 164.0, 152.3, 148.2, 139.4, 128.9, 124.6, 61.6, 14.1; Anal. Calcd for C₉H₉NO₃: C, 60.33; H, 5.06; N, 7.82%; Found: C, 60.41; H, 5.11; N, 7.78%.

Methyl-2-bromo-5-formylfuran-4-carboxylate (40): White solid; 87% yield; mp. = 58.3-58.7 °C; Rf (10% EtOAc/hexane) 0.45; v_max(KBr) 1721, 1676, 1473, 1245, 1066 cm⁻¹; ¹H NMR (400MHz, DMSO-d₆) 9.89 (1 H, s, CHO), 7.22 (1 H, s, Ph), 3.86 (3 H, s, COOMe); ¹³C NMR (100.6MHz, DMSO-d₆) 177.5, 160.7, 153.3, 130.6, 127.6, 114.6, 52.8; Anal. Calcd for C₇H₅BrO₄ C, 36.08; H, 2.16%; Found: C, 36.17; H, 2.21%.

Methyl-3-formylthiophene-2-carboxylate (41): Light brown solid; 91% yield; mp. = 52.5-54.4 °C; ¹H NMR (400MHz, DMSO-d₆) 10.46 (1 H, s, CHO), 7.94-7.93 (1 H, dd, J = 5.1, 0.7Hz, Ph), 7.53-7.51 (1 H, dd, J = 5.2, 0.5Hz, Ph), 3.89 (3 H, s, COOMe); ¹³C NMR (100.6MHz, DMSO-d₆) 186.5, 161.1, 143.8, 138.2, 132.7, 127.0, 52.9.

Methyl-5-formylisoxazole-3-carboxylate (42): White solid; 72% yield; mp. = 72-73 °C, ¹H NMR (400MHz, DMSO-d₆) 10.04 (1 H, s, CHO), 7.37 (1 H, s, Ph), 4.04 (3 H, s, COOMe); ¹³C NMR (100.6MHz, DMSO-d₆) 177.5, 168.9, 159.1, 156.7, 108.8, 53.3.

Methyl-5-formylthiophene-2-carboxylate (43): Yellow solid; 76% yield; mp. = 81-82 °C, ¹H NMR (400MHz, DMSO-d₆) 9.98 (1 H, s, CHO), 7.85-7.84 (1 H, d, J = 3.9Hz, Ph), 7.75-7.74 (1 H, d, J = 3.9Hz, Ph), 3.95 (3 H, s, COOMe); ¹³C NMR (100.6MHz, DMSO-d₆) 183.3, 161.9, 147.7, 140.9, 135.0, 133.3, 52.8.

Methyl-2-chloro-6-formylpyridine-4-carboxylate (44): White solid; 70% yield; mp. = 68-69.8 °C; Rf (10% EtOAc/hexane) 0.40; v_max(KBr) 1736, 1712, 1310, 1217, 761, 683 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) 10.06 (1 H, s, CHO), 8.40 (1 H, s, Ph), 8.13 (1 H, s, Ph), 4.02
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(3 H, s, COOMe); $^{13}$C NMR (100.6MHz, CDCl$_3$) 190.8, 163.4, 153.6, 152.9, 141.5, 128.3, 119.4, 53.3; Anal. Calcd for C$_8$H$_6$ClNO$_3$: C, 48.14; H, 3.03; N, 7.02%; Found: C, 48.10; H, 3.06; N, 6.96%.

4-Formylbenzeneboronicacid neopentylester (45): White solid; 93% yield; mp. = 58-60 °C; R$_f$ (10% EtOAc/hexane) 0.60; $\nu$$_{max}$(KBr) 2958, 1702, 1481, 1314, 1129 cm$^{-1}$; $^1$H NMR (400MHz, DMSO-$d_6$) 10.02 (1H, s, CHO), 7.89-7.85 (4 H, m, Ph), 3.77 (4 H, s, OCH$_2$), 0.93 (6 H, s, CMe$_2$); $^{13}$C NMR (100.6MHz, DMSO-$d_6$) 193.9, 138.1, 134.4, 128.9, 71.9, 31.9, 21.7; Anal. Calcd for C$_{12}$H$_{15}$BO$_3$: C, 66.10; H, 6.93%; Found: C, 66.18; H, 6.98%.

5-Formylbenzo[b]thiophene-2-boronicacid pinacolester (46): White solid; 89% yield; mp. = 102.5-103.7 °C; R$_f$ (10% EtOAc/hexane) 0.55; $\nu$$_{max}$(KBr) 2977, 1701, 1552, 1349, 1325, 1141 cm$^{-1}$; $^1$H NMR (400MHz, DMSO-$d_6$) 10.09 (1 H, s, CHO), 8.52 (1 H, s, Ph), 8.23-8.20 (1 H, d, $J$ 11.2Hz, Ph), 8.09 (1 H, s, Ph), 7.90-7.86 (1 H, dd, $J$ 11.2, 2.0Hz), 1.32 (12 H, s, CMe$_2$-CMe$_2$); $^{13}$C NMR (100.6MHz, DMSO-$d_6$) 193.7, 149.2, 141.1, 136.4, 134.2, 129.0, 125.2, 124.4, 85.6, 25.5; Anal. Calcd for C$_{15}$H$_{17}$BO$_3$S: C, 62.52; H, 5.95%; Found: C, 62.48; H, 5.98%.

3-Formyl-4-fluorobenzeneboronicacid pinacolester (47): White solid; 83% yield; mp. = 51-53.7 °C; R$_f$ (10% EtOAc/hexane) 0.60; $\nu$$_{max}$(KBr) 2982, 1692, 1605, 1361, 1144, 1109, 851, 662 cm$^{-1}$; [Found: C, 62.49; H, 6.48. C$_{13}$H$_{16}$BFO$_3$ requires C, 62.44; H, 6.45%]; $^1$H NMR (400MHz, DMSO-$d_6$) 10.21 (1 H, s, CHO), 8.12-8.11 (1 H, d, Ph), 7.98-7.95 (1 H, m, Ph), 7.42-7.37 (1 H, m, Ph), 1.29 (12 H, s, CMe$_2$-CMe$_2$); $^{13}$C NMR (100.6MHz, DMSO-$d_6$) 188.5, 188.5, 166.8, 164.2, 142.9, 142.8, 136.6, 136.6, 123.9, 123.8, 117.1, 116.9, 84.7, 25.0; Anal. Calcd for C$_{13}$H$_{16}$BFO$_3$: C, 62.44; H, 6.45%; Found: C, 62.49; H, 6.48%.
Figure 2.8 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (34)
Figure 2.9 $^1$H NMR and $^{13}$C NMR in DMSO- $d_6$ (37)
Figure 2.10 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (39)
Figure 2.11 $^1$H NMR and $^{13}$C NMR in CDCl$_3$ (42)
Figure 2.12 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (45)

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Figure 2.13 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (47)
2.5.3 General procedure for the synthesis of cinnamic acids from gem-dibromomethyl aromatics

To a mixture of gem-dibromomethylarene (0.10 mol) and malonic acid (0.2 mol) in pyridine (1.5 mol) was added piperidine (0.01 mol) and the mixture was refluxed for 1-2 hours. The completion of reaction was confirmed by TLC. The brown reaction mixture was cooled and poured onto ice containing hydrochloric acid. The solid precipitated was collected by filtration, washed with water (3 x 75ml) and dried under suction to afford the corresponding cinnamic acid in good yield and purity.

Alternatively, the reaction mixture could be poured into water and extracted with ethyl acetate. The organic phase could be evaporated and directly loaded onto a silica gel column. This method is suitable for isolating \( \alpha,\beta \)-unsaturated carboxylic acids obtained from nitrogen heterocycles. The characterization data of 52 and newly synthesized cinnamic acids (48b-48o) are given below.

3-(4-Methoxy-2-nitrophenyl)acrylic acid (48b): Off-white solid; mp.= 237.5-239.4°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.59 (bs, 1H), 7.92-7.90 (d, 1H, \(J = 8.8Hz\)), 7.72-7.68 (d, 1H, \(J = 16Hz\)), 7.56 (s, 1H), 7.33-7.30 (dd, 1H, \(J_y = 8.8Hz, J_z = 2.8Hz\)), 6.49-6.45 (d, 1H, \(J = 16Hz\)), 3.87 (s, 3H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.52, 161.04, 150.05, 138.22, 130.64, 122.32, 121.30, 120.25, 109.78, 56.71; Anal.Calc’d for C\(_{10}\)H\(_9\)NO\(_5\): C, 53.82; H, 4.06; N, 6.28. Found: C, 53.88; H, 4.11; N, 6.21.

3-[4-(Methoxycarbonyl)-1-naphthyl]acrylic acid (48c): White solid; mp.= 223-225°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.81 (bs, 1H), 8.76-8.74 (dd, 1H, \(J_1 = 6.48Hz, J_2 = 2.2Hz\)), 8.39-8.35 (d, 1H, \(J = 15.76Hz\)), 8.26-8.24 (dd, 1H, \(J = 7.32Hz, J_z = 3.04Hz\)), 8.09-8.07 (d, 1H, \(J = 7.68Hz\)), 7.96-7.94 (d, 1H, \(J = 7.68Hz\)), 7.71-7.76 (m, 2H), 6.66-6.62 (d, 1H, \(J = 15.72Hz\)), 3.93 (s, 3H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.54, 167.52, 140.04, 136.42, 131.43, 130.99, 129.60, 128.80, 128.39, 127.78, 126.23, 124.85, 124.56, 124.34, 52.89; Anal.Calc’d for C\(_{15}\)H\(_{12}\)O\(_4\): C, 70.31; H, 4.72. Found: C, 70.40; H, 4.77.
3-[(5-(Methoxycarbonyl)-2-nitrophenyl)acrylic acid (48d): Pale yellow solid; mp.= 170-172°C; $^1$H NMR (400MHz, DMSO-d6) δ 12.80 (bs, 1H), 8.30-8.29 (d, 1H, $J = 1.12$Hz), 8.20-8.12 (m, 2H), 7.84-7.80 (d, 1H, $J = 15.84$Hz), 6.60-6.56 (d, 1H, $J = 15.80$Hz), 3.91 (s, 3H); $^{13}$C NMR (100MHz, DMSO-d6) δ 167.08, 164.93, 150.96, 138.56, 134.40, 131.48, 130.39, 130.32, 125.80, 125.32, 53.38; Anal.Calc’d for C$_{11}$H$_9$NO$_6$: C, 52.60; H, 3.61; N, 5.58. Found: C, 52.66; H, 3.69; N, 5.47.

3-[(2-Bromo-4-(methoxycarbonyl)phenyl)acrylic acid (48e): White solid; mp.= 222.5-224°C; $^1$H NMR (400MHz, DMSO-d6) δ 12.84 (bs, 1H), 8.12-8.12 (d, 1H, $J = 1.52$Hz), 8.02-8.00 (d, 1H, $J = 8.2$Hz), 7.91-7.89 (dd, 1H, $J_1 = 8.2$Hz, $J_2 = 1.2$Hz), 7.81-7.77 (d, 1H, $J = 15.88$Hz), 6.67-6.63 (d, 1H, $J = 15.92$Hz), 3.85 (s, 3H); $^{13}$C NMR (100MHz, DMSO-d6) δ 167.24, 164.94, 140.63, 138.45, 133.83, 132.46, 129.12, 128.96, 125.21, 124.74, 53.07; Anal.Calc’d for C$_{11}$H$_9$BrO$_4$: C, 46.34; H, 3.18. Found: C, 46.43; H, 3.24.

3-(2,2-Dimethyl-4-oxo-4H-1,3-benzodioxin-7-yl)acrylic acid (48f): White solid; mp.= 253-255°C; $^1$H NMR (400MHz, DMSO-d6) δ 12.76 (bs, 1H), 7.87-7.85 (d, 1H, $J = 8.04$Hz), 7.62-7.58 (d, 1H, $J = 16$Hz), 7.54-7.52 (d, 1H, $J = 8.04$Hz), 7.48 (s, 1H), 6.73-6.69 (d, 1H, $J = 16$Hz), 1.64 (s, 6H); $^{13}$C NMR (100MHz, DMSO-d6) δ 167.57, 160.27, 156.13, 143.04, 142.23, 130.01, 123.80, 122.89, 117.11, 114.16, 107.03, 25.72; Anal.Calc’d for C$_{13}$H$_{12}$O$_5$: C, 62.90; H, 4.87. Found: C, 62.93; H, 4.91.

3-(6-Bromopyridin-3-yl)acrylic acid (48g): White solid; mp.= 231-232°C; $^1$H NMR (400MHz, DMSO-d6) δ 12.62 (bs, 1H), 8.68-8.67 (d, 1H, $J = 2.16$Hz), 8.13-8.10 (dd, 1H, $J_1 = 8.36$Hz, $J_2 = 2.36$Hz), 7.71-7.69 (d, 1H, $J = 8.32$Hz), 7.61-7.57 (d, 1H, $J = 16.16$Hz), 6.74-6.70 (d, 1H, $J = 16.12$Hz); $^{13}$C NMR (100MHz, DMSO-d6) δ 167.53, 150.90, 142.93, 139.67, 138.16, 130.39, 128.70, 122.73; Anal.Calc’d for C$_8$H$_6$BrNO$_2$: C, 42.14; H, 2.65; N, 6.14. Found: C, 42.18; H, 2.73; N, 6.05.
3-[5-(Methoxycarbonyl)pyridin-2-yl]acrylic acid (48h): White solid; mp. = 224-225°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.79 (bs, 1H), 9.08 (s, 1H), 8.32-8.30 (dd, 1H, \(J_1 = 8.08\)Hz, \(J_2 = 1.72\)Hz), 7.87-7.85 (d, 1H, \(J = 8.12\)Hz), 7.66-7.62 (d, 1H, \(J = 15.72\)Hz), 6.94-6.90 (d, 1H, \(J = 15.72\)Hz), 3.88 (s, 1H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.41, 165.27, 156.54, 150.72, 142.15, 138.37, 125.98, 125.66, 124.67, 52.93; Anal. Calc’d for C\(_{10}\)H\(_9\)NO\(_4\): C, 57.97; H, 4.38; N, 6.76. Found: C, 58.02; H, 4.44; N, 6.67.

3-[5-Bromo-3-(methoxycarbonyl)-2-furyl]acrylic acid (48i): White solid; mp. = 213-214°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.81 (bs, 1H), 7.79-7.75 (d, 1H, \(J = 15.96\)Hz), 7.05 (s, 1H), 6.40-6.36 (d, 1H, \(J = 16\)Hz), 3.81 (s, 3H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.05, 161.89, 154.82, 127.82, 126.53, 122.36, 120.92, 114.71, 52.75; Anal. Calc’d for C\(_9\)H\(_7\)BrO\(_5\): C, 39.30; H, 2.57. Found: C, 39.34; H, 2.62.

3-[2-(Acetylamino)-5-bromo-1,3-thiazol-4-yl]acrylic acid (48j): Brown solid; mp. = >350°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.70 (bs, 1H), 12.57 (bs, 1H), 7.43-7.39 (d, 1H, \(J = 15.32\)Hz), 6.45-6.41 (d, 1H, \(J = 15.36\)Hz), 2.15 (s, 3H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 169.66, 167.30, 157.33, 143.19, 132.56, 122.09, 107.13, 22.31.

3-[5-(Methoxycarbonyl)-2-thienyl]acrylic acid (48k): Pale yellow solid; mp. = 182-184°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.64 (bs, 1H), 7.76-7.71 (m, 2H), 7.57-7.56 (d, 1H, \(J = 3.6\)Hz), 6.41-6.38 (d, 1H, \(J = 15.84\)Hz), 3.82 (s, 3H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.28, 161.95, 145.55, 136.14, 134.79, 134.47, 131.87, 121.41, 52.94; Anal. Calc’d for C\(_9\)H\(_8\)O\(_4\)S: C, 50.94; H, 3.80. Found: C, 50.99; H, 3.86.

3-[6-Chloro-4-(methoxycarbonyl)pyridin-2-yl]acrylic acid (48l): White solid; mp. = 183-185°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.77 (bs, 1H), 8.14-8.13 (d, 1H, \(J = 1.08\)Hz), 7.84 (d, 1H, \(J = 1.08\)Hz), 7.67-7.63 (d, 1H, \(J = 15.64\)Hz), 6.86-6.82 (d, 1H, \(J = 15.64\)Hz), 3.89 (s, 1H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.18, 164.08, 154.81, 151.63, 141.87,
140.84, 125.60, 124.40, 123.13, 53.60; Anal. Calc'd for C_{10}H_8ClNO_4: C, 49.71; H, 3.34; N, 5.80. Found: C, 49.76; H, 3.39; N, 5.72.

3-(2-Cyanopyridin-3-yl)acrylic acid (48m): White solid; mp. = 243-244°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.96 (bs, 1H), 8.74-8.73 (dd, 1H, \(J_1 = 4.48\)Hz, \(J_2 = 0.88\)Hz), 8.55-8.52 (dd, 1H, \(J_1 = 8.24\)Hz, \(J_2 = 0.72\)Hz), 7.80-7.77 (m, 1H), 7.74-7.70 (d, 1H, \(J = 15.92\)Hz), 6.92-6.88 (d, 1H, \(J = 15.88\)Hz); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.00, 152.32, 136.44, 135.68, 134.61, 132.75, 128.32, 126.72, 116.46; Anal. Calc’d for C_{9}H_{6}N_{2}O_{2}: C, 62.07; H, 3.47; N, 16.08. Found: C, 62.11; H, 3.49; N, 16.01.

3-[2-Fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]acrylic acid (48n): White solid; mp. = 187-189°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 12.60 (bs, 1H), 7.98-7.96 (d, 1H, \(J = 7.84\)Hz), 7.74-7.71 (m, 1H), 7.65-7.61 (d, 1H, \(J = 16.2\)Hz), 7.32-7.27 (m, 1H), 6.57-6.53 (d, 1H, \(J = 16.2\)Hz), 1.29 (s, 12H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.60, 164.30, 161.76, 159.96, 138.72, 138.63, 135.98, 135.95, 135.86, 135.83, 122.91, 122.86, 122.18, 122.07, 116.49, 116.28, 84.51, 25.09; Anal. Calc’d for C_{15}H_{18}BFO_4: C, 61.68; H, 6.21. Found: C, 61.73; H, 6.24.

3-[2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-1-benzothien-5-yl]acrylic acid (48o): White solid; mp. = 172-174°C; \(^1\)H NMR (400MHz, CDCl_3) \(\delta\) 7.99 (s, 1H), 7.94-9.1 (m, 3H), 7.62-7.59 (dd, 1H, \(J_1 = 8.48\)Hz, \(J_2 = 1.56\)Hz), 6.55-6.51 (d, 1H, \(J = 15.96\)Hz), 1.39 (s, 12H); \(^{13}\)C NMR (100MHz, CDCl_3) \(\delta\) 171.89, 147.14, 145.87, 140.86, 134.56, 130.45, 125.42, 124.09, 123.07, 116.80, 84.66, 24.81; Anal. Calc’d for C_{17}H_{19}BO_4S: C, 61.84; H, 5.80. Found: C, 61.89; H, 5.84.

1,1’-(Phenylmethylene)bis-pyridiniumdibromide (52): Yellow solid; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 9.55 (s, 1H), 9.42-9.40 (m, 4H), 8.92-8.88 (m, 2H), 8.40-8.36 (m, 4H), 7.69-7.61 (m, 3H), 7.42-7.40 (m, 2H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 149.60, 145.02, 132.02, 130.03, 129.37, 128.96, 128.73, 86.98.
Figure 2.14 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (48c)
Figure 2.15 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (48e)
Figure 2.16 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (48f)
Figure 2.17 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (48h)
Figure 2.18 $^1H$ NMR and $^{13}C$ NMR in DMSO-$d_6$ (48i)
Figure 2.19 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (48j)
Figure 2.20 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (481)
Figure 2.21 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (48n)
Figure 2.22 $^1$H NMR and $^{13}$C NMR in CDCl$_3$ (48o)
Figure 2.23 $^1$H NMR and $^{13}$C NMR in DMSO-$d_6$ (52)
2.5.4 General procedure for the synthesis of tert-butyl cinnamates from gem-dibromomethyl aromatics

To a mixture of gem-dibromomethyl arene (0.10 mol) and malonic acid (0.2 mol) in pyridine (1.5 mol) was added piperidine (0.01 mol) followed by BOC₂O (0.11 mol). The mixture was refluxed for 2-4 hours. The completion of reaction was confirmed by TLC. The brown reaction mixture was cooled and poured onto ice-water. The product was extracted with diethyl ether (2 x 50 mL). The combined organic phase was washed with water and dried over sodium sulfate. The ether layer was concentrated under vacuum to afford the corresponding tert-butyl cinnamate in good yield and purity.

tert-Butyl-3-(4-methoxy-2-nitrophenyl)acrylate (49a): Colourless liquid; \(^{1}\)H NMR (400MHz, CDCl₃) \(\delta\) 7.94-7.90 (d, 1H, \(J = 15.8\) Hz), 7.58-7.56 (d, 1H, \(J = 8.76\) Hz), 7.48-7.47 (d, 1H, \(J = 2.6\) Hz), 7.16-7.13 (dd, 1H, \(J = 8.76, 2.68\) Hz), 6.25-6.21 (d, 1H, \(J = 15.8\) Hz), 3.88 (s, 3H), 1.52 (s, 9H); \(^{13}\)C NMR (100MHz, DMSO-d₆) \(\delta\) 165.3, 160.6, 149.2, 138.1, 129.9, 129.7, 128.8, 128.4, 123.4, 122.6, 119.8, 109.3, 80.9, 56.0, 29.6.

Methyl 3-bromo-4-[3-tert-butoxy-3-oxoprop-1-en-1-yl]benzoate (49b): Off-white solid; mp. = 91.2-92.7°C; \(^{1}\)H NMR (400MHz, DMSO-d₆) \(\delta\) 8.28 (s, 1H), 7.88-7.68 (m, 3H), 6.63-6.59 (d, 1H, \(J = 15.8\) Hz), 3.86 (s, 3H), 1.48 (s, 9H); \(^{13}\)C NMR (100MHz, DMSO-d₆) \(\delta\) 165.6, 165.2, 140.6, 134.6, 134.2, 132.0, 130.2, 129.9, 129.1, 124.7, 81.0, 52.9, 28.2.

Methyl 2-[3-tert-butoxy-3-oxoprop-1-en-1-yl]-4-fluorobenzoate (49c): Colourless liquid; \(^{1}\)H NMR (400MHz, CDCl₃) \(\delta\) 8.36-8.32 (d, 1H, \(J = 15.8\) Hz), 8.01-7.98 (m, 1H), 7.29-7.25 (m, 1H), 7.12-7.08 (m, 1H), 6.25-6.21 (d, 1H, \(J = 15.8\) Hz), 3.92 (s, 3H), 1.47 (s, 9H);

tert-Butyl-3-(6-bromopyridin-3-yl)acrylate (49d): Off-white solid; mp. = 116.5-118.7°C; \(^{1}\)H NMR (400MHz, DMSO-d₆) \(\delta\) 8.68-8.67 (d, 1H, \(J = 2.16\) Hz), 8.13-8.10 (dd, 1H, \(J = 8.40, 2.36\) Hz), 7.70-7.68 (d, 1H, \(J = 8.4\) Hz), 7.57-7.73 (d, 1H, \(J = 15.8\) Hz), 6.73-6.69 (d, 1H, \(J = 15.8\) Hz), 1.47 (s, 9H); \(^{13}\)C NMR (100MHz, DMSO-d₆) \(\delta\) 165.4, 150.9, 142.9, 139.3, 138.2, 130.2, 128.6, 123.2, 80.8, 28.2.
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**tert-Butyl-3-(5-bromopyridin-3-yl)acrylate (49e):** Off-white solid; mp. = 103.5-105.7°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 8.84 (d, 1H, \(J = 1.6\) Hz), 8.68 (d, 1H, \(J = 2.12\) Hz), 8.49-8.48 (t, 1H), 7.56-7.52 (d, 1H, \(J = 15.8\) Hz), 6.79-6.75 (d, 1H, \(J = 15.8\) Hz), 1.47 (s, 9H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 164.9, 151.1, 148.1, 138.7, 137.0, 132.0, 123.5, 120.6, 80.4, 27.7.

**tert-Butyl-3-(2-bromopyridin-4-yl)acrylate (49f):** Off-white solid; mp. = 67.1-69.4°C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 8.40-8.39 (d, 1H, \(J = 5.12\) Hz), 7.98 (s, 1H), 7.75-7.73 (dd, 1H, \(J = 5.16, 1.04\) Hz), 7.51-7.47 (d, 1H, \(J = 15.8\) Hz), 6.88-6.84 (d, 1H, \(J = 15.8\) Hz), 1.46 (s, 9H); \(^{13}\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 164.6, 150.8, 144.8, 142.2, 139.3, 126.4, 126.0, 121.5, 80.0, 27.7.

**Methyl 6-[3-tert-butoxy-3-oxoprop-1-en-1-yl]-2-chloronicotinate (49g):** Off-white solid; mp. = 77.1-79.4°C; \(^1\)H NMR (400MHz, CDCl\(_3\)) \(\delta\) 8.18-8.16 (d, 1H, \(J = 7.84\) Hz), 7.52-7.48 (d, 1H, \(J = 15.64\) Hz), 7.39-7.37 (d, 1H, \(J = 7.84\) Hz), 6.96-6.92 (d, 1H, \(J = 15.64\) Hz), 3.96 (s, 3H), 1.52 (s, 9H); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \(\delta\) 165.2, 164.5, 155.8, 150.1, 141.1, 139.3, 128.0, 126.2, 121.7, 81.2, 52.8, 28.0.

**tert-Butyl-3-(8-chloroquinolin-2-yl)acrylate (49h):** Off-white solid; mp. = 99.1-101.7°C; \(^1\)H NMR (400MHz, CDCl\(_3\)) \(\delta\) 8.49-8.47 (d, 1H, \(J = 8.4\) Hz), 8.05-8.02 (d, 1H, \(J = 8.8\) Hz), 7.97-7.95 (m, 2H), 7.73-7.69 (d, 1H, \(J = 15.8\) Hz), 7.61-7.57 (t, 1H), 7.06-7.02 (d, 1H, \(J = 15.8\) Hz), 1.51 (s, 9H); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \(\delta\) 164.9, 153.3, 143.3, 142.6, 137.7, 132.4, 130.2, 129.1, 127.4, 127.3, 125.9, 121.7, 80.6, 27.7.

**tert-Butyl-3-(3-bromo-4-methoxyphenyl)acrylate (49i):** Colourless liquid; \(^1\)H NMR (400MHz, CDCl\(_3\)) \(\delta\) 7.73 (s, 1H), 7.49-7.40 (m, 2H), 6.90-6.87 (d, 1H, \(J = 8.48\) Hz), 6.27-6.23 (d, 1H, \(J = 15.8\) Hz), 3.92 (s, 3H), 1.53 (s, 9H); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \(\delta\) 166.2, 157.1, 141.6, 132.4, 128.7, 119.1, 112.1, 111.7, 80.4, 56.3, 28.1.
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Methyl 4-[3-tert-butoxy-3-oxoprop-1-en-1-yl]-3-iodobenzoate (49j): Colourless liquid; \(^1\)H NMR (400MHz, CDCl\(_3\)) \(\delta\) 7.73 (s, 1H), 7.49-7.40 (m, 2H), 6.90-6.87 (d, 1H, \(J = 8.48\) Hz), 6.27-6.23 (d, 1H, \(J = 15.8\) Hz), 3.92 (s, 3H), 1.53 (s, 9H); \(^13\)C NMR (100MHz, CDCl\(_3\)) \(\delta\) 166.2, 157.1, 141.6, 132.4, 128.7, 119.1, 112.1, 111.7, 80.4, 56.3, 28.1.

Methyl 5-[3-tert-butoxy-3-oxoprop-1-en-1-yl]thiophene-2-carboxylate (49k): Colourless liquid; \(^1\)H NMR (400MHz, CDCl\(_3\)) \(\delta\) 7.69-7.67 (t, 1H), 7.62-7.58 (d, 1H, \(J = 15.72\) Hz), 7.18-7.17 (d, 1H, \(J = 3.88\) Hz), 6.29-6.25 (d, 1H, \(J = 15.72\) Hz), 3.88 (s, 3H), 1.51 (s, 9H); \(^13\)C NMR (100MHz, CDCl\(_3\)) \(\delta\) 165.4, 162.1, 145.6, 135.0, 134.5, 133.8, 129.9, 121.9, 81.0, 52.3, 28.1.

Methyl 4-[3-tert-butoxy-3-oxoprop-1-en-1-yl]-1-naphthoate (49m): Off-white solid; mp. = 109.1-111.2\(^\circ\)C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 8.77-8.74 (m, 1H), 8.37-8.34 (d, 1H, \(J = 15.8\) Hz), 8.27-8.25 (dd, 1H, \(J = 7.36, 4.44\) Hz), 8.09-8.07 (d, 1H, \(J = 7.68\) Hz), 8.00-7.98 (d, 1H, \(J = 7.68\) Hz), 7.74-7.68 (m, 2H), 6.66-6.62 (d, 1H, \(J = 15.8\) Hz), 3.94 (s, 3H), 1.52 (s, 9H); \(^13\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 167.0, 165.0, 139.2, 135.8, 130.9, 130.0, 129.1, 128.3, 127.9, 127.3, 125.7, 124.8, 124.1, 123.8, 80.4, 52.4, 27.8.

4-[3-tert-Butoxy-3-oxoprop-1-en-1-yl]-3-nitrobenzene boronic acid pinacol ester (49n): Colourless liquid; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 8.18 (s, 1H), 7.95-7.91 (m, 2H), 7.87-7.83 (d, 1H, \(J = 15.8\) Hz), 6.56-6.52 (d, 1H, \(J = 15.8\) Hz), 1.47 (s, 9H); \(^13\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 164.6, 147.8, 138.9, 138.4, 131.9, 129.7, 129.1, 125.0, 84.5, 80.6, 27.7, 24.5.

tert-Butyl-3-(5-bromo-2-cyanophenyl)acrylate (49o): Off-white solid; mp. = 123.6-125.2\(^\circ\)C; \(^1\)H NMR (400MHz, DMSO-\(d_6\)) \(\delta\) 8.38 (s, 1H), 7.86-7.79 (m, 2H), 7.65-7.61 (d, 1H, \(J = 15.8\) Hz), 6.93-6.89 (d, 1H, \(J = 15.8\) Hz), 1.48 (s, 9H); \(^13\)C NMR (100MHz, DMSO-\(d_6\)) \(\delta\) 164.6, 138.4, 136.8, 134.9, 133.4, 130.2, 127.9, 126.0, 116.7, 110.7, 80.8, 27.7.
Figure 2.24 $^1$H NMR (400MHz) and $^{13}$C NMR (100MHz) in CDCl$_3$ (49a)
Figure 2.25 $^1$H NMR (400MHz) and $^{13}$C NMR (100MHz) in DMSO-$d_6$ (49b)
Figure 2.26 $^1$H NMR (400MHz) and $^{13}$C NMR (100MHz) in DMSO-$d_6$ (49e)
Figure 2.27 $^1$H NMR (400MHz) and $^{13}$C NMR (100MHz) in DMSO-$d_6$ (49g)
Figure 2.28 $^1$H NMR (400MHz) and $^{13}$C NMR (100MHz) in DMSO-$d_6$ (49h)
Figure 2.29 $^1H$ NMR (400MHz) and $^{13}C$ NMR (100MHz) in DMSO-\(d_6\) (49j)
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