Construction of C-X bond

Metal-Free, Green and Efficient Oxidative Functionalization: Aq. Halo acid and DMSO promoted α-Halogenation of Enaminones

1.1 Introduction

Halogenation is the process in which halogen atom is incorporated into the organic molecule. These halogenated organic compounds are drawn special attention in the centre of synthetic organic chemistry. These are the fundamental and valuable building blocks with suitable key precursors being used to construct carbon – carbon, carbon – heteroatom bonds. Apart from being ample in natural products and pharmaceuticals, Halogenated organic molecules have always been extremely important synthetic intermediates for various chemical transformations. On this context, the cross – coupling reactions have gained more insight into one of the hot areas in organic reactions that entail the pre-functionalized starting materials such as aryl halides, α-halo compounds and pseudo-halide. Therefore, installing the halogens especially bromine and iodine due to their high affinity towards oxidative insertion, on aromatic molecules has gained admirable interest from synthetic point of view.

Scheme 1.1: Traditional halogenation with X₂

Traditional methods for incorporating halogen make use of molecular halogens (X₂; X = Br, I, Cl) which suffer from distinct limitations (Scheme 1.1) such as 1) Except iodine, all the other halogens are hazardous, toxic and corrosive reagents, 2) These methods provide very low halogen atom economy due to the formation of HX as by-product and 3) During the course of reactions sometimes, undesirable by-products are unavoidable. In order to avoid the use of molecular halogens, some altered reagents were introduced such as halo-succinimides (NBS, NCS and NIS). These reagents showed more prominent, safer to operational in comparison of molecular halogens (X₂) and they do not produce by-product HX. However, these reagents are not up to the mark to make use in industrial processes for large-scale

production of halogenated products because of their high cost and produce succinimide as organic waste. Hence, it is very much essential to develop the in-situ methods for the preparation molecular halogens and their further use in organic synthesis. Interestingly, hydrogen halide (HX), the byproduct of X₂ based halogenations, is willingly available, easily operable, having low cost and require simple storage and transportation. Therefore, the concept of oxidative halogenations inspired by biomimetic halogenation, which works as an electrophilic halogenation via oxidation of the halide ion from aq. HX, is enormously increasing as an alternative tool for the use of molecular halogens in organic transformations. Besides, it incorporates only one halogen atom into the substrate allowing the regeneration of the electrophilic halogen through oxidation of residual halide ions. In this context, a variety of stoichiometric oxidants have been employed for the oxidation of halide ions such as H₂O₂, O₂ Selectfluor, Oxone and metal-based oxidants. However, there is a need for the continuous investigations for the development of more greener reaction conditions in this field since the available methods suffer selectivity issue, longer reaction time, expensive reagents demands high resources and high waste generation except the combination of aq. HBr/H₂O₂ which has proven safe.

Utility of enaminoes containing multiple reactive sites i.e. alkene, enamine and enone is more fascinating in organic synthesis due to their wide applicability for the preparation of various of heterocycles, organic molecules, and biologically important

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molecules\textsuperscript{18}. In addition, these enaminones have also been examined as ligands\textsuperscript{19} for the metal mediated organic transformations. Accordingly, functionalization of simple enaminones has become an important area of research for many chemists. In this direction, enaminones have been widely employed for various chemical transformations via direct $\alpha$-C-H functionalization/activation processes by both metal\textsuperscript{20} and metal free\textsuperscript{21} conditions. These functionalized enaminones gained enormous attention in synthetic chemistry due to their flexibility as valuable precursors and can provide new avenue for further modification. Though, the metal catalyzed C-H activation\textsuperscript{22} transformations have considered as indispensable tool in organic synthesis, the metal free C-H activations have also emerged rapidly as highly significant strategy in the preparation of diverse organic molecules\textsuperscript{23}. Due to increasing concern on development of sustainable chemistry, the metal free catalysis has increasingly gaining worth attention\textsuperscript{24} as these can completely eliminate the possibility of metal contamination, which is crucial for the synthesis of biologically important molecules\textsuperscript{25}. Therefore, developing metal free environmentally benign conditions for easy access to C-H bond functionalization is truly a highly demanding task. On the other hand, research findings have found wide applications of DMSO as solvent\textsuperscript{26}, reagent\textsuperscript{27} and an oxidizing agent\textsuperscript{28}. This

DMSO has gained more attention in organic synthesis due to its high abundance, inexpensive, low toxicity and eco-friendly nature. We therefore were interested in investigating the potential reactivity of low toxic, inexpensive and green DMSO for oxidative halogenations. Literature precedence showed that, the research on the use of aq. HBr/DMSO combination indeed resulted in several oxidative transformations.

Jakob Magolan et.al., showed, facile and efficient protocol for synthesis of 1,2-dibromoalkanes from alkene by using aq. HBr and DMSO system (Scheme 1.2). During this reaction, bromide ion is oxidized by dimethyl sulfoxide to generate the molecular bromine, which then reacts with alkene to give the corresponding 1,2-dibromoalkanes with good yield.

\[ \text{Scheme 1.2: Synthesis of 1,2-dibromoalkanes} \]

Ning Jiao et.al., reported an easy preparation of bromohydrins in good yields, from alkenes using aq. HBr-DMSO system (Scheme 1.3). They claimed that dimethyl sulfoxide served as co-solvent as well as oxidant for this transformation. Authors also demonstrated successfully the application of aq. HBr-DMSO in electrophilic bromination of arenes and heteroarenes with very good yields. Similar bromination has also been studied by George Majetich’s research group using aq. HBr-DMSO combination (Scheme 1.4).

\[ \text{Scheme 1.3: Synthesis of bromohydrin using aq. HBr-DMSO system} \]

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Masanao Inagaki\textsuperscript{33} et al., have developed benzylic oxidation by applying aq. HBr-DMSO under mild condition as shown in the (Scheme 1.5).

\begin{equation}
\text{Scheme 1.4: Electrophilic aromatic bromination of arenes}
\end{equation}

Similarly, Zhiling Cao\textsuperscript{34} et al., showed the oxidation of alkyl ketones to the corresponding 1,2-dicarbonyl compounds by using aq. HBr in dimethyl sulfoxide.

\begin{equation}
\text{Scheme 1.5: Benzylic oxidation by HBr:DMSO}
\end{equation}

1.2 Our hypothesis

Although aq. HBr-DMSO system gave several useful chemical transformations, the enaminones have not been explored so far with it for oxidative halogenation reaction. Interestingly, albeit the construction of C–C\textsuperscript{35}, C–N\textsuperscript{36}, C–S\textsuperscript{37}, and C–O\textsuperscript{38} bonds on enaminones through C–H bond functionalization have been achieved largely, the

\begin{equation}
\text{Scheme 1.6: Preparation 1,2-dicarbonyl compounds}
\end{equation}


\textsuperscript{34} Z. Cao, D. Shi, Y. Qu, C. Tao, W. Liu and G. Yao, \textit{Molecules}, 2013, 18, 15717.


corresponding C–halogen bond formation is studied in very rare occasion\textsuperscript{39}. Recently, Shen and Yu developed α-chlorination\textsuperscript{40} of acyclic \textit{N}-aryl enaminones using cupric chloride as source of chlorine atom (Scheme 1.7). However, this chlorination limits its applicability in terms of 1) excess quantity of cupric chloride, 2) moderate to good yield, 3) less atom economy and 4) longer reaction time. Authors have also disclosed the bromination products with moderate yields. However, a similar C-halogen bond formation on enaminone under environmentally safer and metal free conditions has not been reported to the best of our knowledge. With the knowledge of utility on aq. HBr–DMSO system and the limitations of previous work on halogenations on enaminones, we thought, we can explore the reactivity of aq. HBr–DMSO on enaminones. Subsequently, we begin our study on optimizing the reaction conditions as discussed in the following section.

1.3 Results and Discussion

\textbf{Optimization of reaction condition}

We herein wish to report our research findings of a mild and efficient oxidative halogenation of \textit{N}-aryl enaminones employing hydrohalic acid along with DMSO, which furnished clean and effortless synthesis of various α-halo enaminones. We initiated our study with \textit{N}-Phenyl enaminone 1a as benchmark substrate to define the suitable reaction conditions for the present study. The reaction of 1a was carried out with aq. HBr (2.2 equiv.) using various oxidizing agents in different solvents as shown in the Table 1.1. The reaction of 1a with aq. HBr and H\textsubscript{2}O\textsubscript{2} (2.2 equiv.) as oxidant in water at reflux conditions gave the corresponding brominated product 2-bromo-1-phenyl-3-(phenylamino) prop-2-en-1-one 2a in


20% yield (Table 1.1, Entry 1). Interestingly, the same reaction in EtOAc at 45 °C furnished the product 2a in 72% yield (Table 1.1, Entry 2). We assumed that, the less solubility of reactants in water might be the reason for low yield in water as solvent. Hence, continued to investigate the suitable oxidants in EtOAc. Reactions using both aq. TBHP and solution of TBHP in decane produced the desired product 2a in 78% and 74% respectively (Table 1.1, Entries 3&4). Subsequently, the reactions with CPBA and K₂S₂O₈ were not efficient and lead to only 65% and 40% of yields respectively (Table 1.1, Entries 5&6). To our delight, the use of DMSO as oxidant under similar reaction conditions underwent complete conversion and furnished the desired product 2a in yield of 99% (Table 1.1, Entry 7). Interestingly, there was no formation of product in absence of DMSO and the starting material 1a was recovered completely (Table 1.1, Entry 8) indicating the fact that, an oxidizing agent is necessary. Additionally, the lowering of DMSO quantity resulted in reducing the yield of product (Table 1.1, Entries 9&10). In addition, the Oxone also produced the desired product 2a in 75% yield (Table 1.1, Entry 11). We also employed molecular oxygen as environmentally benign oxidant for the reaction, however the reaction was slow and we could obtain the product 2a in only 45% (Table 1.1, Entry 12). Thus, among several oxidizing agents studied, the DMSO was more promising as it was resulting in to complete conversion with excellent yield of isolated product. With set oxidizing agent in hand, we then continued to explore the solvent medium for the present oxidative halogenation reaction. A moderate yield of around 65% is observed in an alcoholic solvent ethanol (Table 1.1, Entry 13). Similarly, reactions in non-polar solvents such as Toluene and

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Table 1.1: Optimization of reaction condition

![Table 1.1: Optimization of reaction condition](image)
All reactions were carried out by using 0.45 mmol of 1a, 0.99 mmol of 47% aq. HBr and DMSO in EtOAc (2 mL) at 45 °C for 1.5-2 h under aerobic condition. Isolated yields. Reaction was performed at RT to 100 °C. NR = No Reaction. Equiv. = equivalent.

Hexane produced the corresponding product 2a in 65% and 75% yields respectively (Table 1.1, Entries 14 and 15). Ethereal solvents THF and 1,4-Dioxane were better than non-polar solvents in producing the product 2a in yield of 86% and 82% respectively (Table 1.1, Entries 16 &17). However, acetonitrile was appeared to be poor solvent and furnished the product 2a in only 53% (Table 1.1, Entry 18). In addition, DMF and halogenated solvents also gave the desired product in the yield range of 75-85% (Table 1.1, Entries 19-21). Surprisingly, DMSO itself as solvent did not produce success and obtained the product in only moderate yield of 68% (Table 1.1, Entry 22).

After screening of several oxidizing agents and solvents, we decided to choose the entry 7 of Table 1.1 as the optimized reaction conditions for the present halogenation reaction. Thus, continued to explore the substrate scope for present halogenation as shown in the Table 1.2 using aq. HBr (2.2 equiv.) and DMSO (2.2 equiv.) in EtOAc (2 mL) as solvent.
medium. The reaction of enaminones with electron donating group furnished the corresponding brominated products 2b, 2c, 2d and 2e in 94%, 95%, 96% and 99% respectively. Enaminone containing naphthyl under the optimal conditions also afforded the product 2f, 2g and 2h in 90%, 94% and 91% respectively. In addition, chlorine substituted enaminones also underwent clean reactions and furnished the desired brominated products 2i and 2j in 92 and 98% yields. Similarly, fluorine substituted enaminones resulted in to the desired products 2k and 2l in excellent yields 97 and 98% respectively. In the same way, the enaminone containing both chlorine and fluorine atoms was tested under similar conditions. It was found that, the reaction proceeded smoothly affording the corresponding product 2m in 95% yield. We also investigated the reactivity of enaminone that contain heterocyclic moiety under present methodology. Accordingly, thiophene and furan derived enaminones on subjecting to present oxidative bromination afforded their corresponding products 2n, 2o and 2p in 95, 93 and 98% yields respectively.

However, the N,N-dimethyl analogue of enaminone 1q did not take part in oxidative bromination successfully. The corresponding brominated product 2q was not formed and produced unidentifiable impurities might be due to more basic nature of tertiary amine in 1q. We then changed our attention towards investigating the substrate scope on chlorination reactions using aq. HCl and DMSO combination. Chlorination of enaminone derivatives also gave fruitful results under similar reaction conditions by consuming aq. HCl (5 equiv.) and DMSO (5 equiv.). This excess amount reagent is in accordance to the higher oxidation potential\(^{41}\) of more electronegative halide ion than less electronegative halide ion.

Table 1.2: Substrate scope of Enaminone\(^a\)

All bromination reactions were carried out by using 1 (1.0 equiv.), 47% aq. HBr (2.2 equiv.) and DMSO (2.2 equiv.) in EtOAc (2 mL) at 45 °C for 1-3.5 h. All chlorination reactions were carried out by using 1 (1.0 equiv.), 37% HCl (5.0 equiv.) and DMSO (5.0 equiv.) in EtOAc (2 mL) at 45 °C for 1-3.5 h. ND = not detected

The unsubstituted enaminone 1a under standard conditions worked well for the oxidative chlorination and gave the chlorinated product 2r in 81% yield. The enaminones containing electron-donating group afford the related chlorinated products 2s and 2t in 77 and 83% respectively. The halogen substituted enaminones reacted smoothly and furnished their
products \(2u\) and \(2v\) in 85 and 80\% yields respectively. In addition, the enaminone containing thiophene moiety was also proceeded smoothly to afford the product \(2w\) in 79\% yield.

To further explore the scope of present methodology, we tested the synthesis of chromenone derivatives as shown in the Scheme 1.8. The hydroxy enaminone derivative 3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one \(3\) reacted smoothly under optimized oxidative halogenation conditions and gave the corresponding chlorinated \((3a)\), brominated \((3b\) and \(3c)\) and iodinated \((3d)\) products of chromenones in excellent yields of 86, 92, 94, and 89\% respectively.

![Scheme 1.8: Synthesis of halogenated chromone](image)

Due to simple and highly efficient strategy, we also examined the efficiency of present halogenation by scaling up the reaction quantity as outlined in the Scheme 1.9. The reaction of 2.0 gm scale also went well in furnishing the brominated product with very good yield of 95\% indicating the practical applicability of present method in large scale. In our present study, the \(N,N\)-dimethyl analogue of enaminone \(1q\) did not give success (see Table 1.2, \(2q\)) which made us to think alternatively to generate the halogenated products by one pot reactions since the enaminone \(1q\) is the starting material for the preparation of \(N\)-aryl enaminone. Thus, we planned to prepare halogenated \(N\)-aryl enaminones starting from \(N,N\)-dimethyl analogue of enaminones and anilines without the isolation of \(N\)-aryl enaminones as shown in the Scheme 1.10. Accordingly, we initially reacted \(N,N\)-dimethyl analogue of enaminones and anilines with PTSA in xylene solvent at 110 \(^\circ\)C for 2 h, then maintained the optimized reaction conditions. We found the formation of desired brominated products in good yields. The brominated products \(2a\) and \(2x\) were synthesized through one pot reaction in 70 and 75\% yield respectively.
After all the above success, we were trying to figure out the reaction mechanism for the present halogenation reaction. To understand the mechanism of reaction, we performed few controlled experiments as shown in the Scheme 1.11. The (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl TEMPO a radical scavenger was used with an intention to trap any free radical formed during the oxidative halogenation of enamiones 1a and 3. These reactions produced brominated products 2a and 3b in 95 and 90% yields respectively, suggesting the reaction is not proceeding through free radical mechanism. Thus, based on the literature precedence\textsuperscript{30-34}, controlled experiment and earlier optimization studies, we proposed a tentative reaction mechanism as shown in the Figure 1.1. We believe that, the DMSO oxidizes the halo acid and results in the formation of an adduct DMS.Br\textsubscript{2} which will further take part in reaction to furnish the desired halogenated enaminone derivative.
1.4 Conclusions

In summary, a new method of an oxidative halogenation for N-aryl enaminones under transition metal free and mild reaction conditions is developed. The success of this method is the use of readily available and inexpensive aqueous halo acid and DMSO as an oxidising reagent. This method furnished variety of halogenated enaminone derivative in short reaction time with excellent yields. The present reaction represents considerable advancement over previously reported halogenation of enaminones and is a straightforward approach for halogenation without the use of molecular halogens. We also demonstrated successfully the practical feasibility of present by scaling up the reaction quantity. The developed strategy was also found to be useful in synthesis of halogenated chromone derivatives in very good yields, which is very important.

1.5 Experimental Section
All the enaminone starting materials were synthesized using the procedure given in literature.42

1.5.1 General Experimental Procedure for The Preparation of α-brominated Enaminone Products

![Chemical structure](image)

To the solution of enaminone 1 (1.0 equiv./0.45 mmol) in ethyl acetate (2 mL), was added hydrobromic acid (47% aq. HBr, 2.2 equiv./0.99 mmol) followed by dimethyl sulfoxide (2.2 equiv./0.99 mmol). The reaction mixture was stirred at 45 °C till completion of reaction. The progress of reaction was monitored by TLC. After completion of reaction, evaporated the solvent completely under reduced pressure and the residue was purified by column chromatography to afford pure α-halogenated enaminone 2.

The above procedure is used for chlorination and iodination reactions using DMSO (5.0 equiv.) with 37% aq. HCl (5.0 equiv./2.24 mmol) & 57% aq. HI (5.0 equiv./2.24 mmol) in EtOAc (2 mL) respectively.

1.5.2 Procedure for One Pot Oxidative Halogenation Reaction

![Chemical structure](image)

To the solution of enaminone 1q (1.0 equiv./0.57 mmol) in xylene (2 mL), was added amines (1.0 equiv./0.57 mmol) followed by p-Toluene sulfonylic acid (p-TSA) (0.028 mmol). The resultant reaction mixture was heated up 110 °C for 2 h and progression of the reaction was monitored by TLC. After the formation N-aryl enaminone (1) allowed the reaction mixture for room temperature then, without isolation of (1) added the hydrobromic acid (47% aq. HBr, 0.99 mmol) followed by dimethyl sulfoxide (0.99 mmol) in ethyl acetate (2 mL). The reaction mixture was stirred at 45 °C till completion of reaction. The progress of reaction was monitored by TLC. After completion of reaction, evaporated the solvent completely under reduced pressure and the residue was purified by column chromatography to afford pure α-halogenated enaminone

1.5 Spectroscopic Data of New Enaminone Derivatives and α-Halogenated Enaminones

3-(2-Chlorophenyl)amino-1-(thiophen-2-yl)prop-2-en-1-one (1o)

Physical state of the compound : Yellow solid; m.p. 182-184 °C.

Rf value : 0.7 in 10% EtOAc/PET.

1H NMR (400 MHz, CDCl3) : δ = 5.8 (d, J = 8.0Hz, 1H, alkene-α-H), 6.77 - 6.83 (m, 1H, ArH), 6.92 - 9.96 (m, 1H, ArH), 6.98 - 7.02 (m, 1H, ArH), 7.03 -
7.09 (m, 1H, ArH), 7.20 - 7.29 (m, 2H, ArH), 7.38 –
7.41 (m, 1H, ArH), 7.48 - 7.51 (m, 1H, ArH), 11.97 (d,
J = 12.0Hz, 1H, -NH).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 95.4, 114.0, 122.4, 123.4, 127.7, 127.9, 129.3,$
129.9, 131.7, 137.0, 142.4, 145.7, 183.7.

MS (ESI): $m/z$ calcd for C$_{13}$H$_{10}$ClNOS 263.01, found 264.04
[M+H], 266.02 [M+H+2].

$^{3}$-(4-Chlorophenyl)amino-1-((4-fluorophenyl)prop-2-en-1-one (1m)

Physical state of the compound: Yellow solid; m.p. 182-184 °C.

R$_f$ value: 0.8 in 10% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 5.98$ (d, $J = 8.0Hz$, 1H, alkene-α-H), 7.0 - 7.05 (m,
2H, ArH), 7.09 - 7.15 (m, 2H, ArH), 7.29 - 7.33 (m, 2H, ArH), 7.40 -
7.47 (m, 1H, ArH), 7.90 - 7.97 (m, 2H, ArH), 12.08 (d, $J = 12.0Hz$, 1H,
-NH).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 93.8, 115.5$ (d, $J = 22Hz$), 117.5,
128.8, 129.8, 135.3 (d, $J = 2.9Hz$), 138.8, 144.7, 163.8,
166.3, 189.7.

MS (ESI): $m/z$ calcd for C$_{15}$H$_{11}$ClFNO 275.05, found 276.1
[M+H], 278.1 [M+H+2].
**Figure 1.2**: $^1$H NMR Spectrum of 3-(2-Chlorophenyl)amino-1-(thiophen-2-yl)prop-2-en-1-one (1o)

**Figure 1.3**: $^{13}$C NMR Spectra of 3-(2-Chlorophenyl)amino-1-(thiophen-2-yl)prop-2-en-1-one (1o)
Figure 1.4: $^1$H NMR spectra of 3-(4-Chlorophenyl)amino-1-(4-fluorophenyl)prop-2-en-1-one (1m)

Figure 1.5: $^{13}$C NMR spectrum of 3-(4-Chlorophenyl)amino-1-(4-fluorophenyl)prop-2-en-1-one (1m)

3-(4-Methoxyphenyl)amino-1-(thiophen-2-yl)prop-2-en-1-one (1n)

Physical state of the compound: Yellow solid; m.p. 179-181 ºC.
R$_f$ value: 0.8 in 10% EtOAc/PET.
\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta = 3.7\) (s, 3H, -OMe), 5.75 (d, \(J = 7.6\)Hz, 1H, alkene-\(\alpha\)-H), 6.8 (d, \(J = 7.8\)Hz, 2H, ArH), 6.94 (d, \(J = 7.8\)Hz, 2H, ArH), 7.00 - 7.03 (m, 1H, ArH), 7.25 - 7.35 (m, 1H, ArH), 7.43 - 7.45 (m, 1H, ArH), 7.53 - 7.55 (m, 1H, ArH), 11.83 (d, \(J = 12.0\)Hz, 1H, -NH).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) : \(\delta = 55.5, 92.8, 115.0, 117.7, 127.9, 128.6, 131.2, 133.7, 145.4, 146.3, 156.3, 183.3\).

MS (ESI) : \(m/z\) calcld for C\(_{14}\)H\(_{13}\)NO\(_2\)S 259.06, found 260.09 [M+H].

\(1\)-(2,4-Dichlorophenyl)-3-(phenylamino)prop-2-en-1-one (Ii)

Physical state of the compound : Yellow solid; m.p. 169-171 °C.

R\(_f\) value : 0.8 in 10% EtOAc/PET.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta = 5.7\) (d, \(J = 7.6\)Hz, 1H, alkene-\(\alpha\)-H), 7.09 - 7.14 (m, 1H, ArH), 7.28 - 7.32 (m, 1H, ArH), 7.33 - 7.39 (m, 2H, ArH), 7.43 (d, \(J = 2.0\)Hz, 1H, ArH), 7.46 - 7.53 (m, 2H, ArH), 11.94 (d, \(J = 12.0\)Hz, 1H, -NH).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) : \(\delta = 97.5, 116.6, 124.2, 127.0, 129.7, 130.1, 130.3, 132.5, 136.0, 138.6, 139.8, 145.3, 190.7\).

MS (ESI) : \(m/z\) calcld for C\(_{15}\)H\(_{11}\)Cl\(_2\)NO 291.02, found 292.06 [M+H], 293.98 [M+H+2], 295.92 [M+H+4].
Figure 1.6: $^1$H NMR spectrum of 3-(4-Methoxyphenyl)amino-1-(thiophen-2-yl)prop-2-en-1-one (1n)

Figure 1.7: $^{13}$C NMR spectrum of 3-(4-Methoxyphenyl)amino-1-(thiophen-2-yl)prop-2-en-1-one (1n)
GS-SM-Di-Cl

Figure 1.8: $^1$H NMR spectrum of 1-(2,4-Dichlorophenyl)-3-(phenylamino)prop-2-en-1-one (1i)

GS-SM-Di-Cl

Figure 1.9: $^{13}$C NMR spectrum of 1-(2,4-Dichlorophenyl)-3-(phenylamino)prop-2-en-1-one (1i)

1-(Furan-2-yl)-3-(4-methoxyphenylamino)prop-2-en-1-one (1p)

Physical state of the compound : Yellow solid; m.p. 182-184 °C.

Rf value : 0.8 in 10% EtOAc/PET.
$^1$H NMR (400 MHz, CDCl$_3$) : $\delta = 3.68$ (s, 3H, -OMe), 5.77 (d, $J = 7.6$Hz, 1H, alkene-$\alpha$-H), 6.35 - 6.42 (m, 1H), 6.77 (d, $J = 9.2$Hz, 2H, ArH), 6.92 (d, $J = 9.2$Hz, 2H, ArH), 6.98 (d, $J = 3.2$Hz, 1H, ArH), 7.26 - 7.32 (m, 1H, ArH), 7.42 (d, $J = 1.2$Hz, 1H, ArH), 11.85 (d, $J = 12.0$Hz, 1H, -NH).

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta = 55.4$, 92.5, 111.9, 113.5, 114.8, 117.7, 133.6, 144.7, 145.6, 153.7, 156.2, 179.5.

MS (ESI) : $m/z$ calcd for C$_{14}$H$_{13}$NO$_3$ 243.08, found 244.1 [M+H].

*I-(4-Chlorophenyl)-3-((2-chlorophenyl)amino)prop-2-en-1-one (1j)*

Physical state of the compound : Yellow solid; m.p. 199-201 °C.

R$_f$ value : 0.7 in 10% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$) : $\delta = 6.02$ (d, $J = 7.6$Hz, 1H, alkene-$\alpha$-H), 6.72 - 6.78 (m, 1H, ArH), 6.90 - 7.08 (m, 1H, ArH), 7.20 - 7.29 (m, 2H, ArH), 7.41 (d, $J = 8.2$Hz, 2H, ArH), 7.47 - 7.53 (m, 1H, ArH), 7.89 (d, $J = 8.2$Hz, 2H, ArH), 12.39 (d, $J = 11.6$Hz, 1H, -NH).

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta = 95.0$, 115, 117, 119.0, 123.9, 127.6, 127.9, 128.7, 129.4, 130.3, 138.0, 143.5, 189.8.

MS (ESI) : $m/z$ calcd for C$_{15}$H$_{12}$Cl$_2$NO 291.01, found 292.0 [M+H], 294.0 [M+H+2] 296.0 [M+H+4].
Figure 1.10: $^1$H NMR spectrum of 1-(Furan-2-yl)-3-(4-methoxyphenylamino)prop-2-en-1-one (1p)

Figure 1.11: $^{13}$C NMR spectrum of 1-(Furan-2-yl)-3-(4-methoxyphenylamino)prop-2-en-1-one (1p)
Figure 1.12: $^1$H NMR spectrum of 1-(4-Chlorophenyl)-3-((2-chlorophenyl)amino)prop-2-en-1-one (1j)

Figure 1.13: $^{13}$C NMR spectrum of 1-(Naphthalen-2-yl)-3-(phenylamino)prop-2-en-1-one (1g)

**1-(Naphthalen-2-yl)-3-(phenylamino)prop-2-en-1-one (1g)**

**Physical state of the compound**: Yellow solid; m.p. 189-191 °C.

**R$_f$ value**: 0.8 in 10% EtOAc/PET.
**1H NMR (400 MHz, CDCl₃)**: δ = 5.82 (d, J = 8.0Hz, 1H, alkene-α-H), 7.07 - 7.17 (m, 3H, ArH), 7.33 - 7.39 (m, 2H, ArH), 7.45 - 7.58 (m, 4H, ArH), 7.71 – 7.74 (m, 1H, ArH), 7.85 - 7.93 (m, 2H, ArH), 8.52 (d, J = 8.0Hz, 2H, ArH), 12.14 (d, J = 11.6Hz, 1H, -NH).

**13C NMR (100 MHz, CDCl₃)**: δ = 98.3, 116.4, 123.7, 124.7, 125.9, 126.0, 126.8, 128.2, 128.4, 129.7, 130.2, 130.6, 133.8, 138.9, 140.2, 144.6, 195.3.

**MS (ESI)**: m/z calcd for C₁₉H₁₅NO 273.11, found 274.1 [M+H].

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3-(4-Methoxyphenyl)amino)-1-(naphthalen-1-yl)prop-2-en-1-one (1h)

**Physical state of the compound**: Yellow solid; m.p. 193-195 °C.

**R_f value**: 0.8 in 10% EtOAc/PET.

**1H NMR (400 MHz, CDCl₃)**: δ = 3.81 (s, 3H, -O Me), 5.77 (d, J = 7.6Hz, 1H, alkene-α-H), 6.91 (d, J = 8.8Hz, 2H, ArH), 7.09 (d, J = 8.8Hz, 2H, ArH), 7.40 - 7.58 (m, 4H, ArH), 7.71 (d, J = 6.8Hz, 1H, ArH), 7.84 - 7.93 (m, 2H, ArH), 8.52 (d, J = 8.4Hz, 1H, ArH), 12.20 (d, J = 12.4Hz, 1H, -NH).

**13C NMR (100 MHz, CDCl₃)**: δ = 55.6, 97.6, 115.1, 118.1, 124.8, 125.8, 126.0, 126.0, 126.7, 128.3, 130.2, 130.4, 133.8, 133.9, 139.2, 145.6, 156.5, 194.9.

**MS (ESI)**: m/z calcd for C₂₀H₁₇NO₂ 303.12, found 304.1 [M+H].
Figure 1.14: $^1$H NMR spectrum of 1-(Naphthalen-2-yl)-3-(phenylamino)prop-2-en-1-one (1g)

Figure 1.15: $^{13}$C NMR spectrum of 1-(Naphthalen-2-yl)-3-(phenylamino)prop-2-en-1-one (1g)
Figure 1.16: $^1$H NMR spectrum of 3-(4-Methoxyphenyl)amino)-1-(naphthalen-1-yl)prop-2-en-1-one (1h)

Figure 1.17: $^{13}$C NMR spectrum of 3-(4-Methoxyphenyl)amino)-1-(naphthalen-1-yl)prop-2-en-1-one (1h)
**2-Bromo-1-phenyl-3-(phenylamino)prop-2-en-1-one (2a)**

Physical state of the compound : Yellow solid; m.p. 152–154 °C.

Yield : 200 mg, 99%.

R<sub>f</sub> value : 0.35 in 20% EtOAc /PET.

1<sup>H</sup> NMR (400 MHz, CDCl<sub>3</sub>) : δ = 6.9 - 6.92 (m, 2H, ArH), 7.06 - 7.10 (m, 1H, ArH), 7.28 - 7.32 (m, 2H, ArH, -NH), 7.38 - 7.55 (m, 4H, ArH), 7.56 - 7.62 (m, 2H, ArH), 7.87 (d, J = 13.60Hz, 1H, C=CH).

13<sup>C</sup> NMR (100 MHz, CDCl<sub>3</sub>) : δ = 101.9, 116.1, 118.1, 124.2, 128.5, 129.9, 130.9, 131.1, 132.8, 143.6, 188.3.

MS (ESI) : m/z calcd for C<sub>15</sub>H<sub>12</sub>BrNO 301.01; found 302.09 [M+H], 304.01 [M+H+2].

**2-Bromo-3-(4-methoxyphenyl)amino-1-phenylprop-2-en-1-one (2b)**

Physical state of the compound : Yellow solid; m.p. 178-180 °C.

Yield : 184 mg, 94%.

R<sub>f</sub> value : 0.32 in 20% EtOAc/PET.

1<sup>H</sup> NMR (400 MHz, CDCl<sub>3</sub>) : δ = 3.76 (s, 3H, -OMe), 6.81 (d, J = 1.2Hz, 2H), 7.0 - 7.15 (m, 1H), 7.42 - 7.54 (m, 4H), 7.58 - 7.64 (m, 3H, -NH), 7.77 (d, J = 13.2Hz, 1H, C=CH).

13<sup>C</sup> NMR (100 MHz, CDCl<sub>3</sub>) : δ = 55.9, 102.6, 113.7, 115.04, 116.8, 118.4, 128.5, 130.8, 131.0, 138.8, 143.2, 156.4, 188.2.

MS (ESI) : m/z calcd for C<sub>16</sub>H<sub>14</sub>BrNO<sub>2</sub> 331.02; found 332.10 [M+H], 334.01 [M+H+2].
Figure 1.18: $^1$H NMR spectrum of 2-Bromo-1-phenyl-3-(phenylamino)prop-2-en-1-one (2a)

Figure 1.19: $^{13}$C NMR spectrum of 2-Bromo-1-phenyl-3-(phenylamino)prop-2-en-1-one (2a)
Figure 1.20: $^1$H NMR spectrum of 2-Bromo-3-(4-methoxyphenyl)amino-1-phenylprop-2-en-1-one (2b)

Figure 1.21: $^{13}$C NMR spectrum of 2-Bromo-3-(4-methoxyphenyl)amino-1-phenylprop-2-en-1-one (2b)
2-Bromo-1-(4-fluorophenyl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2c)  

Physical state of the compound: Dark brown solid; m.p. 179–181 °C.

Yield: 183 mg, 95%.

Rf value: 0.35 in 20% EtOAc/PET.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta = 3.78\) (s, 3H, -OMe), 6.83–6.92 (m, 4H, ArH), 7.11-7.22 (m, 3H, ArH + NH), 7.58-7.64 (m, 2H, ArH), 7.74 (d, \(J = 13.6\)Hz, 1H, C=CH).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 55.6, 100.6, 115.2, 115.4, 115.6\) (d, \(J = 21.0\)Hz), 115.6 (d, \(J = 21.0\)Hz), 118.4, 130.7 (d, \(J = 9.0\)Hz), 130.7 (d, \(J = 9.0\)Hz), 132.6, 135.1, 144.3, 156.9, 164.2 (d, \(J = 251.0\)Hz), 186.8.

MS (ESI): \(m/z\) calcd for C\(_{16}\)H\(_{13}\)BrFNO\(_2\) 349.01; found 350.04 [M+H], 352.02 [M+H+2].

2-Bromo-1-phenyl-3-(p-tolylamino)prop-2-en-1-one (2d)  

Physical state of the compound: Dark brown solid; m.p. 161–163 °C.

Yield: 191 mg, 96%.

Rf value: 0.28 in 20% EtOAc/PET.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta = 2.29\) (s, 3H, -CH\(_3\)), 6.81 (d, \(J = 8\)Hz, 2H, ArH), 7.10 (d, \(J = 8\)Hz, 2H, ArH), 7.22 (db, \(J = 13.6\)Hz, 1H, NH), 7.43 – 7.48 (m, 2H, ArH), 7.49 – 7.55 (m, 1H, ArH), 7.57 – 7.63 (m, 2H, ArH), 7.84 (d, \(J = 13.2\) Hz, 1H, C=CH).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 20.7, 101.5, 116.6, 128.4, 128.5, 130.4, 130.8, 134.1, 136.7, 139.0, 143.9, 188.1.

MS (ESI): \(m/z\) calcd for C\(_{16}\)H\(_{14}\)BrNO 315.02; found 316.04 [M+H], 318.02 [M+H+2].
Figure 1.22: $^1$H NMR spectrum of 2-Bromo-1-(4-fluorophenyl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2c)

Figure 1.23: $^{13}$C NMR spectrum of 2-Bromo-1-(4-fluorophenyl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2c)
Figure 1.24: $^1$H NMR spectrum of 2-Bromo-1-phenyl-3-(p-tolylamino)prop-2-en-1-one (2d)

Physical state of the compound: Dark yellow solid; m.p. 159–161 °C.
Yield : 191 mg, 99%.

R_f value : 0.31 in 10% EtOAc/PET.

^1^H NMR (400 MHz, CDCl_3) : δ = 2.29 (s, 3H, ArCH_3), 3.87 (s, 3H, -OMe), 6.83 (d, J = 8.4Hz, 2H, ArH), 6.95 (d, J = 8.4Hz, 2H, ArH), 6.90 - 7.21 (m, 3H, -NH), 7.60 (d, J = 8.8Hz, 2H, ArH), 7.86 (d, J = 13.2Hz, 1H, C=CH).

^1^3^C NMR (100 MHz, CDCl_3) : δ = 20.7, 55.4, 101.4, 116.5, 130.0, 130.8, 131.0, 131.2, 133.8, 136.9, 142.9, 161.9, 187.3.

MS (ESI) : m/z calcd for C_{17}H_{16}BrNO_2 345.03; found 346.05 [M+H], 348.02 [M+H+2].

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2-Bromo-1-(naphthalen-1-yl)-3-(phenylamino)prop-2-en-l-one (2f)

Physical state of the compound : Pale yellow solid; m.p. 175-177 ºC.

Yield : 173 mg, 90%.

R_f value : 0.4 in 10% EtOAc/PET.

^1^H NMR (400 MHz, CDCl_3) : δ = 6.72 (d, J = 8.0Hz, 2H, ArH), 6.97 (t, J = 7.2Hz, 1H, ArH), 7.15 (t, J = 8.0Hz, 2H, ArH), 7.41 - 7.52 (m, 5H, ArH + NH), 7.71 (d, J = 13.6Hz, 1H, C=CH) 7.83-7.98 (m, 3H, ArH).

^1^3^C NMR (100 MHz, CDCl_3) : δ = 103.2, 116.8, 118.4, 124.5, 125.7, 126.7, 127.2, 128.4, 129.9, 130.3, 130.9, 132.7, 133.8, 136.9, 138.9, 144.4, 188.8.

MS (ESI) : m/z calcd for C_{19}H_{14}BrNO 351.02; found 352.0 [M+H], 354.0 [M+H+2].
**Figure 1.26:** $^1$H NMR spectrum of 2-Bromo-1-(4-methoxyphenyl)-3-(p-tolylamino)prop-2-en-1-one (2e)

**Figure 1.27:** $^{13}$C NMR spectrum of 2-Bromo-1-(4-methoxyphenyl)-3-(p-tolylamino)prop-2-en-1-one (2e)
**Figure 1.28:** $^1$H NMR spectrum of 2-Bromo-1-(naphthalen-1-yl)-3-(phenylamino)prop-2-en-1-one (2f)

**Figure 1.29:** $^1$H NMR spectrum of 2-Bromo-1-(naphthalen-2-yl)-3-(phenylamino)prop-2-en-1-one (2g)

**Physical state of the compound**: Yellow solid; m.p. 168-170 °C.
Yield : 181 mg, 94%.

Rf value : 0.35 in 10% EtOAc/PET.

1H NMR (400 MHz, CDCl3) : \( \delta = 6.41 (d, J = 8.8 \text{ Hz}, 1 \text{H, ArH}), 7.12 (dd, J_1 = 4.0 \text{ Hz}, J_2 = 8.8 \text{ Hz}, 1 \text{H, ArH}), 7.45-7.51 (m, 5 \text{H, ArH}), 7.58 (d, J = 2.0 \text{ Hz}, 1 \text{H, ArH}), 7.63 - 7.67 (m, 1 \text{H}), 7.73 (d, J = 12.8 \text{ Hz}, 1 \text{H, } - \text{NH}), 7.84 - 7.97 (m, 4 \text{H, ArH}). \)

13C NMR (100 MHz, CDCl3) : \( \delta = 105.8, 113.3, 116.1, 116.2, 124.6, 125.4, 125.8, 126.7, 127.3, 128.4, 130.6, 130.8, 131.8, 133.7, 135.4, 136.0, 136.3, 142.0, 188.7. \)

MS (ESI) : m/z calcd for C19H14BrNO 351.02; found 352.0 [M+H], 354.0 [M+H+2].

2-Bromo-3-((4-methoxyphenyl)amino)-1-(naphthalen-1-yl)prop-2-en-1-one (2h)

Physical state of the compound : Yellow solid; m.p. 177-179 °C.

Yield : 171 mg, 91%.

Rf value : 0.32 in 10% EtOAc/PET.

1H NMR (400 MHz, CDCl3) : \( \delta = 3.70 (s, 3 \text{H, } - \text{OMe}), 6.52 - 6.56 (m, 1 \text{H, ArH}), 6.64 - 6.68 (m, 1 \text{H, ArH}), 6.90 (d, J = 13.2 \text{ Hz}, 1 \text{H, } - \text{NH}), 6.69 (s, 1 \text{H, ArH}), 7.05 (d, J = 2.8 \text{ Hz}, 1 \text{H, ArH}), 7.48 - 7.54 (m, 3 \text{H, ArH}), 7.62 (s, 2 \text{H, ArH}), 7.87 - 7.89 (m, 1 \text{H, ArH}), 7.91 - 7.98 (m, 2 \text{H, ArH}). \)

13C NMR (100 MHz, CDCl3) : \( \delta = 55.6, 103.8, 115.1, 118.1, 124.8, 125.4, 125.8, 126.0, 128.3, 130.2, 130.4, 133.8, 133.9, 139.2, 145.6, 156.5, 188.5. \)

MS (ESI) : m/z calcd for C20H16BrNO2 381.03; found 382.03 [M+H], 384.02 [M+H+2].
Figure 1.30. $^1$H NMR spectrum of 2-Bromo-1-(naphthalen-2-yl)-3-(phenylamino)prop-2-en-1-one (2g)

Figure 1.31: $^{13}$C NMR spectrum of 2-Bromo-1-(naphthalen-2-yl)-3-(phenylamino)prop-2-en-1-one (2g)
1.32: $^1H$ NMR spectrum of 2-Bromo-3-((4-methoxyphenyl)amino)-1-(naphthalen-1-yl)prop-2-en-1-one (2h)

Figure 1.33: $^{13}C$ NMR spectrum of 2-Bromo-3-((4-methoxyphenyl)amino)-1-(naphthalen-1-yl)prop-2-en-1-one (2h)

2-Bromo-1-(2,4-dichlorophenyl)-3-(phenylamino)prop-2-en-1-one (2i)
Physical state of the compound: Yellow semi solid.

Yield: 174 mg, 92%.

R_f value: 0.3 in 10% EtOAc/PET.

^1H NMR (400 MHz, CDCl_3): \( \delta = 6.92 \) (d, \( J = 8.00 \) Hz, 2H, ArH), 7.13 (t, \( J = 7.2 \) Hz, 1H, ArH), 7.25 - 7.38 (m,5H, ArH + NH), 7.48 (d, \( J = 2 \) Hz 1H, ArH), 7.63 (d, \( J = 13.2 \) Hz, 1H, C=CH).

^13C NMR (100 MHz, CDCl_3): \( \delta = 101.9, 117.1, 118.6, 125.1, 127.5, 130.0, 130.3, 133.2, 136.4, 137.2, 139.9, 144.1, 185.0 \).

MS (ESI): \( m/z \) calcd for C_{15}H_{10}BrCl_2NO 368.93; found 370.05 [M+H], 371.96 [M+H+2], 373.88 [M+H+4], 375.82 [M+H+6].

2-Bromo-1-(4-chlorophenyl)-3-((2-chlorophenyl)amino)prop-2-en-1-one (2j)

Physical state of the compound: Yellow solid; m.p. 161–163 °C.

Yield: 185 mg, 98%.

R_f value: 0.35 in 20% EtOAc/PET.

^1H NMR (400 MHz, CDCl_3): \( \delta = 6.8 \) (dd, \( J_1 = 2.0Hz, J = 8.0Hz, 1H, ArH), 6.95 \) (t, \( J = 2.0Hz, 1H, ArH), 7.05-7.08 \) (m, 1H, ArH), 7.22 - 7.24 \) (m, 1H, ArH), 7.31 \) (d, \( J = 12.8Hz, 1H, -NH), 7.43 - 7.47 \) (m, 2H, ArH), 7.54 - 7.58 \) (m, 2H, ArH), 7.79 \) (d, \( J = 13.2Hz, 1H, C=CH).\n
^13C NMR (100 MHz, CDCl_3): \( \delta = 102.5, 114.7, 116.0, 117.0 118.5, 124.5, 129.0, 130.2, 131.2, 136.9, 137.7, 139.6, 142.6, 187.2 \).

MS (ESI): \( m/z \) calcd for C_{15}H_{10}BrCl_2NO 368.93; found 370.12 [M+H], 372.00 [M+H+2], 373.88 [M+H+4], 375.86 [M+H+6].
Figure 1.34: $^1$H NMR spectrum of 2-Bromo-1-(2,4-dichlorophenyl)-3-(phenylamino)prop-2-en-1-one (2i)

Figure 1.35: $^{13}$C NMR spectrum of 2-Bromo-1-(2,4-dichlorophenyl)-3-(phenylamino)prop-2-en-1-one (2i)
Figure 1.36: $^1$H NMR spectrum of 2-Bromo-1-(4-chlorophenyl)-3-((2-chlorophenyl)amino)prop-2-en-1-one (2j)

Figure 1.37: $^1$H NMR spectrum of 2-Bromo-1-(4-chlorophenyl)-3-((2-chlorophenyl)amino)prop-2-en-1-one (2j)

2-Bromo-3-((2-fluorophenyl)amino)-1-phenylprop-2-en-1-one (2k)
Physical state of the compound: Dark brown solid; m.p. 157–159 °C.

Yield: 175 mg, 97%.

Rf value: 0.35 in 20% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): \( \delta = 6.90 \text{ (dt, } J_1 = 1.6 \text{Hz, } J_2 = 8.0 \text{Hz, 1H, ArH)}, 6.97 - 7.16 \text{ (m, 3H, ArH)}, 7.35 \text{ (d, br, } J = 13.2 \text{Hz, 1H, -NH}), 7.43-7.48 \text{ (m, 2H, ArH)}, 7.49 - 7.55 \text{ (m, 1H, ArH)}, 7.58 - 7.62 \text{ (m, 2H, ArH)}, 7.86 \text{ (d, } J = 13.2 \text{Hz, 1H, C=CH}).

$^{13}$C NMR (100 MHz, CDCl$_3$): \( \delta = 103.3, 116.1, 116.2, 116.4, 124.3 \text{ (d, } J =7.3 \text{ Hz}), 124.3 \text{ (d, } J = 7.3 \text{Hz}), 125.2 \text{ (d, } J = 3.7 \text{Hz}), 125.2 \text{ (d, } J = 3.7 \text{Hz}), 128.6 \text{ (d, } J = 6.7 \text{Hz)}, 128.6 \text{ (d, } J = 6.7 \text{Hz}), 131.3, 142.0, 142.7, 151.3 \text{ (d, } J = 243 \text{Hz}), 153.7 \text{ (d, } J = 243 \text{Hz}), 188.4.

MS (ESI): \( m/z \) calcd for C$_{15}$H$_{11}$BrFNO 319.00; found 320.05 [M+H], 322.02 [M+H+2].

**2-Bromo-3-((4-fluorophenyl)amino)-1-(p-tolyl)prop-2-en-1-one (2l)**

Physical state of the compound: Pale yellow solid; m.p. 173–174 °C.

Yield: 192 mg, 98%.

Rf value: 0.35 20% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): \( \delta = 2.42 \text{ (s, 3H, -Me)}, 6.87 - 6.92 \text{ (m, 2H, ArH)}, 6.99 - 7.06 \text{ (m, 2H, ArH)}, 7.15 \text{ (db, } J = 13.2 \text{Hz, 1H, -NH}) 7.24 - 7.28 \text{ (m, 2H, ArH)} 7.49 - 7.53 \text{ (m, 2H, ArH)}, 7.80 \text{ (d, } J = 13.2 \text{Hz, 1H, C=CH}).

$^{13}$C NMR (100 MHz, CDCl$_3$): \( \delta = 21.7, 102.1, 116.7 \text{ (d, } J = 23 \text{Hz)}, 116.9 \text{ (d, } J = 23 \text{Hz)}, 118.3 \text{ (d, } J = 8.0 \text{Hz)}, 118.4 \text{ (d, } J = 8.0 \text{Hz)}, 128.8 \text{ (d, } J = 44 \text{Hz}), 129.3 \text{ (d, } J = 44 \text{Hz}), 135.8 \text{ (d, } J = 3 \text{Hz}), 135.8 \text{ (d, } J = 3 \text{Hz}), 136.0, 141.7, 143.7, 158.4 \text{ (d, } J = 242 \text{Hz}), 160.8 \text{ (d, } J = 242 \text{Hz}), 188.3.

MS (ESI): \( m/z \) calcd for C$_{16}$H$_{13}$BrFNO 333.01; found 334.02 [M+H], 336.02 [M+H+2].
Figure 1.38: $^1$H NMR spectrum of 2-Bromo-3-((2-fluorophenyl)amino)-1-phenylprop-2-en-1-one (2k)

Figure 1.39: $^1$H NMR spectrum of 2-Bromo-3-((2-fluorophenyl)amino)-1-phenylprop-2-en-1-one (2k)
Figure 1.40: $^1$H NMR spectrum of 2-Bromo-3-((4-fluorophenyl)amino)-1-(p-tolyl)prop-2-en-1-one (2l)

$^{13}$C NMR spectrum of 2-Bromo-3-((4-fluorophenyl)amino)-1-(p-tolyl)prop-2-en-1-one (2l)

2-Bromo-3-((4-chlorophenyl)amino)-1-(4-fluorophenyl)prop-2-en-1-one (2m)

Physical state of the compound: Pale yellow solid; m.p. 168-170 °C.
Yield: 182 mg, 95%.

Rf value: 0.28 in 10% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$) : $\delta = 6.87$ (d, $J = 8.8$ Hz, 2H, ArH), 7.11 - 7.32 (m, 5H, ArH + NH), 7.60 - 7.66 (m, 2H, ArH), 7.79 (d, $J = 12.8$ Hz 1H, C=CH).

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta = 102.0, 115.5$ (d, $J = 22$ Hz), 115.7 (d, $J = 22$ Hz), 117.7(d, $J = 21$ Hz), 117.9 (d, $J = 21$ Hz), 129.5(d, J = 54Hz), 130.0 (d, $J = 54$ Hz), 130.8 (d, $J = 9$ Hz), 130.9 (d, $J = 9$ Hz), 134.7,137.7, 142.6, 163.2 (d, $J = 251$ Hz), 165.7 (d, $J = 251$ Hz), 186.9.

MS (ESI) : m/z calcd for C$_{15}$H$_{10}$BrClFNO 352.96; found 354.17 [M+H], 356.00 [M+H+2], 357.90 [M+H+4].

2-Bromo-3-((4-methoxyphenyl)amino)-1-(thiophen-2-yl)prop-2-en-1-one (2n)

Physical state of the compound: Dark brown semi solid.

Yield: 185 mg, 95%.

Rf value: 0.3 in 10% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$) : $\delta = 3.79$ (s, 3H, -OMe), 6.85-6.91 (m, 2H, ArH), 6.95 - 7.01 (m, 2H, ArH), 7.09 - 7.13 (m, 1H, ArH), 7.21 (db, $J = 13.2$ Hz, 1H, -NH), 7.56 - 7.62 (m, 2H, ArH), 8.19 (d, $J = 13.2$ Hz, 1H, C=CH).

$^{13}$C NMR (100 MHz, CDCl$_3$) : $\delta = 55.8, 99.7, 115.3, 118.6, 127.4, 131.3, 131.4, 132.9, 143.1, 149.0, 156.9, 179.1.$

MS (ESI) : m/z calcd for C$_{14}$H$_{12}$BrNO$_2$S 336.97; found 338.04 [M+H], 340.02 [M+H+2].
Figure 1.42: $^1$H NMR spectrum of 2-Bromo-3-((4-chlorophenyl)amino)-1-(4-fluorophenyl)prop-2-en-1-one (2m)

Figure 1.43: $^{13}$C NMR spectrum of 2-Bromo-3-((4-chlorophenyl)amino)-1-(4-fluorophenyl)prop-2-en-1-one (2m)
Figure 1.44: $^1$H NMR spectrum of 2-Bromo-3-(4-methoxyphenyl)amino)-1-(thiophen-2-yl)prop-2-en-1-one (2n)

Figure 1.45: $^1$H NMR spectrum of 2-Bromo-3-(4-methoxyphenyl)amino)-1-(thiophen-2-yl)prop-2-en-1-one (2n)

2-Bromo-3-(2-chlorophenyl)amino)-1-(thiophen-2-yl)prop-2-en-1-one (2o)
**Physical state of the compound**: Dark brown semi solid.

**Yield**: 180 mg, 93%.

**R_f** value: 0.3 in 10% EtOAc/PET.

**1H NMR (400 MHz, CDCl_3)**: δ = 6.9 - 7.04 (m, 1H, ArH), 7.05 - 7.09 (m, 1H, ArH), 7.13 - 7.17 (m, 1H, ArH), 7.23 - 7.28 (m, 1H, ArH), 7.39 - 7.44 (m, 1H ArH), 7.60 - 7.64 (m, 1H, ArH), 7.66 - 7.70 (m, 1H, ArH), 7.77 (db, J = 12.0Hz, 1H, -NH) 8.27 (d, J = 13.2Hz, 1H, C=CH).

**13C NMR (100 MHz, CDCl_3)**: δ = 102.2, 115.1, 116.2, 127.6, 127.6, 128.4, 130.2, 131.4, 131.8, 132.6, 137.9, 139.2, 180.7.

**MS (ESI)**: m/z calcd for C_{13}H_{9}BrClNOS 340.92, found 342.0 [M+H], 344.0 [M+H+2], 345.9 [M+H+4].

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**2-Bromo-1-(furan-2-yl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2p)**

**Physical state of the compound**: Dark brown solid; m.p. 144–146 °C.

**Yield**: 194 mg, 98%.

**R_f** value: 0.3 in 30% EtOAc/PET.

**1H NMR (400 MHz, CDCl_3)**: δ = 3.79 (s, 3H, -OMe), 6.53 (dd, J_1 = 2Hz, J = 3.6Hz, 1H, ArH), 6.88 - 6.92 (m,2H, ArH) 7.01 - 7.05 (m, 2H, ArH), 7.2 - 7.21 (m, 1H, ArH), 7.30 (d, br, J = 13.2Hz 1H, -NH), 7.56 (d, J = 0.8Hz, 1H, ArH), 8.65 (d, J = 13.6Hz, 1H, C=CH).

**13C NMR (100 MHz, CDCl_3)**: δ = 55.7, 100.1, 112.0, 115.3, 117.4, 118.6, 133.0, 143.4, 144.9, 152.1, 156.9, 173.1.

**MS (ESI)**: m/z calcd for C_{14}H_{12}BrNO_3 321.00, found 322.08 [M+H], 324.02 [M+H+2].
Figure 1.46: $^1$H NMR spectrum of 2-Bromo-3-(2-chlorophenylamino)-1-(thiophen-2-yl)prop-2-en-1-one (2o)

Figure 1.47: $^{13}$C NMR spectrum of 2-Bromo-3-(2-chlorophenylamino)-1-(thiophen-2-yl)prop-2-en-1-one (2o)
Figure 1.48: $^1$H NMR spectrum of 2-Bromo-1-(furan-2-yl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2p)

Figure 1.49: $^{13}$C NMR spectrum of 2-Bromo-1-(furan-2-yl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2p)

2-Chloro-1-phenyl-3-(phenylamino)prop-2-en-1-one (2r)

Physical state of the compound: Pale yellow solid; m.p. 162–164 °C.
Yield: 140 mg, 81%.

Rf value: 0.35 in 20% EtOAc/PET.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta = 6.90 - 6.92\) (m, 2H, ArH), 7.06 - 7.10 (m, 1H, ArH), 7.28 - 7.32 (m, 2H, ArH, -NH), 7.38 – 7.55 (m, 4H, ArH), 7.56 – 7.62 (m, 2H, ArH), 7.87 (d, \(J = 13.60\)Hz, 1H, C=CH).

2-Chloro-1-(4-chlorophenyl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2s)

Physical state of the compound: White solid; m.p. 170–172 °C.

Yield: 129 mg, 77%.

Rf value: 0.3 in 10% EtOAc/PET.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta = 3.78\) (s, 3H, Ar-OCH\(_3\)), 6.84 – 6.91 (m, 4H, ArH), 7.19 - 7.34 (m, 4H, ArH + NH), 7.45 (m, 2H, ArH + C=CH).

\(^13\)C NMR (100 MHz, CDCl\(_3\)) : \(\delta = 55.6, 108.3, 115.1, 118.7, 127.2, 132.2, 136.0, 136.9, 142.8, 157.1, 184.4.

2-Chloro-1-phenyl-3-(p-tolylamino)prop-2-en-1-one (2t)

Physical state of the compound: Pale yellow solid; m.p. 160–162 °C.

Yield: 142 mg, 83%.

Rf value: 0.32 in 20% EtOAc/PET.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta = 2.29\) (s, 3H, Ar-Me), 6.81 (d, \(J = 8.4\)Hz, 2H, ArH), 7.09 - 7.17 (m, 3H, ArH + NH), 7.43 - 7.48 (m, 2H, ArH), 7.49 - 7.55 (m, 1H, ArH), 7.59 - 7.63 (m, 2H, ArH), 7.8 (d, \(J = 13.2\)Hz, 1H, C=CH).
Figure 1.50: $^1$H NMR spectrum of 2-Chloro-1-phenyl-3-(phenylamino)prop-2-en-1-one (2r)

Figure 1.51: $^1$HNMR spectrum of 2-Chloro-1-(4-chlorophenyl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2s)
Figure 1.52: $^{13}C$ NMR spectrum of 2-Chloro-1-(4-chlorophenyl)-3-((4-methoxyphenyl)amino)prop-2-en-1-one (2s)

Figure 1.53: $^1H$ NMR spectrum of 2-Chloro-1-phenyl-3-(p-tolylamino)prop-2-en-1-one (2t)

2-Chloro-1-(2,4-dichlorophenyl)-3-(phenylamino) prop-2-en-1-one (2u)
Physical state of the compound: Pale yellow solid; m.p. 145-147 °C.

Yield: 142 mg, 85%.

Rf value: 0.3 in 20% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.92 (d, $J$ = 7.6 Hz, 2H, ArH), 7.09 - 7.15 (m, 1H, ArH), 7.29 - 7.36 (m, 5H, ArH), 7.47 (d, $J$ = 2.0 Hz 1H, ArH), 7.6 (d, $J$ = 13.2 Hz, 1H, -NH).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 109.2, 116.8, 124.7, 127.2, 130.0, 130.0, 132.3, 136.2, 136.6, 138.8, 141.8, 144.9, 184.8.

MS (ESI): $m/z$ calcd for C$_{15}$H$_{10}$Cl$_3$NO 324.98, found 326.17 [M+H], 328.00 [M+H+2], 329.92 [M+H+4], 331.90 [M+H+6].

2-Chloro-3-((2-fluorophenyl)amino)-1-phenylprop-2-en-1-one (2v)

Physical state of the compound: Yellow solid; m.p. 137–139 °C.

Yield: 137 mg, 80%.

Rf value: 0.3 in 10% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.92 (dt, $J_1$ = 1.6 Hz, $J_2$ = 8 Hz, 1H, ArH), 7.08 - 7.19 (m, 3H, ArH), 7.27 (d, $J$ = 11.2Hz, 1H, -NH), 7.44 - 7.48 (m, 2H, ArH), 7.50 - 7.56 (m, 1H, ArH), 7.62 (dd, $J_1$ = 4.8 Hz, $J_2$ = 6.8 Hz, 2H,ArH), 7.83 (d, $J$ = 13.2Hz, 1H, C=CH).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 111.0, 115.9, 116.2, 116.4, 124.2 (d, $J$ = 7.0 Hz), 124.2 (d, $J$ = 7.0 Hz), 125.2 (d, $J$ = 4.0Hz), 125.2 (d, $J$ = 4.0 Hz), 128.5 (d, $J$ = 8.0 Hz), 128.5 (d, $J$ = 8.0Hz), 131.3, 138.6, 140.3, 151.3 (d, $J$ = 243.0 Hz), 153.7 (d, $J$ = 243.0 Hz), 188.2.

MS (ESI): $m/z$ calcd for C$_{15}$H$_{11}$ClFNO 275.05, found 276.05 [M+H], 278.02 [M+H+2].
Figure 1.54: $^1$H NMR spectrum of 2-Chloro-1-(2,4-dichlorophenyl)-3-(phenylamino) prop-2-en-1-one (2u)

Figure 1.55: $^{13}$C NMR spectrum of 2-Chloro-1-(2,4-dichlorophenyl)-3-(phenylamino) prop-2-en-1-one (2u)
**Figure 1.56:** $^1$H NMR spectrum of 2-Chloro-3-((2-fluorophenyl)amino)-1-phenylprop-2-en-1-one (2v)

**Figure 1.57:** $^1$H NMR spectrum of 2-Chloro-3-((2-fluorophenyl)amino)-1-phenylprop-2-en-1-one (2v)

### 2-Chloro-3-((2-chlorophenyl)amino)-1-(thiophen-2-yl)prop-2-en-1-one (2w)

**Physical state of the compound:** Dark brown semi solid.
Yield: 134 mg, 79%.

Rf value: 0.3 in 10% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 6.95 - 7.02 (m, 1H, ArH), 7.07 (d, $J$ = 7.6 Hz, 1H, ArH), 7.11 - 7.15 (m, 1H, ArH), 7.21 - 7.28 (m, 1H, ArH), 7.35 - 7.39 (m, 1H ArH), 7.59 - 7.68 (m, 2H, ArH + NH), 7.77 (dd, $J_1$ = 0.8 Hz, $J_2$ = 4 Hz, 1H, ArH), 8.21 (d, $J$ = 13.2 Hz, 1H, C=C=CH).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 109.8, 114.9, 123.9, 124.3, 127.6, 128.3, 130.1, 132.2, 132.4, 135.9, 137.4, 142.2, 181.4.

MS (ESI): $m/z$ calcd for C$_{13}$H$_9$Cl$_2$NOS 296.97, found 298.0 [M+H], 299.9 [M+H+2], 301.9 [M+H+4].

2-Bromo-3-((2,6-dimethylphenyl)amino)-1-(furan-2-yl)prop-2-en-1-one (2x)

Physical state of the compound: Dark brown semi solid.

Yield: 149 mg, 75%.

Rf value: 0.3 in 10% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 2.38 (s, 6H, -Me), 6.51 - 6.53 (m, 1H, ArH), 6.87 (d, $J$ = 13.2 Hz 1H, -NH), 7.11 - 7.20 (m, 4H, ArH), 7.50(d, 1H, $J$ = 0.8 Hz, ArH), 8.31 (d, $J$ = 13.2 Hz, 1H, C=C=CH).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 18.6, 99.0, 111.9, 120.2, 126.1, 128.9, 129.1, 131.6, 131.8, 138.6, 144.7, 152.5, 180.1.

MS (ESI): $m/z$ calcd for C$_{15}$H$_{14}$BrNO$_2$ 296.97, found 298.02 [M+H], 300.0 [M+H+2].
Figure 1.58: $^1$H NMR spectrum of 2-Chloro-3-((2-chlorophenyl) amino)-1-(thiophen-2-yl)prop-2-en-1-one (2w)

Figure 1.59: $^{13}$C NMR spectrum of 2-Chloro-3-((2-chlorophenyl) amino)-1-(thiophen-2-yl)prop-2-en-1-one (2w)
Figure 1.60: $^1$H NMR spectrum of 2-Bromo-3-((2,6-dimethylphenyl)amino)-1-(furan-2-yl)prop-2-en-1-one (2x)

Figure 1.61: $^{13}$C NMR spectrum of 2-Bromo-3-((2,6-dimethylphenyl)amino)-1-(furan-2-yl)prop-2-en-1-one (2x)
3-Chloro-4H-chromen-4-one (3a)

Physical state of the compound: White solid; m.p. 112-114 °C.
Yield: 120 mg, 86%.
Rf value: 0.35 in 20% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.43 - 7.5 (m, 2H, ArH), 7.71 (m, 1H, ArH), 8.15 (s, 1H, C=CH), 8.28 (dd, $J_1$ = 1.6Hz, $J_2$ = 1.6Hz, 1H, ArH).

3-Bromo-4H-chromen-4-one (3b)

Physical state of the compound: White solid; m.p. 176-178 °C.
Yield: 157 mg, 92%.
Rf value: 0.35 in 20% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.41 - 7.47 (m, 2H, ArH), 7.66 - 7.73 (m, 1H, ArH), 8.21 - 8.26 (m, 2H, ArH).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 110.6, 118.1, 123.0, 125.8, 126.3, 134.1, 153.7, 155.9, 172.2.

3-Bromo-6,8-dichloro-4H-chromen-4-one (3c)

Physical state of the compound: White solid; m.p. 176-178 °C.
Yield: 158 mg, 94%.
Rf value: 0.35 in 20% EtOAc/PET.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.75 (d, $J$ = 2.4Hz, 1H, ArH), 8.12 (d, $J$ = 2.4Hz, 1H, ArH), 8.3 (s, 1H, ArH).

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Figure 1.62: $^1$H NMR spectrum of 3-Chloro-4H-chromen-4-one (3a)

Figure 1.63: $^1$H NMR spectrum of 3-Bromo-4H-chromen-4-one (3b)
Figure 1.64: $^{13}$C NMR spectrum of 3-Bromo-4H-chromen-4-one (3b)

Figure 1.65: $^1$H NMR spectrum of 3-Bromo-6,8-dichloro-4H-chromen-4-one (3c)
3-Iodo-4H-chromen-4-one (3d)\textsuperscript{45}

Physical state of the compound: White solid; m.p. 95-97 °C.
Yield: 184 mg, 89%.
Rf value: 0.35 in 20% EtOAc/PET.
$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.41 - 7.47$ (m, 2H, ArH), 7.66 - 7.73 (m, 1H, ArH), 8.21 (dd, $J_1 = 1.2$ Hz, $J_2 = 6.8$ Hz, 1H, ArH), 8.28 (s, 1H, CH).

\textbf{Figure 1.66:} $^1$H NMR of spectrum of 3-Iodo-4H-chromen-4-one (3d)