Chapter 4

Tandem Reactions of 2-Aminopyridinium Salts and 2-Bromoaldehyde Derivatives: Access to Chromone-fused Imidazo[1,2-*a*]pyridines

4.1 INTRODUCTION

Heterocyclic compounds comprises almost half of the basket of naturally occurring molecules, in which the nitrogen and oxygen containing scaffolds are part of the largest of the classical divisions of organic chemistry. The enormous importance of these molecules is encountered in the fields of pharmaceutics, agro-chemistry and material sciences. The mainstream of pharmaceutical products that mimic natural products with biological activity are *N*- or *O*-heterocycles (**Figure 4.1**).

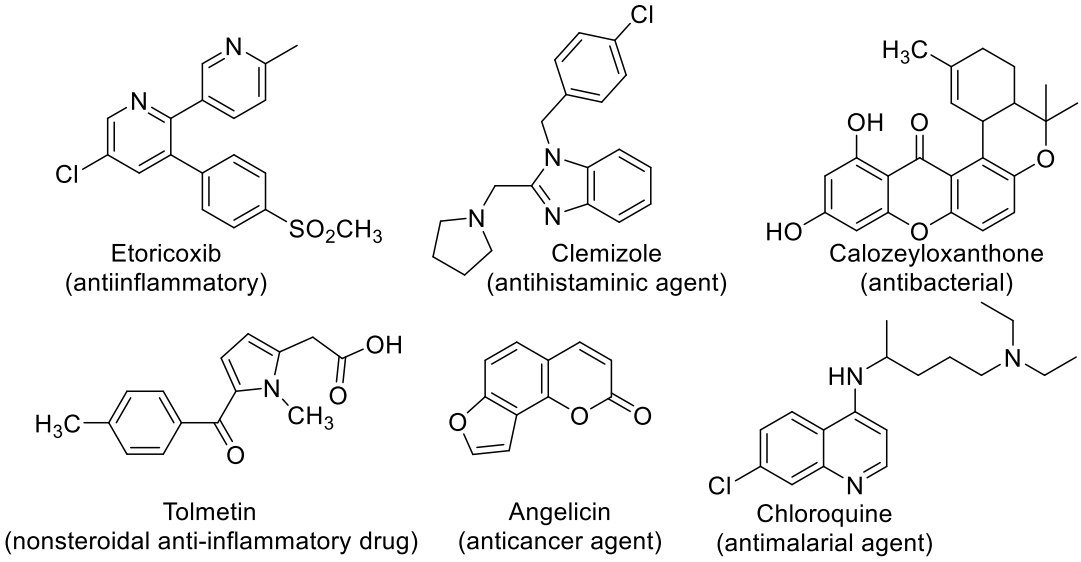


Figure 4.1 Some of the medicinally important heterocyclic compounds

Moreover, the annulated aromatic systems containing two or more heterocycles are frequently encountered in numerous natural and non-natural drug like products.[1-3] The unique architecture of these molecules benefits in their fundamental applications in pharmaceutical fields and development of organic materials. The amalgamation of nitrogen and oxygen containing heterocyclic systems have gained considerable attention in organic synthesis since the resulting hybrid molecules have found broad spectrum of physiological and biological activities, such as anti-allergic, antibacterial, and anti-inflammatory properties.[4-6] The fused heterocyclic systems also serve as innovative starting materials as well as highly fluorescent materials.

In particular, chromone/pyranone represent a class of oxygen-containing heterocyclic molecule abundantly occurring in natural plant alkaloids such as flavones and flavonoids. The molecule is endowed with wide range of biological properties, including anti-inflammatory, antifungal,

antimicrobial, antiallergenic, antitubulin, antiviral, anti-hypertensive, and antitumor activities, as well as the capacity to inhibit several enzymes involved in a wide range of disease states (**Figure 4.2**).[7-10]

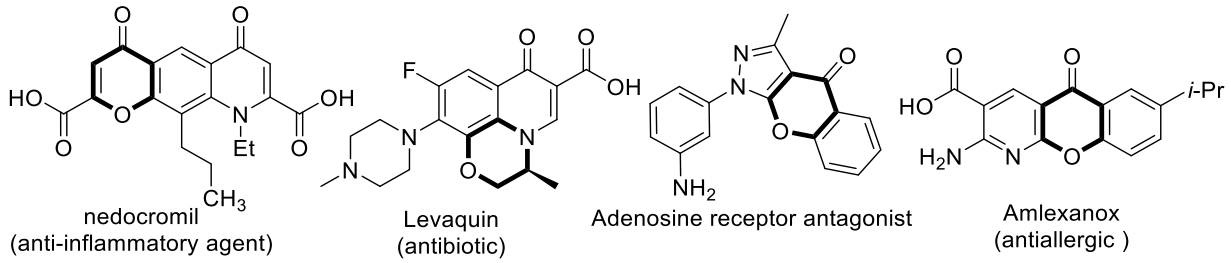
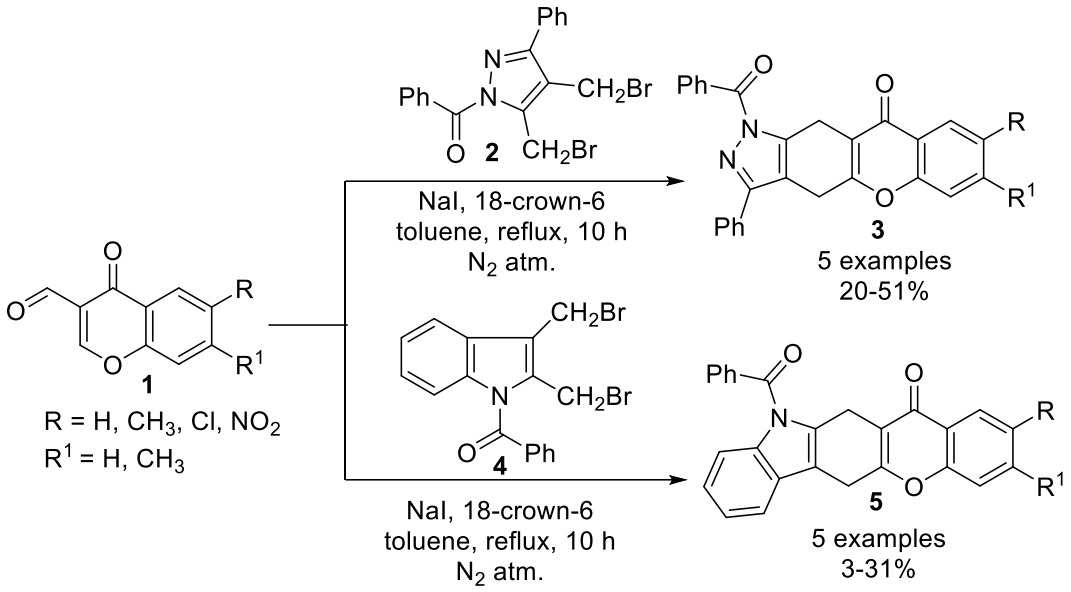


Figure 4.2 Representative examples of biologically important fused nitrogen and oxygen-containing heterocyclic scaffolds

In light of their applications, the preparation of functionalized chromones has received considerable synthetic attention.[11-13] Recently, the synthesis of chromeno-fused heterocyclic derivatives,[14] concisely, *N*-heterocyclic derivatives has evolved as a fascinating area of research for synthetic chemist due to their wide applications in the field of pharmaceuticals.

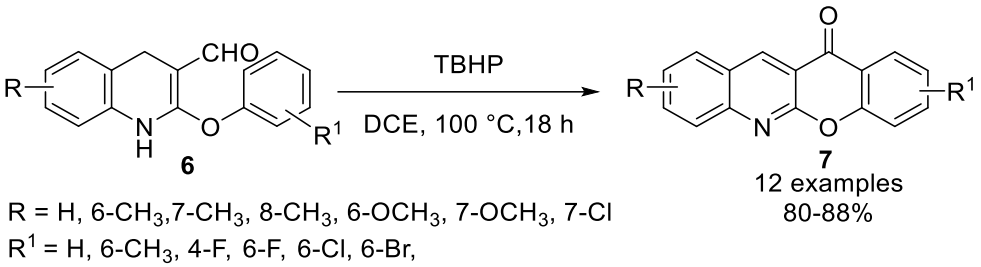
4.1.1 Synthesis of Chromone-fused *N*-Heterocyclic Compounds

Tsoleridis and co-workers reported the synthesis of chromeno-fused carbazoles (**5**) and pyrazoles (**3**) from the Diels-Alder cycloaddition reaction of 3-formylchromones (**1**) with *o*-quinodimethanes (*o*-QDMs) of indole (**4**) and pyrazole (**2**) respectively. The reactive (*o*-QDMs) of indole and pyrazole were prepared *in situ* through reaction of sodium iodide to the appropriate dibromo-derivatives indole and pyrazole. The reaction proceeded through the *in situ* deformylation of chromenone Diels–Alder adducts (**Scheme 4.1**).[15]



Scheme 4.1 Synthesis of chromeno-fused carbazoles and pyrazoles *via* Diels-Alder reaction

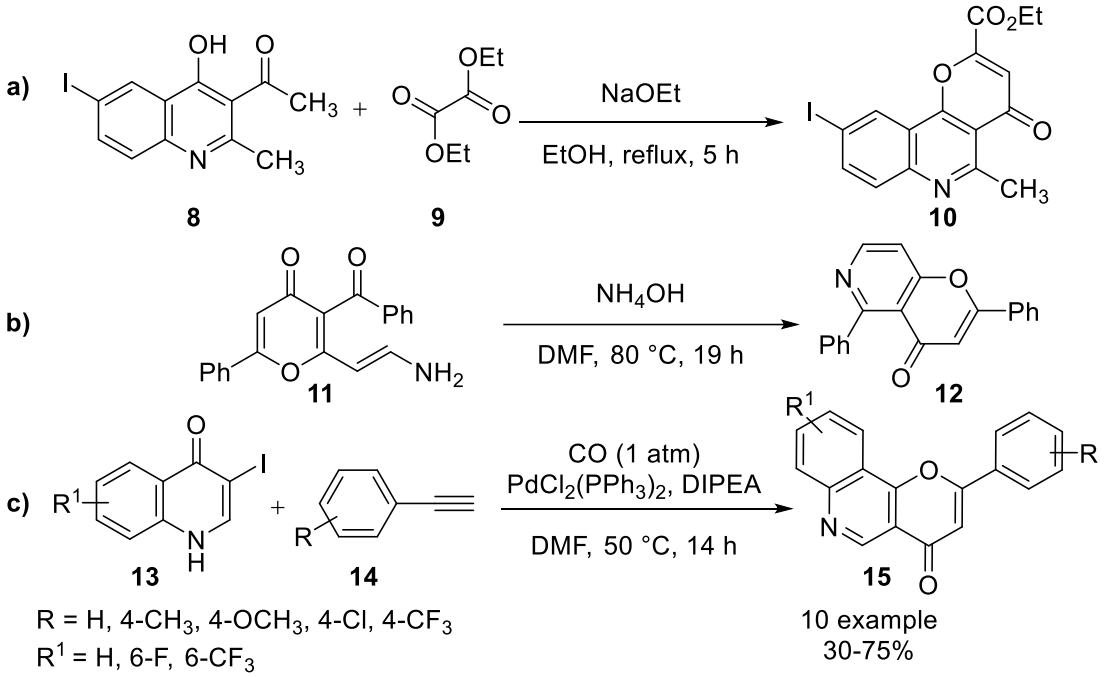
Singh *et al.* synthesized chromone-fused quinolines (**7**) using TBHP-promoted intramolecular cross-dehydrogenative coupling reaction of aldehydic C-H bond with arene C-H bond of 2-phenoloxyquinolinyl-3-carboxaldehydes (**6**). The reaction progressed through TBHP-mediated radical cyclization reaction involving single electron transfer (SET) process. The methodology was extended to synthesize chromone-fused pyridine and pyrazole (**Scheme 4.2**).[16]



Scheme 4.2 Synthesis of chomone-fused quinoline derivatives.

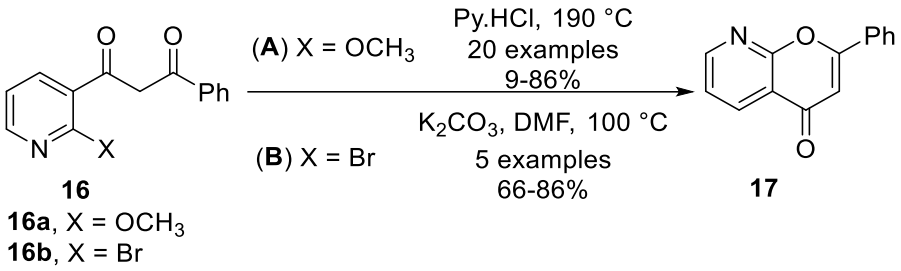
Ghorab and co-workers attempted the synthesis of medicinally important frameworks *i.e.* 6-aza-chromones by the condensation reaction of 3-acetyl-quinolinone (**8**) with diethyl oxalate (**9**) (**Scheme 4.3a**). The synthesis of **10** was destined from the multistep synthetic pathway starting from benzoxazinone as starting material in the quest to synthesize antimicrobial agents based on quinoline scaffolds.[17] Stanovnik *et al.* reported the condensation of 3-carbonyl-2-(2-

(dimethylamino) vinyl)-4*H*-pyran-4-one (**11**) with ammonium acetate to prepare 6-aza-chromone derivatives **12** (**Scheme 4.3b**).[18] Sheng and Hu group developed a new method to access 6-aza-chromones by employing palladium-catalyzed cascade reactions. The palladium-catalyzed cascade carbonylation-Sonogashira-cyclization reaction of 3-iodo-4-(1*H*)-quinolone (**13**) and terminal acetylenes (**14**) led to the formation of aza-chomones **15** (**Scheme 4.3c**).[19]



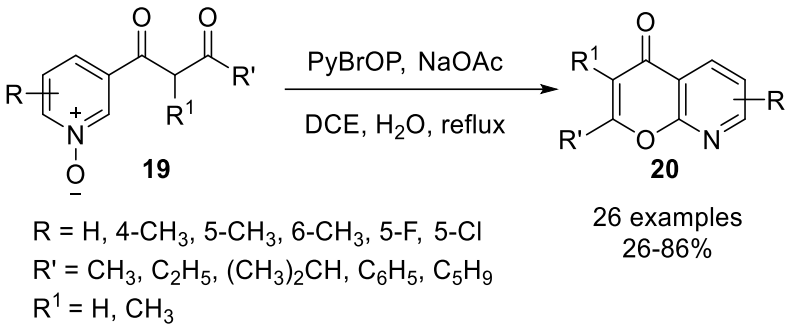
Scheme 4.3 Different synthetic methods to access 6-aza-chromones

C. Hansen *et al*. reported a nucleophilic aromatic substitution reactions (S_NAr) of 2-methoxy substituted pyridines (**17a**) in the presence of pyridinium hydrochloride under very high temperature for synthesis of 8-aza-chromones (**18**) (**Scheme 4.4A**).[20] Fu and co-workers also accessed 8-aza-chromones derivatives (**18**) through base-mediated, transition-metal-free intramolecular Ullmann-type *O*-arylation reaction of 1-(2-halopyridinyl)-propane-1,3-diones (**17b**). The method was found to be inexpensive and environmentally benign to synthesize aza-chromone derivatives (**Scheme 4.4B**).[21]



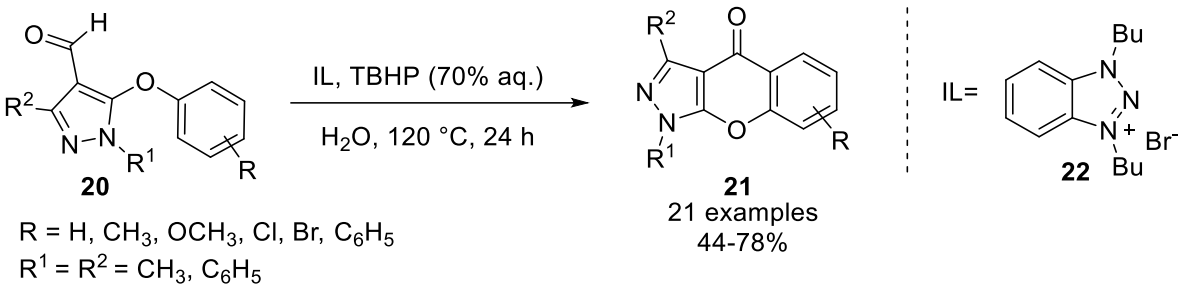
Scheme 4.4 Synthesis of 8-aza-chromones derivatives

Wang and Yu group synthesized the 8-aza-chromones derivatives (**19**) using C-H activation of C-3 functionalized pyridine *N*-oxide (**18**) which in turn was obtained from the Claisen condensation of methyl nicotinate and corresponding ketones followed by oxidation (**Scheme 4.5**). The key step in the synthesis *i.e.* intramolecular O-arylation reaction was realized by nucleophilic attack of enolates to C2 of *N*-oxides under PyBrOP as coupling partner or Ac_2O activation conditions.[22]



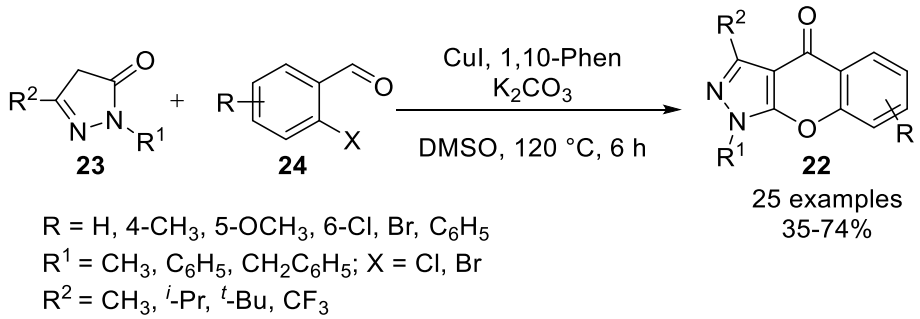
Scheme 4.5 Synthesis of 8-aza-chromones derivatives *via* C-H activation

Liu *et al.* disclosed TBHP-mediated intramolecular annulation of 5-(aryloxy)-1*H*-pyrazole-4-carbaldehydes (**20**) to chromeno[2,3-*c*]pyrazol-4(1*H*)-ones (**21**) *via* oxidative C-H coupling reaction of carbonyl proton and C(sp^2)-H protons in the presence of benzotriazole based ionic liquid (**22**) (**Scheme 4.6**). The reaction was believed to follow single electron transfer (SET) mechanism promoted by ionic liquid (**22**) and TBHP. The advantages of the protocol were aqueous reaction medium and the recyclability and reusability of the promoter up to 5 cycles without any loss in the efficiency.[23]



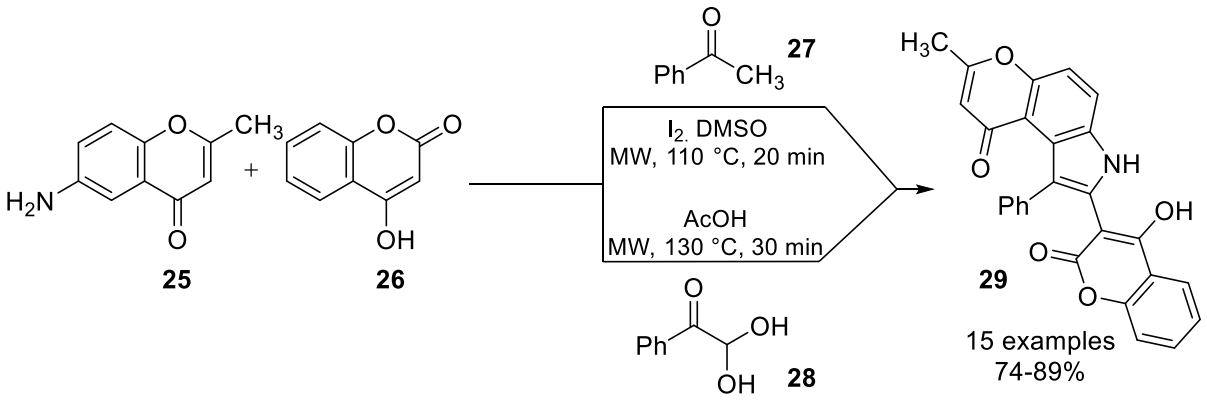
Scheme 4.6 TBHP-mediated synthesis of chromeno[2,3-*c*]pyrazol-4(1*H*)-ones

Suresh and co-workers described intermolecular copper-catalyzed tandem reaction between 2,4-dihydro-3*H*-pyrazol-3-ones (**23**) and *ortho*-haloarylcarboxaldehydes (**24**) to furnish the corresponding chromone-fused pyrazoles (**22**). The reaction proceeded through copper-catalyzed *O*-arylation followed by cross-dehydrogenative coupling (CDC) of acyl proton with C(sp^2)-H protons of pyazole skeleton. The methodology was utilized to synthesize A2-subtype selective adenosine receptor antagonist in only two steps (**Scheme 4.7**).[24]



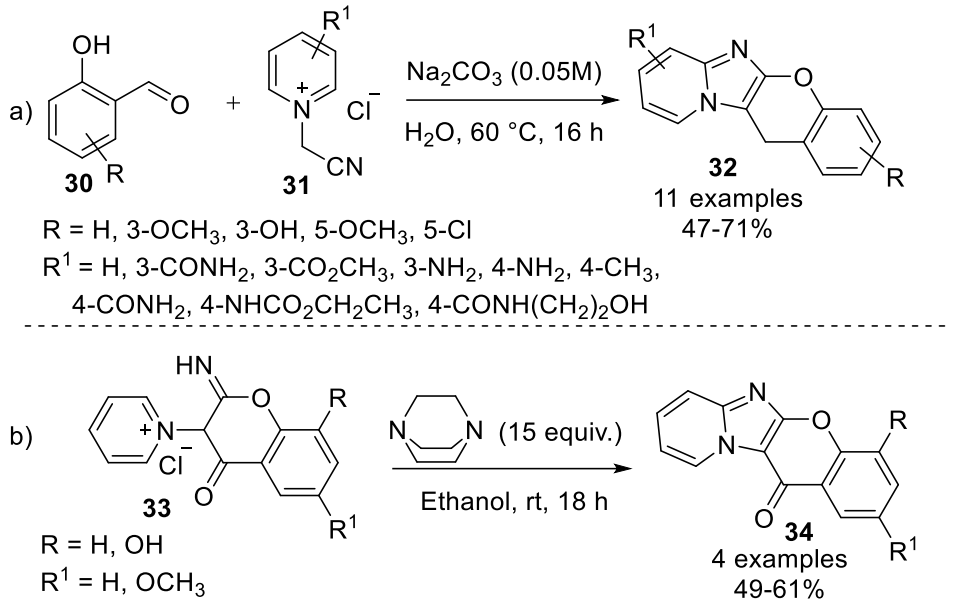
Scheme 4.7 Copper-catalyzed tandem synthesis of chromone-fused pyrazoles

Choudhury and co-workers disclosed a metal-free, multicomponent reaction approach for construction of chromone-fused pyrrole derivatives (**29**). The condensation reaction of phenylglyoxal monohydrates (**28**), 4-hydroxycoumarins (**26**) and 6-aminochromone/7-aminochromones (**25**) under acidic condition yielded complex examples of chromone-fused pyrrole derivatives. They also attempted iodine/DMSO-mediated condensation reaction of acetophenone (**27**), 4-hydroxycoumarins (**26**) and 6-aminochromone/7-aminochromones (**25**) for synthesis of chromone-fused pyrrole derivatives. The I_2/DMSO system helped for *in situ* generation of arylglyoxal from acetophenone (**Scheme 4.8**).[25]



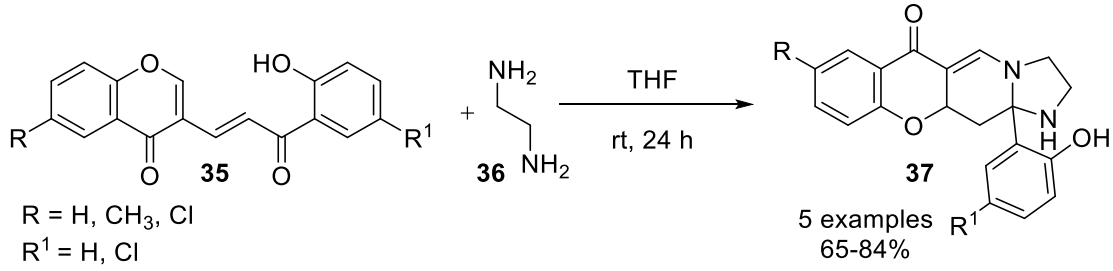
Scheme 4.8 Multicomponent reaction for synthesis of chromone-fused pyrroles

In light of potential biological and functional properties associated with chromenes and imidazo-fused heterocyclic moieties, it is reasonable to prospect that the hybrid of these two privileged structures might be endowed with potent and unique biological activities. Thus synthesis of a heterocyclic system incorporating these 'privileged' fragment is the subject of considerable interest. For examples, Voskressensky *et al.* have synthesized chromeno-annulated imidazo-pyrrolopyridines and imidazocarboline derivatives by base-promoted domino reaction of *o*-hydroxy aryl aldehydes with azaindole-6-cyanomethyl chloride and N^2-(cyanomethyl)-*β*-carbolinium bromide, respectively.[26-27] They also achieved imidazo[2,1-*a*]isoquinolines-fused chromene derivatives by the base-catalyzed reaction of *N*-cyanomethyl-isoquinolinium salts with *o*-hydroxy aryl aldehydes in a DMF/water mixture.[28-29] Proenca and Costa have synthesized chromeno-annulated imidazo[1,2-*a*]pyridines (**32**) by a domino one-pot reaction of 2-(cyanomethyl)-pyridinium chlorides (**31**) and salicylaldehydes (**30**) in aqueous sodium carbonate solution (**Scheme 4.9a**).[30] Same group also reported the synthesis of chromono-fused imidazo[1,2-*a*]pyridines (**34**) by base mediated intramolecular cyclisation of 1-(2-imino-4-oxo-3,4,7,8-tetrahydro-2*H*-chromen-3-yl)pyridin-1-ium chloride (**33**) (**Scheme 4.9b**).[31]



Scheme 4.9 Synthesis of chromene and chromone-fused imidazo[1,2-*a*]pyridine

Bennamane and Silva group synthesized chromeno-imidazopyridinone derivatives (**37**) utilizing a one-pot and catalyst-free tandem reaction of 3-[(2-hydroxyphenyl)-3-oxoprop-1-en-1-yl]chromones (**35**) and ethane-1,2-diamine (**36**) (**Scheme 4.10**). The mechanism of the reaction involved a tandem aza-Michael addition reaction followed by chromone-to-chromanone rearrangement and lastly, heterocyclization sequence, to lead chromeno-imidazopyridinone polyheterocycles. The room temperature and catalyst-free conditions make the approach appealing to design complex poly-cyclic molecules.[32]

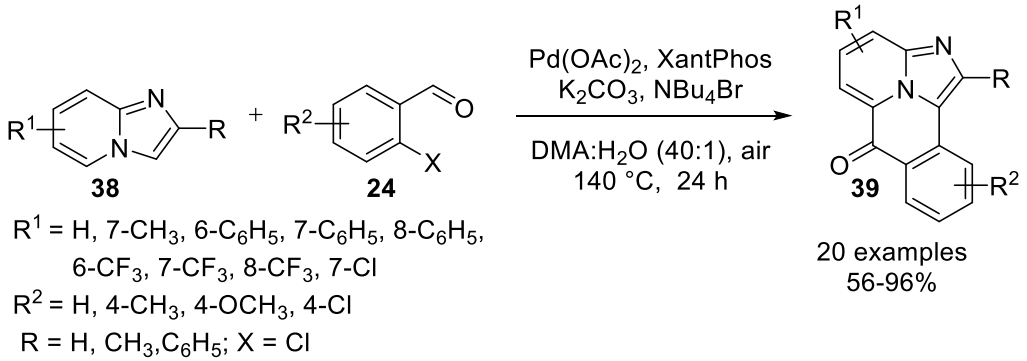


Scheme 4.10 Catalyst-free synthesis of chromeno-fused imidazopyridinones

4.1.2 Palladium-catalyzed Tandem Reactions

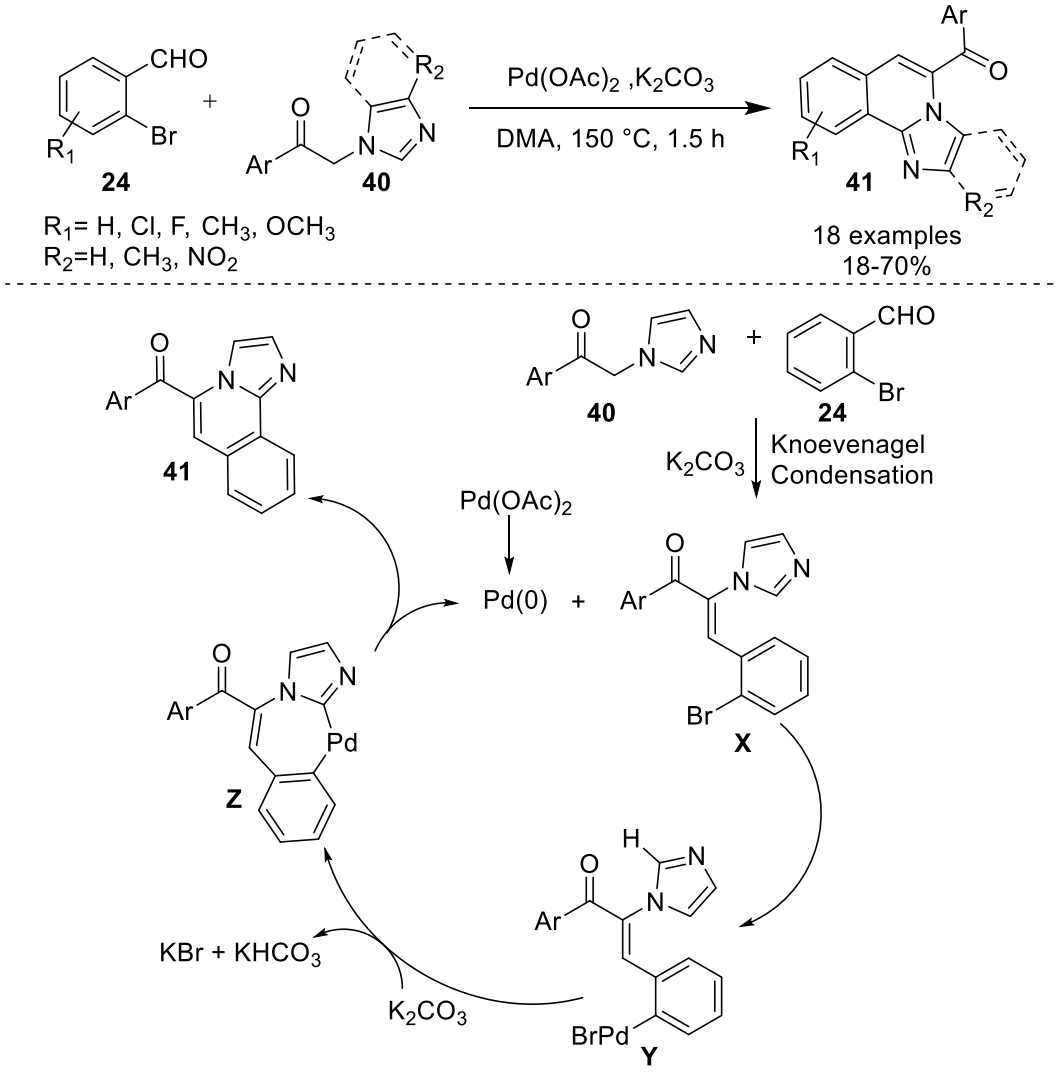
The domino processes also known as cascade or tandem reactions that involve simultaneous formation of multiple new C-C/C-heteroatom bond and generate high levels of diversity and

complexity under the same reaction conditions have become very attractive and highly desirable in organic synthesis.[33-35] These methods reduce generation of chemical waste and reaction time. Transition metal-catalyzed tandem reactions and in particular, palladium-catalyzed domino transformations are an elegant approach to synthesize complex molecular scaffolds.[36-37] For instance, Chang and Wu described the construction of polycyclic 6*H*-benzo[*b*]-imidazo[5,1,2-*de*]quinolizin-6-ones *via* Pd-catalyzed dehydrogenative annulation reaction of imidazo[1,2-*a*]pyridines with 2-chlorobenzaldehydes in presence of air as oxidant. The palladium-catalyzed tandem intermolecular cyclization reaction proceeded through C-H arylation and oxidative acylation (**Scheme 4.11**).[38]



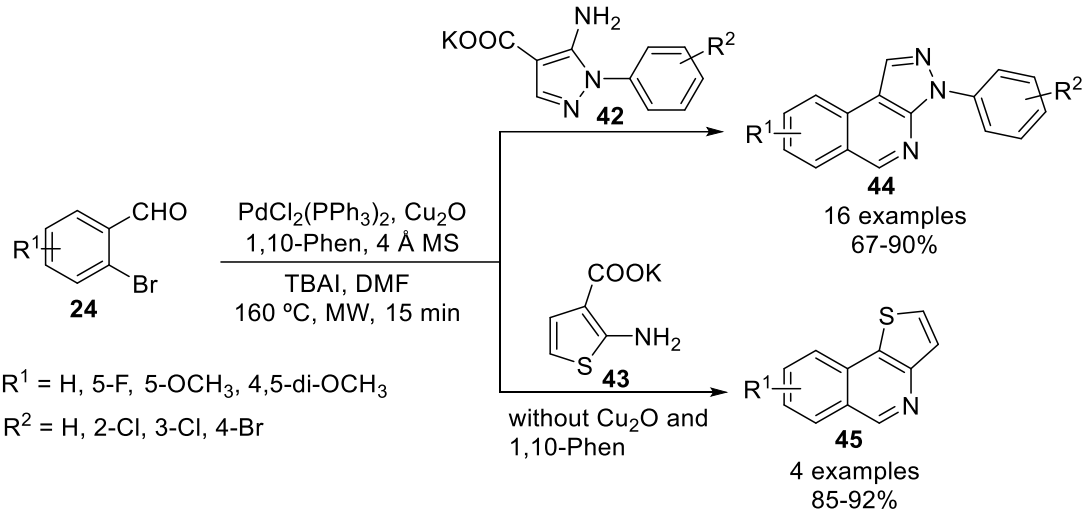
Scheme 4.11 Palladium-catalyzed tandem synthesis of 6*H*-benzo[*b*]-imidazo[5,1,2-*de*]quinolizin-6-ones

Our group also developed a palladium-catalyzed cascade synthesis of aroyl-substituted imidazo-/benzimidazofused isoquinolines (**41**) from reaction of 2-bromobenzaldehyde (**24**) and 2-(1*H*-imidazol-1-yl)-1-phenylethan-1-ones (**40**) (**Scheme 4.12**). The cascade reaction proceeded *via* initial Knoevenagal condensation of 2-(1*H*-imidazol-1-yl/benzimidazolyl-1-yl)-1-arylethanones (**40**) and 2-bromobenzaldehyde (**24**) to form intermediate X, which underwent palladium catalyzed intramolecular C−H activation pathway to afford **41**.[39]



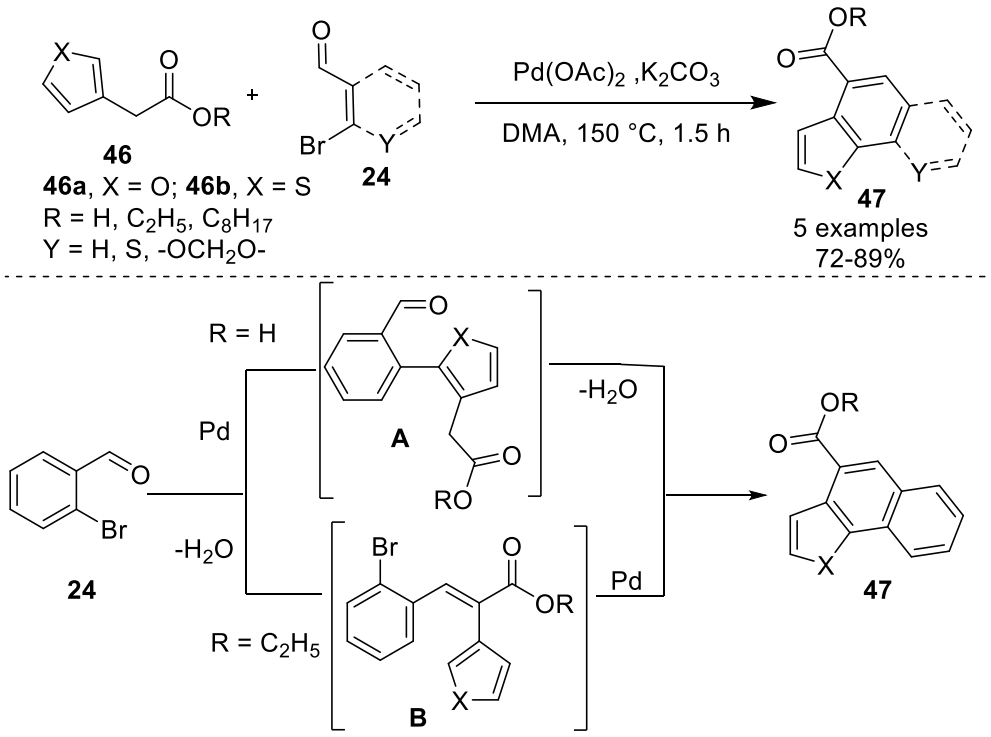
Scheme 4.12 Palladium-catalyzed cascade approach for synthesis of aza-fused isoquinolines

Batra *et al.* described the construction of 3*H*-pyrazolo[3,4-*c*]isoquinolines (**44**) *via* one-pot tandem reaction of 2-bromo benzaldehydes (**24**) with potassium 5-amino-1-aryl-1*H*-pyrazole-4-carboxylate (**42**) under Pd-Cu co-catalyst system. Additionally, they have also synthesized thieno[3,4-*c*]isoquinolines (**45**) using potassium 2-aminothiophene-3-carboxylate (**43**) through Pd(II)-catalyst. The reaction followed Pd-catalyzed tandem condensation and decarboxylative C-H arylation process to achieve thieno/pyrazolo[3,4-*c*]isoquinoline derivatives (**44** & **45**) (**Scheme 4.13**).[40]



Scheme 4.13 Palladium-catalyzed tandem synthesis of 3*H*-pyrazolo[3,4-*c*]isoquinolines

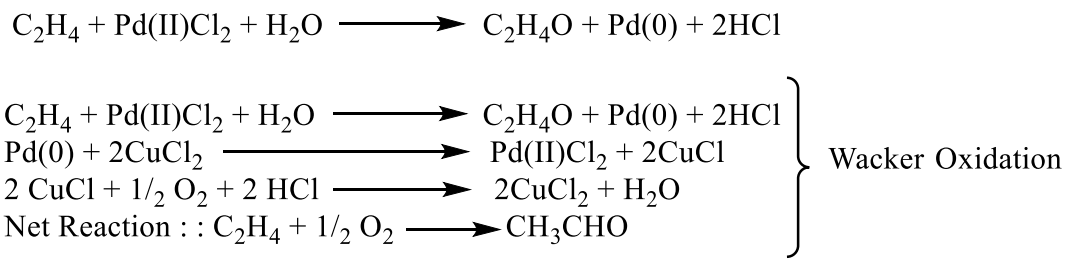
Pasini *et al.* reported an active protocol that included synthesis of thiophene and furan-based π-extended organic materials through one-pot cross-Aldol reaction followed by palladium-catalyzed direct heteroarylation reaction approach. The annulation of alkyl-2-(thiophen-3-yl)acetate (**46b**) or alkyl-2-(furan-3-yl)acetate (**46a**) with 2-halo aryl benzaldehyde (**24**) in presence of $Pd(OAc)_2$ as catalyst and K_2CO_3 as base was performed to obtain naphtha-fused thiophene derivative or naphtha-fused furan derivative (**47**) **(Scheme 4.14)**. The protocol provided an efficient route to access polycyclic extended π-systems with pendant carboxylate or ester groups. The appended carboxylate or ester group in thiophene or furan found to influence the reaction pathway such as the more acidic carboxylic functionality influenced the acidity of the neighboring α-hydrogens thus promoting first direct heteroarylation intermediate (**A**) formation then cross-Aldol cyclisation leading to final product. While the substrates containing less acidic group like ester group followed opposite pathway *i.e.* first cross-Aldol condensation to yield Aldol intermediate (**B**) followed by DHA reaction.[41]



Scheme 4.14 Palladium-catalyzed tandem synthesis of thiophene/furan-based organic molecules

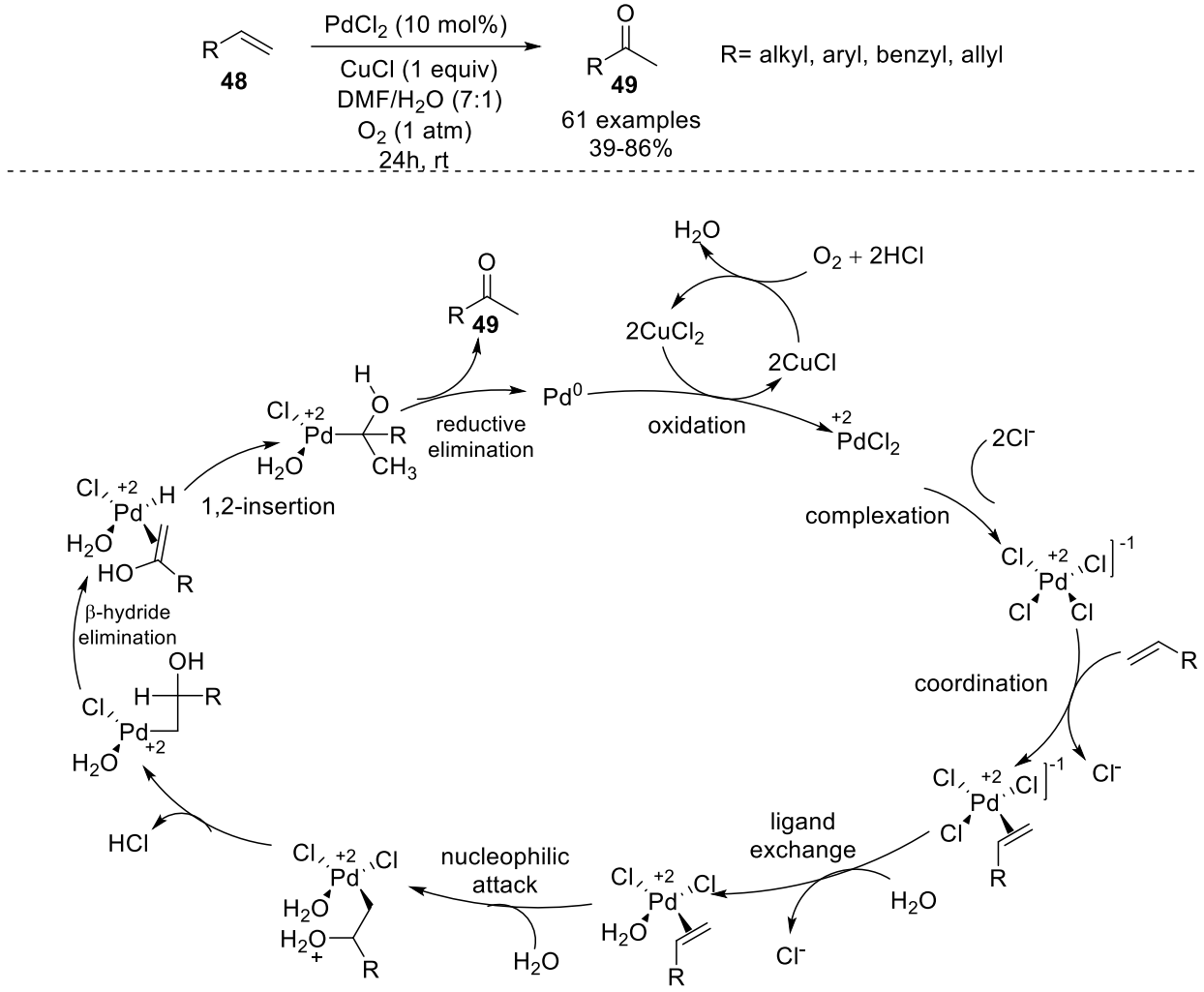
4.1.3 Palladium-catalyzed Wacker Type Oxidation

In 1984, Francis C. Phillips described the oxidation of ethene by palladium(II) chloride solutions, as a test for alkenes since the Pd(II) chloride solutions turned to black in color Pd(0) after the reaction.[42-43] However, the reaction did not come into limelight until 1959, when J. Smidt, an employee of Wacker Chemie revisited the reaction with some modification like adding cupric chloride to regenerate the Pd(II) catalyst. The process was named as Wacker-oxidation process (**Scheme 4.15**).[44]



Scheme 4.15 Reaction sequences involved in Wacker oxidation

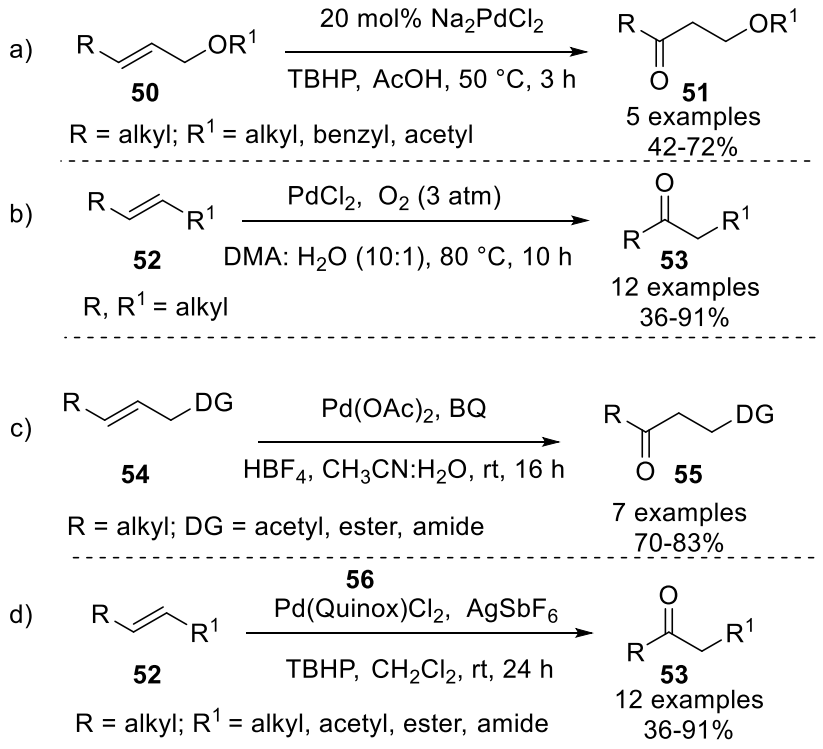
The first synthetic applicability of the method was started by Tsuji by succesfully oxidising terminal olefines (**48**) to ketones (**49**) in good yileds. The reaction was performed using palladium(II) chloride as catalyst and cupric chloride as regerator while molecular oxygen was employed as oxidant (**Scheme 4.16**).[45]



Scheme 4.16 Tsuji-Wacker oxidation and general mechanism involved in process

Eversince, the Tsuji-Waker oxidation which transform terminal olefins to methyl ketones under Pd(II) catalytic system has established as powerful tool in the synthesis of pharmaceuticals, and natural products.[45-47] Interestingly, the application of Tsuji-Waker oxidation for oxidation of internal alkenes has been inadequately reported. This restriction is due to the absence of an efficient methodology to catalyze the oxidation of internal alkenes to carbonyls with regio-control.

Tsuji and co-workers have shown the regioselective oxidation of α,β-unsaturated ester (**50**) to give β-keto ester (**51**) (**Scheme 4.17a**). The authors suggested the high regioselectivity observed was due to coordination of the neighboring oxygen group to the catalyst.[48] Kaneda and co-workers have revealed a direct O_2-coupled Wacker oxidation of internal olefins (**52**) into carbonyl compounds (**53**) using a $PdCl_2$/DMA catalyst system (**Scheme 4.17b**). The group suggested that the copper species used in classical Wacker oxidation process, which promotes the reoxidation of Pd(0) into Pd(II), inhibits the oxidation of internal olefins. Thus exclusion of copper from system would favor oxidation of internal alkenes[49] The oxidation of directing group attached internal alkene (**54**) using palladium acetate as catalyst and benzoquinone as oxidant was suggested by Grubbs and co-workers (**Scheme 4.17c**).[50] Cook and Sigman with co-workers have demonstrated Pd-catalyzed TBHP-mediated Wacker-type oxidation of internal alkenes (**52**). The reaction was performed with 2- (4,5-dihydro-2-oxazolyl)quinoline (Quinox) (**56**) as ligand (**Scheme 4.17d**).[51]



Scheme 4.17 Examples of palladium-catalyzed Wacker oxidation of internal alkenes

After an extensive literature survey, our attention attracted for synthesis of chromone-fused imidazopyridines by the fact that only one report was available for the same which also suffered from one or more limitations such as narrow substrate scope, moderate yields and longer reaction

time. As part of our ongoing interest in developing synthetic methods for the preparation of fused imidazo[1,2-*a*]pyridines[52-55] and on exploration of 2-aminopyridinium salts in the synthesis of imidazo[1,2-*a*]pyridines,[56] we envisioned that a tandem reaction of 2-amino-1-(2-ethoxy-2-oxoethyl)pyridin-1-ium bromide with 2-bromoarylaldehydes in the presence of a base and palladium catalyst could give less explored chromeno-annulated imidazo[1,2-*a*]pyridine derivatives (**Figure 4.3**). In this chapter, we report our results for a one-pot synthesis of chromeno-annulated imidazo[1,2-*a*]pyridine *via* tandem amidation, Knoevenagel condensation, palladium-catalyzed Wacker type oxidation and C-O coupling reactions.

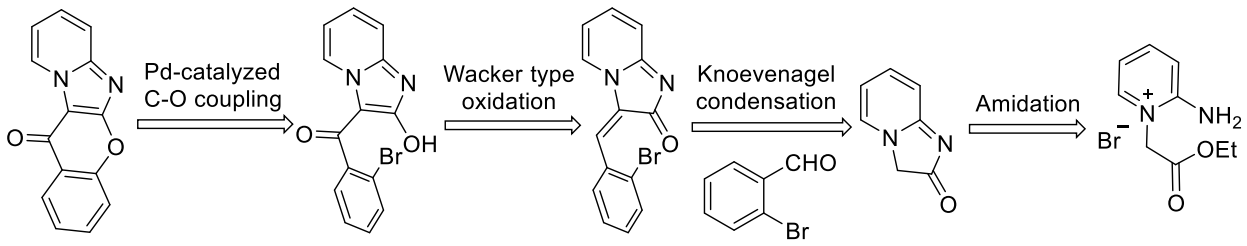


Figure 4.3 Schematic representation of the domino reactions for the synthesis of chromeno-annulated imidazo[1,2-*a*]pyridine

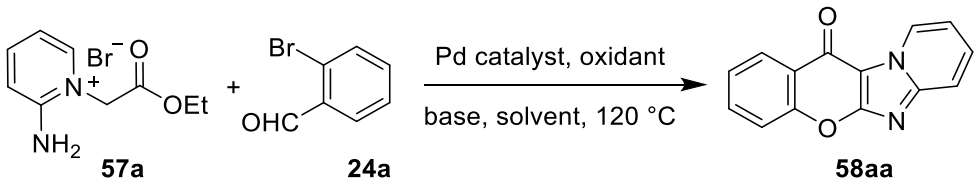
4.2 RESULTS AND DISCUSSION

4.2.1 Optimization of Reaction Conditions

We initiated our study with a model reaction of **57a** and **24a** in the presence of $Pd(OAc)_2$ (10 mol %) and $Cu(OAc)_2$ (2 equiv.) and K_2CO_3 (2.5 equiv.) in DMF at 120 °C for 10 h under air. To our satisfaction, the 12*H*-chromeno[2',3':4,5]imidazo[1,2-*a*]pyridin-12-one **(58aa)** was obtained in 48% isolated yield (**Table 4.1**, entry 1). This encouraging result indicated the feasibility of the envisioned tandem reaction. Thus, we went on to optimize the reaction conditions by varying different parameters such as catalysts, oxidants, bases, and solvents, *etc*. for the model reaction (**Table 4.1**). Replacement of K_2CO_3 base with various other inorganic (KOH, Cs_2CO_3, *t*-BuOK) and organic (DBU) bases demonstrated somewhat lower efficiency compared with K_2CO_3 (**Table 4.1**, entries 2−5). However, improved yield (61%) of **58aa** was observed when the reaction was carried out with K_3PO_4 (**Table 4.1**, entry 6). We further examined the performance of the reaction with a series of palladium catalysts such as $PdCl_2$, $Pd(TFA)_2$ and $PdCl_2(dppf)_2$ in the presence of $Cu(OAc)_2$ and K_3PO_4 (**Table 4.1**, entries 7-9) and to our satisfaction slightly better yield (67%) was obtained with $Pd(TFA)_2$ as compared to $Pd(OAc)_2$. A sharp decrease in the yield of **58aa** was observed when the reaction was performed in the presence of other oxidants such as IBD, oxone,

$AgNO_3$, AgOAc and Ag(TFA) (**Table 4.1**, entries 10-14). In other polar solvents like DMA, DMF: H_2O and PEG-400 moderate yields of **58aa** (48-69%) were obtained, whereas poor yield of **58aa** was obtained in DMSO (**Table 4.1**, entries 15-18), Desired transformation did not occur in non-polar solvents such as toluene and dioxane (**Table 4.1**, entries 19-20). It is also worth mentioning that the yield of **58aa** decreased when the reaction was performed under inert atmosphere (**Table 4.1**, entry 21). Decreasing the loading of $Cu(OAc)_2$ lead to decrease in the yield of **58aa** (**Table 4.1**, entries 22-23). In the absence of $Pd(TFA)_2$, no reaction was observed (**Table 4.1**, entry 24) while in the absence of $Cu(OAc)_2$ only 10% of **58aa** was formed (**Table 4.1**, entry 25). This observation showed that presence of both $Cu(OAc)_2$ and $Pd(TFA)_2$ is necessary for the success of this reaction. Finally, the best yield of **58aa** (77%) was obtained from the reaction of **57a** (2 equiv.) with **24a (**1 equiv.) in the presence of $Pd(TFA)_2$ (10 mol %), $Cu(OAc)_2$ (2.0 equiv.) in DMF: H_2O (1: 1 *v/v*) at 120 °C for 10 h under air (**Table 4.1**, entry 26).

Table 4.1 Optimization of the reaction condition for synthesis of **58aa**.[a]



57a **24a** **58aa**

Entry	Pd catalyst	Oxidant	Base	Solvent	% Yield of **58aa**[b]
1.	$Pd(OAc)_2$	$Cu(OAc)_2$	K_2CO_3	DMF	48
2.	$Pd(OAc)_2$	$Cu(OAc)_2$	KOH	DMF	36
3.	$Pd(OAc)_2$	$Cu(OAc)_2$	Cs_2CO_3	DMF	38
4.	$Pd(OAc)_2$	$Cu(OAc)_2$	DBU	DMF	15
5.	$Pd(OAc)_2$	$Cu(OAc)_2$	*t*-BuOK	DMF	36
6.	$Pd(OAc)_2$	$Cu(OAc)_2$	K_3PO_4	DMF	61
7.	$PdCl_2$	$Cu(OAc)_2$	K_3PO_4	DMF	32
8.	$PdCl_2(dppf)_2$	$Cu(OAc)_2$	K_3PO_4	DMF	30

9.	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	DMF	67
10.	$Pd(TFA)_2$	IBD	K_3PO_4	DMF	5
11.	$Pd(TFA)_2$	Oxone	K_3PO_4	DMF	8
12.	$Pd(TFA)_2$	$AgNO_3$	K_3PO_4	DMF	Trace
13.	$Pd(TFA)_2$	AgOAc	K_3PO_4	DMF	30
14	$Pd(TFA)_2$	Ag(TFA)	K_3PO_4	DMF	10
15.	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	DMA	48
16.	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	DMF: H_2O[c]	69
17.	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	PEG-400	50
18.	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	DMSO	25
19.	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	Dioxane	NR
20	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	Toluene	Trace
21.	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	DMF	52[d]
22	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	DMF	27[e]
23	$Pd(TFA)_2$	$Cu(OAc)_2$	K_3PO_4	DMF	50[f]
24	-	$Cu(OAc)_2$	K_3PO_4	DMF	NR
25	$Pd(TFA)_2$	-	K_3PO_4	DMF	10
26.	**$Pd(TFA)_2$**	**$Cu(OAc)_2$**	**K_3PO_4**	**DMF: H_2O[c]**	**77[g]**

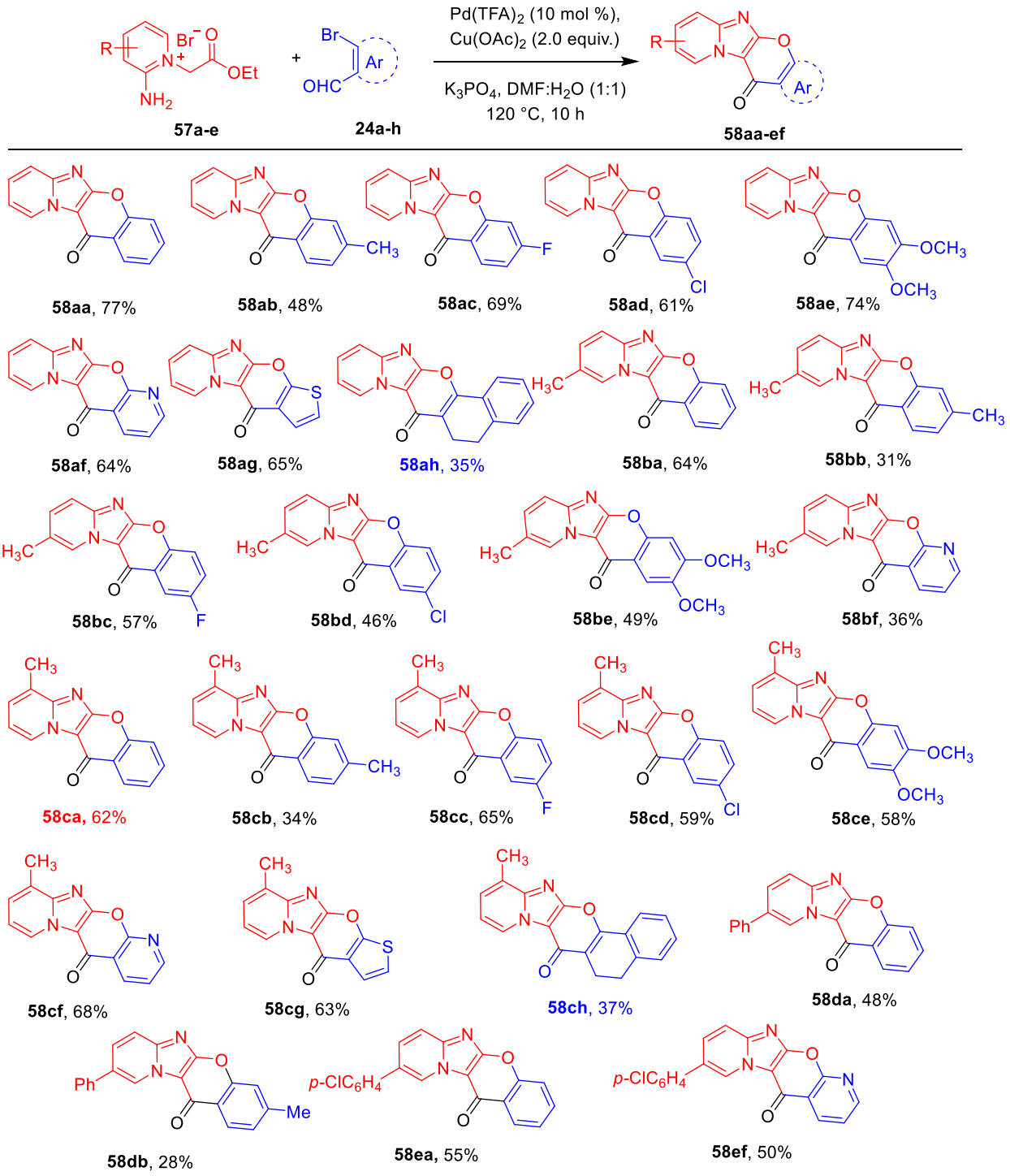
[a]Reaction conditions: **57a** (0.54 mmol), **24a** (0.54 mmol) Pd catalyst (10 mol %), oxidant (2.0 equiv.), base (2.5 equiv.), solvent (8 mL), 120 °C, 10 h under open air; [b]Isolated yields; [c]DMF: H_2O (1: 1 *v/v*); [d]Reaction performed under N_2 atm; [e]1.0 equiv. of $Cu(OAc)_2$ was used; [f]1.5 equiv. of $Cu(OAc)_2$ was used; [g]2.0 equiv. of **57a** was used.

4.2.2 Synthesis of 12*H*-Chromeno[2',3':4,5]imidazo[1,2-*a*]pyridin-12-ones (58)

With the optimized condition in hand, we embarked on investigation of the scope and limitation of the methodology. As shown in table **4.2**, different substituted 2-aminopyridinium salts (**57**) reacted smoothly with 2-bromoarylaldehydes (**24**) to give corresponding chromeno-annulated imidazo[1,2-*a*]pyridines (**58**) in moderate to good yield (28-77%) under standardized reaction conditions. First scope of the tandem process was evaluated by using different 2-bromo-arylaldehydes (**24a-e**) having substituents such as methyl, fluoro, chloro, *etc*. No significant electronic influence was observed on the yield of **58aa**. Interestingly, heteroaromatic aldehydes 2-bromopyridine-3-carbaldehyde (**24f**) and 2-bromothiophene-3-carbaldehyde (**24g**) also reacted to furnish corresponding chromeno-fused imidazo[1,2-*a*]pyridines **58af** and **58ag** in 64% and 65% yields, respectively. Finally, 1-bromo-3,4-dihydronaphthalene-2-carbaldehyde (**24h**) was reacted with 2-aminopyridinium salts **57a** to give corresponding 5,6-dihydro-7*H*-benzo[7',8']chromeno[2',3':4,5]imidazo[1,2-*a*]pyridin-7-ones (**58ah**) in 35% yield.

Next, scope of 2-aminopyridinium salts was examined. It was found that the substituents on the pyridine ring of 2-aminopyridinium salts significantly influenced the reaction outcome. For example, slightly lower yields of the desired product were obtained from the C-5 substituted 2-aminopyridinium salts as compared to the unsubstituted or C-3-substituted 2-aminopyridinium salts. Along with formation of the desired chromeno-annulated imidazo[1,2-*a*]pyridines, cleavage of salts leading to *N*-acetyl-2-aminopyridine derivatives (**62d** and **62e**) was observed in case of the 5-substituted 2-aminopyridinium salts (**57d** and **57e**). On the other hand, 5-nitro-2-aminopyridinium salt (**57f**) failed to give desired product under these conditions.

Table 4.2 Substrate scope for synthesis of chromeno-annulated imidazo[1,2-*a*]pyridines.[a,b]



[a]Reaction conditions: **57** (1.08 mmol), **24** (0.54 mmol), $Pd(TFA)_2$ (18 mg, 0.054 mmol), $Cu(OAc)_2$ (216 mg, 1.08 mmol), K_3PO_4 (286 mg, 1.351 mmol), DMF: H_2O (8 mL, *v/v*), 120 °C, 10 h under open air; [b]Isolated yields.

Structures of all the synthesized compounds were elucidated by IR, ^{1}H NMR, ^{13}C NMR and HRMS data. The exact structure of the product **58cd** (CCDC 1585320) was unambiguously determined by single X-ray diffraction analysis (**Figure 4.4**). The molecular structure of **58cd** is planar in nature with all four fused rings including the substituted atoms such as chlorine, oxygen atom of the carbonyl group and the carbon atom of the methyl group.

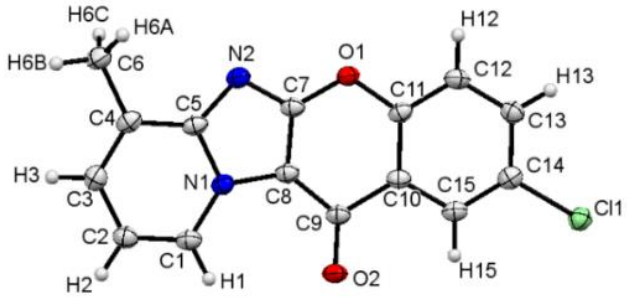


Figure 4.4 ORTEP diagram of **58cd**. The displacement ellipsoids are drawn at 50% probability level.

The presence of carbonyl group in the molecule was indicated by a peak at 1643 cm^{-1} corresponding to C=O stretching in the IR spectrum of **58aa**. The peaks ranging from 1442-1604 cm^{-1} corresponding to aromatic C=C stretching and peak for C-O stretching at 1249 cm^{-1} were also observed (**Figure 4.5**).

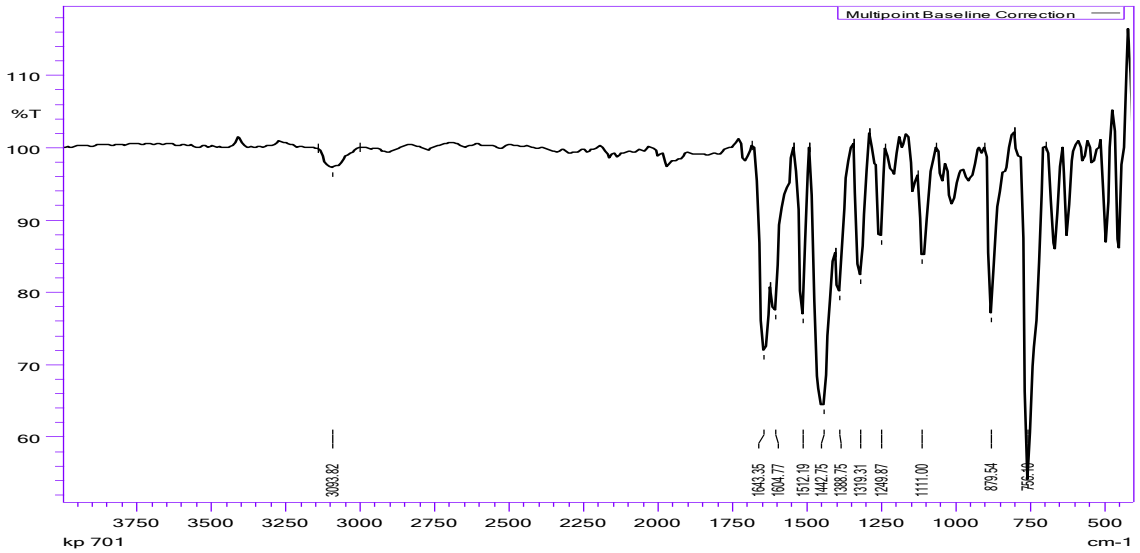


Figure 4.5 IR spectrum of compound **58aa**

In the ^{1}H NMR spectrum of **58aa**, all the peaks appeared in aromatic region along with distinctive doublet for most deshielded C10-H proton at δ 9.46 ppm with J = 6.6 Hz was observed (**Figure 4.6**). In the ^{13}C NMR spectrum of **58aa**, the presence C=O carbon at δ 168 ppm, C-O carbons at δ 161 and δ 154 ppm along with all other corresponding carbon peaks were observed (**Figure 4.7**).

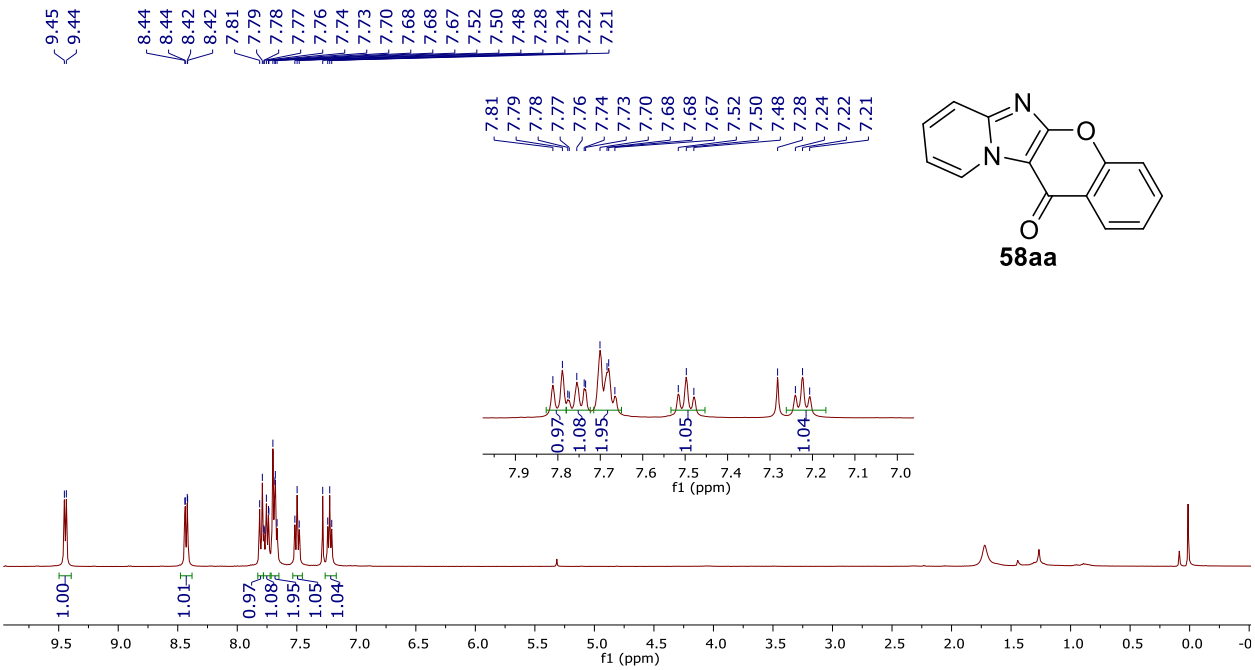


Figure 4.6 ^{1}H NMR spectrum of **58aa**

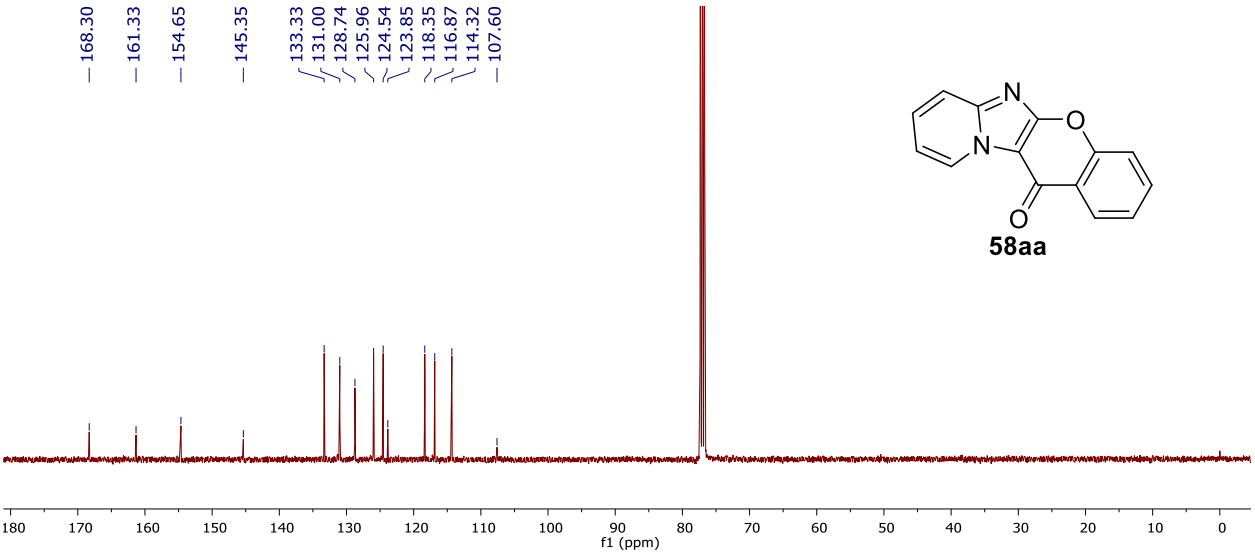
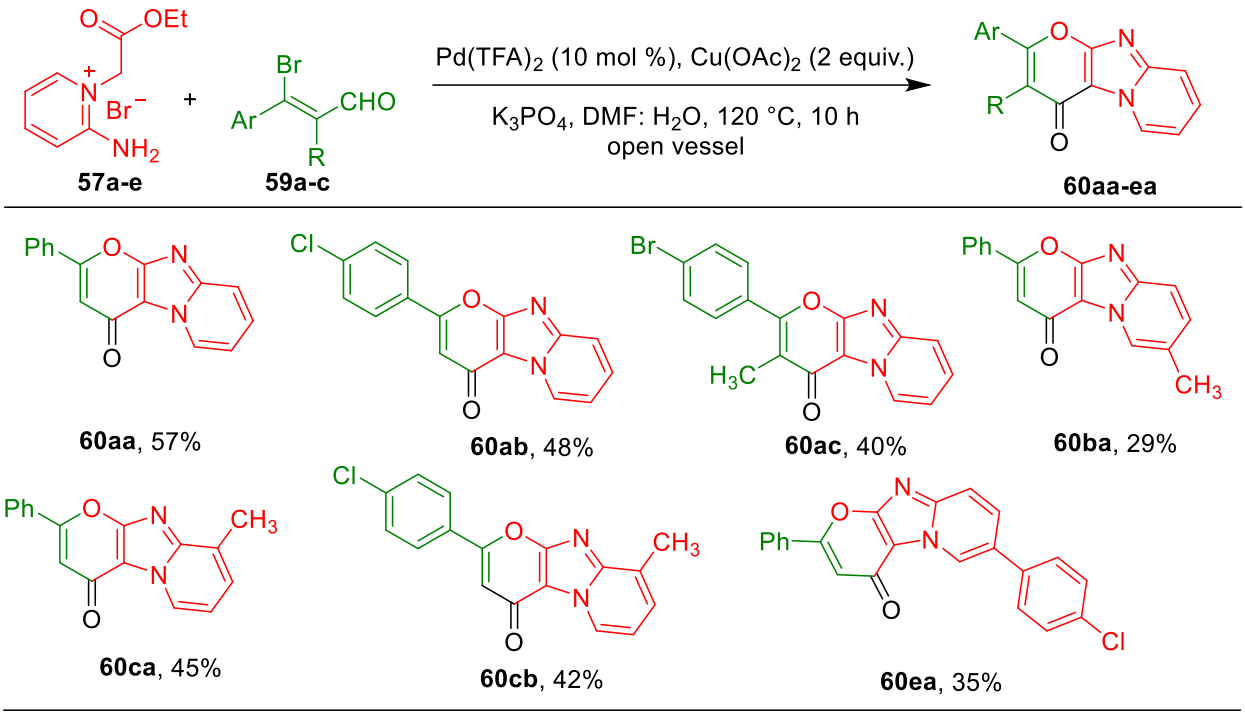


Figure 4.7 ^{13}C NMR spectrum of **58aa**

4.2.3 Synthesis of Pyrano[2',3':4,5]imidazo[1,2-*a*]pyridin-4-ones

The compatibility of the method was further explored by reacting 2-amino-1-(2-ethoxy-2-oxoethyl)pyridinium salts (**57a-e**) with 3-bromo-3-arylacrylaldehydes (**59a-b**) and 3-bromo-3-(4-bromophenyl)-2-methylacrylaldehyde (**59c**) (**Table 4.3**). The tandem reaction worked successfully to give pyrano[2',3':4,5]imidazo[1,2-*a*]pyridin-4-ones (**60aa-ea**) in moderate (29-57%) yields.

Table 4.3 Synthesis of pyrano[2',3':4,5]imidazo[1,2-*a*]pyridin-4-ones (**60**).[a,b]

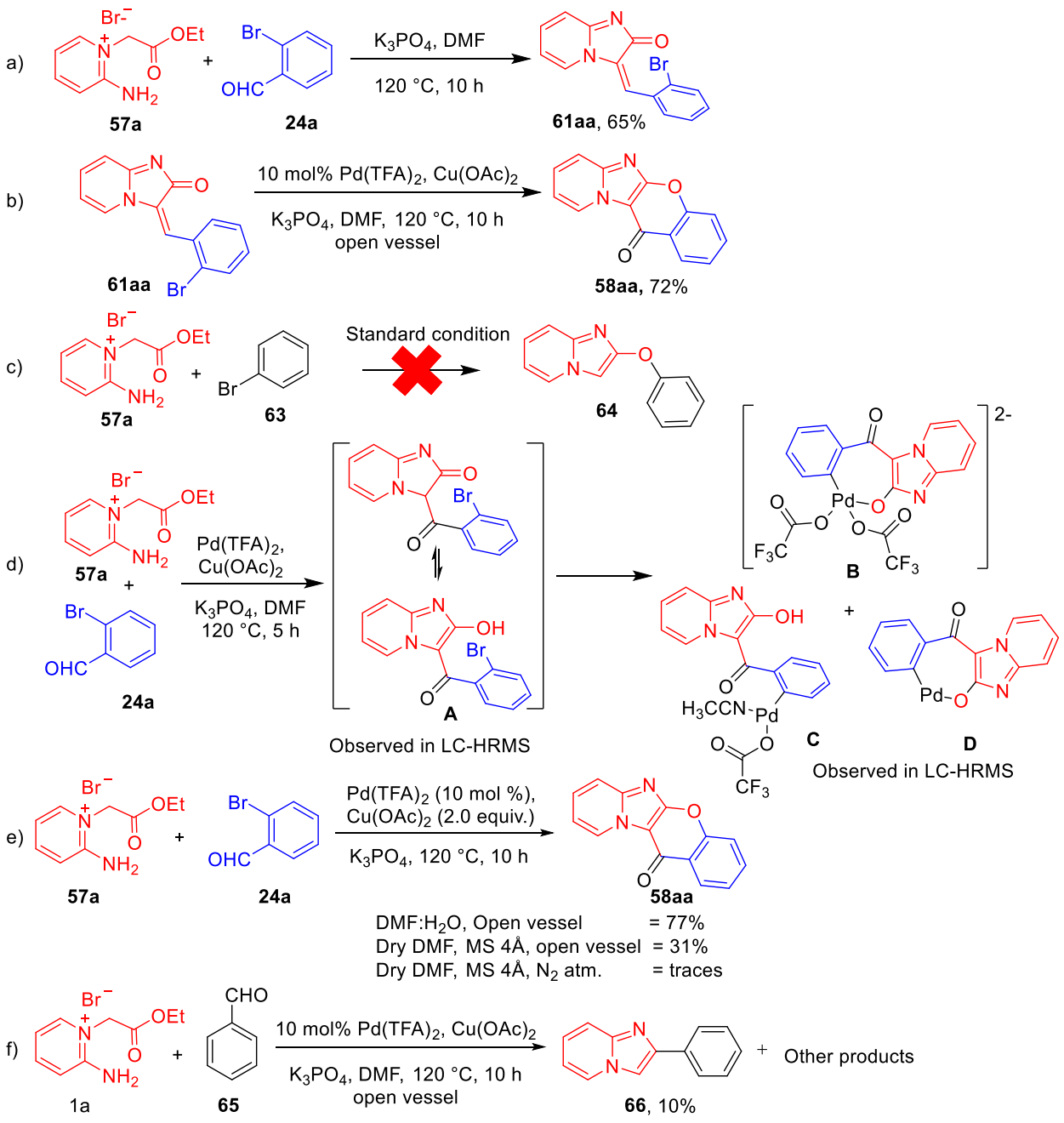


[a]Reaction conditions: **57** (1.08 mmol), **59** (0.54 mmol), $Pd(TFA)_2$ (18 mg, 0.054 mmol), $Cu(OAc)_2$ (216 mg, 1.08 mmol), K_3PO_4 (286 mg, 1.351 mmol), DMF: H_2O (8 mL, *v/v*), 120 °C, 10 h under open air; [b]Isolated yields.

4.2.4 Control Experiments

Some control experiments were carried out in order to gain better understanding of the mechanism and are presented in scheme **4.18**. Initially, reaction of **57a** and **24a** under standard reaction conditions without the addition of palladium catalyst resulted in the formation of 3-(2-bromobenzylidene)imidazo[1,2-*a*]pyridin-2(3*H*)-one (**61aa**) in 65% yield (**Scheme 4.18**, **a**). Next,

treatment of isolated **61aa** with $Pd(TFA)_2$ under the standard reaction conditions resulted in the formation of **58aa** in 72% yield (**Scheme 4.18**, **b**). This indicated that the reaction proceeds through **61aa**. Reaction of **57a** and bromobenzene (**63**) under optimized reaction condition did not occur to give 2-phenoxyimidazo[1,2-*a*]pyridine (**64**) which indicated that *O*-arylation is not taking place in the tandem reaction (**Scheme 4.18**, **c**).



Scheme 4.18 Control experiments

Further, aliquots of reaction between **57a** and **24a** under standard reaction conditions at different time intervals were diluted with acetonitrile and analyzed by LC-HRMS isocratic method using acetonitrile-water as eluent. Peaks corresponding to the mass of intermediates **A**, **B**, **C** and **D** were observed at *m/z* 316.9921 (calcd for $C_{14}H_{10}BrN_2O_2$ 316.9926), 568.9393 (calcd for $C_{18}H_9F_6N_2O_6Pd$ 568.9400), 497.9824 (calcd for $C_{18}H_{12}F_3N_3O_4Pd$ 497.9893) and 364.9524 (calcd for $C_{14}H_8N_2O_2PdNa$ 364.9518), respectively in HRMS spectrum (**Scheme 4.18**, **d**) (**Figure 4.8**) indicating that the tandem reaction might be proceeding through these intermediates.

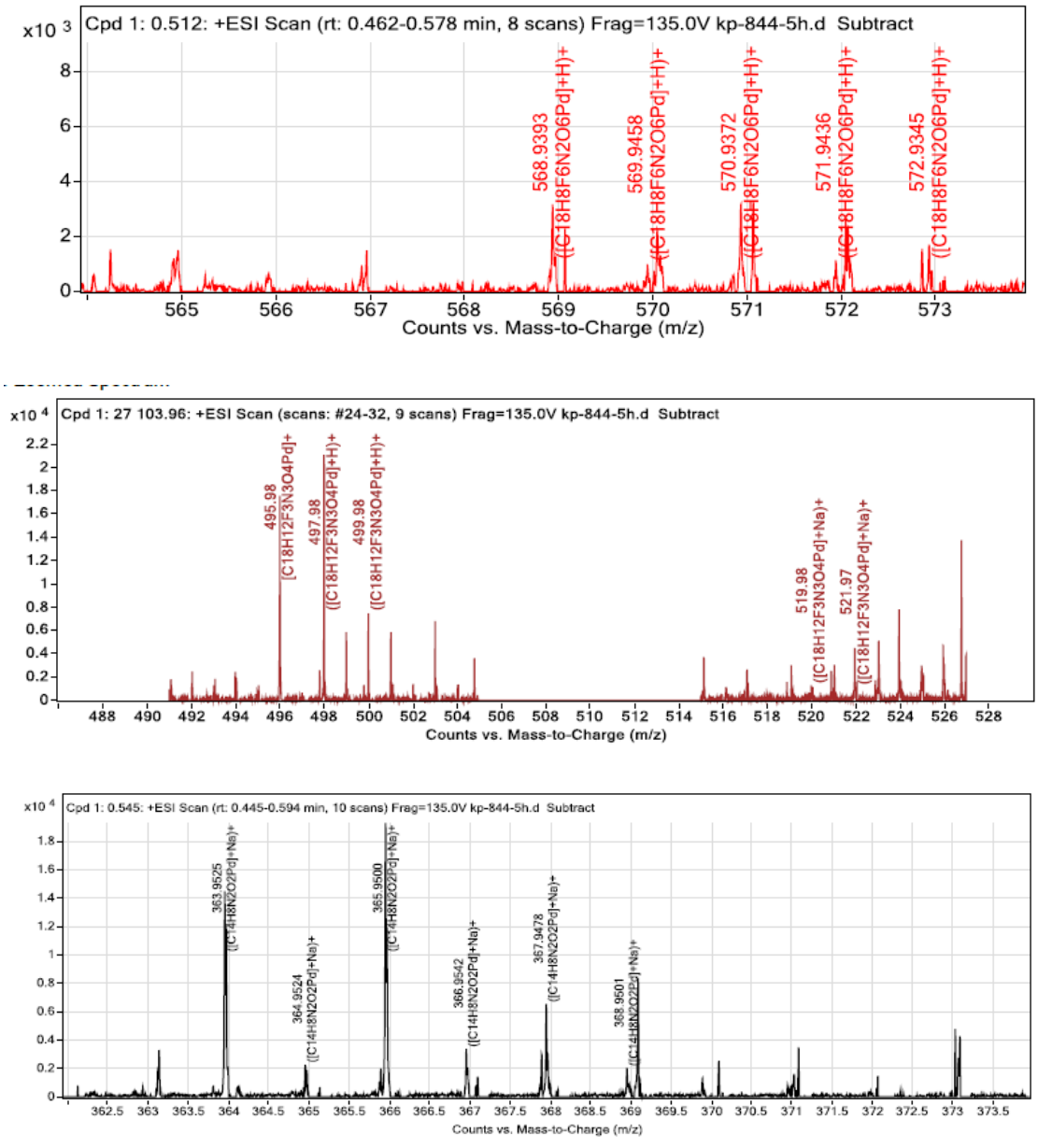
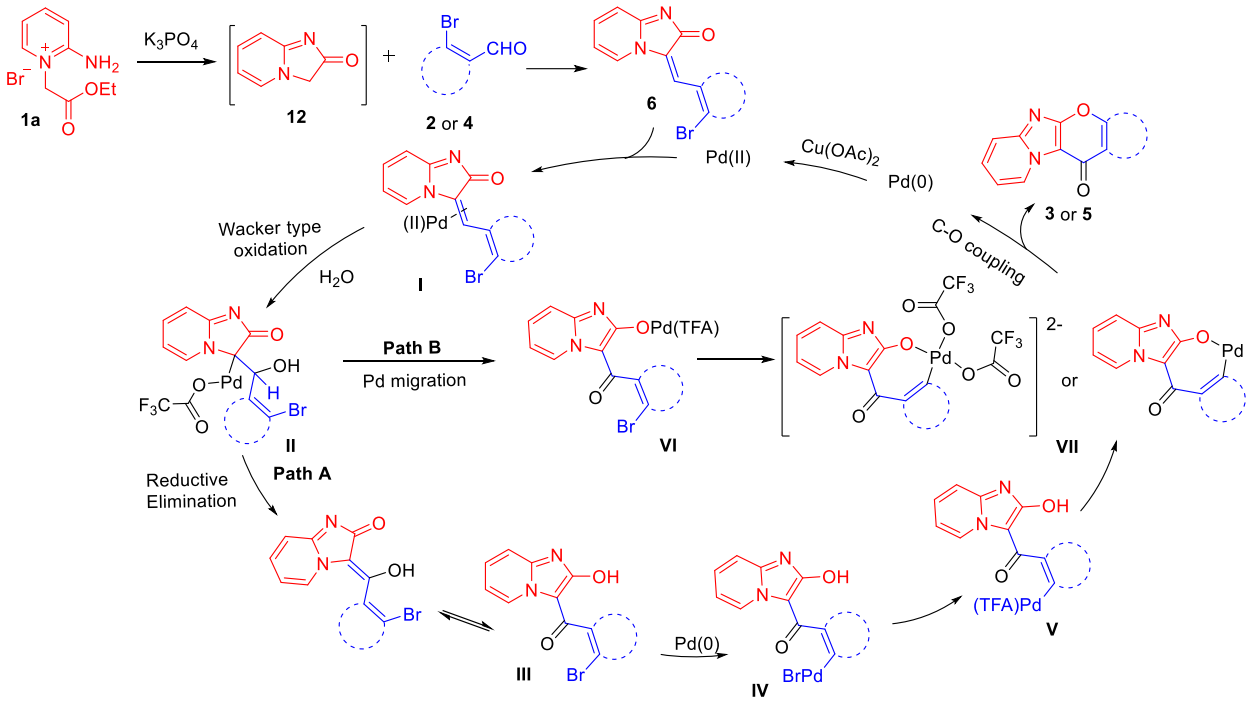


Figure 4.8 HRMS spectra of reaction mixture

Finally, reaction of **57a** and **24a** under optimized reaction conditions using i) anhydrous DMF in the presence of molecular sieves (MS 4Å) and ii) anhydrous DMF in the presence of MS 4Å under nitrogen atmosphere led to drastic decrease in the yield of **58aa** (**Scheme 4.18**, **e**). This indicates that oxygen and H_2O play very important role in the tandem reaction. Reaction of **57a** with benzaldehyde (**65**) resulted in the formation of 2-phenylimidazo[1,2-*a*]pyridine (**66**) in 10% yield along with other unidentified products (**Scheme 4.18**, **f**). Formation of **66** from **57a** may be proceeding in a similar fashion as reported by Katritzky group from 2-amino-1-[α-benzotriazol-1-ylmethyl]pyridinium chlorides.[57]

4.2.5 Plausible Mechanism

Although exact mechanism for the tandem reaction is unclear, based on the experimental results and literature a plausible pathway for the formation of **58** or **60** from **57** is proposed in scheme **4.19**. Initially, base catalyzed intramolecular amidation of 2-aminopyridinium salt **57** gives imidazo[1,2-*a*]pyridin-2(3*H*)-one (**67**) which on Knoevenagel condensation with 2-bromoaldehyde (**24** or **59**) affords intermediate **61**.[58] The intermediate **6** then coordinates with Pd(II) to give **I** which then on reaction with water produces **II** *via* Wacker type oxidation.[47, 59-61] Intermediate **II** may lead to formation of palladacycle **VII** either through **path A** or **path B**. In path B, palladium migrates to give intermediate **VI** which then results in the formation of **VII** (observed in HRMS, **Scheme 4.18**, **d**). In path A, reductive elimination of **II** lead to formation of **III**. Oxidative addition to Pd(0) leads to formation of intermediate **IV** which on exchange of bromide with trifluroacetate leads to formation of **V** (observed in HRMS, **Scheme 4.18**, **d**). Intermediate **V** converts to intermediate **VII** which on reductive elimination leads to the formation of C-O bond and gives cyclized product **58** or **60**.[62]



Scheme 4.19 Proposed mechanism for the formation of chromeno-annulated imidazo[1,2-*a*]pyridines

4.3 CONCLUSIONS

In summary, we have developed a new synthetic methodology to access less explored chromeno-annulated imidazo[1,2-*a*]pyridines through a one-pot tandem reaction of 2-amino-1-(2-ethoxy-2-oxoethyl)pyridinium salts with 2-bromoarylaldehydes. The reaction involves tandem intramolecular amidation, Knoevenagel condensation followed by palladium-catalyzed Wacker type oxidation and intramolecular C-O coupling reactions. Compared with previously reported methods, this protocol is versatile, tolerates different functional groups and gives moderate to good yields of chromeno[2',3':4,5]imidazo[1,2-*a*]pyridin-12-one derivatives.

4.4 EXPERIMENTAL SECTION

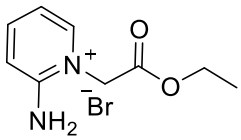
4.4.1 Materials and Methods

All reagents and solvents were purchased from commercial sources and used without further purification. Melting points were measured using an automatic capillary point apparatus and are uncorrected. The thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60-F_{254}

and a UV-lamp was used as visualizing agent. Column chromatography was performed using silica gel (100-200 mesh) and hexane and ethyl acetate were used as eluents. The ^{1}H and ^{13}C NMR spectra were obtained on 400 MHz and 100 MHz spectrometer. Coupling constant and chemical shifts were reported in hertz (Hz) and parts per million (ppm) respectively, relative to the internal standard of tetramethylsilane (TMS). IR spectroscopy was performed as a neat sample on a FT-IR instrument and values are expressed in cm^{-1}. The HRMS were analyzed by electrospray ionization (ESI) method in positive mode on a Q-TOF LC-MS spectrometer. Synthesis of β-bromo-α,β-unsaturated aldehydes (**24h**, **59a-c**) was achieved from the reaction of corresponding ketones and $POBr_3$ following literature method.[63]

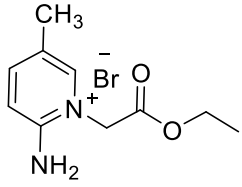
4.4.2 General Procedure for the Synthesis of 2-Aminopyridinium Bromides (57): An oven dried round bottom (RB) flask was charged with 2-aminopyridine (0.500 g, 5.31 mmol) and tetrahydrofuran (15 mL). The RB flask was capped with rubber septum and after purging N_2 gas, ethyl bromoacetate (1.33 g, 7.96 mmol) was added *via* syringe and stirred the reaction mixture under N_2 gas atmosphere at 0 °C. The temperature of the reaction mixture was slowly raised to room temperature and stirred for 8 h to obtain pink colored precipitate. After complete consumption of 2-aminopyridine as monitored by thin layer chromatography, reaction mixture was filtered and residue was washed with diethyl ether to provide pure solid compound.

2-Amino-1-(2-ethoxy-2-oxoethyl)pyridin-1-ium bromide (57a).



Pink solid (1.3 g, 93%); Decomposed after 200 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (s, 1H), 8.08-8.07 (m, 1H), 7.99 – 7.75 (m, 1H), 7.20 (d, J = 8.1 Hz, 1H), 7.01 – 6.75 (m, 1H), 5.22 (s, 2H), 4.17 (q, J = 7.1 Hz, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.3, 155.1, 143.3, 140.8, 115.4, 113.1, 62.4, 54.2, 14.4. FT-IR ν_{max} (neat) 3286, 3062, 1739, 1651, 1577, 1338, 1126, 1099, 771 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_9H_{13}N_2O_2^+$ $[M\text{-}Br]^+$ 181.0972, found 181.0970.

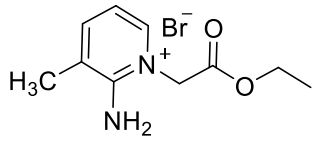
2-Amino-5-methyl-1-(2-ethoxy-2-oxoethyl)pyridin-1-ium bromide (57b).



Pink solid (1.2 g, 96%); MP 280 – 282 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (s, 1H), 7.89 (s, 1H), 7.82 (d, J = 9.0 Hz, 1H), 7.09 (d, J = 9.1 Hz, 1H), 5.12 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 2.15 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.3, 153.7, 145.5,

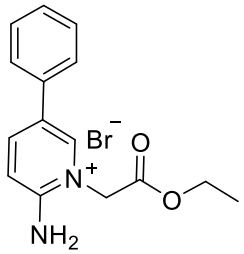
138.2, 122.3, 115.2, 62.4, 54.0, 16.8, 14.4; FT-IR ν_{max} (neat) 3329, 3290, 3124, 1743, 1658, 1523, 1373, 1211, 1022, 759 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{10}H_{15}N_2O_2^+$ $[M\text{-}Br]^+$ 195.1128, found 195.1135.

2-Amino-3-methyl-1-(2-ethoxy-2-oxoethyl)pyridin-1-ium bromide (57c).



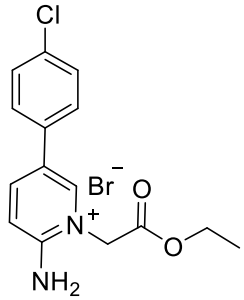
Pink solid (1.2 g, 96%); MP 296 – 298 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35 (s, 2H), 8.04 (d, J = 7.5 Hz, 1H), 7.86 (d, J = 7.2 Hz, 1H), 7.04 – 6.77 (m, 1H), 5.32 (s, 2H), 4.20 (q, J = 7.7 Hz, 2H), 2.26 (s, 3H), 1.25 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.4, 154.2, 142.2, 138.9, 124.0, 112.8, 62.4, 54.8, 18.0, 14.4; FT-IR ν_{max} (neat) 3286, 3070, 1743, 1666, 1585, 1342, 1219, 1022, 767 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{10}H_{15}N_2O_2^+$ $[M\text{-}Br]^+$ 195.1128, found 195.1128.

2-Amino-1-(2-ethoxy-2-oxoethyl)-5-phenylpyridin-1-ium bromide (57d).



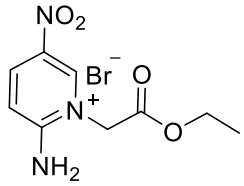
Pink solid (0.90 g, 90%); MP 285 – 287 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.79 (s, 2H), 8.53 (s, 1H), 8.36 (d, J = 8.9 Hz, 1H), 7.68 (d, J = 7.3 Hz, 2H), 7.52 (t, J = 7.2 Hz, 2H), 7.44 (d, J = 7.0 Hz, 1H), 7.25 (d, J = 9.2 Hz, 1H), 5.25 (s, 1H), 4.23 (q, J= 6.7 Hz, 2H), 1.27 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.3, 154.1, 142.0, 138.1, 134.2, 129.7, 128.9, 126.3, 125.3, 115.8, 62.5, 54.5, 14.4; ; FT-IR ν_{max} (neat) 3271, 3244, 3074, 1751, 1662, 1346, 1288, 1095, 759 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{17}N_2O_2^+$ $[M\text{-}Br]^+$ 257.1287, found 257.1306.

2-Amino-5-(4-chlorophenyl)-1-(2-ethoxy-2-oxoethyl)pyridin-1-ium bromide (57e).



Off-white solid (0.86 g, 95%); MP 180 – 182 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.83 (s, 2H), 8.57 (d, J = 1.6 Hz, 1H), 8.35 (dd, J = 9.3, 1.8 Hz, 1H), 7.71 (d, J = 8.6 Hz, 2H), 7.59 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 9.3 Hz, 1H), 5.23 (s, 2H), 4.23 (q, J = 7.1 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.2, 154.2, 141.7, 138.3, 133.7, 133.1, 129.7, 128.1, 125.2, 124.0, 115.8, 62.5, 54.5, 14.4; FT-IR ν_{max} (neat) 3271, 3244, 3074, 1747, 1662, 1539, 1342, 1207, 1161, 1095, 813,752 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{16}ClN_2O_2^+$ $[M\text{-}Br]^+$ 291.0895 found 291.0878.

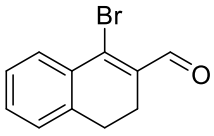
2-Amino-1-(2-ethoxy-2-oxoethyl)-5-nitropyridin-1-ium bromide (57f).



Off-white solid (0.25 g, 23%); MP 135 – 138 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.10 (bs, 1H), 9.42 (s, 1H), 8.55 (d, J = 9.4 Hz, 1H), 7.27 (d, J = 9.8 Hz, 1H), 5.31 (s, 2H), 4.23 (q, J = 6.7 Hz, 2H), 1.27 (t, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.8, 156.6, 141.8, 136.3, 135.4, 115.8, 62.6, 55.0, 14.4; FT-IR ν_{max} (neat) 3325, 3147, 1762, 1658, 1543, 1361, 1215, 1168, 1053, 991,783 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_9H_{12}N_3O_4^+$ [M-Br]$^+$ 226.0822, found 226.0809.

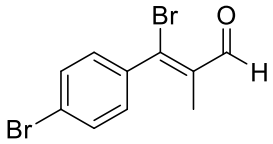
4.4.3 General Procedure for the Synthesis of β-Bromo-α,β-unsaturated Aldehydes[63]: A dry round bottom flask was charged with $POBr_3$ (3 equiv.) in $CHCl_3$ at 0 °C under N_2 atmosphere. To this cooled solution, *N*,*N*-dimethylformamide (6 equiv.) was added drop wise over 10 min. and stirred at room temperature for 45-60 min. Over the time, white precipitate was observed. To this mixture, ketone (1 equiv.) dissolved in $CHCl_3$ was added at 0 °C and then the resulting reaction mixture was stirred for 10-15 h at 60 °C. After complete consumption of ketone as monitored by thin layer chromatography, reaction mass was poured in ice-cold water and the aqueous layer was neutralized with solid K_2CO_3 and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $NaSO_4$, filtered, and concentrated in rotatory evaporator. The crude product obtained was subjected to column chromatography using SiO_2 and EA: hexane (5: 95 *v/v*) as eluting mixture to afford the β-bromo-α,β-unsaturated aldehydes.

1-Bromo-3,4-dihydronaphthalene-2-carbaldehyde (24h).



Yellow solid (0.580 g, 65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.92 (dd, J = 7.2, 2.0 Hz, 1H), 7.43 – 7.31 (m, 2H), 7.22 (ddd, J = 5.9, 2.1, 1.0 Hz, 1H), 2.86 (dd, J = 9.2, 6.7 Hz, 2H), 2.71 – 2.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.14, 139.07, 138.95, 134.56, 133.03, 131.36, 128.75, 127.61, 127.15, 27.20, 22.91; FT-IR ν_{max} (neat): 2864, 1682, 1570, 1500, 1220, 1149, 1040, 847, 712 cm^{-1}; HRMS (APCI-TOF, *m/z*): calcd for $C_{11}H_{10}BrO$ [M + H]$^+$ 236.9910, 238.9890; found 236.9901, 238.9881.

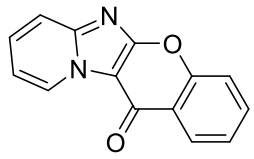
3-Bromo-3-(4-bromophenyl)-2-methylacrylaldehyde (59c).



Yellow liquid (0.550 g, 76%); ^{1}H NMR (400 MHz, $CDCl_3$: 10:1 mixture of (E)/(Z)-isomers) signals of (E)-isomer: δ 9.42 (s, 1 H, CHO), 7.74–7.48 (m, 2 HAr), 7.38–7.04 (m, 2 HAr), 2.11 (s, 3 H, Me); additional signals of (Z)-isomer: δ = 10.21 (s, CHO), 1.80 (s, Me); ^{13}C NMR (100 MHz, $CDCl_3$; 10:1 mixture of (E)/(Z)-isomers): δ = 193.95 (Z), 188.34 (E), 146.12 (E), 139.84 (E), 138.23 (Z), 137.61 (Z), 136.54 (E), 135.05 (Z), 131.78 (Z), 131.72 (E), 131.44 (E), 129.99 (Z), 124.65 (E), 124. 10 (Z), 16.43 (E), 14.85 (Z); FT-IR ν_{max} (neat): 2862, 1673, 1598, 1504, 1229, 1159, 1027, 906, 872, 835, 702 cm^{-1}; HRMS (APCI-TOF, *m/z*): calcd for $C_{10}H_9Br_2O$ $[M + H]^+$ 302.9015, 304.8994; found 302.8998, 304.8976.

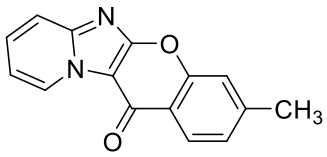
4.4.4 Representative Procedure for the Synthesis of Chromeno/pyrano-annulated Imidazo[1,2-*a*]pyridine (58 & **60).** An oven-dried 10 mL round bottom flask was charged with 2-amino-1-(2-ethoxy-2-oxoethyl)pyridin-1-ium bromide (0.282 g, 1.081 mmol), 2–bromoaldehyde (0.100 g, 0.540 mmol), K_3PO_4 (0.286 g, 1.351 mmol), $Cu(OAc)_2$ (0.216 g, 1.08 mmol), and $Pd(TFA)_2$ (0.018 g, 0.054 mmol) in DMF: H_2O (8 mL, *v/v*). The resulting reaction mixture was heated at 120 °C for 10 h. The reaction was monitored by TLC over the time. On completion, the reaction mass was cooled to ambient temperature, diluted with ice cold water (20 mL), extracted with ethyl acetate (2 × 30 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and evaporated to dryness under reduced pressure. The crude residue was subjected to column chromatography (30% EtOAc: hexane) to afford **58aa** in 77% (98 mg) yield.

12H-Chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58aa).



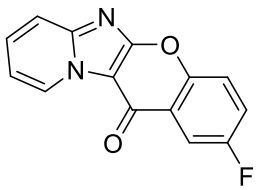
Cream colored solid (0.098 g, 77%); MP 289 – 291 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (d, *J* = 6.6 Hz, 1H), 8.43 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.70-7.67 (m, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.22 (t, *J* = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 161.3, 154.6, 145.3, 133.3, 131.0, 128.7, 125.9, 124.5, 123.8, 118.3, 116.8, 114.3, 107.6; FT-IR ν_{max} (neat) 3093, 1643, 1604, 1442, 1249, 1111, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_9N_2O_2$ $[M + H]^+$ 237.0659, found 237.0660.

3-Methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58ab).



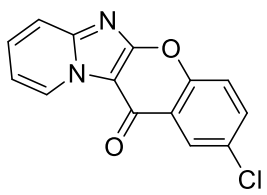
Cream colored solid (0.060 g, 48%); MP 266 – 268 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 – 9.41 (m, 1H), 8.31 (d, J = 8.1 Hz, 1H), 7.81-7.78 (m, 1H), 7.71 – 7.63 (m, 1H), 7.49 (s, 1H), 7.31 (dd, J = 8.1, 0.9 Hz, 1H), 7.21 (td, J = 6.9, 1.1 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 161.3, 152.9, 145.5, 133.3, 131.4, 130.5, 128.8, 125.5, 125.0, 119.9, 116.9, 114.5, 107.5, 21.8; FT-IR ν_{max} (neat) 1643, 1612, 1442, 1381, 1249, 1111, 762 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{11}N_2O_2$ $[M + H]^+$ 251.0815, found 251.0815.

2-Fluoro-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58ac).



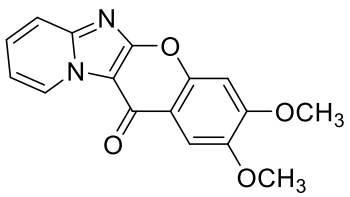
Cream colored solid (0.086 g, 69%); MP 234-236 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (dt, J = 6.7, 1.1 Hz, 1H), 8.06 (dd, J = 8.4, 3.1 Hz, 1H), 7.80 (dt, J = 9.0, 1.0 Hz, 1H), 7.74 – 7.63 (m, 2H), 7.46 (ddd, J = 9.1, 7.4, 3.2 Hz, 1H), 7.24 (td, J = 6.9, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (d, J = 2.2 Hz), 161.4, 160.4, 158.0, 150.6, 145.5, 131.3, 128.8, 125.1 (d, J = 7.2 Hz), 121.0 (d, J = 25.1 Hz), 120.1 (d, J = 8.1 Hz), 115.7 (d, J = 242.7 Hz), 111.2 (d, J = 24.3 Hz), 107.3; FT-IR ν_{max} (neat) 3060, 1643, 1620, 1450, 1319, 1242, 1134, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_8FN_2O_2$ $[M + H]^+$ 255.0564, found 255.0566.

2-Chloro-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58ad).



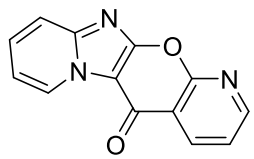
Cream colored solid (0.075 g, 61%); MP 261 – 263 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (d, J = 6.4 Hz, 1H), 8.38 (s, 1H), 7.81 (d, J = 8.9 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.64 (d, J = 8.8 Hz, 1H), 7.25 (t, J = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 161.3, 152.9, 145.5, 133.3, 131.4, 130.5, 128.8, 125.5, 125.0, 119.9, 116.9, 114.5, 107.5; FT-IR ν_{max} (neat) 2916, 1635, 1612, 1442, 1372, 1249, 1026, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_8ClN_2O_2$ $[M + H]^+$ 271.0269, found 271.0271.

***2,3-Dimethoxy-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58ae*).**



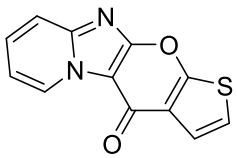
Cream colored solid (0.089 g, 74%); MP 280 – 282 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (d, J = 6.6 Hz, 1H), 7.78 (d, J = 9.0 Hz, 1H), 7.76 (s, 1H), 7.69 – 7.62 (m, 1H), 7.21 (dd, J = 10.2, 3.5 Hz, 1H), 7.13 (s, 1H), 4.06 (s, 3H), 4.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 161.0, 153.8, 150.3, 146.8, 144.8, 130.5, 128.6, 116.7, 116.5, 114.0, 105.0, 100.4, 56.5, 56.41; FT-IR ν_{max} (neat) 2916, 1635, 1612, 1442, 1372, 1249, 1026, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{16}H_{13}N_2O_4$ $[M + H]^+$ 297.0870, found 297.0866.

***Pyrido[2",3":5,6]-5H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-5-one* (*58af*).**



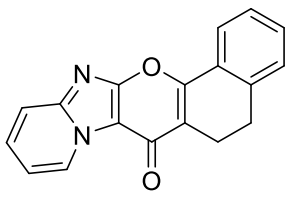
Yellow solid (0.081 g, 64%); MP >300 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (d, J = 6.6 Hz, 1H), 8.82 (dd, J = 7.7, 1.7 Hz, 1H), 8.78 (dd, J = 4.4, 1.7 Hz, 1H), 7.86 (d, J = 9.0 Hz, 1H), 7.73 (t, J = 7.7 Hz, 1H), 7.56 (dd, J = 7.6, 4.7 Hz, 1H), 7.26 (d, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 161.2, 159.0, 152.2, 145.9, 136.6, 131.5, 128.7, 121.3, 118.9, 117.2, 114.8, 107.6; FT-IR ν_{max} (neat) 3063, 1635, 1620, 1519, 1458, 1327, 1257, 1111, 1041, 763 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_8N_3O_2$ $[M + H]^+$ 238.0611, found 238.0612.

***4H-Thieno[3'',2'':5',6']pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*58ag*).**



Yellow solid (0.082 g, 65%); MP 202 – 204 °C; ^{1}H NMR (400 MHz, $CDCl_3$ δ 9.40 (d, J = 6.6 Hz, 1H), 7.79 (dd, J = 6.8, 4.5 Hz, 2H), 7.66 (t, J = 7.9 Hz, 1H), 7.34 (d, J = 5.4 Hz, 1H), 7.21 (t, J = 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 161.6, 156.0, 144.7, 131.3, 130.5, 128.5, 123.8, 118.1, 116.9, 114.2, 107.8; FT-IR ν_{max} (neat) 3074, 2954, 2920, 1624, 1512, 1458, 1307, 1249, 1145, 1029, 763 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{12}H_7N_2O_2S$ $[M + H]^+$ 243.0223, found 243.0228.

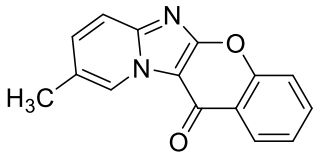
5,6-Dihydro-7H-benzo[7',8']chromeno[2',3':4,5]imidazo[1,2-a]pyridin-7-one (58ah).



Yellow solid (0.042, 35%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37 (dt, J = 6.7, 1.3 Hz, 1H), 8.08 (dd, J = 5.6, 3.5 Hz, 1H), 7.77 (dt, J = 9.1, 1.2 Hz, 1H), 7.63 (ddd, J = 8.9, 7.0, 1.4 Hz, 1H), 7.42 (dd, J = 5.6, 3.3 Hz, 2H), 7.32 (dd, J = 5.4, 3.4 Hz, 1H), 7.17 (td, J = 6.9, 1.2 Hz, 1H), 3.03-3.00

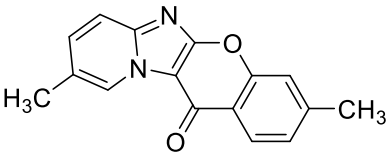
(m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 160.3, 155.2, 144.4, 138.6, 130.6, 130.2, 128.4, 128.4, 128.0, 127.1, 123.9, 118.8, 116.8, 113.8, 27.2, 18.9; FT-IR ν_{max} (neat): 3093, 2935, 1647, 1600, 1450, 1258, 1100, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{18}H_{13}N_2O_2$ $[M + H]^+$ 289.0972 found 289.0979.

9-Methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58ba).



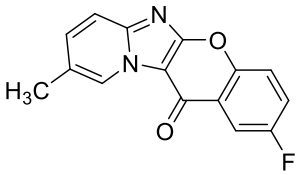
Cream colored solid (0.086 g, 64%); MP 215 – 217 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (d, *J* = 0.8 Hz, 1H), 8.43 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.75 (ddd, *J* = 8.6, 7.1, 1.7 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.53 (dd, *J* = 9.2, 1.7 Hz, 1H), 7.52 – 7.47 (m, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 161.2, 154.6, 144.1, 133.8, 133.2, 126.8, 125.9, 124.4, 124.4, 123.8, 118.3, 116.1, 107.4, 18.2; FT-IR ν_{max} (neat) 3093, 3039, 2916, 1643, 1519, 1458, 1317, 1248, 1188, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{11}N_2O_2$ $[M + H]^+$ 251.0815, found 251.0813.

3,9-Dimethyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58bb).



Off white solid (0.041 g, 31%); MP 207 – 209 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (d, *J* = 0.8 Hz, 1H), 8.29 (d, *J* = 8.1 Hz, 1H), 7.68 (d, *J* = 9.1 Hz, 1H), 7.50 (dd, *J* = 9.1, 1.6 Hz, 1H), 7.46 (s, 1H), 7.30 -7.28 (m, 1H), 2.55 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 161.2, 152.8, 144.3, 134.2, 133.2, 130.3, 126.8, 125.5, 125.0, 124.8, 119.8, 116.2, 107.4, 18.2; FT-IR ν_{max} (neat) 3032, 2929, 2854, 1620, 1519, 1465, 1303, 1234, 1118, 1041, 817, 763 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{16}H_{13}N_2O_2$ $[M + H]^+$ 265.0972, found 265.0980.

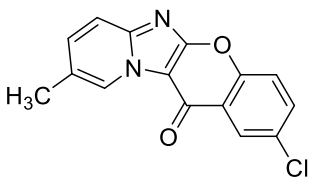
2-Fluoro-9-methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58bc).



Cream colored solid (0.075 g, 57%); MP 230 – 232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 – 9.17 (m, 1H), 8.07 (dd, *J* = 8.4, 3.1 Hz, 1H), 7.71 (d, *J* = 9.5 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.56 (dd, *J* = 9.1, 1.7 Hz, 1H), 7.46 (ddd, *J* = 9.1, 7.4, 3.2 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 161.4, δ 159.2 (d, *J* = 245.5 Hz), 157.8, 150.6, 144.3, 134.2, 126.8, 125.2 (d, *J* = 7.2 Hz), 124.7, 120.9 (d, *J* = 25.1 Hz), 120.0 (d, *J* = 8.1 Hz), 116.2, 111.2 (d, *J* = 24.3 Hz),

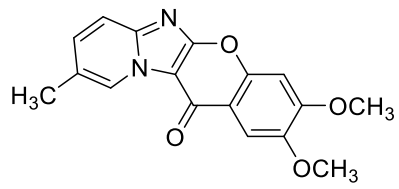
107.2, 18.2; FT-IR ν_{max} (neat) 3063, 1635, 1519, 1465, 1303, 1234, 1118, 1041, 817, 763 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{10}FN_2O_2$ $[M + H]^+$ 269.0721, found 269.0722.

***2-Chloro-9-methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58bd*).**



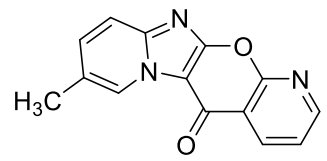
Off-white solid (0.060 g, 46%); MP 248 – 249 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.38 (d, J = 2.5 Hz, 1H), 7.71 (d, J = 8.9 Hz, 1H), 7.69-7-67 (m, 1H), 7.63 (d, J = 8.8 Hz, 1H), 7.56 (dd, J = 9.1, 1.6 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 161.2, 152.8, 144.3, 134.2, 133.2, 130.3, 126.8, 125.5, 125.0, 124.8, 119.8, 116.2, 107.4, 18.2; FT-IR ν_{max} (neat) 3063, 1635, 1519, 1465, 1303, 1234, 1118, 1041, 817, 763 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{10}ClN_2O_2$ $[M + H]^+$ 285.0425, found 285.0422.

***2,3-Dimethoxy-9-methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58be*).**



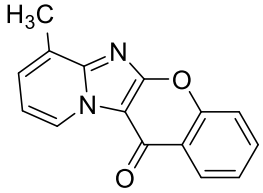
Yellow viscous liquid (0.062 g, 49%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 7.76 (s, 1H), 7.68 (d, J = 9.1 Hz, 1H), 7.50 (dd, J = 9.1, 1.5 Hz, 1H), 7.12 (s, 1H), 4.06 (s, 6H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 160.9, 153.7, 150.3, 146.7, 143.6, 133.4, 126.6, 124.1, 116.6, 116.0, 107.1, 105.1, 100.4, 56.5, 56.4, 18.2; FT-IR ν_{max} (neat) 2958, 2924, 1631, 1612, 1504, 1462, 1427, 1261, 1222, 1111, 1020, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{17}H_{15}N_2O_4$ $[M + H]^+$ 311.1026, found 311.1031.

8-Methyl-pyrido[2",3":5',6']-5H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-5-one (58bf).



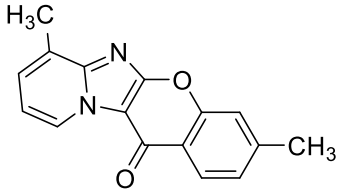
White solid (0.048 g, 36%); MP 271 – 273 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.82 (dd, J = 7.7, 2.0 Hz, 1H), 8.77 (dd, J = 4.6, 2.0 Hz, 1H), 7.75 (d, J = 9.1 Hz, 1H), 7.60 – 7.56 (m, 1H), 7.56 – 7.52 (m, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 161.1, 159.0, 152.1, 144.7, 136.7, 134.45, 126.7, 125.0, 121.2, 118.9, 116.5, 107.4, 18.2; FT-IR ν_{max} (neat) 3085, 2927, 1637, 1519, 1458, 1340, 1240, 1020, 757 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{14}H_{10}N_3O_2$ $[M + H]^+$ 252.0768, found 252.0770.

***7-Methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58ca*).**



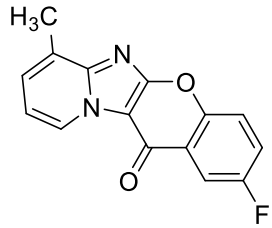
Cream colored solid (0.083 g, 62%); MP 253 – 254 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (d, J = 6.5 Hz, 1H), 8.44 (d, J = 7.9 Hz, 1H), 7.80 – 7.72 (m, 1H), 7.68 (d, J = 8.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.14 (t, J = 6.9 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 154.6, 133.2, 130.1, 126.9, 126.42, 125.9, 124.5, 123.9, 118.3, 114.3, 107.9, 16.8; FT-IR ν_{max} (neat) 3063, 2916, 1643, 1512, 1450, 1381, 1257, 1056, 779 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{11}N_2O_2$ $[M + H]^+$ 251.0815, found 251.0816.

***3,7-Dimethyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58cb*).**



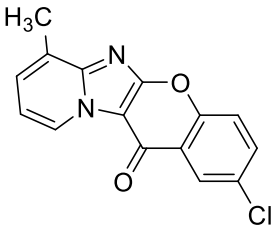
Cream colored solid (0.045 g, 34%); MP 256 – 258 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (d, J = 6.6 Hz, 1H), 8.30 (d, J = 8.1 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.46 (s, 1H), 7.31 (d, J = 9.1 Hz, 1H), 7.12 (t, J = 6.9 Hz, 1H), 2.72 (s, 1H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 160.9, 154.7, 145.2, 144.6, 129.9, 126.8, 126.3, 125.8, 125.7, 121.5, 118.2, 114.2, 107.8, 21.8, 16.8; FT-IR ν_{max} (neat) 3117, 2916, 1651, 1620, 1519, 1450, 1381, 1272, 1111, 771 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{16}H_{13}N_2O_2$ $[M + H]^+$ 265.0972, found 265.0980.

***2-Fluoro-7-methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58cc*).**



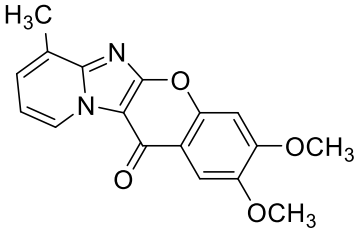
Cream colored solid (0.085 g, 65%); MP 227 – 228 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (d, J = 6.5 Hz, 1H), 8.07 (dd, J = 8.3, 3.0 Hz, 1H), 7.67 (dd, J = 9.1, 4.1 Hz, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.49 – 7.41 (m, 1H), 7.15 (t, J = 6.9 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 161.1, 160.4, 158.0, 150.6, 145.6, 130.5, 127.0, 126.4, 125.1, δ 120.9 (d, J = 25.1 Hz), 120.0 (d, J = 8.1 Hz), 114.5, 111.2 (d, J = 24.3 Hz), 16.8; FT-IR ν_{max} (neat) 3063, 1658, 1612, 1450, 1373, 1257, 1056, 779 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{10}FN_2O_2$ $[M + H]^+$ 269.0721, found 269.0722.

***2-Chloro-7-methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58cd*).**



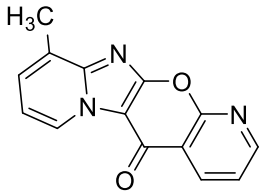
Cream colored solid (0.076 g, 59%); MP 273 – 275 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (d, J = 6.6 Hz, 1H), 8.37 (d, J = 2.5 Hz, 1H), 7.68 (dd, J = 8.9, 2.6 Hz, 1H), 7.62 (d, J = 8.8 Hz, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.15 (t, J = 6.9 Hz, 1H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 160.9, 152.9, 145.6, 133.2, 130.51, 130.4, 127.1, 126.4, 125.4, 125.0, 119.8, 114.6, 107.8, 16.8; FT-IR ν_{max} (neat) 3063, 1658, 1612, 1450, 1373, 1257, 1056, 779 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{15}H_{10}ClN_2O_2$ $[M + H]^+$ 285.0425, found 285.0430.

***2,3-Dimethoxy-7-methyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one* (*58ce*).**



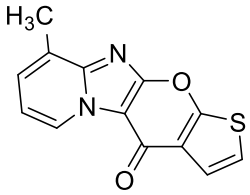
Cream colored solid (0.073 g, 58%); MP 250 – 252 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (d, J = 6.6 Hz, 1H), 7.77 (s, 1H), 7.46 (d, J = 7.1 Hz, 1H), 7.13 (d, J = 6.9 Hz, 1H), 7.10 (s, 1H), 4.06 (s, 3H), 4.05 (s, 3H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 160.7, 153.7, 150.3, 147.2, 146.8, 131.1, 129.6, 126.8, 126.3, 116.6, 114.1, 105.1, 100.4, 56.5, 56.4, 16.9; FT-IR ν_{max} (neat) 2924, 2850, 1666, 1635, 1612, 1504, 1458, 1438, 1257, 1226, 1114, 1026, 740 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{17}H_{15}N_2O_4$ $[M + H]^+$ 311.1026, found 311.1028.

***10-Methyl-pyrido[2",3":5',6']-5H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-5-one* (*58cf*).**



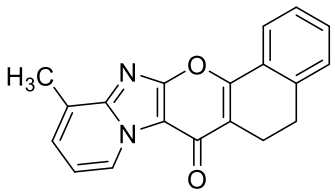
White solid (0.091 g, 68%); MP 238 – 239 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (d, J = 6.5 Hz, 1H), 8.82 (dd, J = 7.7, 1.9 Hz, 1H), 8.78 (dd, J = 4.6, 1.9 Hz, 1H), 7.58 – 7.54 (m, 1H), 7.54 – 7.50 (m, 1H), 7.17 (t, J = 6.9 Hz, 1H), 2.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 160.9, 159.0, 152.1, 145.9, 136.6, 130.7, 127.4, 126.3, 121.2, 119.0, 114.8, 107.9, 16.9; FT-IR ν_{max} (neat) 3085, 1640, 1609, 1519, 1458, 1357, 1240, 1109, 1041, 757 cm^{-1}; HRMS (+ESI-TOF, m/z): calcd for $C_{14}H_{10}N_3O_2$ $[M + H]^+$ 252.0768, found 252.0767

9-Methyl-4H-thieno[3'',2'':5',6']pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one (58cg).



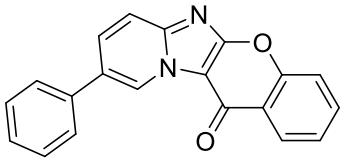
Yellow solid (0.084 g, 63%); MP 248 – 250 °C; ^{1}H NMR (400 MHz, $CDCl_3$ δ 9.25 (d, J = 6.6 Hz, 1H), 7.76 (d, J = 5.4 Hz, 1H), 7.45 (d, J = 7.1 Hz, 1H), 7.32 (d, J = 5.4 Hz, 1H), 7.11 (t, J = 6.9 Hz, 1H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 161.2, 156.0, 144.81, 131.15, 129.52, 127.00, 126.20, 123.81, 118.11, 114.22, 108.16, 16.88; FT-IR ν_{max} (neat) 3097, 2954, 2920, 1654, 1620, 1512, 1450, 1381, 1253, 1161, 1053, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_9N_2O_2S$ $[M + H]^+$ 257.0379, found 257.0381.

12-Methyl-5,6-dihydro-7H-benzo[7',8']chromeno[2',3':4,5]imidazo[1,2-a]pyridin-7-one (58ch).



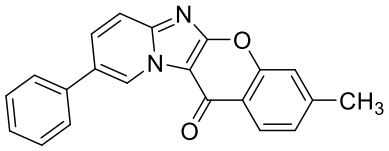
Red solid (0.047, 37%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (d, J = 6.7 Hz, 1H), 8.15 – 8.01 (m, 1H), 7.53 – 7.36 (m, 2H), 7.35 – 7.27 (m, 1H), 7.08 (t, J = 6.9 Hz, 1H), 3.03-2.99 (m, 4H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 159.9, 155.1, 144.5, 138.6, 130.5, 129.3, 128.5, 127.9, 127.1, 126.8, 126.1, 123.9, 118.7, 113.9, 27.2, 18.9, 16.9; FT-IR ν_{max} (neat): 3093, 2854, 1650, 1604, 1420, 1250, 1149, 1040, 847, 712, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{19}H_{15}N_2O_2$ $[M + H]^+$ 303.1128 found 303.1148.

9-Phenyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58da).



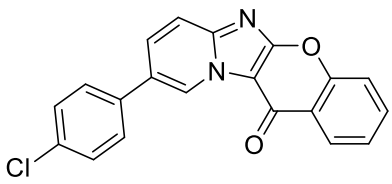
Off-white solid (0.080 g, 48%); MP 248 – 250 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 8.45 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.87 (d, J = 9.2 Hz, 1H), 7.78 (t, J = 7.0 Hz, 1H), 7.74 – 7.65 (m, 3H), 7.57 (s, 1H), 7.56 – 7.51 (m, 2H), 7.50 – 7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 161.5, 154.6, 144.5, 136.1, 133.3, 131.2, 129.3, 129.0, 128.5, 127.1, 126.0, 125.9, 124.5, 123.8, 118.3, 116.6, 107.8; FT-IR ν_{max} (neat) 3063, 1635, 1519, 1458, 1327, 1257, 1080, 1018, 802, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{20}H_{13}N_2O_2$ $[M + H]^+$ 313.0972, found 313.0974.

3-Methyl-9-phenyl-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58db).



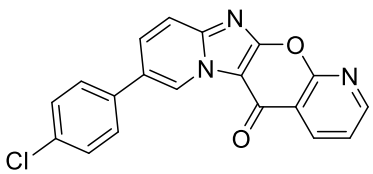
Off-white solid (0.045 g, 28%); MP 260 – 262 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 8.31 (d, J = 8.1 Hz, 1H), 7.93 (dd, J = 9.3, 1.8 Hz, 1H), 7.85 (d, J = 9.2 Hz, 1H), 7.69 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.5 Hz, 2H), 7.50 (s, 1H), 7.50 – 7.45 (m, 1H), 7.32 (d, J = 7.9 Hz, 1H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 161.4, 154.8, 144.7, 144.3, 136.1, 131.0, 129.3, 128.9, 128.4, 127.1, 125.9, 125.9, 125.7, 121.5, 118.3, 116.6, 107.7, 21.8; FT-IR ν_{max} (neat) 3063, 1635, 1620, 1519, 1458, 1327, 1257, 1111, 1041, 763 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{21}H_{15}N_2O_2$ $[M + H]^+$ 327.1128, found 327.1137.

9-(4-Chlorophenyl)-12H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-12-one (58ea).



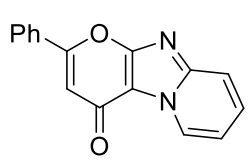
Off-white solid (0.102 g, 55%); MP 261 – 263 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 2H), 8.44 (dd, J = 7.9, 1.5 Hz, 1H), 7.93 – 7.83 (m, 2H), 7.82 – 7.75 (m, 1H), 7.71 (d, J = 7.6 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.55 – 7.52 (m, 2H), 7.52 – 7.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 161.5, 154.6, 144.4, 134.8, 134.6, 133.5, 130.8, 129.5, 128.4, 127.8, 126.00, 125.8, 124.6, 123.8, 118.4, 116.8, 107.9; FT-IR ν_{max} (neat) 3097, 3062, 1666, 1635, 1519, 1465, 1334, 1257, 1095, 1010, 810, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{20}H_{12}ClN_2O_2$ $[M + H]^+$ 347.0582, found 347.0594.

8-(4-Chlorophenyl)-pyrido[2",3":5',6']-5H-chromeno[2',3':4,5]imidazo[1,2-a]pyridin-5-one (58ef).



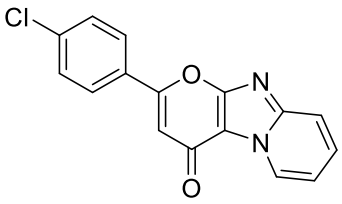
Sticky white compound (0.093 g, 50%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 8.83 (dd, J = 7.7, 2.0 Hz, 1H), 8.80 (dd, J = 4.6, 2.0 Hz, 1H), 7.95-7.89 (m, 2H), 7.65 – 7.60 (m, 2H), 7.58 (dd, J = 7.7, 4.7 Hz, 1H), 7.55 – 7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 161.4, 159.0, 152.3, 145.0, 136.7, 134.9, 134.3, 131.4, 129.6, 128.4, 128.3, 125.8, 121.4, 118.9, 117.2, 107.8; FT-IR ν_{max} (neat) 2948, 1640, 1519, 1460, 1320, 1223, 1020, 815, 757 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{19}H_{11}ClN_3O_2$ $[M + H]^+$ 348.0534, found 348.0531.

***2-Phenyl-4H-pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*60aa*).**



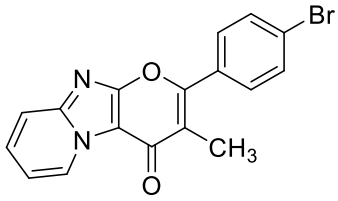
Brown viscous liquid (0.070 g, 57%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (d, J = 6.0 Hz, 1H), 8.05 – 7.89 (m, 2H), 7.78 (d, J = 8.7 Hz, 1H), 7.70 – 7.60 (m, 1H), 7.59 – 7.49 (m, 3H), 7.18 (t, J = 6.2 Hz, 1H), 6.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 161.1, 160.8, 150.4, 144.5, 131.4, 131.2, 130.5, 129.1, 128.5, 126.3, 116.9, 114.1, 109.7; FT-IR ν_{max} (neat) 3063, 1653, 1600, 1439, 1249, 1109, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{16}H_{11}N_2O_2$ $[M + H]^+$ 263.0815, found 263.0822.

***2-(4-Chlorophenyl)-4H-pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*60ab*).**



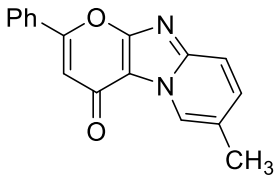
Viscous liquid (0.058 g, 48%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (d, J = 6.7 Hz, 1H), 7.96 – 7.87 (m, 2H), 7.79 (d, J = 9.1 Hz, 1H), 7.71 – 7.61 (m, 1H), 7.57 – 7.50 (m, 2H), 7.20 (td, J = 6.9, 1.0 Hz, 1H), 6.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 161.0, 159.7, 144.6, 137.5, 131.4, 130.7, 129.9, 129.4, 128.5, 127.5, 116.9, 114.2, 109.8; FT-IR ν_{max} (neat) 3020, 2920, 2850, 1643, 1627, 1524, 1450, 1257, 1114, 1091, 1006, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{16}H_{10}ClN_2O_2$ $[M + H]^+$ 297.0425, 299. 0401 found 297.0427 and 299.0399.

***2-(4-Bromophenyl)-3-methyl-4H-pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*60ac*).**



Viscous solid (0.054, 40%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (d, J = 6.7 Hz, 1H), 7.77 (d, J = 9.1 Hz, 1H), 7.69 (d, J = 8.1 Hz, 2H), 7.64 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 8.2 Hz, 2H), 7.18 (t, J = 6.9 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 160.6, 156.6, 153.9, 131.9, 131.7, 130.8, 130.5, 130.5, 128.4, 124.6, 119.6, 116.8, 113.9, 11.7; FT-IR ν_{max} (neat): 3035, 2839, 1656, 1600, 1389, 1250, 1111, 756, 715 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{17}H_{12}BrN_2O_2$ $[M + H]^+$ 355.0077, found 355.0065 and 357.0044.

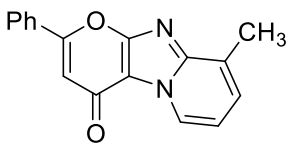
***7-Methyl-2-phenyl-4H-pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*60ba*).**



Cream solid (0.038 g, 29%); MP 284 – 286 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.06 – 7.90 (m, 2H), 7.67 (d, J = 9.1 Hz, 1H), 7.59 – 7.52 (m, 3H), 7.49 (d, J = 9.1 Hz, 1H), 6.89 (s, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 161.0, 160.6, 143.4, 133.5, 131.5,

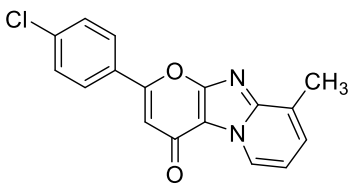
131.1, 129.0, 126.5, 126.2, 124.2, 116.2, 109.6, 18.1; FT-IR ν_{max} (neat) 3093, 1650, 1604, 1420, 1256, 1111, 756 cm^{-1}; HRMS (ESI-TOF, m/z): calcd for $C_{17}H_{13}N_2O_2$ $[M + H]^+$ 277.0972, found 277.0969.

***9-Methyl-2-phenyl-4H-pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*60ca*).**



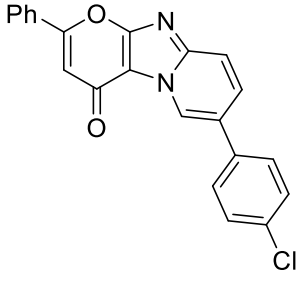
Cream solid (0.059 g, 45%); δ 9.18 (d, J = 6.5 Hz, 1H), 8.00 (d, J = 3.5 Hz, 2H), 7.58 – 7.49 (m, 3H), 7.46 (d, J = 7.0 Hz, 1H), 7.10 (t, J = 6.9 Hz, 1H), 6.91 (s, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ δ 170.4, 160.7, 151.3, 144.7, 131.5, 131.2, 129.6, 129.0, 126.9, 126.3, 126.2, 114.1, 109.7, 16.9; FT-IR ν_{max} (neat) 3097, 2924, 2854, 1627, 1573, 1446, 1253, 1161, 1111, 867, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{17}H_{13}N_2O_2$ $[M + H]^+$ 277.0972, found 277.0979.

***2-(4-Chlorophenyl)-9-methyl-4H-pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*60cb*).**



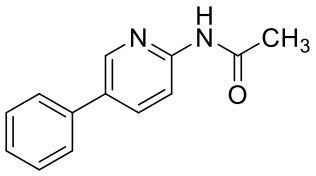
Cream colored solid (0.053 g, 42%); MP 284 – 286 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (d, J = 6.7 Hz, 1H), 7.96 – 7.87 (m, 2H), 7.79 (d, J = 9.1 Hz, 1H), 7.71 – 7.61 (m, 1H), 7.57 – 7.50 (m, 2H), 7.20 (td, J = 6.9, 1.0 Hz, 1H), 6.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 160.6, 159.5, 144.7, 137.4, 129.9, 129.7, 129.4, 127.5, 127.0, 126.2, 114.2, 109.8, 16.9; FT-IR ν_{max} (neat) 3084, 1656, 1608, 1434, 1256, 1111, 1056, 756 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{17}H_{12}ClN_2O_2$ $[M + H]^+$ 311.0582, found 311.0586.

***7-(4-Chlorophenyl)-2-phenyl-4H-pyrano[2',3':4,5]imidazo[1,2-a]pyridin-4-one* (*60ea*).**



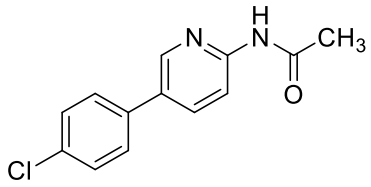
Viscous liquid (0.060 g, 35%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 3H), 8.00 (d, J = 2.7 Hz, 1H), 7.98 (d, J = 3.3 Hz, 1H), 7.86 (d, J = 1.6 Hz, 2H), 7.62 (d, J = 8.5 Hz, 3H), 7.59 – 7.55 (m, 3H), 7.52 (d, J = 8.5 Hz, 2H), 6.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 161.3, 161.0, 146.6, 143.6, 134.7, 134.6, 134.6, 131.3, 130.5, 129.5, 129.1, 128.4, 127.6, 126.3, 125.6, 116.9, 109.7; FT-IR ν_{max} (neat) 3062, 2924, 2854, 1643, 1631, 1577, 1465, 1261, 1091, 817, 694 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{22}H_{14}ClN_2O_2$ $[M + H]^+$ 373.0738, found 373.0744.

N-(5-Phenylpyridin-2-yl)acetamide (62d).[64]



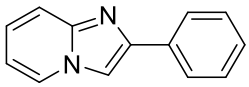
Cream solid (0.021 g, 18%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.52 (s, 1H), 8.32 (d, J = 8.5 Hz, 1H), 7.95 (dd, J = 8.6, 2.2 Hz, 1H), 7.59-7.56 (m, 2H), 7.49 (t, J = 7.5 Hz, 2H), 7.44 – 7.35 (m, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 145.9, 141.0, 132.6, 132.2, 128.1, 124.3, 123.0, 122.0, 109.2, 20.0; FT-IR ν_{max} (neat) 3240, 3039, 2924, 1658, 1527, 1373, 1303, 1018, 763 cm^{-1}.

N-(5-(4-Chlorophenyl)pyridin-2-yl)acetamide (62e).



Cream solid (0.020 g, 15%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.32 (s, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.2 Hz, 2H), 7.45 (d, J = 7.8 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.67, 150.71, 145.75, 136.72, 135.85, 133.99, 131.73, 129.26, 127.99, 113.79, 24.79; FT-IR ν_{max} (neat) 3242, 3037, 2923, 1657, 1524, 1371, 1305, 1011, 761 cm^{-1}; HRMS (ESI-TOF, *m/z*): calcd for $C_{13}H_{11}ClN_2O$ $[M + H]^+$ 246.0560, found 246.0558.

2-Phenylimidazo[1,2-a]pyridine (66).[65]



Cream colored solid (0.018, 10%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dt, J = 6.8, 1.2 Hz, 1H), 8.02 – 7.95 (m, 2H), 7.87 (s, 1H), 7.65 (dq, J = 9.1, 1.1 Hz, 1H), 7.51 – 7.41 (m, 2H), 7.39 – 7.32 (m, 1H), 7.18 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.78 (td, J = 6.7, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 145.7, 133.8, 128.7, 127.9, 126.0, 125.5, 124.6, 117.5, 112.4, 108.1.

4.4.5 Single X-ray Analysis of 2-Chloro-7-methyl-12*H*-chromeno[2',3':4,5]imidazo[1,2-*a*]pyridin-12-one (58cd).

4.4.5.1 Experimental

Single crystals of $C_{15}H_9ClN_2O_2$ (**58cd**) were generated. A suitable crystal was selected and analyzed on a XtaLAB Pro: Kappa dual home/near diffractometer. The crystal was kept at 93(2) K during data collection. Using Olex2 [66], the structure was solved with the ShelXT [67] structure

solution program using Intrinsic Phasing and refined with the ShelXL [68] refinement package using Least Squares minimisation.

Crystal Data for $C_{15}H_9ClN_2O_2$ (M =284.69 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 7.7771(3) Å, b = 21.9081(4) Å, c = 7.8071(2) Å, β = 115.213(4)°, V = 1203.46(7) Å^3, Z = 4, T = 93(2) K, μ(CuKα) = 2.841 mm^{-1}, *Dcalc* = 1.571 g/cm^3, 3647 reflections measured (8.072° ≤ 2Θ ≤ 148.528°), 1912 unique (R_{int} = 0.0180, R_{sigma} = 0.0254) which were used in all calculations. The final R_1 was 0.0372 (I > 2σ(I)) and wR_2 was 0.1062 (all data).

Refinement Model Description

Number of restraints - 0, number of constraints - unknown.

Details:

1.Fixed Uiso At 1.2 times of: All C(H) groups At 1.5 times of: All C(H, H, H) groups
2.a) Aromatic/amide H refined with riding coordinates: C15(H15), C2(H2), C12(H12), C1(H1), C13(H13),C3(H3)
2.b) Idealized Me refined as rotating group: C6(H6A, H6B, H6C)

Table 4.4 Crystal data and structure refinement for **58cd**.

Identification code	EXP-186-KP-806_reduced
Empirical formula	$C_{15}H_9ClN_2O_2$
Formula weight	284.69
Temperature/K	93(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	7.7771(3)
b/Å	21.9081(4)
c/Å	7.8071(2)
α/°	90

β/°	115.213(4)
γ/°	90
Volume/Å^3	1203.46(7)
Z	4
ρ_{calc}g/cm^3	1.571
μ/mm^{-1}	2.841
F(000)	584.0
Crystal size/mm^3	0.2 × 0.05 × 0.02
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.072 to 148.528
Index ranges	-8 ≤ h ≤ 8, -26 ≤ k ≤ 26, -9 ≤ l ≤ 9
Reflections collected	3647
Independent reflections	1912 [R_{int} = 0.0180, R_{sigma} = 0.0254]
Data/restraints/parameters	1912/0/182
Goodness-of-fit on F^2	1.070
Final R indexes [I>=2σ (I)]	R_1 = 0.0372, wR_2 = 0.1050
Final R indexes [all data]	R_1 = 0.0385, wR_2 = 0.1062
Largest diff. peak/hole / e Å^{-3}	0.27/-0.39

Table 4.5 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) **58cd**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***X***	***y***	***Z***	**U(eq)**
Cl1	6048.7(7)	2533.3(2)	4006.9(6)	26.56(18)
O1	1955.3(19)	4872.0(6)	2052.3(15)	23.9(3)
O2	4353(2)	4317.1(6)	7729.5(16)	27.1(3)
N1	2058(2)	5494.7(6)	6219(2)	21.7(4)

N2	853(2)	5729.9(7)	3078.1(19)	24.1(4)
C8	2570(3)	5025.2(8)	5334(2)	21.9(4)
C7	1785(3)	5202.9(8)	3433(2)	21.9(4)
C10	3788(3)	4127.7(8)	4502(2)	21.1(4)
C9	3636(3)	4485.7(8)	6058(2)	22.7(4)
C11	2936(3)	4327.4(8)	2610(2)	22.2(4)
C4	274(3)	6433.3(8)	5289(2)	24.1(4)
C15	4749(3)	3570.4(8)	4913(2)	23.0(4)
C5	1015(3)	5909.7(8)	4806(2)	22.6(4)
C14	4839(3)	3230.1(8)	3474(2)	23.7(4)
C2	1692(3)	6072.4(8)	8561(2)	26.1(4)
C12	3031(3)	3978.2(9)	1166(2)	25.6(4)
C1	2397(3)	5569.6(8)	8087(2)	24.8(4)
C13	3980(3)	3425.3(8)	1598(2)	25.1(4)
C3	625(3)	6504.3(8)	7165(2)	25.9(4)
C6	-889(3)	6874.7(9)	3755(3)	29.5(5)

Table 4.6 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **58cd**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
Cl1	28.8(4)	22.5(3)	26.0(3)	0.58(14)	9.4(2)	1.36(16)
O1	25.8(9)	23.6(6)	18.7(6)	2.3(4)	5.9(5)	2.7(5)
O2	30.6(9)	28.0(7)	17.5(6)	3.1(5)	5.3(5)	2.5(6)
N1	21(1)	20.5(7)	20.9(7)	0.9(5)	6.4(6)	-0.9(6)
N2	24.3(11)	23.0(7)	21.0(7)	1.9(5)	5.6(6)	-0.3(6)
C8	21.0(12)	21.9(8)	19.2(8)	0.3(6)	5.1(7)	-2.6(8)

C7	21.5(11)	22.0(8)	18.5(8)	0.2(6)	5.0(7)	-3.2(7)
C10	19.3(11)	22.6(8)	18.9(8)	1.1(6)	5.6(7)	-4.0(7)
C9	20.9(12)	24.8(9)	18.4(8)	0.1(6)	4.6(7)	-2.4(7)
C11	18.8(11)	21.5(8)	21.7(8)	1.8(6)	4.3(7)	-1.5(7)
C4	19.3(12)	21.5(9)	26.8(9)	1.8(6)	5.3(7)	-1.9(7)
C15	21.5(12)	24.7(9)	19.2(8)	2.5(6)	5.2(7)	-2.1(7)
C5	19.2(12)	22.7(8)	21.1(8)	2.3(6)	3.9(7)	-3.2(7)
C14	20.8(12)	22.3(8)	25.8(8)	0.7(6)	7.7(7)	-2.5(7)
C2	25.4(12)	27.6(9)	22.5(8)	-2.1(7)	7.4(7)	-3.1(8)
C12	23.5(12)	31.3(9)	18.8(8)	2.4(6)	6.1(7)	-0.5(8)
C1	24.1(12)	26.1(9)	19.0(8)	1.4(6)	4.2(7)	-2.7(7)
C13	26.0(12)	25.6(9)	22.2(8)	-2.7(6)	8.9(7)	-2.1(8)
C3	23.4(12)	22.8(9)	29.8(9)	-1.8(7)	9.8(8)	-1.7(8)
C6	29.4(13)	24.9(9)	28.4(9)	2.8(7)	6.9(8)	2.4(8)

Table 4.7 Bond Lengths for **58cd**.

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
Cl1	C14	1.7479(19)	C10	C11	1.407(2)
O1	C7	1.351(2)	C10	C15	1.396(3)
O1	C11	1.383(2)	C11	C12	1.390(3)
O2	C9	1.237(2)	C4	C5	1.406(3)
N1	C8	1.389(2)	C4	C3	1.380(3)
N1	C5	1.393(2)	C4	C6	1.505(2)
N1	C1	1.376(2)	C15	C14	1.375(3)
N2	C7	1.328(2)	C14	C13	1.393(2)

N2	C5	1.359(2)	C2	C1	1.351(3)
C8	C7	1.399(2)	C2	C3	1.415(3)
C8	C9	1.416(2)	C12	C13	1.383(3)
C10	C9	1.492(2)			

Table 4.8 Bond Angles for **58cd**.

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
C7	O1	C11	116.13(13)	O1	C11	C12	115.62(15)
C8	N1	C5	106.43(14)	C12	C11	C10	121.11(18)
C1	N1	C8	130.47(15)	C5	C4	C6	119.13(16)
C1	N1	C5	123.08(15)	C3	C4	C5	117.30(16)
C7	N2	C5	103.52(14)	C3	C4	C6	123.55(18)
N1	C8	C7	103.53(15)	C14	C15	C10	119.68(15)
N1	C8	C9	131.54(15)	N1	C5	C4	119.14(15)
C7	C8	C9	124.93(16)	N2	C5	N1	111.95(16)
O1	C7	C8	123.39(16)	N2	C5	C4	128.91(16)
N2	C7	O1	122.03(14)	C15	C14	Cl1	119.24(14)
N2	C7	C8	114.57(15)	C15	C14	C13	121.62(18)
C11	C10	C9	121.75(17)	C13	C14	Cl1	119.15(14)
C15	C10	C9	119.56(15)	C1	C2	C3	120.49(16)
C15	C10	C11	118.67(16)	C13	C12	C11	119.41(16)
O2	C9	C8	126.48(16)	C2	C1	N1	118.08(16)
O2	C9	C10	123.03(17)	C12	C13	C14	119.51(16)
C8	C9	C10	110.50(14)	C4	C3	C2	121.90(18)
O1	C11	C10	123.27(16)				

Table 4.9 Hydrogen Atom Coordinates ($Å \times 10^4$) and Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **58cd.**

Atom	*X*	*y*	*z*	U(eq)
H15	5327.1	3430.04	6154.6	28
H2	1909.46	6135.14	9815.5	31
H12	2461.59	4115.02	-79.98	31
H1	3092.1	5282.3	8995.48	30
H13	4044.16	3185.75	643.67	30
H3	146.34	6845.96	7522.28	31
H6A	-230.82	6967.91	2989.08	44
H6B	-1079.32	7243.01	4317.62	44
H6C	-2098.19	6694.7	2978.93	44

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