JOC The Journal of Organic Chemistry

Article

Copper [Cu]-Catalyzed Tandem O-Arylation–Oxidative Cross Coupling: Synthesis of Chromone Fused Pyrazoles

Surisetti Suresh, Owk Obulesu, K. Harish Babu, and Jagadeesh Babu Nanubolu

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b02890 • Publication Date (Web): 22 Feb 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

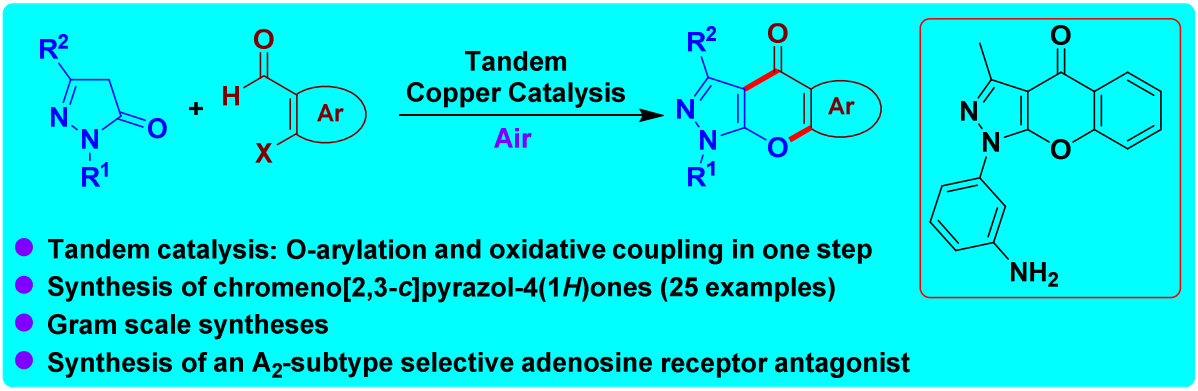
Copper [Cu]-Catalyzed Tandem O-Arylation–Oxidative Cross Coupling: Synthesis of Chromone Fused Pyrazoles

Owk Obulesu,[†,‡] K. Harish Babu,[†] Jagadeesh Babu Nanubolu[§] and Surisetti Suresh*[,†,‡]

[†]Organic and Biomolecular Chemistry Division, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500 007, India

[‡]Academy of Scientific and Innovative Research (AcSIR), CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500 007, India

[§]Center for X-Ray Crystallography, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad, 500 007, India



ABSTRACT: Intermolecular tandem copper catalyzed O-arylation–oxidative acylation (cross dehydrogenative coupling-CDC) has been developed under air as an oxidant. The reaction between 2,4-dihydro-3*H*-pyrazol-3-ones and *ortho*-halo aryl carboxaldehydes furnished the corresponding chromone fused pyrazoles, in a straightforward manner. The synthetic utility of the presented tandem catalysis has been demonstrated with the synthesis of an A_2-subtype selective adenosine receptor antagonist in only two steps.

INTRODUCTION

Owing to its outstanding atom and step efficiencies, direct C-H bond functionalization has emerged as a powerful tool in organic synthesis over the past decades. Transition metal catalyzed C-H functionalization *via* C-H activation has received a great deal of attention from organic chemists.[1] In most of the cases, the success of these processes depends on the assistance from the deliberate installation/design of the directing groups. Direct coupling between two C-H centers, known as CDC or oxidative cross coupling (often *via* dual C-H activation), has proven to be one of the most important methods for the construction of C-C bonds in the plethora of C-H functionalization reactions.[2] Intermolecular CDC between (aryl)aldehyde C-H bonds and olefin[3] or arene[4] C-H bonds, acylation of sp^2 C-H bonds using aldehydes, has emerged as a method of interest for the synthesis of aryl ketones (Figure 1, i). The intramolecular CDC processes provide privileged bicyclic and tricyclic compounds with a ketone functionality.[5] Xanthones,[5c,d,f,h] thioxanthones,[5h] fluorenones,[5d,g,h] acridinones,[5e,i] isatins,[5b] pyrazole-chromone[5j] and indole-indolone[5k] scaffolds *etc.* have been synthesized using this synthetic strategy (Figure 1, ii). However, for such intramolecular transformations, the necessary precursor need to be pre-synthesized. In most of these methods, the acylation of arenes with aldehydes rely on the use of stoichiometric/excess amounts of expensive or unfriendly oxidizing agents.[5] Although pure molecular oxygen[5b] has been used as the oxidant of choice in the transition metal catalyzed CDC, use of atmospheric air[4a,6] would be more attractive. Development of methods to synthesize cyclic ketones in an intermolecular fashion involving arylation-oxidative coupling (Figure 1, iii) using air as an oxidant would be highly beneficial from the synthetic standpoint.

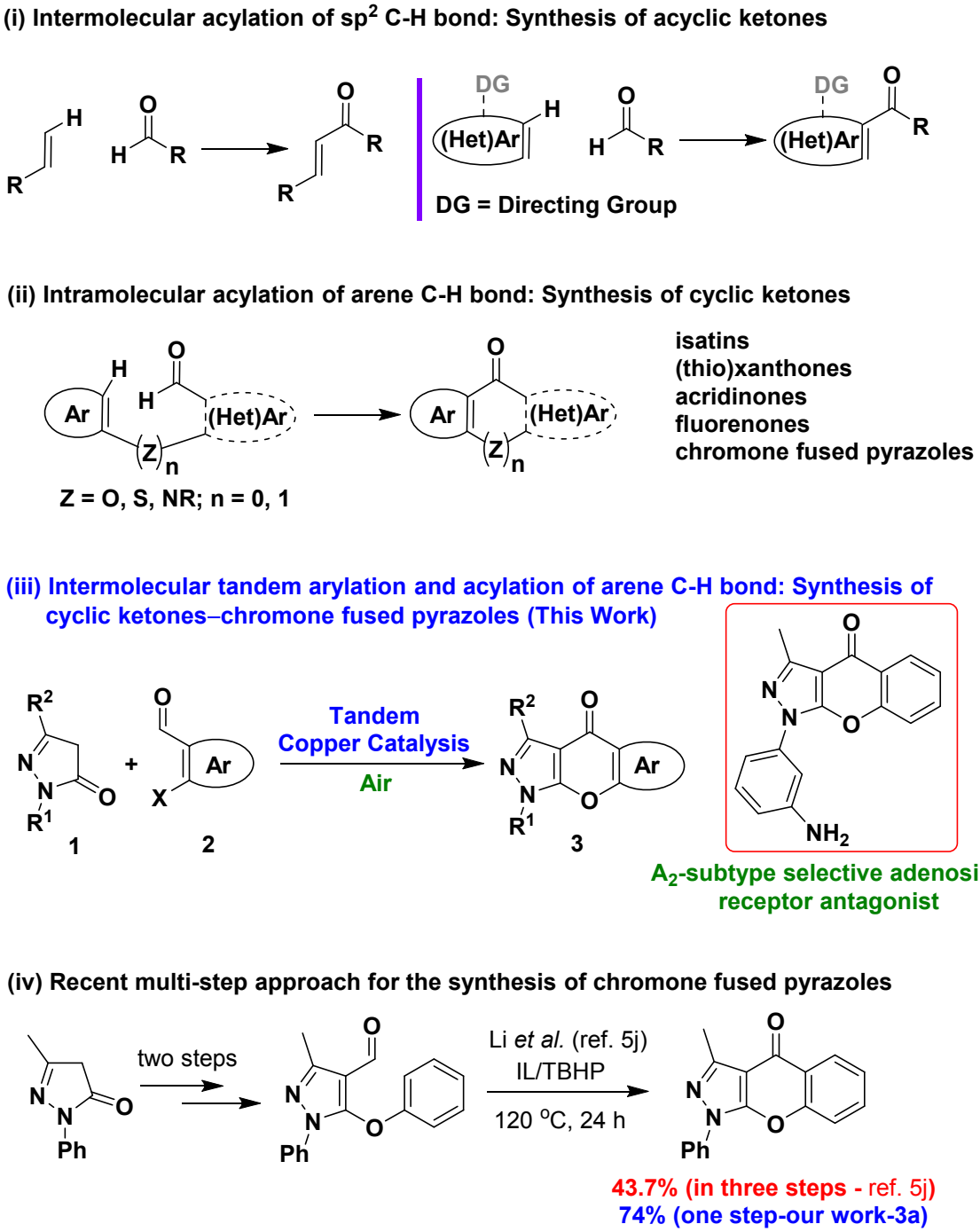


Figure 1. Inter- and intramolecular CDC between sp^2 C-H bonds of aldehydes and olefin/arene; This Work.

RESULTS AND DISCUSSION

We envisioned a synthetic strategy for the construction of cyclic ketones from intermolecular reaction with the development of tandem arylation-oxidative coupling, obviating the synthesis of specific intermediates. Continuing our interest in the development of tandem reactions triggered by copper catalysis,[7] we envisaged to develop tandem O-arylation-oxidative coupling process. To test this hypothesis we have selected 2,4-dihydro-3*H*-pyrazol-3-ones **1** and 2-haloaryl aldehydes **2** as coupling partners that would eventually lead to the synthesis of chromone fused pyrazoles, chromeno[2,3-*c*]pyrazol-4(1*H*)-ones **3** (Figure 1, iii).[8,9] Indeed, this kind of chromone fused pyrazoles have shown important biological activities such as selective (A_{2A} or A_1) adenosine receptor antagonist.[8] It should be mentioned that the chromone fused pyrazoles have been prepared using multi-step synthesis associated with harsh reaction conditions, use of excess amounts of reagents/oxidants, prolonged reaction times and with the outcome of low overall yields[5j,8a-b,9] (for example, see Figure 1, iv).

At the outset, we engaged in the development of tandem[10] copper-catalyzed[11] O-arylation[12] followed by oxidative cyclization to synthesize **3—**starting from 2,4-dihydro-3*H*-pyrazol-3-ones **1** and *ortho*-halo substituted aryl aldehydes **2** (Figure 1, iii). Initially, we chose 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one **1a** and 2-bromobenzaldehyde **2a** as partners to test this tandem reaction process.

We have preformed the reaction by using $Cu(OAc)_2$ as a catalyst, 1,10-phenanthroline as a ligand, and K_2CO_3 as a base in a vial, closed in the presence of air. Gratifyingly, this reaction afforded the desired chromone fused pyrazole **3a** in 54% yield (Table 1, entry 1). Encouraged by this result, we have conducted an optimization study with respect to different transition metal catalysts, ligands, and bases (Table 1; entries 1-12, for a detailed optimization study, see

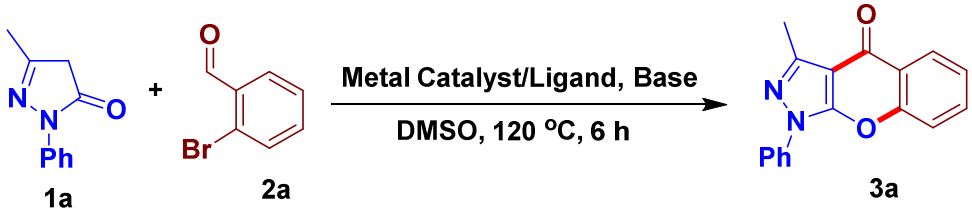
supporting information). As a result of this study, it turned out that the combination of CuI–1,10-phenanthroline–K_2CO_3 proved to be the best among a set of conditions screened (Table 1, entry 4). Performing the reaction with optimized conditions (Table 1, entry 4) under inert atmosphere of argon resulted in very low yield of the desired product which indicated that the reaction requires air/oxygen (Table 1, entry 9). When the reaction was conducted under an oxygen atmosphere, there was a decrease in the yield (Table 1, entry 10)—probably due to the oxidation of the aldehyde under this condition. However, this tandem process was not successful with the use of other transition metal compounds of Pd, Ru, Fe and In, under the reaction conditions (see supporting information). It should be mentioned that in the absence of CuI/ligand the reaction did not proceed (Table 1, entries 11 and 12). These experiments suggest that CuI is the choice of the transition metal catalyst and air serves as the oxidant for such tandem catalysis.

After having the set of optimized conditions, we focused our attention on extending the scope of this process by using different 2,4-dihydro-3*H*-pyrazol-3-ones **1** and various *ortho*-halo aromatic aldehydes **2** (Scheme 1). Primarily, we set on to evaluate the leaving halogen group in this tandem process. It turned out that *ortho*-bromo substituted benzaldehyde gave better yields of the desired product when compared to 2-chlorobenzaldehyde or 2-iodobenzaldehyde (see **3a**, Scheme 1 and supporting information for other leaving groups).

Later we studied the scope of this reaction using differently substituted *ortho*-bromobenzaldehydes and **1a**. Electron donating groups on *ortho*-bromobenzaldehydes **2d**-**2f** have tolerated well to give the corresponding chromone fused pyrazoles **3b**-**3d** in good yields (Scheme 1). The structure of the chromone fused pyrazole derivative **3d** was also confirmed by X-ray crystal structure analaysis (supporting information). Electron withdrawing group like fluorine on *ortho*-bromobenzaldehyde gave the corresponding product **3e**, albeit in moderate

yield (Scheme 1). The reaction of **1a** and 2,5-dibromobenzaldehyde **2h** gave the corresponding bromo substituted chromone fused pyrazole **3f** in 68% yield (Scheme 1).

Table 1. Optimization study.[a]



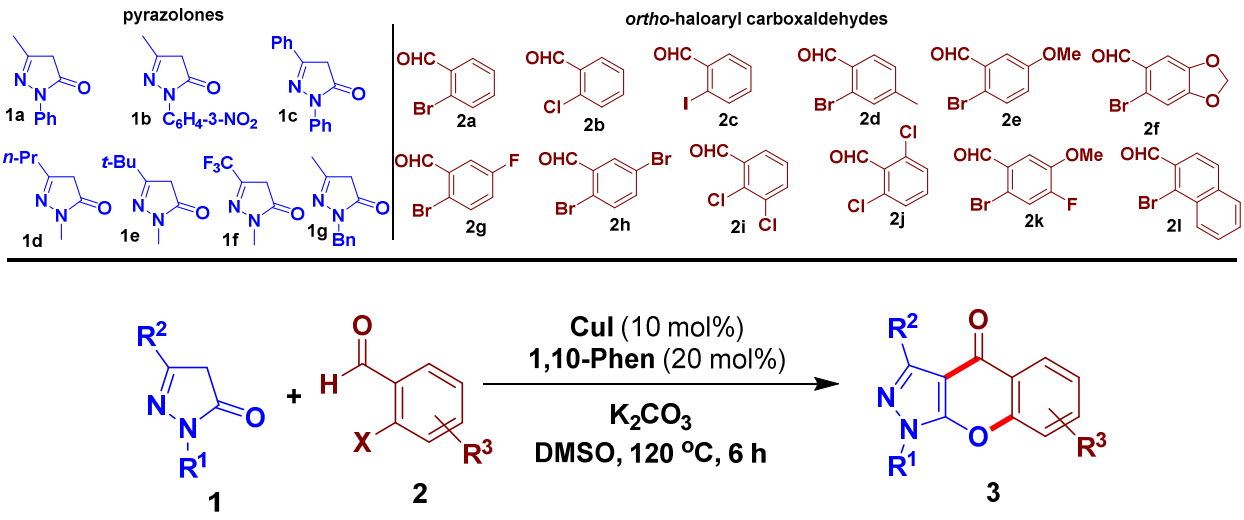
Entry	Metal Catalyst	Ligand	Base	%yield of 3a
1	$Cu(OAc)_2$	1,10-phenanthroline	K_2CO_3	54
2	Cu_2O	1,10-phenanthroline	K_2CO_3	32
3	CuBr	1,10-phenanthroline	K_2CO_3	58
4	**CuI**	**1,10-phenanthroline**	**K_2CO_3**	**74**[b]
5	CuI	DMEDA	K_2CO_3	56
6	CuI	IMes	K_2CO_3	45
7	CuI	(L)-proline	K_2CO_3	64
8	CuI	1,10-phenanthroline	K_3PO_4	39
9	CuI	1,10-phenanthroline	K_2CO_3	18[c]
10	CuI	1,10-phenanthroline	K_2CO_3	16[d]
11	CuI	—	K_2CO_3	NR
12	—	—	K_2CO_3	NR

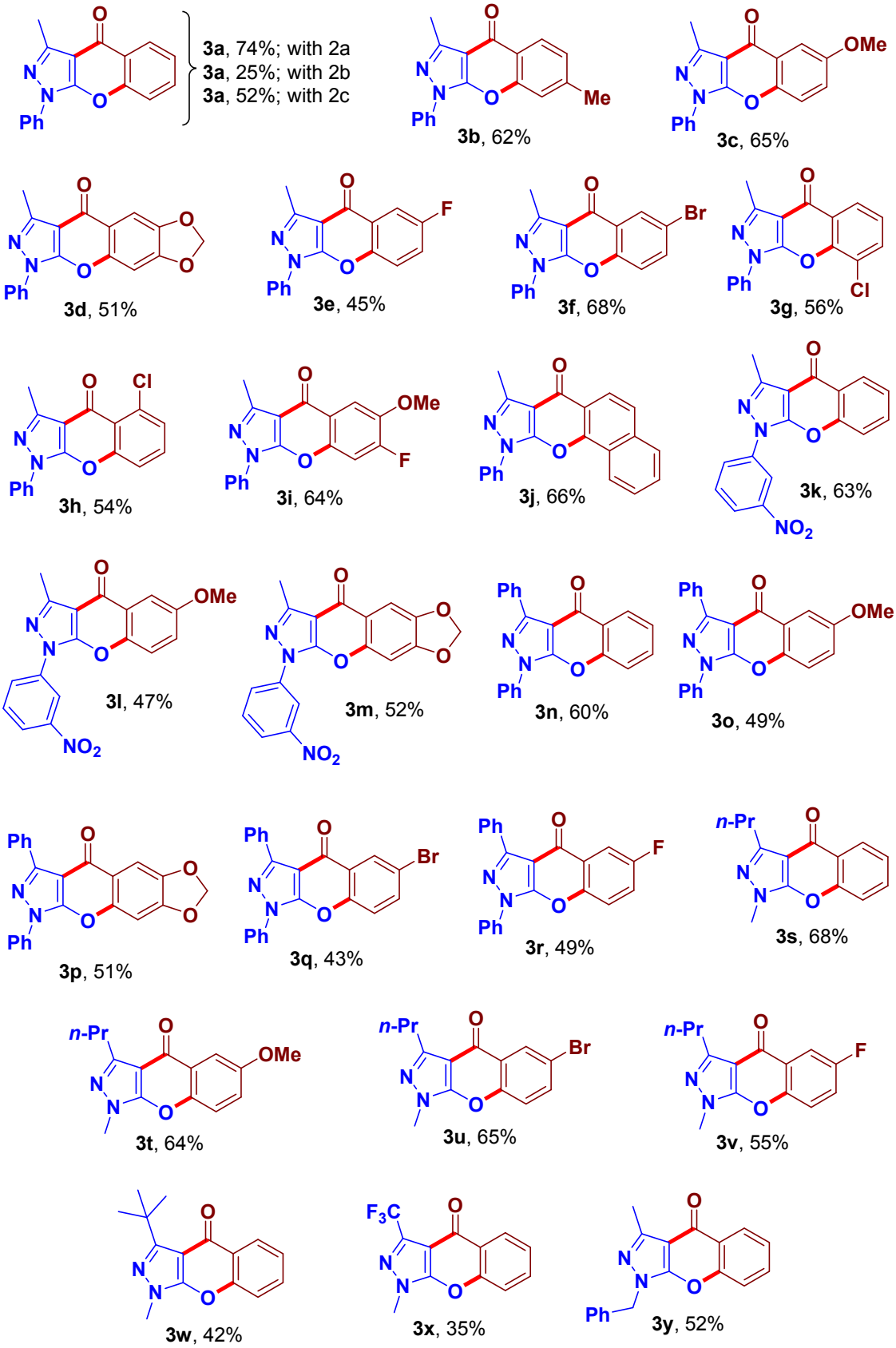
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), metal catalyst (0.05 mmol), ligand (0.1 mmol), base (1.65 mmol), DMSO (2 mL); [b] same result was obtained when the reaction was performed in a open vial; [c] Reaction was performed under argon atmosphere in dry DMSO; [d] Reaction was performed under oxygen atmosphere in dry

DMSO; DMEDA: *N*,*N*′-dimethylethylenediamine; IMes: 1,3-bis(2,4,6-trimethylphenyl)-imidazolium chloride; NR: No Reaction.

It is also interesting to note that chlorine also served as a good leaving group as 2,3-dichlorobenzaldehyde **2i** and 2,6-dichlorobenzaldehyde **2j** provided the corresponding chromone fused pyrazoles bearing chlorine substituents (**3g** and **3h**, Scheme 1). *ortho*-Bromobenzaldehyde bearing both electron withdrawing and donating substituents **2k** afforded the corresponding product **3i** in good yield (Scheme 1). Tetracyclic chromone fused pyrazole **3j** was synthesized in good yield using of 1-bromo-2-napththaldehyde **2l** (Scheme 1). The tandem process was well successful by using different electron withdrawing groups and donating groups on pyrazole systems **1b**-**1f**, furnishing the diversely substituted chromone fused pyrazole frameworks **3k**-**3y** in moderate to good yields (Scheme 1). However, the reaction of *N*-Boc pyrazolone and 2-bromobenzaldehyde did not give the desired product. The starting materials have been recovered. This transformation was also not successful with heteroaromatic aldehydes such as 2-chloronicotinaldehyde and pyrazolone **1a**.

Scheme 1. Reaction of pyrazolones 1 and *ortho*-halo aryl aldehydes 2.[a]



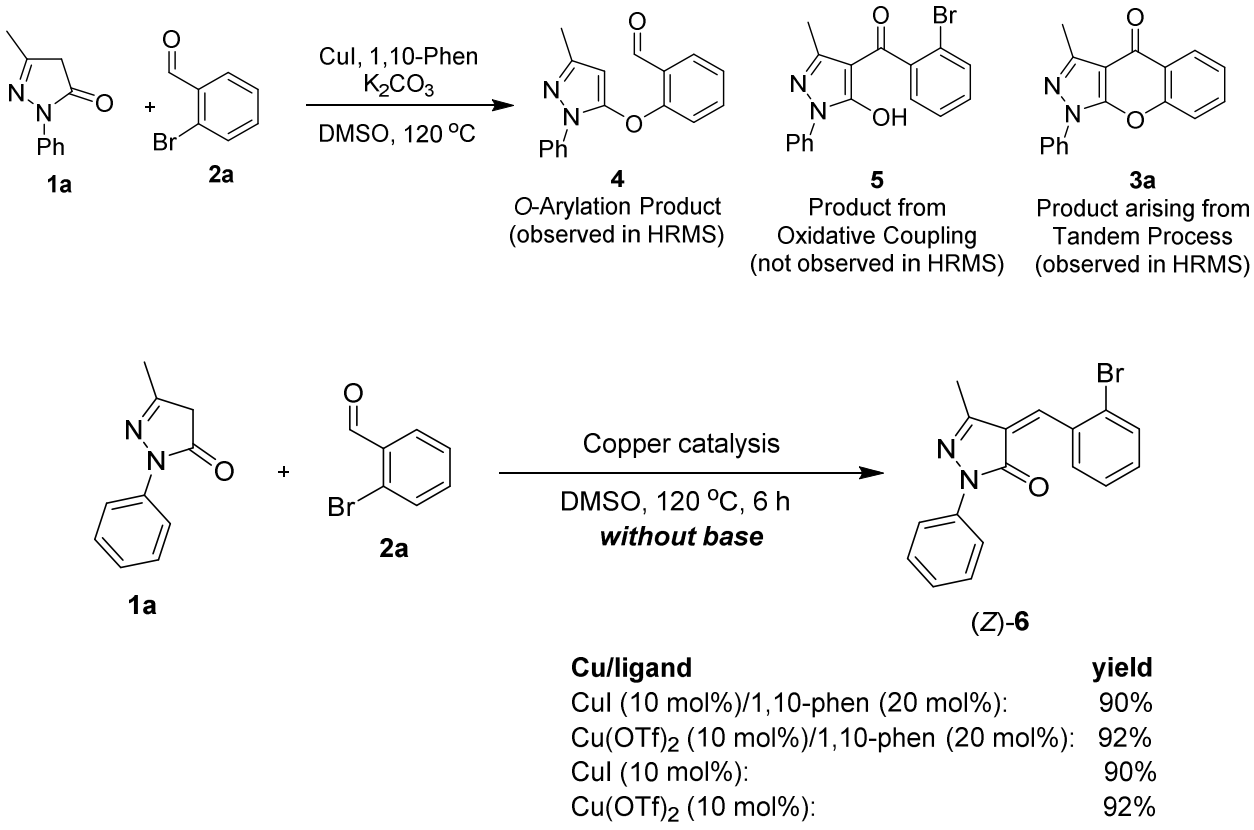

3a, 74%; with 2a
3a, 25%; with 2b
3a, 52%; with 2c
3b, 62%
3c, 65%
3d, 51%
3e, 45%
3f, 68%
3g, 56%
3h, 54%
3i, 64%
3j, 66%
3k, 63%
3l, 47%
3m, 52%
3n, 60%
3o, 49%
3p, 51%
3q, 43%
3r, 49%
3s, 68%
3t, 64%
3u, 65%
3v, 55%
3w, 42%
3x, 35%
3y, 52%

[a] Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), CuI (0.05 mmol), 1,10-phen (0.1 mmol), K_2CO_3 (1.65 mmol), DMSO (2 mL).

To understand the reaction mechanism, we conducted some control experiments. To know whether the reaction goes through a radical intermediate, we have added TEMPO (1 equiv) to the reaction. In this case, the product **3a** was formed in good yield which may indicate that no radical intermediate is involved in this reaction pathway (see supporting information).

It was thought that the present tandem copper catalyzed O-arylation–oxidative acylation would involve the intermediates **4** or **5** that could result from the sole O-arylation or sole oxidative coupling, respectively (Scheme 2, top). We have monitored the reaction of **1a** and **2a** by HRMS at different time intervals (after 1 h, 2 h, 4 h and 6 h) to find out whether the formation of intermediates **4** or **5** occurs. From HRMS analysis, mass corresponding to the product **3a** was observed as a major peak while mass corresponding to the O-arylation intermediate **4** was also observed as a minor peak. Our efforts to isolate this intermediate were not successful. No peak corresponding to **5** was observed in HRMS. This suggests that the reaction might be going through O-arylation followed by oxidative cross coupling *via* C-H activation. However, the Friedel-Crafts type intermediate in the present tandem reaction may be ruled out due to the reasons: (i) the reaction is conducted under basic medium, (ii) formation of condensation product **6** in the absence of the base (Scheme 2, bottom), probably *via* Friedel-Crafts type reaction,[13] (iii) significant drop in the yield of the product **3a** with deuterated **1a-D** (see, supporting information). These experiments may suggest that C-H activation is the key step in the present tandem process.

Scheme 2. Control experiments.

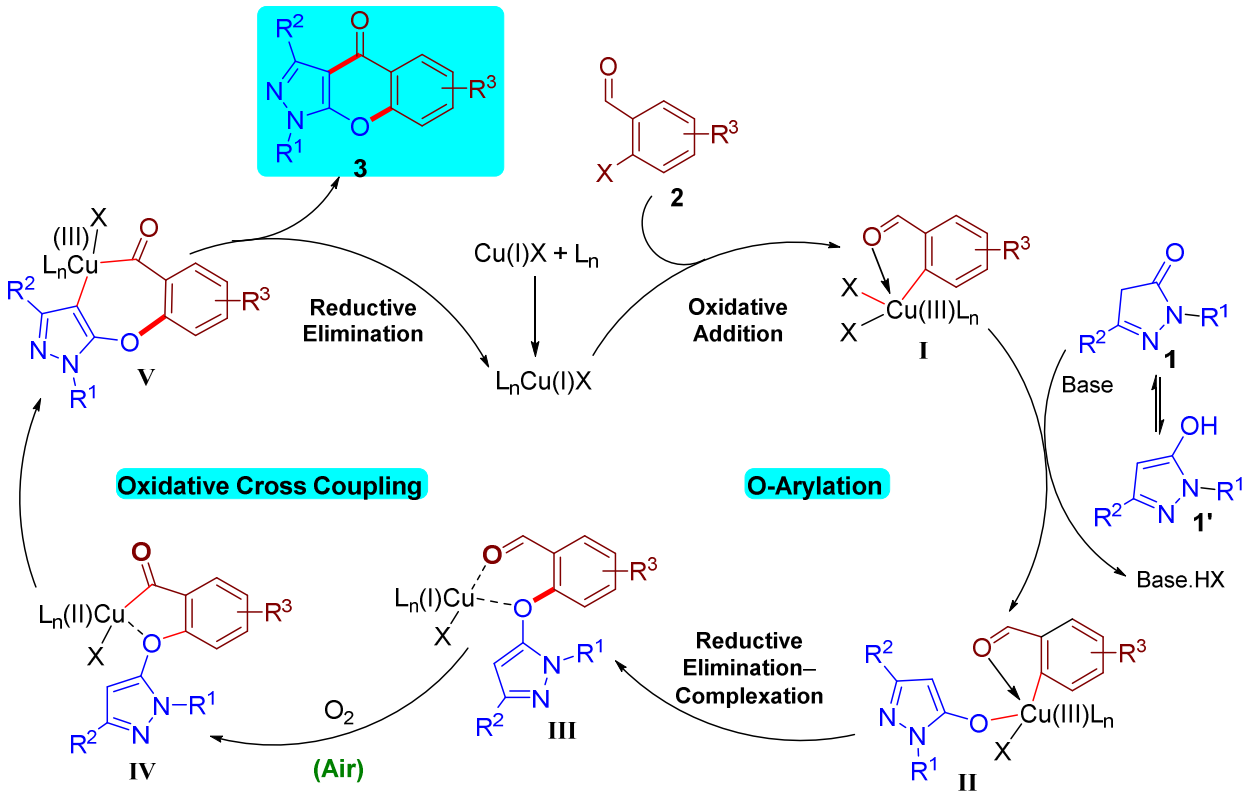


Cu/ligand	yield
CuI (10 mol%)/1,10-phen (20 mol%):	90%
$Cu(OTf)_2$ (10 mol%)/1,10-phen (20 mol%):	92%
CuI (10 mol%):	90%
$Cu(OTf)_2$ (10 mol%):	92%

Based on the literature report by Li and co-workers on a copper-catalyzed intramolecular C-H oxidation/acylation[5b] and above control experiments, a plausible reaction mechanism may be tentatively proposed for the present tandem catalysis (Scheme 3). Initially, intermediate **I** would be formed by the oxidative addition of *ortho*-haloaryl aldehyde **2** with copper catalyst. In the presence of base, pyrazole **1** would undergo complexation with intermediate **I** to give intermediate **II**. Reductive elimination of **II** followed by complexation with the Cu(I) would lead to the formation of intermediate **III**. The thus generated **III** would form an intermediate **IV** upon oxidative insertion in the presence of oxygen. The intermediate **IV** would lead to the cyclized

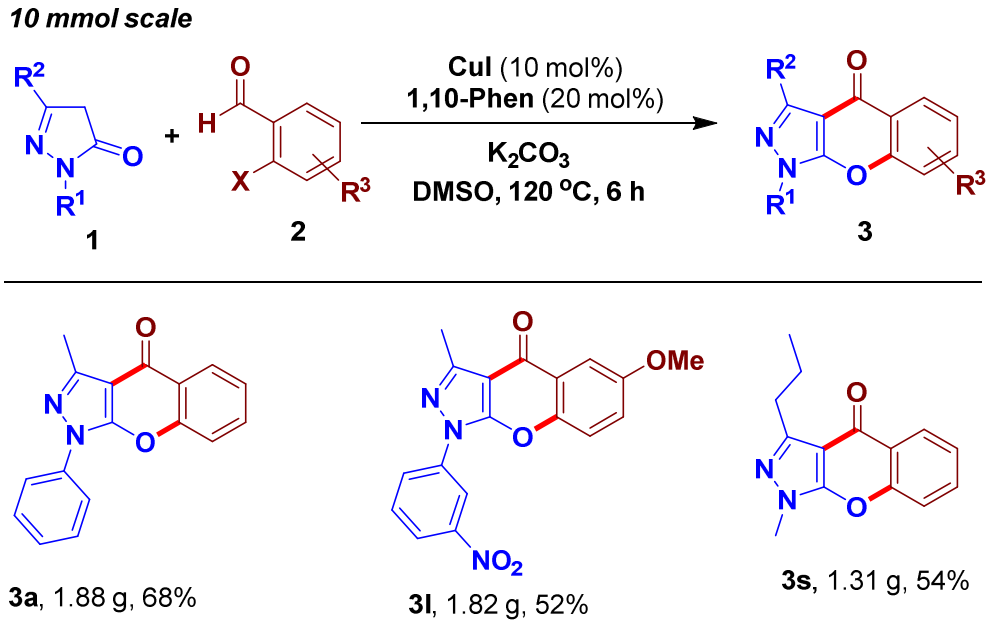
copper complex **V** that could finally undergo cyclization to give the product **3** upon reductive elimination.

Scheme 3. Plausible Mechanism.



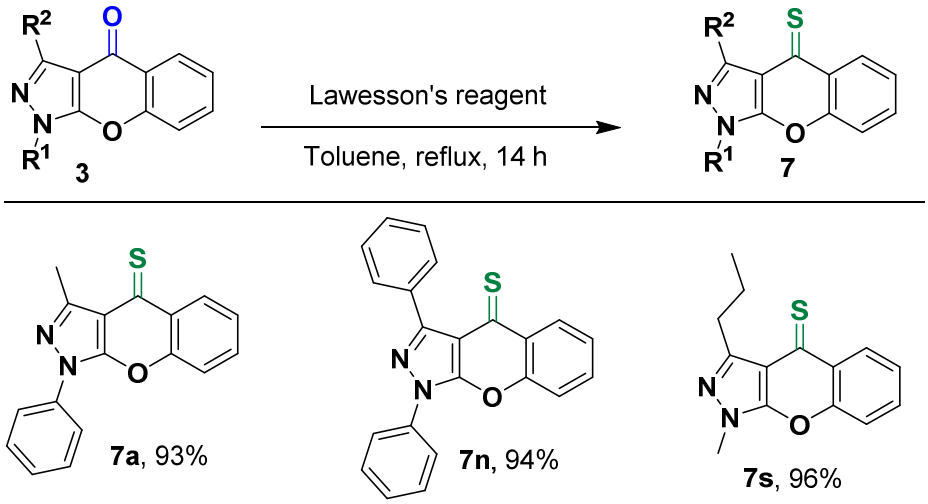
It is worth mentioning that the developed method has enabled to scale up the reaction to a gram scale for the synthesis of **3a** while maintaining high yield. Gram scale synthesis of chromone fused pyrazole **3l** and **3s** was also performed (Scheme 4).

Scheme 4. Gram-scale syntheses of chromone fused pyrazoles 3a, 3l and 3s.



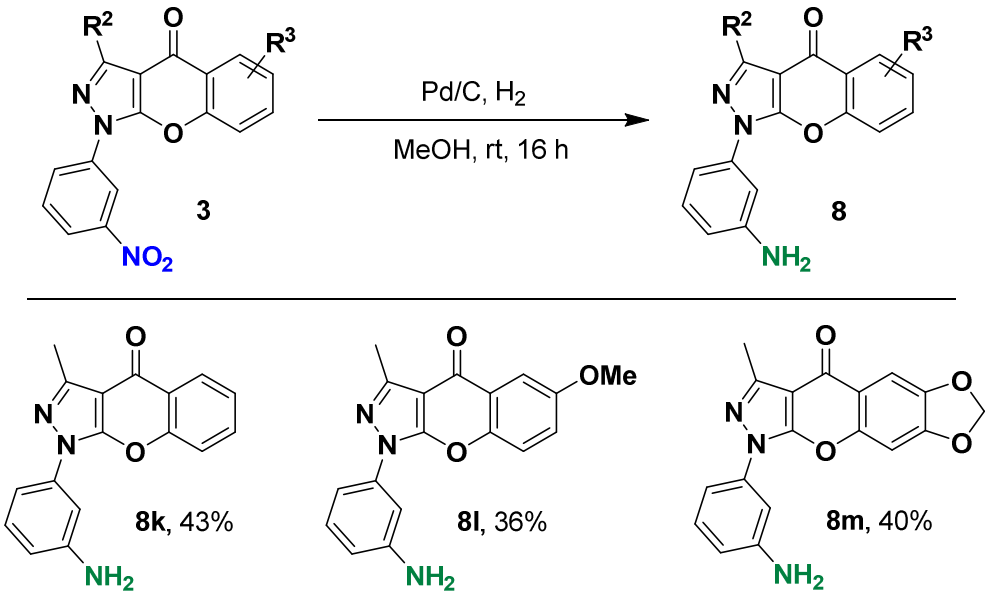
We have subjected **3a** to thionation using Lowesson's reagent to obtain the thione derivative of the chromone fused pyrazole **7a** in 93% yield.[14] The thione analogs **7n** and **7s** were also obtained in excellent yields (Scheme 5).

Scheme 5. Thionation of chromone fused pyrazole 3a, 3n and 3s.



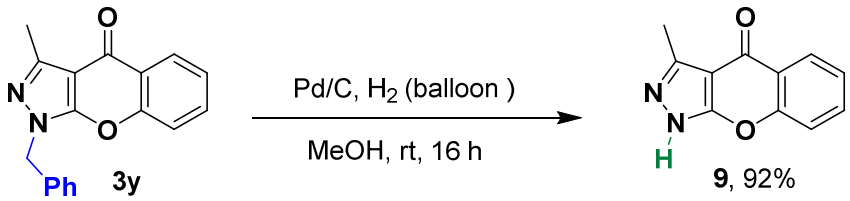
It is noteworthy that the potential of the present tandem method is demonstrated by the synthesis of an A_2-subtype selective adenosine receptor antagonist **8k**. The method has also been extended to the synthesis of interesting analogs **8l** and **8m** (Scheme 6). It is worth mentioning that this synthesis has been accomplished in just couple of steps compared to the reported multi-step synthesis for the same.[8a,b]

Scheme 6. Synthesis of A_2-subtype selective adenosine receptor antagonist 8a and congeners 8l, 8m.



The benzyl group of *N*-benzyl substituted chromone fused pyrazole **3y** was deprotected using Pd/C catalyzed hydrogenolysis to obtain *N*-unsubstituted chromone fused pyrazole, 3-methylchromeno[2,3-*c*]pyrazol-4(1*H*)-one **9** in excellent yield (Scheme 7).

Scheme 7. Deprotection of benzyl group of 3y.



CONCLUSIONS

In conclusion, we have successfully developed copper catalyzed intermolecular tandem *O*-arylation–oxidative cyclization using 2,4-dihydro-3*H*-pyrazol-3-ones and *ortho*-haloaryl aldehydes under aerobic conditions. Notably, this method furnished the direct synthesis of diversely substituted tricyclic and tetracyclic chromone fused pyrazoles in moderate to good yields using commercially available starting materials. The synthetic utility of the chromone fused pyrazoles has also been described for the synthesis of a representative A_2-subtype selective adenosine receptor antagonist in only two steps.

EXPERIMENTAL SECTION

General: All the reactions were carried out with an oven dried glassware or screw caped vials. Reactions are magnetically stirred and monitored by analytical thin layer chromatography (TLC). TLC was performed on silica gel 60 F_{254}, UV lamp was used as visualizing agent. Iodine, 5% aqueous potassium permanganate solution were used as a developing agents followed by heating. Purification of products was carried out by column chromatography by using 60-120 mesh silica and hexane, ethyl acetate were used as eluents, concentration under reduced pressure was performed by rotary evaporator at 40-45 ^{o}C. All the reagents and solvents are purchased from commercial suppliers. Anhydrous/LR DMSO, catalysts, ligands, bases, and deuterated solvents were used without further purification. ^{1}H-NMR spectra were recorded on 300, 400 and

500 MHz instruments. Chemical shifts (δ) are reported in ppm with the reference solvent and the internal standards (TMS = 0; $CDCl_3$ = 7.26). The following abbreviations were used to explain the multiplicity of the spectra (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet). ^{13}C-NMR spectra were recorded on 75, 100, and 125 MHz spectrometers. Mass spectra was analysed by Electrospray Ionization (ESI) method on a LCMS mass spectrometer. High resolution mass spectra were recorded on a quadrupole mass spectrometer. Melting points (MP) were determined using a capillary point apparatus. MPs are uncorrected. Infrared spectroscopy was performed as a neat sample or as a KBr sample on a FT-IR instrument.

General procedure for the synthesis of chromone fused pyrazoles 3a-y:- In a 10 mL screw caped vial 2,4-dihydro-3*H*-pyrazol-3-one **1** (0.5 mmol), *ortho*-halo aryl aldehyde **2** (0.6 mmol), CuI (0.05 mmol, 9.5 mg), K_2CO_3 (1.65 mmol, 228 mg), 1,10-phenanthroline (0.1 mmol, 18 mg), and dimethyl sulfoxide (2 mL) were taken. Then the reaction vial was closed in the presence of air. Then the reaction mixture was stirred at 120 ^{o}C for 6 h. The reaction mixture was cooled to room temperature, diluted with water, extracted with ethyl acetate (2 x 20 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in *vacuo* to afford a crude residue. The residue was purified by flash column chromatography (hexane/EtOAc, 95:5) on silica gel to afford chromone fused pyrazole derivatives **3a-y**.

3-Methyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one[5j] 3a:- White solid, 102 mg (0.37 mmol), 74%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 169-171 ^{o}C; **IR** (KBr) 1448, 1531, 1610, 1660, 2925, 3050 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 2.72 (s, 3H), 7.38-7.44 (m, 1H), 7.47-7.49 (m, 1H), 7.53-7.58 (m, 3H), 7.69-7.74 (m, 1H), 7.89-7.90 (m, 2H), 8.37 (dd, J_1 = 7.9 Hz, J_2 = 1.5 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.1, 105.0, 117.6, 121.2, 123.4, 125.2,

126.8, 127.3, 129.4, 133.7, 137.0, 148.1, 153.0, 154.5, 173.5; **MS** (ESI) m/z 277 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{13}N_2O_2$ $[M+H]^+$ 277.0971, found 277.0974.

3,7-Dimethyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3b:- Light green solid, 90 mg (0.31 mmol), 62%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 159-160 ^oC; **IR** (KBr) 1139, 1438, 1534, 1621, 1658, 2923, 3060 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.51 (s, 3H), 2.71 (s, 3H), 7.28 (s, 1H), 7.35 (s, 1H), 7.38-7.41 (m, 1H), 7.52-7.57 (m, 2H), 7.88-7.90 (m, 2H), 8.24 (d, *J* = 8.0 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.1, 21.7, 117.6, 121.2, 121.3, 126.6, 126.7, 127.3, 129.4, 137.3, 145.2, 148.2, 154.8, 173.6; **MS** (ESI) m/z 291 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{15}N_2O_2$ $[M+H]^+$ 291.1128, found 291.1124.

6-Methoxy-3-methyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one[5j] 3c:- Yellow solid, 100 mg (0.32 mmol), 65%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 158-160 ^oC; **IR** (KBr) 1281, 1469, 1536, 1617, 1660, 2926, 3070 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.72 (s, 3H), 3.93 (s, 3H), 7.26-7.28 (m, 1H), 7.38-7.41 (m, 1H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.53-7.56 (m, 2H), 7.76 (d, *J* = 3.5 Hz, 1H), 7.88-7.90 (m, 2H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.2, 56.0, 104.7, 107.0, 118.8, 121.2, 122.8, 124.0, 127.3, 129.5, 137.2, 148.1, 149.1, 153.2, 160.0, 173.5; **MS** (ESI) m/z 307 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{15}N_2O_3$ $[M+H]^+$ 307.1077, found 307.1069.

3-Methyl-1-phenyl-[1,3]dioxolo[4',5':6,7]chromeno[2,3-*c*]pyrazol-4(1*H*)-one 3d:- Yellow solid, 82 mg (0.25 mmol), 51%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 168-170 ^oC; **IR** (KBr) 1257, 1482, 1533, 1629, 1652, 2911, 3065 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.70 (s, 3H), 6.13 (s, 2H), 6.95 (s, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 8.5 Hz, 2H), 7.67 (s, 1H), 7.85-7.87 (m, 2H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.1, 98.1, 102.8, 103.6, 104.6, 117.9, 121.1, 121.9, 126.5, 127.3, 129.0, 129.4, 137.1, 146.0, 147.8, 151.4, 152.6, 153.0, 172.8; **MS**

(ESI) m/z 321 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{13}N_2O_4$ $[M+H]^+$ 321.0870, found 321.0877.

6-Fluoro-3-methyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one[5j,9c] 3e:- White solid, 66 mg (0.22 mmol), 45%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 168-170 ^oC; **IR** (KBr) 1125, 1186, 1257, 1534, 1619, 1662, 2925, 3056 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.69 (s, 3H), 7.39-7.43 (m, 2H), 7.51-7.56 (m, 3H), 7.85-7.89 (m, 2H), 7.99 (dd, J_1 = 8.2 Hz, J_2 = 3.1 Hz, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 13.9, 104.4, 111.8-112.0 (d, $J_{C\text{-}F}$ = 24.2 Hz), 119.3-119.4, (d, $J_{C\text{-}F}$ = 8.1 Hz), 120.9, 121.2, 124.4-124.5 (d, $J_{C\text{-}F}$ = 7.3 Hz), 127.4, 129.4, 136.8, 147.8, 150.3, 152.8, 158.3, 160.7, 172.1; **MS** (ESI) m/z 295 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{12}FN_2O_2$ $[M+H]^+$ 295.0877, found 295.0883.

6-Bromo-3-methyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one[5j] 3f:- White solid, 121 mg (0.34 mmol), 68%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 156-158 ^oC; **IR** (KBr) 1447, 1531, 1597, 1662, 2920, 3077 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.68 (s, 3H), 7.38-7.44 (m, 2H), 7.52-7.56 (m, 2H), 7.76-7.78 (m, 1H), 7.85 (d, J = 8.0 Hz, 2H), 8.44 (s, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 14.1, 104.9, 118.7, 119.5, 121.4, 124.9, 127.6, 129.5, 129.6, 136.6, 136.9, 148.3, 152.8, 153.3, 172.1; **MS** (ESI) m/z 355 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{12}BrN_2O_2$ $[M+H]^+$ 355.0077, found 355.0090.

8-Chloro-3-methyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3g:- White solid, 87 mg (0.28 mmol), 56%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 157-159 ^oC; **IR** (KBr) 1461, 1504, 1600, 1671, 2926, 3075 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.72 (s, 3H), 7.38-7.42 (m, 2H), 7.55-7.58 (m, 2H), 7.78 (dd, J_1 = 1.7 Hz, J_2 = 7.8 Hz, 1H), 8.02-8.04 (m, 2H), 8.28 (dd, J_1 = 1.7 Hz, J_2 = 7.9 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.2, 104.8, 120.5, 122.8, 125.1,

125.4, 125.5, 127.3, 129.5, 134.2, 137.1, 148.3, 150.4, 152.5, 172.7; **MS** (ESI) m/z 311 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{12}ClN_2O_2$ $[M+H]^+$ 311.0587, found 311.0589.

5-Chloro-3-methyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3h:- White solid, 84 mg (0.27 mmol), 54%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 158-160 ^oC; **IR** (KBr) 1450, 1532, 1604, 1662, 2926, 3058 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.72 (s, 3H), 7.39-7.44 (m, 2H), 7.53-7.58 (m, 3H), 7.84-7.86 (m, 2H), 8.30 (d, *J* = 8.5 Hz, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 14.2, 105.1, 117.9, 121.4, 122.1, 126.0, 127.7, 128.1, 129.5, 136.9, 139.7, 148.3, 152.8, 154.6, 172.7; **MS** (ESI) m/z 311 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{12}ClN_2O_2$ $[M+H]^+$ 311.0587, found 311.0589.

7-Fluoro-6-methoxy-3-methyl-1-phenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3i:- White solid, 104 mg (0.32 mmol), 64%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 194-195 ^oC; **IR** (KBr) 1457, 1504, 1618, 1663, 2964, 3058 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.70 (s, 3H), 4.00 (s, 3H), 7.29 (d, *J* = 10.5 Hz, 1H), 7.39-7.41 (m, 1H), 7.53-7.56 (m, 2H), 7.83-7.86 (m, 3H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 14.1, 56.6, 104.6, 105.7-105.9 (d, J_{C-F} = 23.5 Hz), 108.5-108.6 (d, J_{C-F} = 2.9 Hz), 119.7, 121.3, 127.5, 129.5, 136.9, 146.1, 146.2, 148.5-148.6 (d, J_{C-F} = 11.7 Hz), 153.1, 154.1, 156.7, 172.6; **MS** (ESI) m/z 325 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{14}FN_2O_3$ $[M+H]^+$ 325.0983, found 325.0989.

8-Methyl-10-phenylbenzo[7,8]chromeno[2,3-*c*]pyrazol-7(10*H*)-one 3j:- Yellow solid, 108 mg (0.33 mmol), 66%, R_f = 0.25 (EtOAc/Hexane, 5:95); **MP** 196-197 ^oC; **IR** (KBr) 1458, 1504, 1595, 1656, 2923, 3056 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.76 (s, 3H), 7.45-7.48 (m, 1H), 7.62-7.66 (m, 2H), 7.69-7.74 (m, 2H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.96-8.02 (m, 3H), 8.32 (d, *J* = 8.5 Hz, 1H), 8.43-8.47 (m, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.2, 105.6, 119.3, 121.3, 121.6, 121.9, 123.6, 125.2, 127.4, 127.5, 128.2, 129.2, 129.7, 136.3, 137.2, 148.1, 151.6, 152.7,

173.7; **MS** (ESI) m/z 327 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{21}H_{15}N_2O_2$ $[M+H]^+$ 327.1128, found 327.1128.

3-Methyl-1-(3-nitrophenyl)chromeno[2,3-*c*]pyrazol-4(1*H*)-one 3k:- White solid, 102 mg (0.32 mmol), 63%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 210-211 ^oC; **IR** (KBr) 1455, 1532, 1612, 1664, 2924, 3113 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.73 (s, 3H), 7.49-7.53 (m, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.73-7.79 (m, 2H), 8.23-8.25 (m, 1H), 8.33-8.36 (m, 1H), 8.38 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 8.90 (t, *J* = 2.5 Hz, 1H); **^{13}C{1H}NMR** (75 MHz, $CDCl_3$) δ = 14.2, 105.5, 115.5, 117.8, 121.5, 123.4, 125.8, 126.0, 127.0, 130.5, 134.2, 138.2, 148.9, 149.3, 153.5, 154.5, 173.4; **MS** (ESI) m/z 322 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{12}N_3O_4$ $[M+H]^+$ 322.0822, found 322.0821.

6-Methoxy-3-methyl-1-(3-nitrophenyl)chromeno[2,3-*c*]pyrazol-4(1*H*)-one[8b] 3l:- White solid, 83 mg (0.24 mmol), 47%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 205-206 ^oC; **IR** (KBr) 1424, 1492, 1533, 1610, 1667, 2933, 3102 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.72 (s, 3H), 3.94 (s, 3H), 7.32 (dd, J_1 = 9.2 Hz, J_2 = 3.2 Hz, 1H), 7.54 (d, J_1 = 9.2 Hz, 1H), 7.71-7.76 (m, 2H), 8.21-8.24 (m, 1H), 8.32-8.35 (m, 1H), 8.89 (t, *J* = 7.9 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.2, 56.1, 105.2, 107.1, 115.4, 118.9, 121.4, 123.1, 124.0, 125.9, 130.5, 138.2, 148.9, 149.0, 149.2, 153.6, 157.3, 173.3; **MS** (ESI) m/z 352 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{18}H_{14}N_3O_5$ $[M+H]^+$ 352.0928, found 352.0929.

3-Methyl-1-(3-nitrophenyl)-[1,3]dioxolo[4',5':6,7]chromeno[2,3-c]pyrazol-4(1*H*)-one 3m:- Yellow solid, 96 mg (0.26 mmol), 52%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 206-208 ^oC; **IR** (KBr) 1256, 1535, 1664, 2919, 3099 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.70 (s, 3H), 6.16 (s, 2H), 7.02 (s, 1H), 7.68 (s, 1H), 7.73 (t, *J* = 8.2 Hz, 1H), 8.21-8.23 (m, 1H), 8.29-8.31 (m, 1H), 8.85 (t, *J* = 2.2 Hz, 1H); **^{13}C{1H}NMR** (100 MHz $CDCl_3$) δ = 14.1, 98.2, 102.9, 103.7,

105.2, 115.3, 118.0, 121.4, 125.9, 130.5, 138.2, 146.4, 148.8, 148.9, 151.4, 152.9, 153.5, 172.6; **MS** (ESI) m/z 366 $[M+H]^+$; **HRMS** (ESI, m/z):calcd for $C_{18}H_{12}N_2O_6$ $[M+H]^+$ 366.0721, found 366.0741.

1,3-Diphenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one[9b] 3n:-White solid, 101 mg (0.30 mmol), 60%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 174-176 ^oC; **IR** (KBr) 1403, 1457, 1517, 1609, 1659 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.43-7.47 (m, 2H), 7.49-7.54 (m, 3H), 7.55-7.62 (m, 3H), 7.71-7.75 (m, 1H), 7.98-8.01 (m, 2H), 8.42-8.44 (m, 1H), 8.46-8.48 (m, 2H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 104.0, 117.4, 121.9, 123.5, 125.4, 127.4, 127.8, 128.4, 128.7, 129.5, 131.5, 133.9, 137.1, 149.9, 153.7, 153.8, 172.8; **MS** (ESI) m/z 339 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{22}H_{15}N_2O_2$ $[M+H]^+$ 339.1128, found 339.1128.

6-Methoxy-1,3-diphenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3o:- White solid, 90 mg (0.24 mmol), 49%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 198-199 ^oC; **IR** (KBr) 1456, 1486, 1521, 1606, 1652, 2923 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 3.93 (s, 3H), 7.30 (dd, J_1 = 3.0 Hz, J_2 = 9.0 Hz, 1H), 7.42-7.53 (m, 5H), 7.60 (t, J = 7.5 Hz, 2H), 7.83 (d, J = 3.2 Hz, 1H), 7.97-8.02 (m, 2H), 8.44-8.49 (m, 2H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 56.0, 103.7, 107.3, 118.6, 121.8, 123.2, 124.0, 127.7, 128.3, 128.7, 129.5, 131.6, 137.2, 148.4, 149.7, 153.9, 157.1, 172.7; **MS** (ESI) m/z 369 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{23}H_{17}N_2O_3$ $[M+H]^+$ 369.1234, found 369.1237.

1,3-Diphenyl-[1,3]dioxolo[4',5':6,7]chromeno[2,3-*c*]pyrazol-4(1*H*)-one 3p:- White solid, 98 mg (0.26 mmol), 51%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 218-219 ^oC; **IR** (KBr) 1457, 1533, 1597, 1650 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 6.13 (s, 2H), 6.96 (s, 1H), 7.42-7.46 (m, 2H), 7.51 (t, J = 7.0 Hz, 2H), 7.58 (t, J = 7.5 Hz, 2H), 7.72 (s, 1H), 7.95-7.97 (m, 2H), 8.44-8.46 (m, 2H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 97.8, 102.8, 103.6, 104.0, 117.9, 121.7,

127.7, 128.3, 128.7, 129.4, 129.5, 131.6, 137.1, 146.2, 149.5, 150.7, 152.8, 153.7, 171.9; **MS** (ESI) m/z 383 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{23}H_{15}N_2O_4$ $[M+H]^+$ 383.1026, found 383.1032.

6-Bromo-1,3-diphenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3q:- White solid, 89 mg (0.21 mmol), 43%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 208-209 ^oC; **IR** (KBr) 1248, 1454, 1517, 1597, 1665, 2922 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.44-7.49 (m, 3H), 7.50-7.53 (m, 2H), 7.57-7.61 (m, 2H), 7.81 (dd, J_1 = 2.8 Hz, J_2 = 9.0 Hz, 1H), 7.95-7.97 (m, 2H), 8.42-8.45 (m, 2H), 8.53 (d, J = 2.8 Hz, 1H); **^{13}C{1H}NMR** (75 MHz, $CDCl_3$) δ = 103.9, 118.7, 119.3, 121.9, 124.9, 128.0, 128.4, 128.6, 129.5, 129.6, 130.1, 131.2, 136.8, 136.9, 149.9, 152.6, 153.5, 171.3; **MS** (ESI) m/z 417 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{22}H_{14}BrN_2O_2$ $[M+H]^+$ 417.0233, found 417.0228.

6-Fluoro-1,3-diphenylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3r:- White solid, 88 mg (0.25 mmol), 49%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 197-198 ^oC; **IR** (KBr) 1449, 1465, 1520, 1622, 1659 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 7.42-7.48 (m, 3H), 7.50-7.53 (m, 2H), 7.55-7.57 (m, 1H), 7.57-7.61 (m, 2H), 7.96-7.98 (m, 2H), 8.07 (dd, J_1 = 3.0 Hz, J_2 = 8.5 Hz, 1H), 7.43-7.45 (m, 2H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 103.5, 112.5-112.7 (d, $J_{C\text{-}F}$ = 24.2 Hz), 119.2-119.3 (d, $J_{C\text{-}F}$ = 8.0 Hz), 121.8, 121.9, 127.9, 128.4, 128.6, 129.5, 129.6, 131.3, 136.9, 149.7-149.8 (d, $J_{C\text{-}F}$ = 5.1 Hz), 153.8, 158.5, 160.9, 171.7; **MS** (ESI) m/z 357 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{22}H_{14}N_2O_2F$ $[M+H]^+$ 357.1034, found 357.1038.

1-Methyl-3-propylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3s:- Yellow solid, 82 mg (0.34 mmol), 68%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 85-87 ^oC; **IR** (KBr) 1455, 1563, 1613, 1665, 1828, 1959, 2959, 3067 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.01 (t, J = 7.5 Hz, 3H), 1.80-1.88 (m, 2H), 2.94 (t, J = 7.7 Hz, 2H), 3.90 (s, 3H), 7.41-7.44 (m, 1H), 7.47-7.49 (m, 1H), 7.66-

7.69 (m, 1H), 8.34 (dd, J_1 = 1.6 Hz, J_2 = 7.9 Hz, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 13.9, 21.9, 30.6, 33.7, 103.0, 117.3, 123.2, 124.9, 126.9, 133.5, 151.2, 153.8, 154.3, 173.1; **MS** (ESI) m/z 243 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{14}H_{15}N_2O_2$ $[M+H]^+$ 243.1128, found 243.1128.

6-Methoxy-1-methyl-3-propylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3t:- White solid, 88 mg (0.32 mmol), 64%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 169-171 ^oC; **IR** (KBr) 1428, 1565, 1612, 1658, 1903, 2956, 3072 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.01 (t, J = 7.5 Hz, 3H), 1.80-1.88 (m, 2H), 2.94 (t, J = 7.5 Hz, 2H), 3.89 (s, 3H), 3.91 (s, 3H), 7.23-7.25 (m, 1H), 7.41 (d, J = 9.5 Hz, 1H), 7.44 (d, J = 3.0 Hz, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 13.9, 21.9, 30.6, 33.7, 55.9, 102.8, 107.2, 118.5, 122.5, 123.9, 148.9, 151.1, 154.1, 156.7, 173.1; **MS** (ESI) m/z 273 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{15}H_{17}N_2O_3$ $[M+H]^+$ 273.1234, found 273.1233.

6-Bromo-1-methyl-3-propylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3u:- Yellow solid, 104 mg (0.32 mmol), 65%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 169-171 ^oC; **IR** (KBr) 1448, 1535, 1599, 1660, 1921, 2954, 3069 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.00 (t, J = 7.5 Hz, 3H), 1.80-1.86 (m, 2H), 2.93 (t, J = 7.5 Hz, 2H), 3.90 (s, 3H), 7.36-7.39 (m, 1H), 7.73-7.76 (m, 1H), 8.41-8.43 (m, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 13.9, 21.8, 30.5, 33.8, 103.0, 118.3, 119.2, 124.9, 129.8, 136.3, 151.4, 153.2, 153.8, 171.7; **MS** (ESI) m/z 321 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{14}H_{14}N_2O_2Br$ $[M+H]^+$ 321.0233, found 321.0233.

6-Fluoro-1-methyl-3-propylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3v:- White solid, 72 mg (0.28 mmol), 55%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 188-189 ^oC; **IR** (KBr) 1451, 1569, 1622, 1664, 1909, 2963, 3081 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.02 (t, J = 7.0 Hz, 3H), 1.79-1.87 (m, 2H), 2.94 (t, J = 7.5 Hz, 2H), 3.90 (s, 3H), 7.37-7.41 (m, 1H), 7.48 (dd, J_1 = 4.0 Hz, J_2 = 9.0 Hz, 1H), 7.97 (dd, J_1 = 3.5 Hz, J_2 = 8.0 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$)

δ = 13.9, 21.9, 30.6, 33.8. 102.7, 112.3-112.5 (d, J_{C-F} = 24.5 Hz), 119.0-119.1 (d, J_{C-F} = 8.2 Hz), 121.1-121.3 (d, J_{C-F} = 25.4 Hz), 124.8-124.9 (d, J_{C-F} = 7.3 Hz), 150.4, 151.2, 154.0, 158.5, 160.5, 172.1; **MS** (ESI) m/z 261 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{14}H_{14}N_2O_2F$ $[M+H]^+$ 261.1033, found 261.1034.

3-*tert*-Butyl-1-methylchromeno[2,3-*c*]pyrazol-4(1*H*)-one 3w:- White solid, 55 mg (0.21 mmol), 42%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 163-164 ^oC; **IR** (KBr) 1171, 1261, 1366, 1466, 1505, 1601, 2854, 2925, 2962, 3010 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 1.50 (s, 9H), 3.90 (s, 3H), 7.41-7.44 (m, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.65-7.69 (m, 1H), 8.36 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ =28.3, 33.7, 33.8, 102.4, 117.0, 123.4, 124.9, 127.4, 133.4, 153.8, 154.6, 159.1, 172.3; **MS** (ESI) m/z 257 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{15}H_{17}N_2O_2$ $[M+H]^+$ 257.1281, found 257.1280.

1-Methyl-3-(trifluoromethyl)chromeno[2,3-*c*]pyrazol-4(1*H*)-one 3x:- White solid, 47 mg (0.18 mmol), 35%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 183-185 ^oC; **IR** (KBr) 1455, 1558, 1610, 1671, 2924, 3060 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 4.04 (s, 3H), 7.46-7.50 (m, 1H), 7.52-7.54 (m, 1H), 7.72-7.77 (m, 1H), 8.37 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 34.8, 102.6, 117.5, 118.7, 121.4, 122.9, 125.7, 127.5, 131.0, 134.5, 154.0, 154.1, 170.8; **MS** (ESI) m/z 269 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{12}H_8N_2O_2F_3$ $[M+H]^+$ 269.0532, found 269.0534.

1-Benzyl-3-methylchromeno[2,3-c]pyrazol-4(1*H*)-one 3y:- White solid, 75 mg (0.26 mmol), 52%, R_f = 0.5 (EtOAc/Hexane, 10:90); **MP** 148-151 ^oC; **IR** (KBr) 1493, 1554, 1611, 1659, 2929 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.62 (s, 3H), 5.38 (s, 3H), 7.29-7.37 (m, 5H), 7.41 (t, *J* = 7.2. Hz, 1H), 7.45-7.47 (m, 1H), 7.64-7.68 (m, 1H), 7.73 (dd, J_1 = 1.6. Hz, J_2 = 7.9. 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.4, 50.9, 103.7, 117.4, 123.4, 124.9, 126.9, 127.6,

128.2, 128.9, 133.5, 135.2, 147.3, 153.7, 154.5, 173.4; **MS** (ESI) m/z 291 $[M+H]^+$; **HRMS** (ESI, m/z):calcd for $C_{18}H_{15}N_2O_2$ $[M+H]^+$; 291.1128, found 291.1144.

Experimental procedure for the synthesis of 6:- In a 10 mL screw caped vial 2,4-dihydro-3*H*-pyrazol-3-one **1a** (0.5 mmol 87 mg), 2-bromobenzaldehyde **2a** (0.6 mmol, 0.07 mL), copper catalyst CuI or $Cu(OTf)_2$ (0.05 mmol) and 1,10-phenanthroline (0.1 mmol, 18 mg) were taken in DMSO (2 mL). The reaction vial was closed in the presence of air and it was stirred at 120 ^oC for 6 h. The reaction mixture was cooled to room temperature, diluted with water, extracted with ethyl acetate (2 x 20 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in *vacuo* to afford a crude residue. The residue was purified by flash column chromatography (hexane/EtOAc) on silica gel to afford the condensation product **6**. The geometry of this compound was found to be (*Z*) by nOe (see supporting information).

(*Z*)-4-(2-Bromobenzylidene)-5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one 6:- Red colour solid, 157 mg (0.46 mmol), 92%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 128-130 ^oC; **IR** (KBr) 1463, 1593, 1635, 1687, 2920, 3425 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.38 (s, 3H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.33-7.45 (m, 4H), 7.68 (dd, J_1 = 1.0 Hz, J_2 = 1.0 Hz, 1H), 7.79 (s, 1H), 7.91 (d, *J* = 9.6 Hz, 2H), 8.78 (dd, J_1 = 1.5 Hz, J_2 = 7.7 Hz, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ =13.3, 118.9, 125.0, 126.8, 127.3, 128.7, 128.8, 131.7, 132.9, 133.3, 133.5, 138.2, 144.5, 150.8, 161.4; **MS** (ESI) m/z 341 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{14}N_2OBr$ $[M+H]^+$ 341.0284, found 341.0294.

Gram scale synthesis of chromone fused pyrazoles 3a, **3l** and **3s:-** In a 100 mL two necked round bottom flask pyrazolone **1a** or **1b** or **1d** (10 mmol), *ortho*-bromobenzaldehyde **2a** or **2e** (12 mmol), CuI (1 mmol, 190 mg), K_2CO_3 (33 mmol, 4.55 g), 1,10-phenanthroline (2 mmol, 360

mg), and dimethyl sulfoxide (30 mL) were taken. Then the reaction mixture was stirred at 120 ^{o}C for 6 h in the presence of air. The reaction mixture was cooled to room temperature, diluted with water, extracted with ethyl acetate (2 x 200 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in *vacuo* to afford a crude residue. The residue was purified by flash column chromatography (hexane/EtOAc) on silica gel to afford chromone fused pyrazole derivative **3a** or **3l** or **3s.**

Experimental procedure for thionation of chromone fused pyrazoles 3a, **3n** and **3s:-** Chromone fused pyrazole **3a** or **3n** or **3s** (0.5 mmol) was dissolved in 15 mL toluene and then added Lawesson's reagent (0.25 mmol, 101 mg). Then the reaction mixture was heated at 140 ^{o}C for 14 h and cooled to room temperature. The reaction mixture was extracted with ethyl acetate (2 x 20 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed *in vacuo* to afford a crude residue. The residue was purified by flash column chromatography (hexane/EtOAc, 90:10) on silica gel to afford thione analogs **7a** or **7n** or **7s**.

3-Methyl-1-phenylchromeno[2,3-c]pyrazole-4(1H)-thione[14] 7a:- Red solid, 136 mg (0.46 mmol), 93%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 185-187 ^{o}C; **IR** (KBr) 1440, 1537, 1588, 2921 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.84 (s, 3H), 7.39-7.48 (m, 2H), 7.51-7.59 (m, 3H), 7.70-7.74 (m, 1H), 7.89-7.93 (m, 2H), 8.81 (dd, J_1 = 8.2 Hz, J_2 = 2.0 Hz, 1H); **^{13}C{1H}NMR** (75 MHz, $CDCl_3$) δ = 16.0, 116.3, 117.8, 121.3, 125.8, 127.6, 128.0, 129.4, 129.5, 133.7, 136.8, 146.6, 149.8, 150.9, 198.1; **MS** (ESI) m/z 293 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{13}N_2OS$ $[M+H]^+$ 293.0743, found 293.0744.

1,3-Diphenylchromeno[2,3-c]pyrazole-4(1*H*)-thione 7n:- Brown solid, 167 mg (0.47 mmol), 94%, R_f = 0.3 (EtOAc/Hexane, 10:90); **MP** 210-212 ^{o}C; **IR** (KBr) 1454, 1507, 1583, 1661, 2925 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 7.42-7.47 (m, 5H), 7.53-7.59 (m, 3H), 7.70-

7.73 (m, 1H), 7.88-7.90 (m, 2H), 7.98 (d, J = 7.6 Hz, 2H), 8.97 (dd, J_1 = 1.3 Hz, J_2 = 8.0 Hz, 1H); **^{13}C{1H}NMR** (100 MHz, $CDCl_3$) δ = 115.2, 117.6, 121.7, 125.8, 127.6, 127.8, 128.4, 129.2, 129.5, 129.7, 130.2, 131.8, 133.7, 136.8, 147.0, 149.2, 152.1, 197.5; MS (ESI) m/z 355 $[M+H]^+$; **HRMS** (ESI, m/z):calcd for $C_{22}H_{15}N_2OS$ $[M+H]^+$ 355.0900, found 355.0917.

1-Methyl-3-propylchromeno[2,3-*c*]pyrazole-4(1*H*)-thione 7s:- Brown solid, 124 mg (0.48 mmol), 96%, R_f = 0.3 (EtOAc/Hexane, 10:90); **MP** 120-122 ^oC; IR (KBr) 1448, 1527, 1580, 1665, 2863, 2928 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 1.04 (t, J = 7.5 Hz, 3H), 1.74-1.87 (m, 2H), 3.14 (t, J = 7.7 Hz, 2H), 3.91 (s, 3H), 7.40-7.48 (m, 2H), 7.64-7.72 (m, 1H), 8.80 (dd, J_1 = 1.6 Hz, J_2 = 8.2 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 13.9, 21.5, 30.8, 33.6, 114.7, 117.4, 125.3, 127.6, 129.4, 133.3, 147.5, 149.5, 153.4, 197.3; **MS** (ESI) m/z 259 $[M+H]^+$; **HRMS** (ESI, m/z):calcd for $C_{14}H_{15}N_2OS$ $[M+H]^+$ 259.0900, found 259.0911.

Experimental procedure for the reduction of nitro group of 1-(3-nitrophenyl)chromeno[2,3-*c*]pyrazol-4(1*H*)-ones:- 1-(3-Nitrophenyl)chromeno[2,3-*c*]pyrazol-4(1*H*)-ones **3k** or **3l** or **3m** (0.5 mmol), was dissolved in methanol (5 mL) and added Pd/C (10 wt.%, 106 mg). The reaction mixture was stirred at room temperature under hydrogen atmosphere (H_2 balloon) for 16 h. The reaction mixture was filtered on celite® pad, washed with chloroform (20 mL) and the filtrate was concentrated to obtain the products, 1-(3-aminophenyl)-chromeno[2,3-*c*]pyrazol-4(1*H*)-ones **8k** or **8l** or **8m** without further purification.

1-(3-Aminophenyl)-3-methylchromeno[2,3-c]pyrazol-4(1H)-one[8b] 8k:- White solid, 63 mg (0.22 mmol), 43%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 259-260 ^oC; **IR** (KBr) 1494, 1534, 1611, 1658, 2922, 3420 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 2.70 (s, 3H), 6.68-6 71 (m, 1H), 7.20 (d, J = 2.0 Hz, 1H), 7.28-7.33 (m, 2H), 7.47 (t, J = 7.6 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.68-7.72 (m, 1H), 8.37 (dd, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ =

14.2, 105.0, 107.9, 111.2, 114.1, 117.7, 123.5, 125.2, 126.9, 130.2, 133.8, 138.0, 147.6, 148.0, 153.1, 154.6, 173.7; **MS** (ESI) m/z 292 $[M+H]^+$; **HRMS** (ESI, m/z): calcd for $C_{17}H_{14}N_3O_2$ $[M+H]^+$ 292.1080, found 292.1082.

1-(3-Aminophenyl)-6-methoxy-3-methylchromeno[2,3-c]pyrazol-4(1*H*)-one[8b] 8l:- White solid, 58 mg (0.18 mmol), 36%, R_f = 0.3 (EtOAc/Hexane, 5:95); **MP** 189-191 ^oC; **IR** (KBr) 1470, 1613, 1659, 2928, 3371 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.69 (s, 3H), 3.90 (s, 3H), 6.68 (d, J_1 = 7.5. Hz, 1H), 7.19 (s, 1H), 7.24-7.25 (m, 1H), 7.27-7.32 (m, 2H), 7.44 (d, J = 9.2. Hz, 1H), 7.73 (d, J = 3.0. Hz, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.1, 55.9, 104.6, 106.9, 107.7, 110.9, 113.9, 118.8, 122.7, 123.9, 130.1, 137.9, 147.5, 147.8, 149.1, 153.2, 156.9, 173.5; **MS** (ESI) m/z 322 $[M+H]^+$; **HRMS** (ESI, m/z):calcd for $C_{18}H_{16}N_3O_3$ $[M+H]^+$ 322.1186, found 322.1204.

1-(3-Aminophenyl)-3-methyl-[1,3]dioxolo[4',5':6,7]chromeno[2,3-c]pyrazol-4(1*H*)-one 8m:- Yellow solid, 68 mg (0.20 mmol), 40%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 195-197 ^oC; **IR** (KBr) 1254, 1538, 1651, 2917, 3352 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 2.68 (s, 3H), 6.12 (s, 2H), 6.68 (s, 1H), 6.69 (s, 1H), 7.17 (s, 1H), 7.22-7.24 (m, 1H), 7.27-7.30 (m, 1H), 7.67 (s, 1H); **^{13}C{1H}NMR** (125 MHz, $CDCl_3$) δ = 14.1, 98.1, 102.7, 103.7, 110.9, 113.5, 117.9, 130.1, 137.9, 145.9, 147.6, 151.4, 152.5, 153.0, 172.7; **MS** (ESI) m/z 336 $[M+H]^+$; **HRMS** (ESI, m/z):calcd for $C_{18}H_{14}N_3O_4$ $[M+H]^+$ 336.0979, found 336.0994.

Experimental procedure for the synthesis of 3-Methylchromeno[2,3-*c*]pyrazol-4(1*H*)-one[15] 9:- 1-Benzyl-3-methylchromeno[2,3-*c*]pyrazol-4(1*H*)-one (0.5 mmol, 145 mg), was dissolved in methanol (5 mL) and added Pd/C (10 wt.%, 106 mg). The reaction mixture was stirred at room temperature under hydrogen atmosphere (H_2 balloon) for 16 h. The reaction

mixture was filtered on celite® pad, washed with chloroform (20 mL) and the filtrate was concentrated to obtain the product **9** in 92% yield, without further purification.

3-Methylchromeno[2,3-*c*]pyrazol-4(1*H*)-one[15] 9:- White solid, 92 mg (0.46 mmol), 92%, R_f = 0.5 (EtOAc/Hexane, 10:90); **MP** 299-301 ^oC; **IR** (KBr) 1450, 1519, 1595, 1641, 3200 cm^{-1}; **^{1}H-NMR** (300 MHz, DMSO-d_6) δ = 2.60 (s, 3H), 7.26 (t, J = 7.2. Hz, 1H), 7.35-7.38 (m, 1H), 7.54-7.60 (m, 1H), 8.13 (dd, J_1 = 1.4 Hz, J_2 = 7.7 1H), 12.96 (broad singlet NH, 1H); **^{13}C{1H}NMR** (75 MHz, DMSO-d_6) δ = 11.0, 103.1, 117.3, 122.1, 122.9, 125.7, 133.3, 140.4, 155.3, 161.2, 175.1; **MS** (ESI) m/z 201 $[M+H]^+$; **HRMS** (ESI, m/z):calcd for $C_{11}H_9N_2O_2$ $[M+H]^+$ 201.0659, found 201.0671.

AUTHOR INFORMATION

Corresponding Author

* E-Mail: surisetti@iict.res.in; suresh.surisetti@yahoo.in

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We thank Department of Science and Technology (DST), India for Fast track grant (SB/FT/CS-055/2012) and CSIR, New Delhi for financial support as part of XII Five Year plan under title ORIGIN (CSC-0108). OO thanks CSIR, KHB thanks DST for fellowship and project assistantship, respectively. We also thank Dr. G. V. Karunakar, CSIR-IICT, Dr. J. Raju Reddy, Osmania University and Dr. D. V. Ramana, Central University of Jammu for their support.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.

Optimization data, control experiments, and spectra (PDF)

REFERENCES

(1) For selected recent reviews on C-H functionalization, see: (a) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792. (b) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (c) Rouquet, G.; Chatani, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 11726. For a recent book on C-H functionalization, see: (d) *C-H Bond Activation in Organic Synthesis*; Li, J. J., Ed.; CRC Press: New York, 2015 and references cited therein.

(2) (a) *From C-H to C-C Bonds: Cross-Dehydrogenative-Coupling*; Li, C.-J., Ed.; Royal Society of Chemistry: Cambridge, 2015. (b) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (c) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem. Int. Ed.* **2014**, *53*, 74. (d) Topczewski, J. J.; Sanford, M. S. *Chem. Sci.* **2015**, *6*, 70.

(3) (a) Shi, Z.; Schröder, N.; Glorius, F. *Angew. Chem. Int. Ed.* **2012**, *51*, 8092. (b) Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Angew. Chem. Int. Ed.* **2013**, *52*, 2256.

(4) (a) Jia, X.; Zhang, S.; Wang, W.; Luo, F.; Cheng, J. *Org. Lett.* **2009**, *11*, 3120. (b) Baslé, O.; Bidange, J.; Shuai, Q.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 1145. (c) Chan, C.-W.; Zhou, Z.; Chan, A. S. C.; Yu, W.-Y. *Org. Lett.* **2010**, *12*, 3926. (d) Wu, Y.; Li, B.; Mao, F.; Li, X.; Kwong, F. Y. *Org. Lett.* **2011**, *13*, 3258. (e) Li, C.; Wang, L.; Li, P.; Zhou, W. *Chem. Eur. J.* **2011**, *17*, 10208. (f) Zhou, B.; Yang, Y.; Li, Y. *Chem. Commun.* **2012**, *48*, 5163. (g) Matcha, K.;

Antonchick, A. P. *Angew. Chem. Int. Ed.* **2013**, *52*, 2082. (h) Lee, H.; Yi, C. S. *Eur. J. Org. Chem.* **2015**, 1899.

(5) For the synthesis of cyclic ketones *via* intramolecular CDC, see: (a) Barluenga, J.; Trincado, M.; Rubio, E.; González, J. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 3140. (b) Tang, B.-X.; Song, R.-J.; Wu, C.-Y.; Liu, Y.; Zhou, M.-B.; Wei, W.-T.; Deng, G.-B.; Yin, D.-L.; Li, J.-H. *J. Am. Chem. Soc.* **2010**, *132*, 8900. (c) Wang, P.; Rao, H.; Hua, R.; Li, C.-J. *Org. Lett.* **2012**, *14*, 902. (d) Wertz, S.; Leifert, D.; Studer, A. *Org. Lett.* **2013**, *15*, 928. (e) Li, X.-A.; Wang, H.-L.; Yang, S.-D. *Org. Lett.* **2013**, *15*, 1794. (f) Rao, H.; Ma, X.; Liu, Q.; Li, Z.; Cao, S.; Li, C.-J. *Adv. Synth. Catal.* **2013**, *355*, 2191. (g) Shia, Z.; Glorius, F. *Chem. Sci.* **2013**, *4*, 829. (h) Manna, S. K.; Manda, S. L. K.; Panda, G. *Tetrahedron Lett.* **2014**, *55*, 5759. (i) Zheng, Z.; Dian, L.; Yuan, Y.; Zhang-Negrerie, D.; Du, Y.; Zhao, K. *J. Org. Chem.* **2014**, *79*, 7451. (j) Li, H.; Liu, C.; Zhang, Y.; Sun, Y.; Wang, B.; Liu, W. *Org. Lett.* **2015**, *17*, 932. (k) Wang, X.; Li, Z.; Cao, S.; Rao, H. *Adv. Synth. Catal.* **2016**, *358*, 2059.

(6) For the synthesis of xanthones via intermolecular reaction, see: Hu, J.; Adogla, E. A.; Ju, Y.; Fan, D.; Wang, Q. *Chem. Commun.* **2012**, *48*, 11256.

(7) (a) Obulesu, O.; Nanubolu, J. B.; Suresh, S. *Org. Biomol. Chem.* **2015**, *13*, 8232. (b) Murugesh, V.; Harish, B.; Adiseshu, M.; Nanubolu, J. B.; Suresh, S. *Adv. Synth. Catal.* **2016**, *358*, 1309. (c) Harish, B.; Subbireddy, M.; Suresh, S. *Chem. Commun.* **2017**, DOI: 10.1039/C6CC10292A.

(8) (a) Colotta, V.; Cecchi, L.; Catarzi, D.; Melani, F.; Filacchioni, G.; Martini, C.; Tacchi, P.; Lucacchini, A. *Pharm. Pharmacol. Lett.* **1992**, *2*, 74 (*Chem. Abstr.* **1993**, *118*, 32807). (b) Catarzi, D.; Cecchi, L.; Colotta, V.; Filacchioni, G. *J. Med. Chem.* **1995**, *38*, 1330. (c) for A_1 and A_{2A} adenosine binding activity of some pyrano fused pyrazoles, see: Colotta, V.; Catarzi, D.;

Varano, F.; Melani, F.; Filacchioni, G.; Cecchi, L.; Trincavelli, L.; Martini, C.; Lucacchini, A. *Farmaco* **1998**, *53*, 189.

(9) (a) Sarenko, A. S.; Éfros, L. S.; Kvitko, I. Ya.; *Pharm. Chem. J.* **1970**, *4*, 488; (b) Chantegrel, B.; Nadi, A.-I.; Gelin, S. *Synthesis* **1983**, 214. (c) Holzer, W.; Ebner, A.; Schalle, K.; Batezila, G.; Eller, G. A. *J. Fluorine Chem.* **2010**, *131*, 1013.

(10) (a) Fogg, D. E.; dos Santos, E. N. *Coord. Chem. Rev.* **2004**, *248*, 2365. (b) Chapman, C. J.; Frost, C. G. *Synthesis* **2007**, 1.

(11) For selected examples on copper-catalyzed tandem reactions, see: (a) Guo, S.; Wang, J.; Fan, X.; Zhang, X.; Guo, D. *J. Org. Chem.* **2013**, *78*, 3262. For a review see, (b) Liao, Q.; Yang, X.; Xi, C. *J. Org. Chem.* **2014**, *79*, 8507 and references cited therein. (c) Wen, L.-R.; Jin, X.-J.; Niu, X.-D.; Li, M. *J. Org. Chem.* **2015**, *80*, 90.

(12) For selected examples on O-arylation, see: (a) Shafir, A.; Lichtor, P. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3490. (b) Bistri, O.; Correa, A.; Bolm, C. *Angew. Chem. Int. Ed.* **2008**, *47*, 586. For a review see, (c) Monnier, F.; Taillefer, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 6954 and references cited therein.

(13) Poulsen, T. B.; Jørgensen, K. A. *Chem. Rev.* **2008**, *108*, 2903.

(14) Huemer, V.; Eller, G. A.; Holzer, W. *Magn. Reson. Chem.* **2010**, *48*, 476.

(15) (a) Butler, D. E.; DeWald, H. A. *J. Org. Chem.* **1975**, *40*, 1353. (b) Eiden, F.; Rademacher, G. *Arch. Pharm.* **1983**, *316*, 34.