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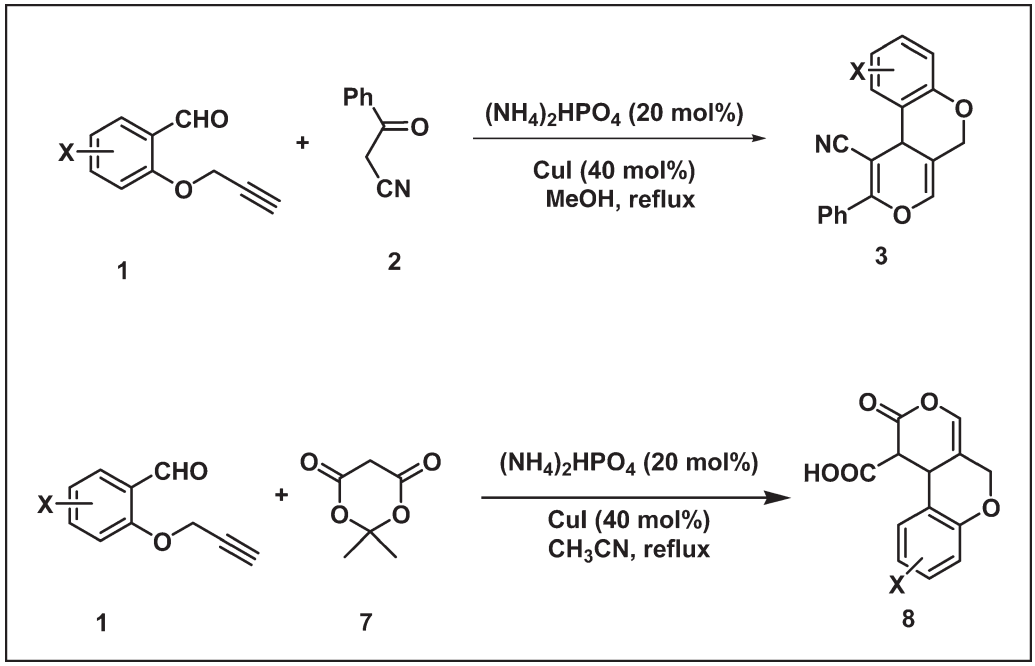

A new strategy involving domino Knoevenagel hetero-Diels-Alder reaction is described for the preparation of pyrano[3,4-*c*]chromenes scaffold. Reaction of *O*-propargylated salicylaldehyde with benzoylacetonitrile or Meldrum's acid in the presence of CuI and diammonium hydrogen phosphate affords pyrano[3,4-*c*]chromenes with good yields and high bond-forming efficiency.

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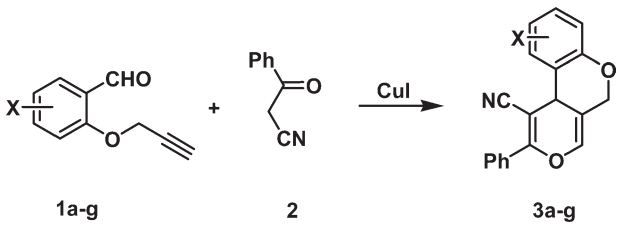
INTRODUCTION

The hetero-Diels-Alder reaction is one of the most powerful methods for the preparation of heterocyclic compounds and it has wide applications in the synthesis of biologically active compounds and natural products [1]. Among these reactions, domino Knoevenagel hetero-Diels-Alder reactions provide efficient and rapid means for the construction of polyheterocyclic compounds [2], especially pyran moieties. 2H-pyran derivatives are present in many natural products with different biological activities [3]. A family of xanthone natural products with potent antiviral activity has been isolated from plants, and it is a potent inhibitor of human immunodeficiency virus-1 reverse transcriptase [4]. Some 2H-chromene family are effective photoaffinity reagents for the cytochrome P450 superfamily of enzymes and probably other proteins as well [5]. Because of the unique properties of pyranochromene skeletons, the developments of synthetic methods that enable facile access to these useful entities are desirable.

In most reported reactions, in domino Knoevenagel hetero-Diels-Alder reactions, alkenes were used as a dienophile. The use of alkynes was limited due to their less reactivity when compared with alkenes. The activation of alkynes toward a variety of organic transformations is an exciting field in organic synthesis. In the recent years, the most important strategy for this aim usually consists of applying transition metal catalysts [6]. The activation of alkynes using various metals has

Scheme 1. Synthesis of pyrano[3,4-*c*]chromene in the presence of CuI.



1a-g 2 3a-g

been extensively investigated and described in the literature [7]. Selection of the proper Lewis acid to achieve this purpose is more important. Among the metal catalysts, coinage metals including copper, silver, and gold play an essential role in this field [8]. Therefore, development of new synthetic strategy based on coinage metals is very attractive.

During the past decade, copper (Cu) (I)-catalyzed cyclization of alkynes has represented a convenient tool for the preparation of heterocycles [8]. Copper (I) iodide (CuI), which has been applied in the synthetic and medicinal chemistry, has received much attention due to several advantages over the other coinage metals; including the low cost, insensitivity to air, simple experimental procedure, and no toxicity. Therefore, discovery of novel Cu (I)-catalyzed reaction of alkynes is of great interest [9].

RESULTS AND DISCUSSION

Following our research work to introduce domino Knoevenagel hetero-Diels-Alder reaction using unactivated alkynes with CuI [10] and to enlarge the scope of this synthetic methodology, herein, we report a domino Knoevenagel hetero-Diels-Alder reaction using *O*-propargylated salicyclaldehyde derivatives **1**(**a**–**g**) and benzoylacetonitrile **2** as unactivated terminal alkynes and an active methylene compound, respectively, in the presence of CuI (Scheme 1). The products are functionalized pyrano[3,4-*c*]chromenes **3**(**a**–**g**).

Initially, *O*-propargylated salicylaldehydes as the starting material were prepared in excellent yields using reaction of propargyl bromide and salicylaldehydes derivatives in dimethyl formamide and in the presence of K_2CO_3. To optimize the desired reaction conditions, the reaction of compound **1a** with benzoylacetonitrile **2** was used as the model system. The experimental results are summarized in Table 1.

Heating aldehyde **1a** and **2** in methanol under reflux condition for 72 h did not lead to the desired product. So, CuI was used as the Lewis acid. The reaction was done using different ratios of CuI in the presence of diammonium hydrogen phosphate (DAHP) or triethylamine as the base. The yields and reaction times are summarized in Table 1.

According to the obtained results, methanol was selected as the best solvent and the optimized molar ratio of CuI was 40%.

Under the optimal reaction conditions, pyrano[2,3-*c*]chromenes **3a**–**g** were prepared in 61–75% yields (Table 2). The best result was obtained using aldehyde **1d** (entry 4) that contained a nitro group. It seems that the electron-withdrawing substituent increase the yields of this transformation, as opposed to decreased yield obtained with electron-donating substituent (entry 3).

Structures of the products were confirmed by their spectroscopic data. In ^{1}H NMR of compounds **3a**–**g**, the —OCH_2 group resonates at $\delta = 4.60$ and 4.72 ppm as a doublet with $J = 11.5$–11.8 Hz. The —CH proton appears at $\delta = 4.79$–4.93 ppm as a singlet, and the olefinic proton =CH resonates at $\delta = 7.12$–7.22 ppm as a singlet. The corresponding signal of the —OCH_2 and the shielded olefinic =C—CN carbons in ^{13}C NMR appear at 65.0–66.4 and 83.8–85.7 ppm, respectively.

This reaction involves two steps: (a) the Knoevenagel condensation between benzoylacetonitrile **2** and the propargylated salicylaldehydes **1a**–**g**. DAHP acts as a mild base for Knoevenagel condensation and formation of 1-oxa-1,3-butadiene that could react as a heterodiene to form the intermediate. (b) hetero-Diels-Alder reaction of olefinic intermediate in the presence of CuI to afford compounds **3a**–**g**. Although the mechanism for this transformation is not clear, it seems that CuI could active the unactivated triple bond to act as a dienophile in hetero-Diels-Alder reaction (Scheme 2).

As a logical extension of domino Knoevenagel hetero-Diels-Alder reaction with unactivated alkynes, we became interested in the synthesis of functionalized pyranochromene derivatives, whose structures have been found in vast numbers of natural products and pharmaceuticals. Reaction of *O*-propargylated salicylaldehyde

Table 1

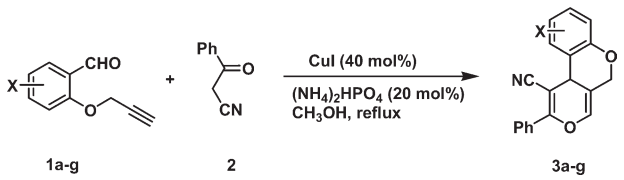
Synthesis of pyrano[3,4-*c*]chromene using domino Knoevenagel hetero-Diels-Alder reaction, the role of base type and molar ratio of CuI on the formation of product **3a**.

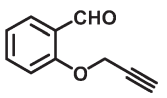
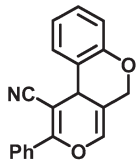
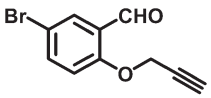
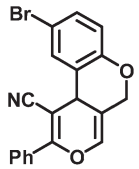
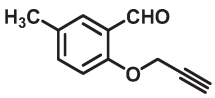
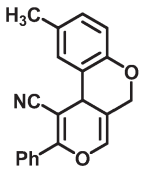
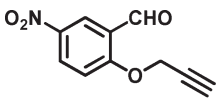
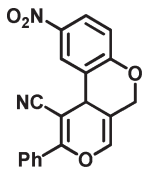
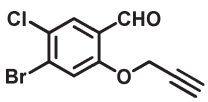
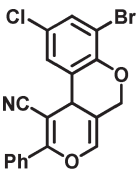
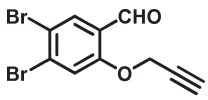
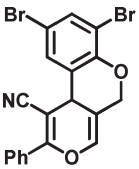
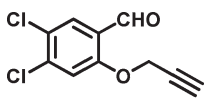
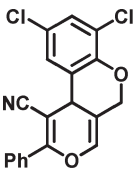
Entry	Lewis acid	Solvent	Base	Time (h)[a]	Yield (%)
1	–	MeOH	$(NH_4)_2HPO_4$	72	–
2	CuI (20%)	MeOH	$(NH_4)_2HPO_4$	72	Trace
3	CuI (30%)	MeOH	$(NH_4)_2HPO_4$	48	40
4	CuI (40%)	MeOH	$(NH_4)_2HPO_4$	48	61
5	CuI (50%)	MeOH	$(NH_4)_2HPO_4$	48	57
5	CuI (40%)	MeOH	–	72	–
6	CuI (40%)	MeCN	$(NH_4)_2HPO_4$	48	50
7	CuI (40%)	MeCN	Et_3N	48	28

[a] Completion of the reaction.

Table 2

CuI-mediated domino hetero-Diels-Alder reaction of aldehydes **1a**–**g** with **2**[a].

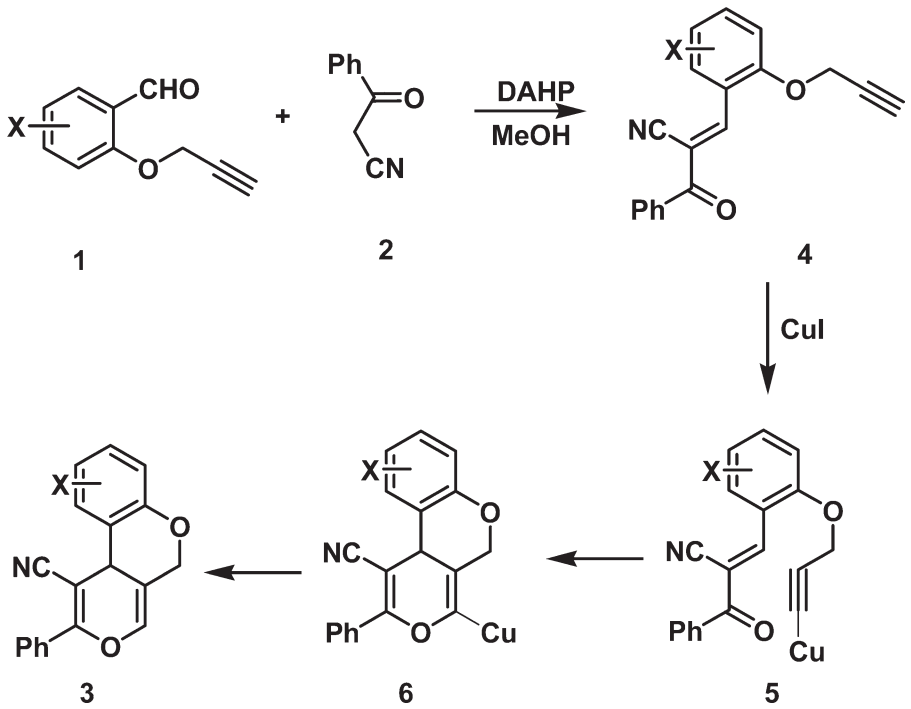


Entry	Aldehyde	Product	Time (h)	Yield (%)[b]
1	 **1a**	 **3a**	48	61
2	 **1b**	 **3b**	32	65
3	 **1c**	 **3c**	24	61
4	 **1d**	 **3d**	20	75
5	 **1e**	 **3e**	12	70
6	 **1f**	 **3f**	16	67
7	 **1g**	 **3g**	12	67

[a] All of the reaction were performed with propargylated aldehydes **1a**–**g** (1 mmol), benzoylacetonitrile **2** (1.2 mmol), $(NH_4)_2HPO_4$ (20 mol %), and CuI (40 mol %) in methanol at reflux.

[b] Isolated yield.

Scheme 2. Plausible mechanism for the synthesis of pyrano[3,4-*c*]chromene skeleton *via* domino Knoevenagel hetero-Diels-Alder reaction using CuI.



Scheme 3. Synthesis of pyrano[3,4-*c*]chromenes **8** in the presence of CuI and Meldrum's acid.

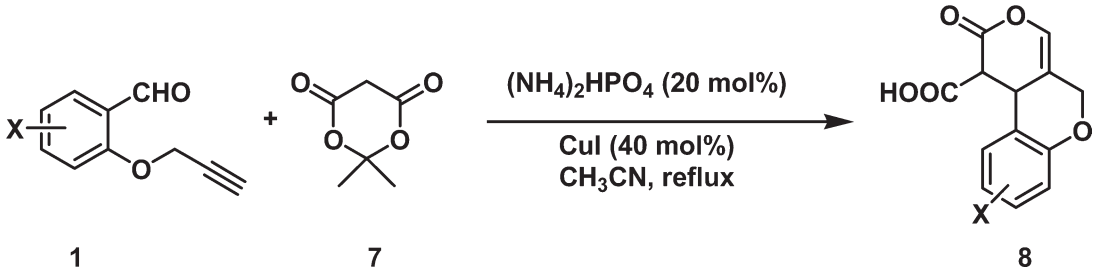
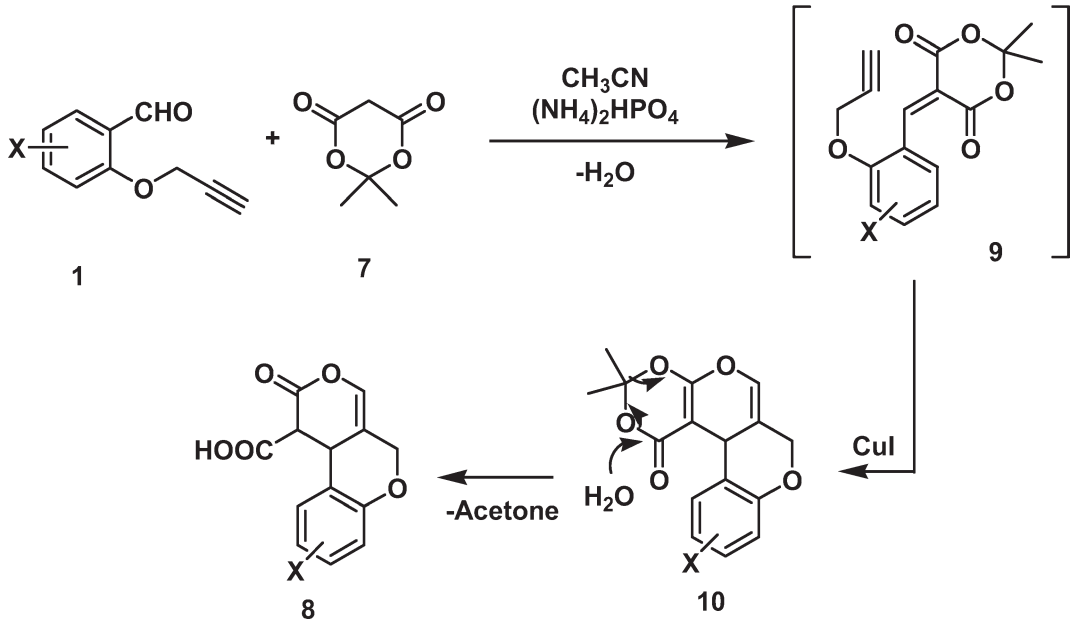


Table 3

Synthesis of pyrano[3,4-*c*]chromene using domino Knoevenagel hetero-Diels-Alder reaction, the role of solvent, base type, and molar ratio of CuI on the formation of product **8a**.

Entry	Lewis acid	Solvent	Base	Time (h)	Yield (%)
1	–	MeCN	$(NH_4)_2HPO_4$	120	–
2	CuI (20%)	MeCN	$(NH_4)_2HPO_4$	120	40
3	CuI (30%)	MeCN	$(NH_4)_2HPO_4$	72	45
4	CuI (40%)	MeCN	$(NH_4)_2HPO_4$	72	68
5	CuI (50%)	MeCN	$(NH_4)_2HPO_4$	72	60
6	CuI (40%)	MeOH	$(NH_4)_2HPO_4$	80	50
7	CuI (40%)	EtOH	$(NH_4)_2HPO_4$	96	Trace
8	CuI (40%)	H_2O	$(NH_4)_2HPO_4$	96	Trace
9	CuI (40%)	MeCN	–	72	–
13	CuI (40%)	MeCN	Et_3N	48	33
14	CuI (40%)	MeCN	K_2CO_3	72	38

Scheme 4. Plausible mechanism for the synthesis of pyrano[3,4-*c*]chromene skeleton *via* activation of π-triple bond using CuI.



with Meldrum's acid **7** in the presence of CuI should afford the desired pyranochromenes **8** (Scheme 3).

Reaction of *O*-propargylated salicylaldehyde **1a** with Meldrum's acid **7** was selected as a model, and the reaction was done in the presence of different ratios of CuI and also diammonium hydrogen phosphate as a base. The details were summarized in Table 3. In this reaction, the best yield was obtained using 40% CuI. The presence of CuI is necessary for the progress of reaction and without CuI, the Knoevenagel product were obtained as the sole product.

On the basis of established Meldrum's acid chemistry, it is reasonable to assume that the formation of aryliden Meldrum's acid apparently results from initial addition of Meldrum's acid with *O*-propargylated salicylaldehyde to obtain *in situ* dieneone **8** (Scheme 4). This intermediate under the reflux conditions and hetero-Diels-Alder reaction converted to pyran skeleton.

The presence of the pyran skeleton is supported by the spectroscopic data. In the ^{1}H NMR of compound **8a**, the —OCH_2 group shows two separated doublet with $J = 12$ Hz and also a carboxylic acid peak at $\delta = 12.75$ ppm. The high J value is related to the torsion angle that is 174.6°. The structure of compound **8a** was confirmed using X-ray structure data. The product **8a** could form a dimmer *via* intermolecular hydrogen bonding between two carboxylic acid groups (Figs. 1 and 2).

Under the optimal reaction conditions, the best result was obtained using aldehyde **1d** (entry 4) that contained a nitro group (Table 4). In entry 4, the desired product could be decarboxylated and the final product does not contain the carboxylic acid functional group and the product **8d** is the sole product of reaction. Existence of a catalyst such as CuI is necessary to activate the triple bond through complexation. CuI could coordinate the triple bond and the activated triple bond is ready to proceed hetero-Diels-Alder reaction to form pyrano[3,4-*c*]chromene. Reactions were done under Argon conditions to prevent the oxidation of Cu (I) to Cu (II).

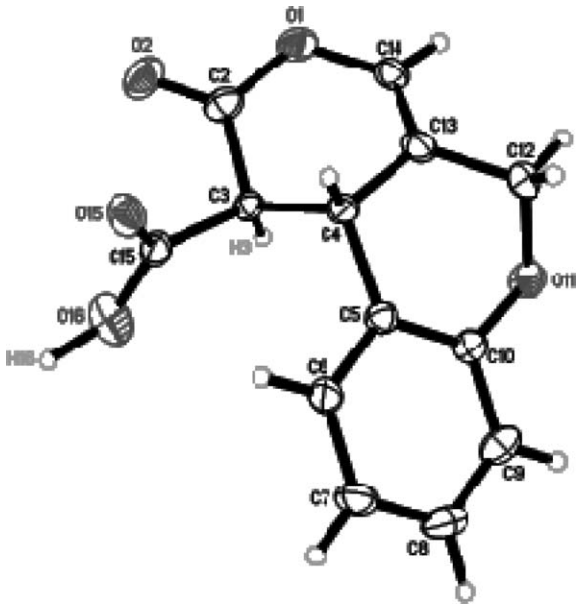


Figure 1. X-ray structure of compound **8a**.

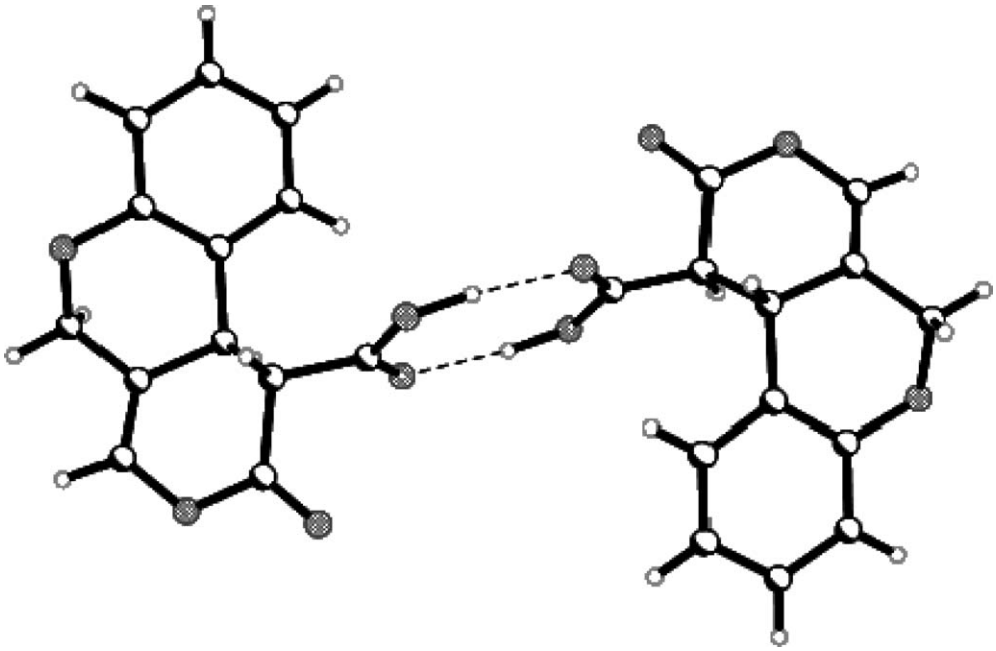


Figure 2. Intermolecular hydrogen bonding in compound **8a**.

CONCLUSIONS

In conclusion, we have described an efficient approach with a high bond-forming efficiency for the synthesis of pyrano[3,4-*c*]chromene skeleton *via* domino Knoevenagel hetero-Diels-Alder reaction started from simple and inexpensive materials. Reaction of *O*-propargylated salicylaldehyde with active methylene compounds such as benzoylacetonitrile and Meldrum's acid leads to functionalized pyranochromenes. In this reaction, CuI (40%) was used as Lewis acid for the activation of unactivated alkynes and DAHP (20%) as the base. The products have nitrile and carboxylic acid functional groups that could be used for further conversion.

EXPERIMENTAL

Commercially available materials were used without further purification. Melting points were determined with Electrothermal 9100 apparatus and were uncorrected. IR spectra were obtained on an ABB FTIR (FTLA 2000) spectrometer. ^{1}H NMR and ^{13}C NMR were run on a Bruker DRX-300 AVANCE at 500 and 300 MHz for ^{1}H NMR and 125 and 75 MHz for ^{13}C NMR. $CDCl_3$ and DMSO-d_6 were used as solvents. High resolution mass spectra were recorded on JEOL JMS-700 (HR-EI) spectrometer and Mass spectra were obtained using a GC-MS Hewlett Packard (EI, 70 eV) instrument.

General procedure for the synthesis of pyranochromenes 3a–g derivatives *via* hetero-Diels-Alder reactions. A solution of *O*-propargylated salicylaldehydes **1a–g** (1 mmol), benzoylacetonitrile (174 mg, 1.2 mmol), CuI (0.4 equiv., 76 mg), and $(NH_4)_2HPO_4$ (28 mg, 0.2 equiv.) in methanol (25 mL) was refluxed. The progress of reaction was monitored by thin layer chromatography (Petroleum ether: EtOAc 3:1). After completion of the reaction, the mixture of reaction was filtered and the solvent was evaporated under reduced pressure. The obtained oil was crystalizated in diethyl ether.

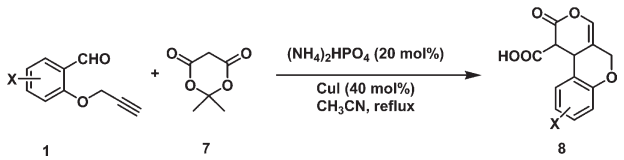
2-Phenyl-5H,10bH-pyrano[3,4-c]chromene-1-carbonitri le (3a). This compound was obtained as a white solid; yield 61%; mp (Dec) 200.3°C; ir (potassium bromide): 2203, 1710, 1615, 1578 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.60 (d, J = 11.5 Hz, 1H, —OCH_2), 4.72 (d, J = 11.5 Hz, 1H, —OCH_2), 4.79 (s, 1H, —CH), 6.85 (d, J = 7.9 Hz, 1H, H_{Ar}), 7.01 (t, J = 7.5 Hz, 1H, H_{Ar}), 7.15 (s, 1H, =CH), 7.22 (t, J = 7.5 Hz, 1H, H_{Ar}), 7.53–7.61 (m, 3H, H_{Ar}), 7.69 (d, J = 7.9 Hz, 1H, H_{Ar}), 7.75 ppm (d, J = 7.2 Hz, 2H, H_{Ar}); ^{13}C NMR (125 MHz, DMSO-d_6): δ 31.8, 66.0, 85.7, 110.3, 118.3, 120.7, 121.8, 125.7, 127.0, 129.0, 129.3, 129.5, 132.2, 132.3, 137.8, 155.1, 163.6 ppm; HR ms (70 eV, electron impact): m/z $[M]^{+\cdot}$ Calcd. for $C_{19}H_{13}NO_2$: 287.0946; Found: 287.0959.

9-Bromo-2-phenyl-5H,10bH-pyrano[3,4-c]chromene-1-carbonitrile (3b). This compound was obtained as a white solid; yield 65%; mp 197–198°C; IR (potassium bromide): 2204, 1707, 1614, 1577 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.58 (d, J = 11.6 Hz, 1H, —OCH_2), 4.73 (d, J = 11.6 Hz, 1H, —OCH_2), 4.80 (s, 1H, —CH), 6.81 (d, J = 8.7 Hz, 1H, H_{Ar}), 7.16 (s, 1H, =CH), 7.36 (dd, J = 8.7, 2.1 Hz, 1H, H_{Ar}), 7.49–7.60 (m, 3H, H_{Ar}), 7.74 (d, J = 7.2 Hz, 2H, H_{Ar}), 7.80 ppm (d, J = 2.1 Hz, 1H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ 30.6, 65.3, 84.3, 108.4, 112.0, 119.7, 126.8, 128.2, 128.6, 128.8, 131.1, 131.2, 131.5, 137.4, 153.6, 163.0 ppm; HR ms (70 eV, electron impact): m/z $[M]^{+\cdot}$ Calcd. for $C_{19}H_{12}NO_2$ ^{79}Br: 365.0052; Found: 365.0039. $[M + 2]^{+\cdot}$ Calcd. for $C_{19}H_{12}NO_2$ ^{81}Br: 367.0031; Found: 367.0026.

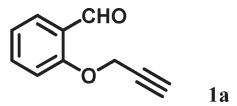
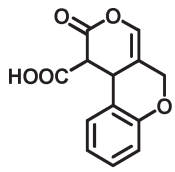
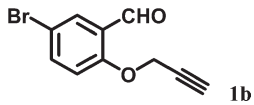
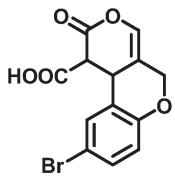
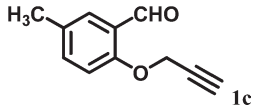
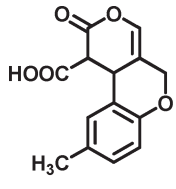
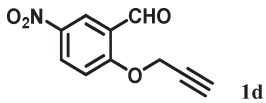
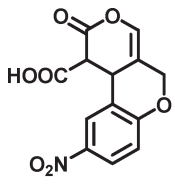
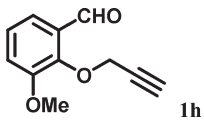
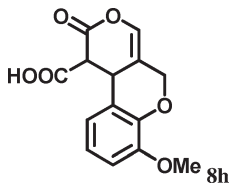
9-Methyl-2-phenyl-5H,10bH-pyrano[3,4-c]chromene-1-carbonitrile (3c). This compound was obtained as a white solid,

Table 4

One-pot synthesis of pyrano[3,4-*c*]chromene *via* domino Knoevenagel hetero-Diels-Alder reaction.



1 7 8

Entry	Aldehyde	Product	Time (h)	Yield (%)[b]
1	 **1a**	 **8h**	72	68
2	 **1b**	 **8b**	48	65
3	 **1c**	 **8c**	48	63
4	 **1d**	 **8d**	48	81
5	 **1h**	 **8h**	72	61

yield 61%; mp 169–171°C; IR (potassium bromide): 2205, 1708, 1620, 1600 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 2.25 (s, 3H, Me), 4.54 (d, J = 11.6 Hz, 1H, —OCH_2), 4.66 (d, J = 11.6 Hz, 1H, —OCH_2), 4.71 (s, 1H, —CH), 6.72 (d, J = 8.2 Hz, 1H, H_{Ar}), 7.00 (d, J = 8.2 Hz, 1H, H_{Ar}), 7.12 (s, 1H, =CH), 7.46 (s, 1H, H_{Ar}), 7.50–7.60 (m, 3H, H_{Ar}), 7.74 ppm (dd, J = 7.7, 1.5 Hz, 2H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ 20.4, 30.9, 65.0, 84.9, 109.6, 117.2, 119.9, 124.4, 126.4, 128.1, 128.6, 128.9, 129.5, 131.3, 131.4, 136.8, 152.0, 162.7 ppm; HR ms (70 eV, electron impact): m/z $[M]^{+\cdot}$ Calcd. for $C_{20}H_{15}NO_2$: 301.1103; Found: 301.1067.

9-Nitro-2-phenyl-5H,10bH-pyrano[3,4-c]chromene-1-carbonitrile (3d). This compound was obtained as a white solid, yield 75%; mp 185.5–187.5°C; IR (potassium bromide): 2209, 1708, 1616, 1580, 1514, 1343 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 4.76 (d, J = 11.7 Hz, 1H, —OCH_2), 4.89 (d, J = 11.7 Hz, 1H, —OCH_2), 4.93 (s, 1H, —CH), 7.05 (d, J = 9.1 Hz, 1H, H_{Ar}), 7.22 (s, 1H, =CH), 7.51–7.61 (m, 3H, H_{Ar}),

7.75 (d, J = 6.6 Hz, 2H, H_{Ar}), 8.10 (dd, J = 9.1, 2.0 Hz, 1H, H_{Ar}), 8.63 ppm (d, J = 2.0 Hz, 1H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ 30.7, 66.3, 83.8, 107.2, 118.5, 119.7, 122.3, 124.5, 125.4, 128.1,128.7, 131.0, 131.7, 137.8, 140.6, 159.9, 162.9 ppm; HR ms (70 eV, electron impact): m/z $[M]^{+\cdot}$ Calcd. for $C_{19}H_{12}N_2O_4$: 332.0797; Found: 332.0769.

7-Bromo-9-chloro-2-phenyl-5H,10bH-pyrano[3,4-c]chromene-1-carbonitrile (3e). This compound was obtained as a white solid, yield 70%; mp 195–196°C; IR (potassium bromide): 2205, 1710, 1613, 1450 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.71 (d, J = 11.8 Hz, 1H, —OCH_2), 4.86 (s, 1H, —CH), 4.89 (d, J = 11.8 Hz, 1H, —OCH_2), 7.20 (s, 1H, =CH), 7.51–7.59 (m, 3H, H_{Ar}), 7.67 (s, 2H, H_{Ar}), 7.76 ppm (d, J = 6.79 Hz, 2H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.0, 66.4, 83.9, 107.7, 111.6, 119.6, 124.6, 125.3, 127.7, 128.2, 128.6, 131.0, 131.6, 137.7, 149.8, 163.1 ppm; HR ms (70 eV, electron impact): m/z $[M]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{79}Br^{35}Cl$: 398.9662; Found: 398.9637. $[M + 2]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{79}Br^{37}Cl$: 400.9641; Found: 400.9629. $[M + 4]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{81}Br^{37}Cl$: 402.9612; Found: 402.9644.

7,9-Dibromo-2-phenyl-5H,10bH-pyrano[3,4-c]chromene-1-carbonitrile (3f). This compound was obtained as a white solid, yield 67%; mp 202.4–203.5°C; IR (potassium bromide): 2204, 1709, 1613, 1599 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.71 (d, J = 11.8 Hz, 1H, —OCH_2), 4.87 (s, 1H, —CH), 4.89 (d, J = 11.8 Hz, 1H, —OCH_2), 7.20 (s, 1H, =CH), 7.50–7.61 (m, 3H, H_{Ar}), 7.74–7.80 ppm (m, 3H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ 30.9, 66.4, 83.9, 107.7, 111.9, 112.0, 119.6, 128.2, 128.6, 131.0, 131.6, 133.6, 137.7, 150.2, 163.1 ppm; HR ms (70 eV, electron impact): m/z $[M]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{79}Br_2$: 442.9157; Found: 442.9195. $[M + 2]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{79}Br^{81}Br$: 444.9136; Found: 444.9091. $[M + 4]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{81}Br_2$: 446.9115; Found: 446.9069.

7,9-Dichloro-2-phenyl-5H,10bH-pyrano[3,4-c]chromene-1-carbonitrile (3g). This compound was obtained as a white solid, yield 67%; mp 193–195°C; ir (potassium bromide): 2205, 1710, 1611, 1600 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.72 (d, J = 11.6 Hz, 1H, H-5), 4.85 (s, 1H, —CH), 4.90 (d, J = 11.6 Hz, 1H, —OCH_2), 7.20 (s, 1H, =CH), 7.50–7.61 (m, 4H, H_{Ar}), 7.64–7.65 (m, 1H, H_{Ar}), 7.76 ppm (dd, J = 7.3, 1.6 Hz, 2H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.0, 66.3, 83.8, 107.6, 119.6, 122.2, 124.19, 124.2, 124.7, 127.9, 128.2, 128.3, 128.6, 131.0, 131.6, 137.7, 148.9, 163.1 ppm; HR ms (70 eV, electron impact): m/z $[M]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{35}Cl_2$: 355.0166; Found: 355.0198. $[M+2]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{35}Cl^{37}Cl$: 357.0138; Found: 357.0185. $[M + 4]^{+\cdot}$ Calcd. for $C_{19}H_{11}NO_2{}^{37}Cl_2$: 359.0108; Found: 359.0138.

General procedure for the synthesis of pyranochromenes 8 derivatives *via* hetero-Diels-Alder reactions. A solution of *O*-propargylated salicylaldehydes (1 mmol), Meldrum's acid (172 mg, 1.2 mmol), CuI (0.4 equiv., 76 mg), and $(NH_4)_2HPO_4$ (28 mg, 0.2 equiv.) in acetonitrile (25 mL) was refluxed. The progress of reaction was monitored by TLC (Petroleum ether:EtOAc 4:1). After completion of the reaction, the mixture of reaction was filtered and the solvent was evaporated under reduced pressure. Further purification was done using crystallization in acetonitrile.

2-Oxo-1,10b-dihydro-2H,5H-pyrano[3,4-c]chromene-1-carboxylic acid (8a). This compound was obtained as a white solid, yield 72%; mp (Dec) 250°C; ir (potassium bromide): 3414, 1761, 1692 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.43 (d, J = 12.9 Hz, 1H, —CHCOOH), 4.34–4.38 (m, 2H, —OCH_2, —CH), 4.65 (d, J = 12.0 Hz, 1H, —OCH_2), 6.87 (d, J = 7.7 Hz, 1H, H_{Ar}), 6.92 (t, J = 7.4 Hz, 1H, H_{Ar}), 7.05 (s, 1H, =CH), 7.16 (t, J = 7.4 Hz, 1H, H_{Ar}), 7.24 (d, J = 7.7 Hz, 1H, H_{Ar}), 12.50 ppm (brs, 1H, —COOH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 32.1, 53.2, 65.0, 115.0, 118.5, 122.3, 123.8, 129.1, 129.4, 137.7, 155.6, 166.9, 170.2 ppm; ms (70 eV, electron impact): m/z 246 (M^+), 245 (M^+ − H), 201 (M^+ − COOH), 173 (M^+ − C_2HO_3).

Colorless crystal (polyhedron), dimensions 0.37 × 0.22 × 0.13 mm^3, crystal system monoclinic, space group $P2_1/n$, Z = 4, a = 8.9193(12) Å, b = 12.4115(16) Å, c = 9.9814(13) Å, α = 90°, β = 97.889(3) deg, γ = 90 deg, V = 1094.5(2) Å^3, ρ = 1.494 g/cm^3, T = 200(2) K, Θ_{max} = 28.31°, radiation Mo Kα, λ = 0.71073 Å, 0.3° omega scans with CCD area detector, covering a whole sphere in reciprocal space, 11,243 reflections measured, 2724 unique [R(int) = 0.0243], 2510 observed [$I > 2\sigma(I)$], intensities were corrected for Lorentz and polarization effects, an empirical absorption correction was applied using SADABS[1] based on the Laue symmetry of the reciprocal space, mu = 0.12 mm^{-1}, T_{min} = 0.96, T_{max} = 0.99, structure solved by direct methods and refined against F^2 with a Full-matrix least-squares algorithm using the SHELXTL-PLUS (6.10) software package [11], 171 parameters refined, hydrogen atoms were treated using appropriate riding models, except of H3 and H16 at the carboxyl group, which were refined isotropically, goodness of fit 1.13 for observed reflections, final residual values $R1(F)$ = 0.061, $wR(F^2)$ = 0.158 for observed reflections, residual electron density −0.58 to 0.75 eÅ^{-3}. CCDC 742487 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

9-Bromo-2-oxo-1,10b-dihydro-2H,5H-pyrano[3,4-c]chromene-1-carboxylic acid (8b). This compound was obtained as a white solid, yield 65%; mp (°C) 230°C; IR (potassium bromide): 3447, 1768, 1680 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.47 (d, J = 13.0 Hz, 1H, —CHCOOH), 4.34–4.40 (m, 2H, —OCH_2, —CH), 4.69 (d, J = 12.1 Hz, 1H, —OCH_2), 6.87 (d, J = 8.6 Hz, 1H, H_{Ar}), 7.07 (s, 1H, H_{Ar}), 7.32–7.38 (m, 2H, =CH, H_{Ar}), 12.65 ppm (brs, 1H, —COOH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.1, 52.0, 64.2, 112.7, 113.1, 119.7, 125.3, 130.8, 130.9, 137.1, 154.1, 165.6, 169.0 ppm; ms (70 eV, electron impact): m/z 326 (M^+ +2), 324 (M^+), 281 ([$C_{13}H_9O_5{}^{81}Br$ – COOH]$^+$), 279 ([$C_{13}H_9O_5{}^{79}Br$ – COOH]$^+$), 253 ([$C_{13}H_9O_5{}^{81}Br$ – C_2HO_3]$^+$), 251 ([$C_{13}H_9O_5{}^{79}Br$ – C_2HO_3]$^+$).

9-Methyl-2-oxo-1,10b-dihydro-2H,5H-pyrano[3,4-c]chromene-1-carboxylic acid (8c). This compound was obtained as a white solid; yield 63%; mp (°C) 235°C; IR (potassium bromide): 3416, 1764, 1690 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.14 (s,3H, Me), 3.39 (d, J = 12.7 Hz, 1H, —CHCOOH), 4.27–4.30 (m, 2H, —OCH_2, —CH), 4.59 (d, J = 12.0 Hz, 1H, —OCH_2), 6.74 (d, J = 7.5 Hz, 1H, H_{Ar}), 6.93–7.04 (m, 3H, H_{Ar}, =CH), 12.55 ppm (brs, 1H, —COOH); ms (70 eV, electron impact): m/z 260 (M^+), 215 (M^+ − COOH). Because of the low solubility of this compound in DMSO-d_6, we were not successful to have ^{13}C NMR.

9-Nitro-2-oxo-1,10b-dihydro-2H,5H-pyrano[3,4-c]chromene (8d). This compound was obtained as a white solid; yield 81%; mp 242–243°C; IR (potassium bromide): 3407, 1782, 1680 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.49–2.62 (m,

1H, ═CH), 3.32–3.43 (m, 1H, ═CH_2), 4.16 (dd, J = 13.3, 4.4 Hz, 1H, ═CH_2), 4.56 (d, J = 12.3 Hz, 1H, ═OCH_2), 4.84 (d, J = 12.3 Hz, 1H, ═OCH_2), 7.07 (d, J = 8.5 Hz, 2H, H_{Ar}, =CH), 8.03 (dd, J = 8.5, 2.3 Hz, 1H, H_{Ar}), 8.33 (d, J = 2.3 Hz, 1H, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.4, 34.4, 64.2, 111.9, 118.0, 123.6, 124.7, 124.8, 138.1, 141.2, 159.2, 167.0 ppm; ms (70 eV, electron impact): m/z 247 (M^+), 230 ($M^+ - OH$), 219 ($M^+ - CO$).

7-Methoxy-2-oxo-1,10b-dihydro-2H,5H-pyrano[3,4-c]chromene-1-carboxylic acid (8h). This compound was obtained as a white solid; yield 61%; mp (°C) 240°C; IR (potassium bromide): 3447, 1768, 1680 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.41 (d, J = 12.6 Hz, 1H, ═CHCOOH), 3.72 (s, 3H, OMe), 4.28–4.36 (m, 2H, ═OCH_2, ═CH), 4.68(d, J = 12.0 Hz, 1H, ═OCH_2), 6.79–6.90 (m, 3H, H_{Ar}), 7.05 (s, 1H, =CH), 12.60 ppm (brs, 1H, ═COOH); ^{13}C NMR (75 MHz, DMSO-d_6): δ 30.4, 51.5, 54.7, 63.2, 109.8, 113.3, 118.9, 120.0, 122.6, 135.9, 143.6, 147.9, 165.2, 168.4 ppm; ms (70 eV, electron impact): m/z 276 (M^+), 275 ($M^+ - H$), 231 ($M^+ - COOH$), 203 ($M^+ - C_2HO_3$).

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