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Efficient synthesis of pyrano[2,3-*c*]coumarins via intramolecular domino Knoevenagel hetero-Diels–Alder reactions

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ABSTRACT

The domino Knoevenagel hetero-Diels–Alder reaction of the *O*-propargylated salicylaldehydes and 4-hydroxycoumarin leads to pyrano[2,3-*c*]coumarins **3** and pyrano[2,3-*c*]chromones **4** in high yield in the presence of CuI as a Lewis acid. In all cases, the reaction was shown to exhibit high regioselectivity and form product **3** as main product.

1. Introduction

Heterocyclic compounds are widely distributed in natural products and comprise a huge number of biologically active compounds. Amongst the various heterocyclic systems, pyran rings are one of the most widely investigated.[1] Recently, it was shown that some natural products with a tricyclic benzopyrone core structure belong to a new class of inhibitors for bacterial metallo-β lactams. This skeleton also exists in the fungal metabolite fulvic acid.[2] As a result, the development of efficient methods for the synthesis of these compounds is one of the most attractive fields in preparative chemistry.

One area of interest in the field of heterocyclic synthesis is in the use of domino reactions. During the past decade, domino reactions have emerged as a powerful and efficient method for the construction of heterocyclic compounds.[3] Amongst such reactions, the domino Knoevenagel-hetero-Diels–Alder reaction has proven to be a useful tool for the synthesis of polyheterocyclic compounds.[4] This synthetic methodology employing oxa-dienes represents a straightforward approach to the synthesis of oxygen-containing heterocycles. The field of domino Knoevenagel hetero-Diels–Alder reaction is dominated by alkenes. The use of alkyne analogous as a dienophile has imposed an important problem due to the reduced reactivity of alkynes as compared to alkenes. In recent years, the activation of alkynes by transition metal catalysts leads to more effective substrates in a variety of organic transformations.[5,6] Recently, CuI-catalyzed cyclization of alkynes has been represented as one of the most important processes in organic synthesis.[7]

We have previously described a new hetero-Diels–Alder reaction of 1-oxa-1,3-butadienes with inactivated terminal acetylene using a CuI catalyst.[8] In continuation of this work and because of the biological activities of pyran rings, we report a new domino Knoevenagel-hetero-Diels–Alder reaction of *O*-propargylated salicylaldehydes **1** and 4-hydroxycoumarins **2** using CuI as a catalyst. This reaction shows a remarkable regioselectivity (Scheme 1).

2. Results and discussion

The substrates **1a**–**e** for the copper-catalyzed domino Knoevenagel hetero-Diels–Alder reaction were synthesized in high yields and excellent purity by addition of the propargyl bromide to the salicylaldehydes derivatives in DMF.

The domino Knoevenagel hetero-Diels–Alder reactions of **1a**–**e** with 4-hydroxycoumarins **2a**,**b** were performed using CuI as a Lewis acid in 1,4-dioxane at reflux. We first chose **1a** and **2a** as

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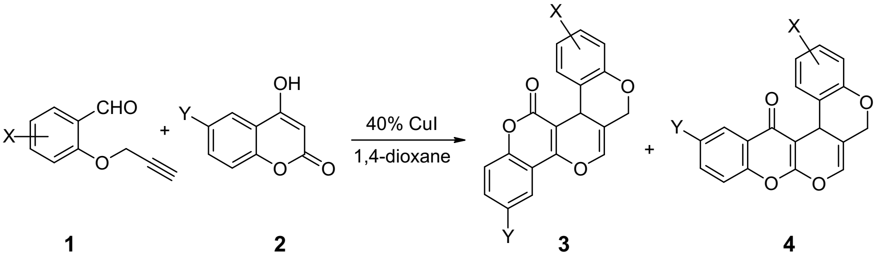


Scheme 1.

model substrates to optimize the reaction conditions to achieve the best outcome. The experimental results are summarized in Table 1.

In the first attempt, the reaction of **1a** and **2a** in absence of a CuI catalyst did not yield any of the desired compound **3a** (entry 1). When 20 mol % of CuI was employed, compound **3a** formed in 50% yield (entry 4). A series of solvents (toluene, 1,4-dioxane, and methanol) were investigated (entries 2–7). Amongst the solvents tested, 1,4-dioxane provided the best yield. Then the amount of CuI catalyst was varied. When 40 mol % of CuI was employed, the desired product **3a** was isolated in 72% yield and no product **4a** was observed.

Using the optimized conditions, we studied the domino Knoevenagel-hetero-Diels–Alder reaction of **1a**–**e** and **2a**–**b**. The results are summarized in Table 2. The structures of the products were determined by NMR spectroscopic data and X-ray crystallography. In some cases (entries 2 and 7–9) a mixture of products was formed. For example, in the ^{1}H NMR spectra of compounds **3b** and **4b**, there were two separate signals. One of the H_{Ar} of **3b** resonate at δ=6.97 with J=7.9 Hz. The same hydrogen atom signal for **4b** is observed at δ=6.88 with J=7.7 Hz. Based on these peaks, the ratio of **3b**/**4b** was determined to be 72:28. In the ^{13}C NMR spectra, carbonyl signal appeared at 161.6 ppm for coumarin **3b**, and at δ=176.4 ppm for chromone **4b**.

The characteristic peaks for **4a**–**i** in the ^{1}H NMR spectra are an AB quartet for the OCH_2 group between 4.7 and 5.0 ppm followed closely by a singlet for the =CH group. The corresponding signals of the OCH_2 and =CH groups in the ^{13}C NMR spectra appear at 66 and 99 ppm, respectively. The diastereotopicity of the two protons of the OCH_2 groups is due to the helical shape of rings in the products. The helical shape of **3a** and **3e** was confirmed by an X-ray study (Fig. 1). The angles between the faces are 61.8° for **3a** and 69.8° for **3b**.

The mixture of products could be formed as a result of a competitive hetero-Diels–Alder reaction including two different heterodienes. Due to the reaction conditions, an alkene intermediate is formed (Scheme 2). The alkene intermediate provides two different heterodiene fragments that give the corresponding hetero-Diels–Alder reaction (intermediates **5** and **6**). Therefore, two pathways can be imagined for a hetero Diels–Alder reaction. In one case, the keto carbonyl group could be involved in the cycloaddition reaction leading to the pyrano[2,3-*c*]coumarins **3** (path A in Scheme 2). In another form, the lactone carbonyl group could be reacted, affording to the pyrano[2,3-*c*]chromone **4** (path B in Scheme 2). As it was shown in Table 2, electron-withdrawing substituents (such as NO_2, entry 9) accelerate the reaction. The results can be understood in terms of the frontier molecular orbital (FMO) theory. According to FMO theory, the reactions having small HOMO–LUMO gaps manifest faster rates. It seems that the effective interaction takes place between the LUMO of diene and the HOMO of the alkyne, thus we are dealing with an inverse Diels–Alder reaction. Similarly, chemoselectivity observed in this reaction can be explained in frontier orbital terms. It seems that two important factors control the synthesis of major product **3** that could be classified as (a) more efficient HOMO–LUMO interaction for α,β-unsaturated ketone as diene and alkyne as dienophile in the intermediate **5** compared to intermediate **6**. (b) More steric hinderance in the intermediate **6** compared to **5**. The steric hinderance is much more when the carbonyl group of ester acts as the heterodiene compared to the carbonyl group of α,β-unsaturated ketone system.

In all of the cases, the major products probably arise from the hetero-Diels–Alder reaction of the keto carbonyl (product **3**). The structures and the ratio of the products were established on the basis of their spectroscopic data. In the ^{1}H NMR spectrum, there are two distinct groups of peaks with different intensity proportional to the ratio of products.

Table 1
Effect of reaction conditions for the Domino Knoevenagel hetero-Diels–Alder reaction of **1a** and **2a**

Entry	Lewis acid	Solvent	Base	Time (h)	Yield[a] (%)
1	—	1,4-Dioxane	Et_3N	30	—
2	CuI (20%)	Acetonitrile	Et_3N	30	—
3	CuI (20%)	Toluene	Et_3N	30	—
4	CuI (20%)	1,4-Dioxane	Et_3N	30	50
5	CuI (30%)	1,4-Dioxane	Et_3N	30	66
6	CuI (40%)	1,4-Dioxane	Et_3N	24	72
7	CuI (40%)	Methanol	Et_3N	18	50
8	CuI (40%)	1,4-Dioxane	—	40	—
9	CuI (40%)	1,4-Dioxane	DIEA[b]	24	20

[a] Compounds **3a** and **4a**.
[b] *i*-Pr_2NEt.

3. Conclusion

The CuI-catalyzed domino Knoevenagel-hetero-Diels–Alder reaction of *O*-propargylated salicylaldehydes **1a**–**g** with 4-hydroxycoumarin **2a**,**b** represents a new route to the efficient synthesis of the pyrano[2,3-*c*]coumarins **3a**–**j** and pyrano[2,3-*c*]chromones **4a**–**j**. Remarkable feature of this approach is the efficient preparation of predominately one of the possible products. The yields are good to high in most cases. Initial studies have shown that the pyrano[2,3-c]coumarins have interesting biological properties. Further investigations for determination of these properties are in progress.

4. Experimental section

4.1. General

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

Table 2
CuI-catalyzed domino Knoevenagel-hetero-Diels–Alder reaction **1a–e** with **2a–b**

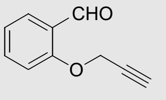
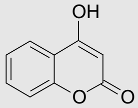
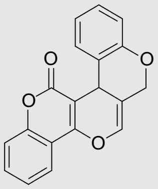
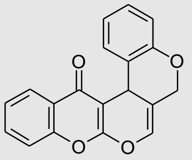
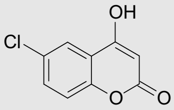
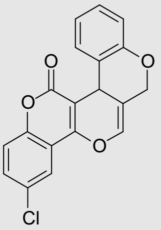
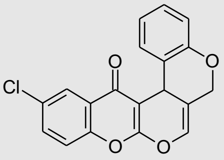
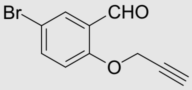
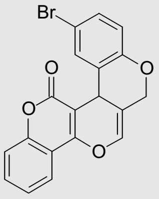
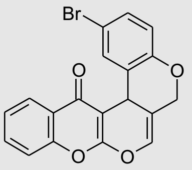
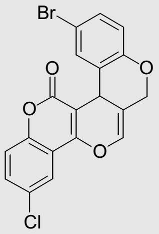
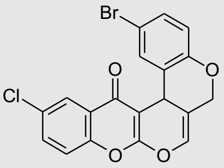
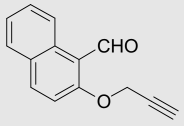
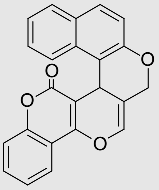
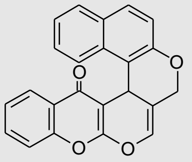
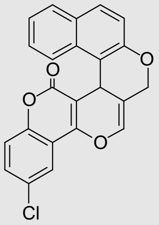
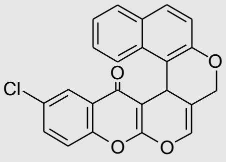
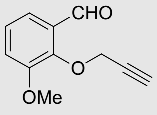
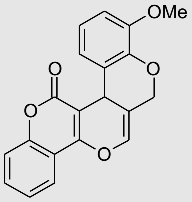
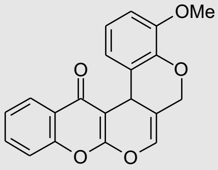
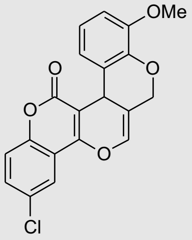
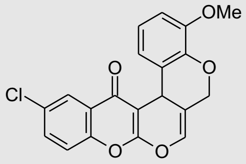
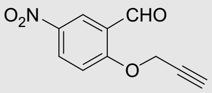
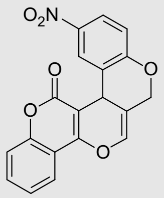
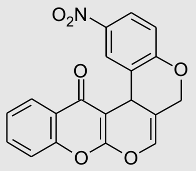
Entry	Aldehyde		Products		Time (h)	Yield[a] (%)	Ratio (**3**/**4**)
1	 **1a**	 **2a**	 **3a**	 **4a**	24	72	100:00
2	**1a**	 **2b**	 **3b**	 **4b**	25	75	72:28
3	 **1b**	**2a**	 **3c**	 **4c**	24	94	90:10
4	**1b**	**2b**	 **3d**	 **4d**	48	93	100:00
5	 **1c**	**2a**	 **3e**	 **4e**	18	66	100:00
6	**1c**	**2b**	 **3f**	 **4f**	46	68	100:00

Table 2 (*continued*)

Entry	Aldehyde		Products		Time (h)	Yield[a] (%)	Ratio (**3**/**4**)
7	 **1d**	**2a**	 **3g**	 **4g**	22	70	80:20
8	**1d**	**2a**	 **3h**	 **4h**	45	78	80:20
9	 **1e**	**2a**	 **3i**	 **4i**	24	95	65:35

[a] Isolated yields.

spectrometer. X-ray structure determinations were carried out on Bruker Smart (**3a**) and APEX (**3e**) diffractometers. CCDC 699807 (**3a**) and 699808 (**3e**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4.2. General procedure

A mixture of propargylated salicylaldehyde **1a–e** (1 mmol), 4-hydroxycoumarin **2a–b** (1.2 mmol), Et_3N (0.6 ml, 1 mmol), and copper(I) iodide (76 mg, 0.40 mmol) in 1,4-dioxane (20 ml) was heated to reflux. Water (15–20 ml) was added, and the precipitated solid was filtered and recrystallized from ethyl acetate. Compounds

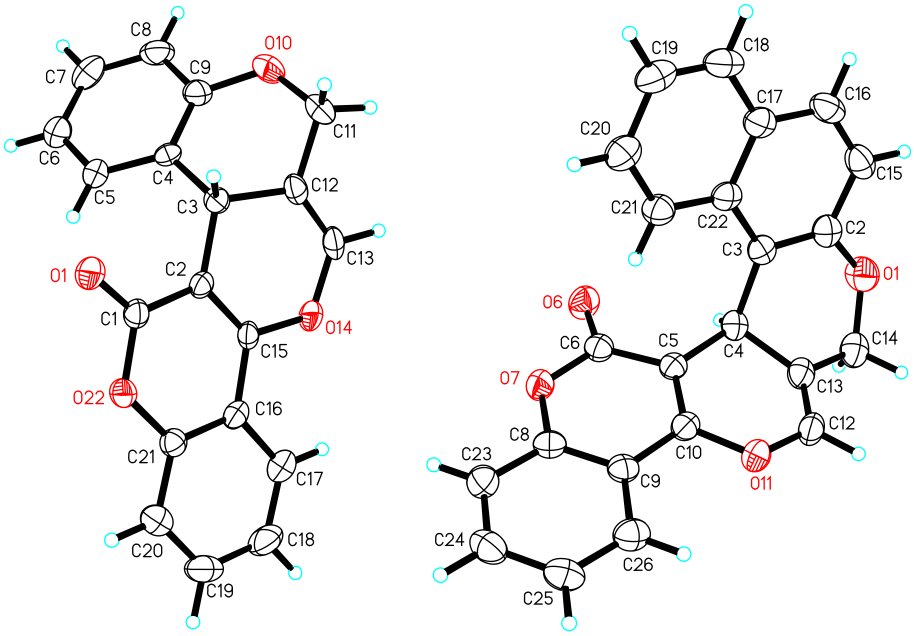
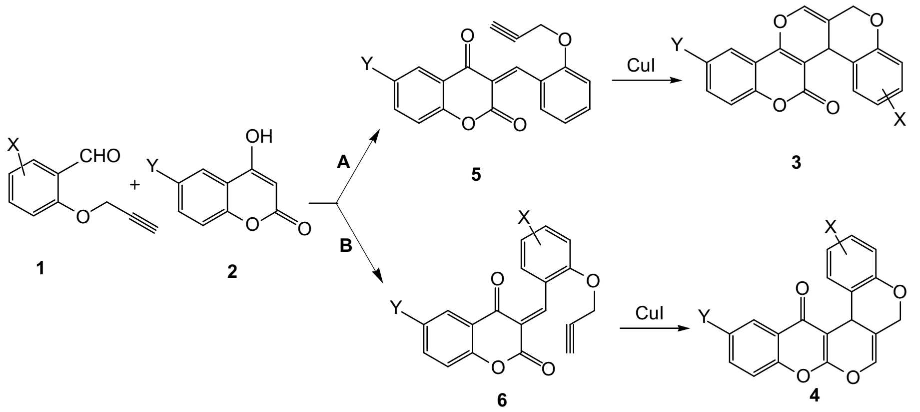


Figure 1. ORTEP representation of the structure of **3a** and **3e**.



Scheme 2.

3 and **4** have the same polarity, therefore our try to separate these compounds using different solid supports such as silicagel and alumina was not successful.

4.3. 1*H*,6b*H*,7*H*-Chromeno[3′,4′:5,6]pyrano[3,4-*c*]-chromen-7-one (3a)

Following the general procedure the reaction afforded **3a** (219 mg, 72%) as a yellow solid; mp 216.5–218 °C; ν_{max} (KBr) 1706, 1617; δ_H (500 MHz, DMSO-d_6) 4.71 (1H, s, C*H*), 4.74 (2H, d, *J* 11.8 Hz, OC*H*), 4.86 (1H, d, *J* 11.8 Hz, OC*H*), 6.75 (2H, m, H_{Ar}), 6.98 (1H, d, *J* 7.7 Hz, H_{Ar}), 7.10 (1H, t, *J* 7.7 Hz, H_{Ar}), 7.19 (1H, s, =C*H*), 7.41 (1H, t, *J* 7.7 Hz, H_{Ar}), 7.51 (1H, d, *J* 8.3 Hz, H_{Ar}), 7.71 (1H, t, *J* 8.3 Hz, H_{Ar}), 7.77 (1H, d, *J* 7.7 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 29.0, 66.1, 99.2, 112.1, 113.1, 116.2, 116.5, 120.0, 122.3, 124.4, 125.4, 126.3, 127.6, 132.7, 134.5, 151.9, 153.2, 156.1, 161.8; HRMS (EI): $[M]^+$, found 304.0733. $C_{19}H_{12}O_4$ requires 304.0735.

4.4. Mixture of 3b and 4b

Following the general procedure the reaction afforded a mixture of **3b** and **4b** (72:28, 254 mg, 75%) as a brown solid; mp 194–196 °C; ν_{max} (KBr) 1714, 1621.

*4.4.1. 11-Chloro-1H,6bH,7H-chromeno[3′,4′:5,6]pyrano[3,4-c]-chromen-7-one (**3b**)*

δ_H (500 MHz, DMSO-d_6) 4.70 (1H, s, C*H*), 4.74 (1H, d, *J* 11.7 Hz, OC*H*), 4.86 (1H, d, *J* 11.7 Hz, OC*H*), 6.76–6.80 (2H, m, H_{Ar}), 6.97 (1H, d, *J* 7.6 Hz, H_{Ar}), 7.09 (1H, m, H_{Ar}), 7.17 (1H, s, H_{Ar}), 7.54 (1H, d, *J* 8.5 Hz, H_{Ar}), 7.73 (1H, s, =C*H*), 7.74 (1H, m, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 29.3, 66.3, 100.4, 112.4, 114.8, 116.8, 118.6, 120.1, 121.8, 125.7, 126.3, 127.9, 128.7, 132.6, 134.7, 150.8, 153.4, 155.3, 161.7.

*4.4.2. 12-Chloro-6H,14H,14bH-chromeno[4′,3′:4,5]pyrano[2,3-b]-chromen-14-one (**4b**)*

δ_H (500 MHz, DMSO-d_6) 4.70 (1H, s, C*H*), 4.73 (1H, d, *J* 7.2 Hz, OC*H*), 4.86 (1H, d, *J* 7.2 Hz, OC*H*), 6.75–6.80 (2H, m, H_{Ar}), 6.88 (1H, d, *J* 7.7 Hz, H_{Ar}), 7.09–7.12 (2H, m, H_{Ar}), 7.70 (1H, s, H_{Ar}), 7.85 (1H, d, *J* 7.3 Hz, H_{Ar}), 8.03 (1H, d, *J* 1.5 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 30.1, 66.2, 95.4, 113.4, 116.5, 120.2, 123.7, 124.2, 126.4, 126.5, 127.8, 130.3, 133.9, 134.3, 150.9, 153.3, 161.3, 176.4.

HRMS (EI): $[M]^+$, found 338.0328. $C_{19}H_{11}O_4^{35}Cl$ requires 338.0345; $[M+2]^+$, found 340.0305. $C_{19}H_{11}O_4^{37}Cl$ requires 340.0316.

4.5. Mixture of 3c and 4c

Following the general procedure the reaction afforded a mixture of **3c** and **4c** (90:10, 358 mg, 94%) as a dark yellow solid; mp 263–265 °C; ν_{max} (KBr) 1711, 1622.

*4.5.1. 5-Bromo-1H,6bH,7H-chromeno[3′,4′:5,6]pyrano[3,4-c]-chromen-7-one (**3c**)*

δ_H (500 MHz, DMSO-d_6) 4.76 (1H, s, C*H*), 4.77 (1H, d, *J* 12.0 Hz, OC*H*), 4.87 (1H, d, *J* 12.0 Hz, OC*H*), 6.75 (1H, d, *J* 8.7 Hz, H_{Ar}), 7.15 (1H, d, *J* 2.2 Hz, H_{Ar}), 7.23 (1H, s, =C*H*), 7.27 (1H, dd, *J* 2.2, 8.6 Hz, H_{Ar}), 7.42 (1H, t, *J* 7.9 Hz, H_{Ar}), 7.51 (1H, d, 1H, *J* 7.9 Hz, H_{Ar}), 7.73 (1H, t, *J* 7.9 Hz, H_{Ar}), 7.79 (1H, d, *J* 7.9 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 29.1, 66.3, 98.9, 111.1, 111.2, 113.1, 116.4, 119.0, 122.5, 124.5, 128.2, 128.4, 130.5, 132.9, 135.2, 152.0, 152.7, 156.5, 162.1.

*4.5.2. 5-Bromo-6H,14H,14bH-chromeno[3′,4′:4,5]pyrano[2,3-b]-chromen-14-one (**4c**)*

δ_H (500 MHz, DMSO-d_6) 4.74 (1H, d, *J* 11.5 Hz, OC*H*), 4.86 (1H, d, *J* 11.5 Hz, OC*H*), 4.94 (1H, s, C*H*), 6.74 (1H, d, *J* 7.1 Hz, H_{Ar}), 7.04 (1H, d, *J* 2.3 Hz, H_{Ar}), 7.13 (1H, s, =C*H*), 7.24 (1H, m, H_{Ar}), 7.55 (1H, t, *J* 7.9 Hz, H_{Ar}), 7.65 (1H, d, *J* 7.9 Hz, H_{Ar}), 7.82 (1H, t, *J* 7.9 Hz, H_{Ar}), 8.14 (1H, d, *J* 7.9 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 30.0, 65.9, 98.8, 111.3, 117.0, 118.8, 125.0, 125.8, 129.0, 130.4, 134.2, 134.9, 149.9, 152.6.

HRMS (EI): $[M]^+$, found 381.9823. $C_{19}H_{11}O_4^{79}Br$ requires 381.9841; $[M+2]^+$, found 383.9817. $C_{19}H_{11}O_4^{81}Br$ requires 383.9821.

4.6. 5-Bromo-11-chloro-1*H*,6b*H*,7*H*-chromeno[3′,4′:5,6]-pyrano[3,4-*c*]chromen-7-one (3d)

Following the general procedure the reaction afforded **3d** (288 mg, 93%) as a dark yellow solid; mp 216.5–218 °C; ν_{max} (KBr) 1720, 1621; δ_H (300 MHz, DMSO-d_6) 4.76 (1H, s, C*H*), 4.77 (1H, d, *J* 11.0 Hz, OC*H*), 4.87 (1H, d, *J* 11.0 Hz, OC*H*), 6.76 (1H, d, *J* 8.3 Hz, H_{Ar}), 7.15 (1H, s, =C*H*), 7.22 (1H, s, H_{Ar}), 7.27 (1H, d, *J* 8.3 Hz, H_{Ar}), 7.56 (1H, d, *J* 9.1 Hz, H_{Ar}), 7.76 (2H, br s, H_{Ar}); δ_C (75 MHz, DMSO-d_6) 29.4, 67.0, 100.0, 111.3, 119.2, 121.9, 128.4, 128.7, 130.8, 132.7, 135.3, 150.9. HRMS (EI): $[M]^+$, found 415.9493. $C_{19}H_{10}O_4^{35}Cl^{79}Br$ requires 415.9451; $[M+2]^+$, found 417.9472. $C_{19}H_{11}O_4^{35}Cl^{81}Br$ requires 417.9430. $[M+4]^+$, found 419.9470. $C_{19}H_{11}O_4^{37}Cl^{81}Br$ requires 419.9430.

4.7. 8c,15-Dihydro-1*H*,9*H*-benzo[*f*]benzo[3,4]-isochromeno[7,8-*c*]chromen-9-one (3e)

Following the general procedure the reaction afforded **3e** (234 mg, 66%) as a yellow solid; mp 243–245 °C; ν_{max} (KBr) 1709, 1620; δ_H (500 MHz, DMSO-d_6) 4.84 (2H, br s, OC*H* and C*H*), 4.92 (1H, br s, OC*H*), 7.16 (1H, d, *J* 8.7 Hz, H_{Ar}), 7.19 (1H, s, =C*H*), 7.26–7.28 (2H, m, H_{Ar}), 7.42 (1H, t, *J* 7.5 Hz, H_{Ar}), 7.50 (1H, d, *J* 8.2 Hz, 1H, H_{Ar}), 7.68–7.74 (2H, m, H_{Ar}), 7.76 (1H, d, *J* 8.7 Hz, H_{Ar}), 7.81–7.84 (2H, m, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 28.8, 66.1, 100.6, 113.6, 116.3, 116.4, 119.1, 119.6, 121.8, 122.3, 123.1, 124.4, 125.8, 128.4, 128.6, 129.1, 131.9, 132.5, 135.0, 151.7, 153.6, 157.8, 160.3. HRMS (EI): $[M]^+$, found 354.0894. $C_{23}H_{14}O_4$ requires 354.0892.

4.8. 13-Chloro-8c,15-dihydro-1*H*,9*H*-benzo[*f*]benzo[3,4]-isochromeno[7,8-*c*]chromen-9-one (3f)

Following the general procedure afforded **3f** (265 mg, 68%) as a green solid; mp 232–235 °C; ν_{max} (KBr) 1725, 1627; δ_H (500 MHz, DMSO-d_6) 4.80 (1H, d, *J* 12.8 Hz, OC*H*), 4.87 (1H, d, *J* 12.8 Hz, OC*H*), 4.96 (1H, s, C*H*), 7.16 (1H, d, *J* 8.8 Hz, H_{Ar}), 7.23 (1H, s, =C*H*), 7.29 (1H, d, *J* 6.3 Hz, H_{Ar}), 7.30 (1H, d, *J* 6.3 Hz, H_{Ar}), 7.55 (1H, d, *J* 8.8 Hz, H_{Ar}), 7.70–7.85 (5H, m, 5H, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 29.0, 66.2, 101.8, 115.4, 116.7, 118.7, 119.3,119.4, 121.8, 122.3, 123.4, 126.2, 128.6, 128.7, 128.9, 129.3, 132.3, 132.4, 135.5, 150.6, 153.9, 157.3, 159.9. HRMS (EI): $[M]^+$, found 388.0493. $C_{23}H_{13}O_4^{35}Cl$ requires 388.0502; $[M+2]^+$, found 390.0455. $C_{23}H_{13}O_4^{37}Cl$ requires 390.0473.

4.9. Mixture of 3g and 4g

Following the general procedure the reaction afforded a mixture of **3g** and **4g** (80:20, 234 mg, 70%) as a yellow solid; mp 214–216 °C; ν_{max} (KBr) 1715, 1622.

*4.9.1. 3-Methoxy-1H,6bH,7H-chromeno[3′,4′:5,6]-pyrano[3,4-c]chromen-7-one (**3g**)*

δ_H (500 MHz, DMSO-d_6) 3.72 (3H, s, O*Me*), 4.67 (1H, s, C*H*), 4.76 (1H, d, *J* 11.7 Hz, OC*H*), 4.86 (1H, d, *J* 11.7 Hz, OC*H*), 6.55 (1H, d, *J* 7.9 Hz, H_{Ar}), 6.73 (1H, t, *J* 7.9 Hz, H_{Ar}), 6.82 (1H, d, *J* 8.2 Hz, H_{Ar}), 7.17 (1H, s, 1H, =C*H*), 7.41 (1H, t, *J* 8.2 Hz, H_{Ar}), 7.50 (1H, d, *J* 8.2 Hz, H_{Ar}), 7.72 (1H, dt, *J* 7.9, 1.5 Hz, H_{Ar}), 7.78 (1H, dd, *J* 7.9, 1.3 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 29.3, 55.6, 66.3, 95.1, 110.8, 112.5, 113.3, 116.5, 117.1, 119.8, 122.6, 124.6, 127.4, 132.9, 134.5, 142.7, 148.4, 152.1, 156.1, 162.0.

*4.9.2. 4-Methoxy-6H,14H,14bH-chromeno[3′,4′:4,5]pyrano[2,3-b]-chromen-14-one (**4g**)*

δ_H (500 MHz, DMSO-d_6) 3.71 (3H, s, O*Me*), 4.67 (1H, s, C*H*), 4.86 (2H, m, OC*H*), 6.47 (1H, d, *J* 7.7 Hz, H_{Ar}), 6.69 (1H, t, *J* 8.0 Hz, H_{Ar}), 6.81 (1H, d, *J* 8.0 Hz, H_{Ar}), 7.07 (1H, s, =C*H*), 7.54 (1H, t, *J* 7.7 Hz, H_{Ar}), 7.64 (1H, d, *J* 8.3 Hz, H_{Ar}), 7.82 (1H, dt, *J* 7.7, 1.6 Hz, H_{Ar}), 8.10 (1H, dd, *J* 8.0, 1.5 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 30.0, 65.8, 66.3, 99.4, 110.8, 113.5, 117.5, 117.6, 118.0, 119.7, 125.1, 125.8, 134.1, 134.2, 142.7, 148.2, 152.4, 156.2, 161.0, 177.4.

HRMS (EI): $[M]^+$, found 334.0815. $C_{20}H_{14}O_5$ requires 334.0841.

4.10. Mixture of 3h and 4h

Following the general procedure the reaction afforded a mixture of **3h** and **4h** (80:20, 288 mg, 78%) as a dark yellow solid; mp 214–215 °C; ν_{max} (KBr) 1715, 1622.

*4.10.1. 11-Chloro-3-methoxy-1H,6bH,7H-chromeno[3′,4′:5,6]-pyrano[3,4-c]chromen-7-one (**3h**)*

δ_H (500 MHz, DMSO-d_6) 3.72 (3H, s, O*Me*), 4.67 (1H, s, C*H*), 4.76 (1H, d, *J* 11.8 Hz, OC*H*), 4.86 (1H, d, *J* 11.8 Hz, OC*H*), 6.54 (1H, d, *J* 7.9 Hz, H_{Ar}), 6.73 (1H, t, *J* 7.9 Hz, H_{Ar}), 6.83 (1H, d, *J* 7.9 Hz, H_{Ar}), 7.14 (1H, s, =C*H*), 7.54 (1H, d, *J* 9.0 Hz, H_{Ar}), 7.72–7.75 (2H, m, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 29.3, 55.5, 66.2, 100.3, 110.9, 112.6, 114.8, 117.1, 118.6, 119.9, 121.8, 127.2, 128.7, 132.6, 134.4, 142.7, 148.4, 150.7, 155.3, 161.5.

*4.10.2. 12-Chloro-3-methoxy-6H,14H,14bH-chromeno[4′,3′:4,5]-pyrano[2,3-b]chromen-14-one (**4h**)*

δ_H (500 MHz, DMSO-d_6) 3.71 (3H, s, O*Me*), 4.67 (1H, s, C*H*), 4.73 (1H, d, *J* 12.0 Hz, OC*H*), 4.86 (1H, d, *J* 12.0 Hz, OC*H*), 6.46 (1H, d, *J* 7.9 Hz, H_{Ar}), 6.70 (1H, t, *J* 7.9 Hz, H_{Ar}), 6.81 (1H, d, *J* 7.9 Hz, H_{Ar}), 7.07 (1H, s, =C*H*), 7.70 (1H, d, *J* 8.9 Hz, H_{Ar}), 7.85(1H, dd, *J* 8.9, 2.6 Hz, H_{Ar}), 8.02 (1H, d, *J* 2.6 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 30.0, 55.6, 66.3, 110.8, 113.6, 117.9, 119.7, 120.1, 123.7, 124.2, 130.3, 133.8, 133.9, 142.6, 150.9, 161.2, 176.3.

HRMS (EI): $[M]^+$, found 368.0428. $C_{20}H_{13}O_5^{35}Cl$, requires 368.0451; $[M+2]^+$, found 370.0429. $C_{20}H_{13}O_5^{37}Cl$ requires 370.0422.

4.11. Mixture of 3i and 4i

Following the general procedure the reaction afforded a mixture of **3i** and **4i** (65:35, 332 mg, 95%) as a dark yellow solid; mp (dec) 243 °C; ν_{max} (KBr) 1704, 1617.

*4.11.1. 5-Nitro-1H,6bH,7H-chromeno[3′,4′:5,6]pyrano[3,4-c]-chromen-7-one (**3i**)*

δ_H (500 MHz, DMSO-d_6) 4.91 (1H, s, C*H*), 4.92 (1H, d, *J* 11.8 Hz, OC*H*), 5.02 (1H, d, *J* 11.8 Hz, OC*H*), 6.99 (1H, d, *J* 9.0 Hz, H_{Ar}), 7.31 (1H, s, =C*H*), 7.42 (1H, t, *J* 7.6 Hz, H_{Ar}), 7.54 (1H, d, *J* 8.3 Hz, H_{Ar}), 7.74 (1H, dt, *J* 7.8, 1.4 Hz, H_{Ar}), 7.80 (1H, dd, *J* 7.9, 1.0 Hz, H_{Ar}), 7.98 (1H, dd, *J* 2.5, 1.0 Hz, H_{Ar}), 8.05 (1H, dd, *J* 9.0, 2.7 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 29.3, 67.4, 98.8, 116.6, 117.8, 122.6, 122.7, 124.0, 124.7, 126.0, 126.5, 133.1, 136.2, 152.1, 156.8, 159.4, 162.3.

*4.11.2. 2-Nitro-6H,14H,14bH-chromeno[4′,3′:4,5]pyrano[2,3-b]-chromen-14-one (**4i**)*

δ_H (500 MHz, DMSO-d_6) 4.89 (1H, d, *J* 11.8 Hz, OC*H*), 5.02 (1H, d, *J* 11.8 Hz, OC*H*), 5.07 (1H, s, C*H*), 6.97 (1H, d, *J* 9.0 Hz, H_{Ar}), 7.21 (1H, s, =C*H*), 7.58 (1H, t, *J* 7.1 Hz, H_{Ar}), 7.67 (1H, d, *J* 8.4 Hz, H_{Ar}), 7.85 (1H, t, *J* 7.8 Hz, H_{Ar}), 7.89 (1H, dd, *J* 2.7, 1.0 Hz, H_{Ar}), 8.01 (1H, d, *J* 7.5 Hz, H_{Ar}), 8.18 (1H, d, *J* 7.5 Hz, H_{Ar}); δ_C (125 MHz, DMSO-d_6) 30.1, 66.9, 94.8, 117.6, 117.7, 122.4, 123.4, 124.1, 125.1, 126.9, 134.4, 135.8, 152.4, 156.9, 159.3, 161.3, 177.8.

HRMS (EI): $[M]^+$, found 349.0605. $C_{19}H_{11}NO_6$ requires 349.0587.

4.12. Crystal structure

*4.12.1. Crystal data of **3a***

Compound **3a** (CCDC 699807): $C_{19}H_{12}O_4$, yellowish crystals, orthorhombic, *Pna*2_1, $Z=4$, $a=22.014(5)$ Å, $b=14.846(3)$ Å, $c=4.1845(9)$ Å, $\alpha=90°$, $\beta=90°$, $\gamma=90°$. $V=1367.5(5)$ Å^3, $D_{calcd}=1.48$ g/cm^3, $\mu=0.10$ mm^{-1}, 13,870 reflections collected, 3405 independent ($R_{int}=0.0613$), 3029 observed, $R_1=0.079$, $wR2=0.161$ ($I>2\sigma(I)$).

*4.12.2. Crystal data of **3e***

Compound **3e** (CCDC 699808): $C_{23}H_{14}O_4$, colorless crystals, monoclinic, $P2_1/n$, $Z=4$, $a=13.7593(4)$ Å, $b=9.0833(2)$ Å, $c=13.9962(4)$ Å, $\alpha=90°$, $\beta=112.489(1)°$, $\gamma=90°$. $V=1616(7)$ Å^3, $D_{calcd}=1.46$ g/cm^3, $\mu=0.10$ mm^{-1}, 15,953 reflections collected, 3701 independent ($R_{int}=0.0708$), 2326 observed, $R_1=0.051$, $wR2=0.101$ ($I>2\sigma(I)$).

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References and notes

1. (a) Boulton, A. J.; Mckillop, A. *Comprehensive Heterocyclic Chemistry*; Pergamon: New York, NY, 1984; (b) Norcross, R. D.; Paterson, I. *Chem. Rev.* **1995**, *95*, 2041–2114; (c) Faulkner, D. J. *Nat. Prod. Rep.* **1997**, *14*, 259–302; (d) Danishefsky, S. J. *Aldrichimica Acta* **1986**, *19*, 59–68; (e) Schmidt, R. R. *Acc. Chem. Res.* **1986**, *19*, 250–259.
2. (a) Payne, D. J.; Hueso-Rodríguez, J. A.; Boyd, H.; Concha, N. O.; Janson, C. A.; Gilpin, M.; Bateson, J. H.; Cheever, C.; Niconovich, N. L.; Pearson, S.; Rittenhouse, S.; Tew, D.; Díez, E.; Pérez, P.; de La Fuente, J.; Rees, M.; Rivera-Sagredo, A. *Antimicrob. Agents Chemother.* **2002**, *46*, 1880–1886; (b) Dean, F. M. *Naturally Occurring Oxygen Ring Compounds*; Butterworths: London, 1963.
3. (a) Tietze, L. F. *Domino Reaction in Organic Synthesis*; Wiley-VCH: Weinheim, 2006; (b) Chapman, C. J.; Frost, C. G. *Synthesis* **2007**, 1–21; (c) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570–1581; (d) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136; (e) Gaddam, V.; Nagarajan, R. *J. Org. Chem.* **2007**, *72*, 3573–3576; (f) Chebanov, V. A.; Saraev, V. E.; Desenko, S.; Chernenko, V. N.; Shishkina, S. V.; Chishkin, O. V.; Kobzar, K. M.; Kappe, C. O. *Org. Lett.* **2007**, *9*, 1691–1694.
4. (a) Tietze, L. F.; Rackelman, N. In *Multicomponent Reactions*; Zhu, J., Bienaymé, H., Eds.; Wiley-VCH: Weinheim, 2005; pp 121–167; (b) Tietze, L. F.; Rackelman, N. *Pure Appl. Chem.* **2004**, *76*, 1967–1983; (c) Tietze, L. F. *J. Heterocycl. Chem.* **1990**, *27*, 47–69; (d) Tietze, L. F.; Rackelman, N.; Müller, I. *Chem.—Eur. J* **2004**, *10*, 2722–2731; (e) Yadav, J. S.; Reddy, B. V. S.; Narsimhaswamy, D.; Lakahmi, P. N.; Narsimulu, K.; Srinivasulu, G.; Kunwar, A. C. *Tetrahedron Lett.* **2004**, *45*, 3493–3497; (f) Jayashankaran, J.; Manian, R. D. R. S.; Raghunathan, R. *Tetrahedron Lett.* **2006**, *47*, 2265–2270.
5. (a) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180–3211; (b) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271–2296; (c) Asao, N.; Sato, K.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 3682–3685; (d) Asao, N.; Yudha, S.; Nogami, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2005**, *44*, 5526–5528; (e) Ermolat, D. S.; Mehta, V. P.; Eycken, E. V. V. *Synlett* **2007**, 3117–3122; (f) Wender, P. A.; Paxton, T. J.; Williams, T. J. *J. Am. Chem. Soc.* **2006**, *128*, 14814–14815.
6. (a) Michelet, V.; Toullea, P. Y.; Genêt, J.-P. *Angew. Chem., Int. Ed* **2008**, *47*, 4268–4315; (b) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650–12651; (c) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079–3160; (d) Asao, N.; Kasahara, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 3504–3506; (e) Kamijo, S.; Sasaki, Y.; Yamamoto, Y. *Tetrahedron Lett.* **2004**, *45*, 35–38; (f) Liu, X.-Y.; Che, C.-N. *Angew. Chem., Int. Ed.* **2008**, *47*, 3805–3810; (g) Bi, H.-P.; Guo, L.-N.; Gou, F.-R.; Duan, X.-H.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2008**, *73*, 4713–4716.
7. (a) Chen, C.; Dormer, P. G. *J. Org. Chem.* **2005**, *70*, 6964–6967; (b) Evindar, G.; Batey, R. *J. Org. Chem.* **2006**, *71*, 1802–1808; (c) Zhu, W.; Ma, D. *Chem. Commun.* **2004**, 888–889; (d) Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 14844–14845; (e) Sreedhar, B.; Reddy, P. S.; Kumar, N. S. *Tetrahedron Lett.* **2006**, *47*, 3055–3058; (f) Bock, V. D.; Hiemstra, H.; Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51–68; (g) Black, D. A.; Arndtsen, B. A. *Org. Lett.* **2004**, *6*, 1107–1110.
8. (a) Khoshkholgh, M. J.; Balalaie, S.; Gleiter, R.; Rominger, F. *Tetrahedron* **2008**, *64*, 10924–10929; (b) Khoshkholgh, M. J.; Balalaie, S.; Bijanzadeh, H. R.; Rominger, F.; Gross, J. H. *Tetrahedron Lett.* **2008**, *49*, 6965–6968; (c) Khoshkholgh, M. J.; Balalaie, S.; Bijanzadeh, H. R.; Gross, J. H. *ARKIVOC* **2009**, *ix*, 114–121; (d) Khoshkholgh, M. J.; Balalaie, S.; Bijanzadeh, H. R.; Gross, J. H. *Synlett* **2009**, 55–58.