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NH_4OAc-promoted Cascade Approach towards Aberrant Synthesis of Chromene-fused Quinolinones

Santosh Kumari,[a] S. M. Abdul Shakoor,[a] Datta Markad,[b] Sanjay K. Mandal,[b] Rajeev Sakhuja*[a]

Abstract: A concise cascade strategy for the synthesis of 6*H*-chromeno[4,3-*b*]quinolin-6-ones was developed from 4-hydroxycoumarins and arylhydrazine hydrochlorides in DMSO. The synthetic strategy relies on dual role of ammonium acetate in generating aromatic amine from arylhydrazine *via* aryl radical formation, and Csp^2-H formylation of coumarin using DMSO as a methine source. The strategy is scalable, and an array of arylhydrazine hydrochlorides delivered chromene-fused quinolinones in good-to-excellent yields.

Introduction

The accountability of fluorescent fused heterocycles in the developed organic light-emitting diodes (OLEDs),[1] biological markers,[2] sensors,[3] organic rectifiers and dyes[4] has received tremendous hike in recent years. Strikingly, chromene nucleus has displayed a center-stage role in designing a number of fascinating fluorescent heterocyclic architectures of immense potential in medicinal and material chemistry.[5] In particular, chromene-fused quinolines constitute an integral part of several natural products including santiagonamine,[6] and have been identified as antibacterial,[7] and anticancer agents,[8] sensors,[9] dyes for mitocondrial imaging,[10] estrogen receptor *β*-selective ligands,[11] selective non-steroidal progesterone receptor modulators,[12] and glucocorticoid modulators[13] (Figure 1).

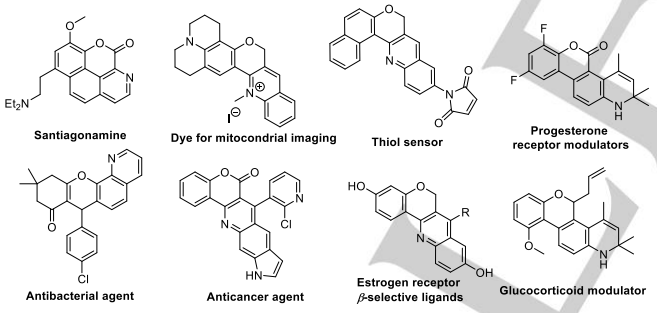

Figure 1. Selective examples of reported chromene-fused quinolines

Further, the applicative value of substituted 6*H*-chromeno[4,3-*b*]quinolin-6-ones has stimulated considerable interest of organic chemists towards their construction, in the past decade. Traditional strategies reported for the synthesis of 6*H*-chromeno[4,3-*b*]quinolin-6-ones include, cyclization of 4-chloro-3-formylcoumarin (obtained by formylation using toxic $POCl_3$) with aromatic amines or aryl isocyanates.[5a],[14] However, the disadvantages associated with Vilsmeier–Haack formylation has led to the use of aldehydes as methine source substrate, for preparing 6*H*-chromeno[4,3-*b*]quinolin-6-ones. Under this realm, Choudhury and co-workers disclosed a bismuth triflate-catalyzed strategy for preparing 6*H*-chromeno[4,3-*b*]quinolin-6-ones *via* multicomponent reaction between 4-hydroxycoumarin, aldehydes and aromatic amines under neat conditions (Scheme 1a).[15] Sashidhara group reported iodine-catalyzed tandem process for annulation between 4-hydroxycoumarin, aromatic aldehydes, and aromatic amines under MW irradiation, affording 6*H*-chromeno[4,3-*b*]quinolin-6-ones in high yields (Scheme 1b).[12] Yao and co-workers synthesized 6*H*-chromeno[4,3-*b*]quinolin-6-ones through reductive cyclization between 4-hydroxycoumarin and *ortho*-nitrobenzaldehydes using excess of Fe and acetic acid (Scheme 1c).[16] With the advent of elegant Csp^2-H formylation protocols,[17] Su and co-workers reported a Cu-catalyzed cyclization protocol from 4-(phenylamino)-2*H*-chromen-2-ones, employing DMF as formyl-generating source and TBPB as oxidant, affording functionalized 6*H*-chromeno[4,3-*b*]quinolin-6-ones in moderate-to-good yields (Scheme 1d).[18] In spite of reasonable advancements, designing metal-free/oxidant-free strategy from commercially available starting materials to obtain 6*H*-chromeno[4,3-*b*]quinolin-6-ones in a single step is highly desirable.

Metal-free cascade strategies have developed a significant repute for constructing different heterocycles in an environmentally sustainable and atom-economical manner.[19] In this regard, the use of NH_4OAc as an inexpensive nitrogen source has been exemplified in various C-C/C-X bond forming/breaking transformations.[20] In addition, it is reported as a promoter for Pummerer reaction for successful formylation of indoles using DMSO as carbonyl source.[21]

On the other hand, arylhydrazines are valuable coupling partners in organic synthesis, capable of constructing aryl-(hetero)aryl C-C bonds *via* generating aryl radical[22] under appropriate conditions. To the best of our knowledge, the use of arylhydrazines remains unexplored for the synthesis of chromene-fused quinolinones. We envisioned the dual use of NH_4OAc to promote Pummerer reaction for C-3 formylation of coumarin using DMSO as a methine source, and simultaneously act as a nitrogen source for trapping aryl radical that is expected to generate from arylhydrazine, to consecutively afford 6*H*-chromeno[4,3-*b*]quinolin-6-ones in a tandem manner. With our continuous zeal in developing C-H activation based cascade strategies,[23] and inspired from significant applications of 6*H*-chromeno[4,3-*b*]quinolin-6-ones, herein, we report an operationally simple ammonium-promoted method for the one-pot synthesis of 6*H*-chromeno[4,3-*b*]quinolin-6-ones from 4-

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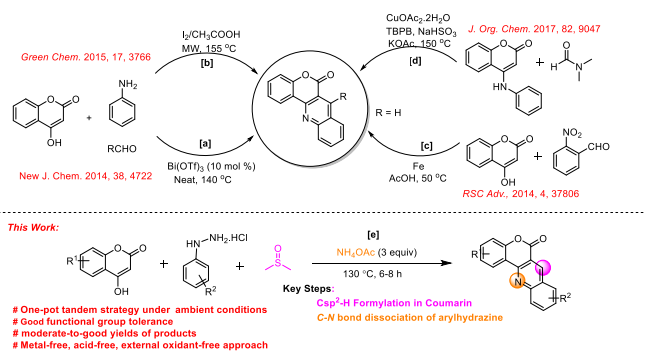
hydroxycoumarin, arylhydrazine hydrochlorides using NH_4OAc in DMSO (Scheme 1e).

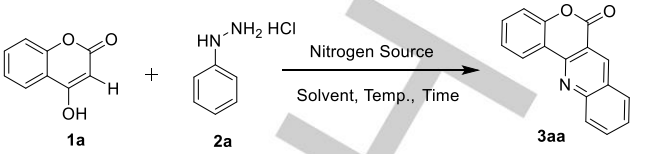


Scheme 1. Summary of previous and present synthesis of 6*H*-chromeno[4,3-*b*]quinolin-6-one

Results and Discussion

From the outset of the proposed work, we began investigating the model reaction between 4-hydroxycoumarin (**1a**) (1 equiv), and phenylhydrazine hydrochloride (**2a**) (1.2 equiv) under ammonium-promoted conditions (Table 1). Gratifyingly, we witnessed the formation of a product in 35% yield after heating **1a** and **2a** using NH_4OAc (1 equiv) at 130 °C in DMSO for 5 h under ambient conditions (Table, 1 entry 1). Purification and characterization of the product using ^1H NMR, ^{13}C NMR, HRMS unequivocally confirmed it to be 6*H*-chromeno[4,3-*b*]quinolin-6-one (**3aa**). This unprecedented formation of a chromene-fused quinolinone from phenylhydrazine hydrochloride as an aryl source propel us to further optimize this tandem protocol with respect to time, solvent, and reactant/reagent concentrations. Time optimization studies revealed that heating the model reaction up to 6 h produces an increment in the yield of **3aa** to 42%, however no further noticeable amelioration in its yield was observed by further increasing the reaction time (Table 1, entries 2-3). Delightfully, a step-wise change in the equivalents of NH_4OAc from 1 to 3 aids an augmentation in the yield of **3aa** to 70%, albeit the use of 4 equivalents of NH_4OAc produced no further noticeable change (Table 1, entries 4-6). Also, no enrichment in the yield of **3aa** was noticed by increasing the concentration of **2a** to 1.5 equivalents (Table 1, entry 7). Next, solvent screening studies were performed which suggested DMF and DMA to be poor solvents for the desired transformation, yielding <10% of **3aa**, while MeOH and 1,4-dioxane to be completely unsuitable as expected (Table 1, entries 8-11). The use of external oxidants were next investigated; the results of which inferred that no product was formed in presence of TBHP, H_2O_2, $K_2S_2O_8$ under nitrogen atmosphere, while the use of molecular O_2 furnished **3aa** in 73% yield (Table 1, entries 12-15). Finally, the use of other amine sources, including $(NH_4)_2CO_3$, NH_4Cl, NH_2NH_2 and NH_3 were explored; these amine sources produced lower yields of **3aa** under similar reaction conditions. (Table 1, entries 16-19).

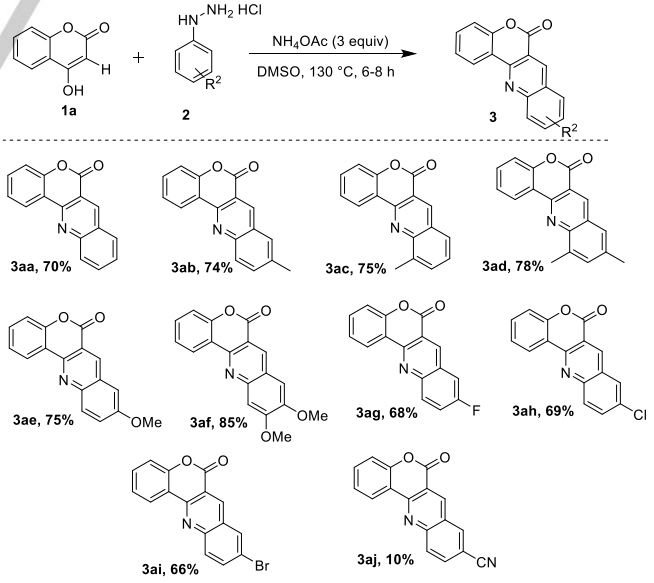
Table 1. Selected Optimization conditions[a] for the synthesis of **3aa**



Entry	Nitrogen source	Reaction Conditions			Oxidant	Yield of**3aa**
	(equiv)	Solvent	T (°C)	Time (h)	(equiv)	(%)[b]
1.	NH_4OAc (1)	DMSO	130	5	Air	35
2.	NH_4OAc (1)	DMSO	130	6	Air	42
3.	NH_4OAc (1)	DMSO	130	8	Air	43
4.	NH_4OAc (2)	DMSO	130	6	Air	50
5.	**NH_4OAc (3)**	**DMSO**	**130**	**6**	**Air**	**70**
6.	NH_4OAc (4)	DMSO	130	6	Air	71
7.[c]	NH_4OAc (3)	DMSO	130	6	Air	70
8.	NH_4OAc (3)	DMF	130	6	Air	<10
9.	NH_4OAc (3)	DMA	130	6	Air	<10
10.	NH_4OAc (3)	MeOH	70	6	Air	-
11.	NH_4OAc (3)	Dioxane	115	6	Air	-
12.[d]	NH_4OAc (3)	DMSO	130	6	TBHP (3)	0
13.[d]	NH_4OAc (3)	DMSO	130	6	H_2O_2 (3)	0
14.[d]	NH_4OAc (3)	DMSO	130	6	$K_2S_2O_8$ (3)	0
15.	NH_4OAc (3)	DMSO	130	6	O_2	73
16.	$(NH_4)_2CO_3$ (3)	DMSO	130	6	Air	50
17.	NH_4Cl (3)	DMSO	130	6	Air	30
18.	NH_2NH_2 (3)	DMSO	130	6	Air	20
19.	Aq. NH_3	DMSO	130	6	Air	26

[a] **1a** (0.30 mmol), **2a** (0.36 mmol), nitrogen source (as specified), oxidant (as specified, if applicable), solvent (3 mL) under air (except for entry 12-15). [b] Isolated yields. [c] **1a** (0.30 mmol), **2a** (0.45 mmol). [d] Nitrogen atmosphere.

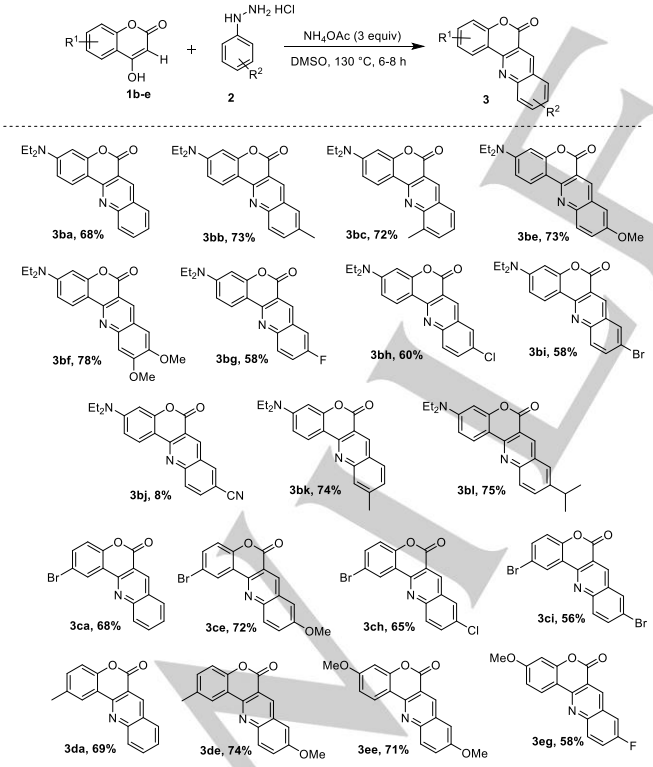
Having optimized reaction conditions in hand, we next investigated the generality of this cascade process with a wide range of arylhydrazine hydrochlorides (**2a-j**) as coupling partners with 4-hydroxycoumarin (**1a**) (Scheme 2).



Scheme 2. Substrate Scope of arylhydrazine hydrochlorides

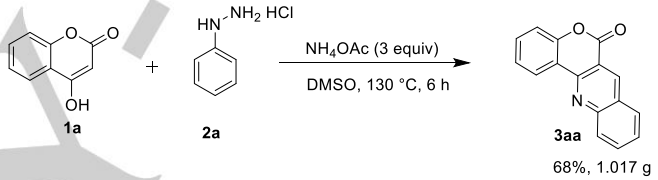
Arylhydrazine hydrochlorides possessing electron-donating and electron-withdrawing groups were well tolerated under optimized conditions to deliver corresponding substituted 6*H*-chromeno[4,3-*b*]quinolin-6-ones (**3aa-ai**) in 66-85% yields. Overall, some variation in the electronic environment of arylhydrazine hydrochlorides has shown noticeable results. Electronically-rich arylhydrazine hydrochlorides (**2b-f**: R^2 = 4-Me, 2-Me, 4-OMe, 2,4-diMe, 3,4-diOMe) exhibited good reactivity and furnished substituted chromene-fused quinolinones (**3ab-af**) in 74-85% yields, while moderately electronically-deficient arylhydrazine hydrochlorides (**2g-i**: R^2 = F, Cl, Br) afforded the cyclized products **3ag-ai** in comparatively lower yields (66-69%). Unfortunately, the use of 4-cyanophenylhydrazine hydrochloride (**2j**) yielded only 10% of the cyano functionalized 6*H*-chromeno[4,3-*b*]quinolin-6-one (**3aj**). The lower reactivity of arylhydrazine possessing electron withdrawing group (CN) could be either due to instability of the corresponding aryl radical, and/or due to lower nucleophilicity of *in situ* generated substituted 4-aminoaryl coumarin, to promote C-3 formylation and subsequent nucleophilic addition.

With our advent interest in synthesizing highly fluorescent heterocycles, we next explored the performance of 7-(*N,N*-diethylamino)-4-hydroxycoumarin (**1b**) with a variety of arylhydrazine hydrochlorides under optimized conditions. Pleasingly, **1b** reacted quite well with electron-rich and electron-deficient arylhydrazine hydrochlorides (**2a-c**, **2e-i**, **2k-l**), affording their corresponding chromene-fused quinolinones (**3ba-bc**, **3be-bi**, **3bk-bl**) in 58-78% yields (Scheme 3).



Scheme 3. Substrate scope of 4-hydroxycoumarins and arylhydrazine hydrochlorides

Here again, electronically-rich arylhydrazine hydrochlorides exhibited better reactivity over the electron-deficient ones. The only exception in this case was the reaction of 4-cyanophenylhydrazine hydrochloride with **1b**, which afforded cyano functionalized 7-(diethylamino)-6*H*-chromeno[4,3-*b*]quinolin-6-one **3aj** in only 8% yield. Also, electron-deficient 6-bromo-4-hydroxycoumarin (**1c**) showcased moderate reactivity for a number of arylhydrazine hydrochlorides (**2a, 2e, 2h** & **2i**), affording their corresponding chromene-fused quinolinones **3ca**, **3ce**, **3ch** & **3ci** in 56-72% yields. On the other hand, methyl and methoxy substituted 4-hydroxycoumarins (**1d** & **1e**) displayed slightly better reactivity towards different arylhydrazine hydrochlorides (**2a**, **2e**, **2g**) to furnished their corresponding chromene-fused quinolinones (**3da**, **3de**, **3ee** & **3eg**) in 58-74% yields. All the synthesized compounds were isolated by column chromatography, and characterized by detailed spectroscopic analysis. To assess the scalability of this metal-free cascade process, a gram scale reaction was performed between **1a** and **2a** under optimized conditions to afford **3aa** in 68% yield (1.017 g), which is similar to that obtained on a smaller scale (Scheme 4).



Scheme 4. Gram scale synthesis of **3aa**

To further confirm the proposed structure, as a representative example, single crystals of **3ba** were grown from a mixture of ethyl acetate and hexane for X-ray diffraction (XRD) studies. Compound **3ba** crystallizes in the $R\bar{3}$ (No. 148) group. An ORTEP diagram of the **3ba** (CCDC No. 1862858) is shown in Figure 2.

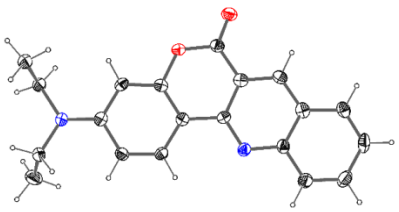
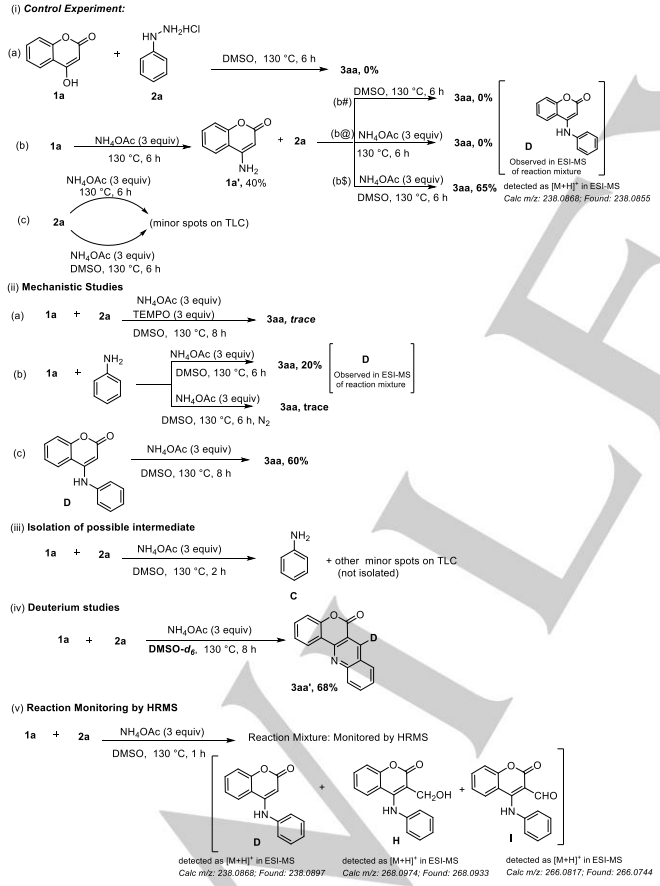


Figure 2. ORTEP diagram of **3ba**

To gain insights into the mechanistic pathway, a series of preliminary experiments were performed. Reaction of 4-hydroxycoumarin (**1a**) and phenylhydrazine hydrochloride (**2a**) in DMSO at 130 °C produced no product at all, thereby indicating a crucial participation of NH_4OAc in this cascade process (Scheme 5ia). Reaction of **1a** with NH_4OAc (3 equiv) under neat conditions at 130 °C for 6 h furnished 4-aminocoumarin (**1a´**) in only 40% yield, which on further reaction with **2a** in DMSO (without NH_4OAc, Scheme 5ib#) or using NH_4OAc (in absence of DMSO, Scheme 5ib@) did not yield **3aa** at all. It is worth

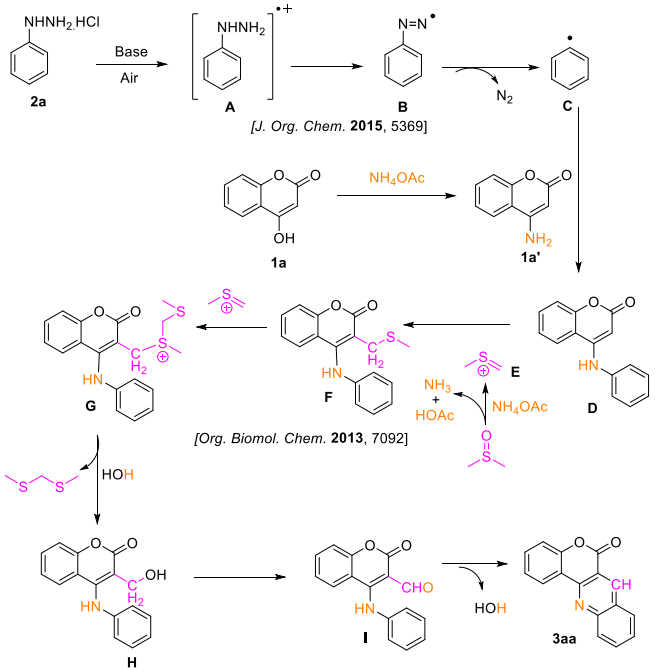
mentioning that 4-aminophenyl coumarin (**D**) was observed in ESI-MS of their respective reaction mixtures (Supporting Information). On the other hand, reaction of 4-aminocoumarin (**1a´**) with **2a** using NH_4OAc in DMSO under optimized conditions afforded **3aa** in 65% yield (Scheme 5ib). No prominent product was isolated by reacting **2a** with NH_4OAc, in presence or absence of DMSO under described reaction conditions (Scheme 5ic). Notably, the failure of model reaction to proceed in presence of radical scavenger TEMPO (3 equiv) advocates about the involvement of radical species during the course of reaction mechanism (Scheme 5iia). The reaction of aniline instead of phenylhydrazine with **1a** under optimized conditions yielded the product **3aa**, albeit in only 20% after 6 h under ambient conditions, whereas trace amount of **3aa** was observed (on TLC) in nitrogen atmosphere (Scheme 5iib). This indicates a crucial role of atmospheric oxygen in the reaction pathway. To further confirm the formation of 4-(phenylamino)-2*H*-chromen-2-one (**D**) as one of the intermediates in the reaction between **1a** and **2a**, **D** was synthesized by standard procedure.[18] Pleasingly, **D** on further heating in DMSO using ammonium acetate (3 equiv) yielded the desired product **3aa** in 60% yield after 8 h, thereby indicating that its formation is involved in the reaction mechanism (Scheme 5iic).



Scheme 5. Control experiments for investigation of the mechanism

Interestingly, aniline was isolated (*via* column chromatography) as one of the intermediates in only minor amounts from the mixture obtained by reacting **1a** and **2a** after 2 h (Scheme 5iii), however, this is contradictory to the results obtained in Scheme 5ic. Thus, it appears that aniline formation might not be involved in the operating reaction mechanism, and aniline could be a result of a side reaction. Contentedly, the formation of **3aa'** in presence of deuterated DMSO-d_6 affirmed DMSO as a methine source in the disclosed transformation (Scheme 5iv). Unfortunately, no other intermediate was isolated in pure form, even on repeated attempts. Thus, we planned to monitor the model reaction *via* analyzing its mass spectra (Scheme 5v). To our delight, ESI-HRMS of the crude mixture recorded after 1 h detected the presence of the peaks at *m/z* 238.0897, 268.0933 and 266.0744, corresponding to the molecular formula $C_{15}H_{12}NO_2$ $[M + H]^+$, $C_{16}H_{14}NO_3$ $[M + H]^+$ and $C_{16}H_{12}NO_3$ $[M + H]^+$, respectively, which indicated the possible formation of intermediates **D**, **H**, and **I** during the course of the reaction (supporting Information). After all the investigations, it appears that the intermediate, 4-aminophenyl coumarin (**D**) has been formed by the reaction of *in situ* generated aniline (**C**) with 4-hydroxycoumarin (**1a**), or by *N*-arylation of *in situ* generated 4-aminocoumarin (**1a´**).

Based upon the above studies and literature reports,[5],[17],[21],[24] a postulated mechanism is illustrated in scheme 6. The overall process consists of two main steps that could be assumed to proceed either simultaneously or consecutively. The first step of the reaction is believed to be initiated by the decomposition of phenylhydrazine hydrochloride (**2a**) to phenyl radical (**C**) *via* formation of **A** and diazonium radical (**B**) *via* single electron transfer (SET) mechanism.[24] Subsequently, amination of 4-hydroxycoumarin (**1a**) with ammonium acetate, followed by arylation by phenyl radical (**C**) furnishes 4-(phenylamino)-2*H*-chromen-2-one (**D**). Thereafter, the second step involves the activation of DMSO by ammonium acetate to produce thionium ion (**E**), which undergoes a nucleophilic attack by **1a** to produce **F** *via* Pummerer-type reaction, as established by Cheng.[21] The sulfur atom in **F** attacks another molecule of thionium ion (**E**) to generate intermediate **G**, which upon nucleophilic attack by water affords C-3 hydroxymethylation intermediate (**H**). Subsequently oxidation of **H** takes place to produce 4-(phenylamino)-2*H*-chromen-2-one-3-carbaldehyde (**I**). Finally, aldol-type intramolecular nucleophilic addition in **I,** followed by dehydration affords the desired product **3aa**. However, there is still one question that remains to be addressed, *i.e*. the source of water (as nucleophile) in the proposed mechanism. We anticipated that either the hygroscopic behavior of ammonium acetate under ambient conditions, or nucleophilic substitution of hydroxyl group with aniline could be possible source(s) of water in the reaction mixture.



Scheme 6. Plausible mechanism

Conclusions

In summary we have developed an efficient, atom-economical and metal-free cascade process for the synthesis of coumarin-fused quinolinones; wherein DMSO, NH_4OAc and arylhydrazine served as methine, nitrogen and aryl sources, respectively. The deuterium study implies that the carbon added is from the methyl group of DMSO, with the inexpensive, economical reagent, easy availability of the substrates, and moderate functional group tolerability. This protocol could be recognized as an inexpensive and opens a new avenue for the green and challenging synthesis of chromeno-quinoline derivatives

Experimental Section

General materials and methods

All reagent and chemical were purchased from commercial source and used as received. Required solvent for reaction were dried by standard procedures prior to use. All reactions were performed under air atmosphere, unless otherwise noted. ^{1}H NMR spectra were recorded on 400 MHz spectrometer and chemical shifts are reported in δ units, parts per million (ppm), and referred to the internal standard TMS set as 0.00 ppm , relative to residual chloroform (7.26 ppm) in the deuterated solvent. Data are reported as follows: the following abbreviations were used to describe peak splitting patterns : s = singlet, d = doublet, t = triplet, dd = doublet of doublet and m = multiplet. Coupling constants *J* were reported in Hz. The ^{13}C NMR spectra were reported in ppm relative to deuterochloroform (77.0 ppm). Melting points were determined on a capillary point apparatus equipped with a digital thermometer and are uncorrected. High resolution mass spectra were recorded with a TOF analyzer spectrometer by using electrospray mode. IR spectra were recorded on Shimadzu IR Prestige-21 FT-IR spectrophotometer. Flash column chromatography was performed on silica gel, 60−120 mesh. Analytical and preparative thin-layer chromatography was carried out on silica gel 60 F-254 plates. Products were visualized using UV and shown blue colour and yellow colour under uv light.

General procedure for the synthesis of 6*H*-chromeno[4,3-*b*]quinolin-6-ones

A mixture of 4-hydroxycoumarin (**1**, 0.30 mmol, 1.0 equiv), arylhydrazine hydrochloride (**2**, 0.36 mmol, 1.2 equiv), NH_4OAc (0.90 mmol, 3.0 equiv) were heated in DMSO (3.0 mL) at 130 °C under ambient conditions for 6-8 h. On completion of the reaction as indicated by TLC, the reaction mixture was cooled to room temperature, and diluted with ice-water. The mixture was extracted with ethyl acetate (3 × 20 mL), and the organic layer was separated and dried over Na_2SO_4. The organic layer was concentrated, and the crude product was subjected to silica gel column chromatography [SiO_2 (100-200 mesh), with (hexanes/EtOAc, 19:1) as the eluent to afford pure 6*H*-chromeno[4,3-*b*]quinolin-6-one (**3**).

6*H*-Chromeno[4,3-*b*]quinolin-6-one (3aa): White solid; yield: 52.3 mg (70%); mp: 223–224 °C (lit.[18] 221.9−223.1 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.78 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.24 (d, *J* = 8.6 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.96 – 7.91 (m, 1H), 7.68 – 7.59 (m, 2H), 7.47 – 7.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 152.7, 151.1, 149.6, 141.1, 133.4, 132.4, 129.6, 129.4, 127.4, 127.3, 125.3, 125.0, 119.6, 117.4, 115.8; IR ($\tilde{\nu}$, cm^{-1}): 3055, 3013, 1735, 1604, 1496, 1242, 1172, 1033, 987, 756; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_{10}NO_2^+$: 248.0706; found 248.0707 $[M + H]^+$.

9-Methyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ab): White solid; yield: 58.5 mg (74%); mp: 211–213 °C (lit.[18] 234.4−235.1 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.77 (dd, *J* = 7.8, 1.0 Hz, 1H), 8.14 (d, *J* = 9.2 Hz, 1H), 7.76 (d, *J* = 6.8 Hz, 2H), 7.64 – 7.57 (m, 1H), 7.47 – 7.38 (m, 2H), 2.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 152.5, 149.8, 148.8, 140.1, 137.6, 135.9, 132.1, 129.2, 127.9, 127.3, 125.1, 124.9, 119.7, 117.3, 115.7, 21.7; IR ($\tilde{\nu}$, cm^{-1}): 2962. 2919, 1728, 1597, 1489, 1458, 1303, 1180, 1056, 1026, 802, 748; HRMS (ESI-TOF) (*m/z*) calculated $C_{17}H_{12}NO_2$: 262.0863; found 262.0862 $[M + H]^+$.

11-Methyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ac): White solid; yield: 59.3 mg (75%); mp: 221–223 °C (lit.[18] 209.6−211.7 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.93 – 8.83 (m, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.83 – 7.77 (m, 1H), 7.65 – 7.60 (m, 1H), 7.60 – 7.54 (m, 1H), 7.50 – 7.47 (m, 1H), 7.46 – 7.42 (m, 1H), 2.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 152.6, 149.9, 148.2, 140.9, 137.7, 133.1, 132.1, 127.2, 127.2, 127.2, 125.2, 124.8, 120.0, 117.3, 115.3, 17.9; IR ($\tilde{\nu}$, cm^{-1}): 3066, 2970, 1728, 1612, 1489, 1411, 1350, 1118, 1018, 840, 748; HRMS (ESI-TOF) (*m/z*) calculated $C_{17}H_{12}NO_2^+$: 262.0863; found 262.0859 $[M + H]^+$.

9,11-Dimethyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ad): White solid; yield: 65.0 mg (78%); mp: 228–230 °C (lit.[18] 219.8−220.5 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.81 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.62 – 7.57 (m, 3H), 7.47 – 7.39 (m, 2H), 2.91 (s, 3H), 2.56 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 152.5, 148.8, 147.6, 140.1, 137.3, 137.3, 135.8, 131.8, 127.5, 125.8, 125.1, 124.8, 120.2, 117.3, 115.4, 21.7, 17.8; IR ($\tilde{\nu}$, cm^{-1}): 2962, 2924, 1728, 1597, 1496, 1373, 1257, 1087, 894, 748; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{14}NO_2^+$: 276.1019; found 276.1003 $[M + H]^+$.

9-Methoxy-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ae): White solid; yield: 62.9 mg (75%); mp: 234–2 36 °C (lit.[18] 233.5−235.0 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.78 (dd, *J* = 7.9, 1.6 Hz, 1H), 8.18 (d, *J* = 9.3 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.48 – 7.41 (m, 2H), 7.26 (d, *J* = 2.8 Hz, 1H), 4.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 158.4, 152.3, 147.7, 147.5, 139.0, 131.8, 131.0, 128.5, 127.1, 124.9, 124.9, 119.9, 117.3, 115.9, 105.6, 55.8; IR ($\tilde{\nu}$, cm^{-1}): 3052, 2986, 1735, 1620, 1496, 1381, 1234, 1180, 1087, 948, 748; HRMS (ESI-TOF) (*m/z*) calculated $C_{17}H_{12}NO_3^+$: 278.0812; found 278.0800 $[M + H]^+$.

9,10-Dimethoxy-6*H*-chromeno[4,3-*b*]quinolin-6-one (3af): White solid; yield: 79.0 mg (85%); mp: 280–282 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.75 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.56 (s, 1H), 7.49 – 7.39 (m, 2H), 7.22 (s, 1H), 4.16 (s, 3H), 4.10 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 156.0, 152.4, 150.8, 149.3, 148.1, 137.9, 131.7, 124.8, 124.7, 123.6, 119.9, 117.4, 114.0, 107.6, 105.8, 56.5, 56.3; IR ($\tilde{\nu}$, cm^{-1}): 3056, 2993, 1728, 1604, 1504, 1257, 1188, 756; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{14}NO_4^+$: 308.0917; found 308.0913 $[M + H]^+$.

9-Fluoro-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ag): White solid; yield: 54.6 mg (68%); mp: 244–245 °C (lit.[18] 242.3−243.0°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.76 (dd, *J* = 7.9, 1.6 Hz, 1 H), 8.26 (dd, *J* = 9.3, 5.2 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.67 – 7.60 (m, 2H), 7.48 – 7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5 ($J_{C\text{-}F}$ = 85.3 Hz), 159.4, 152.6, 149.0 ($J_{C\text{-}F}$ = 2.7 Hz), 148.3, 140.2 ($J_{C\text{-}F}$ = 6.1 Hz), 132.4, 132.2 ($J_{C\text{-}F}$ = 8.9 Hz), 127.9, 127.8, 125.1 ($J_{C\text{-}F}$ = 3.3 Hz), 124.0 ($J_{C\text{-}F}$ = 26.2 Hz), 119.4, 117.4, 116.4, 112.0 ($J_{C\text{-}F}$ = 21.8 Hz); IR ($\tilde{\nu}$, cm^{-1}): 3066, 2963, 1735, 1604, 1496, 1458, 1357, 1226, 1118, 864, 756; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_9FNO_2^+$: 266.0612; found 266.0603 $[M + H]^+$.

9-Chloro-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ah): White solid; yield: 58.7 mg (69%); mp: 240–242 °C (lit.[18] 245.7−246.4°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.75 (d, *J* = 6.9 Hz, 1H), 8.18 (d, *J* = 9.0 Hz, 1H), 8.00 (d, *J* = 1.5 Hz, 1H), 7.85 (dd, *J* = 9.0, 1.9 Hz, 1H), 7.63 (t, *J* = 7.0 Hz, 1H), 7.49 – 7.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 152.7, 149.8, 149.4, 140.0, 134.3, 133.4, 132.7, 131.1, 127.8, 127.7, 125.2, 125.1, 119.3, 117.5, 116.5; IR ($\tilde{\nu}$, cm^{-1}): 3065, 2918, 1735, 1604, 1481, 1458, 1303, 1195, 1080, 925, 756; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_9ClNO_2^+$: 282.0316; found 282.0314 $[M + H]^+$.

9-Bromo-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ai): White solid; yield: 65.9 mg (66%); mp: 232–234 °C (lit.[18] 230.0−231.0°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.72 (d, *J* = 7.9 H z, 1H), 8.14 (d, *J* = 1.7 Hz, 1H), 8.08 (d, *J* = 9.0 Hz, 1H), 7.96 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.47 – 7.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 152.7, 149.9, 149.6, 139.9, 136.8, 132.7, 131.2, 131.1, 128.2, 125.2, 125.1, 121.5, 119.3, 117.5, 116.4; IR ($\tilde{\nu}$, cm^{-1}): 3065, 2924, 1735, 1604, 1481, 1373, 1172, 987, 910, 756; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_9BrNO_2^+$: 325.9811; found 325.9809 $[M + H]^+$.

6-Oxo-6*H*-chromeno[4,3-*b*]quinoline-9-carbonitrile (3aj): White solid; yield: 8.24 mg (10%); mp: 229–231 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.81 (d, *J* = 2.4 Hz, 1H), 8.46 (d, *J* = 1.6 Hz, 1H), 8.38 – 8.34 (m, 1H), 8.06 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.52 – 7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 153.2, 152.3, 151.7, 141.7, 135.5, 133.6, 133.4, 131.1, 126.5, 125.7, 125.3, 119.0, 117.8, 117.6, 117.3, 111.2; IR ($\tilde{\nu}$, cm^{-1}): 2978, 2930, 2222, 1735, 1604, 1450, 1350, 1195, 1018, 817; HRMS (ESI-TOF) (*m/z*) calculated $C_{17}H_9N_2O_2^+$: 273.0659; found 273.0620 $[M + H]^+$.

3-(Diethylamino)-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ba): Yellow solid; yield: 46.4 mg (68%); mp: 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.47 (d, *J* = 9.0 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.86 – 7.80 (m, 1H), 7.55 – 7.48 (m, 1H), 6.71 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.52 (d, *J* = 2.5 Hz, 1H), 3.46 (q, *J* = 7.1 Hz, 4H), 1.26 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 154.7, 151.5, 151.1, 150.6, 140.9, 133.0, 129.4, 128.9, 126.3, 126.2, 126.0, 114.7, 109.1, 107.3, 97.9, 44.8, 12.6; IR ($\tilde{\nu}$, cm^{-1}): 2962, 2924, 1720, 1597, 1442, 1350, 1273, 1126, 1018, 941, 817, 779; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{19}N_2O_2^+$: 319.1441; found 319.1459 $[M + H]^+$.

3-(Diethylamino)-9-methyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bb): Yellow solid; yield: 52.0 mg (73%); mp: 179–181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.47 (d, *J* = 9.0 Hz, 1H), 8.02 (d, *J* = 9.2 Hz, 1H), 7.67 (d, *J* = 4.5 Hz, 2H), 6.72 (dd, *J* = 9.0, 2.3 Hz, 1H), 6.54 (d, *J* = 2.2 Hz, 1H), 3.47 (q, *J* = 7.1 Hz, 4H), 2.56 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 154.5, 150.9, 150.2, 149.9, 140.1, 136.0, 135.5, 128.6, 128.0, 126.4, 126.1, 114.6, 109.1, 107.5, 97.9, 44.8, 21.5, 12.6; IR ($\tilde{\nu}$, cm^{-1}): 2962, 2893, 1728, 1597, 1350, 1195, 1126, 941, 817; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{21}N_2O_2^+$: 333.1598; found 333.1598 $[M + H]^+$.

3-(Diethylamino)-11-methyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bc): Yellow solid; yield: 51.2 mg (72%); mp: 175–177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.19 – 8.16 (m, 1H) , 7.93 (d, *J* = 8.5 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.50 – 7.46 (m, 1H), 6.78 – 6.69 (m, 2H), 3.52 (q, *J* = 7.1 Hz, 4H), 2.87 (s, 3H), 1.31 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 154.0, 150.6, 149.6, 147.7, 139.3, 136.0, 135.9, 132.6, 129.4, 128.6, 127.4, 125.6, 109.4, 100.0, 97.1, 45.1, 18.3, 12.5; IR ($\tilde{\nu}$, cm^{-1}): 2970, 2916, 1720, 1597, 1489, 1350, 1134, 779; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{21}N_2O_2^+$: 333.1598; found 333.1554 $[M + H]^+$.

3-(Diethylamino)-9-methoxy-6*H*-chromeno[4,3-*b*]quinolin-6-one (3be): Red solid; yield: 54.4 mg (73%); mp: 183–185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.60 (d, *J* = 8.9 Hz, 1 H), 8.18 (d, *J* = 9.3 Hz, 1H), 7.65 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 6.88 (dd, *J* = 8.9, 2.1 Hz, 1H), 6.70 (d, *J* = 2.0 Hz, 1H), 4.12 (s, 3H), 3.63 (q, *J* = 7.0 Hz, 4H), 1.43 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 157.3, 154.3, 150.6, 148.6, 147.9, 138.9, 130.3, 127.2, 126.4, 125.8, 114.7, 109.0, 107.5, 105.8, 97.9, 55.6, 44.7, 12.6; IR (KBr, $\tilde{\nu}$, cm^{-1}): 2970, 2938, 1712, 1620, 1597, 1496, 1411, 1342, 1234, 1126, 1010, 779; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{21}N_2O_3^+$: 349.1547; found 349.1542 $[M + H]^+$.

3-(Diethylamino)-9,10-dimethoxy-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bf): Red solid; yield: 62.9 mg (78%); mp: 192–194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.44 (d, *J* = 9.0 H z, 1H), 7.45 (s, 1H), 7.13 (s, 1H), 6.75 – 6.72 (m, 1H), 6.57 (d, *J* = 2.5 Hz, 1H), 4.13 (s, 3H), 4.06 (s, 3H), 3.46 (t, *J* = 7.1 Hz, 4H), 1.26 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.61, 155.7, 154.4, 150.7, 149.7, 138.0, 125.6, 122.2, 112.7, 109.0, 107.6, 107.3, 106.4, 106.0, 100.7, 98.0, 56.4, 56.2, 44.8, 12.6; IR ($\tilde{\nu}$, cm^{-1}): 2970, 2940, 1712, 1620, 1597, 1496, 1342, 1126, 779; HRMS (ESI-TOF) (*m/z*) calculated $C_{22}H_{23}N_2O_4^+$: 379.1652; found 379.1653 $[M + H]^+$.

3-(Diethylamino)-9-fluoro-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bg): Yellow solid; yield: 41.8 mg (58%); mp: 188–190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.43 (d, *J* = 9.0 Hz, 1H), 8.11 (dd, *J* = 9.3, 5.2 Hz, 1H), 7.64–7.58 (m, 1H), 7.52 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.71 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.52 (d, *J* = 2.5 Hz, 1H), 3.47 (q, *J* = 7.1 Hz, 4H), 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5 ($J_{C\text{-}F}$ = 88.3 Hz), 158.6, 154.6, 151.1, 150.1 ($J_{C\text{-}F}$ = 2.3 Hz), 148.6, 140.0 ($J_{C\text{-}F}$ = 5.8 Hz), 131.4 ($J_{C\text{-}F}$ = 8.8 Hz), 126.6 ($J_{C\text{-}F}$ = 10.0 Hz), 126.1, 123.3 ($J_{C\text{-}F}$ = 25.9 Hz), 115.3, 112.0 ($J_{C\text{-}F}$ = 21.6 Hz), 109.1, 107.1, 97.9, 44.8, 12.5; IR ($\tilde{\nu}$, cm^{-1}): 3062, 2970, 1735, 1604, 1527, 1489, 1350, 1257, 1195, 802 ; HRMS

(ESI-TOF)(*m/z*) calculated $C_{20}H_{18}FN_2O_2^+$: 337.1347; found 337.1331 [M + H]$^+$.

9-Chloro-3-(diethylamino)-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bh): Yellow solid; yield: 45.2 mg (60%); mp: 185–187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.46 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 9.1 Hz, 1H), 7.90 (d, *J* = 2.3 Hz, 1H), 7.76 (dd, *J* = 9.1, 2.4 Hz, 1H), 6.73 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.54 (d, *J* = 2.5 Hz, 1H), 3.48 (q, *J* = 7.1 Hz, 4H), 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 154.7, 151.3, 150.9, 149.9, 139.9, 133.8, 131.6, 130.5, 127.7, 126.7, 126.2, 115.4, 109.2, 107.0, 97.9, 44.8, 12.5; IR ($\tilde{V}$, cm^{-1}): 3062, 2970, 1728, 1597, 1442, 1350, 1126, 825; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{18}ClN_2O_2^+$: 353.1051; found 353.1065 [M + H]$^+$.

9-Bromo-3-(diethylamino)-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bi): Yellow solid; yield: 49.2 mg (58%); mp: 184–186 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.42 (d, *J* = 9.0 Hz, 1H), 8.04 (d, *J* = 2.2 Hz, 1H), 7.96 (d, *J* = 9.1 Hz, 1H), 7.86 (dd, *J* = 9.1, 2.2 Hz, 1H), 6.71 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.51 (d, *J* = 2.5 Hz, 1H), 3.47 (q, *J* = 7.1 Hz, 4H), 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 154.7, 151.3, 150.9, 150.0, 139.7, 136.2, 131.1, 130.5, 127.2, 126.3, 119.5, 115.3, 109.2, 106.9, 97.9, 44.8, 12.6; IR ($\tilde{V}$, cm^{-1}): 2970, 2923, 1735, 1597, 1535, 1481, 1404, 1350, 1234, 1188, 1018, 941, 817; HRMS (ESI-TOF) (*m/z*) calculated $C_{20}H_{18}BrN_2O_2^+$: 397.0546; found 397.0538 [M + H]$^+$.

3-(Diethylamino)-6-oxo-6*H*-chromeno[4,3-*b*]quinoline-9-carbonitrile (3bj): Yellow solid; yield: 5.88 mg (8%); mp: 191–193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.48 (d, *J* = 9.0 Hz, 1H), 8.31 (d, *J* = 1.8 Hz, 1H), 8.16 (d, *J* = 8.9 Hz, 1H), 7.93 (dd, *J* = 8.9, 1.9 Hz, 1H), 6.75 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.55 (d, *J* = 2.5 Hz, 1H), 3.50 (q, *J* = 7.1 Hz, 4H), 1.29 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 155.2, 153.0, 152.3, 152.0, 141.3, 135.5, 133.0, 130.2, 126.8, 125.4, 118.4, 116.1, 109.4, 109.2, 106.6, 97.8, 44.9, 12.5; IR ($\tilde{V}$, cm^{-1}): 2978, 2930, 2222, 1735, 1604, 1450, 1396, 1234, 1018, 817; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{18}N_3O_2^+$: 344.1394; found 344.1387 [M + H]$^+$.

3-(Diethylamino)-10-methyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bk): Yellow solid; yield: 52.7 mg (74%); mp: 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.47 (d, *J* = 9.0 Hz, 1H), 7.92 – 7.87 (m, 1H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.35 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.72 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.54 (d, *J* = 2.5 Hz, 1H), 3.46 (q, *J* = 7.1 Hz, 4H), 2.60 (s, 3H),1.26 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 154.7, 151.6, 151.0, 150.7, 144.1, 140.5, 129.0, 128.4, 127.8, 126.2, 124.5, 113.9, 109.0, 107.4, 97.9, 44.8, 22.3, 12.6; IR ($\tilde{V}$, cm^{-1}): 2970, 2915, 1720, 1597, 1489, 1396, 1195, 879, 779; HRMS (ESI-TOF) (*m/z*) calculated $C_{21}H_{21}N_2O_2^+$: 333.1598; found 333.1605 [M + H]$^+$.

3-(Diethylamino)-9-isopropyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3bl): Red solid; yield: 57.9 mg (75 %); mp: 180–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.48 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.79 – 7.70 (m, 2H), 6.72 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.55 (d, *J* = 2.5 Hz, 1H), 3.47 (q, *J* = 7.1 Hz, 4H), 1.39 (s, 3H), 1.38 (s, 3H), 1.28 (brs, 1H), 1.26 (t, *J* = 6.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 154.6, 150.9, 150.5, 150.0, 146.7, 140.4, 133.2, 128.7, 126.4, 126.1, 125.3, 114.6, 109.0, 107.5, 97.9, 44.8, 34.0, 29.7, 23.7, 12.6; IR ($\tilde{V}$, cm^{-1}): 2970, 2892, 1728, 1620, 1597, 1527, 1489, 1404, 1226, 1118, 1072, 879; HRMS (ESI-TOF) (*m/z*) calculated $C_{23}H_{25}N_2O_2^+$: 361.1911; found 361.1908 [M + H]$^+$.

2-Bromo-6*H*-chromeno[4,3-b]quinolin-6-one (3ca): White solid; yield: 46.0 mg (68%); mp: 218– 220 °C; ^{1}H NMR (400 MHz, DMSO–d_6) δ 9.39 (s, 1H), 8.73 (brs, 1H), 8.35 (d, *J* = 8.2 Hz, 1H), 8.24 (d, *J* = 9.5 Hz, 1H), 8.10 – 8.04 (m, 1H), 7.89 – 7.83 (m, 1H), 7.82 – 7.77 (m, 1H), 7.47 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO–d_6) δ 160.5, 152.0, 150.3, 148.3, 141.5, 135.4, 134.5, 130.4, 129.3, 128.4, 127.8, 127.0, 121.8, 120.2, 117.3, 116.5; IR ($\tilde{V}$, cm^{-1}): 2916, 2853, 1743, 1604, 1550, 1489,1373,1172, 995, 802; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_9BrNO_2^+$: 325.9811; found 325.9810 [M + H]$^+$.

2-Bromo-9-methoxy-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ce): White solid; yield: 53.3 mg (72%); mp: 220–224 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.88 (d, *J* = 2.4 Hz, 1H), 8.17 (brs, 1H), 7.66 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.61 (dd, *J* = 9.3, 2.8 Hz, 1H), 7.30 (s, 1H), 7.25 (d, *J* = 2.8 Hz, 1H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 158.7, 151.2, 147.6, 146.2, 139.0, 134.4, 131.0, 128.8, 127.5, 127.4, 121.5, 119.1, 118.0, 115.7, 105.6, 55.8; IR ($\tilde{V}$, cm^{-1}): 2954, 2924, 1735, 1620, 1597, 1234, 1180, 1026, 810; HRMS (ESI-TOF) (*m/z*) calculated $C_{17}H_{11}BrNO_3^+$: 355.9917; found 355.9911 [M + H]$^+$.

2-Bromo-9-chloro-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ch): White solid; yield: 48.9 mg (65 %); mp: 221–223 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.89 (d, *J* = 2.4 Hz, 1H), 8.21 (d, *J* = 9.1 Hz, 1H), 8.04 (d, *J* = 2.3 Hz, 1H), 7.90 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.71 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 151.5, 149.4, 148.6, 140.2, 135.4, 134.7, 133.9, 131.2, 128.0, 127.9, 127.8, 121.0, 119.3, 118.2, 116.3; IR ($\tilde{V}$, cm^{-1}): 2924, 2854, 1728, 1612, 1504, 1458, 1249, 1219, 1080, 833, 723; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_8BrClNO_2^+$: 361.9400; found 361.9316 [M + H]$^+$.

2-Bromo-9-bromo-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ci): White solid; yield: 47.0 mg (56%); mp: 232–234 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.92 (brs, 1H), 8.23 (d, *J* = 2.2 Hz, 1H), 8.16 (d, *J* = 9.1 Hz, 1H), 8.03 (dd, *J* = 9.1, 2.2 Hz, 1H), 7.73 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.32 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 151.6, 149.6, 148.7, 142.3, 140.1, 137.1, 135.4, 131.2, 131.2, 128.5, 128.0, 122.0, 121.0, 119.3, 118.2, 116.3; IR ($\tilde{V}$, cm^{-1}): 2916, 2847, 1743, 1651, 1543, 1265, 1172, 995, 825; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_8Br_2NO_2^+$: 403.8916; found 403.8906 [M + H]$^+$.

2-Methyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3da): White solid; yield: 51.5 mg (69%); mp: 231–233 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.61 (s, 1H), 8.28 (d, *J* = 8.6 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.96 – 7.93 (m, 1H), 7.70 – 7.66 (m, 1H), 7.44 – 7.41 (m, 1H), 7.32 (d, *J* = 8.4 Hz, 1H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 151.1, 150.9, 149.8, 141.2, 134.8, 133.4, 129.5, 129.5, 127.4, 127.3, 125.0, 119.2, 117.2, 115.9, 21.0; IR ($\tilde{V}$, cm^{-1}): 2954, 2916, 1735, 1620, 1597, 1458, 1373, 1280, 1226, 1026, 825; HRMS (ESI-TOF) (*m/z*) calculated $C_{17}H_{12}NO_2^+$: 262.0863; found 262.0843 [M + H]$^+$.

9-Methoxy-2-methyl-6*H*-chromeno[4,3-*b*]quinolin-6-one (3de): White solid; yield: 61.1 mg (74%); mp: 237–239 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 8.54 – 8.48 (m, 1H), 8.13 (d, *J* = 9.3 Hz, 1H), 7.58 (dd, *J* = 9.3, 2.8 Hz, 1H), 7.37 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.21 (d, *J* = 2.8 Hz, 1H), 4.00 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 158.3, 150.4, 147.6, 147.5, 139.0, 134.6, 132.7, 130.8, 128.4, 127.0, 124.6, 119.3, 117.1, 116.0, 105.6, 55.8, 21.0; IR ($\tilde{V}$, cm^{-1}): 2954, 2916, 1735, 1620, 1504, 1450, 1234, 1126, 1010, 833, 810; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{14}NO_3^+$: 292.0968; found 292.0948 [M + H]$^+$.

3,9-Dimethoxy-6*H*-chromeno[4,3-*b*]quinolin-6-one (3ee): White solid; yield: 56.6 mg (71%); mp: 235–237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.65 (d, *J* = 8.8 Hz, 1H), 8.13 (d, *J* = 9.3 Hz, 1H), 7.58 (dd, *J* = 9.3, 2.8 Hz, 1H), 7.22 (d, *J* = 2.8 Hz, 1H), 7.01 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.90 (d, *J* = 2.4 Hz, 1H), 4.00 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 158.0, 153.7, 147.7, 147.6, 139.2, 130.6, 128.0, 127.1,

126.0, 115.1, 112.8, 105.7, 101.4, 55.8, 55.8; IR ($\tilde{V}$, cm^{-1}): 3080, 2994, 1735, 1627, 1496, 1458, 1381, 1234, 1157, 1126, 779; HRMS (ESI-TOF) (*m/z*) calculated $C_{18}H_{14}NO_4^+$: 308.0917; found 308.0893 $[M + H]^+$.

9-Fluoro-3-methoxy-6*H*-chromeno[4,3-*b*]quinolin-6-one (3eg): White solid; yield: 44.5 mg (58%); mp: 239–241°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.65 (d, *J* = 8.8 Hz, 1H), 8.22 (dd, *J* = 9.3, 5.2 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.62 (dd, *J* = 8.3, 2.8 Hz, 1H), 7.02 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.90 (d, *J* = 2.4 Hz, 1H), 3.95 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 161.5 ($J_{C\text{-}F}$ = 28.7 Hz), 159.1, 154.0, 149.3 ($J_{C\text{-}F}$ = 2.5 Hz), 148.4, 140.3 ($J_{C\text{-}F}$ = 6.1 Hz), 131.8 ($J_{C\text{-}F}$ = 8.9 Hz), 127.3 ($J_{C\text{-}F}$ = 10.2 Hz), 126.28, 123.9 ($J_{C\text{-}F}$ = 26.1 Hz), 115.6, 112.9, 112.5 112.0 ($J_{C\text{-}F}$= 21.1 Hz), 101.5, 55.8; IR ($\tilde{V}$, cm^{-1}): 2954, 2916, 1728, 1604, 1465, 1357, 1203, 1157, 1026, 941, 848; HRMS (ESI-TOF) (*m/z*) calculated $C_{17}H_{11}FNO_3^+$: 296.0717; found 296.0690 $[M + H]^+$.

6*H*-chromeno[4,3-*b*]quinolin-6-one-7-d (3aa''): White solid; yield: 51.1 mg (68%); mp: 210–212 °C; ^{1} H NMR (400 MHz, $CDCl_3$) δ 8.84 (dd, *J* = 7.9, 1.6 Hz, 1H), 8.29 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 8.1 Hz, 1H), 8.09 – 8.04 (m, 1H), 7.71 – 7.61 (m, 2H), 7.50 – 7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 152.8, 151.2, 149.7, 133.4, 132.4, 129.6, 129.4, 127.4, 127.3, 125.3, 125.0, 119.7, 117.4, 115.8; IR (KBr, $\tilde{V}$, cm^{-1}): 3055, 2957, 1735, 1604, 1573, 1458, 1242, 1157, 1187, 948, 756; HRMS (ESI-TOF) (*m/z*) calculated $C_{16}H_9DNO_2^+$: 249.0769; found 249.0735 $[M + H]^+$.

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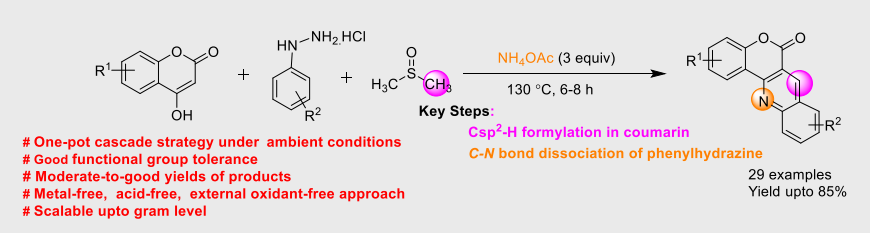

Key Topic*

*Santosh Kumari, S. M. Abdul Shakoor, Datta Markad, Sanjay K. Mandal, Rajeev Sakhuja**

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NH_4OAc-promoted Cascade Approach towards Aberrant Synthesis of Chromene-fused Quinolinones

Metal-free strategy for chromene-fused quinolinones