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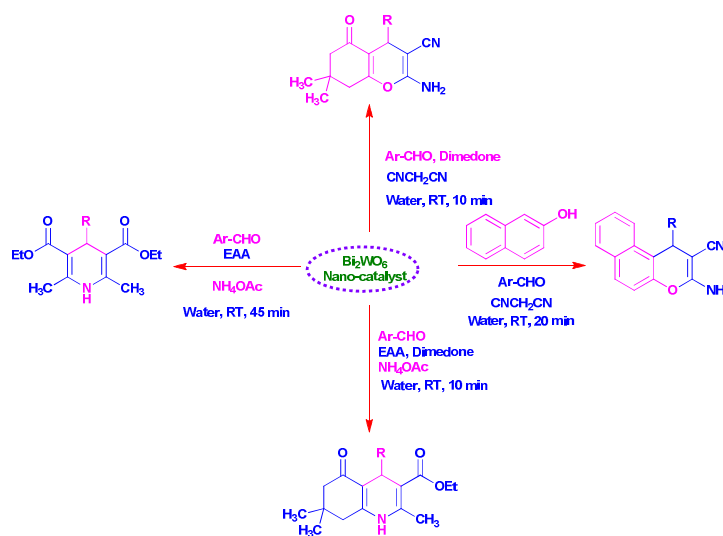
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Recyclable Bi₂WO₆-nanoparticle mediated one-pot multicomponent reactions in aqueous medium at room temperature^{†‡}

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Different types of multicomponent reactions (MCRs) are reported using Bi₂O₃, BiVO₄, and Bi₂WO₆ (nanoparticle) as heterogeneous catalysts. Among these, Bi₂WO₆ nano particles showed excellent reactivity for the synthesis of functionalized dihydropyridine, polyhydroquinoline, 4H-chromene and 2-amino-4H-benzo[b]pyran derivatives at ambient temperature in aqueous medium. All the reactions gave good to excellent yields in 10-45 minutes in the presence of 5 mol% (optimized) of the catalyst. The catalyst was regenerated and reused up to 5 cycles without losing catalytic activity. The gram scale synthesis of dihydropyridine gave the desired product in 82 % yield in 2 h



ARTICLE

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Different types of multicomponent reactions (MCRs) are reported using Bi₂O₃, BiVO₄, and Bi₂WO₆ (nanoparticle) as heterogeneous catalysts. Among these, Bi₂WO₆ nano particles showed excellent reactivity for the synthesis of functionalized dihydropyridine, polyhydroquinoline, 4*H*-chromene and 2-amino-4*H*-benzo[*b*]pyran derivatives at ambient temperature in aqueous medium. All the reactions gave good to excellent yields in 10-45 minutes in the presence of 5 mol% (optimized) of the catalyst. The catalyst was regenerated and reused up to 5 cycles without losing catalytic activity. The gram scale synthesis of dihydropyridine gave the desired product in 82 % yield in 2 h.

Introduction

Research in multicomponent reactions (MCRs) has well established and known for quite a period of time.¹ One can generate a library of compounds with minimum number of steps (most of the times, single step) and high atom economy² using MCRs. Many methods are available in the literature where a complex organic molecule (with diverse hetero atoms)³ or a natural product scaffold with certain biological activity⁴ has generated using MCRs as concept under asymmetric⁵ homogeneous⁶ and heterogeneous⁷ catalysis conditions. Along with these, recently, the organocatalytic,⁸ pseudo,⁹ enzyme-mediated¹⁰ and catalyst free¹¹ MCRs also gaining attention for the generation of complex molecules with biological, materials and polymers applications.¹²

Along with the conventional synthesis, last couple of decades have witnessed the development of environmentally friendly/greener approaches for organic transformations. In this direction, many techniques (solid phase,¹³ sonication,¹⁴ microwave mediated reactions,¹⁵ micellar catalysis¹⁶) are

developed along with ionic liquids¹⁷ and water¹⁸ as reaction medium and solvent free conditions.¹⁹

Because of the realization of interdisciplinary research, the synthesis and applications of nanomaterials have become an integral part of material science²⁰ and biology.²¹ Similar to this, synthetic organic chemistry also benefits from the use of nanomaterials as catalysts for organic reactions. In this regard, various nanomaterials-based catalysts (magnetic and non-magnetic)^{22,23} with different metal combinations were prepared and successfully applied for organic reactions.

Bismuth salts in +3 and +5 oxidation states play an important role in organic synthesis.²⁴ Compared to other metals, Bismuth reagents have the advantage of non-toxicity, non-carcinogenicity (green element), low cost and tolerance for sensitive functional groups. Because of this, bismuth reagents are used for a variety of reactions including oxidation, reduction, protection-deprotection sequences, esterification, etherification and other C–C and C–heteroatom bond formation reactions.^{24,25}

Results and discussion

From the above discussion, it is clear that the MCRs are performed under various conditions.^{5-19,22,23} Along with these, Bismuth-based reagents such as Bi(OTf)₃, Bi(NO₃)₃, Bi(NO₂)₃·5H₂O, BiCl₃ and Bi₂(SO₄)₃ have been used for the MCRs and Mannich type reactions.²⁶ However, some of these reactions are performed under thermal or microwave conditions in organic solvents and take more time for completion at room temperature.

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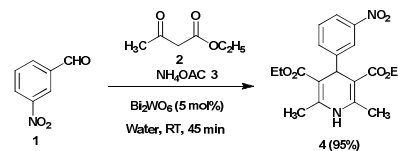
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^{†‡}Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

The synthesis of bismuth-based nanomaterials particularly Bi_2WO_6 is gaining importance because of its photo catalytic application for water splitting with UV-Vis radiation and oxidation of glycerol to dihydroxy acetone.²⁷ However, this material is not been explored for core organic transformations. Thus, here in were port the application of Bi_2WO_6 nanoparticle for the multicomponent reactions and explore its Lewis acidic properties.

Dihydropyridines (DHPs) known as *Hantzsch esters* are useful intermediates for hydrogen transfer reactions²⁸ and can be used as precursors for the preparation of substituted pyridine derivatives.²⁹ Also, the derivatives of DHPs act as neuroprotective agents, calcium channel blockers, radical scavenging agents.³⁰ Considering the importance of DHPs, we plan to explore the utility of Bi_2WO_6 nanoparticle as a heterogeneous catalyst for the synthesis of DHPs. Thus, the treatment of 3-nitrobenzaldehyde **1** (1 equiv) with ethyl acetoacetate **2** (EAA, 2 equiv) and ammonium acetate (NH_4OAc) **3** (2.5 equiv) in presence of catalytic amount Bi_2WO_6 (30 mol%) in EtOH (at 70 °C, 2 h) gave the DHP derivative **4** in 80% yield. After confirming the formation of the product (by Melting point and comparing with the literature value),³¹ the focus was shifted towards the optimization of the reactions conditions. Accordingly, the reactivity of 3-nitrobenzaldehyde **1**, EAA **2** and NH_4OAc **3** was tested with variation in the catalyst loading (from 30 mol% to 2 mol%) with simultaneous screening of the solvents (starting from diethyl ether to water) at room temperature (**Tables 1 and 2**). It was observed that the reaction was successful with moderate yields in organic solvents (irrespective of the polarity and protic/aprotic nature). Among all, water was found to be effective, giving desired product **4** in 95% yields with 5 mol% catalyst in 45 minutes (**Scheme-1**). Same reaction was carried out using Bi_2O_3 , BiVO_4 and $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ (water, RT, 4-6 h). However, all three catalysts were less reactive giving 33%, 56% and 49% yields respectively. It is noteworthy to mention that $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ is less reactive compared to BiVO_4 towards Hantzsch synthesis. This may be due to the Lewis acidic property of BiVO_4 and acceleration effect of water^{27,32} as it is observed in the present study. After optimization of the reaction conditions (**Scheme-1**), different aliphatic (formaldehyde, acetaldehyde), aromatic aldehydes (with electron donating and withdrawing groups) and heterocyclic aldehydes (furfural, pyrazole, quinoline and chromene based) were treated with EAA and NH_4OAc in presence of Bi_2WO_6 (5 mol%) in water at room temperature. In all the cases, the reaction was completed in 40-45 min with excellent yields (82-95%) irrespective of the starting material (aliphatic or aromatic), substitution (electron donating or withdrawing group) on benzene and aromatic moiety as summarized in **Figure-1**. All the products **5-17** were compared with the literature data or characterized using ^1H , ^{13}C -NMR and mass spectral data (see supporting information). To test the feasibility of the reaction and catalytic activity of Bi_2WO_6 , the gram scale,^{4a} synthesis of DHP derivative **5** using formaldehyde was attempted. Towards this, the formaldehyde (1 g, 33 mmol), ethylacetoacetate (8.4 g, 66 mmol) and



Scheme-1. Synthesis of dihydropyridine (**4**) (Optimized conditions)

S. No.	Solvent	Reaction time (h)	Isolated yield (%) ^a
1	Diethylether	2.5	60
2	Toluene	3.5	53
3	Dichloromethane	4.0	63
4	Chloroform	2.5	60
5	Tetrahydrofuran	3.5	60
6	MeOH	2.0	65
7	EtOH	2.0	68
8	DMF	3.0	50
9	DMSO	2.5	55
10	Acetonitrile	2.0	66
11	Water	45 min	95

Table-1. Solvent screening for the synthesis of dihydropyridine **4** (using 5 mol% catalyst)

S. No.	Catalyst loading (mol%)	Reaction time (min)	Isolated Yield ^a (%)
1	30	30	97
2	20	35	96
3	10	40	96
4	5	45	95
5	2	120	80

Table-2. Screening of the catalyst loading for the synthesis of DHP **4**;

^aWater is used as reaction medium

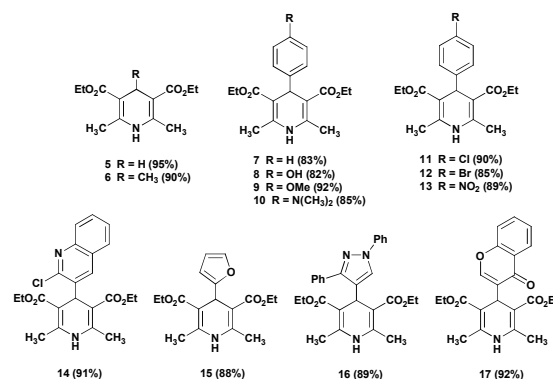


Figure-1. Different dihydropyridine (DHP) derivatives (**5-17**)

NH_4OAc (6.5 g, 82.5 mmol) were stirred in presence of Bi_2WO_6 (1.1 g, 15 mmol) in water (20 mL) at room temperature. As expected the formation of desired product **5** was observed in 2 h with 82% yield (7 g).

Later, the reusability of the catalyst was checked by regenerating the catalyst after every cycle of the reaction. Thus, above reaction was performed [3.3 mmol scale, Bi_2WO_6 (5

mol%), water, RT, 45 min] and catalyst was separated from the reaction mixture (by simple filtration), washed with distilled water (2 X 10 mL) and acetone (5 mL), dried at 70 °C (hot air oven) for 10 min. The regenerated catalyst was again used for a fresh reaction under similar conditions. The catalytic activity was tested up to 5 cycles and the results are summarized in **Table 3**. From the powder XRD data, it is confirmed that there is no change in the morphology in the catalyst (for powder XRD data, please see supporting information).

Cycle No.	Reaction time (min)	Isolated yield (5) (%) ^a
1	45	95
2	45	92
3	45	90
4	45	86
5	45	82

Table-3. Studies on the recyclability of the catalyst (with regeneration of the catalyst); ^aReaction was carried out at 3.3 mmol scale using 4 mL of water and 5 mol % of the catalyst.

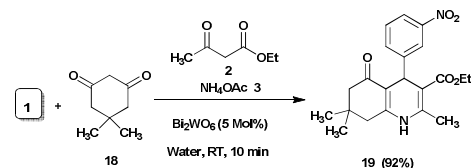
Along with the above, separate experiments were performed to see the feasibility of the reaction without separation of the catalyst. Hence, EtOAc (2 X 10 mL) was added to the reaction mixture (after completion of the reaction, as monitored by TLC) stirred for 10 min and the solvent layers were allowed to separate. EtOAc was removed using a separating funnel, leaving the catalyst in aqueous layer. To this aqueous layer, starting materials were added and stirred (see **Table 4**) till the completion of the reaction (checked by TLC). Same procedure was repeated for 5 times. It was observed that the catalyst is active giving the desired product in good yields even after 5 cycles as summarised in **Table-4**.

Cycle No.	Reaction time (min) ^a	TLC Conversion (%) ^a	Isolated yield (5) (%) ^a
1	35	100	95
2	35	100	95
3	45	98	92
4	50	95	90
5	60	95	86

Table-4. Studies on the recyclability of the catalyst (without regeneration of the catalyst); ^aReaction was performed at 3.3 mmol scale using 4 mL of water and 5mol % of the catalyst.

After successfully demonstrating the synthesis of DHPs, the attention shifted towards the synthesis of poly hydroquinolines that are structurally similar to that of DHPs and have importance in medicinal chemistry.³³ Towards this, aliphatic aldehydes like formaldehyde, acetaldehyde, aromatic aldehydes with electron donating and withdrawing groups (3-nitrobenzaldehyde **1**) and heterocyclic aldehydes (furfural, quinoline and chromene based) were reacted with dimedone **18** and NH₄OAc **3** (equimolar molar ratio) in presence of Bi₂WO₆ (5 mol%) in water at room temperature (**Scheme-2**). To our surprise, the formation of the product was observed in 10 min

(TLC) for all the substrates with good to excellent yields (80-95%) as shown in **Figure-2**. All the compounds **19-31** were characterised using complimentary spectral data (see supporting information).



Scheme-2. Synthesis of polyhydroquinoline derivative (**19**)

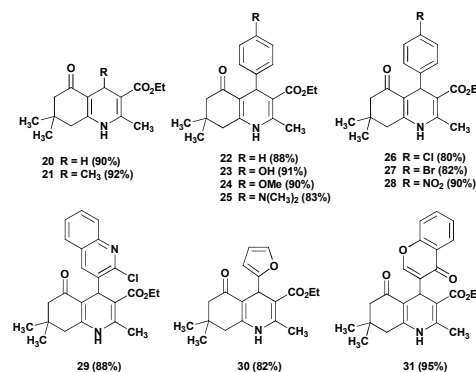
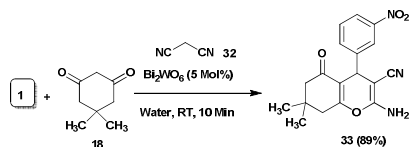


Figure-2. Different polyhydroquinoline derivatives (**20-31**)

In an extension to the present study of the catalytic activity of Bi₂WO₆, we continued our efforts for the construction of oxygen containing heterocyclic scaffolds such as 4H-chromenes which show biological properties.^{34,35} The preparation of 4H-chromenes was achieved under similar reaction conditions as described above (**Scheme 2**). The reaction of 3-nitrobenzaldehyde **1** with dimedone **18** and malononitrile **31** (in equimolar ratio) in presence of Bi₂WO₆ (5 mol%) in water at room temperature for 10 min gave desired chromene derivative **33** in 89% yield (**Scheme-3**). After confirmation of the product, other aldehydes (aliphatic, aromatic and heteroaromatic) were treated with dimedone and malononitrile to give desired products **34-45** with good to excellent yields as summarized in **Figure-3** (see supporting information for the spectral data of new compounds).

Similar to above, the synthesis of biologically active (anticancer, insulin-regulated amino peptidase inhibitors)^{34,35} 2-amino-4H-benzo[b]pyrans was conceived using the reaction conditions as mentioned in **Scheme-3** and β -naphthol as coupling partner. Towards this, different aldehydes were treated with β -naphthol **46** and malononitrile **32** in presence of Bi₂WO₆ (5 mol%) in water (**Scheme-4**). Unlike earlier results, the reaction times were slightly longer (i.e. 10-20 min) with yields ranging from 75-95%. This variation in the yields could be attributed to the bulkier size of β -naphthol **46**. All the compounds **47-60** were characterized using literature data or ¹H-, ¹³C-NMR and mass spectroscopic data (see supporting information).



Scheme-3. Synthesis of 4H-chromene derivative (33)

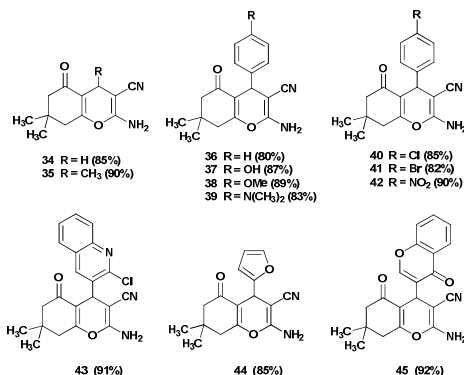
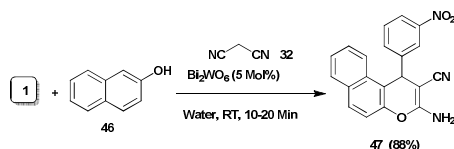


Figure-3. Different 4H-chromene derivatives (34–45)



Scheme-4. 2-amino-4H-benzo[b]pyran (47)

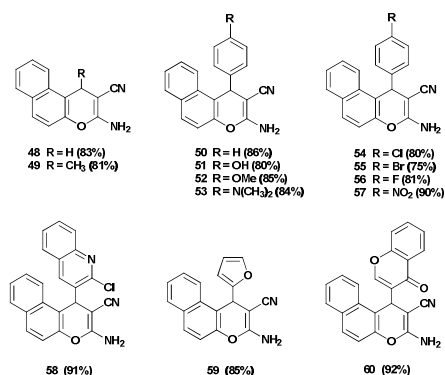


Figure-4. Different 2-amino-4H-benzo[b]pyran derivatives (48–60)

Conclusion

In conclusion, we have demonstrated Bi₂WO₆ nanoparticle mediated multicomponent reactions (at RT, in aq. medium) for the generation of a library of compounds with different scaffolds (DHPs, poly hydroquinolines, 4H-chromene and 2-amino-4H-benzo[b]pyran). In all the cases, random reactivity was observed irrespective of the substrate with good yields in a short period of time (10-45 min; 5 mol% of catalyst). The regenerated catalyst was found to be active up to 5 cycles without losing catalytic activity and structural changes. It was also observed that the catalyst is active for gram scale reactions. Many of the derivatives reported here can be converted in to

active pharmaceutical intermediates using suitable functional group inter conversions.

Experimental

General methods:

All the starting materials were purchased from Spectrochem, SD-Fine and Sigma-Aldrich and used as received. Melting points were determined in open capillaries using Stuart SMP30 melting point apparatus and uncorrected. ¹H and ¹³C-NMR spectra were recorded on Bruker 500 and 100 Mz spectrometer using CDCl₃ solvent (and reported in δ ppm). The mass spectra were recorded on Bruker-micro-TOFMS analyzer. Deionized water was used for the preparation of bismuth stock solution.

General procedure for the synthesis of Dihydropyridines and polyhydro quinolones:

To a mixture of aldehyde (1 equiv), and ethyl acetoacetate (2 equiv) or dimedone (1 equiv) in water (3-5 mL) was added NH₄OAc (2.5 equiv) followed by Bi₂WO₆ (5 mol%). The mixture was stirred at RT for 10-45 min. After completion of the reaction (monitored by TLC), the contents were transferred to separating funnel and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, water, dried over Na₂SO₄ and filtered. Evaporation of the solvent gave the crude product which was purified by recrystallization using EtOH as solvent or purified by silica gel column chromatography (EtOAc:petroleum ether as eluent) to give desired product (see supporting information for details and spectral data).

General procedure for the synthesis of 4H-chromene and 2-amino-4H-benzo[b]pyran derivatives:

To a mixture of aldehyde (1 equiv), and dimedone (1 equiv) or β-naphthol (1 equiv) in water (3-5 mL) was added malononitrile (1 equiv) followed by Bi₂WO₆ (5 mol%). The mixture was stirred at RT for 10–20 min. After completion of the reaction (monitored by TLC), the contents were transferred to separating funnel and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine, water, dried over Na₂SO₄ and filtered. Evaporation of the solvent gave the crude product which was purified by recrystallization or silica gel column chromatography (EtOAc:petroleum ether as eluent). (see supporting information for details and spectral data).

Spectral data for the selected compounds:

Diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (5): Yield = 95% (Yellow solid), M.P: 180-182°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.31 (t, 6H, J = 7 Hz), 2.22 (s, 6H), 3.29 (s, 2H), 4.17-4.22 (m, 4H), 5.15 (s, 1H). ¹³C-NMR (100 MHz, CDCl₃): δ 167.99, 144.65, 99.65, 59.61, 24.81, 19.14, 14.45.; Mass (TOF, ES+): m/z = Calculated: 253.13; Observed: 252.13 (M-H).

Diethyl 2,4,6-trimethyl-1,4-dihydropyridine-3,5-dicarboxylate (6):
Yield = 90% (Yellow solid), M.P: 128-130°C, ¹H-NMR (500 MHz, CDCl₃): δ 0.99 (d, 3H, *J* = 6.5Hz), 1.32 (t, 6H, *J* = 7 Hz), 2.29 (s, 6H), 3.83-3.87 (m, 1H), 4.18-4.23 (m, 4H), 5.53 (s, 1H). ¹³C-NMR (100 MHz, CDCl₃): δ 167.85, 144.19, 104.76, 59.59, 28.54, 22.25, 19.52, 14.45.

Diethyl 4-(2-chloroquinolin-3-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (14):

Yield = 91 % (Yellow solid), M.P: 233-235°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.21 (t, 6H, *J* = 7.5 Hz), 2.39 (s, 6H), 4.06-4.14 (m, 4H), 5.54 (s, 1H), 5.69 (s, 1H), 7.29 (s, 1H), 7.51 (t, 1H, *J* = 7.5 Hz), 7.68 (t, 1H, *J* = 7.5 Hz), 7.75 (d, 1H, *J* = 8.5 Hz), 7.99 (d, 1H, *J* = 8.5 Hz). ¹³C-NMR (100 MHz, CDCl₃): δ 201.45, 167.20, 150.35, 146.36, 144.27, 140.30, 139.46, 129.02, 128.14, 127.76, 110.61, 103.62, 59.95, 30.20, 19.74, 14.35. Mass (TOF, ES⁺): *m/z* Calculated: 414.13; Observed: 415.13 (M+1).

Diethyl 4-(1, 3-diphenyl-1*H*-pyrazole-4-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (16):

Yield = 89 % (Light yellow solid), M.P: 125-128°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.11 (t, 6H, *J* = 7Hz), 2.25 (s, 6H), 3.79-3.86 (m, 2H), 4.02-4.08 (m, 2H), 5.33 (s, 1H), 5.41 (s, 1H), 7.24-7.29 (m, 1H), 7.36 (t, 1H, *J* = 7Hz), 7.43 (t, 4H, *J* = 6.5 Hz), 7.71 (d, 2H, *J* = 8 Hz), 7.77 (s, 1H), 7.85 (d, 2H, *J* = 8 Hz). ¹³C-NMR (100 MHz, CDCl₃): δ 167.52, 151.34, 143.19, 140.36, 134.95, 129.20, 128.56, 127.84, 127.01, 125.92, 110.01, 104.43, 59.67, 29.81, 19.51, 14.30. Mass (TOF, ES⁺): *m/z* Calculated: 471.22; Observed: 472.22 (M+1).

Diethyl 2, 6-dimethyl-4-(4-oxo-4*H*-chromene-3-yl)-1,4-dihydropyridine-3,5-dicarboxylate (17):

Yield = 92% (Pale yellow solid), M.P: 220-222°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.27 (t, 6H, *J* = 7.5 Hz), 2.34 (s, 6H), 4.10-4.16 (m, 4H), 4.89 (s, 1H), 6.00 (s, 1H), 7.29 (s, 3H), 7.97 (s, 1H), 8.19 (d, 1H, *J* = 8Hz). ¹³C-NMR (100 MHz, CDCl₃): δ 176.90, 167.70, 155.90, 154.75, 132.91, 125.62, 125.40, 125.20, 124.72, 110.61, 110.00, 59.59, 35.32, 29.70, 19.03, 14.37.

Ethyl 2,4,7,7-tetramethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (21):

Yield= 92% (Pale yellow solid), M.P: 200-204 °C, ¹H-NMR (500 MHz, CDCl₃): δ 1.02 (d, 3H, *J* = 6.5 Hz), 1.10 (s, 3H), 1.11 (s, 3H), 1.31 (t, 3H, *J* = 7 Hz), 2.19 (d, 1H, *J* = 16.5 Hz), 2.28 (s, 2H), 2.32 (d, 1H, *J* = 16.5 Hz), 3.94 (q, 1H, *J* = 6.5 Hz), 4.20 (m, 2H), 5.84 (s, 1H). ¹³C-NMR (100 MHz, CDCl₃): δ 201.45, 195.81, 167.73, 148.58, 143.49, 112.80, 107.15, 50.86, 41.17, 32.71, 29.52, 27.02, 25.49, 22.16, 19.37, 14.42. Mass (TOF, ES⁺): *m/z* Calculated: 277.17; Observed: 278.17 (M+1).

Ethyl 2-chloro-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydro-(3,4-biquinoline)-3-carboxylate (29):

Yield = 88% (Yellow solid), M.P: 275-278°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.12 (s, 3H), 1.25 (s, 3H), 1.35 (t, 3H, *J* = 7 Hz), 1.79 (s, 2H), 2.40 (s, 3H), 2.65 (s, 2H), 4.12 (q, 2H, *J* = 6.5 Hz), 6.01 (s, 1H), 7.52 (t, 1H, *J* = 7.5 Hz), 7.78 (t, 1H, *J* = 7 Hz), 7.92 (d, 1H, *J* = 7 Hz), 8.01 (d, 1H, *J* = 7 Hz), 8.50 (s, 1H). ¹³C-NMR (100 MHz, CDCl₃): δ 197.17, 164.77, 162.89, 151.75, 141.15, 130.05, 137.46, 135.10, 131.39, 130.35, 129.47, 128.62, 127.78, 125.73, 122.16, 120.33, 115.86, 111.57, 50.91, 41.00, 32.20, 31.22, 29.33, 27.03. Mass (TOF, ES⁺): *m/z* Calculated: 424.16; Observed: 425.21 (M+1).

Ethyl 2,7,7-trimethyl-5-oxo-4-(4-oxo-4*H*-chromene-3-yl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (31):

Yield = 95% (Light yellow solid), M.P: 240-243°C, ¹H-NMR (500 MHz, CDCl₃): δ 0.97(s, 3H), 1.09 (s, 3H), 1.28 (t, 3H, *J* = 7 Hz), 2.17 (s, 2H), 2.34 (m, 5H), 4.12 (q, 2H, *J* = 6.5 Hz), 4.89 (s, 1H), 6.55 (s, 1H), 7.35 (t, 1H, *J* = 7.5 Hz), 7.43 (d, 1H, *J* = 7 Hz), 7.62 (t, 1H, *J* = 7 Hz), 8.13 (d, 1H, *J* = 7 Hz), 8.16 (s, 1H). ¹³C-NMR (100 MHz, CDCl₃): δ 195.70, 177.16, 167.36, 156.04, 155.20, 150.55, 146.02, 132.87, 125.36, 125.20, 124.63, 124.09, 110.12, 107.24, 100.98, 59.65, 50.84, 41.07, 32.72, 32.61, 29.32, 27.25, 19.84, 14.35. Mass (TOF, ES⁺): *m/z* Calculated: 407.17; Observed: 408.17 (M+1).

2-amino-4,7,7-trimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (35):

Yield= 90% (Pale yellow solid), M.P: 180-183°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.09 (s, 3H), 1.11 (s, 3H), 1.51 (t, 3H, *J* = 7 Hz), 2.27 (s, 2H), 2.34 (s, 2H), 4.42 (s, 1H), 4.53 (s, 1H). ¹³C-NMR (100 MHz, CDCl₃): δ 197.14, 161.54, 160.38, 156.10, 119.05, 115.34, 52.48, 50.89, 41.21, 32.09, 28.83, 24.73, 22.52. Mass (TOF, ES⁺): *m/z* Calculated: 232.12; Observed: 233.12 (M+1).

2-amino-4-(2-chloroquinoline-3-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-3-carbonitrile (43):

Yield = 91% (White solid), M.P: 242-245°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.22 (s, 3H), 1.24 (s, 3H), 2.46 (d, 2H, *J* = 1.5 Hz), 2.72-2.81 (m, 2H), 4.61 (d, 1H, *J* = 3.5 Hz), 4.74 (s, 1H), 7.62 (t, 1H, *J* = 8 Hz), 7.84 (t, 1H, *J* = 7 Hz), 7.96 (d, 1H, *J* = 8Hz), 8.04 (d, 1H, *J* = 8.5 Hz), 8.59 (s, 1H). ¹³C-NMR (100 MHz, CDCl₃): δ 197.12, 170.30, 154.13, 146.53, 140.54, 131.92, 120.33, 128.00, 127.19, 126.99, 112.07, 111.85, 110.81, 106.61, 50.47, 41.66, 35.55, 32.40, 29.40, 29.36, 27.08. Mass (TOF, ES⁺): *m/z* Calculated: 379.84; Observed: 344.13 (M-35).

2-amino-7,7-dimethyl-4,5-dioxo-5,6,7,8-tetrahydro-4*H*,4'*H*-(3,4'-bichromene)-3-carbonitrile (45):

Yield = 92% (Pale yellow solid), M.P: 249-251°C, ¹H-NMR (500 MHz, CDCl₃): δ 1.02 (s, 3H), 1.12 (s, 3H), 2.28 (s, 2H), 2.43 (d, 1H, *J* = 17.5 Hz), 2.55 (d, 1H, *J* = 17.5 Hz), 4.15 (s, 1H), 4.65 (s, 2H), 7.38 (t, 1H, *J* = 7.5 Hz), 7.46 (d, 1H, *J* = 8 Hz), 7.66 (t, 1H, *J* = 7.5Hz), 8.08 (s, 1H), 8.15 (d, 1H, *J* = 7.5 Hz). ¹³C-NMR (100 MHz, CDCl₃): δ 196.65, 176.80, 163.79, 159.56, 156.27, 154.29, 151.75, 133.45, 125.46, 124.76, 121.83, 118.22, 110.97, 50.80, 52.34, 50.73, 40.59, 32.22, 30.60, 28.94, 27.45.

Mass (TOF, ES⁺): *m/z* Calculated: 362.13; Observed: 363.13 (M+1).

3-amino-1-(4-oxo-4*H*-chromene-3-yl)-1*H*-benzo(*b*)chromene-2-carbonitrile (60):

Yield = 92% (Bricked solid), M.P: 231-235°C, ¹H-NMR (500 MHz, CDCl₃): δ 4.12 (d, 1H, *J* = 8Hz), 5.87 (s, 1H), 7.07(t, 1H, *J* = 7.5Hz), 7.13 (d, 1H, *J* = 8Hz), 7.42- 7.47 (m, 2H), 7.56-7.60 (m, 2H), 7.69 (d, 1H, *J* = 7Hz), 7.76 (d, 1H, *J* = 1.5Hz), 7.90 (t, 1H, *J* = 3.5Hz), 7.97 (t, 2H, *J* = 8.5Hz), 8.02 (s, 1H). Mass (TOF, ES⁺): *m/z* Calculated: 366.10; Observed: 367.10 (M+1).

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Notes and references

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