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Visible light induced, catalyst free, convenient synthesis of chromene nucleus and its derivatives using water–ethanol mixture as a solvent

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A highly efficient, green, eco-friendly, one pot protocol has been demonstrated for the synthesis of 2-imino-2*H*-chromene-3-carbonitrile **(3)**, 2-aminochromene **(4)** and chromeno(2,3-*b*)pyridines **(5)**. The synthesis of the chromene nucleus has been carried out under visible light irradiation in a water–ethanol mixture at room temperature using salicylaldehyde and malononitrile in different proportions. The adopted method shows significant advantages such as mild and clean reaction conditions, eco-friendly procedures, absence of catalysts and a short reaction time. This protocol involves the use of CFL as the visible light source and shows high selectivity in the presence of a mixture of ethanol and water. The reaction proceeds with good to excellent yield.

Introduction

The safety of the environment and consciousness about the reduction in global warming inspires the use of renewable energy resources and minimization of waste products. In the past several years, the development of a sustainable, eco-efficient energy source for the construction of biologically important heterocycles has become an important research area in the field of synthesis.[1] Visible light induced synthesis of heterocycles has evoked the interest of chemists and researchers due to the easy availability of visible radiation. In addition, cost effective radiation is useful and harmless to human beings.[2] Light is a perfect reagent for the environmentally benign, green synthesis of heterocyclic scaffolds because it activates organic molecules, facilitating a smooth completion of the chemical reaction.[3] Solvents also play an important part in organic synthesis. Water is present in abundance in nature and show environment friendly behaviour.[4] Therefore, we carried out the synthesis of bioactive molecules in a mixture of ethanol and water, which is observed as a green medium for synthesis.[5] Chromenes are an important scaffold having oxygen as a heteroatom,[6] and the chromene nucleus commonly forms a part of various tannins and polyphenols present in tea, vegetables, fruits and red wine. They show different types of bioactivities, such as antiviral, anti-HIV, antidepressant, antioxidative, anticoagulant, antimicrobial, mutagenicity, antiproliferative, antitumor, diuretic, antianaphylactic and for creation of small scaffold ligands with highly noticeable smooth muscle relaxant properties. The chromene nucleus is also broadly found in natural alkaloids, tocopherols, anthocyanins and flavanoids.[7] In addition, they activate potassium channels and inhibit dihydrofolate reductase and phosphodiesterase IV. Chromene moieties have been able to prevent many diseases, including psoriatic arthritis and rheumatoid arthritis and are also widely used in cancer therapy.[8] They have fluorescence properties, and hence are used in brightening agents, optical whiteners and as laser dyes in pharmacy and biology.

In addition, iminocoumarins are an elite class of protein tyrosine kinase inhibitors of low molecular weight. A number of anti-cancer agents contain the protein tyrosine kinase.[9] Similar to coumarin, iminocoumarins are used as dyes and fluorescent sensors for the evaluation of metal ions in micromolar concentrations.[10] 2-Amino-4*H*-pyrans also show some important biological activities such as anticancer activity, central nervous system activity and anti-microbial activity. They are broadly applied in cosmetic and agrochemical industries.[11] The examples of bioactive compounds synthesized by a multicomponent method, involving the iminocoumarin moiety, are diethyl-2-amino-3-cyano-4*H*-chromen-4-ylphosphonate (compound A; Fig. 1),[12] which shows unique pharmacological properties such as being an anticoagulant; 2-(2-hydroxyphenyl)-3*H*-chromeno-[2,3-*d*]pyrimidin-4(5*H*)-one (compound B; Fig. 1) and 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-7-(dimethylamino)-4*H*-chromene-3-carbonitrile (compound C; Fig. 1) as antitumor agents; and compound D, which is used in cancer therapy.

Multicomponent reactions show many advantages over conventional multistep synthesis such as short reaction time, cost

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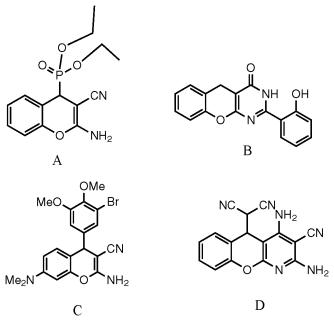
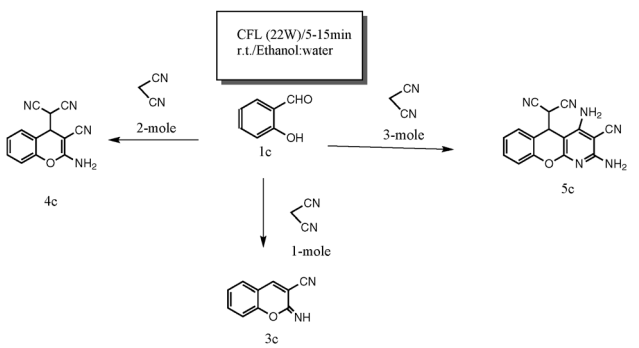


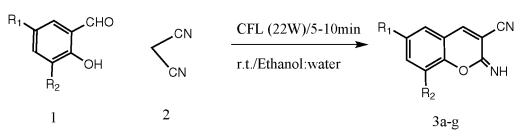
Fig. 1 Some biodynamic chromene nuclei.

effectiveness, energy efficiency and the use of minimum amounts of raw material. They involve the formation of a number of bonds in a single step.[13] A number of methods[14] have been reported for the synthesis of coumarin derivatives. For example, Somnath Ghosh *et al.* synthesized a chromene nucleus using salicylaldehyde and Meldrum's acid via a photochemical method; Majid M. Heravi also synthesized a chromene nucleus in the presence of MCM-41; M. N. Elinson used the grinding method for the synthesis of a chromene nucleus; and M. Costa and co-workers synthesized new dimeric chromene derivatives. It has been observed that all the methods require thermal energy, long reaction time and the use of toxic solvents for the completion of the reaction.[15] Considering these aspects, and in continuation of our previous work,[16] we report a highly efficient visible light catalyzed synthesis of bioactive heterocycles (Scheme 1).

Salicylaldehyde (**1c**) and malononitrile (**2**) were added in stoichiometric amounts to a mixture of water and ethanol (1 : 1, 20 ml) and irradiated under visible light (22 W, CFL) at rt. Corresponding iminocoumarins (**3c**) were obtained in good to excellent yield (Scheme 2).



Scheme 1 Visible light catalyzed synthesis of chromene derivatives.



Scheme 2 Synthesis of 2-imino-2*H*-chromene-3-carbonitrile.

Results and discussion

In order to investigate the effect of solvent, we used a number of polar and nonpolar reaction media to perform the test reactions. It was observed that polar solvents increased the yield of the product more compared to nonpolar ones (Table 1, entry 3).

We know that cyclisation reactions occur more smoothly in polar reaction media;[17] hence, we shifted our attention towards the use of water and ethanol as a solvent.

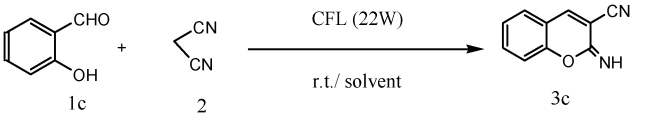
In order to obtain a high yield of the product and to decrease the overall reaction time, the degree of the polarity of the reaction medium was optimized by the addition of ethanol as a co-reaction medium in water in different ratios[18] (Table 2). When the reaction was performed in pure ethanol, the yield of the product was not satisfactory (Table 2, entry 1). The result clearly indicates that 50% ethanol in water proved to be the optimum solvent in which a good yield was obtained in minimum time[15a] (Table 2, entry 4).

Our next step was to optimize the intensity of visible light in order to achieve maximum yield (Table 3). The results showed that the enhancement of illumination intensity of CFL above 22 W does not significantly affect the yield of the product.

Having optimized the reaction conditions, we performed the reaction with different derivatives of salicylaldehyde to prepare a series of chromene nuclei (Table 4).

To extend the scope of this protocol, we used different ratios of reactant molecules. First, the reaction of salicylaldehyde (**1**) was carried out with 2 equivalents of malononitrile (**2**) under

Table 1 Optimization of solvents



Entry	Solvent	Time (min)	Yield[a] (%)
1	Water	15	86
2	Ethanol	20	88
3	Ethanol : water (1 : 1)	5	92
4	Acetonitrile	20	72
5	DMSO	25	74
6	DCM	22	76
7	Neat	12	89

[a] Isolated yield in % salicylaldehyde (1 mmol), malononitrile (1 mmol) in ethanol:water mixture.

Table 2 Effect of solvent ratio on the yield

Entry	Solvent	Time (min)	Yield[a] (%)
1	100% ethanol	5	78
2	80% ethanol in water	5	79
3	70% ethanol in water	5	80
4	50% ethanol in water	5	94
5	30% ethanol in water	5	92
6	10% ethanol in water	5	90
7	5% ethanol in water	5	89

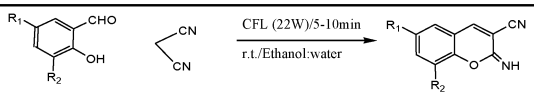
[a] Isolated yield in % salicylaldehyde (1 mmol), malononitrile (1 mmol) in ethanol:water mixture.

Table 3 Optimization of reaction conditions

Entry	Reaction condition	Time (min)	Yield[a] (%)
1	CFL (18 W)	9	94
1	CFL (22 W)	5	97
2	CFL (24 W)	9	97
3	CFL (36 W)	5	97
3	Daylight	12	88
4	Dark	15	64

[a] Isolated yield in % salicylaldehyde (1 mmol), malononitrile (1 mmol) in ethanol:water mixture.

Table 4 Substrate scope for the formation of compound (**3a–g**)

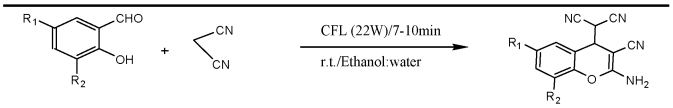


1 2 3a-g

Entry	R_1	R_2	Time (min)	Yield[a] (%)	M.P. (°C)
a	H	OCH_3	9	92	>260
b	OH	H	10	88	>260
c	H	H	5	97	138–140
d	Br	H	8	89	192–194
e	H	OH	7	98	>260
f	CH_3	H	8	90	—
g	Cl	H	10	91	—

Reaction between one mole salicylaldehyde and malononitrile. [a] Is isolated yield in %.

Table 5 Substrate scope for the formation of compound (**4a–h**)



1 2 4a-h

Entry	R_1	R_2	Time (min)	Yield[a] (%)	M.P. (°C)
a	H	OCH_3	8	96	171–172
b	H	OEt	7	98	96–99
c	H	H	9	96	150–151
d	CH_3	H	7	98	138–142
e	Br	H	10	89	163–165
f	OH	H	8	95	—
g	Cl	H	10	88	154–157
h	Br	OCH_3	9	87	161–162

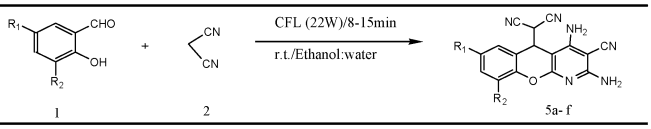
Reaction between one mole salicylaldehyde and two moles of malononitrile. [a] Isolated yield in %.

the same reaction conditions, resulting in 2-amino chromene (**4**) (Table 5). This product was obtained due to Michael addition of malononitrile and iminocoumarins.

Furthermore, in order to enlarge the scope of our reaction, we carried out the reaction of salicylaldehyde with 3 equivalents of malononitrile, which led to the formation of chromeno-(2,3-*b*)pyridines (**5**) (Table 6).

A mechanistic rationalization for the reaction is proposed in (Scheme 3). This plausible mechanism[12a] shows that the active methylene compound, malononitrile, undergoes tautomerisation[19] in the presence of visible light and the solvent (*i.e.*, water and alcohol), which gives (A). Knoevenagel condensation of (A) and salicylaldehyde takes place in a solution with the elimination of

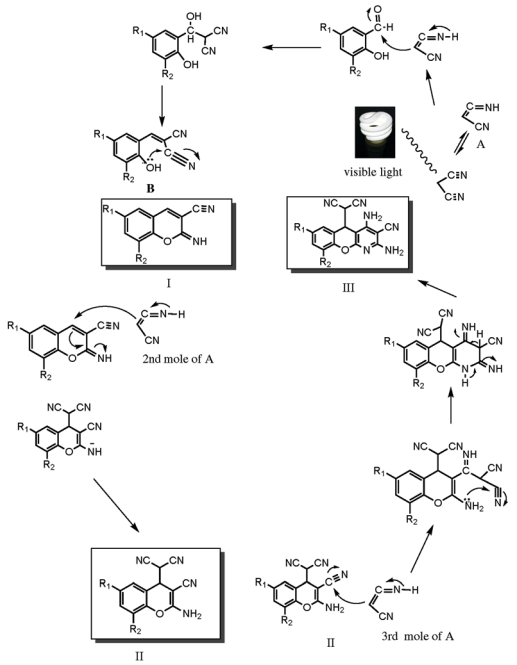
Table 6 Substrate scope for the formation of compound (**5**)



1 2 5a-f

Entry	R_1	R_2	Time (min)	Yield[a]	M.P. (°C)
a	Br	OCH_3	12	88	>300
b	H	OCH_3	10	89	>300
c	H	H	8	97	>300
d	Br	H	15	89	>300
e	H	OEt	15	90	>300
f	CH_3	H	15	96	>300

Reaction between one mole salicylaldehyde and 3 mole of malononitrile. [a] Isolated yield in %.



Scheme 3 A plausible mechanism for the synthesis of chromene and its derivatives.

water and the formation of the corresponding benzylidene malononitrile (B). The subsequent intramolecular cyclization of the Knoevenagel adduct (B) gives substituted 2-imino-2*H*-chromene-3-carbonitriles (**I**).

Furthermore, the addition of a 2nd mole of malononitrile to (**I**) gives (4*H*-chromene-4-yl)malononitrile (**II**), while the addition of a 3rd mole of malononitrile to (**II**) gives (4-*H*-chromene-4-yl) malononitrile (**III**) by an attack on the nitrile group of the pyran ring of (**II**) followed by cyclization.

Conclusion

To conclude, herein, we have put forward a method in which the target products could be isolated by a simple filtration method due to a difference in the solubility of product and reactant materials. To our delight, the products obtained were

analytically so pure that there was no need for further purification, which avoided multiple extraction steps and separation by chromatography. Hence, the choice of the mixture water and ethanol as a solvent over other toxic solvents minimized the impurity of the products, and thereby reduced the generation of waste by chromatographic separation.[20]

Experimental section

A. General information

Reagents were obtained from commercial suppliers, and used without further purification unless otherwise specified by a reference. All the reactions were performed using oven-dried glassware. Organic solutions were concentrated using a Buchi rotary evaporator. TLC was performed using silica gel GF254 (Merck) plates. Melting points were determined by open glass capillary method and are uncorrected. IR spectra in KBr were recorded on an Perkin-Elmer 993 IR spectrophotometer, ^{1}H NMR spectra were recorded on a Bruker AVII 300 spectrometer in $CDCl_3$ using TMS as an internal reference with chemical shift values being reported in ppm. All the coupling constants (J) are reported in Hertz (Hz). Mass (EI) spectra were recorded on a JEOL D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyzer.

B. General method

A mixture of 1 mole of salicyladehyde (1) and malononitrile (2) (1 mol for **3a–g**, 2 mol for **4a–h** and 3 mol for **5a–f**) was added in water and ethanol (1 : 1, 20 ml). The mixture was irradiated with 22 W CFL with stirring at rt. for 5–15 min. After the completion of the reaction (monitored by TLC), water (10 ml) was added and the mixture was filtered. The resulting product was recrystallized using hot ethanol and a yield of 88–98% was obtained. All the compounds that were obtained are known and were characterised by comparison of their spectral data with those reported in literature.

2-Imino-8-methoxy-2*H*-chromene-3-carbonitrile (3a)[15f]. Yellow solid. mp >260 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3420, 2940, 2228, 1650, 1620. ^{1}H NMR δ = 3.80 (s, 3H), 7.13 (dd, J = 7.6 Hz, 1.5 Hz, 1H), 7.120 (t, J = 7.8 Hz, 1H), 7.31 (dd, J = 8.1 Hz, 1.8 Hz, 1H), 8.34 (s, 1H), 8.91 (s, 1H). Anal. Calc. for $C_{11}H_8N_2O_2$; C, 65.41; H, 3.96; N, 13.88. Found: C, 65.78; H, 4.09; N, 13.66. EIMS 200 $(M)^+$.

6-Hydroxy-2-imino-2*H*-chromene-3-carbonitrile (3b)[14b,15f]. Yellowish solid. mp >260 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3245, 2222, 1656. ^{1}H NMR δ = 6.45–7.01 (m, 3H), 8.32 (s, 1H), 8.60 (s, 1H), 9.76 (1H). Anal. Calc. for $C_{10}H_6N_2O_2$; C, 64.52; H, 3.25; N, 15.05. Found: C, 64.45; H, 3.30; N, 15.10. EIMS: 186 $(M)^+$.

2-Imino-2*H*-chromene-3-carbonitrile (3c)[14b,15f]. Yellowish white solid. mp 138–140 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3285, 2225, 1658, ^{1}H NMR δ = 7.16–7.20 (m, 1H), 7.27 (td, J = 7.5 Hz, 0.9 Hz, 1H), 7.52–7.60 (m, 2H), 8.36 (d, J = 1.5 Hz, 1H), 8.85 (s, 1H). Anal. Calc. for $C_{10}H_6N_2O$; C, 69.85; H, 3.49; N, 16.30. Found: C, 70.02; H, 3.55; N, 16.20. EIMS 170 $(M)^+$.

6-Bromo-2-imino-2*H*-chromene-3-carbonitrile (3d)[14b,15f]. Yellowish white solid. mp 192–194 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3338, 2250, 1651, 1585, 1556. ^{1}H NMR δ = 7.14 (d, J = 9.0 Hz, 1H), 7.71 (dd, J = 8.7 Hz, 2.4 Hz, 1H), 7.78 (d, J = 2.4 Hz, 1H), 8.27 (s, 1H), 9.01 (s, 1H). ^{13}C NMR δ = 105.53, 114.97, 115.45, 117.83, 119.31, 131.30, 136.22, 145.65, 150.81 Anal. Calc. for $C_{10}H_5N_2OBr$; C, 48.19; H, 2.01; N, 11.24. Found: C, 47.95; H, 2.03; N, 11.15. EIMS 247 $(M)^+$, 249 $(M + 2)^+$.

8-Hydroxy-2-imino-2*H*-chromene-3-carbonitrile (3e)[15f]. Yellow solid. mp >260 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3330, 2222, 1640. ^{1}H NMR δ = 6.95–7.45 (m, 3H), 8.31 (s, 1H), 8.65 (s, 1H), 10.20 (brs, 1H). ^{13}C NMR δ = 104.11, 113.76, 115.23, 116.35, 117.54, 121.42, 146.83, 146.93, 152.02, 153.46. Anal. Calc. for $C_{10}H_6N_2O_2$; C, 64.52; H, 3.23; N, 15.05. Found: C, 64.35; H, 3.40; N, 15.10. EIMS 186 $(M)^+$.

2-(2-Amino-3-cyano-8-methoxy-4*H*-chromen-4-yl)malononitrile (4a)[14c]. White solid. mp 171–172 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3420, 2930, 2227. ^{1}H NMR δ = 3.39 (s, 3H), 4.56 (d, J = 3.9 Hz, 1H), 5.02 (d, J = 3.9 Hz, 1H), 7.01 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.10 (dd, J = 8.1 Hz, 1.5 Hz, 1H), 7.18 (t, J = 8.1 Hz, 1H), 7.51 (s, 2H). Anal. Calc. for $C_{14}H_{10}N_4O_2$; C; 63.16; H, 3.59; N, 21.05. Found: C, 63.30; H, 3.70; N, 20.80. EIMS 266 $(M)^+$.

2-(2-Amino-3-cyano-4*H*-chromen-4-yl)malononitrile (4c)[15f]. White solid. mp 150–151 °C IR (KBr) ($\nu_{max/cm^{-1}}$) 3320, 2228, 1652, 1641. ^{1}H NMR δ = 4.57 (d, J = 3.9 Hz, 1H), 5.05 (d, J = 3.9 Hz, 1H), 7.14 (dd, J = 8.1 Hz, 0.9 Hz, 1H), 7.27 (dt, J = 7.5 Hz, 0.9 Hz, 1H), 7.41 (dt, J = 7.8 Hz, 1.2 Hz, 1H), 7.46 (dd, J = 7.7 Hz, 1.2 Hz, 1H), 7.51 (s, 2H). Anal. Calc. for $C_{13}H_8N_4O$; C, 66.10; H, 3.39; N, 23.73. Found: C, 65.80; H, 3.45; N, 23.78. EIMS 236 $(M)^+$.

2-(2-Amino-6-bromo-3-cyano-4*H*-chromen-4-yl)malononitrile (4e)[14c,15f]. White solid. mp 163–165 °C; IR (KBr) ($\nu_{max/cm^{-1}}$) 2255, 2148, 2130, 1655, 1638, 1590, 1565 cm^-. ^{1}H NMR δ = 4.62 (d, J = 3.6 Hz, 1H), 5.14 (d, J = 3.9 Hz, 1H), 7.12 (d, J = 9.0 Hz, 1H), 7.52–7.61 (m, 3H), 7.71 (d, J = 2.4 Hz, 1H). ^{13}C NMR δ = 32.41, 36.73, 48.45, 112.74, 112.93, 116.45, 118.63, 119.13, 120.30, 131.42, 131.95, 149.01, 163.23. Anal. Calc. for $C_{13}H_7N_4OBr$; C, 48.83; H, 2.35; N, 17.53. Found: C, 49.12; H, 2.40; N, 17.20. EIMS 313 $(M)^+$, 315 $(M + 2)^+$.

2-(2-Amino-6-bromo-3-cyano-8-methoxy-4*H*-chromen-4-yl)-malononitrile (4h)[15f]. White solid. mp 161–162 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 2248, 2189, 2120, 1675, 1651, 1626, 1590, 1572. ^{1}H NMR δ = 3.87 (s, 3H), 4.58 (d, J = 3.9 Hz, 1H), 5.09 (d, J = 3.9 Hz, 1H), 7.25 (d, J = 2.1 Hz, 1H), 7.32 (d, J = 2.1 Hz, 1H), 7.61 (s, 2H). ^{13}C NMR δ = 32.34, 36.82, 48.56, 56.44, 112.76, 112.93, 115.8, 116.34, 119.12, 120.55, 122.03, 138.65, 148.11, 163.13. Anal. Calc. for $C_{14}H_9N_4O_2Br$; C, 48.70; H, 2.61; N, 16.23. Found: C, 48.75; H, 2.89; N, 16.30. EIMS 343 $(M)^+$, 345 $(M + 2)^+$.

(2,4-Diamino-7-bromo-3-cyano-9-methoxy-5*H*-chromeno[2,3-*b*]-pyridin-5-yl) malononitrile (5a)[12a]. White Yellow solid. mp >300 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3442, 3348, 2948, 2259, 2205, 1627, 1563, 1489, 1403, 1236. ^{1}H NMR δ = 3.89 (s, 3H), 4.90–4.92 (m, 2H), 6.72 (s, 2H), 7.05–7.9 (m, 3H), 7.32 (s, 1H). ^{13}C NMR δ = 30.31, 34.53, 56.40, 70.73, 83.24, 112.72, 113.21, 115.13,

115.85, 116.11, 120.24, 122.26, 140.58, 148.62, 156.95, 160.01, 160.42. Anal. Calc. for $C_{17}H_{12}BrN_6O_2$; C, 49.65; H, 2.70; N, 20.44. Found: C, 49.70; H, 2.80; N, 20.48. EIMS 411 $(M)^+$, 413 $(M + 2)^+$.

(2,4-Diamino-3-cyano-9-methoxy-5*H*-chromeno[2,3-*b*]pyridin-5-yl)malononitrile (5b)[12a]. Whitish yellow solid. mp >300 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3460, 3336, 2958, 2254, 2198, 1643, 1599, 1561, 1493, 1412. ^{1}H NMR δ = 3.84 (s, 3H), 4.86 (d, 1H, *J* = 3.9 Hz), 4.98 (d, 1H, *J* = 3.9 Hz), 6.67 (s, 2H), 6.96 (d, 1H, *J* = 7.3 Hz), 7.05 (s, 2H) 7.12–7.14 (m, 3H). ^{13}C NMR δ = 30.31, 34.83, 55.95, 70.62, 83.87, 112.71, 112.90, 113.42, 116.34, 118.78, 120.01, 123.98, 141.64, 156.91, 160.43. Anal. Calc. for $C_{17}H_{13}N_6O_2$; C, 61.44; H, 3.64; N, 25.29. Found: C, 61.55; H, 3.75; N, 25.35. EIMS 332 $(M)^+$.

(2,4-Diamino-3-cyano-5*H*-chromeno[2,3-*b*]pyridin-5-yl)malononitrile (5c)[12a]. Yellowish solid. mp >300 °C. (KBr) ($\nu_{max/cm^{-1}}$) 3387, 3180, 2895, 2259, 2202, 1643, 1569, 1491, 1409, 1348. ^{1}H NMR δ = 4.87 (d, 1H, *J* = 3.6 Hz), 4.94 (d, 1H, *J* = 3.6 Hz), 6.87 (s, 2H), 7.07 (s, 2H), 7.22–7.31 (m, 2H), 7.42–7.48 (m, 2H). ^{13}C NMR δ = 30.12, 34.84, 70.81, 84.03, 112.96, 113.52, 116.91, 117.94, 124.12, 130.20, 151.11, 157.14, 160.45, 160.52. Anal. Calc. for $C_{16}H_{11}N_6O$; C, 63.57; H, 3.33; N, 27.80. Found: C, 63.65; H, 3.43; N, 27.85. EIMS 303 $(M)^+$.

(2,4-Diamino-3-cyano-9-ethoxy-5*H*-chromeno[2,3-*b*]pyridin-5-yl)malononitrile (5e)[12a]. Yellowish solid. mp >300. IR (KBr) ($\nu_{max/cm^{-1}}$) 3445, 3365, 2970, 2247, 2210, 1652, 1628, 1567, 1475, 1416 cm^{-1}. ^{1}H δ = 1.37 (t, 3H, *J* = 6.9 Hz), 4.05–4.13 (m, 2H), 4.84 (d, 1H, *J* = 3.9 Hz), 4.92 (d, 1H, *J* = 3.9 Hz), 6.70 (s, 2H), 7.05 (s, 2H), 7.12–7.21 (m, 3H). ^{13}C NMR δ = 14.63, 30.30, 34.84, 64.21, 70.68, 83.73, 112.97, 113.40, 113.64, 116.27, 118.71, 119.90, 123.93, 141.11, 146.90, 156.95, 160.43. Anal. Calc. for $C_{18}H_{14}N_6O_2$; C, 62.92; H, 4.07; N, 24.27. Found: C, 62.98; H, 4.12; N, 24.32. EIMS 346 $(M)^+$.

(2,4-Diamino-3-cyano-7-methyl-5*H*-chromeno[2,3-*b*]pyridin-5-yl)malononitrile (5f)[12a]. Yellowish solid. mp >300 °C. IR (KBr) ($\nu_{max/cm^{-1}}$) 3386, 3168, 2260, 2202, 1637, 1608, 1566, 1490, 1403, 1230. ^{1}H NMR δ = 2.34 (s, 3H), 4.83 (d, 1H, *J* = 3.9 Hz), 4.87 (d, 1H, *J* = 3.9 Hz), 6.66 (s, 2H), 7.05 (s, 2H), 7.11 (d, 1H, *J* = 8.3 Hz), 7.21 (s, 1H), 7.27 (d, 1H, *J* = 8.3 Hz). ^{13}C NMR δ = 20.32, 30.45, 34.63, 70.54, 83.88, 112.81, 113.44, 116.23, 116.58, 117.52, 129.01, 130.65, 133.17, 149.8, 156.93, 160.47, 160.51. Anal. Calc. for $C_{17}H_{13}N_6O$; C, 64.55; H, 3.82; N, 26.57. Found: C, 64.52; H, 3.90; N, 26.62. EIMS 317 $(M)^+$.

(**4b**) 14.54, 32.37, 37.35, 48.89, 64.42, 112.91, 113.06, 114.01.118.92, 119.34, 119.71, 124.91, 139.42, 146.37, 163.37 ppm.

(**4d**) 20.33, 32.43, 37.14, 48.78, 112.91, 113.07, 116.10, 117.56, 119.45, 128.84, 130.61, 134.15, 147.70, 163.53 ppm.

(**4g**) 32.30, 36.85, 48.46, 112.69, 112.85, 118.29, 119.08, 119.89, 128.46, 128.51, 130.02, 148.56, 163.22 ppm.

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Notes and references

1 (*a*) M. Costa, F. Areias, L. Abrunhosa, A. Venancio and F. Proenca, *J. Org. Chem.*, 2008, **73**, 1954; (*b*) P. T. Anastas and T. C. Williamson, Frontiers in Benign Chemical Synthesis Process, in *Green Chemistry*, Oxford University Press, Oxford, UK, 1998; (*c*) P. T. Anastas and J. C. Warner, Theory and Practice, in *Green Chemistry*, Oxford University Press, Oxford, UK, 1998.

2 Y. Xi, H. Yi and A. Lei, *Org. Biomol. Chem.*, 2013, **11**, 2387.

3 (*a*) M. mours, *ChemSusChem*, 2008, **1**, 59; (*b*) A. Mordini and F. Faigl, *New methodologies and techniques for a sustainable organic chemistry*, 2008, p. 279.

4 A. Chanda and V. V. Fokin, *Chem. Rev.*, 2009, **109**, 725.

5 (*a*) N. Hoffmann, *Chem. Rev.*, 2008, **108**, 1052; (*b*) M. Fagnoni, D. Dondi, D. Ravellio and A. Albini, *Chem. Rev.*, 2007, **107**, 2725.

6 N. Thomus and S. M. Zachariah, *Asian J. Pharm. Clin. Res.*, 2013, **6**, 11.

7 Y. Abrouki, A. Anouzla, H. Loukili, A. Chakir, M. Idrissi, A. Abrouki, A. Rayadh, M. Zahouily, K. Kacemi, J. Bessiere, B. Marouf and S. Sebti, *American Journal of Biological, Chemical and Pharmaceutical Sciences*, 2013, **1**, 28.

8 G. Shanthi, P. T. Perumal, U. Rao and P. K. Sehgal, *Indian J. Chem.*, 2009, **48B**, 1319.

9 (*a*) J. Mori, M. Iwashima, M. Takeuchi and H. Saito, *Chem. Pharm. Bull.*, 2006, **54**, 391; (*b*) C. K. Denish, K. P. Hetal and K. G. Nilesh, *Asian J. Biochem. Pharm. Res.*, 2012, **2**, 126; (*c*) D. S. Raghuvanshi and K. N. Singh, *ARKIVOC*, 2010, **10**, 305.

10 (*a*) J. Volmajer, R. Toplak, I. Leban, A. Majcen and L. Marechal, *Tetrahedron*, 2005, **61**, 7012; (*b*) G. murugavel and T. Punniyamurthy, *Org. Lett.*, 2013, **15**, 3828.

11 (*a*) S. Makarem, A. A. Mohammadi and A. R. Fakhari, *Tetrahedron Lett.*, 2008, **49**, 7194; (*b*) M. M. Heravi, M. M. Heravi, K. Bakhtiari, V. Zadsirjan, F. F. Bamoharram and O. M. Heravi, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 4265; (*c*) R. Ballini, G. Bosica, M. L. Confort, R. Maggi, A. Mazzacani, P. Righi and G. Sartori, *Tetrahedron*, 2001, **57**, 1395; (*d*) D. Kumar, V. B. Reddy, B. G. Mishra, R. K. Rana, M. N. Nadagouda and R. S. Varma, *Tetrahedron*, 2007, **63**, 3093.

12 (*a*) M. N. Elinson, S. V. Gorbuno, A. N. Vereshchagin, R. F. Nasybullin, A. S. Goloveshkin, I. S. Bushmarinov and M. P. Egorov, *Tetrahedron*, 2014, **70**, 8559; (*b*) T. S. Shaikh, J. D. Patil, D. S. Gaikwad, P. G. Hegade, P. B. Patil, M. M. Mane and D. M. Pore, *Indian J. Chem.*, 2014, **53**, 1288.

13 (*a*) M. S. Singh and S. Chowdhury, *RSC Adv.*, 2012, **2**, 4547; (*b*) Y. Gu, *Green Chem.*, 2012, **14**, 2091; (*c*) R. Ballini, G. Bosica, M. L. Confortio, R. Maggi, A. Mazzacani, P. Righi and G. Sartori, *Tetrahedron*, 2001, **57**, 1395.

14 (*a*) M. M. Heravi, N. Poormohammad, Y. S. Beheshtiha, B. Baghernejad and R. Malakooti, *Bull. Chem. Soc. Ethiop.*, 2010, **24**(2), 273; (*b*) J. Volmajer, R. Toplak, I. Leban and A. Majcen LeMarechal, *Tetrahedron*, 2005, **61**, 7012; (*c*) M. N. Elinson, A. S. Dorofeev, S. K. Feducovich, R. F. Nasybullin,

S. V. Gorbunov and G. I. Nikishin, *Electrochem. Commun.*, 2006, **8**, 1567.

15 (*a*) S. Ghosh, J. Das and S. Chattopadhyay, *Tetrahedron Lett.*, 2011, **52**, 2869; (*b*) E. Corey, *J. Am. Chem. Soc.*, 1952, **74**, 5897; (*c*) Y. Hu, P. Wei, H. Huang, Z.-G. Le and Z.-C. Chen, *Synth. Commun.*, 2005, **35**, 2955; (*d*) E. A. Shirokava, G. M. Segal and I. V. Torgov, *Bioorg. Khim.*, 1988, **14**, 236; (*e*) B. P. Bandgar, L. S. Uppalla and D. S. Kurule, *Green Chem.*, 1999, **1**, 243; (*f*) D. Villemin, A. Venancio and F. Proenca, *J. Org. Chem.*, 2008, **73**, 1954.

16 M. Srivastava, J. Singh, S. B. Singh, K. Tiwari, V. K. Pathak and J. Singh, *Green Chem.*, 2012, **14**, 901.

17 Q. Zhange, B. Liu, W. Chen, Q. Lin and X. Lin, *Green Chem.*, 2008, **10**, 972.

18 J. S. Bennett, K. L. Charles, M. R. Miner, C. F. Heuberger, E. J. Spina, M. F. Bartels and T. Foreman, *Green Chem.*, 2009, **11**, 166.

19 P. P. Ghosh, S. Paul and A. R. Das, *Tetrahedron Lett.*, 2013, **54**, 138.

20 P. P. Ghosh and A. R. Das, *J. Org. Chem.*, 2013, **78**, 6170.

