DBU acetate mediated: one-pot multi component syntheses of dihydropyrano[3,2-c]quinolones

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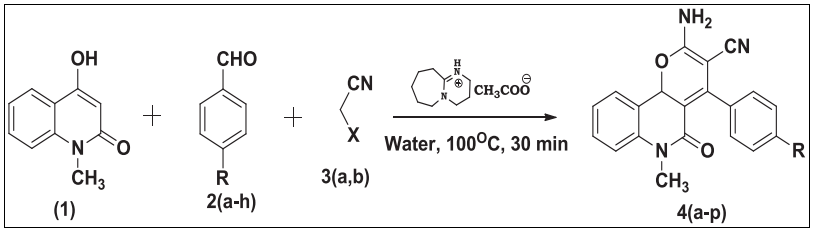

Three-component reaction involving condensation of 1-methylquinoline-2,4(1H,3H)-dione(**1**), aromatic aldehydes **2(a-h)** and malononitrile/cyanoaceticester **3(a,b)** in{(1,8-diazabicyclo[5.4.0]-undec-7-en-8-ium acetate)}[DBU][Ac] as task-specific ionic liquid leading to the efficient synthesis of dihydropyrano[3,2-c] quinolones **4(a-p)** is described. This approach is convenient, mild, and affords the products in high yields without the use of column chromatography.

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INTRODUCTION

Multicomponent reactions (MCRs) [1] have been used extensively in recent years for the synthesis of a large number of heterocyclic, carbocyclic compounds. Such reactions offer a wide range of possibilities for the efficient construction of complex molecules in a single procedural step, thus avoiding the isolation and purification steps of intermediates, giving high yields, and allowing savings of both solvents and reagents. In the past decade, there have been tremendous developments in three-component and four-component reactions, and great efforts continue to be made to develop new MCRs.

Pyrano [3,2-c]quinolone structural units are commonly found in alkaloids showing diverse biological activities like antibacterial [2], antiinflammatory, [3] and antifungal [4]. The methods available for the synthesis of pyranoquinolones are fairly elaborate but somewhat inconvenient.

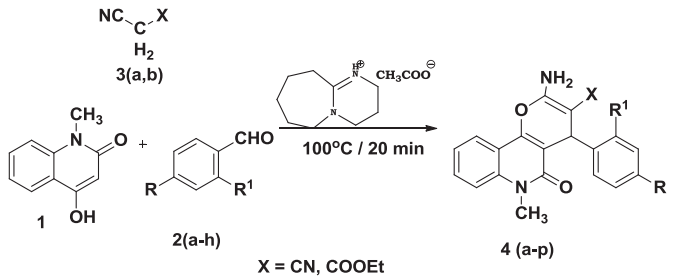
Ionic liquids [5] have attracted much attention because of their mild reaction conditions, short reaction times and better yield, solvating ability, and easy recyclability [6]. Various reactions have been reported recently using ionic liquids as a catalyst, reaction media [7], as rate enhancers [8], and in peptide synthesis [9]. These solvents are playing a key role in multicomponent synthesis for preparation of many heterocyclic compounds. DBU acetate is especially used as solvent and catalyst for many organic reactions. Yu *et al.* [10] reported DBU-based carbonylation of o-phenylenediamines with CO_2 to 2-benzimidazolones under solvent-free condition. Lima *et al.* [11] reported DBU-catalyzed synthesis amides via aminolysis of methyl esters. In literature survey, only a few reactions are reported on DBU acetate-catalyzed multicomponent reactions. Herein, we report on the use of DBU acetate as an efficient catalyst and reaction medium for the synthesis of pyranoquinolones 4(a-p) through the one pot method.

RESULTS AND DISCUSSION

A mixture of 1-methylquinoline-2,4(1H,3H)-dione(**1**), benzaldehyde **2**(**a-h**), malo nonitrile /ethylcyano acetate **3**(**a,b**) was stirred at 100°C in DBU acetate for 20 min. After simple processing of the reaction mixture, pyranoquinolones **4(a-p)** were isolated as products and characterized by IR, ^{1}HNMR,^{13}CMR, and mass spectral data (for details, please see the Experimental section). When the reaction was carried out in the absence of DBU acetate, by refluxing the reactants in ethanol for 2–3 h, no progress in the product formation was observed as found by periodic thin-layer chromatography (TLC) analysis of the reaction mixture. DBU [12] acetate required in this reaction was generated *in situ* by using the reported procedure.

Initially, a mixture of 1-methylquinoline-2,4(1H,3H)-dione (**1**) benzaldehyde (**2a**), and malononitrile (**3a**) was stirred with 5 mL of DBU acetate at room temperature. TLC showed formation of the product in low yield. (Scheme 1) Therefore, the same mixture was heated at 100°C for 20 min to accomplish the reaction. After workup, pyranoquinolones were the only products isolated in high yield. We noticed that reducing in the quantity of DBU acetate (3 mL) did not affect the yields (Table 1).

Scheme 1. Synthesis of 4 (a-p) from 1, 2(a-h) and 3(a-b).



The catalyst/reaction medium plays a vital role in determining the success of the reaction in terms of rate and yields. Various ionic liquids such as [bmim]Br, [bmim]BF_4, and [bmim]$AlCl_4$ were screened for the synthesis of pyranoquinolones **4(a-p)**. Among these ionic liquids, DBU acetate proved to be the most effective as far as completion of reaction in short time and yields are concerned (Table 2). As shown in Chart 1, the ionic liquid [DBU][Ac] could be recycled four times without considerable loss of activity.

The synthesis of pyranoquinolones could also be achieved in a tandem fashion (Scheme 2). Thus, a mixture of benzaldehyde (**2a**), malononitrile (**3a**), and DBU acetate was stirred at 100°C for 20 min. The reaction was monitored by TLC. After the completion of reaction, as shown by disappearance of one of the reactants to the resulting mixture,1-methylquinoline-2,4(1H,3H)-dione (**1**) was added in a tandem way without isolating any product/intermediate and the resulting mixture stirred at 100°C for a further 20 min. At the end of this period, the mixture was processed to obtain the final product, that is, pyranoquinolone **4a**.

Similarly, a mixture of **1, 2a** and DBU acetate was stirred at 100°C for 30 min. The reaction was monitored

Table 2

Ionic liquids screened for the synthesis of pyranoquinolones.

Entry	Ionic liquid used	Time (min) of reaction	Temp (°C)	Yield (%) of product 4a
1	[bmim]Br	90	100	35
2	[bmim]BF_4	90	100	46
3	[bmim]$AlCl_4$	90	100	55
4	[bmim]SbF_6	90	100	45
5	[DBU][AC]	20	100	90

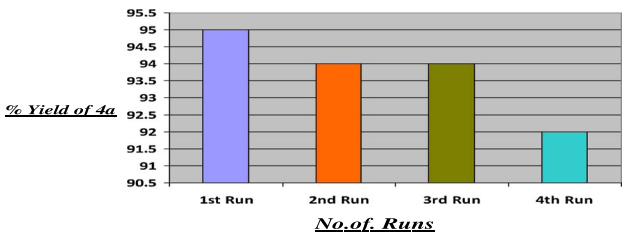


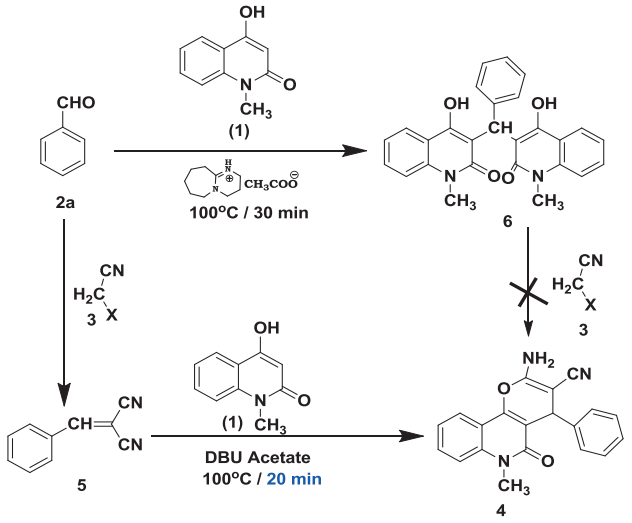
Chart 1. Recyclization of DBU acetate in synthesis of 4a. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table 1

Synthesis of pyranoquinolones derivatives from 1-methylquinoline-2,4(1H,3H)-dione (1).

S. No	Aldehydes (2)	Active methylene (3)	Product	Time (min)	Yield (%)	m.p (°C)
1.	2a (R = H, R^1 = H)	3a (X = CN)	4a	15	90	260-62
2.	2b (R = F, R^1 = H)	3a (X = CN)	4b	18	88	240-42
3.	2c (R = Cl, R^1 = H)	3a (X = CN)	4c	18	85	243-45
4.	2d (R = Br, R^1 = H)	3a (X = CN)	4d	17	86	220-22
5.	2e (R = OCH_3, R^1 = H)	3a (X = CN)	4e	20	86	190-93
6.	2f (R = NO_2, R^1 = H)	3a (X = CN)	4f	15	93	175-177
7.	2 g (R = CH_3, R^1 = H)	3a (X = CN)	4 g	20	85	220-23
8.	2 h (R = H, R^1 = OH)	3a (X = CN)	4 h	20	87	>280
9.	2a (R = H, R^1 = H)	3b (X = $COOC_2H_5$)	4i	18	91	210-12
10.	2b (R = F, R^1 = H)	3b (X = $COOC_2H_5$)	4j	18	90	156-60
11.	2c (R = Cl, R^1 = H)	3b (X = $COOC_2H_5$)	4 k	20	86	150-52
12.	2d (R = Br, R^1 = H)	3b (X = $COOC_2H_5$)	4 l	19	89	160-64
13.	2e (R = OCH_3, R^1 = H)	3b (X = $COOC_2H_5$)	4 m	20	85	180-82
14.	2f (R = NO_2, R^1 = H)	3b (X = $COOC_2H_5$)	4n	16	92	175-77
15.	2 g (R = CH_3, R^1 = H)	3b (X = $COOC_2H_5$)	4o	20	86	218-20
16.	2 h (R = H, R^1 = OH)	3b (X = $COOC_2H_5$)	4p	20	88	183-85

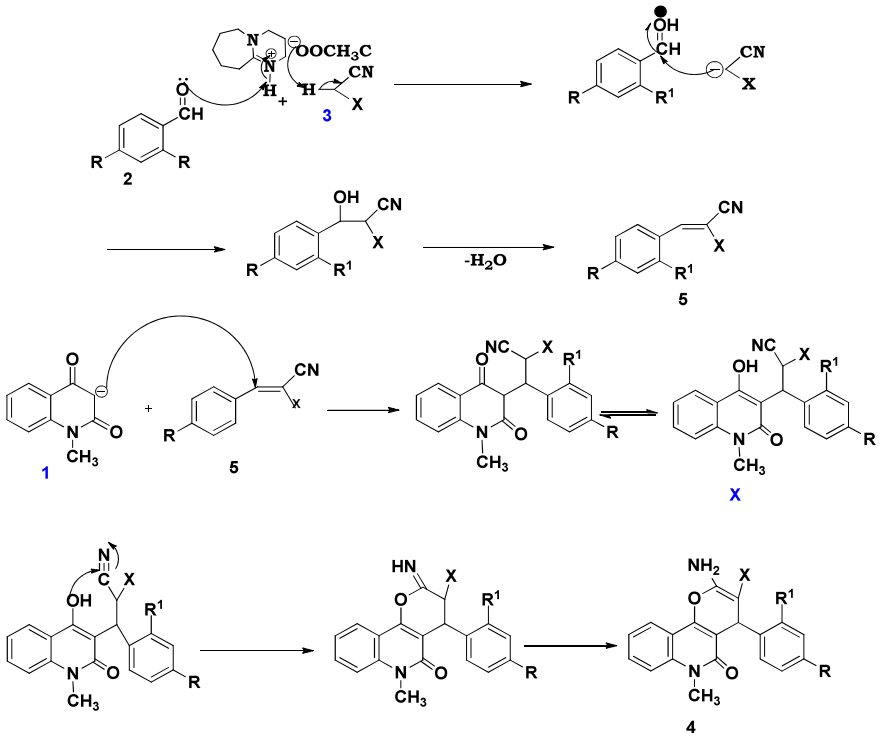
Scheme 2. (Alternate synthesis of pyranoquinolones). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



study of spectral data (IR, ^{1}H-NMR and mass) showed it to be **6a** (for details of spectral data, please see the Experimental section). The product thus obtained, that is, **6a** was thus a combination of one unit of **2a** and two units of **1,** a case which probably seems to be unprecedented in the literature.

In the mechanism, the reaction includes a Knoevenagel condensation catalyzed by DBU acetate between benzaldehyde **(2)** and active methylene group of the cyano compound **(3)** to yield α, β-unsaturated nitrile intermediate **5**. The latter is then attacked by the carbanion of the 1-methylquinoline-2,4(1H,3H)-dione compound **(1)** in the form of Michael addition followed by a keto-enol tautomerization to furnish the enol intermediate **(X)**. Nucleophilic addition of the hydroxyl group of intermediate **(X)** to the cyano moiety afforded imine intermediate, which undergoes enolization to yield the final product **4**.

Mechanism I



A possible mechanism has been proposed for the formation of 4(a-p) from 2(a-h), 3and 1

by TLC. After completion of reaction to the resulting mixture, malononitrile **3a** was added in a tandem fashion without isolating the condensed product and then stirred at R.T. for a further 20 min. At the end of this period, the mixture was processed to obtain a product, which surprisingly was not the expected **4a.** Careful

CONCLUSION

We have developed a general and highly efficient method using DBU acetate as convenient reaction medium for the three-component synthesis of pyranoquinolones. The products are isolated in high yield. Easy workup, high yield, and inexpensive catalyst are the advantages of the present procedure.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. The progress of the reaction was monitored by TLC performed on silica gel G coated Merck plastic sheets (Kenilworth, NJ, USA), and spots were observed by exposure to iodine vapor or UV light. IR spectra were recorded by using KBr disc on a Perkin-Elmer (Waltham, MA, USA) 240c analyzer. 1H NMR spectra were recorded on Brucker DPX-400 (Billerica, MA, USA) at 400 MHz (chemical shifts in δ, ppm) and mass spectra on an Agilent (Agilent Technologies, Sta. Clara, CA, USA) LC-MS instrument giving only M+ values in Q + 1 mode.

General procedure for synthesis of pyranoquinolones 4(a-p). A mixture of methylquinoline-2,4(1H,3H)-dione **1** (1 m*M*), aldehyde **2a-e**(1 mmol), malononitrile or ethyl cyanoacetate **3a-b** (1 m*M*), in DBU acetate (3 ml) was stirred at 100°C for 30 min. To the resulting oily reaction mixture was added 5 mL of ethanol to force out the crude product from the polar ionic liquid reaction medium. Then the precipitated product was filtered and washed with cold ethanol to afford the pure products. The collected ionic liquid along with ethanol as filtrate in the filtration flask was evaporated to remove ethanol, and the obtained ionic liquid was reused for subsequent reactions. To compensate for the loss of some acetic acid during the workup procedure, an amount of acetic acid (2 mL) was added after each run. A volume of DBU (2 mL) was added to the ionic liquid filtrate after three runs.

Procedure for the preparation of 6. A mixture of benzaldehyde **2a** (1 m*M*),1-methyl quinol ine-2,4(1H,3H)-dione **1** (1 m*M*) and DBU acetate (3 mL) was stirred at 100°C for 30 min. After completion of the reaction monitored by TLC, the reaction mixture cooled to room temperature was added 5 mL of ethanol. Then the precipitated product was filtered and washed with cold ethanol to afford the pure product **6**.

2-amino-6-methyl-5-oxo-4-phenyl-5,6-dihydro-4H-pyrano [3,2-c]quinoline-3-carbonitrile 4a. (R = H, R^1 = H, X = CN) : IR (KBr): 3391, 3297 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2205 (sharp, medium, -CN), 1677 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): 3.52 (s, 3H, $-NCH_3$), 4.51 (s, 1H, -CH), 7.16–8.02 (m, 9H, Aromatic hydrogens), 7.55 (s, 2H, $-NH_2$, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.62, 58.31, 109.53, 113.02, 115.27, 120.08, 122.50, 122.52, 127.04, 127.80, 128.68, 131.94, 138.98, 144.57, 150.50, 159.21, 160.13; *m/z* (M^++1): 330. *Anal.* Calcd for $C_{20}H_{15}N_3O_2$ (329.12): C, 72.94; H, 4.59; N, 12.76; Found: C, 72.23; H, 4.93; N, 12.35;

2-amino-4-(4-fluorophenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carbonitrile (4b). (R = F, R^1 = H, X = CN) : IR (KBr): 3395, 3299 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2197 (sharp, medium, -CN), 1670 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 3.48 (s, 3H, $-NCH_3$), 4.61 (s, 1H, -CH), 7.11–8.12 (m, 8H, Aromatic hydrogens), 7.48 (s, 2H, $-NH_2$, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.34, 58.57, 109.35, 113.28, 115.43, 120.46, 122.64, 122.85, 127.13, 127.43, 128.57, 131.78, 138.78, 144.86, 150.84, 159.32, 160.25; *m/z* (M^++1): 348. *Anal.* Calcd for $C_{20}H_{14}FN_3O_2$ (347.11): C, 69.16; H, 4.06; N, 12.10; Found: C, 69.65; H, 4.32; N, 12.84.

2-amino-4-(4-chlorophenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carbonitrile (4c). (R = Cl, R^1 = H, X = CN) : IR (KBr): 3391, 3302 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2190 (sharp, medium, -CN), 1671 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 3.54 (s, 3H, $-NCH_3$), 4.72 (s, 1H, -CH), 7.14–8.05 (m, 8H, Aromatic hydrogens), 7.52 (s, 2H, $-NH_2$, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.46, 58.64, 109.84, 113.31, 115.87, 120.23, 122.72, 122.21, 127.42, 127.52, 128.82, 131.84, 138.87, 144.43, 150.92, 159.74, 160.19; *m/z* (M^++1): 364. *Anal.* Calcd for $C_{20}H_{14}ClN_3O_2$ (363.00): C, 66.03; H, 3.88; N, 11.55; Found: C, 66.56; H, 3.32; N, 11.12.

2-amino-4-(4-bromophenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carbonitrile (4d). (R = Br, R^1 = H, X = CN) : IR (KBr): 3390, 3299 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2194 (sharp, medium, -CN), 1669 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 3.44 (s, 3H, $-NCH_3$), 4.62 (s, 1H, -CH), 7.11–7.96 (m, 8H, Aromatic hydrogens), 7.47 (s, 2H, $-NH_2$, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.43, 58.87, 109.74, 113.97, 115.75, 120.32, 122.71, 122.90, 127.54, 127.73, 128.57, 131.66, 138.40, 144.39, 150.57, 159.29, 160.85; *m/z* (M^++1): 408. *Anal.* Calcd for $C_{20}H_{14}BrN_3O_2$ (407.03): C, 58.84; H, 3.46; Br, 19.57; N, 10.29; O, 7.84% Found: C, 58.31; H, 3.91; N, 10.64.

2-amino-4-(4-methoxyphenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carbonitrile (4e). (R = OCH_3, R^1 = H, X = CN) : IR (KBr): 3389, 3291 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2190 (sharp, medium, -CN), 1665 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 2.89 (s, 3H, $-OCH_3$), 3.56 (s, 3H,$-NCH_3$),4.45(s,1H,-CH),6.96–7.88(m,8H,Aromatic hydrogens),7.32(s,2H,$-NH_2$,D_2Oexchangeable);^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.31, 50.43, 58.39, 109.22, 113.84, 115.72, 120.91, 122.73, 122.98, 127.24, 127.75, 128.48, 131.53, 138.94, 144.86, 150.84, 159.32, 160.25; *m/z* (M^++1): 360. *Anal.* Calcd for $C_{21}H_{17}N_3O_3$ (359.38): C, 70.18; H, 4.77; N, 11.69; Found: C, 70.54; H, 4.14; N, 11.23.

2-amino-6-methyl-4-(4-nitrophenyl)-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carbonitrile (4f). (R = NO_2, R^1 = H, X = CN) : IR (KBr): 3386, 3297 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2220 (sharp, medium, -CN), 1675 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSOd_6/TMS):δ3.46(s,3H,$-NCH_3$),4.77(s,1H,-CH),7.06–8.12 (m, 8H, Aromatic hydrogens), 7.44 (s, 2H, $-NH_2$, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.26, 58.54,109.83,113.92,115.33,120.81,122.32,122.72,127.56,

127.24,128.54,131.88,138.84,144.21,150.33,159.53,160.43; *m/z* (M^++1): 375. *Anal*. Calcd for $C_{20}H_{14}N_4O_4$ (374.35): C, 64.17; H, 3.77; N, 14.97; Found: C, 64.53; H, 3.23; N, 14.32.

2-amino-6-methyl-5-oxo-4-(p-tolyl)-5,6-dihydro-4H-pyrano [3,2-c]quinoline-3-carbonitrile (4g). (R = CH_3, R^1 = H, X = CN) : IR (KBr): 3380, 3290 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2189 (sharp, medium, -CN), 1656 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.80 (s, 3H, -CH_3), 3.21 (s, 3H, -NCH_3), 4.12 (s, 1H, -CH), 6.92–7.82 (m, 8H, Aromatic hydrogens), 7.38 (s, 2H, -NH_2, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 25.84, 29.84, 58.33, 109.23, 113.76, 115.65, 120.95, 122.36, 122.99, 127.26, 127.84, 128.74, 131.21, 138.46, 144.34, 150.67, 159.26, 160.55; *m/z* (M^++1): 344. *Anal*. Calcd for $C_{21}H_{17}N_3O_2$ (343.13): C, 73.45; H, 4.99; N, 12.24; Found: C, 73.91; H, 4.32; N, 12.71.

2-amino-4-(2-hydroxyphenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carbonitrile (4h). (R = H, R^1 = OH, X = CN) : IR (KBr): 3387, 3198 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 2195 (sharp, medium,-CN), 1667 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 3.44 (s, 3H, -NCH_3), 4.14 (s, 1H, -CH), 6.86–7.69 (m, 8H, Aromatic hydrogens), 7.21 (s, 2H, -NH_2, D_2O exchangeable), 9.44 (s, 1H, -OH, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.65, 58.42, 109.65, 113.26, 115.95, 120.47, 122.87, 122.34, 127.22, 127.27, 128.56, 131.76, 138.33, 144.66, 150.87, 159.32, 160.44; *m/z* (M^++1): 346. *Anal*. Calcd for $C_{20}H_{15}N_3O_3$ (345.11): C, 69.56; H, 4.38; N, 12.17; Found: C, 69.12; H, 4.87; N, 12.57.

Ethyl-2-amino-6-methyl-5-oxo-4-phenyl-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3carboxylate (4i). (R = H, R^1 = H, X = $COOC_2H_5$) : IR (KBr): 3375, 3281 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 1685, 1655 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.11 (t, 3H, -CH_3), 3.54 (s, 3H, -NCH_3), 3.96 (q, 2H, -CH_2), 4.85 (s, 1H, -CH), 7.06–8.09 (m, 9H, Aromatic hydrogens), 7.75 (s, 2H, -NH_2, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.28, 35.22, 58.84, 77.43, 111.94, 112.87, 114.92, 122.15, 122.79, 123.65, 125.99, 126.22, 127.78, 127.92, 131.35, 138.49, 145.89, 149.98, 159.46, 160.09, 167.82; *m/z* (M^++1): 377. *Anal*. Calcd for $C_{22}H_{20}N_2O_4$ (376.14): C, 70.20; H, 5.36; N, 7.44; Found: C, 70.73; H, 5.93; N, 7.91.

Ethyl-2-amino-4-(4-fluorophenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carboxylate (4j). (R = F, R^1 = H, X = $COOC_2H_5$) : IR (KBr): 3371, 3280 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 1680, 1653 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.13 (t, 3H, -CH_3), 3.48 (s, 3H, -NCH_3), 3.98 (q, 2H, -CH_2), 4.92 (s, 1H, -CH), 7.05–8.09 (m, 8H, Aromatic hydrogens), 7.81 (s, 2H, -NH_2, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.34, 35.32, 58.43, 77.53, 111.82, 112.43, 114.53, 122.23, 122.84, 123.33, 125.24, 126.89, 127.24, 127.45, 131.84, 138.45, 145.34, 149.54, 159.32, 160.43, 167.32; *m/z* (M^++1): 395. *Anal*. Calcd for $C_{22}H_{19}FN_2O_4$ (394.13): C, 67.00; H, 4.86; N, 7.10; Found: C, 67.53; H, 4.23; N, 7.94.

Ethyl-2-amino-4-(4-chlorophenyl)6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carboxylate (4k). (R = Cl, R^1 = H, X = $COOC_2H_5$) : IR (KBr): 3370, 3278 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 1682, 1650 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.16 (t, 3H, -CH_3), 3.49 (s, 3H, -NCH_3), 4.01 (q, 2H, -CH_2), 4.96 (s, 1H, -CH), 7.06–8.11 (m, 8H, Aromatic hydrogens), 7.82 (s, 2H, -NH_2, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.23, 35.45, 58.65, 77.32, 111.43, 112.47, 114.66, 122.35, 122.95, 123.45, 125.65, 126.76, 127.46, 127.74, 131.56, 138.52, 145.64, 149.68, 159.75, 160.76, 167.44; *m/z* (M^++1): 411. *Anal*. Calcd for $C_{22}H_{19}ClN_2O_4$ (410.10): C, 64.31; H, 4.66; N, 7.10; Found: C, 64.71; H, 4.13; N, 7.61.

Ethyl-2-amino-4-(4-bromophenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carboxylate (4l). (R = Br, R^1 = H, X = $COOC_2H_5$) : IR (KBr): 3378, 3289 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 1675, 1645 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.12 (t, 3H, -CH_3), 3.46 (s, 3H, -NCH_3), 4.04 (q, 2H, -CH_2), 4.95 (s, 1H, -CH), 7.04–8.08 (m, 8H, Aromatic hydrogens), 7.81 (s, 2H, -NH_2, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.43, 35.22, 58.62, 77.54, 111.94, 112.26, 114.84, 122.83, 122.98, 123.32, 125.49, 126.23, 127.83, 127.95, 131.84, 138.22, 145.35, 149.53, 159.82, 160.43, 167.86; *m/z* (M^++1): 455. *Anal*. Calcd for $C_{22}H_{19}BrN_2O_4$ (454.05): C, 58.04; H, 4.21; N, 6.15; Found: C, 58.72; H, 4.82; N, 6.82.

Ethyl-2-amino-4(4-methoxyphenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c] quinoline-3-carboxylate (4m). (R = OCH_3, R^1 = H, X = $COOC_2H_5$) : IR (KBr): 3368, 3279 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 1667, 1649 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.14 (t, 3H, -CH_3), 3.45 (s, 3H, -NCH_3), 3.92 (s, 3H, -OCH_3), 4.01 (q, 2H, -CH_2), 4.98 (s, 1H, -CH), 7.02–8.12 (m, 8H, Aromatic hydrogens), 7.91 (s, 2H, -NH_2, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.33, 35.43, 50.33, 58.84, 77.34, 111.25, 112.43, 114.34, 122.39, 122.56, 123.24, 125.53, 126.43, 127.61, 127.84, 131.73, 138.82, 145.74, 149.77, 159.35, 160.64, 167.97; *m/z* (M^++1): 407. *Anal*. Calcd for $C_{23}H_{22}N_2O_5$ (406.15): C, 67.97; H, 5.46; N, 6.89; Found: C, 67.12; H, 5.92; N, 6.11.

Ethyl-2-amino-6-methyl-4-(4-nitrophenyl)-5-oxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carboxylate (4n). (R = NO_2, R^1 = H, X = $COOC_2H_5$) : IR (KBr): 3369, 3285 (unequal doublet, asymmetric and symmetric stretchings of $–NH_2$), 1660, 1644 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.18 (t, 3H, -CH_3), 3.46 (s, 3H, -NCH_3), 4.05 (q, 2H, -CH_2), 4.97 (s, 1H, -CH), 7.11–8.16 (m, 8H, Aromatic hydrogens), 7.92 (s, 2H, -NH_2, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.77, 35.63, 58.72, 77.42, 111.68, 112.93,114.54,122.46,122.78,123.46,125.84,126.32,127.49,

127.84,131.54,138.33,145.64,149.48,159.53,160.73,167.49; *m/z* (M^++1): 422. *Anal*. Calcd for $C_{22}H_{19}N_3O_6$ (421.13): C, 62.70; H, 5.54; N, 9.97; Found: C, 62.11; H, 5.91; N, 9.22.

Ethyl-2-amino-6-methyl-5-oxo-4-(p-tolyl)-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carboxylate (4o). ($R = CH_3$, $R^1 = H$, $X = COOC_2H_5$) : IR (KBr): 3360, 3270 (unequal doublet, asymmetric and symmetric stretchings of $-NH_2$), 1661, 1640 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.12 (t, 3H, $-CH_3$), 1.41 (s, 3H, $-CH_3$), 3.42 (s, 3H, $-NCH_3$), 4.01 (q, 2H, $-CH_2$), 4.91 (s, 1H, -CH), 7.04–7.98 (m, 8H, Aromatic hydrogens), 7.86 (s, 2H, $-NH_2$, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 25.83, 29.32, 35.43, 58.54, 77.63, 111.84, 112.11, 114.32, 122.34, 122.54, 123.42, 125.46, 126.67, 127.65, 127.74, 131.64, 138.43, 145.67, 149.32, 159.79, 160.67, 167.85; *m/z* (M^++1): 391. *Anal*. Calcd for $C_{23}H_{22}N_2O_4$ (390.16): C, 70.75; H, 5.68; N, 7.17; Found: C, 70.98; H, 5.13; N, 7.87.

Ethyl-2-amino-4-(2-hydroxyphenyl)-6-methyl-5-oxo-5,6-dihydro-4H-pyrano[3,2-c] quinoline-3-carboxylate (4p). ($R = H$, $R^1 = OH$, $X = COOC_2H_5$) **:** IR (KBr): 3369, 3278 (unequal doublet, asymmetric and symmetric stretchings of $-NH_2$), 1669, 1645 cm^{-1} (-CO- group, broad); ^{1}H-NMR (DMSO d_6/TMS): δ 1.15 (t, 3H, $-CH_3$), 3.41 (s, 3H, $-NCH_3$), 4.02 (q, 2H, $-CH_2$), 4.79 (s, 1H, -CH), 7.01–7.99 (m, 8H, Aromatic hydrogens), 7.78 (s, 2H, $-NH_2$, D_2O exchangeable), 10.23 (s, 1H, -OH, D_2O exchangeable); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 29.64, 35.73, 58.35, 77.85, 111.64, 112.42, 114.13, 122.32, 122.53, 123.65, 125.62, 126.78, 127.83, 127.86, 131.79, 138.42, 145.64, 149.84, 159.74, 160.56, 167.34; *m/z* (M^++1): 393. *Anal*. Calcd for $C_{22}H_{20}N_2O_5$ (392.14): C, 67.34; H, 5.14; N, 7.14; Found: C, 67.87; H, 5.68; N, 7.77.

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REFERENCES AND NOTES

[1] Esther, V. G.; Rosario, R.; Sara, P. Beilstein J Org Chem 2011, 7, 980.

[2] Agui, H.; Mitani, T.; Izawa, A.; Komatsu, T.; Nakagome, T. J Med Chem 1977, 20, 791.

[3] Chia, E. W.; Pearce, A. N.; Berridge, M. V.; Larsen, L. Bioorg Med Chem 2008, 16, 9432.

[4] Ryu, C. K.; Lee, J. Y.; Jeong, S. H.; Nho, J. H. Bioorg Med Chem Lett 2009, 19, 146.

[5] Thomas, W. Chem Rev 1999, 99, 2071.

[6] Zhu, H. P.; Yang, F.; Tang, J.; He, M. Y. Green Chem 2003, 5, 38.

[7] Yadav, J. S.; Reddy, B. V. S.; Reddy, J. S. S.; Srinivasa Rao, R. Tetrahedron 2003, 59.

[8] Chen, H.; Shi, D. J Comb Chem 2010, 12, 571.

[9] Miao, W.; Chan, T. H. J Org Chem 2005, 70, 3251.

[10] Yu, B.; Zhang, H.; Zhao, Y.; Chen, S.; Xu, J.; Hao, L.; Liu, Z. ACS catal 2013, 3, 2076.

[11] Lima, E. C.; De souza, C. C.; Soares, R. O.; Vaz, B. G.; Eberlin, M. N.; Dias, A. G.; Costa, P. R. R. C. J Braz Chem Soc 2011, 22, 2186.

[12] Boger, D. L.; Brotherton, C. E.; Panek, J. S.; Yohannes, D. J Org Chem 1984, 49, 4056.