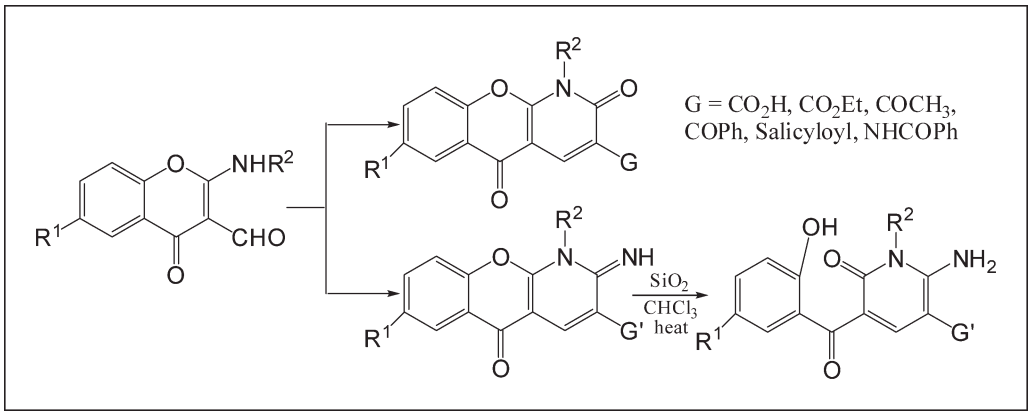
A One-Pot Synthesis of the 1-Benzopyrano[2,3-*b*]pyridine Moiety from 2-(Alkyl/arylamino)-4-oxo-4*H*-1-Benzopyran-3-Carbaldehyde

Sourav Maiti, Suman Kalyan Panja, and Chandrakanta Bandyopadhyay*

Department of Chemistry, R. K. Mission Vivekananda Centenary College, Rahara, Kolkata, West Bengal 700 118, India
*E-mail: kantachandra@rediffmail.com

Received September 22, 2009
DOI 10.1002/jhet.397
Published online 24 June 2010 in Wiley InterScience (www.interscience.wiley.com).



2-(Alkyl/arylamino)chromone-3-carbaldehyde reacts with Meldrum's acid, hippuric acid, 4-hydroxycoumarin, diethyl malonate, ethyl acetoacetate, or ethyl benzoylacetate to produce 1-benzopyrano[2,3-*b*]pyridine-2,5-dione moiety, but ethyl cyanoacetate and malononitrile react differently.

J. Heterocyclic Chem., **47**, 973 (2010).

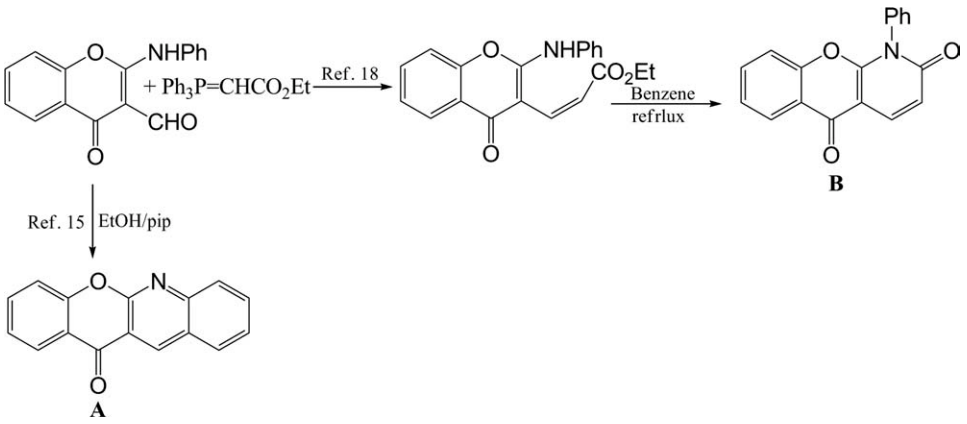
INTRODUCTION

1-Benzopyranopyridine derivatives have found diverse application in the field of medicinal chemistry. 1-Benzopyrano[3,4-*c*]pyridine-5-ones act as human dopamine D_4 receptor antagonists and serve as potential antipsychotic agents [1]. Some nonsteroidal human androgen receptor agonists were synthesized based on 4-(trifluoromethyl)-2*H*-pyrano[3,2-*g*]-2-quinolone [2]. 1-Benzopyrano[2,3-*b*]pyridine-2,5-dione **1** (R^2 = H, G = $COCH_2COCH_3$) functions as a polyketide, which are involved in the biosynthesis of natural products [3]. Some chromenopyridines are designed and synthesized as an analogue of tetracycline [4]. 5-Salicyloyl-2-oxopyridine-3-carbonitriles play comparable roles as the nonglycosidic cardiotonic agents milrinone or amrinone [5]. Compounds **1**(R^2 = H, G = CN, CO_2R, CO_2H) exhibit antiallergic properties and are used in the preparation of bronchodialators [6]. 1-Benzopyrano[2,3-*b*]pyridine-4,5-dione having a CO_2H group at 3-position provides 100% inhibition in the passive cutaneous anaphylaxis screen when applied in a dose of 0.9 mg/kg [7]. Recently, some chromenopyridines are proved to be effective sensitizers for europium and terbium luminescence [8].

Synthesis of the 1-Benzopyrano[2,3-*b*]pyridine motif have been accomplished (a) from chromone-3-carbonitrile by reaction either with acetylacetone in the presence of piperidine [9] or with 1-ethoxy-1,3-bis(trimethylsilyloxy)-1,3-butadiene in the presence of Me_3SiOTf [10], (b) from chromone-3-carbaldehyde by the reaction of 2-aminochromone [11] or with aniline in the presence of TMSCl in DMF [12]. 2-Aminochromone-3-carbaldehyde **3** (R^2 = H) has also been used for the synthesis of **1**(R^2 = H) [13].

Although the reactions of 2-aminochromone-3-carbaldehyde **3** (R^2 = H) and 2-(*N*,*N*-dialkylamino)chromone-3-carbaldehyde **3** (NR_2 in place of NHR^2) have been studied in detail [13], the chemistry of 2-(mono substituted amino)chromone-3-carbaldehyde **3** has only been little explored. Most of its reactions were carried out by converting it into *N*,*N*-disubstituted analogue [14a,b]. Reaction of **3** with primary amine produces corresponding Schiff base [14], but with aliphatic secondary amines like diethylamine or piperidine compound **3** (R^2 = aryl) produces 1-benzopyranoquinolones (**A**) (Scheme 1) [15]. Recently, diethyl 1-benzopyrano[2,3-*b*]pyridine-2,3-dicarboxylate has been synthesized from **3** and diethyl acetylenedicarboxylate in the presence of Ph_3P [16]. Synthesis of 2-pyridone moiety having ester or carbamoyl functionality at its 3-positions from β-formyl-β-nitroenamine has recently been reported [17].

Scheme 1



A literature survey revealed that functionlization at the 3-position of 1-benzopyrano [2,3-*b*]pyridine-2,5-dione made this system medicinally efficacius [6]. 1-Benzopyrano[2,3-*b*]pyridine-2,5-dione (**B**) having no functionality at its 3-position had been synthesized by the reaction of **3** (R^2 = Ph) with ethyl (triphenylphosphoranylidene)acetate followed by heating in benzene (Scheme 1) [18].

Our objective was to synthesize **1** with varying substituents at its 3-position utilizing the C3N1 building block of the β-amino-α, β-unsaturated aldehyde moiety of **3.** We report herein a few new one-pot syntheses of compound **1** from **3** by condensation with 2,2-dimethyl-1,3-dioxan-4,6-dione (Meldrum's acid), *N*-benzoylglycine (hippuric acid), 4-hydroxycoumarin, and other active methylene compounds under suitable reaction conditions. Compound **3** can readily be obtained from *N*-alkyl/aryl-*C*-(4-oxo-4*H*-1-benzopyran-3-yl)nitrones **2** [19] or directly from chromone-3-carbaldehyde [20].

RESULTS AND DISCUSSION

Meldrum's acid (**4**), an active methylene compound having strong electrophillic centres, has made its position in the synthesis of many organic compounds having use in the fields of drugs and pharmaceuticals [21]. Very recently, its chemical bonding and structure-reactivity relation have been studied both experimentally and theoretically [22]. Its chemical versatility has also been discussed in several review articles [23]. We have used Meldrum's acid in the synthesis of 1-benzopyrano[2,3-*b*]pyridine-2,5-dione moiety from **3**.

An equimolar mixture of **3** and **4** was heated under reflux in ethanol in the presence of catalytic amount of pyridine for 2–4 h. White solids (**1a–e**) were found to precipitate under this reaction condition in moderate to good yields (Table 1, entries 1–5). Compound **3** undergoes Knoevenagel condensation with Meldrum's acid to form **5**, which cyclizes to **1a–e** under the reaction condition (Scheme 2, path-a). The structures of the

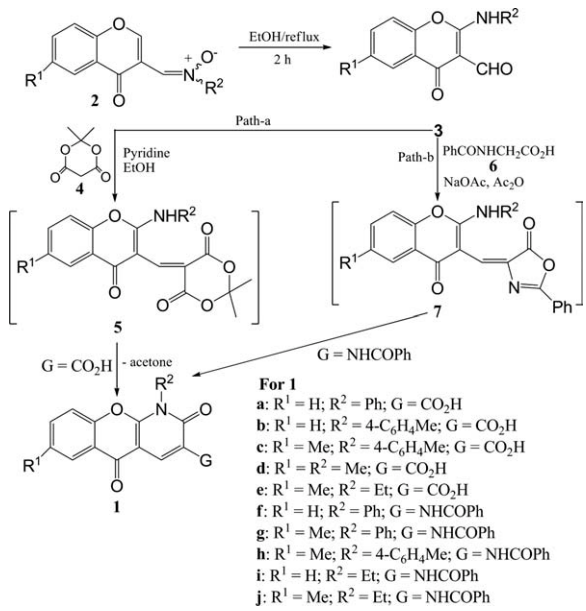
Table 1

Results of the reactions of **3** with **4** or **6** or **8** under different conditions.

Entry	R^1	R^2	Reagent	Reaction condition	Time (h)	Product	Yield (%)	Mps (°C)
1	H	Ph	**4**	A	3	**1a**	70	>320
2	H	Ar	**4**	A	4	**1b**	68	>320
3	Me	Ar	**4**	A	3	**1c**	70	298–300
4	Me	Me	**4**	A	2	**1d**	52	296–298
5	Me	Et	**4**	A	2.5	**1e**	50	276–278
6	H	Ph	**6**	B	7	**1f**	41	>320
7	Me	Ph	**6**	B	6	**1g**	40	>320
8	Me	Ar	**6**	B	7	**1h**	45	>320
9	H	Et	**6**	B	6.5	**1i**	32	258–260
10	Me	Et	**6**	B	6	**1j**	30	286–288
11	Me	Ph	**8**	A	5	**10a**	85	284–286
12	H	Ph	**8**	A	6	**10b**	79	268–270
13	H	Et	**8**	A	5.5	**10c**	79	238–240

A, Heated in EtOH under reflux containing catalytic amount of pyridine.
B, Heated a mixture of **3**, **6** and fused NaOAc in Ac_2O on a water bath.
Ar stands for 4-C_6H_4Me.

Scheme 2



compounds were established on the basis of IR, ^{1}H NMR, and mass spectral analysis. It is to be mentioned here that the carboxylic acid protons for compounds **1a** and **1b** were not observed in their ^{1}H NMR spectra. The presence of carboxylic acid group in **1a** and **1b** was confirmed from their mass spectral analyses and the singlet appearance of C_4-H in the ^{1}H NMR spectra of **1a,b**.

In connection to our earlier studies [24] on the reactions of different nitrogenous nucleophiles on 4-[(4-oxo-4*H*-1-benzopyran-3-yl)methylene]-2-phenyl-5-oxazolone **7** (R^1 = NHR^2 = H)(Scheme 2), derived from 3-formylchromone, it has been observed that nitrogenous nucleophiles are prone to interact on the carbonyl function of oxazolone moiety. Compound **3** can be considered as 3-formylchromone moiety having an inbuilt amino function in appropriate position. To utilize this special structural feature of **3**, an equimolar mixture of **3** (R^2 = aryl) and hippuric acid (**6**) was heated in the presence of excess amount of fused sodium acetate in acetic anhydride on water bath for 6–7 h and after usual work-up, compounds **1f–h** were obtained as white solids in moderate yields (Table 1, entries 6–8). On similar treatment of **3** (R^2 = alkyl), the reaction mixture yielded **1i** and **1j** (entries 9, 10) after chromatographic separation on silica gel using 10% ethyl acetate in benzene as eluent. Formation of **1f–j** from **3** may be rationalized by the initial formation of azlactone **7**, followed by intramolecular attack of the amino function to the carbonyl carbon of oxazolone moiety (Scheme 2, path-b).

This reaction was further extended by using 4-hydroxycoumarin (**8**). On heating an equimolar mixture of **3** and **8** in ethanol under reflux for 5–6 h in the presence of catalytic amount of pyridine, the reaction mixture produced compound **10** in good yields *via* the Knoevenagel condensate **9** (Scheme 3) (Table 1, entries 11–13). Suitably placed NHR^2 group in **9** reacted intramolecularly on the carbonyl function with a lesser decrease in entropy compared to the Michael addition of second molecule of **8**, which is the common feature for the reaction of an aldehyde with **8** [25].

With an endeavor to synthesize **1**(G = CO_2Et), compound **3** (R^2 = aryl) was stirred at room temperature with diethyl malonate in pyridine, but no change in **3** was observed (Table 2, entry 1). Ethyl acetoacetate also failed to cause any change in **3** on stirring at room temperature in pyridine (entry 2), even on heating **3** with ethyl acetoacetate in ethanol for 25 h in the presence of pyridine showed no considerable change (entry 3). On stirring an ethanolic solution of **3** (R^2 = aryl) with diethyl malonate at room temperature in the presence of piperidine for 40 h resulted in the formation of 1-benzopyrano[2,3-*b*]-12-quinolone (**A**) [15,18,19] (Scheme 1) (Table 2, entry 4). No pure compound could be isolated from the reaction mixture obtained by heating a mixture of **3**, diethyl malonate, fused NaOAc in Ac_2O on a water bath for 5 h (entry 5). Surprisingly, compound **3** reacted with diethyl malonate in $CHCl_3$ under reflux in the presence of piperidine to produce **1k,l** (entries 6, 7) (Scheme 4). It was observed that more than stoichiometric amounts of diethyl malonate (1.5 equiv) and piperidine (1.5 equiv) were required for complete consumption of **3**. This methodology was then applied for the synthesis of **1** having various substituents at its 3-position. On heating **3** (R^2 = aryl) with ethyl acetoacetate and piperidine in equimolar amounts in $CHCl_3$ for 4 h produced **1o** (entry 8). Similarly, ethyl benzoylacetate reacted stoichiometrically with **3** (R^2 = aryl) within 2 h to produce **1q,r** (entries 9, 10).

Scheme 3

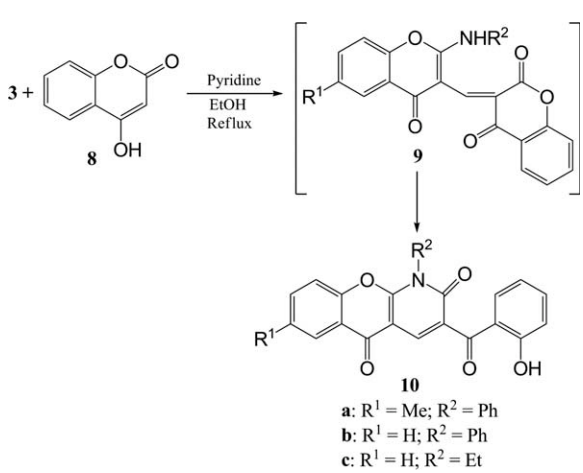


Table 2

Results of the reactions of **3** with active methylene compounds (EtO_2C-CH_2-G) under different conditions.

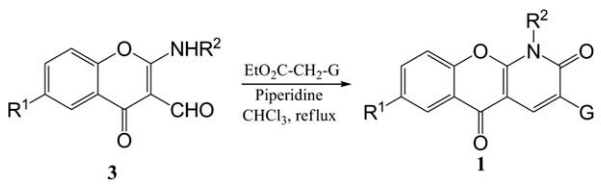
Entry	R^1	R^2	G	Reaction condition	Time (h)	Product	Yield (%)	Mps (°C)
1	H	Ph	CO_2Et	Py/RT	40	N. R.	–	–
2	Me	Ph	$COCH_3$	Py/RT	20	N. R.	–	–
3	Me	Ph	$COCH_3$	Py/EtOH/Reflux	25	N. R.[a]	–	–
4	H	Ph	CO_2Et	Pip/EtOH/RT	40	**A**	70	236–238
5	H	Ph	CO_2Et	$NaOAc/Ac_2O$/heat	5	Not isolated	–	–
6	H	Ph	CO_2Et	Pip/$CHCl_3$/reflux	18	**1k**	55	278–280
7	Me	Ph	CO_2Et	Pip/$CHCl_3$/reflux	12	**1l**	74	208–210
8	Me	Ph	$COCH_3$	Pip/$CHCl_3$/reflux	4	**1o**	68	278–280
9	H	Ph	COPh	Pip/$CHCl_3$/reflux	2	**1q**	72	264–266
10	Me	Ph	COPh	Pip/$CHCl_3$/reflux	2	**1r**	74	278–280
11	H	Me	COPh	Pip/$CHCl_3$/reflux	2	**1s**	60	256–258
12	H	Et	COPh	Pip/$CHCl_3$/reflux	2	**1t**	62	224–226
13	H	Et	$COCH_3$	Pip/$CHCl_3$/reflux	4	**1p**	43	218–220
14	H	Et	CO_2Et	Pip/$CHCl_3$/reflux	28	**1m**	42	178–180
15	Me	Et	CO_2Et	Pip/$CHCl_3$/reflux	25	**1n**	40	192–194
16	H	Et	COPh	Pip/EtOH/reflux	6	**1t**	70	224–226
17	Me	Ph	$COCH_3$	Pip/EtOH/reflux	2	**1o**	20[b]	278–280
18	H	Et	$COCH_3$	Pip/EtOH/reflux	7	**1p**	62	218–220
19	H	Ph	COPh	Morpholine/ $CHCl_3$/reflux	5	**1q**	60	264–266
20	H	Ph	COPh	$Et_2NH/CHCl_3$/ reflux	13	**1q**	56	264–266

''Py'' stands for Pyridine; ''Pip'' stands for piperidine; ''RT'' stands for room temperature.
''N. R.'' stands for No Reaction.
[a] 80% **3** was recovered.
[b] 40% of compound **A** was isolated.

The reaction was extended with **3** (R^2 = alkyl). Ethyl benzoylacetate (entries 11,12), ethyl acetoacetate (entry 13), and diethyl malonate (entries 14, 15) produced corresponding **1** but in lower yields. On changing the solvent from $CHCl_3$ to ethanol, the yield of **1** (R^2 = alkyl) was found to improve, but a little longer reaction time was required (entries 12,16 and 13, 18). Similar reaction with **3** (R^2 = aryl) in ethanol always produced some 1-benzopyrano quinolone (**A**) along with **1** (entry 17). Use of triethylamine or pyridine as a base in the reaction between **3** and $PhCOCH_2CO_2Et$ either in $CHCl_3$ or in EtOH failed to show the formation of **1** even after heating under reflux for 30 h. Piperidine was found to be a better reagent than morpholine or diethylamine for this transformation (entries 9, 19, 20).

Compound **3** reacted differently when ethyl cyanoacetate or malononitrile were used as active methylene component. On stirring an equimolar mixture of **3** and ethyl cyanoacetate in ethanol in the presence of piperidine at room temperature, followed by usual work-up [*vide* experimental Section ''General procedure for the reaction of ethyl cyanoacetate on 2-alkyl/arylaminochromone-3-carbaldehyde (3)''] and chromatographic purification produced **11** (G' = CO_2Et) (Scheme 5, path a). But malononitrile yielded **12** when reacted with **3** under similar reaction condition (Scheme 5, path b). In an attempt to purify compound **12** (G' = CN) by column chromatography, a partial change in **12** was observed and finally the new compound was assigned to be **11** (G′ = CN). This observation led us to check the silica-induced conversion of **12** (G′ = CN) to **11** (G′ = CN). A chloroform solution of **12** (G′ = CN) containing some silica gel was heated under reflux for 5 h with stirring. Indeed, complete conversion of **12** (G′ = CN) to **11** (G′ = CN) was observed. Use of benzene in place of chloroform also accomplished this transformation under identical condition. However, on heating under reflux in ordinary $CHCl_3$ or benzene in the absence of silica gel, compound **12** failed to show any change. In an earlier report [17], β–allylamino-2-nitroacrolein was made to react with malononitrile and was supposed to

Scheme 4

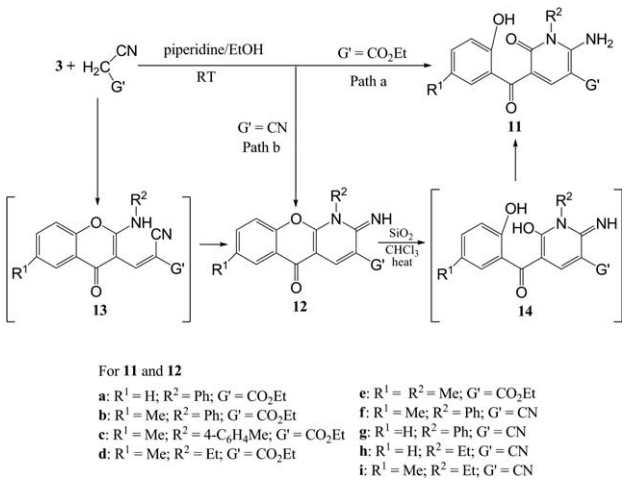


3 **1**

For **1**

k: R^1 = H; R^2 = Ph; G = CO_2Et
l: R^1 = Me; R^2 = Ph; G = CO_2Et
m: R^1 = H; R^2 = Et; G = CO_2Et
n: R^1 = Me; R^2 = Et; G = CO_2Et
o: R^1 = Me; R^2 = Ph; G = $COCH_3$
p: R^1 = H; R^2 = Et; G = $COCH_3$
q: R^1 = H; R^2 = Ph; G = COPh
r: R^1 = Me; R^2 = Ph; G = COPh
s: R^1 = H; R^2 = Me; G = COPh
t: R^1 = H; R^2 = Et; G = COPh

Scheme 5



For **11** and **12**

a: R^1 = H; R^2 = Ph; G' = CO_2Et
b: R^1 = Me; R^2 = Ph; G' = CO_2Et
c: R^1 = Me; R^2 = 4-C_6H_4Me; G' = CO_2Et
d: R^1 = Me; R^2 = Et; G' = CO_2Et
e: R^1 = R^2 = Me; G' = CO_2Et
f: R^1 = Me; R^2 = Ph; G' = CN
g: R^1 =H; R^2 = Ph; G' = CN
h: R^1 = H; R^2 = Et; G' = CN
i: R^1 = Me; R^2 = Et; G' = CN

pass through an amidine like intermediate as in **12**, but the intermediate could not be isolated. Isolation of **12** (G′ = CN) gave us an impetus to take an attempt for the isolation of **12** (G′ = CO_2Et). But careful investigation of the solid [*vide* experimental Section ''General procedure for the reaction of ethyl cyanoacetate on 2-alkyl/arylaminochromone-3-carbaldehyde (3)''] obtained from the reaction mixture of **3** (R^1 = H, R^2 = Ph) and ethyl cyanoacetate revealed that there was more than one product (TLC). However, chromatographic separation yielded only **11a** in moderate yield. The other components were separated by preparative TLC and the bands corresponding to two different spots were extracted separately with $CHCl_3$. Unfortunately, the isolated compounds were same in both cases and the compound was **11a**. Compound **12** (R^2 = aryl, G′ = CO_2Et) could not be isolated even after using neutral Al_2O_3 as adsorbent in the column chromatography. The only such compound **12d** was obtained by stirring a pyridine solution of **3** (R^1 = Me, R^2 = Et) and ethyl cyanoacetate at room temperature. Compound **12d** was readily converted to **11d** within 1 h when heated in ordinary $CHCl_3$ in the presence of silica gel. Formation of **12** can be rationalized *via* the Knoevenagel condensate **13** (Scheme 5). It was presumed that the conversion of **12** to **11** took place by silica-induced hydration. The source of water was supposed to be from silica adsorbent or solvent or atmosphere. Water molecule attacks **12** and opens the pyran ring to form **14** and subsequently tautomerizes to **11**. To justify this presumption, compound **12** was heated in dry $CHCl_3$ in the presence of dry silica gel and under argon atmosphere and indeed compound **12** failed to show any change.

CONCLUSION

We have reported a few new efficient one-pot methods for the synthesis of 1-benzopyrano [2,3-*b*]pyridine-2,5-dione moiety bearing various functionalities at its 3-position. The differential behavior of the active methylene compounds bearing cyano group toward **3** has also been reported.

EXPERIMENTAL

General. The recorded mps are uncorrected. IR spectra were recorded in KBr on a Beckman IR 20a, ^{1}H NMR/^{13}C NMR spectra on a bruker 300 MHz/75 MHz spectrometer, mass spectra on a Qtof micro YA 263 instrument and elemental analysis on a Perkin Elmer 240c elemental analyzer. Light petroleum refers to the fraction with 60–80°C. All chemicals used were of commercial grade and were used as such.

General procedure for the synthesis of 1-alkyl/aryl-2*H*,5*H*-1-benzopyrano[2,3-*b*]pyridine-3-carboxylic acids (1a–e). An ethanolic solution (10 mL) of a mixture of **3** (1 mmol), **4** (144 mg, 1 mmol), and catalytic amount of pyridine (2 drops) was heated under reflux for 2–4 h. The white solid separated out during the reaction was filtered off and crystallized from benzene to obtain **1a–e** as white crystalline solids.

1-Phenyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylic acid (1a). This compound was obtained in 70% yield as white crystalline solid, mp > 320°C; IR: 3493, 3064, 2784, 1754, 1646, 1533, 1427 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.23 (br d, 1H, 9-H, *J* = 8.1 Hz), 7.56–7.64(m, 6H, ArH), 7.75–7.80 (m, 1H, 8-H), 8.17 (br d, 1H, 6-H, *J* = 7.5 Hz), 8.86 (s, 1H, 4-H); ms: m/z 356 (M^+ +Na). *Anal*. Calcd for $C_{19}H_{11}NO_5$: C, 68.47; H, 3.33; N, 4.20. Found: C, 68.67; H, 3.37; N, 4.12.

1-p-Tolyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylic acid (1b). This compound was obtained in 68% yield as white crystalline solid, mp > 320°C; IR: 3453, 2976, 2755, 1767, 1652, 1540, 1453 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.36 (s, 3H, CH_3), 7.27 (br d, 1H, 9-H, *J* = 8.4 Hz), 7.38–7.50 (m, 4H, ArH), 7.57 (br t, 1H, 7-H, *J* = 7.5 Hz), 7.75–7.80 (m, 1H, 8-H), 8.17 (br d, 1H, 6-H, *J* = 7.5 Hz), 8.86 (s, 1H, 4-H); ms: m/z 370 (M^+ +Na). *Anal*. Calcd for $C_{20}H_{13}NO_5$: C, 69.16; H, 3.77; N, 4.03. Found: C, 68.98; H, 3.72; N, 3.95.

7-Methyl-1-p-tolyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylic acid (1c). This compound was obtained in 70% yield as white crystalline solid, mp 298–300°C; IR: 3460, 3015, 2812, 1743, 1647, 1553, 1437 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.46 (s, 3H, $ArCH_3$), 2.53 (s, 3H, $ArCH_3$), 7.12–7.47 (m, 6H, ArH), 8.03 (br s, 1H, 6-H), 9.32 (s, 1H, 4-H), 12.94 (s, 1H, COOH, deuterium oxide exchangeable)). *Anal*. Calcd for $C_{21}H_{15}NO_5$: C, 69.80; H, 4.18; N, 3.88. Found: C, 70.01; H, 4.11; N, 3.79.

1,7-Dimethyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylic acid (1d). This compound was obtained in 52% yield as white crystalline solid, mp 296–298°C; IR: 3456, 3045, 2934, 1741, 1634, 1542, 1475 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.51 (s, 3H, $ArCH_3$), 3.89 (s, 3H, NCH_3), 7.47 (d, 1H, 9-H, *J* = 8.4 Hz), 7.62 (br d, 1H, 8-H, *J* = 8.4 Hz), 8.11 (br s, 1H, 6-H), 9.35 (s, 1H, 4-H), 13.20 (s, 1H, COOH, deuterium oxide exchangeable)). *Anal*. Calcd for $C_{15}H_{11}NO_5$: C, 63.16; H, 3.89; N, 4.91. Found: C, 62.98; H, 3.82; N, 4.83.

1-Ethyl-7-methyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylic acid (1e). This compound was obtained in 50% yield as white crystalline solid, mp 276–278°C; IR: 3420,

3050, 2945, 1750, 1634, 1530, 1466 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.51 (t, 3H, CH_2CH_3, J = 6.9 Hz), 2.51 (s, 3H, $ArCH_3$), 4.52 (q, 2H, CH_2CH_3, J = 6.9 Hz), 7.47 (d, 1H, 9-H, J = 8.1 Hz), 7.62 (br d, 1H, 8-H, J = 8.1 Hz), 8.10 (br s, 1H, 6-H), 9.32 (s, 1H, 4-H), 13.27 (s, 1H, COOH, deuterium oxide exchangeable)). *Anal*. Calcd for $C_{16}H_{13}NO_5$: C, 64.21; H, 4.38; N, 4.68. Found: C, 64.32; H, 4.43; N, 4.59.

General procedure for the synthesis of 3-benzoylamino-1-alkyl/aryl-2H,5H-1-benzopyrano[2,3-*b*]pyridine-2,5-diones (1f–j). A mixture of **3** (1 mmol), **6** (180 mg, 1 mmol), NaOAc (250 mg, 3 mmol), and acetic anhydride (5 mL) was heated on water bath for 6–7 h. Crushed ice (50 g) was then added to the cold reaction mixture. A solid mass was separated when the reaction was carried out with **3** (R^2 = aryl). The solid was filtered off, washed with water, dried in air, and recrystallized from $CHCl_3$ to afford **1f–h**. But the reaction mixture obtained from **3** (R^2 = alkyl) afforded a semisolid mass when ice-water was added. The semisolid mass was extracted with $CHCl_3$. The organic layer was washed with water, dried over Na_2SO_4, and chromatographed over silica gel (100–200) using 10% EtOAc in benzene as eluent to get **1i–j** as white crystalline solid.

3-Benzoylamino-1-phenyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1f). This compound was obtained in 41% yield as white crystalline solid, mp > 320°C; IR: 3379, 3050, 1655, 1520, 1459 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.13 (br d, 1H, 9-H, J = 8.1 Hz), 7.36–7.66 (m, 10H, ArH), 7.93 (dd, 2H, ArH, J = 8.1, 1.2 Hz), 8.32 (dd, 1H, 6-H, J = 7.8, 1.5 Hz), 8.99 (br s, 1H, NH, deuterium oxide exchangeable), 9.35 (s, 1 H, 4-H); ms: m/z 409 (M^+ + H), 431 (M^+ +Na). *Anal*. Calcd for $C_{25}H_{16}N_2O_4$: C, 73.52; H, 3.95; N, 6.86. Found: C, 73.67; H, 3.86; N, 6.75.

3-Benzoylamino-7-methyl-1-phenyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1g). This compound was obtained in 40% yield as white crystalline solid, mp > 320°C; IR: 3360, 3120, 1640, 1545, 1422 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.44 (s, 3H, $ArCH_3$), 7.03 (d, 1H, 9-H, J = 8.1 Hz), 7.40-7.63 (m, 9H, ArH), 7.92 (dd, 2H, ArH, J = 8.0, 1.2 Hz), 8.10 (brs, 1H, 6-H), 8.97 (br s, 1H, NH, deuterium oxide exchangeable), 9.34 (s, 1H, 4-H). *Anal*. Calcd for $C_{26}H_{18}N_2O_4$: C, 73.92; H, 4.29; N, 6.63. Found: C, 73.80; H, 4.26; N, 6.58.

3-Benzoylamino-7-methyl-1-p-tolyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1h). This compound was obtained in 45% yield as white crystalline solid, mp > 320°C; IR: 3350, 3074, 1635, 1533, 1428 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.45 (s, 3H, $ArCH_3$), 2.51 (s, 3H, $ArCH_3$), 6.90 (d, 1H, 9-H, J = 8.4 Hz), 7.39–7.56 (m, 8H, ArH), 7.93 (br d, 2H, ArH, J = 7.2 Hz), 8.11 (brs, 1H, 6-H), 8.99 (br s, 1H, NH, deuterium oxide exchangeable), 9.34 (s, 1H, 4-H). *Anal*. Calcd for $C_{27}H_{20}N_2O_4$: C, 74.30; H, 4.62; N, 6.42. Found: C, 74.15; H, 4.55; N, 6.34.

3-Benzoylamino-1-ethyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1i). This compound was obtained in 32% yield as white crystalline solid, mp 256–258°C; IR: 3385, 3096, 1680, 1651, 1628, 1518, 1482 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.50 (t, 3H, CH_2CH_3, J = 6.5 Hz), 4.52 (q, 2H, CH_2CH_3, J = 6.5 Hz), 7.49–7.53 (m, 5H, ArH), 7.68–7.70 (m, 1H, 8-H), 7.93 (br d, 2H, ArH, J = 7.2 Hz), 8.31 (br d, 1H, 6-H, J = 7.2 Hz), 8.97 (br s, 1H, NH, deuterium oxide exchangeable), 9.21 (s, 1H, 4-H). *Anal*. Calcd for $C_{21}H_{16}N_2O_4$: C, 69.99; H, 4.48; N, 7.77. Found: C, 70.18; H, 4.43; N, 7.84.

3-Benzoylamino-1-ethyl-7-methyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1j). This compound was obtained in 30% yield as white crystalline solid, mp 286–288°C; IR: 3390, 3100, 2968, 1670, 1651, 1626, 1500, 1468 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.48 (t, 3H, CH_2CH_3, J = 6.6 Hz), 2.46 (s, 3H, $ArCH_3$), 4.50 (q, 2H, CH_2CH_3, J = 6.6 Hz), 7.39 (d, 1H, 9-H, J = 8.4 Hz), 7.47–7.56 (m, 4H, ArH), 7.93 (brd, 2H, ArH, J = 7.2 Hz), 8.07 (br s, 1H, 6-H), 8.96 (br s, 1 H, NH, deuterium oxide exchangeable), 9.19 (s, 1H, 4-H). *Anal*. Calcd for $C_{22}H_{18}N_2O_4$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.41; H, 4.78; N, 7.39.

General procedure for the synthesis of 1-alkyl/aryl-3-salicyloyl-2H,5H-1-benzopyrano[2,3-*b*]pyridine-2,5-diones (10a–c). An ethanolic solution of a mixture of **3** (1 mmol), **8** (162 mg, 1 mmol), and pyridine (2 drops) was heated under reflux for 5–6 h. A white solid, separated out during the reaction, was filtered off and crystallized from benzene-light petroleum (80:20) to obtain **10a–c** as white crystalline solid.

7-Methyl-1-phenyl-3-salicyloyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (10a). This compound was obtained in 85% yield as white crystalline solid, mp 284–286°C; IR: 3448, 2925, 1681, 1648, 1623, 1544 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.46 (s, 3H, $ArCH_3$), 6.87 (br t, 1H, ArH, J = 7.8 Hz), 7.05 (br t, 2H, ArH, J = 7.8 Hz), 7.36–7.59 (m, 8H, ArH), 8.06 (br s, 1H, 6-H), 8.52 (s, 1H, 4-H), 11.90 (s, 1H, OH, deuterium oxide exchangeable); ^{13}C NMR ($CDCl_3$): δ 20.8, 101.7, 117.4, 118.4, 118.9, 119.5, 121.6, 126.1, 126.2, 128.2, 128.3, 129.7, 132.7, 133.3, 135.6, 136.6, 136.9, 137.8, 151.9, 156.9, 159.1, 163.2, 173.4, 197.2; ms: m/z 424 (M^++H), 446 (M^++Na). *Anal*. Calcd for $C_{26}H_{17}NO_5$: C, 73.75; H, 4.05; N, 3.31. Found: C, 73.61; H, 4.12; N, 3.22.

1-Phenyl-3-salicyloyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (10b). This compound was obtained in 79% yield as white crystalline solid, mp 268–270°C; IR: 3400, 2940, 1692, 1660, 1630, 1524 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.87 (br t, 1H, ArH, J = 7.5 Hz), 7.03 (br d, 1H, 9-H, J = 8.4 Hz), 7.16 (br d, 1H, ArH, J = 8.4 Hz), 7.36–7.41 (m, 3H, ArH), 7.44–7.52 (m, 2H, ArH), 7.58–7.67 (m, 4H, ArH), 8.27 (br d, 1H, 6-H, J = 7.5 Hz), 8.51 (s, 1H, 4-H), 11.88 (s, 1 H, OH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{25}H_{15}NO_5$: C, 73.35; H, 3.69; N, 3.42. Found: C, 73.52; H, 3.63; N, 3.35.

1-Ethyl-3-salicyloyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (10c). This compound was obtained in 79% yield as white crystalline solid, mp 238–240°C; IR: 3425, 2920, 1690, 1640, 1620, 1500 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.48 (t, 3H, CH_2CH_3, J = 6.9 Hz), 4.47 (q, 2H, CH_2CH_3, J = 6.9 Hz), 6.86 (br t, 1H, ArH, J = 7.5 Hz), 7.04 (br d, 1H, 9-H, J = 8.4 Hz), 7.48–7.59 (m, 4H, ArH), 7.79 (br t, 1H, 8-H, J = 8.4 Hz), 8.30 (br d, 1H, 6-H, J = 7.8 Hz), 8.39 (s, 1H, 4-H), 11.92 (s, 1 H, OH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{21}H_{15}NO_5$: C, 69.80; H, 4.18; N, 3.88. Found: C, 69.62; H, 4.12; N, 3.95.

General procedure for the synthesis of ethyl 1-alkyl/aryl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-*b*]pyridine-3-carboxylates (1k-n) and 3-acetyl/benzoyl-1-alkyl/aryl-2H,5H-1-benzopyrano[2,3-*b*]pyridine-2,5-diones (1o-t). A mixture of **3** (1 mmol), diethyl malonate (240 mg, 1.5 mmol) and piperidine (130 mg, 1.5 mmol) or **3** (1 mmol), ethyl acetoacetate (130 mg, 1 mmol) and piperidine (85 mg, 1 mmol) or **3** (1 mmol), ethyl benzoylacetate (190 mg, 1 mmol) and piperidine (85 mg, 1 mmol) in $CHCl_3$ (10 mL) was heated under reflux

for several hours (Table 2) till the completion of reaction (TLC). Solvent was removed from the reaction mixture under reduced pressure and resulted residue was stirred with water (10 mL) for 10 min. The separated solid was filtered off, dried, and purified by column chromatography over silica gel (100–200) using 10% EtOAc in benzene as eluent to obtain **1k–t**.

Ethyl 1-phenyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylate (1k). This compound was obtained in 55% yield as white crystalline solid, mp 278–280°C; IR: 2927, 1752, 1717, 1657, 1542 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.40 (t, 3H, CH_2CH_3, J = 7.2 Hz), 4.39 (q, 2H, CH_2CH_3, J = 7.2 Hz), 7.13 (br d, 1H, 9-H, J = 8.4 Hz), 7.34 (br d, 2H, ArH, J = 7.5 Hz), 7.46 (br t, 1H, ArH, J = 7.2 Hz), 7.59–7.66 (m, 4H, ArH), 8.28 (br d, 1H, 6-H, J = 7.2 Hz), 9.08 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$): δ 14.2, 61.4, 101.4, 117.6, 117.8, 121.7, 126.3, 126.5, 128.1, 129.6, 129.7, 133.2, 134.5, 141.7, 153.4, 157.5, 158.4, 163.5, 173.3; ms: m/z 362 (M^++H), 384 (M^++Na). *Anal.* Calcd for $C_{21}H_{15}NO_5$: C, 69.80; H, 4.18; N, 3.88. Found: C, 69.67; H, 4.09; N, 3.81.

Ethyl 7-methyl-1-phenyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylate (1l). This compound was obtained in 74% yield as white crystalline solid, mp 208–210°C; IR: 2940, 1740, 1710, 1648, 1535 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.39 (t, 3H, CH_2CH_3, J = 7.2 Hz), 2.44 (s, 3H, $ArCH_3$), 4.39 (q, 2H, CH_2CH_3, J = 7.2 Hz), 7.01 (d, 1H, 9-H, J = 8.4 Hz), 7.41 (br d, 1H, 8-H, J = 8.4 Hz), 7.40–7.43 (m, 2H, ArH,), 7.50–7.58 (m, 3H, ArH), 8.10 (br s, 1H, 6-H), 9.06 (s, 1H, 4-H). *Anal.* Calcd for $C_{22}H_{17}NO_5$: C, 70.39; H, 4.56; N, 3.73. Found: C, 70.25; H, 4.52; N, 3.68.

Ethyl 1-ethyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylate (1m). This compound was obtained in 42% yield as white crystalline solid, mp 178–180°C; IR: 2939, 1728, 1685, 1610, 1537 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.41 (t, 3H, NCH_2CH_3, J = 7.2 Hz), 1.46 (t, 3H, OCH_2CH_3, J = 7.2 Hz), 4.38 (q, 2H, NCH_2CH_3, J = 7.2 Hz), 4.46 (q, 2H, OCH_2CH_3, J = 7.2 Hz), 7.49–7.56 (m, 2H, ArH), 7.78 (br t, 1H, 8-H, J = 7.2 Hz), 8.29 (br d, 1H, 6-H, J = 7.8 Hz), 8.95 (s, 1H, 4-H). *Anal.* Calcd for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 64.95; H, 4.78; N, 4.49.

Ethyl 1-ethyl-7-methyl-2H,5H-2,5-dioxo-1-benzopyrano[2,3-b]pyridine-3-carboxylate (1n). This compound was obtained in 40% yield as white crystalline solid, mp 192–194°C; IR: 2956, 1712, 1690, 1618, 1540 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.41 (t, 3H, NCH_2CH_3, J = 7.2 Hz), 1.44 (t, 3H, OCH_2CH_3, J = 7.2 Hz), 2.50 (s, 3H, $ArCH_3$), 4.38 (q, 2H, NCH_2CH_3, J = 7.2 Hz), 4.44 (q, 2H, OCH_2CH_3, J = 7.2 Hz), 7.43 (d, 1H, 9-H, J = 8.4 Hz), 7.56 (br d, 1H, 8-H, J = 8.4 Hz), 8.08 (br s, 1H, 6-H,), 8.96 (s, 1H, 4-H). *Anal.* Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 65.90; H, 5.17; N, 4.21.

3-Acetyl-7-methyl-1-phenyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1o). This compound was obtained in 68% yield as white crystalline solid, mp 278–280°C; IR: 2940, 1696, 1654, 1527, 1478 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.45 (s, 3H, $ArCH_3$), 2.68 (s, 3H, $COCH_3$), 7.03 (d, 1H, 9-H, J = 8.4 Hz), 7.36–7.38 (m, 2H, ArH), 7.43 (br d, 1H, 8-H, J = 8.4 Hz), 7.63–7.65 (m, 3H, ArH), 8.05 (br s, 1H, 6-H), 9.08 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$): δ 20.8, 30.8, 102.0, 117.4, 121.3, 124.1, 126.0, 128.0, 129.7, 129.8, 133.4, 135.6, 136.5, 141.0, 151.7, 157.7, 160.5, 173.5, 195.4; ms: m/z 346 (M^++ H), 368 (M^++Na). *Anal.* Calcd for $C_{21}H_{15}NO_4$: C, 73.04; H, 4.38; N, 4.06. Found: C, 72.90; H, 4.34; N, 3.99.

3-Acetyl-1-ethyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1p). This compound was obtained in 43% yield as white crystalline solid, mp 218–220°C; IR: 2940, 1700, 1660, 1540, 1480 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.47 (t, 3H, CH_2CH_3, J = 6.9 Hz), 2.70 (s, 3H, $COCH_3$), 4.45 (q, 2H, CH_2CH_3, J = 6.9 Hz), 7.49–7.56 (m, 2H, ArH), 7.75–7.80 (m, 1H, 8-H), 8.27 (br d, 1H, 6-H, J = 7.8 Hz), 8.92 (s, 1H, 4-H). *Anal.* Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.70; H, 4.56; N, 4.87.

3-Benzoyl-1-phenyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1q). This compound was obtained in 72% yield as white crystalline solid, mp 264–266°C; IR: 2930, 1671, 1643, 1540, 1458 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.16 (br d, 1H, 9-H, J = 8.4 Hz), 7.37–7.40 (m, 2H, ArH), 7.43–7.48 (m, 3H, ArH), 7.55–7.67 (m, 5H, ArH), 7.87 (br d, 2H, ArH, J = 7.8 Hz), 8.28 (br d, 1H, 6-H, J = 7.8Hz), 8.64 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$): δ 101.8, 117.7, 121.8, 126.3, 126.4, 126.6, 128.1, 128.4, 129.4, 129.7, 129.8, 133.1, 133.2, 134.5, 137.0, 139.0, 153.5, 157.0, 159.4, 173.4, 192.3; ms: m/z 394 (M^++H), 416 (M^++Na). *Anal.* Calcd for $C_{25}H_{15}NO_4$: C, 76.33; H, 3.84; N, 3.56. Found: C, 76.20; H, 3.80; N, 3.49.

3-Benzoyl-7-methyl-1-phenyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1r). This compound was obtained in 74% yield as white crystalline solid, mp 278–280°C; IR: 2936, 1680, 1650, 1550, 1480 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.46 (s, 3H, $ArCH_3$), 7.05 (d, 1H, 9-H, J = 8.4 Hz), 7.36–7.60 (m, 9H, ArH), 7.86 (br d, 2H, ArH, J = 7.5 Hz), 8.06 (br s, 1H, 6-H), 8.64 (s, 1H, 4-H). *Anal.* Calcd for $C_{26}H_{17}NO_4$: C, 76.65; H, 4.21; N, 3.44. Found: C, 76.50; H, 4.16; N, 3.47.

3-Benzoyl-1-methyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1s). This compound was obtained in 60% yield as white crystalline solid, mp 256–258°C; IR: 3010, 1675, 1660, 1540, 1470 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.80 (s, 3H, CH_3), 7.44–7.62 (m, 5H, ArH), 7.79 (br t, 1H, ArH, J = 8.1 Hz), 7.84 (br d, 2H, ArH, J = 8.1 Hz), 8.30 (br d, 1H, 6-H, J = 8.1 Hz), 8.52 (s, 1H, 4-H). *Anal.* Calcd for $C_{20}H_{13}NO_4$: C, 72.50; H, 3.95; N, 4.23. Found: C, 72.40; H, 3.88; N, 4.19.

3-Benzoyl-1-ethyl-2H,5H-1-benzopyrano[2,3-b]pyridine-2,5-dione (1t). This compound was obtained in 62% yield as white crystalline solid, mp 224–226°C; IR: 2958, 1690, 1662, 1548, 1474 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.47 (t, 3H, CH_2CH_3, J = 6.9 Hz), 4.45 (q, 2H, CH_2CH_3, J = 6.9 Hz), 7.44–7.61 (m, 5H, ArH), 7.76–7.79 (m, 1H, ArH), 7.84 (br d, 2H, ArH, J = 7.5 Hz), 8.30 (br d, 1H, 6-H, J = 7.5 Hz), 8.51 (s, 1H, 4-H). *Anal.* Calcd for $C_{21}H_{15}NO_4$: C, 73.04; H, 4.38; N, 4.06. Found: C, 72.91; H, 4.32; N, 3.98.

General procedure for the reaction of ethyl cyanoacetate on 2-alkyl/arylaminochromone-3-carbaldehyde (3). An ethanolic solution (30 mL) of a mixture of **3** (1 mmol), ethyl cyanoacetate (115 mg, 1 mmol), and piperidine (85 mg, 1 mmol) was stirred at room temperature for 3.5 h to afford a solid. The solid was filtered off, washed with ethanol, and purified by column chromatography over silica gel (100–200) using 10% EtOAc in benzene as eluent to afford **11a–e** in moderate yields.

Ethyl 2-amino-1,6-dihydro-5-(salicyloyl)-6-oxo-1-phenylpyridine-3-carboxylate (11a). This compound was obtained in 60% yield as yellow crystalline solid, mp 166–168°C; IR: 3351, 3253, 2983, 1694, 1654, 1574 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.36 (t, 3H, CH_2CH_3, J = 6.9 Hz), 4.30 (q, 2H, CH_2CH_3, J = 6.9 Hz), 4.93 (br s, 1H, NH_2, deuterium oxide exchangeable), 6.83–6.85 (br t, 1H, 5'-H, J = 7.2 Hz), 6.97 (br d, 1H, 3'-H, J = 8.1 Hz),

7.29–7.31 (m, 2H, ArH), 7.36–7.44 (m, 1H, ArH), 7.54–7.62 (m, 4H, ArH), 8.41 (s, 1H, 4-H), 9.18 (br s, 1H, NH_2, deuterium oxide exchangeable), 12.03 (s, 1 H, OH, deuterium oxide exchangeable); ^{13}C NMR ($CDCl_3$): δ 14.3, 60.8, 89.6, 114.9, 117.8, 118.4, 119.7, 128.4, 130.2, 130.7, 132.8, 133.5, 135.8, 145.2, 156.6, 159.5, 162.4, 166.6, 197.7; ms: m/z 379 (M^+ +H), 401 (M^+ +Na). *Anal*. Calcd for $C_{21}H_{18}N_2O_5$: C, 66.66; H, 4.79; N, 7.40. Found: C, 66.80; H, 4.85; N, 7.45.

Ethyl 2-amino-1,6-dihydro-5-(5-methylsalicyloyl)-6-oxo-1-phenylpyridine-3-carboxylate (11b). This compound was obtained in 57% yield as yellow crystalline solid, mp 116–118°C; IR 3400, 3156, 2985, 1691, 1650, 1554 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.35 (t, 3H, CH_2CH_3, J = 6.9 Hz), 2.25 (s, 3H, $ArCH_3$), 4.30 (q, 2H, CH_2CH_3, J = 6.9 Hz), 4.94 (br s, 1H, NH_2, deuterium oxide exchangeable), 6.88 (d, 1H, 3'-H, J = 8.4Hz), 7.23–7.31 (m, 3H, ArH), 7.36–7.39 (m, 1H, ArH), 7.54–7.63 (m, 3H, ArH), 8.36 (s, 1H, 4-H), 9.15 (br s, 1H, NH_2, deuterium oxide exchangeable), 11.81 (s, 1H, OH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{22}H_{20}N_2O_5$: C, 67.34; H, 5.14; N, 7.14. Found: C, 67.55; H, 5.08; N, 7.08.

Ethyl 2-amino-1,6-dihydro-5-(5-methylsalicyloyl)-6-oxo-1-p-tolylpyridine-3-carboxylate (11c). This compound was obtained in 52% yield as yellow crystalline solid, mp 202–204°C; IR 3320, 3148, 2976, 1685, 1663, 1562 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.34 (t, 3H, CH_2CH_3, J = 6.9 Hz), 2.24 (s, 3H, $ArCH_3$), 2.42 (s, 3H, $ArCH_3$), 4.30 (q, 2H, CH_2CH_3, J = 6.9 Hz), 5.02 (br s, 1H, NH_2, deuterium oxide exchangeable), 6.87 (d, 1H, 3'-H, J = 8.4 Hz), 7.16 (d, 2H, ArH, J = 7.8 Hz), 7.23 (br d, 1H, 4'-H, J = 8.4 Hz), 7.36–7.40 (m, 3H, ArH), 8.35 (s, 1H, 4-H), 9.12 (br s, 1H, NH_2, deuterium oxide exchangeable), 11.82 (s, 1H, OH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{23}H_{22}N_2O_5$: C, 67.97; H, 5.46; N, 6.89. Found: C, 67.80; H, 5.41; N, 6.82.

Ethyl 2-amino-1,6-dihydro-1-ethyl-5-(5-methylsalicyloyl)-6-oxo-pyridine-3-carboxylate (11d). This compound was obtained in 40% yield as yellow crystalline solid, mp 160–162°C; IR 3359, 3204, 2977, 1689, 1604, 1542 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.33 (t, 6H, $2\times CH_2CH_3$, J = 6.9 Hz), 2.25 (s, 3H, $ArCH_3$), 4.12 (q, 2H, CH_2CH_3, J = 6.9 Hz), 4.29 (q, 2H, CH_2CH_3, J = 6.9 Hz), 5.11 (br s, 1H, NH_2, deuterium oxide exchangeable), 6.91 (d, 1H, 3′-H, J = 8.4 Hz), 7.25 (br d, 1H, 4′-H, J = 8.4 Hz), 7.32 (br s, 1H, 6′-H), 8.24 (s, 1H, 4-H), 8.99 (br s, 1H, NH_2, deuterium oxide exchangeable), 11.87 (s, 1H, OH, deuterium oxide exchangeable); ms: m/z 345 (M^++H), 367 (M^++Na). *Anal*. Calcd for $C_{18}H_{20}N_2O_5$: C, 62.78; H, 5.85; N, 8.13. Found: C, 62.62, H, 5.80; N, 8.10.

Ethyl 2-amino-1,6-dihydro-1-methyl-5-(5-methylsalicyloyl)-6-oxo-pyridine-3-carboxylate (11e). This compound was obtained in 45% yield as yellow crystalline solid, mp 208–210°C; IR 3333, 3194, 2970, 1684, 1635, 1574 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.33 (t, 3H, CH_2CH_3, J = 6.9 Hz), 2.25 (s, 3H, $ArCH_3$), 3.50 (s, 3H, NCH_3), 4.29 (q, 2H, CH_2CH_3, J = 6.9 Hz), 5.12 (br s, 1H, NH_2, deuterium oxide exchangeable), 6.91 (d, 1H, 3′-H, J = 8.4 Hz), 7.26 (br d, 1H, 4′-H, J = 8.4 Hz), 7.32 (br s, 1H, 6′-H), 8.23 (s, 1H, 4-H), 8.98 (br s, 1H, NH_2, deuterium oxide exchangeable), 11.86 (s, 1H, OH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48. Found: C, 61.74; H, 5.45; N, 8.42.

General procedure for the reaction of malononitrile on 2-alkyl/arylaminochromone-3-carbaldehyde (3). A mixture of **3** (1 mmol), malononitrile (66 mg, 1 mmol), and piperidine (85 mg, 1 mmol) in ethanol (30 mL) was stirred at room temperature for 1 h. The deposited solid was filtered off, washed with ethanol, and recrystallized from benzene to afford **12f–i**.

7-Methyl-1-phenyl-2H,5H-2-imino-5-oxo-1-benzopyrano[2,3-b]pyridine-3-carbonitrile (12f). This compound was obtained in 80% yield as faint yellow crystalline solid, mp 286–288°C; IR 3316, 2210, 1637, 1533, 1475 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.44 (s, 3H, $ArCH_3$), 6.95 (d, 1H, 9-H, J = 8.4 Hz), 7.27–7.39 (m, 5H, ArH), 7.60–7.67 [m, 2H (1 H, deuterium oxide exchangeable), NH+ArH)], 7.98 (br s, 1H, 6-H), 8.23 (s, 1H, 4-H); ms: m/z 328 (M^++H), 350 (M^++Na). *Anal*. Calcd for $C_{20}H_{13}N_3O_2$: C, 73.39; H, 4.00; N, 12.84. Found: C, 73.25; H, 3.92; N, 12.78.

1-Phenyl-2H,5H-2-imino-5-oxo-1-benzopyrano[2,3-b]pyridine-3-carbonitrile (12g). This compound was obtained in 83% yield as faint yellow crystalline solid, mp > 320°C; IR 3330, 2230, 1648, 1520, 1460 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.05 (br d, 1H, 9-H, J = 8.1 Hz), 7.44 (br t, 1H, 7-H, J = 7.2 Hz), 7.58–7.63 (m, 1H, 8-H), 7.64–7.67 (m, 6H, NH+ArH), 8.22 (br d, 1H, 6-H, J = 7.2 Hz), 8.30 (s, 1H, 4-H). *Anal*. Calcd for $C_{19}H_{11}N_3O_2$: C, 72.84; H, 3.54; N, 13.41. Found: C, 72.72; H, 3.48; N, 13.48.

1-Ethyl-2H,5H-2-imino-5-oxo-1-benzopyrano[2,3-b]pyridine-3-carbonitrile (12h). This compound was obtained in 86% yield as faint yellow crystalline solid, mp 266–268°C; IR 3298, 3022, 2222, 1626, 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.45 (t, 3H, CH_2CH_3, J = 6.9 Hz), 4.49 (q, 2H, CH_2CH_3, J = 6.9 Hz), 7.48–7.52 (m, 2H, ArH), 7.62 (br s, 1H, NH, deuterium oxide exchangeable), 7.75 (ddd, 1H, 8-H, J = 8.4, 7.9, 1.8 Hz), 8.19 (s, 1H, 4-H), 8.24 (dd, 1H, 6-H, J = 7.8, 1.8 Hz). *Anal*. Calcd for $C_{15}H_{11}N_3O_2$: C, 67.92; H, 4.18; N, 15.84. Found: C, 68.10; H, 4.23; N, 15.76.

1-Ethyl-7-methyl-2H,5H-2-imino-5-oxo-1-benzopyrano[2,3-b]pyridine-3-carbonitrile (12i). This compound was obtained in 64% yield as faint yellow crystalline solid, mp 256–258°C; IR 3300, 2983, 2254, 1645, 1615 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.44 (t, 3H, CH_2CH_3, J = 6.9 Hz), 2.48 (s, 3H, $ArCH_3$), 4.46 (q, 2H, CH_2CH_3, J = 6.9 Hz), 7.39 (br d, 1H, 9-H, J = 8.4 Hz), 7.54 (br d, 1H, 8-H, J = 8.4 Hz), 7.58 (br s, 1H, NH, deuterium oxide exchangeable), 8.01 (br s, 1H, 6-H), 8.17 (s, 1H, 4-H). *Anal*. Calcd for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.70; H, 4.62; N, 14.96.

Silica-induced hydrolysis of 12 to 1-alkyl/aryl-2-amino-1,6-dihydro-5-(salicyloyl)-6-oxo-pyridine-3-carbonitrile (11f). Compound **12** (1 mmol) was dissolved in $CHCl_3$ (25 mL). Silica gel (1 g) was added to the $CHCl_3$ solution and the resultant mixture was heated under reflux with stirring for 5 h. Silica gel was filtered off and it was eluted with 20% ethyl acetate in benzene. Filtrate ($CHCl_3$ solution) and eluents were mixed together and was concentrated under reduced pressure. The residue was crystallized from benzene to afford **11f–i**.

2-Amino-1,6-dihydro-1-phenyl-5-(5-methylsalicyloyl)-6-oxo-pyridine-3-carbonitrile (11f). This compound was obtained in 70% yield as yellow crystalline solid, mp 194–196°C; IR 3400, 3388, 3220, 2981, 2255, 1690, 1647, 1540 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.26 (s, 3H, $ArCH_3$), 5.50 (br s, 2H, NH_2, deuterium oxide exchangeable), 6.89 (d, 1H, 3'-H, J = 8.7 Hz), 7.29–7.31 (m, 4H, ArH), 7.57–7.65 (m, 3H, ArH), 7.74 (s, 1H, 4-H), 11.61 (s, 1H, OH, deuterium oxide exchangeable); ^{13}C NMR ($CDCl_3$): δ 20.6, 72.0, 116.2, 117.1, 118.0, 119.1, 127.7, 128.1, 128.3, 130.8, 131.0, 132.1, 133.2, 137.6, 144.2, 156.5, 160.7, 196.4; ms: m/z 346 (M^++H), 368

(M^++Na). *Anal*. Calcd for $C_{20}H_{15}N_3O_3$: C, 69.56; H, 4.38; N, 12.17. Found: C, 69.38; H, 4.40; N, 12.12.

2-Amino-1,6-dihydro-1-phenyl-5-salicyloyl-6-oxo-pyridine-3-carbonitrile (11g). This compound was obtained in 72% yield as yellow crystalline solid, mp 228–230°C; IR 3410, 3398, 3213, 2922, 2216, 1681, 1638, 1526 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.41 (br s, 2H, NH_2, deuterium oxide exchangeable), 6.85 (ddd, 1H, 5'-H, J = 7.5, 7.2, 0.6 Hz), 6.98 (dd, 1H, 3'-H, J = 8.1, 0.6 Hz), 7.28–7.31 (m, 2H, ArH), 7.42–7.48 (m, 1H, ArH), 7.55–7.65 (m, 4H, ArH), 7.81 (s, 1H, 4-H), 11.81 (s, 1H, OH, deuterium oxide exchangeable); *Anal*. Calcd for $C_{19}H_{13}N_3O_3$: C, 68.88; H, 3.95; N, 12.68. Found: C, 68.75; H, 3.92; N, 12.63.

2-Amino-1-ethyl-1,6-dihydro-5-salicyloyl-6-oxo-pyridine-3-carbonitrile (11h). This compound was obtained in 69% yield as yellow crystalline solid, mp 252–254°C; IR 3344, 3314, 3227, 2941, 2212, 1631, 1581 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.09 (t, 3H, CH_2CH_3, J = 6.9 Hz), 4.0 (q, 2H, CH_2CH_3, J = 6.9 Hz), 6.81–6.88 (m, 2H, ArH), 7.34–7.36 (m, 2H, ArH), 7.78 (s, 1H, 4-H), 8.14 (br s, 2H, NH_2, deuterium oxide exchangeable), 10.61 (s, 1H, OH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{15}H_{13}N_3O_3$: C, 63.60; H, 4.63; N, 14.83. Found: C, 63.45; H, 4.56; N, 14.74.

2-Amino-1-ethyl-1,6-dihydro-5-(5-methylsalicyloyl)-6-oxo-pyridine-3-carbonitrile (11i). This compound was obtained in 67% yield as yellow crystalline solid, mp 248–250°C; IR 3340, 3324, 3220, 2955, 2220, 1640, 1578 cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.10 (t, 3H, CH_2CH_3, J = 6.9 Hz), 2.20 (s, 3H, $ArCH_3$), 4.00 (q, 2H, CH_2CH_3, J = 6.9 Hz), 6.77 (d, 1H, 3'-H, J = 7.5 Hz), 7.16–7.18 (m, 2H, ArH), 7.75 (s, 1H, 4-H), 8.12 (br s, 2H, NH_2, deuterium oxide exchangeable), 10.42 (s, 1H, OH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{16}H_{15}N_3O_3$: C, 64.64; H, 5.03; N, 14.13. Found: C, 64.74; H, 5.06; N, 14.19.

Synthesis of Ethyl 1-ethyl-7-methyl-2H,5H-2-imino-5-oxo-1-benzopyrano[2,3-b]pyridine-3-carboxylate (12d) from 3 (R^1 = Me, R^2 = Et). A mixture of **3** (R^1 = Me, R^2 = Et) (230 mg, 1 mmol), ethyl cyanoacetate (115 mg, 1 mmol) in pyridine (5 mL) was stirred at room temperature for 2 h when a solid was found to separate. It was filtered off, washed with water, dried in air, and crystallized from benzene-light petrol (80:20) to produce **12d**.

Ethyl 1-ethyl-7-methyl-2H,5H-2-imino-5-oxo-1-benzopyrano[2,3-b]pyridine-3-carboxylate (12d). This compound was obtained in 40% yield as faint yellow crystalline solid, mp 256–258°C; IR 3303, 2985, 1702, 1625, 1537, 1478 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.37–1.44 (m, 6H, 2×CH_2CH_3), 2.47 (s, 3H, $ArCH_3$), 4.34 (q, 2H, NCH_2CH_3, J = 6.9 Hz), 4.47 (q, 2H, OCH_2CH_3, J = 6.6 Hz), 7.36 (d, 1H, 9-H, J = 8.4 Hz), 7.48 (br d, 1H, 8-H, J = 8.4 Hz), 8.01 (br s, 1H, 6-H), 8.63 (s, 1H, 4-H), 9.57 (br s, 1H, NH, deuterium oxide exchangeable). *Anal*. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.40; H, 5.49, N, 8.52.

Acknowledgments. Financial assistance from the Department of Biotechnology (DBT), India (No. BT/PR8217/Med/14/1239/2006) is gratefully acknowledged. We also gratefully acknowledge IICB and IACS, Jadavpur for spectral analysis and the college authorities for providing research facilities.

REFERENCES AND NOTES

[1] Unangst, P. C.; Capiris, T.; Connor, D. T.; Heffner, T. G.; Mackenzie, R. G.; Miller, S. R.; Pugsley, T. A.; Wise, L. D. J Med Chem 1997, 40, 2688.

[2] Edwards, J. D.; Higuchi, R. I.; Winn, D. T.; Pooley, C. F.; Caferro, T. R.; Hamann, L. G.; Zhi, L.; Marschke, K. B.; Goldman, M. E.; Jones, T. K. Bioorg Med Chem Lett 1999, 9, 1003.

[3] Siddique, Z. N.; Khuwaja, G.; Asad, M. Indian J Chem 2006, 45B, 2341.

[4] Weng, L. L.; Ln, G.; Zheng, H. Chin Chem Lett 2002, 13, 13.

[5] Ryabukhin, S. V.; Plaskon, A. S.; Volochnyuk, D. M.; Tolmachev, A. A. Synlett 2004, 2287.

[6] (a) Nohara, A.; Sugihara, H.; Ukawa, K. Ger. Pat. 2,809,720; (b) Nohara, A.; Ishiguro, T.; Ukawa, K. Ger. Pat. 2,841,644; (c) Nohara, A.; Sugihara, H.; Ukawa, K. Jpn. Pat. 7,988,298; (d) Nohara, A.; Sugihara, H.; Ukawa, K. U.S. Pat. 4,255,576;

[7] Connor, D. T.; Strandtmann, V. U.S. Pat. 4,117,134;

[8] Atkinson, P.; Findlay, K. S.; Kielar, F.; Pal, R.; Parker, D.; Poole, R. A.; Puschmann, H.; Richardson, S. L.; Stenson, P. A.; Thompson, A. L.; Yu, J. Org Biomol Chem 2006, 4, 1707.

[9] Ghosh, C. K.; Sinha Roy, D. K.; Mukhopadhyay, K. K. J Chem Soc Perkin Trans1 1979,1964.

[10] (a) Langer, P.; Appel, B. Tetrahedron Lett 2003, 44, 5133; (b) Rashid, M. A.; Rasool, N.; Appel, B.; Adeel, M.; Karapetyan, V.; Mkrtchyan, S.; Reinke, H.; Fischer, C.; Langer, P. Tetrahedron 2008, 64, 5416.

[11] Ghosh, T.; Bandyopadhyay, C. J Heterocycl Chem 2006, 43, 1431.

[12] Plaskon, A. S.; Ryabukhin, S. V.; Volochnyuk, D. M.; Gavrilenko, K. S.; Shivanyuk, A. N.; Tolmachev, A. A. J Org Chem 2008, 73, 6010.

[13] Ghosh, C. K.; Bandyopadhyay, C.; Maiti, J. Heterocycles 1987, 26, 1623.

[14] (a) Sottofattori, E.; Anzaldi, M.; Balbi, A.; Artali, R.; Bombieri, G. Helv Chim Acta 2002, 85, 1698; (b) Singh, G.; Singh, L.; Ishar, M. P. S. Tetrahedron 2002, 58, 7883; (c) Maiti, S.; Panja, S. K.; Bandyopadhyay, C. Indian J Chem 2009, 48B, 1447.

[15] Maiti, S.; Panja, S. K.; Bandyopadhyay, C. Tetrahedron Lett 2009, 50, 3966.

[16] Esmaeili, A. A.; Gharenghani, O. Helv Chim Acta 2007, 90, 1712.

[17] Nakaike, Y.; Hayashi, D.; Nishiwaki, N.; Tobe, Y.; Ariga, M. Org Biomol Chem 2009, 7, 325.

[18] Singh, G; Singh, G.; Ishar, M. P. S. Helv Chim Acta 2003, 86, 169.

[19] (a) Ishar, M. P. S.; Kumar, K.; Singh, R. Tetrahedron Lett 1998, 39, 6547; (b) Ghosh, T.; Bandyopadhyay, C. Tetrahedron Lett 2004, 45, 6169.

[20] (a) Bandyopadhyay, C.; Sur, K. R.; Patra, R.; Banerjee, S. J Chem Res (S) 2003,459; (b) Bandyopadhyay, C.; Sur, K. R.; Patra, R.; Banerjee, S. J Chem Res (M) 2003, 847.

[21] (a) Song, A.; Wang, X.; Lam, K. S. Tetrahedron Lett 2003, 44, 1755; (b) Gao, S.; Tsai, C. H.; Yao, C.-F. Synlett 2009, 949.

[22] Chopra, D.; Zhurov, V. V.; Zhurova, E. A.; Pinkerton, A. A. J Org Chem 2009, 74, 2389.

[23] (a) Mc Nab, H. Chem Soc Rev 1978, 7, 345; (b) Ivanor, A. S. Chem Soc Rev 2008, 37, 789.

[24] Ghosh, C. K.; Bandyopadhyay, C. Indian J Chem 1984, 23B, 1048.

[25] (a) Trivedi, K. N.; Madhava Rao, S. S.; Mistry, S. V.; Desai, S. M. J Indian Chem Soc 2001, 78, 579; (b) Mitra, A. K.; De, A.; Karchaudhuri, N.; Misra, S. K.; Mukhopadhyay, A. K. J Indian Chem Soc 1998, 75, 666.