Regio- and Stereoselective Synthesis of 1-Benzopyrano[2,3-*b*]pyrrolo[2,3-*d*]pyridines: A Microwave-Accelerated Intramolecular [3+2] Cycloaddition Reaction of Azomethine Ylide

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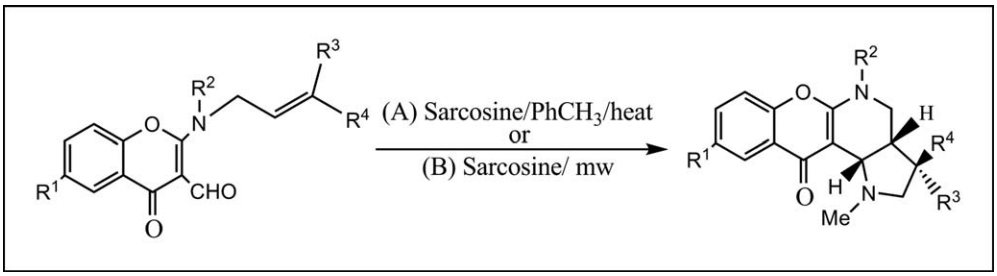

Regio- and stereoselective syntheses of tetracyclic compounds having chromone, pyrrolidine, and piperidine rings have been accomplished by an intramolecular [3+2] cycloaddition reaction involving azomethine ylide. The reactions were carried out thermally as well as by irradiation with microwave. The latter process accelerates the reaction. The selectivities were investigated by density functional theory computation.

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INTRODUCTION

Intramolecular 1,3-dipolar cycloaddition reaction is an effective method for double annulation in a single-step reaction [1]. Intramolecular nitrone–olefin cycloaddition reaction has been widely used for the synthesis of complex heterocyclic compounds including alkaloids [2,3], modified nucleosides [4], β-lactam antibiotics [5], and natural products [6]. *O*-Allylated salicylaldehyde [7,8], 4-allylamino-3-formyl-α-pyrone [9], and 2-allylamino-3-formylchromone [10] have been used in intramolecular [3+2] nitrone–olefin cycloaddition reaction for the synthesis of isoxazolidines fused with different heterocycles [11–15]. Analogous pyrrolidine derivatives, which may be obtained by azomethine ylide–olefin cycloaddition, possess antiviral [16] and local anesthetic activities [17]. Some of them are potential antileukemic and anticonvulsant agents [18]. Benzopyranopyridines or pyrrolidines act as selective dopamine D_3 receptor antagonist [19,20], can bind with DNA [21], and have potential antiplatelet activities [22]. Compounds having piperidine substructures display spasmolytic activity and potent cytotoxicity toward human Molt 4/C8 and CEM T-lymphocytes as well as Murine P 388 and L 1210 leukemic cells [23]. Some naturally occurring chromone-based alkaloids such as schumanniophytine and isoschumanniophytine were found to possess antiviral activity [24,25]. [3+2] Cycloaddition reaction involving azomethine ylide for the synthesis of pyrrolidine moiety has been studied by ultrasonication [26], microwave irradiation [27] in addition to classical heating condition. However, reports on intramolecular cycloaddition reaction involving azomethine ylide, assisted by microwave irradiation or by ultrasonication, are few [28].

2-Alkyl/arylamino-3-formylchromone **3** has become an attractive building block for the synthesis of various heterocycles. Synthesis of **3** was achieved directly from 3-formylchromone **1** [29] or by the rearrangement of nitrone **2** [30,31]. Use of **3** as a synthon has drawn attention markedly in this decade [32–38]. In most of the cases, **3** was further alkylated and nucleophilic substitution reactions were studied using suitable nucleophiles [32–34]. Recently, we have reported deformylative Mannich reaction [39] on **3** for the synthesis of bischromones [36], reactions of different amines with **3** [37], and conversion of **3** into chromeno[2,3-*b*]pyridines with various substituents at their 3-position [38]. Many

Table 1

Synthesis of 1-benzopyrano[2,3-*b*]pyrrolo[2,3-*d*]pyridines using [3+2] cycloaddition reaction.

Entry	R^1	R^2	R^3	R^4	Conditions	Product	Yield (%)	Mp (°C)
1	H	Ph	H	H	MeOH/heat/30 h	–	–	–
2	Me	Ar	H	H	$PhCH_3$/heat/26 h	**6a**	64	198–200
3	H	Ph	H	H	$PhCH_3$/TsOH/heat/36 h	–	–	–
4	H	Ar	H	H	$PhCH_3$/heat/28 h	**6b**	65	182–184
5	Me	Ph	H	H	$PhCH_3$/heat/25 h	**6c**	56	168–170
6	H	Ph	H	H	$PhCH_3$/heat/26 h	**6d**	55	162–164
7	Me	Ar	H	H	DMF/Et_3N/3.5 h	**6a**	30	198–200
8	H	Ph	H	H	MW/4 min	**6d**	60	162–164
9	Me	Ph	H	H	MW/5 min	**6c**	62	168–170
10	H	Ar	H	H	MW/5 min	**6b**	62	182–184
11	Me	Ar	H	H	MW/3 min	**6a**	62	198–200
12	Me	Ar	H	Ph	$PhCH_3$/heat/25 h	**6e**	75	Semisolid
13	H	Ph	H	Ph	$PhCH_3$/heat/25 h	**6f**	81	Semisolid
14	Me	Ar	H	Ph	MW/3 min	**6e**	70	Semisolid
15	H	Ph	H	Ph	MW/3 min	**6f**	71	Semisolid

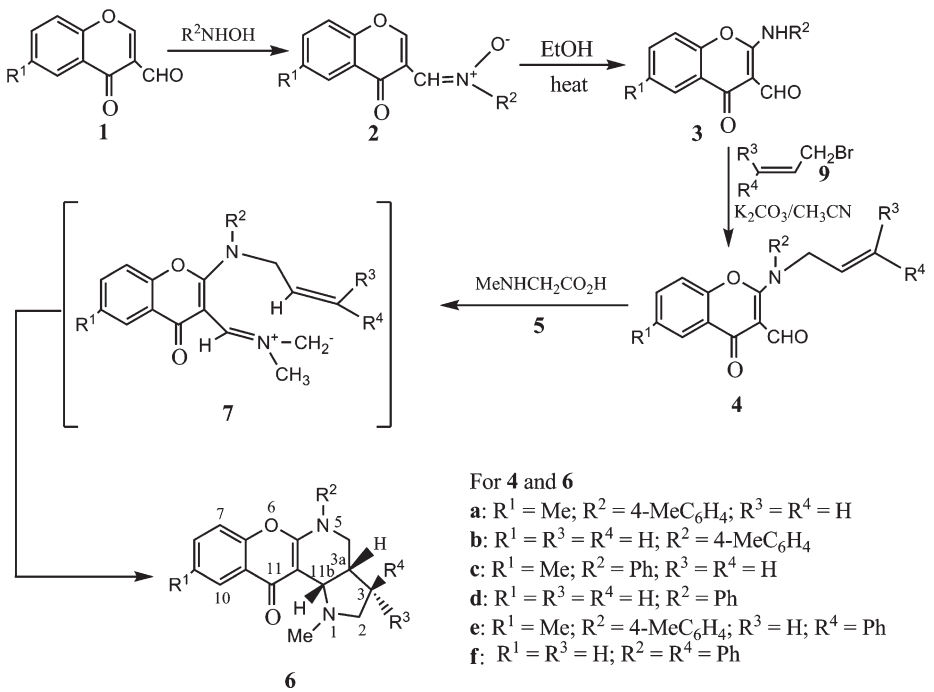
Ar stands for 4-MeC_6H_4; MW stands for microwave irradiation.

attempts for the intramolecular nitrone–olefin cycloaddition reaction using *N*-allyl-*N*-arylamino-3-formylchromone (**4**) led to nitrone–amide rearrangement. However, intramolecular [3+2] cycloaddition was accomplished only under cold condition using MeNHOH as nitrone precursor [10]. Our recent interest on azomethine ylides [40,41] prompted us to generate azomethine ylide on **4**. Earlier reports on the reaction of sarcosine (**5**) with **1** revealed that azomethine ylide derived from **1** and **5** underwent [3+2] cycloaddition and electrocyclic ring closure reactions [40,42–44]. We report herein the results of intramolecular [3+2] cycloaddition reactions involving azomethine ylide derived from **4** and **5** under various conditions.

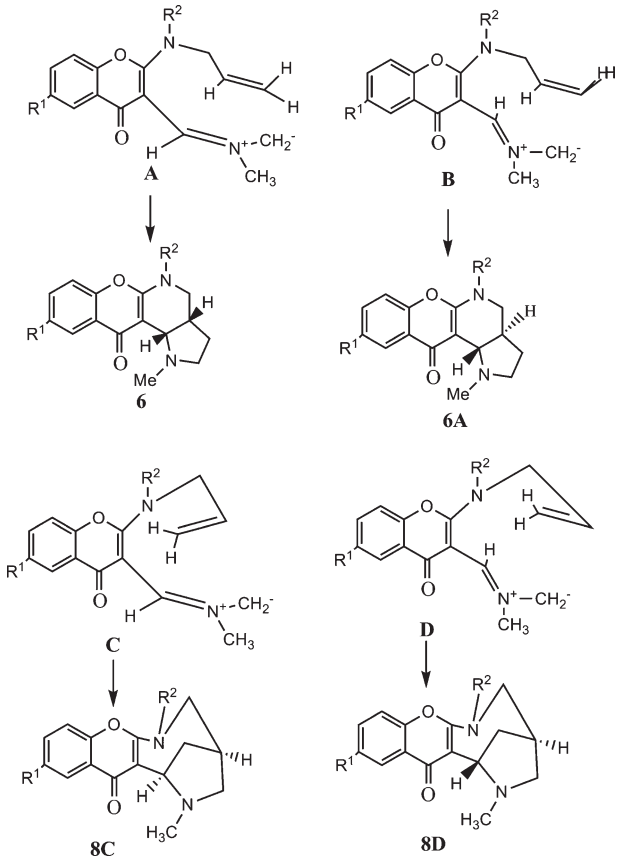
RESULTS AND DISCUSSION

On heating an equimolar mixture of **4** ($R^3 = R^4 = H$) and **5** in methanol under reflux for 30 h produced no suitable result (Table 1, entry 1), but produced **6** (R^3 =

Scheme 1



Scheme 2



R^4 = H) in 64% yield when heated in toluene for 26 h (entry 2; Scheme 1). Addition of TsOH in the above reaction mixture showed adverse effect and no suitable product was isolated (entry 3). Compound **6** with different substituents was synthesized by heating **4** (R^3 = R^4 = H) and **5** in freshly distilled toluene for 25–30 h (entries 4–6). Use of DMF as solvent in the presence of Et_3N shortens the reaction time markedly but isolated yield of **6** was poor (entry 7). When an equimolar mixture of **4** and **5** was irradiated by microwave, surprisingly, it yielded **6** within 3–5 min in moderate to good yields (entries 8–11). Compound **4** (R^3 = H, R^4 = Ph) produced **6** (R^3 = H, R^4 = Ph) in better yield both by classical heating (entries 12 and 13) and by microwave-induced cycloaddition reaction (entries 14 and 15). Although microwave irradiation does not improve the yield, it shortens the reaction time markedly. When the above reactions were performed under sonication, the reactions were not complete even after 40 h.

The structure of compound **6** was established on the basis of IR, ^{1}H-NMR, ^{13}C–NMR, and mass spectral analysis. Formation of **6** may be rationalized as follows: compound **4** reacts with **5** to produce an azomethine ylide intermediate **7** (Scheme 1), which undergoes intramolecular [3+2] cycloaddition reaction to give **6**. Structure of **6** was supported by its mass spectrum. ^{1}H-NMR spectrum of **6** showed the disappearance of vinylic as well as aldehydic protons of **4**. The stereochemistry of C/D ring juncture of **6** deserves special mention. Literature survey revealed that reduced form of pyrano[4,3-*b*]pyrrole system exhibited trans-fusion with *J*-values 10–12 Hz and corresponding cis-fusion with *J*-values 5–7 Hz in their ^{1}H-NMR spectra [11,15,45–47]. However, a recent report claimed that reduced form of pyridino[4,3-*c*]isoxazole in the trans-fused condition exhibited negligible coupling (broad singlet) [10]. In the ^{1}H-NMR spectrum of **6**, C_{11b}—H appears around δ 3.7 (for **6a**–**6d**) and around δ 4.3 (for **6e**, **6f**) with a small coupling constant (J = 3–5 Hz), which supports cis-fusion [15,45–47]. ^{1}H NOESY experiments on **6a** exhibited a very strong cross peak between protons C_{3a}—H and C_{11b}—H. This corroborates the cis-fusion. The C—H attachments were established with the help of ^{1}H–^{13}C correlation spectroscopy. Irradiation of proton at C_{11b} showed NOE enhancement of the signal for the proton at C_{3b}, which further supports the cis-fusion.

The probable modes of approaches of the 1,3-dipolar azomethine ylide and olefin moieties in the intermediate **7** were considered (Scheme 2). Of the four probable approaches (**A**–**D**), **A** or **B** and **C** or **D** can produce two different regiomers **6** and **8**, respectively.

For a critical understanding of the mechanistic pathways for the regio- and stereoselective formation of the various possible products, a detailed density functional theory (DFT) computation was performed at the B3LYP/6-31+G(d) level [48–50]. All the calculations were performed in Gaussian 03 suite of program [51]. Geometry optimization was performed on all the structures without any symmetry constraints for locating the minimum energy structures as well as the transition-state geometries. Additional frequency calculations were performed on all the geometries to confirm the absence of any imaginary frequencies in the harmonic vibrational modes for the minimum energy structures and one imaginary mode corresponding to the saddle—points in the transition states (TSs). The reactive intermediate **7** (Scheme 1) can exist in two isomeric forms **A** or **B**

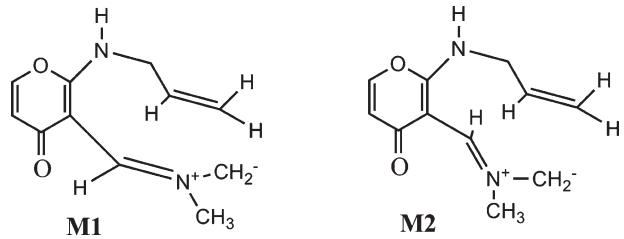


Figure 1. Model structures for DFT calculation.

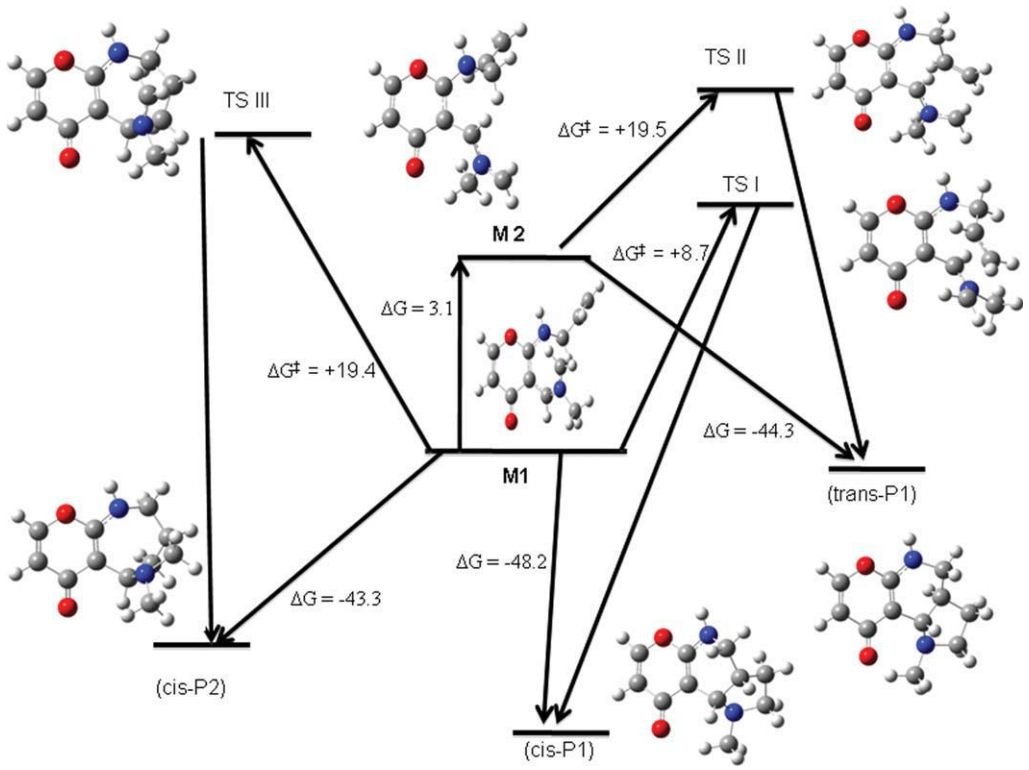


Figure 2. Exothermicity (ΔG) and free energies for activation ($\Delta G^{\ddagger}$; in kcal/mol) of the various pathways leading to different products. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

(Scheme 2), which are designated by **M1** and **M2**, respectively, in the model (Fig. 1), which keep the active reaction site similar to that of the experimental molecules.

M1 having cis relationship between CH_2^- and chromonyl moiety is more stable than **M2**, where the relationship is trans by 3.1 kcal/mol (Fig. 2). Although the low energy intermediate (**M1**) can produce two regiomers **cis-P1** and product **cis-P2** *via* the TSs TSI ($\Delta G^{\ddagger} = 8.7$ kcal/mol) and TS III ($\Delta G^{\ddagger} = 19.4$ kcal/mol), respectively, the high energy intermediate (**M2**) can produce only **trans-P1** *via* TS II ($\Delta G^{\ddagger} = 19.5$ kcal/mol). An attempt to get an energy-minimized structure of the model compound corresponding to **8D** (Scheme 2), the corresponding cis-isomer (**cis-P2**) was obtained, hence, the possibility of getting other regiomer from **M2** was ruled out. The energy profile diagram (Fig. 2) explains the preferable formation of cis-isomer *via* the TS TSI and this finding corroborates the results of the spectral analysis. So, both kinetic and thermodynamic preferences for the regio- and stereoselective synthesis of **6** may be predicted.

CONCLUSIONS

In conclusion, we have reported a microwave-accelerated intramolecular [3+2] cycloaddition reaction involving azomethine ylide. This led to a one-pot regio- and stereoselective synthesis of hitherto unreported chromone-fused pyrrolidino-piperidines in moderate yields. The selectivities have been supported by DFT calculations.

EXPERIMENTAL

General. The recorded melting points 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 in $CDCl_3$ unless stated otherwise, 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 are of commercial grade and are used as such.

General procedure for the synthesis of 2-[*N*-aryl-*N*-allylamino]-4-oxo-4*H*-1-benzopyran-3-carboxaldehyde (4a–f). A mixture of **3** (4 mmol), anhydrous K_2CO_3 (2 g), NaI (50 mg), and **9** [8 mmol for ($R^3 = R^4 = H$) and 6 mmol for ($R^3 = H$; $R^4 = Ph$)] in dry acetonitrile (100 mL) was heated under reflux with stirring for 9 h. The reaction mixture was filtered hot and the residue was washed with acetonitrile. All the washings and the filtrate were mixed together and solvent was removed under reduced pressure. The residue was purified by column chromatography over silica gel using 10% ethyl acetate in benzene as eluent to produce white crystalline solid **4**.

6-Methyl-2-[N-(4-methylphenyl)-N-(prop-2-enyl)]amino-4-oxo-4H-1-benzopyran-3-carboxaldehyde (4a). Yield 80%,

mp 164–166°C; IR (KBr) ν_{max}: 2910, 1680, 1665, 1614, 1590 cm^{-1}; ^{1}H-NMR: δ 2.33 (s, 3H), 2.44 (s, 3H), 4.56 (brs, 2H), 5.22 (brd, J = 11.4 Hz, 1H), 5.27 (brd, J = 20.1 Hz, 1H), 5.92–6.01 (m, 1H), 7.08–7.20 (m, 5H), 7.42 (brd, J = 7.8 Hz, 1H), 7.98 (brs, 1H), 9.98 (s, 1H). Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.80; H, 5.65; N, 4.10.

[N-(4-Methylphenyl)-N-(prop-2-enyl)]amino-4-oxo-4H-1-benzopyran-3-carboxaldehyde (4b). Yield 77%, mp 116–118°C; IR (KBr) ν_{max}: 2985, 1676, 1660, 1615, 1510 cm^{-1}; ^{1}H-NMR: δ 2.34 (s, 3H), 4.59 (d, J = 4.8 Hz, 2H), 5.23 (brd, J = 10.8 Hz, 1H), 5.29 (brd, J = 20.7 Hz, 1H), 5.91–6.01 (m, 1H), 7.05–7.20 (m, 4H), 7.25 (brd, J = 8.4 Hz, 1H), 7.37–7.42 (m, 1H), 7.59–7.64 (m, 1H), 8.20 (brd, J = 7.5 Hz, 1H), 9.99 (s, 1H). Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.08; H, 5.22; N, 4.28.

6-Methyl-4-oxo-2-[N-(phenyl)-N-(prop-2-enyl)]amino-4H-1-benzopyran-3-carboxaldehyde (4c). Yield 75%, mp 162–164°C; IR (KBr) ν_{max}: 3010, 1690, 1665, 1610, 1500 cm^{-1}; ^{1}H-NMR: δ 2.45 (s, 3H), 4.61 (d, J = 3.9 Hz, 2H), 5.23 (brd, J = 10.2 Hz, 1H), 5.29 (brd, J = 17.7 Hz, 1H), 5.93–6.02 (m, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.23–7.26 (m, 3H), 7.34–7.39 (m, 2H), 7.43 (brd, J = 8.4 Hz, 1H), 7.99 (brs, 1H), 9.99 (s, 1H). Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.10; H, 5.29; N, 4.30.

4-Oxo-2-[N-(phenyl)-N-(prop-2-enyl)]amino-4H-1-benzopyran-3-carboxaldehyde (4d). Yield 75%, mp 132–134°C (lit. [35] mp 110–111°C); IR (KBr) ν_{max}: 3005, 1685, 1660, 1640, 1515 cm^{-1}; ^{1}H-NMR: δ 4.62 (d, J = 5.4 Hz, 2H), 5.24 (d, J = 10.5 Hz, 1H), 5.30 (d, J = 17.0 Hz, 1H), 5.92–6.04 (m, 1H), 7.22–7.27 (m, 4H), 7.35–7.43 (m, 3H), 7.63 (dt, J = 7.2, 1.2 Hz, 1H), 8.20 (dd, J = 7.8, 1.2 Hz, 1H), 10.00 (s, 1H). Anal. Calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59. Found: C, 74.66; H, 4.84; N, 4.45.

6-Methyl-2-[N-(4-methylphenyl)-N-(3-phenylprop-2(E)-enyl) amino]-4-oxo-4H-1-benzopyran-3-carboxaldehyde (4e). Yield 75%, mp 178–80°C; IR (KBr) ν_{max}: 3050, 1682, 1640, 1520, 1423 cm^{-1}; ^{1}H-NMR: δ 2.33 (s, 3H), 2.44 (s, 3H), 4.71 (d, J = 5.7 Hz, 2H), 6.31 (td, J = 15.9, 5.7 Hz, 1H), 6.57 (d, J = 15.9 Hz, 1H), 7.10–7.20 (m, 5H), 7.23–7.33 (m, 5H), 7.41 (dd, J = 8.4, 1.5 Hz, 1H), 7.98 (brs, 1H), 10.01 (s, 1H). Anal. Calcd for $C_{27}H_{23}NO_3$: C, 79.20; H, 5.66; N, 3.42. Found: C, 79.35; H, 5.53; N, 3.32.

4-Oxo-2-[N-(phenyl)-N-(3-phenylprop-2(E)-enyl)amino]-4H-1-benzopyran-3-carboxaldehyde (4f). Yield 75%, mp 142–144°C (lit. [35] mp 117–118°C); IR (KBr) ν_{max}: 3058, 1675, 1633, 1515, 1428 cm^{-1}; ^{1}H-NMR: δ 4.76 (d, J = 6.0 Hz, 2H), 6.32 (td, J = 15.6, 6.0 Hz, 1H), 6.59 (d, J = 15.6 Hz, 1H), 7.27–7.42 (m, 12H), 7.62 (brt, J = 7.5Hz, 1H), 8.20 (brd, J = 7.8 Hz, 1H), 10.03 (s, 1H). Anal. Calcd for $C_{25}H_{19}NO_3$: C, 78.72; H, 5.02; N, 3.67. Found: C, 78.60; H, 4.92; N, 3.58.

General procedure for the synthesis of 1-benzopyrano[2,3-*b*]pyrrolo[2,3-*d*]pyridines (6a–f). Method A: A mixture of **4** (1 mmol) and **5** (1 mmol) was heated under reflux in freshly distilled toluene (15 mL) for several hours (Table 1). The progress of the reaction was monitored by TLC. Solvent from the reaction mixture was removed under reduced pressure. The residual mass was dissolved in $CHCl_3$, the organic extract was washed with water, dried over Na_2SO_4, and chromatographed over silica gel (100–200) using 10% methanol in ethyl acetate to afford **6a–6d** as a white crystalline solid, and **6e** and **6f** were obtained as a semisolid mass when eluted with 1:1 benzene–ethyl acetate mixture.

Method B: A well-ground mixture of **4** (1 mmol) and **5** (1.1 mmol) in a small conical flask was irradiated in a domestic microwave oven (Bajaj 1700MT, operating frequency 2450 MHz, 1200 W) with full capacity for 3–5 min. Absence of **4** in the reaction mixture was monitored by TLC. The resultant mixture was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with water and dried over Na_2SO_4, and compound **6** was isolated by column chromatography as described above.

1,9-Dimethyl-2,3,4,5,3a,11b-hexahydro-5-(4-methylphenyl)-1-benzopyrano[2,3-b]pyrrolo[2,3-d]pyridine-11H-11-one (6a). Yield 64%, mp 198–200°C; IR (KBr) ν_{max}: 3050, 2783, 1650, 1613, 1546 cm^{-1}; ^{1}H-NMR: δ 1.44–1.47 (m, 1H), 2.12–2.19 (m, 1 H), 2.25–2.27 (m, 1H), 2.39 (s, 3H), 2.40 (s, 3H), 2.41–2.44 (m, 1H), 2.51 (s, 3H), 3.12–3.17 (m, 1H), 3.44 (dd, J = 12.0, 5.7 Hz, 1H), 3.68 (d, J = 4.5 Hz, 1H), 3. 85 (t, J = 11.4 Hz, 1H), 6.91 (d, J = 8.1 Hz, 1H), 7.19–7.27 (m, 5H), 7.95 (brs, 1H); ^{13}C-NMR: δ 20.8, 21.0, 26.4, 32.8, 40.8, 53.6, 53.9, 58.4, 95.1, 115.9, 122.6, 125.2, 125.8 (2 C), 129.6 (2 C), 132.6, 134.0, 136.6, 139.3, 150.9, 159.0, 175.5; mass *m/z* 361 ($M + H^+$). Anal. Calcd for $C_{23}H_{24}N_2O_2$: C, 76.64; H, 6.71; N, 7.77. Found: C, 76.80; H, 6.80; N, 7.69.

2,3,4,5,3a,11b-Hexahydro-1-methyl-5-(4-methylphenyl)-1-benzopyrano[2,3-b]pyrrolo[2,3-d]pyridine-11H-11-one (6b). Yield 65%, mp 182–184°C; IR (KBr) ν_{max}: 3010, 2920, 1640, 1612 cm^{-1}; ^{1}H-NMR: δ 1.26–1.38 (m, 1H), 1.65–1.75 (m, 1H), 2.30–2.41 (m, 1H), 2.41 (s, 3H), 2.43–2.53 (m, 1H), 2.78 (s, 3H), 3.52–3.62 (m, 2H), 4.20–4.28 (m, 2H), 7.01 (d, J = 7.8 Hz, 1H), 7.26–7.29 (m, 4H), 7.43–7.46 (m, 2H), 8.11 (brd, J = 6.9 Hz, 1H). Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.39; H, 6.31; N, 7.94.

1,9-Dimethyl-2,3,4,5,3a,11b-hexahydro-5-phenyl-1-benzopyrano[2,3-b]pyrrolo[2,3-d]pyridine-11H-11-one (6c). Yield 62%, mp 168–170°C; IR (KBr) ν_{max}: 3007, 2910, 1650, 1620 cm^{-1}; ^{1}H-NMR: δ 1.42–1.52 (m, 1H), 2.10–2.20 (m, 1H), 2.28–2.29 (m, 1H), 2.40 (s, 3H), 2.40–2.50 (m, 1H), 2.50 (s, 3H), 3.11–3.17 (m, 1H), 3.46–3.51 (m, 1H), 3.71 (d, J = 3.9 Hz, 1H), 3. 88 (t, J = 11.7 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 7.23–7.27 (m, 1H), 7.29–7.34 (m, 3H), 7.41–7.46 (m, 2H), 7.96 (brs, 1H). Anal. Calcd for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.40; H, 6.48; N, 7.98.

2,3,4,5,3a,11b-Hexahydro-1-methyl-5-phenyl-1-benzopyrano[2,3-b]pyrrolo[2,3-d]pyridine-11H-11-one (6d). Yield 60%, mp 162–164°C; IR (KBr) ν_{max}: 3054, 2930, 1660, 1613, 1546 cm^{-1}; ^{1}H-NMR: δ 1.42–1.52 (m, 1H), 2.11–2.21 (m, 1H), 2.24–2.29 (m, 1H), 2.41–2.50 (m, 1H), 2.50 (s, 3H), 3.11–3.16 (m, 1H), 3.49 (dd, J = 11.7, 5.5 Hz, 1H), 3.70 (d, J = 4.5 Hz, 1H) 3.89 (t, J = 11.7 Hz, 1H), 7.01 (brd, J = 8.4 Hz, 1H), 7.27–7.36 (m, 4H), 7.42–7.47 (m, 3H), 8.17 (dd, J = 7.8, 0.9 Hz, 1H). Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.95; H, 5.98; N, 8.34.

1,9-Dimethyl-2,3,4,5,3a,11b-hexahydro-5-(4-methylphenyl)-3-phenyl-1-benzopyrano[2,3-b]pyrrolo[2,3-d]pyridine-11H-11-one (6e). Yield 75%, semisolid mass; IR (KBr) ν_{max}: 3014, 2910, 1672, 1610, 1556 cm^{-1}; ^{1}H-NMR: δ 0.86–0.88 (m, 1H), 2.40 (s, 6H), 2.42–2.48 (m, 1H), 2.62 (s, 3H), 2.99–3.05 (m, 1H), 3.62–3.73 (m, 2H), 4.01 (t, J = 11.4 Hz, 1H), 4.28 (d, J = 5.1 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 7.17–7.31 (m, 10H), 7.96 (brs, 1H); ^{13}C-NMR: δ 20.8, 21.0, 40.7, 42.1, 46.6, 52.7, 59.6, 63.5, 93.7, 116.1, 122.3, 125.2, 125.8 (2 C), 126.8, 127.4 (2 C), 128.7 (2 C), 129.8 (2 C), 133.0, 134.3, 136.9, 138.9, 143.2, 151.0, 159.4, 175.8; mass *m/z* 437 ($M + H^+$), 459 (M

+ Na^+). Anal. Calcd for $C_{29}H_{28}N_2O_2$: C, 79.79; H, 6.46; N, 6.42. Found: C, 79.71; H, 6.52; N, 6.36.

3,5-Diphenyl-2,3,4,5,3a,11b-hexahydro-1-methyl-1-benzopyrano[2,3-b]pyrrolo[2,3-d]pyridine-11H-11-one (6f). Yield 81%, semisolid mass; IR (KBr) ν_{max}: 3010, 2920, 1680, 1615 cm^{-1}; ^{1}H-NMR: δ 0.86–0.88 (m, 1H), 2.43 (brs, 1H), 2.64 (s, 3H), 2.91–3.08 (m, 1H), 3.61–3.70 (m, 2H), 4.03 (t, J = 11.0 Hz, 1H), 4.21 (brs, 1H), 7.02 (brd, J = 8.1 Hz, 1H), 7.25–7.46 (m, 12H), 8.19 (brd, J = 7.2 Hz, 1H). Anal. Calcd for $C_{27}H_{24}N_2O_2$: C, 79.39; H, 5.92; N, 6.86. Found: C, 79.48; H, 5.83; N, 6.76.

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REFERENCES AND NOTES

[1] Nair, V.; Suja, T. D. Tetrahedron 2007, 63, 12247.

[2] Confalone, P. N.; Huie, E. M. Org React 1988, 36, 1.

[3] Carruthers, W.; Coggins, P.; Weston, J. B. J Chem Soc Perkin Trans 1 1990, 2323.

[4] Rong, J.; Roselt, P.; Plavec, J.; Chattopadhyay, J. Tetrahedron 1994, 50, 4921.

[5] Ihara, M.; Takahashi, M.; Fukumoto, K.; Kametani, T. J Chem Soc Chem Commun 1988, 9.

[6] Bhattacharjya, A.; Chattopadhyay, P.; McPhail, A. T.; McPhail, D. R. J Chem Soc Chem Commun 1990, 1508.

[7] Broggini, G.; Folcio, F.; Sardone, N.; Zecchi, G. Tetrahedron 1996, 52, 11849.

[8] Broggini, G.; Zecchi, G. Synthesis 1996, 1280.

[9] Gotoh, M.; Mizui, T.; Sun, B.; Hirayama, K.; Noguchi, M. J Chem Soc Perkin Trans 1 1995, 1857.

[10] Singh, G.; Ishar, M. P. S.; Gupta, V.; Singh, G.; Kalyan, M.; Bhella, S. S. Tetrahedron 2007, 63, 4773.

[11] Confalone, P. N.; Huie, E. M. J Am Chem Soc 1984, 106, 7175.

[12] Wenkert, D.; Ferguson, S. B.; Porter, B.; Qvarnstorm, A.; McPhail, A. T. J Org Chem 1985, 50, 4114.

[13] Vedejs, E.; Piotrowski, D. W.; Tucci, F. C. J Org Chem 2000, 65, 5498.

[14] Coldham, I.; Crapnell, K. M.; Moseley, J. D.; Robot, R. J Chem Soc Perkin Trans 1 2001, 1758.

[15] Novikov, M. S.; Khlebnikov, A. F.; Besidina, O. V.; Kastikov, R. R.; Tetrahedron Lett 2001, 42, 533.

[16] Lundahl, K.; Schutt, J.; Schlatmann, J. L. M. A.; Paerels, G. B.; Peters, A. J Med Chem 1972, 15, 129.

[17] Kornett, M. J.; Thio, A. P. J Med Chem 1976, 19, 892.

[18] Abou-Gharbia, M. A.; Doukas, P. H. Heterocycles 1979, 12, 637.

[19] Dubuffet, T.; Muller, O.; Simonef, S. S.; Descomhes, J.-J.; Laubie, M.; Verheuren, T. J.; Lavidle, G. Bioorg Med Chem Lett 1996, 6, 349.

[20] Dubuffet, T.; Newman-Tancerdi, A.; Cussac, D.; Audinot, V.; Loutz, A.; Millan, M. J.; Lavielle, G. Bioorg Med Chem Lett 1999, 9, 2059.

[21] Guillo, L. A.; Beylot, B.; Vigny, P.; Spassky, A. Photochem Photobiol 1996, 64, 349.

[22] Guinn, D. E.; Summers, J. B.; Heyman, H. R.; Conway, R. G.; Rhein, D. A.; Albert, D. H.; Magoc, T.; Carter, G. W. J Med Chem 1992, 35, 2055.

[23] Kumar, R. R.; Perumal, S. Tetrahedron 2007, 63, 12220.

[24] Houghton, P. J.; Woldemariam, T. Z.; Mahmood, N. J Pharm Pharmacol 1994, 46, 1061.

[25] Houghton, P. J.; Woldemariam, T. Z.; Khan, A. I.; Mahmood, N. Antivir Res 1994, 25, 235.

[26] Suresh Babu, A. R.; Raghunathan, R. Tetrahedron Lett 2007, 48, 6809.

[27] Ramesh, E.; Kathiresan, M.; Raghunathan, R. Tetrahedron Lett 2007, 48, 1835.

[28] Ramesh, E.; Raghunathan, R. Tetrahedron Lett 2008, 49, 1125.

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

[30] Ishar, M. P. S.; Kumar, K.; Singh, R. Tetrahedron Lett 1998, 39, 6547.

[31] Ghosh, T.; Bandyopadhyay, C. Tetrahedron Lett 2004, 45, 6169.

[32] Singh, G.; Singh, L.; Ishar, M. P. S. Tetrahedron 2002, 58, 7883.

[33] Sattofattori, E.; Anzaldi, M.; Balbi, A.; Artali, R.; Bombieri, G. Helv Chim Acta 2002, 85, 1698.

[34] Singh, G.; Singh, G.; Ishar, M. P. S. Synlet 2003, 256.

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

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

[37] Maiti, S.; Panja, S. K.; Bandyopadhyay, C. Indian J Chem B 2009, 48, 1447.

[38] Maiti, S.; Panja, S. K.; Bandyopadhyay, C. J Heterocycl Chem 2010, 47, 973.

[39] Panja, S. K.; Maiti, S.; Drew, M. G. B.; Bandyopadhyay, C. Tetrahedron 2009, 65, 1276.

[40] Ghosh, T.; Bandyopadhyay, C. J Chem Res 2007, 190.

[41] Panja, S. K.; Karmakar, P.; Chakraborty, J.; Ghosh, T.; Bandyopadhyay, C. Tetrahedron Lett 2008, 49, 4397.

[42] Clarke, P. D.; Fitton, A. O.; Kosmirak, M.; Suschitzky, H.; Suschitzky, J. L. J Chem Soc Perkin Trans 1 1985, 1747.

[43] de la Torre, M. D. L.; Rodrigues, A. G. P.; Tome, A. C.; Silva, A. M. S.; Cavaleiro, J. A. S. Tetrahedron 2004, 60, 3581.

[44] Figueiredo, A. G. P. R.; Tome, A. C.; Silva, A. M. S.; Cavaleiro, J. A. S. Tetrahedron 2007, 63, 910.

[45] Barr, D. A.; Grigg, R.; Gunaratne, H. Q. N.; Kemp, J.; McMeekin, P.; Sridharan, V. Tetrahedron 1988, 44, 557.

[46] Grigg, R.; Donegan, G.; Gunaratne, H. Q. N.; Kennedy, D. A.; Malone, J. F.; Sridharan, V.; Thianpatanagul, S. Tetrahedron 1989, 45, 1723.

[47] Najdi, S.; Park, K.-H.; Olmstead, M. M.; Kruth, M. J. Tetrahedron Lett 1998, 39, 1685.

[48] Becke, A. D. J Chem Phys 1993, 98, 5648.

[49] Lee, C.; Yang, W.; Parr, R. G. Phys Rev B 1988, 37, 785.

[50] Hariharan, P. C.; Pople, J. A. Theor Chim Acta 1973, 28, 213.

[51] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Vreven, T., Jr.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Mallick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian 03, Revision C.01; Gaussian, Inc.: Wallingford CT, 2004.