The Facile and Efficient Three-Component One-Pot Mannich-Type Reaction of Indoles Catalyzed by $In(OTf)_3$ Under Microwave Irradiations

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Abstract: Indium triflate catalysed the three-component one-pot reaction of indole **1** with a heteroimine generated *in situ* under microwave irradiations and afforded predominately secondary indolyl amines **4** in excellent yields as well as bisindolyl methane **5** in poor yields. The catalyst indium triflate can be recovered after the reaction and reused in the subsequent experiments.

Keywords: Indoles, indium triflate, microwave irradiations, multicomponent reactions, Mannich-type reactions, bisindolyl methane.

INTRODUCTION

In recent years, indoles [1], chromones [2] and their derivatives occupied an unique place in medicinal and synthetic organic chemistry due to their wide range of biological activities. Indole, being an integral part of many natural products of therapeutic importance, possesses potentially reactive sites for a variety of chemical reactions to generate molecular diversity. Bisindolyl alkanes and their analogues constitute an important group of bioactive metabolites of terrestrial and marine origin [3]. Over the past few years a variety of methods has been developed for the synthesis of 3-substituted indoles [4,5]. Of these, the Mannich [6], Michael [7] and Vilsmeier-Haack [8] reactions have been studied extensively. The application of the Vilsmeier-Haack reaction to form long acyl chain derivatives usually proceeds in low yields [9]. Acid catalysed electrophilic substitution of indoles requires careful control of acidity to prevent side reactions such as dimerization and polymerization [10]. Other less used method for the 3- substitution of indole have also been reported, but they have their own limitations. Thus treatment of indole with various isocyanates is reported to afford 3-amidoindoles, a method attempted with a limited array of substrates [11]. Reaction of indole with lactams has been reported to generate 3-(iminyl)indoles, which can be hydrolyzed to generate *o*-aminoacyl groups [12]. Various 3-aminomethyl indole derivatives have been synthesized, but they are reported to be intrinsically unstable [13]. Therefore we sought to find a method for the direct synthesis of substituted 3-aminomethyl indoles, by employing a three-component one-pot reaction strategy.

In continuation to our studies on indoles and indium metals [14], we have investigated herein a new indium-catalyzed three-component one-pot reaction under microwave irradiations, for the synthesis of novel 3-[3'-(aryliminomethyl) benzopyranyl]indoles **4** in high yields. The catalyst indium triflate can be recovered after the reaction quantitatively and reused in the subsequent runs.

Being a one-pot reaction, generally multi-component reactions afford good yields and are fundamentally different from two-component reactions in several aspects [15]. The design of multicomponent reactions (MCR) is an important field of research from point of view of combinatorial chemistry [16]. In the past decade there has been tremendous development in three- and four-component reactions involving Passerini- [17], Ugi- [18] and Mannich-type reactions [19] and great efforts have been and still are being made to find and develop new MCRs [20].

RESULTS AND DISCUSSION

In a typical case, equimolar quantities of 3-formyl chromone and *p*-anisidine were taken in the reaction vassel of the microwave reactor (Synthwave 402 Monomod Reactor from Prolabo) and stirred at room temperature for 5 min. To this 3 equivalent of indole and one equivalent of indium triflate was then added and the resulting mixture was allowed to react under microwave irradiation at 60% power for 5 min. The automatic mode stirrer helps in mixing and uniform heating of the reactants. After completion (monitored by TLC), and on usual work-up the corresponding secondary amine, 3-[3'-(*p*-anisylaminomethyl)benzopyran]indole **4c** was obtained in 80% yield as the main product and benzopyran bisindolyl methane **5a** as the other product in 15% yield.

Rate enhancement of the reaction was observed when 1.5 or 2 equivalent of $In(OTf)_3$ was used but relatively lower yield (70% or 60%) was obtained due to decomposition of the starting material. Moreover, use of lesser amount 0.5 equivalent of $In(OTf)_3$ led to weaker results (40-50%) in longer reaction time. In view of the current interest in environmentally benign catalytic processes, a protocol involving a lower amount of $In(OTf)_3$ would be more appreciable, so we decided to extend the scope of the reaction using only 1 equivalent of the catalyst. Similarly, other primary amines were then reacted with indole and 3-formyl chromone and

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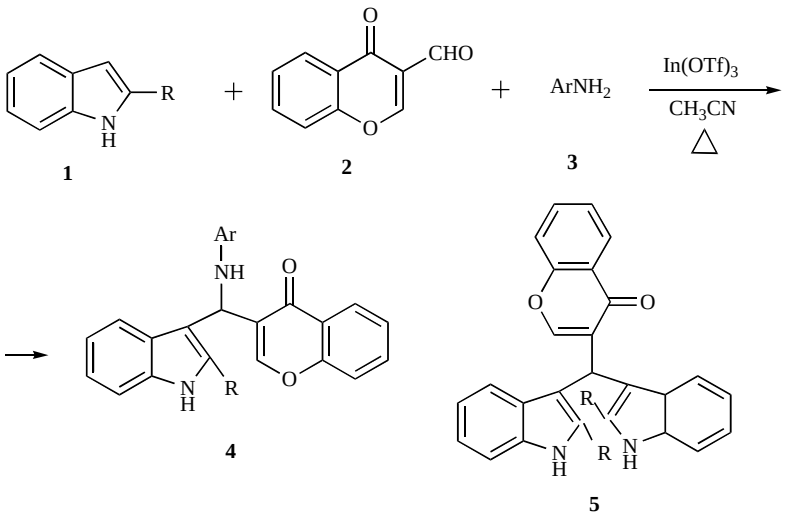


	Ar	R		Ar	R
4a	C_6H_5	H	**4f**	*4*-$N0_2C_6H_4$	H
4b	*4*-MeC_6H_4	H	**4g**	*4*-ClC_6H_4	CH_3
4c	*4*-$Me0C_6H_4$	H	**4h**	*4*-BrC_6H_4	CH_3
4d	*4*-BrC_6H_4	H	**4i**	*4*-$Me0C_6H_4$	CH_3
4e	*4*-ClC_6H_4	H			

Scheme 1.

the corresponding secondary indolyl amines **4b-i** were isolated in 70-82% yields along with bisindolyl methanes **5** (Table **1**). The reaction also proceeded effectively when aromatic aldehydes were employed in lieu of benzopyran 3-carboxaldehyde and the corresponding secondary indolyl amines were obtained in almost comparable yields. Keeping in view the biological significance of benzopyran unit, we have concentrated our studies on 3-formyl chromones only. All the compounds thus obtained were characterised fully by ^{1}H NMR, MS and IR spectroscopy. It is noteworthy that the reaction is not effective when 3-formyl chromone, primary amines and indole were reacted in equimolar quantities in presence of $In(OTf)_3$ and the secondary indolyl amines were obtained in 30-35% yields (entry **1** & **2**). However, when two equivalents of indoles were used, the yield of the products is increased upto 40%. The optimum yields were obtained by using three equivalents of indoles.

Under this reaction condition, we then investigated the Mannich-type reaction using three different catalysts, such as $In(OTf)_3$, $Yb(OTf)_3$ and $Zn(OTf)_2$. Among these, indium triflate was found to give excellent conversions. For instance, 3-formyl chromone and indole with aniline under microwave irradiations gave 82%, 78% and 30% yields, respectively (entry **1**). In the absence of this catalyst, the reaction did not yield any fruitful result even after 10 min of microwave heating. Further increase of reaction time also did not yield any characterizable product rather decomposition of starting materials occurred. All reactions exhibited pronounced rate accelerations and high yields were obtained for

Table 1. $In(OTf)_3$ and $Yb(OTf)_3$ Catalyzed Mannich-Type Reaction of Indoles

Entry	Amines, 3	Reac. time, (min)	Products	M. P. (^{o}C)	Yield In, (%)	Yield[a,b]Yb, (%)	Products	Yield (%)
1	$C_6H_5NH_2$	5	4a	121-123	82	78	5a	10
2	4-$MeC_6H_4NH_2$	5	4b	177-179	80	75	5a	12
3	4-$MeOC_6H_4NH_2$	6	4c	153-155	80	73	5a	15
4	4-$BrC_6H_4NH_2$	5	4d	167-169	83	74	5a	12
5	4-$ClC_6H_4NH_2$	5	4e	154-156	81	76	5a	10
6	4-$NO_2C_6H_4NH_2$	6	4f	186-187	80	75	5a	10
7	4-$ClC_6H_4NH_2$	5	4g	207-208	71	70	5b	15
8	4-$BrC_6H_4NH_2$	5	4h	163-164	70	70	5b	12
9	4-$MeOC_6H_4NH_2$	6	4i	196-198	70	70	5b	10

[a]Isolated yields. [b]All products were characterized by ^{1}H NMR IR and mass spectra.

isolated products **4** with $In(OTf)_3$. In general, the reaction is very clean, rapid, efficient and involves simple work-up procedure. Encouraged by the results obtained with indium triflate, we then turned our attention toward the possibility of recycling the catalyst. Since the products secondary indolyl amines were soluble in chloroform, they could be easily separated by simple extraction with chloroform. The remaining residue containing the catalyst was reused in subsequent experiments with gradual decrease in activity. For example, 3-formyl chromone and *p*-anisidine with indole gave 80%, 76% and 70% yields over three cycles (entry **3**).

In an attempt to react the chromone imines directly with indole in presence of $In(OTf)_3$ in a two-component system was not effective. The corresponding secondary indolyl amines **4** were obtained in 35-40% yields only together with bisindolyl methanes. The formation of benzopyranyl bisindolyl methane was initially thought to be of the result of the reaction of 3-formylchromone which might exist in the system due to the hydrolysis of the chromone imines. So, to reduce the formation of this product we tried an experiment in anhydrous acetonitrile under microwave irradiations, which will minimize the hydrolysis, but the same product was obtained in 20% yields.

Furthermore, when 3-methyl indole was examined for the reaction with 3-formyl chromone and *p*-anisidine and since the C-3 position is blocked in this case, the reaction did not proceed at all during 10 min of microwave irradiation. However, with 2-methyl indole the reaction proceeds effectively under similar conditions. Notably, the reaction also proceeded thermally in refluxing acetonitrile (12-15 h) and the corresponding secondary indolyl amines **4b-i** and bisindolyl methane **5** were obtained in 78-82% and 10-15% yields respectively.

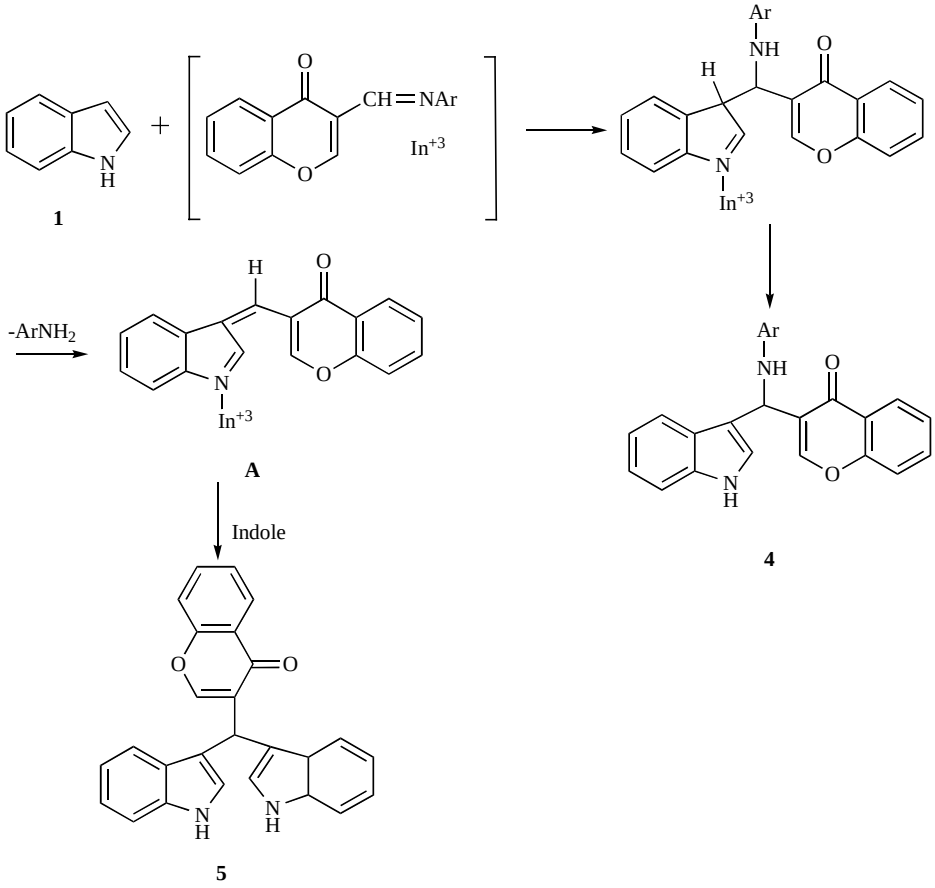
Although, the detailed mechanism of this reaction is not clear at this stage it is likely that the choromone imine generated *insitu* first activated by indium and carried out an electrophilic substitution reaction at the 3-position of indole. After loss of amine, an intermediate **A** is formed. This intermediate **A** is further activated by indium and served as an electrophile to attack a second molecule of indole to form 2+1 adduct **5** (Scheme **2**).

CONCLUSION

In conclusion, indium triflate was found to catalyze the electrophilic substitution reactions of indoles with a variety of chromone imines generated *insitu*. The reaction afforded secondary indolyl amines as the predominant products.

EXPERIMENTAL

Materials are obtained from commercial suppliers and are used without further purification. Melting points are determined by using a Buchi melting point apparatus and are uncorrected. IR spectra are recorded for KBr discs on a Perkin-Elmer 240C analyser. ^{1}H NMR spectra are recorded on 90



Scheme 2.

MHz spectrometers and chemical shift values are recorded in δ units (ppm) relative to Me_4Si as internal standard. The 300 MHz NMR spectra are recorded with tetramethylsilane as internal standard (by RSIC, Shillong). Mass spectra are recorded in an AEIMS-30 spectrometer. Elemental analyses are performed on a Hitachi 026 CHN analyser. All solvents are distilled before use. The progress of most reactions is monitored by TLC and chromatographic purification is performed with silica gel 60 (120 mesh, Merck).

General Procedure for the Preparation of Secondary Indolyl Amines (4) and Bisindolyl Methane (5) Under Microwave Irradiations in a Solvent-Free Condition

Equimolar quantities of 3-formyl chromone (0.17 g, 1 mmol) and *p*-anisidine (0.12 g, 1 mmol) were taken in the reaction vessel of the microwave reactor (Synthwave 402 Monomod Reactor from Prolabo) and stirred at room temperature for 5 min. To this 3 equivalent of indole (0.35 g, 3 mmol), and one equivalent of indium triflate (0.56 g, 1 mmol) was then added and the resulting mixture was allowed to react in a microwave reactor operating at 2450 MHz frequency at 60% power for 5 min. The automatic mode stirrer helps in mixing and uniform heating of the reactants. After completion (monitored by TLC), the resulting mixture was cooled to room temperature, extracted with chloroform and filtered. The residue thus obtained contains indium triflate and this can be reused directly in subsequent experiments. The chloroform extract was then dried over anhydrous sodium sulphate and removed in a rotary evaporator. The residue thus obtained was purified by column chromatography using chloroform as the eluent which afforded a secondary amine, 3-[3'-(*p*-anisylaminomethyl)benzopyran]-indole **4c** mp 153-155 °C in 80% yield as the main product and benzopyran bisindolylmethane **5a** as the byproduct mp 214-216 °C in 15% yield. Similarly other primary amines were reacted with indole or 2-methyl indole and 3-formyl chromone in a one-pot reaction and the corresponding secondary indolyl amines **4b-i** were isolated in (70-83)% yields. The reaction also yields bisindolyl methanes **5a-b** as the other products in 10-15% yields. All the compounds obtained are characterised fully by ^{1}HNMR, MS and IR spectroscopy.

3-[3'-(Phenylaminomethyl)benzopyran]indole (4a)

Yield 82%, m.p.: 121-123 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 3.40 (1H, br); 5.66 (1H, s); 6.68 (1H, d, J=2.5Hz); 7.10 (2H, m); 7.22-7.64 (11H, m); 7.91 (1H, s); 8.10 (1H, br); **^{13}C-NMR (50 MHz, $CDCl_3$)** δ=40.2, 110.7, 112.2, 115.2, 117.8, 120.1, 120.8, 122.1, 124.0, 124.2, 125.7, 125.9, 126.1, 128.8, 129.6, 134.1, 136.8, 153.9, 154.8, 176.6; **MS: *m/z*** = 366 (M^+); **Anal. Calcd for** $C_{24}H_{18}N_2O_{2+}$: C, 78.68; H, 4.92; N, 7.65; Found: C, 78.77; H, 5.02; N, 7.73; **IR (KBr), ν (cm^{-1}):** 3330, 1655, 1560, 1435, 1280, 1170, 895, 860, 835, 744.

3-[3'-(p-Tolylaminomethyl)benzopyran]indole (4b)

Yield 80%, m.p.: 177-179 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 2.10 (3H, s); 3.52 (1H, br); 5.76 (1H, s); 6.68 (1H, d, J=2.5Hz); 7.10 (2H, m); 7.22-7.60 (10H, m); 7.90 (1H, s); 8.12 (1H, br); **^{13}C-NMR (50 MHz, $CDCl_3$)** δ=34.2, 39.8, 110.4, 112.2, 114.8, 117.2, 120.2, 121.2, 122.6, 124.0, 124.6, 125.7, 126.1, 126.6, 128.8, 129.8, 133.8, 137.1, 154.0, 155.2, 175.7; **MS: *m/z*** = 380 (M^+); **Anal. Calcd. for** $C_{25}H_{20}N_2O_2$: C, 78.94; H, 5.26; N, 7.37; Found: C, 79.02; H, 5.15; N, 7.42; **IR (KBr), ν (cm^{-1}):** 3335, 1650, 1565, 1430, 1275 1180, 895, 860, 830, 745.

3-[3'-(p-Anisylaminomethyl)benzopyran]indole (4c)

Yield 80%, m.p.: 153-155 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 3.82 (3H, s); 3.45 (1H, br); 5.70 (1H, s); 6.62 (1H, d, J=2.5Hz); 7.02 (2H, m); 7.16-7.50 (10H, m); 7.85 (1H, s); 8.02 (1H, br); **^{13}C-NMR (50 MHz, CDCl3)** δ=41.2, 60.1, 110.6, 111.8, 115.2, 117.4, 120.2, 121.2, 122.4, 124.0, 124.2, 125.4, 126.0, 127.1, 128.8, 129.4, 134.8, 139.6, 154.2, 154.8, 175.6; **MS *m/z*** = 396 (M^+); **Anal. Calcd. for** $C_{25}H_{20}N_2O_3$: C, 75.76; H, 5.05; N, 7.07; Found: C, 75.66; H, 5.13; N, 6.98; **IR (KBr), ν (cm^{-1}):** 3340, 1650, 1560, 1430, 1280, 1175, 895, 855, 830, 740.

3-[3'-(p-Bromophenylaminomethyl)benzopyran]indole (4d)

Yield 83%, m.p.: 167-169 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 3.50 (1H, br); 5.75 (1H, s); 6.70 (1H, d, J=2.5Hz); 7.08 (2H, m); 7.20-7.56 (10H, m); 7.90 (1H, s); 8.10 (1H, br); **MS: *m/z*** = 445 (M^+); **Anal. Calcd. for** $C_{24}H_{17}N_2O_2Br$: C, 64.72; H, 3.82; N, 6.29; Found: C, 64.81; H, 3.91; N, 6.17; **IR (KBr), ν (cm^{-1}):** 3340, 1655, 1565, 1430, 1285, 1170, 890, 865, 835, 740.

3-[3'-(p-Chlorophenylaminomethyl)benzopyran]indole (4e)

Yield 81%, m.p.: 154-156 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 3.48 (1H, br); 5.75 (1H, s); 6.72 (1H, d, J=2.5Hz); 7.10 (2H, m); 7.22-7.62 (10H, m); 7.92 (1H, s); 8.10 (1H, br); **MS: *m/z*** = 400 (M^+); **Anal. Calcd. for** $C_{24}H_{17}N_2O_2Cl$: C, 72.00; H, 4.25; N, 7.00; Found: C, 72.10; H, 4.31; N, 6.95. **IR (KBr), ν (cm^{-1}):** 3340, 1655, 1560, 1430, 1285, 1175, 890, 860, 830, 745.

3-[3'-(p-Nitrophenylaminomethyl)benzopyran]indole (4f)

Yield 80%, m.p.: 186-187 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 3.45 (1H, br), 5.72 (1H, s), 6.75 (1H, d, J=2.5Hz); 7.12 (2H, m); 7.26-7.66 (10H, m); 7.88 (1H, s), 8.12 (1H, br); **MS: *m/z*** = 411 (M^+); **Anal. Calcd. for** $C_{24}H_{17}N_3O_4$: C, 70.07; H, 4.14; N, 10.22; Found: C, 70.16; H, 4.08; N, 10.31; **IR (KBr), ν (cm^{-1}):** 3340, 1655, 1565, 1430, 1280, 1170, 890, 855, 835, 740.

3-[3'-(p-Chlorophenylaminomethyl)benzopyran]-2-methylindole (4g)

Yield 71%, m.p.: 207-208 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 2.30 (3H, s); 3.45 (1H, br); 5.72 (1H, s); 7.20-7.66 (12H, m); 8.02 (1H, s); 8.15 (1H, br); **MS: *m/z*** = 414 (M^+); **Anal. Calcd. for** $C_{25}H_{19}N_2O_2Cl$: C, 72.46; H, 4.59; N, 6.76; Found: C, 72.37; H, 4.61; N, 6.83; **IR (KBr), ν (cm^{-1}):** 3342, 1642, 1542, 1455, 1260, 796, 772.

3-[3'-(p-Bromophenylaminomethyl)benzopyran]-2-methylindole (4h)

Yield 70%, m.p.: 163-164 °C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 2.25 (3H, s); 3.40 (1H, br); 5.76 (1H, s); 7.15-7.68 (12H, m); 7.98 (1H, s); 8.15 (1H, br); **MS: *m/z*** = 459 (M^+); **Anal. Calcd. for** $C_{25}H_{19}N_2O_2Br$: C, 65.35; H, 4.14; N, 6.10; Found: C, 65.42; H, 4.21; N, 6.02; **IR (KBr), ν (cm^{-1}):** 3342, 1648, 1550, 1450, 1262, 790, 762.

3-[3'-(p-Anisylaminomethyl)benzopyran]-2-methylindole (4i)

Yield 70%, m.p.: 194-196 ^{o}C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 2.34 (3H, s); 3.42 (1H, br); 3.86 (3H, s); 5.70 (1H, s); 6.68-7.52 (12H, m); 7.95 (1H, s); 8.10 (1H, br); **MS: *m/z*** = 410 (M^+); **Anal. Calcd. for** $C_{26}H_{22}N_2O_3$: C, 76.09; H, 5.36; N, 6.83. Found: C, , 76.16; H, 5.43; N, 6.77; **IR (KBr), ν (cm^{-1}):** 3340, 1652, 1550, 1432, 1280, 810, 740.

Benzopyran bisindolyl methane (5a)

Yield: 10-15%, m.p.: 214-216 ^{o}C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 5.82 (1H, s); 6.72 (1H, d); 6.98 (2H, m); 7.18-7.66 (12H, m); 7.90 (1H, s), 8.02 (1H, br); **MS: *m/z*** = 390 $(M)^+$; **Anal. Calcd. for** $C_{26}H_{18}N_2O_2$: C, 79.98; H, 4.65; N, 7.17; Found: C, 80.13; H, 4.45; N, 7.15; **IR (KBr), ν (cm^{-1}):** 3340; 1655; 1560.

Benzopyran bis-(2-methylindolyl)-methane (5b)

Yield 10-15%, m.p.: 175-176 ^{o}C; **^{1}H-NMR ($CDCl_3$), δ(ppm):** 2.38 (6H, s); 5.70 (1H, s); 7.08-7.68 (12H, m); 7.95 (1H, s); 8.12 (1H, br); **MS: *m/z*** = 418 (M^+); **Anal. Calcd. for** $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.26; N, 6.69; Found: C, 80.42; H, 5.32; N, 6.58; **IR (KBr), ν (cm^{-1}):** 3423; 1638; 1545.

General Procedure for the Preparation of Secondary Indolyl Amines and Bisindolyl Methane Under Thermolytic Conditions

In a 100 mL round bottomed flask 3-formyl chromone (0.17 g, 1 mmol) and *p*-anisidine (0.12 g, 1 mmol) were taken in 20 mL of distilled acetonitrile. The mixture was then stirred at room temperature for 5 min. To this solution indole (0.35 g, 3 mmol) and indium triflate (0.56 g, 1 mmol) was added and the resulting mixture was refluxed for 15 h. After completion, (monitored by TLC) the resulting mixture was cooled to room temperature and the solvent was removed in a rotary evaporator. The solid mass thus obtained was then treated with chloroform and filtered. The residue contains indium triflate can be reused in subsequent experiments. The filtrate was then dried over anhydrous sodium sulphate and concentrated and purified by column chromatography using chloroform as the eluent. The reaction afforded a secondary amine, 3-[3'-(*p*-anisylaminomethyl) benzopyran]indole **4c** mp 153-155 ^{o}C in 81% yield as the main product and benzopyran bisindolylmethane **5** as the byproduct mp 214-216 ^{o}C in 12% yield. Similarly other primary amines are reacted with indole or 2-methylindole and 3-formylchromone in a one-pot reaction and the corresponding secondary indolyl amines **4b-i** are obtained in 78-82% yields. All the compounds obtained were characterized fully by ^{1}HNMR, MS and IR spectroscopy.

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REFERENCES AND NOTES

[1] Zhang, H.; Larock, R.C. *Org. Lett*., **2001**, *3*, 3083; Jiang, B.; Yang, C.G.; Wang, J. *J. Org. Chem*., **2001**, *66*, 4865; Mari, M.; Nakamishi, M.; Kajishima, D.; Sato, Y. *Org. Lett*., **2001**, *3*, 1913; Chataigner, L.; Hess, E.; Toupet, L.; Pietre, S.R. *Org. Lett*., **2001**, *3*, 515; Brady, S.F.; Chan, C.J.; Handeisman, J.; Clardy, J. *Org. Lett*., **2001**, *3*, 1981; Wang, T.; Cook, J.M. *Org. Lett*., **2000**, *2*, 2057; Rajeswaran, W.G.; Labroo, R.B.; Cohen, L.A.; King, M.M. *J. Org. Chem*., **1999**, *64*, 1369; Doll, M.K.H. *J. Org. Chem*. **1999**, *62*, 1372 and references cited within section.; Saxton, J.E. In *The Alkaloids*, Cordell, G.A. Ed.; Academic Press: New York, **1998**, Vol. *51*, Chapter 1; Saxton, J.E. *Nat. Prod. Rep*., **1997**, 589.

[2] Ellis, G.P. *Chromones, Chromanones and Chromenes*, Wiley: New York, **1977**, Chapter 7; Ghosh, C.K. *J. Het. Chem*., **1983**, *20*, 1437; Chantegrel, B.; Nadi, A.I.; Gelin, S. *J. Org. Chem*., **1984**, *49*, 4419.

[3] Jones, R.; Bean, G. *The Chemistry of Pyrroles*, Academic Press: London, **1977**.

[4] Iqbal, Z.; Jackson, A.H.; Rao, K.R.N. *Tetrahedron Lett*., **1998**, *29*, 2577; Dujardin, G.; Poiner, J.M. *Bull. Soc. Chem. Fr*., **1994**, *131*, 900; Harrington, P.E.; Kerr, M.A. *Synlett* **1996**, 1047; Manabe, K.; Aoyama, N.; Kobayashi, S. *Adv. Synth. Catal*., **2001**, *343*, 174; Yadav, J.S.; Reddy, B.V.S.; Abraham, S.; Sabitha, G. *Synthesis*, **2001**, 2165; Bandim, M.; Cozzi, P.G.; Giacommi, M.; Mekhiorre, P.; Selva, S.; Ronchi, A.U. *J. Org. Chem*., **2002**, *67*, 3700.

[5] For a comprehensive review see: Boim. C.; Hidebranol, J.P.; Muniz, K.; Hermanns, N. *Angew. Chem. Int. Ed*., **2001**, *40*, 3254.

[6] Smith, A. B.III; Kanoh, N.; Minakawa, N.; Rainer, J.D.; Blasé, F.R.; Hartz, R.A. *Org. Lett*., **1999**, *1*, 1263; Mahboobi, S.; Grothus, G.; Meindl, W. *Arch. Pharm*., **1994**, *327*, 105; Kuhn, H.; Stein, O. *Chem. Ber*., **1937**, *70*, 567.

[7] H. Firouzabadi, N. Iranpoor and F. Nowrouzi, *J. Chem. Soc. Chem. Commun*., 2005, 789.

[8] Joule, J.A.; Mills, K.; Smith, G.F. *Heterocyclic Chemistry*, 3rd ed., Chapman & Hall: New York, **1995**, Chapter 17, pp 305; Iwama, T.; Birnan, V.B.; Kozmin, S.A.; Rawal, V.H. *Org. Lett*., **1999**, *1*, 673.

[9] Abel, E.; Dewall, S.I.; Edwards, W.B.; Lalitha, S.; Covey, D.F.; Gokel, G.W. *J. Org. Chem*., **2000**, *65*, 5901.

[10] Houlihan, W.J. *Indoles*, John Wiley & Sons Inc: New York, **1972**; Vol. *1*. pp 71.

[11] Vorbruggen, H.; Krolikiewicz, K. *Tetrahedron*, **1994**, *50*, 6549; Moody, C.J.; Swann, E. *J. Chem. Soc., Perkin Trans*., **1993**, *1*, 2561.

[12] Powers, J.C. *J. Org. Chem*., **1965**, *30*, 2534; Von Tambelon, E.E.; Knapp, G.G. *J. Am. Chem. Soc*., **1955**, *77*, 1860; Tnesing, J.; Klussendorf, S.; Ballach, P.; Mayer, H. *Chem. Ber*., **1955**, *88*, 1295.

[13] Yamada, F.; Kobayashi, K.; Shimizu, A.; Aoki, N.; Somei, M. *Heterocycles*, **1993**, *36*, 2783.

[14] Using indole see: a) Prajapati, D.; Gadhwal, S. *Tetrahedron*, **2004**, 4909; b) Prajapati, D.; Gohain, M.; Gogoi, B. J. *Tetrahedron Lett*., **2006**, *47*, 3535; Using indium see c) Laskar, D.D.; Prajapati, D.; Sandhu, J.S. *Tetrahedron Lett*., **2000**, *41*, 8639; d) Gohain, M.; Gogoi, B.J.; Prajapati, D.; Devi, G. *Tetrahedron Lett*., **2003**, *44*, 6755; e) Saikia, P.; Prajapati, D.; Sandhu, J.S. *Tetrahedron Lett*., **2003**, *44*, 8725.

[15] Domling, A.; Ugi, E. *Angew. Chem. Int. Ed*., **2000**, *39*, 3168.

[16] a) Weber, L.; Illegen, K.; Almstetter, M. *Synlett*, **1999**, 366; (b) Armstrong, R.W.; Combs, A.P.; Tempest, P.A.; Brown, S.D.; Keating, T.A. *Acc. Chem. Res*., **1996**, *29*, 123.

[17] a) Kobayashi, K.; Matoba, T.; Susumu, I.; Takachi, M.; Morikawa, O.; Konishi, H. *Chem. Lett*., **1998**, 551; (b) Bossio, R.; Marcos, C. F.; Marcaccini, S.; Pepino, R. *Tetrahedron Lett*., **1997**, *38*, 2519.

[18] a) Keatings, T.A.; Armstrong, R.W. *J. Am. Chem. Soc*., **1995**, *117*, 7842; (b) Yamada, T.; Omote, Y.; Yamanaka. Y.; Miyazawa, T.; Kuwata, S. *Synthesis*, **1998**, 991; (c) Ross, G. F.; Herdtweek, E.; Ugi, I. *Tetrahedron*, **2002**, *58*, 6127.

[19] Arend, M.; Westermann, B.; Risch, N. *Angew. Chem. Int. Ed*., **1998**, *37*, 1045.

[20] a) Bagley, M.C.; Dale, J.W.; Bower, J. *Chem. Commun*., **2002**, 1682; (b) Kappe, C.O. *Tetrahedron*, **1993**, *49*, 6973; (c) Bertozgi, F.; Gustafsson, M.; Olsson, R. *Organic Lett*., **2002**, *43*, 6485; (d) Shestopalov, A.M.; Emeliyanova, Y.M.; Shestopalov, A.A.; Rodinovskaya, L.A.; Niazimbetova, Z.I.; Evans, D.H. *Organic Lett*., **2002,** *43*, 423.