

HETEROCYCLES, Vol. 96, No. 5, 2018, pp. 839 - 849. © 2018 The Japan Institute of Heterocyclic Chemistry  
Received, 9th August, 2017, Accepted, 17th April, 2018, Published online, 26th April, 2018  
DOI: 10.3987/COM-17-13796

## SOLVENT-FREE MICROWAVE ACCELERATED SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF PHTHALIDE-FUSED INDOLINES

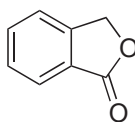
Wong Sheryn, Fatimatul Akma Awang Ngah, Jalifah Latip, Nurul Izzaty Hassan, and Siti Aishah Hasbullah\*

School of Chemical Sciences and Food Technology, Faculty of Science and Technology, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor, Malaysia. E-mail: aishah80@ukm.edu.my

**Abstract** – The 3-substituted phthalides (**3a–3d**) were synthesized by coupling reaction of methylenindoline derivatives (**1**) with 2-formylbenzoic acid derivatives (**2**), under solvent-free microwave irradiation. The reaction rate enhancement resulted from irradiation has proven to be higher and more efficient compared to the conventional method with an excellent yield of 80–98%. The structures of the phthalides were deduced by their analytical and spectral data (FTIR, UV-Vis,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, LC-MS) and confirmed by chemical crystallography. Compounds **3a** and **3b** were successfully crystallized in monoclinic system with space group  $P2_1/c$  and  $C2/c$ , respectively. The molecular structure consists of fused **1** and **2** groups connected by the enamine carbon.

### INTRODUCTION

Phthalides are one of the well-known secondary metabolites or phytochemical compounds classified as lactones,<sup>1</sup> which are commonly produced by biochemical reaction that occurred in endophytic microorganisms.<sup>2</sup> Many phthalide-based compounds have been isolated from plants.<sup>3</sup> The five-membered ring lactones in plants possess a basic structure (Figure 1), which are important building blocks for a large number of biologically active compounds.<sup>4</sup> Therefore, many researchers have designed and developed the



**Figure 1.** The structure of phthalide [isobenzofuran-1(3*H*)-one]

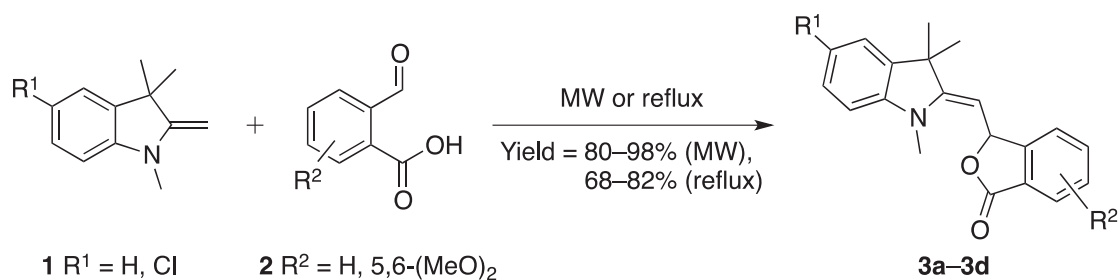
route to synthesize phthalides and their derivatives<sup>5</sup> and consequently screened for their biological activities such as antibacterial, antioxidant and antitumor activities.<sup>6,7</sup>

The common methods for the preparation of phthalides by asymmetric synthesis require chiral auxiliaries or chiral organometallics and a few involved the use of catalysts which needs development in its overall efficiency and atom economy.<sup>8-10</sup> The combination of two active moieties with biological importance through green synthetic methods has gained much attention.<sup>11,12</sup> Microwave Assisted Organic Synthesis (MAOS)<sup>13</sup> has been widely applied in heterocyclic chemistry especially in the synthesis of phthalide derivatives.<sup>14,15</sup> The high irradiating efficiency in a short time gives rise to remarkable rate enhancement. In addition, solventless reaction and no waste production will be in line with the concept of 'green chemistry'.<sup>16</sup> Green method of synthesis was applied in this work, whereby the use of non-toxic solvents was prioritized in the work-up of the reaction through conventional reflux and microwave irradiation method, respectively.

## RESULTS AND DISCUSSION

### Reaction and mechanism of phthalide-fused indolines

To the best of our knowledge, compounds **3a** and **3c** have been synthesized previously.<sup>17,18</sup> Four phthalide-fused indolines were prepared by a one-pot coupling reaction under conventional heating reflux and solventless microwave irradiation (Scheme 1) with reaction conditions as stated in Table 1.



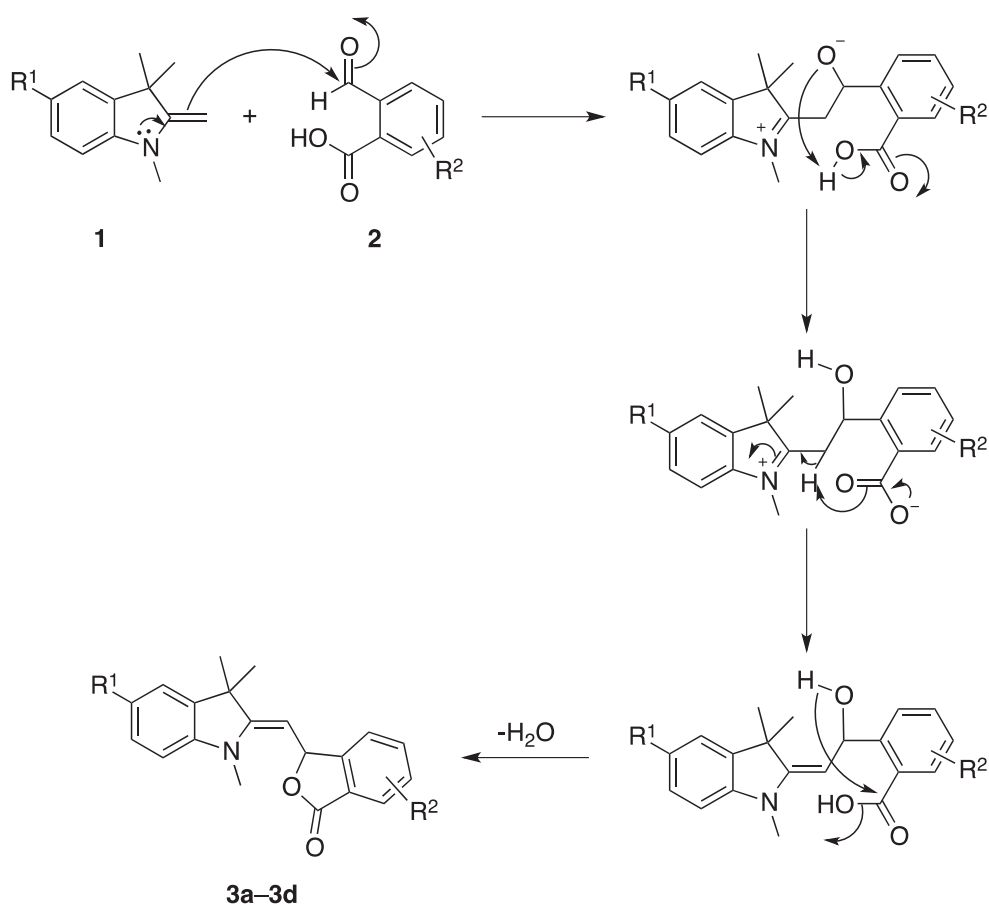
**Scheme 1.** Preparation of phthalide-fused indoline **3a-3d** by microwave irradiation or reflux

**Table 1.** Comparison of different reaction conditions on % yield of synthesized compounds

Product	R <sup>1</sup>	R <sup>2</sup>	Reflux method		Microwave irradiation		
			Time (h)	Yield (%)	Time (min)	Power (W)	Yield (%)
<b>3a</b>	H	H	24	79	5	350	98
<b>3b</b>	H	OMe	24	82	5	350	92
<b>3c</b>	Cl	H	24	77	1	100	85
<b>3d</b>	Cl	OMe	24	68	1	100	80

The percentage yields under different reaction conditions are indicated in Table 1. The synthesized **3a–3d** produces yield 68–82% (reflux) and 80–98% (microwave). The phthalide-fused indolines were obtained at much shorter reaction time by microwave irradiation. Different reaction conditions on microwave irradiation were also tested. A longer reaction time (5 min) and a higher power of microwave irradiation (350 W) afforded better yields as compared to shorter reaction time (1 min) and lower power (100 W). Compound **3b** was found to give a quantitative yield (98%). This was due to the presence of electron-donating group, -OMe, on 2-formylbenzoic acid derivatives. Similarly, compound **3c** was produced in high yield (85%) with the presence of electron-withdrawing group, -Cl, on indoline derivatives.

The proposed mechanism for the synthesis of phthalides is presented in Scheme 2. The reaction occurred by the condensation of Fischer base with aldehydes.<sup>17</sup> The first step involved nucleophilic attack on the aldehyde group of the 2-formylbenzoic acid derivatives by the alpha carbon of Fischer base, which resulted in an iminium intermediate. Next, intramolecular proton transfer formed a carbinol intermediate and freed up the lone pair on amine nitrogen. Lastly, cyclization together with the elimination of water gave a five-membered ring lactone.



**Scheme 2.** Proposed mechanism of compounds **3a–3d**

### Spectroscopic studies of compounds 3a–3d

The UV spectrum of all the four synthesized compounds displayed two absorption peaks at 210–226 nm and 285–290 nm indicative of aromatic ring compounds due to  $\pi \rightarrow \pi^*$  of benzene chromophores and  $n \rightarrow \pi^*$  transition of carbonyl groups. Furthermore, compounds **3b** and **3d** showed weak absorption in the visible region of 435 nm and 445 nm, respectively.

IR spectrum exhibited a strong band at 1745–1755  $\text{cm}^{-1}$  for all compounds and was assigned as C=O stretching vibration, which is characteristic of lactone ring. Presence of electron-donating groups on phthalide moiety and electron-withdrawing groups on indoline moiety showed no significant shift in vibrational frequency of C=O. Bands between 1043  $\text{cm}^{-1}$  and 1294  $\text{cm}^{-1}$  were assigned as C-O and C-N stretching.

According to previous report,<sup>19</sup> the indoline moiety showed a regular  $^1\text{H}$  NMR resonance patterns for the protons on adjacent methyl groups with two singlet peaks for the gem-dimethyl protons. The splitted singlets were observed for compound **3d** at 1.68 and 1.65 ppm. However, the gem-dimethyl protons for compounds **3a–3c** appeared as a singlet instead that resonated in the range of 1.70–1.74 ppm with a total integral of 6 protons. N-methyl protons were observed as a singlet at 2.99–3.03 ppm. For compounds **3b** and **3d** (Figure 2), two sharp singlets appeared at 3.93 and 4.13 ppm, with an integral of 3 each were assigned to the substituted methoxy groups on the phthalide moiety. The chiral *CH*-O proton resonated at 4.18–4.21 ppm as a doublet. A multiplet with an integral of 2 protons that was observed in the range of 6.47–6.65 ppm with a *J* value of 10.4–10.8 Hz, belongs to the olefinic proton that was overlapped with an aromatic proton. The presence of methoxy groups on phthalide moiety resulted in a slightly shielded chiral *CH*-O proton and deshielded olefinic proton due to conjugation effect. Rest of the peaks between 6.0–8.0 ppm was resonated by aromatic protons.

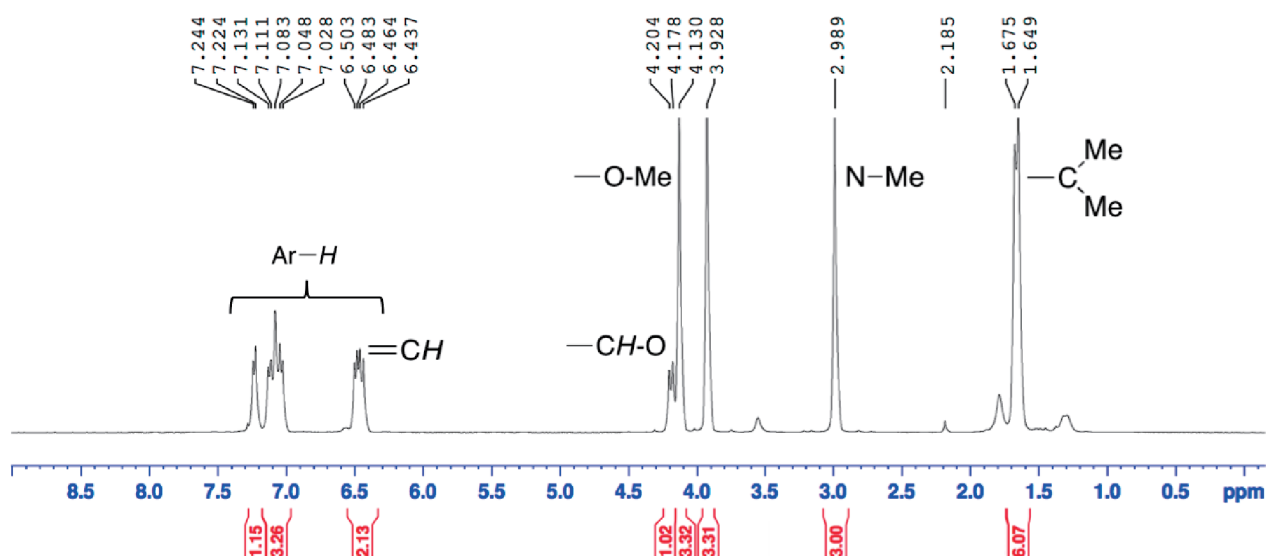


Figure 2.  $^1\text{H}$  NMR spectrum of novel compound **3d**

The  $^{13}\text{C}$  NMR data of compound **3a** was in accordance to the spectrum reported by Chunaev *et al.*<sup>17</sup> In the  $^{13}\text{C}$  NMR spectra of all synthesized compounds, the most downfield quaternary carbon peak at 168.1–170.9 ppm was attributed to the carbonyl group. The carbonyl signal showed an upfield shift of  $\sim 3$  ppm in the spectra of **3b** and **3d** due to its electron rich ring that leads to increased shielding. The methoxy carbon in **3b** and **3d** was observed at 56.9–62.5 ppm as two new peaks. The carbon of gem-dimethyl ( $\text{CH}_3\text{-C-CH}_3$ ) and carbon of N- $\text{CH}_3$  correspond to signals at 29.0–29.9 ppm and 45.0–45.2 ppm, respectively were observed in all spectra. Two peaks in the range of 77.6–79.5 ppm and 87.9–89.5 ppm were also observed and could be ascribed as olefinic carbon and CH-O. Signals between 105.6–152.6 ppm were assigned to the aromatic carbons with distinguishable quaternary carbons. Presence of a quaternary carbon at a very weak field at 160.5–161.5 ppm shows a common shift for a vinyl carbon atom bonded to an electronegative heteroatom ( $\text{N-C=CH}$ ). By comparing the spectrum of **3d** with that of **3b**, the aromatic carbon bonded to chlorine ( $\text{C}_{\text{Ar-Cl}}$ ) was detected as a new quaternary carbon at 124.2 ppm, which was also present in compound **3c** at 124.3 ppm. Two new quaternary signals appeared at 144.0 and 147.9 ppm which were assigned as aromatic carbon attached to methoxy group ( $\text{C}_{\text{Ar-OMe}}$ ) by comparing the  $^{13}\text{C}$  NMR spectra of compounds **3c** and **3d** as shown in Figure 3.

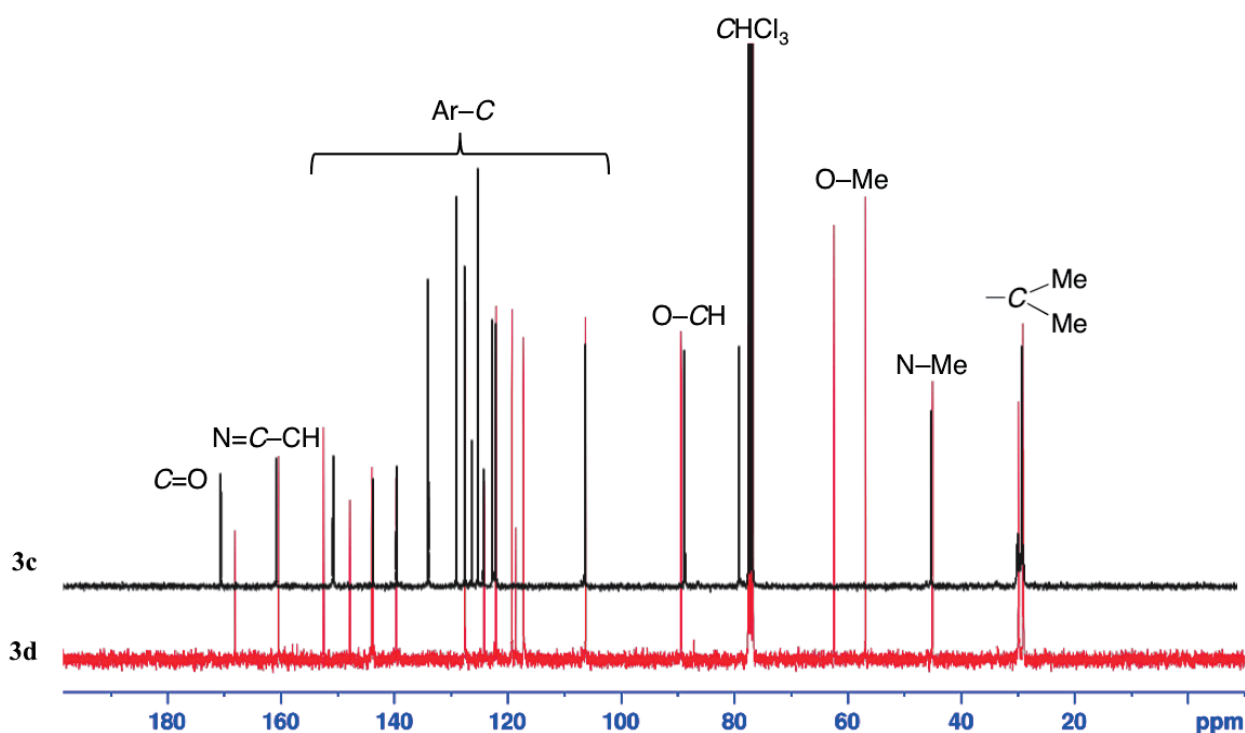


Figure 3.  $^{13}\text{C}$  NMR spectra of compounds **3c** and **3d**

### X-Ray crystallography

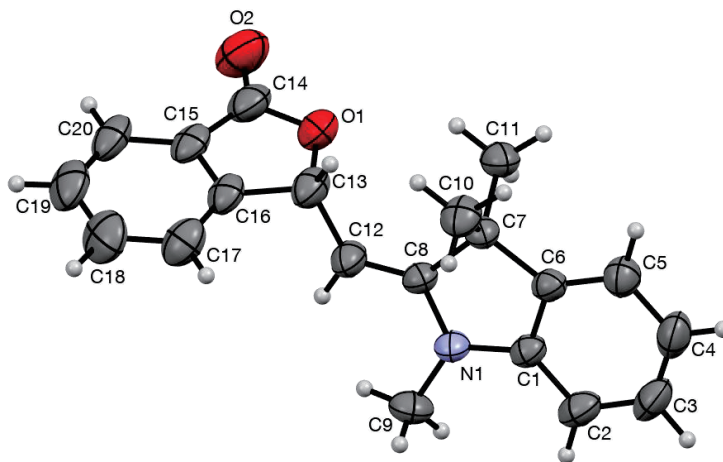
Single crystals of **3a** and **3b** were subjected to X-ray crystallographic analyses to further confirm their chemical structures. The crystals were grown by slow evaporation of acetone solution at room

temperature. Both compounds crystallized in monoclinic system with space group  $P2_1/c$  and  $C2/c$  for **3a** and **3b**, respectively. The crystal system and refinement parameters are shown in Table 2.

**Table 2.** Crystallographic data collection parameters for **3a** and **3b**

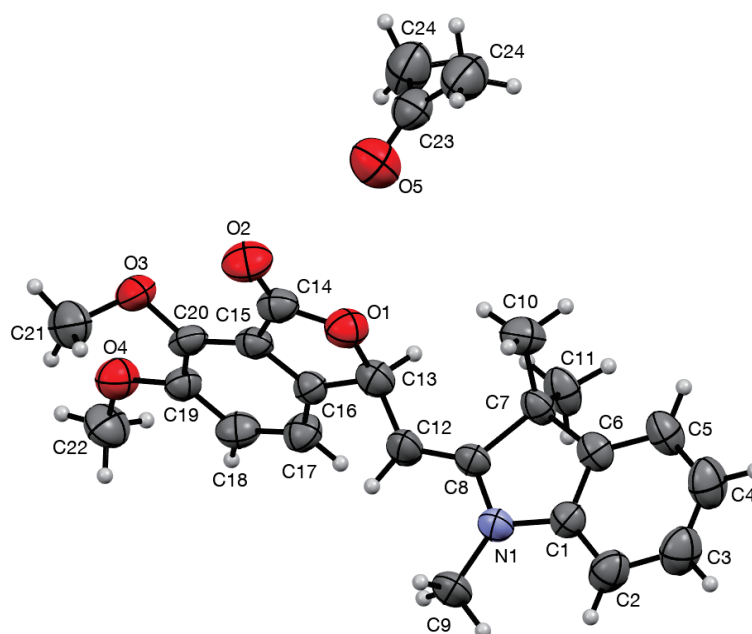
Compound	<b>3a</b>	<b>3b</b>
Empirical formula	$C_{20}H_{19}NO_2$	$C_{47}H_{52}N_2O_9$
Formula weight	305.36	788.90
Temperature (K)	293 (2)	301 (2)
Wavelength (Å)	0.71076	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P 2_1/c$	$C 2/c$
Unit cell dimensions (Å)	a = 11.914 (17) b = 11.26 (2) c = 12.519 (19)	a = 30.793 (7) b = 8.3214 (18) c = 20.680 (4)
$\beta$ (°)	$\beta = 105.53$ (5)°	$\beta = 129.055$ (5)°
Volume (Å <sup>3</sup> )	1618.0 (5)	4115.0 (15)
Z	4	4
Density (calculated) (mg/m <sup>3</sup> )	1.253	1.273
Absorption coefficient (mm <sup>-1</sup> )	0.081	0.088
F (000)	648	1680
Crystal size (mm)	0.53 × 0.27 × 0.23	0.38 × 0.20 × 0.16
$\theta$ range (°)	3.299–26.338	3.113–25.994
Index ranges	-14 ≤ h ≤ 14 -13 ≤ k ≤ 13 -14 ≤ l ≤ 11	-37 ≤ h ≤ 37 -10 ≤ k ≤ 10 -25 ≤ l ≤ 25
Reflections collected	14467	66373
Independent reflections	2864 [R(int) = 0.076]	4038 [R(int) = 0.191]
Completeness to theta	96.9%	99.8%
Refinement method	Full-matrix least-squares on $F^2$	Full-matrix least-squares on $F^2$
Data / restraints / parameters	2864 / 0 / 211	4038 / 0 / 269
Goodness-of-fit on $F^2$	1.160	1.032
Final R indices [ $I > 2\sigma(I)$ ]	R1 = 0.0921, wR2 = 0.1862	R1 = 0.0870, wR2 = 0.2351
R indices (all data)	R1 = 0.1467, wR2 = 0.2184	R1 = 0.1506, wR2 = 0.2788
Largest diff. peak and hole	0.238 and -0.275 e.Å <sup>-3</sup>	0.467 and -0.323 e.Å <sup>-3</sup>
CCDC No.	1564023	1556809

The molecule **3a** consists of two fused 1,3,3-trimethyl-2-methyleneindoline and isobenzofuran-1(3*H*)-one groups connected by the enamine carbon C12 (Figure 4) with C8–C12 and C12–C13 of bond lengths 1.355 (6) and 1.434 (6) Å, respectively.



**Figure 4.** ORTEP diagram of **3a** drawn at 50% probability ellipsoids

The molecular structure of **3b** is similar to that of **3a** but associated with solvated acetone molecule as shown in Figure 5. The isobenzofuran with substituted methoxy groups at positions C19 and C20 (Figure 5) was connected to the 1,3,3-trimethyl-2-methyleneindoline by C12 with C8–C12 and C12–C13 of bond lengths 1.327 (6) and 1.492 (6) Å, respectively and are comparable to those in the **3a**.



**Figure 5.** ORTEP diagram of **3b** drawn at 50% probability ellipsoids

## CONCLUSION

The phthalide-fused indolines were successfully characterized and synthesized through green synthetic method without the use of any solvent. The synthesized **3a–3d** produce yield 68–82% (reflux) and 80–98% (microwave). The microwave irradiation method is proven to be more efficient with increased reaction rate and better yield. Further investigations on the biological activities of the synthesized compounds are being carried out in our laboratory.

## EXPERIMENTAL

### Materials and Instruments

All reactions were performed under conventional and domestic microwave irradiation methods. Microwave irradiation method was performed using domestic microwave oven (Electrolux, model EMM2017X, PCR). Chemicals and solvents were purchased from Sigma Aldrich and Acros and used directly without further purification. UV-vis spectra were recorded on an Agilent Cary 100 UV-vis spectrophotometer; FTIR spectra were recorded on Perkin-Elmer Spectrum GX spectrometer in the range 400–4000  $\text{cm}^{-1}$  using KBr pellet method;  $^1\text{H}$  and  $^{13}\text{C}$  NMR (in  $\text{CDCl}_3$ ) spectra were recorded on a Bruker Avance 400 MHz spectrometer at 400.2 MHz and at 100.6 MHz, respectively using TMS as internal standard; mass spectra were recorded on a Bruker micrOTOF-Q 86 spectrometer equipped with electrospray ionization (ESI) module in the positive ion mode. The source temperature was maintained at 180 °C at an approximate 0.4 bar pressure. Single crystal X-ray experiments were performed on Bruker D8 QUEST diffractometer with  $\text{MoK}\alpha$  radiation.

### General procedure for the synthesis of phthalide-fused indolines under reflux conditions

A mixture of 1,3,3-trimethyl-2-methyleneindoline derivatives, **1** (1.0 mmol) and 2-formylbenzoic acid derivatives, **2** (1.0 mmol) was dissolved in EtOH and stirred at reflux for 24 h. The reaction mixture was then evaporated to approximately half its original volume and the precipitate was filtered. All the crude products were crystallized by slow evaporation from acetone to obtain pure crystal (as monitored on TLC and spectral data) except for **3b**, which was purified by column chromatography.

### General procedure for the synthesis of phthalide-fused indolines under microwave irradiation

A mixture of 1,3,3-trimethyl-2-methyleneindoline derivatives, **1** (1.0 mmol) and 2-formylbenzoic acid derivatives, **2** (1.0 mmol) was sonicated for 1 min to mix well in a reaction vial before placing in a microwave oven. The mixture was then irradiated at the indicated time and power (Table 1). After reaction was completed, cold EtOH (2 mL) was added into the reaction mixture. Precipitate was formed upon sonication for 10 s. The reaction mixture was then evaporated to approximately half its original volume and the precipitate was filtered off. All the crude products were crystallized by slow evaporation from acetone to obtain pure crystal (as monitored on TLC and spectral data) except for **3b**, which was

purified by column chromatography.

### 3-[(1,3,3-Trimethylindolin-2-ylidene)methyl]isobenzofuran-1(3H)-one (3a)<sup>17</sup>

The compound was obtained as yellowish crystal plates in 79% yield (0.73 g) (reflux method), 98% yield (0.89 g) (microwave irradiation). UV (EtOH):  $\lambda_{\max}$  = 225, 285 nm. IR  $\nu_{\max}$  (KBr)/ $\text{cm}^{-1}$ : 3056 (C-H  $\text{sp}^2$ ), 2931, 2966 (C-H  $\text{sp}^3$ ), 1745 (C=O), 1638 (C=C), 1465, 1494, 1604 (aromatic C=C), 1139, 1294 (C-O), 1074, 1097, 1249 (C-N), 894. <sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  1.72 (6H, s,  $\text{CH}_3$ ), 3.03 (3H, s, N- $\text{CH}_3$ ), 4.20 (1H, d,  $J$  = 10.8 Hz, CH-O), 6.62 (1H, m,  $H_{\text{Ar}}$ ), 6.65 (1H, m,  $J$  = 10.8 Hz, C=CH), 6.88 (1H, t,  $J$  = 6.8 Hz,  $H_{\text{Ar}}$ ), 7.18 (2H, m,  $J$  = 6.8 Hz,  $H_{\text{Ar}}$ ), 7.47 (1H, d,  $J$  = 7.2 Hz,  $H_{\text{Ar}}$ ), 7.56 (1H, t,  $J$  = 7.2 Hz,  $H_{\text{Ar}}$ ), 7.70 (1H, t,  $J$  = 7.2 Hz,  $H_{\text{Ar}}$ ), 7.93 (1H, d,  $J$  = 7.2 Hz,  $H_{\text{Ar}}$ ). <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ ) 29.0, 29.6 ( $\text{CH}_3\text{-C-CH}_3$ ), 45.2 (N- $\text{CH}_3$ ), 79.5 (C=CH), 87.9 (CH-O), 105.6 ( $\text{CH}_{\text{Ar}}$ ), 119.5 ( $\text{CH}_{\text{Ar}}$ ), 121.6 ( $\text{CH}_{\text{Ar}}$ ), 122.8 ( $\text{CH}_{\text{Ar}}$ ), 125.3 ( $\text{CH}_{\text{Ar}}$ ), 126.5 ( $\text{C}_{\text{Ar}}$ ), 127.9 ( $\text{CH}_{\text{Ar}}$ ), 129.0 ( $\text{CH}_{\text{Ar}}$ ), 134.0 ( $\text{CH}_{\text{Ar}}$ ), 138.0 ( $\text{C}_{\text{Ar}}$ ), 145.2 ( $\text{C}_{\text{Ar}}$ ), 151.1 ( $\text{C}_{\text{Ar}}$ ), 161.5 (N-C=CH), 170.9 (C=O). DI-MS  $m/z$  calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_2$  [M + H]<sup>+</sup>: 306.1494. Found: 306.1479; DI-MS  $m/z$  calcd for  $\text{C}_{20}\text{H}_{19}\text{NO}_2\text{Na}$  [M + Na]<sup>+</sup>: 328.1313. Found: 328.1314.

### 6,7-Dimethoxy-3-[(1,3,3-trimethylindolin-2-ylidene)methyl]isobenzofuran-1(3H)-one (3b)

The crude compound yield was 82% (0.30 g) (reflux method), 92% yield (0.34 g) (microwave irradiation). UV (EtOH):  $\lambda_{\max}$  = 210, 285, 435 nm. IR  $\nu_{\max}$  (KBr)/ $\text{cm}^{-1}$ : 3056 (C-H  $\text{sp}^2$ ), 2937, 2971 (C-H  $\text{sp}^3$ ), 1755 (C=O), 1640 (C=C), 1456, 1494, 1601 (aromatic C=C), 1139, 1271 (C-O), 1043, 1112, 1244 (C-N), 919. <sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  1.74 (6H, s,  $\text{CH}_3$ ), 3.02 (3H, s, N- $\text{CH}_3$ ), 3.93 (3H, s,  $\text{CH}_3\text{-O}$ ), 4.14 (3H, m,  $\text{CH}_3\text{-O}$ ), 4.18 (1H, m,  $J$  = 10.4 Hz, CH-O), 6.51 (1H, d,  $J$  = 10.0 Hz, C=CH), 6.60 (1H, d,  $J$  = 6.4 Hz,  $H_{\text{Ar}}$ ), 6.86 (1H, t,  $J$  = 6.4 Hz,  $H_{\text{Ar}}$ ), 7.05 (1H, d,  $J$  = 7.6 Hz,  $H_{\text{Ar}}$ ), 7.16 (1H, m,  $J$  = 7.2 Hz,  $H_{\text{Ar}}$ ), 7.19 (1H, m,  $J$  = 7.6 Hz,  $H_{\text{Ar}}$ ), 7.23 (1H, m,  $J$  = 10.8 Hz, 7.6 Hz,  $H_{\text{Ar}}$ ). <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ ) 29.0, 29.1, 31.0 ( $\text{CH}_3\text{-C-CH}_3$ ), 45.0 (N- $\text{CH}_3$ ), 56.9 (O- $\text{CH}_3$ ), 62.4 (O- $\text{CH}_3$ ), 78.0 (C=CH), 88.6 (CH-O), 105.6 ( $\text{CH}_{\text{Ar}}$ ), 117.3 ( $\text{CH}_{\text{Ar}}$ ), 118.7 ( $\text{C}_{\text{Ar}}$ ), 119.3 ( $\text{CH}_{\text{Ar}}$ ), 121.5 ( $\text{CH}_{\text{Ar}}$ ), 127.8 (2 ×  $\text{CH}_{\text{Ar}}$ ), 138.0 ( $\text{C}_{\text{Ar}}$ ), 144.3 ( $\text{C}_{\text{Ar}}\text{-OMe}$ ), 145.2 ( $\text{C}_{\text{Ar}}$ ), 147.8 ( $\text{C}_{\text{Ar}}\text{-OMe}$ ), 152.5 ( $\text{C}_{\text{Ar}}$ ), 161.1 (N-C=CH), 168.2 (C=O). DI-MS  $m/z$  calcd for  $\text{C}_{22}\text{H}_{23}\text{NO}_4\text{Na}$  [M + Na]<sup>+</sup>: 388.1525. Found: 388.1544.

### 3-[(5-Chloro-1,3,3-trimethylindolin-2-ylidene)methyl]isobenzofuran-1(3H)-one (3c)<sup>18</sup>

The compound was obtained as greenish-yellow crystals in 77% yield (0.26 g) (reflux method), 85% yield (0.29 g) (microwave irradiation). UV (EtOH):  $\lambda_{\max}$  = 226, 290 nm. IR  $\nu_{\max}$  (KBr)/ $\text{cm}^{-1}$ : 3053 (C-H  $\text{sp}^2$ ), 2928, 2960 (C-H  $\text{sp}^3$ ), 1750 (C=O), 1649 (C=C), 1466, 1493, 1602 (aromatic C=C), 1139, 1287 (C-O), 1062, 1094, 1265 (C-N), 900. <sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  1.70 (6H, s,  $\text{CH}_3$ ), 3.00 (3H, s, N- $\text{CH}_3$ ), 4.21 (1H, d,  $J$  = 10.8 Hz, CH-O), 6.51 (1H, d,  $J$  = 7.6 Hz,  $H_{\text{Ar}}$ ), 6.60 (1H, d,  $J$  = 10.4 Hz, C=CH), 7.12 (2H, m,  $J$  = 8.0 Hz,  $H_{\text{Ar}}$ ), 7.45 (1H, d,  $J$  = 6.8 Hz,  $H_{\text{Ar}}$ ), 7.56 (1H, t,  $J$  = 6.8 Hz, 7.2 Hz,  $H_{\text{Ar}}$ ), 7.70 (1H, t,  $J$  = 6.4 Hz, 7.2 Hz,  $H_{\text{Ar}}$ ), 7.91 (1H, d,  $J$  = 7.2 Hz,  $H_{\text{Ar}}$ ). <sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ ) 29.2, 29.9

(CH<sub>3</sub>-C-CH<sub>3</sub>), 45.2 (N-CH<sub>3</sub>), 79.1 (C=CH), 88.7 (CH-O), 106.4 (CH<sub>Ar</sub>), 122.1 (CH<sub>Ar</sub>), 122.7 (CH<sub>Ar</sub>), 124.3 (C<sub>Ar</sub>-Cl), 125.4 (CH<sub>Ar</sub>), 126.4 (C<sub>Ar</sub>), 127.7 (CH<sub>Ar</sub>), 129.1 (CH<sub>Ar</sub>), 134.1 (CH<sub>Ar</sub>), 139.7 (C<sub>Ar</sub>), 143.8 (C<sub>Ar</sub>), 150.9 (C<sub>Ar</sub>), 160.9 (N-C=CH), 170.7 (C=O). DI-MS *m/z* calcd for C<sub>20</sub>H<sub>18</sub>ClNO<sub>2</sub>Na [M + Na]<sup>+</sup>: 362.0924. Found: 362.0921.

### 6,7-Dimethoxy-3-[(5-chloro-1,3,3-trimethylindolin-2-ylidene)methyl]isobenzofuran-1(3H)-one (3d)

The novel compound was obtained as yellowish crystals in 68% yield (0.27 g) (reflux method), 80% yield (0.32 g) (microwave irradiation). UV (EtOH): λ<sub>max</sub> = 210, 290, 445 nm. IR ν<sub>max</sub> (KBr)/cm<sup>-1</sup>: 3064 (C-H sp<sup>2</sup>), 2966, 2933 (C-H sp<sup>3</sup>), 1748 (C=O), 1651 (C=C), 1457, 1494, 1603 (aromatic C=C), 1142, 1262 (C-O), 1044, 1096, 1243 (C-N), 929. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> 1.66 (6H, m, CH<sub>3</sub>), 2.99 (3H, s, N-CH<sub>3</sub>), 3.93 (3H, s, CH<sub>3</sub>-O), 4.13 (3H, s, CH<sub>3</sub>-O), 4.19 (1H, d, *J* = 10.4 Hz, CH-O), 6.47 (2H, m, *J* = 8.0 Hz, 10.8 Hz, H<sub>Ar</sub>, C=CH), 7.08 (3H, m, *J* = 8.0 Hz, H<sub>Ar</sub>), 7.23 (1H, d, *J* = 8.0 Hz, H<sub>Ar</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 29.0, 29.2, 29.9 (CH<sub>3</sub>-C-CH<sub>3</sub>), 45.1 (N-CH<sub>3</sub>), 56.9 (O-CH<sub>3</sub>), 62.5 (O-CH<sub>3</sub>), 77.6 (C=CH), 89.5 (CH-O), 106.3 (CH<sub>Ar</sub>), 117.3 (CH<sub>Ar</sub>), 118.6 (C<sub>Ar</sub>), 119.3 (CH<sub>Ar</sub>), 122.1 (CH<sub>Ar</sub>), 124.2 (C<sub>Ar</sub>-Cl), 127.6 (CH<sub>Ar</sub>), 139.7 (C<sub>Ar</sub>), 143.9 (C<sub>Ar</sub>), 144.0 (C<sub>Ar</sub>-OMe), 147.9 (C<sub>Ar</sub>-OMe), 152.6 (C<sub>Ar</sub>), 160.5 (N-C=CH), 168.1 (C=O). DI-MS *m/z* calcd for C<sub>22</sub>H<sub>22</sub>ClNO<sub>4</sub>Na [M + Na]<sup>+</sup>: 422.1135. Found: 422.1134.

## ACKNOWLEDGEMENTS

The authors would like to thank the School of Chemical Sciences and Food Technology, Faculty of Science and Technology, Universiti Kebangsaan Malaysia, Center for Research and Instrumentation Management (CRIM), Research Grants (GUP-2017-86 and DIP-2015-015) and everyone who has involved in this research.

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