

## FACILE SYNTHESIS OF (GUAIAZULEN-1-YL)-1*H*-PYRROLES VIA PAAL-KNORR REACTION

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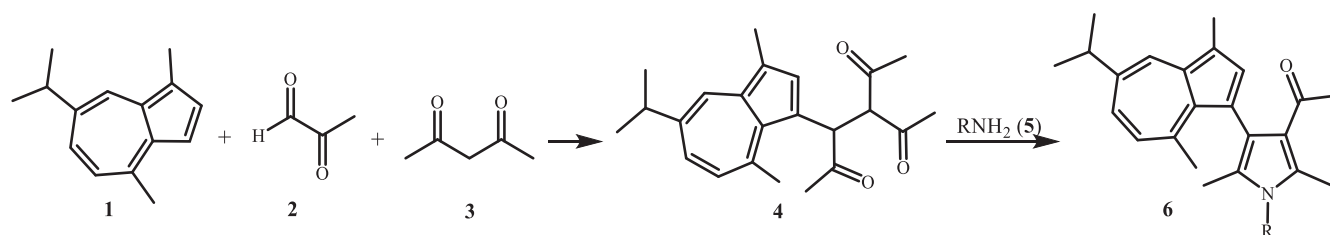
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**Abstract** – An efficient and simple method for the synthesis of (guaiazulen-1-yl)-1*H*-pyrroles was described. The construction of this new heteroarylazulene system was achieved by a the Paal-Knorr reaction of 3-acetyl-4-(guaiazulen-1-yl)hexane-2,5-dione (**4**), easily preparation by a three-component condensation of guaiazulene (**1**), methylglyoxal (**2**) and acetylacetone (**3**), with primary amines (**5**).

Pyrrole is one of the simplest nitrogen heterocycles, and it is an important structural attribute in many bioactive natural products,<sup>1</sup> therapeutic compounds,<sup>2</sup> and new organic materials.<sup>3</sup> Many of these biologically active compounds have emerged as chemotherapeutic agents. In addition, polysubstituted pyrroles are molecular frameworks having immense importance in material science. They have been employed as antioxidants, antibacterial, ionotropic, antitumor, antiinflammatory, and antifungal agents.<sup>4</sup> Moreover, they are a highly versatile class of intermediates in the synthesis of natural products as well as in heterocyclic chemistry.<sup>5</sup>

On the other hand, azulenes have attracted interest in medicine as antiulcer drugs,<sup>6</sup> anticancer agents,<sup>7</sup> and as antioxidant therapeutics for neurodegenerative conditions.<sup>8</sup> A variety of heterocycle-fused azulenes have attracted the interest owing to its unusual chemical properties.<sup>9</sup> Thus, preparation and reactivities of a number of heterocycle-fused azulenes have already been revealed by many research groups.<sup>10</sup>

Recently, our research group has reported the synthesis of new heteroarylazulene derivatives.<sup>11</sup> As part of a continuing effort in our laboratory toward the development of azulene chemistry, we became interested in exploring the reactivity and synthetic applications of guaiazulene<sup>12</sup> to 4-(guaiazulen-1-yl)-1*H*-pyrroles (**6**) by a Paal-Knorr reaction<sup>13</sup> of 3-acetyl-4-(guaiazulen-1-yl)hexane-2,5-dione(**4**), easily preparation by a three-component condensation of guaiazulene (**1**), methylglyoxal (**2**) and acetylacetone (**3**), with primary amines (**5**) (Scheme 1).



**Scheme 1.** Synthesis of 4-(guaiazulen-1-yl)-1*H*-pyrroles

In this study, the key intermediate trione, 3-acetyl-4-(guaiazulen-1-yl)hexane-2,5-dione (**4**), was obtained by the one pot three-component condensation of guaiazulene (**1**) with methylglyoxal (**2**) and acetylacetone (**3**) in 87% yield as blue scaly crystals. Elemental analysis ( $C_{23}H_{28}O_3$ ) and spectral data supported its structure. Its IR spectrum contains absorption peaks at 1727, 1702  $cm^{-1}$ , demonstrating the presence of C=O function. The  $^1H$  NMR spectrum of **4** showed singlet signals at  $\delta$  1.70, 2.08, 2.29, 2.58 and 3.14 ppm for methyl groups. Two methine protons were observed as two doublet signals ( $J = 11.2$  Hz) at  $\delta$  4.64 and 5.64 ppm. The aromatic protons signals at  $\delta$  7.02 (d,  $J = 10.8$  Hz, 1H), 7.39 (d,  $J = 10.8$  Hz, 1H), 7.42 (s, 1H), 8.12 (s, 1H) for azulene nucleus protons.  $^{13}C$  NMR spectrum of **4** exhibited nineteen distinct signals in agreement with the proposed structure, the carbonyl carbons resonated at 201.7, 204.0 and 206.1 ppm.

In an initial endeavor, we selected aniline **5a** as model amine to react with equimolar amounts of intermediate trione **4** for the preparation of 3-acetyl-2,5-dimethyl-4-(guaiazulen-1-yl)-1-phenyl-1*H*-pyrrole **6a** and investigated the optimal reaction conditions. The reaction was carried out under neat conditions at 100 °C without and with different acid catalysts such as *p*-toluenesulfonic acid (*p*-TsOH), trifluoroacetic acid (TFA), and sulfamic acid (SA) each 10 mol% in HOAc. The maximum yield was obtained using *p*-TsOH. It was found that when the reaction was carried out without any catalyst the yield of product was very low (Table 1, entry 1). Although a lower catalyst loading of 5 mol% accomplished this condensation, 10 mol% of *p*-TsOH was optimal in terms of reaction time and isolated yield (entry 5). Increasing the amount from 10 to 15 mol% has no effect on the product yield and reaction time (entry 6). A higher reaction temperature (110 °C) did not make a significant effect in the yield of product (entry 7). In addition, various solvents such as EtOH, MeCN, and DMF were screened for the optimal reaction conditions. The best catalytic activity was observed in HOAc compared to other organic solvents (entries 8-10). As shown in Table 1, *p*-TsOH was the best catalyst for this reaction.

**Table 1.** Optimizing the reaction conditions for the synthesis of **6a**

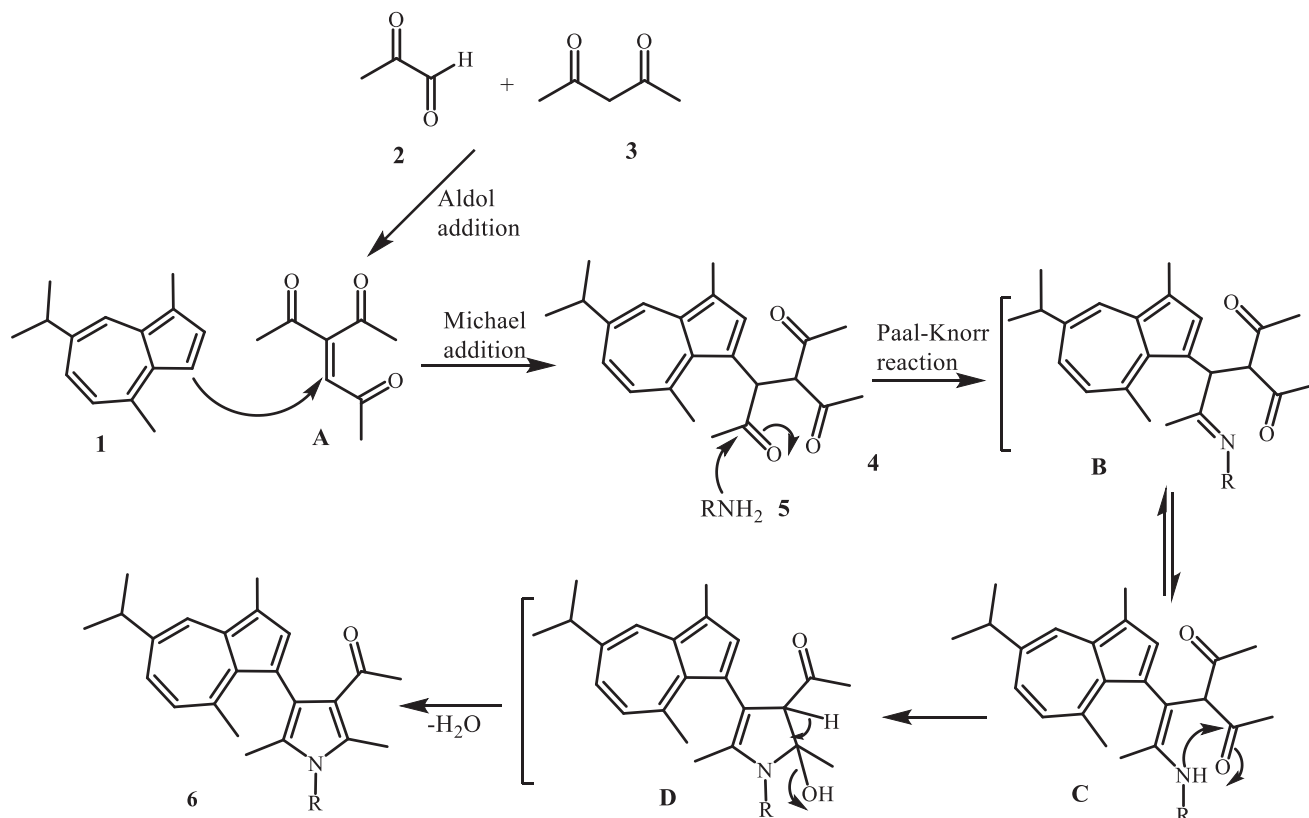
Entry	Catalyst / (mol%)	Solvent	Temp (°C)	Time (h)	Yield (%)
1	none	HOAc	100	24	26
2	<i>p</i> -TsOH (10)	HOAc	100	7	86
3	TFA (10)	HOAc	100	6	71
4	SA (10)	HOAc	100	10	74
5	<i>p</i> -TsOH (5)	HOAc	100	8	80
6	<i>p</i> -TsOH (15)	HOAc	100	6	83
7	<i>p</i> -TsOH (10)	HOAc	110	6	85
8	<i>p</i> -TsOH (10)	EtOH	80	13	79
9	<i>p</i> -TsOH (10)	MeCN	80	11	76
10	<i>p</i> -TsOH (10)	DMF	100	10	67

Having these results in hand, other amines (aliphatic and aromatic) have been subjected to the above-mentioned optimized conditions, and the results are listed in Table 2. The results demonstrated that a wide range of anilines, regardless of electron-donating or electron-withdrawing groups on the benzene ring, could undergo the reaction smoothly to afford the expected products in moderate to good yields (entries 1-5). Anilines bearing a weakly electron-withdrawing were a little bit less efficient in the reaction. Also, it was found that different kinds of aliphatic amines reacted successfully to afford the desired products under the same reaction conditions in apparently shorter reaction time (entries 6-10).

**Table 2.** Synthesis of 4-(guaiazulen-1-yl)-1*H*-pyrroles **6**

Entry	<b>5</b> / R	Time (h)	Product	Yield (%)
1	<b>5a</b> C <sub>6</sub> H <sub>5</sub>	4	<b>6a</b>	86
2	<b>5b</b> 3-MeC <sub>6</sub> H <sub>4</sub>	4	<b>6b</b>	83
3	<b>5c</b> 3,5-Me <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	3	<b>6c</b>	85
4	<b>5d</b> 4-ClC <sub>6</sub> H <sub>4</sub>	5	<b>6d</b>	80
5	<b>5e</b> 4-FC <sub>6</sub> H <sub>4</sub>	5	<b>6e</b>	76
6	<b>5f</b> Me	3	<b>6f</b>	82
7	<b>5g</b> Et	2	<b>6g</b>	85
8	<b>5h</b> <i>n</i> -Bu	2	<b>6h</b>	80
9	<b>5i</b> <i>n</i> -hexyl	3	<b>6i</b>	85
10	<b>5j</b> benzyl	1	<b>6j</b>	87

The proposed mechanism of the process is summarized in Scheme 2. First, an aldol-type addition of methylglyoxal **2** to acetylacetone **3** occurred, enabling the formation of an intermediate **A**. The following Michael addition of guaiiazulene **1** to intermediate **A** then occurs to provide trione **4**, which undergoes Paal-Knorr reaction to form the desired product **6**.



**Scheme 2.** Proposed mechanism for the synthesis of 4-(guaiazulen-1-yl)-1H-pyrroles **6**

In summary, we have demonstrated for the efficient method for the synthesis of (guaiazulen-1-yl)-1H-pyrroles, *via* Paal-Knorr reaction under mild conditions in good yields. This approach offers an effective route for the construction of new heteroarylazulene frameworks in a two-step process from commercially available starting materials.

## EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. The NMR spectra were recorded with a Bruker Avance 400 spectrometer (400 MHz for  $^1\text{H}$  and 100 MHz for  $^{13}\text{C}$ ) using TMS an internal reference. IR spectra were measured on Shimadzu FTIR-8300 spectrophotometer. C, H and N analyses were performed by a HP-MOD 1106 microanalyzer.

**Synthesis of 3-acetyl-2,5-dimethyl-4-((guaiazulen-1-yl)-1-phenyl)-1H-pyrrole (**4**).** An aqueous solution of methylglyoxal **2** (1.80 g, 10.0 mmol, 40 wt%) was mixed with acetylacetone **3** (1.00 g, 10.0 mmol) and guaiiazulene **1** (1.98 g, 10.0 mmol) in EtOH (40.0 mL). The mixture was then stirred at 80 °C for 4 h

(monitored by TLC). After cooling to rt, then water (50.0 mL) was added and stirred for 20 min. The solid was filtered and recrystallized from isopropanol to give **4** (3.06 g, 87%). Blue scaly crystals. mp 260-262 °C; IR (KBr):  $\nu$  1727, 1702  $\text{cm}^{-1}$ ;  $^1\text{H}$ NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.36 (d,  $J = 6.8$  Hz, 6H), 1.70 (s, 3H), 2.08 (s, 3H), 2.29 (s, 3H), 2.58 (s, 3H), 3.02-3.08 (m, 1H), 3.14 (s, 3H), 4.64 (d,  $J = 11.2$  Hz, 1H), 5.64 (d,  $J = 11.2$  Hz, 1H), 7.02 (d,  $J = 10.8$  Hz, 1H), 7.39 (d,  $J = 10.8$  Hz, 1H), 7.42 (s, 1H), 8.12 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  206.1, 204.0, 201.7, 145.2, 141.0, 139.1, 136.7, 135.3, 134.3, 132.8, 128.5, 125.8, 118.2, 70.6, 52.3, 37.6, 32.1, 30.3, 28.8, 27.8, 24.6, 24.5, 13.0. *Anal.* Calcd for  $\text{C}_{23}\text{H}_{28}\text{O}_3$ : C 78.38, H 8.01. Found: C 78.43, H 8.04.

**Typical procedure for the preparation of 4-(guaiazulen-1-yl)-1-phenyl-1H-pyrrole (6).** A solution of 3-acetyl-2,5-dimethyl-4-(guaiazulen-1-yl)-1-phenyl-1H-pyrrole **4** (1.00 mmol) and amines **5** (1.00 mmol) in HOAc (10.0 mL) was heated at 100 °C. After completion monitored by TLC, the reaction mixture was allowed to cool to rt, and then water (30.0 mL) was added to the mixture. EtOAc (50.0 mL) was added to the mixture. The organic layer was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to dryness. The residue was recrystallized from isopropanol to afford the corresponding products **6a-j**.

**3-Acetyl-2,5-dimethyl-4-(guaiazulen-1-yl)-1-phenyl-1H-pyrrole (6a):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1641  $\text{cm}^{-1}$ ;  $^1\text{H}$ NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.38 (d,  $J = 6.8$  Hz, 6H), 1.67 (s, 3H), 1.70 (s, 3H), 2.40 (s, 3H), 2.53 (s, 3H), 2.69 (s, 3H), 3.04-3.11 (m, 1H), 6.88 (d,  $J = 10.8$  Hz, 1H), 7.21-7.24 (m, 1H), 7.32-7.35 (m, 2H), 7.47-7.53 (m, 4H), 8.17 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  197.3, 145.8, 140.7, 139.3, 137.9, 137.7, 135.3, 134.7, 133.6, 133.4, 129.4, 128.5, 128.2, 127.7, 126.5, 124.5, 122.8, 122.1, 120.5, 37.8, 30.5, 25.4, 24.7, 24.6, 13.4, 12.9, 11.4. *Anal.* Calcd for  $\text{C}_{29}\text{H}_{31}\text{NO}$ : C 85.04, H 7.63, N 3.42. Found: C 85.09, H 7.68, N 3.45.

**3-Acetyl-2,5-dimethyl-4-(guaiazulen-1-yl)-1-(*m*-tolyl)-1H-pyrrole (6b):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1643  $\text{cm}^{-1}$ ;  $^1\text{H}$ NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.39 (d,  $J = 7.2$  Hz, 6H), 1.67 (s, 3H), 1.69 (s, 3H), 2.39 (s, 3H), 2.44 (s, 3H), 2.53 (s, 3H), 2.69 (s, 3H), 3.04-3.11 (m, 1H), 6.88 (d,  $J = 10.4$  Hz, 1H), 7.02-7.09 (m, 1H), 7.12-7.14 (m, 1H), 7.28 (s, 1H), 7.33 (d,  $J = 10.4$  Hz, 1H), 7.35-7.41 (m, 1H), 7.50 (s, 1H), 8.17 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  197.3, 145.8, 140.7, 139.3, 137.9, 137.7, 135.3, 134.6, 133.6, 133.4, 129.2, 128.8, 128.7, 127.7, 126.4, 125.3, 125.2, 124.5, 122.7, 122.2, 120.4, 37.8, 30.5, 25.4, 24.7, 24.6, 21.3, 13.4, 12.9, 11.4. *Anal.* Calcd for  $\text{C}_{30}\text{H}_{33}\text{NO}$ : C 85.05, H 7.85, N 3.31. Found: C 85.09, H 7.90, N 3.34.

**3-Acetyl-1-(3,5-dimethylphenyl)-2,5-dimethyl-4-(guaiazulen-1-yl)-1H-pyrrole (6c):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1645  $\text{cm}^{-1}$ ;  $^1\text{H}$ NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.39 (d,  $J = 6.8$  Hz, 6H), 1.67 (s, 3H), 1.69 (s, 3H), 2.40 (s, 3H), 2.45 (s, 3H), 2.53 (s, 3H), 2.70 (s, 6H), 3.04-3.11 (m, 1H), 6.88 (d,  $J = 10.8$  Hz, 1H), 7.02-7.04 (m, 1H), 7.11-7.13 (m, 1H), 7.32-7.35 (m, 2H), 7.50 (s, 1H), 8.18 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  197.8, 145.8, 140.7, 139.3, 137.9, 137.7, 135.3, 133.6, 133.4, 129.2, 128.8, 127.7, 126.4,

125.3, 125.2, 124.5, 122.7, 122.2, 120.4, 37.8, 30.5, 24.7, 24.6, 21.3, 14.1, 13.5, 13.0, 11.5. *Anal.* Calcd for C<sub>31</sub>H<sub>35</sub>NO: C 85.08, H 8.06, N 3.30. Found: C 85.13, H 8.09, N 3.25.

**3-Acetyl-1-(4-chlorophenyl)-2,5-dimethyl-4-(guaiazulen-1-yl)-1H-pyrrole (6d):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1651 cm<sup>-1</sup>; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.38 (d,  $J$  = 6.8 Hz, 6H), 1.67 (s, 3H), 1.68 (s, 3H), 2.39 (s, 3H), 2.52 (s, 3H), 2.69 (s, 3H), 3.06-3.11 (m, 1H), 6.62 (d,  $J$  = 8.8 Hz, 1H), 6.88 (d,  $J$  = 10.8 Hz, 1H), 7.12 (d,  $J$  = 8.4 Hz, 1H), 7.27-7.29 (m, 1H), 7.33-7.37 (m, 2H), 7.49 (d,  $J$  = 8.4 Hz, 2H), 8.18 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  197.3, 145.7, 140.6, 139.4, 137.9, 136.3, 135.1, 134.5, 133.6, 133.5, 129.7, 129.5, 127.6, 126.5, 124.6, 123.1, 121.7, 120.9, 116.3, 37.8, 30.6, 25.4, 24.7, 24.6, 13.4, 12.9, 11.4. *Anal.* Calcd for C<sub>29</sub>H<sub>30</sub>ClNO: C 78.45, H 6.81, N 3.15. Found: C 78.49, H 6.85, N 3.17.

**3-Acetyl-2,5-dimethyl-1-(4-fluorophenyl)-4-(guaiazulen-1-yl)-1H-pyrrole (6e):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1649 cm<sup>-1</sup>; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.40 (d,  $J$  = 6.8 Hz, 6H), 1.67 (s, 3H), 1.69 (s, 3H), 2.39 (s, 3H), 2.52 (s, 3H), 2.70 (s, 3H), 3.05-3.12 (m, 1H), 6.89 (d,  $J$  = 10.8 Hz, 1H), 7.21-7.25 (m, 3H), 7.33-7.36 (m, 2H), 7.49 (s, 1H), 8.18 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  197.3, 163.5, 161.0, 145.7, 140.6, 139.4, 137.9, 135.3, 133.5, 123.0, 129.9, 127.73, 126.5, 124.6, 122.9, 121.8, 120.7, 116.5, 116.3, 37.8, 30.5, 25.4, 24.7, 24.6, 13.4, 12.9, 11.4. *Anal.* Calcd for C<sub>29</sub>H<sub>30</sub>FNO: C 81.47, H 7.07, N 3.28. Found: C 81.82, H 7.09, N 3.32.

**3-Acetyl-2,5-dimethyl-4-(guaiazulen-1-yl)-1-methyl-1H-pyrrole (6f):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1654 cm<sup>-1</sup>; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.38 (d,  $J$  = 6.8 Hz, 6H), 1.61 (s, 3H), 1.90 (s, 3H), 2.50 (s, 3H), 2.63 (s, 3H), 2.67 (s, 3H), 3.50 (s, 3H), 3.04-3.09 (m, 1H), 6.85 (d,  $J$  = 10.8 Hz, 1H), 7.32 (d,  $J$  = 10.8 Hz, 1H), 7.40 (s, 1H), 8.16 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  197.1, 145.9, 140.8, 139.2, 137.8, 134.6, 133.7, 133.5, 133.4, 126.9, 126.3, 124.4, 122.4, 122.3, 120.3, 37.8, 30.4, 30.3, 25.4, 24.7, 24.6, 12.9, 12.2, 10.8. *Anal.* Calcd for C<sub>24</sub>H<sub>29</sub>NO: C 82.95, H 8.41, N 4.04. Found: C 82.98, H 8.45, N 4.06.

**3-Acetyl-2,5-dimethyl-1-ethyl-4-(guaiazulen-1-yl)-1H-pyrrole (6g):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1657 cm<sup>-1</sup>; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  1.31 (t,  $J$  = 7.2 Hz, 3H), 1.38 (d,  $J$  = 6.8 Hz, 6H), 1.61 (s, 3H), 1.90 (s, 3H), 2.40 (s, 3H), 2.64 (s, 3H), 2.67 (s, 3H), 3.03-3.09 (m, 1H), 3.93 (q,  $J$  = 7.2 Hz, 2H), 6.84 (d,  $J$  = 10.8 Hz, 1H), 7.33 (d,  $J$  = 10.8 Hz, 1H), 7.42 (s, 1H), 8.16 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  197.1, 145.9, 140.8, 139.2, 137.8, 134.6, 133.8, 133.5, 133.3, 126.3, 126.1, 124.4, 122.5, 122.4, 120.6, 38.2, 37.8, 30.5, 25.2, 24.7, 24.6, 15.8, 12.9, 11.9, 10.5. *Anal.* Calcd for C<sub>25</sub>H<sub>31</sub>NO: C 83.06, H 8.64, N 3.87. Found: C 83.12, H 8.67, N 3.91.

**3-Acetyl-1-(*n*-butyl)-2,5-dimethyl-4-(guaiazulen-1-yl)-1H-pyrrole (6h):** Blue crystals. mp > 300 °C; IR (KBr):  $\nu$  1658 cm<sup>-1</sup>; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  0.99 (t,  $J$  = 7.2 Hz, 3H), 1.39 (d,  $J$  = 6.8 Hz, 6H), 1.42-1.44 (m, 2H), 1.65 (s, 3H), 1.66-1.69 (m, 2H), 1.88 (s, 3H), 2.42 (s, 3H), 2.62 (s, 3H), 2.67 (s, 3H), 3.03-3.10 (m, 1H), 3.85 (t,  $J$  = 7.2 Hz, 2H), 6.84 (d,  $J$  = 10.8 Hz, 1H), 7.32 (d,  $J$  = 10.8 Hz, 1H), 7.41 (s,

1H), 8.15 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 197.1, 145.9, 140.8, 139.2, 137.8, 134.6, 134.1, 133.5, 133.3, 126.4, 126.3, 124.4, 122.6, 122.4, 120.6, 43.4, 37.8, 32.8, 30.5, 25.2, 24.7, 24.6, 20.1, 13.8, 12.9, 12.2, 10.7. *Anal.* Calcd for C<sub>27</sub>H<sub>35</sub>NO: C 83.24, H 9.06, N 3.60. Found: C 83.28, H 9.09, N 3.64.

**3-Acetyl-2,5-dimethyl-4-(guaiazulen-1-yl)-1-(n-hexyl)-1H-pyrrole (6i):** Blue crystals. mp > 300 °C; IR (KBr): ν 1654 cm<sup>-1</sup>; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>): δ 0.91 (t, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 7.2 Hz, 6H), 1.36-1.39 (m, 4H), 1.61 (s, 3H), 1.86 (s, 3H), 2.40 (s, 3H), 2.62 (s, 3H), 2.67 (s, 3H), 3.06-3.10 (m, 1H), 3.84 (t, *J* = 7.2 Hz, 2H), 6.83 (d, *J* = 10.8 Hz, 1H), 7.33 (d, *J* = 10.8 Hz, 1H), 7.42 (s, 1H), 8.15 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 197.1, 145.9, 140.8, 139.2, 137.8, 134.6, 134.1, 133.5, 133.3, 126.4, 126.3, 124.4, 122.6, 122.4, 120.5, 43.7, 37.8, 31.5, 30.6, 30.5, 29.7, 25.2, 24.7, 24.6, 22.6, 13.9, 12.9, 12.2, 10.8. *Anal.* Calcd for C<sub>29</sub>H<sub>39</sub>NO: C 83.40, H 9.41, N 3.35. Found: C 83.46, H 9.43, N 3.37.

**3-Acetyl-1-benzyl-2,5-dimethyl-4-(guaiazulen-1-yl)-1H-pyrrole (6j):** Blue crystals. mp > 300 °C; IR (KBr): ν 1650 cm<sup>-1</sup>; <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>): δ 1.39 (d, *J* = 6.8 Hz, 6H), 1.66 (s, 3H), 1.81 (s, 3H), 2.50 (s, 3H), 2.58 (s, 3H), 2.68 (s, 3H), 3.06-3.10 (m, 1H), 5.14 (s, 2H), 6.66 (d, *J* = 10.8 Hz, 1H), 6.97 (d, *J* = 7.6 Hz, 2H), 7.29-7.55 (m, 4H), 7.44 (s, 1H), 8.17 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 197.3, 145.8, 140.8, 139.3, 137.9, 137.0, 134.7, 134.7, 133.5, 133.4, 128.9, 127.4, 127.0, 126.4, 125.6, 124.5, 122.7, 122.3, 120.9, 46.8, 37.8, 30.6, 25.4, 24.7, 24.6, 12.9, 12.1, 10.6. *Anal.* Calcd for C<sub>30</sub>H<sub>33</sub>NO: C 85.06, H 7.85, N 3.31. Found: C 85.10, H 7.89, N 3.35.

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