Visible light-induced carbonylation of indoles with arylsulfonyl chlorides and CO

Xiangguang Li a, b, *, Deqiang Liang a, b, **, Wenzhong Huang a, b, Hongfu Zhou a, Zhao Li a, BaoLing Wang a, b, Yinhai Ma a, Hai Wang b

a Department of Chemical Science & Technology, Kunming University, Kunming 650214, China
b Key Laboratory of Yunnan Provincial Higher Education Institutions for Organic Optoelectronic Materials and Devices, Kunming University, Kunming 650214, China

Keywords:
Indol-3-yl aryl ketones
Carbonylation
Arylsulfonyl chlorides
Indoles
Visible light photocatalysis

1. Introduction

The development of new and expedient synthetic strategies for aromatic ketones from readily available starting materials has gained considerable attention in organic chemistry for decades, owing to the biological activity of aromatic ketones and their widespread prevalence in natural products, functional materials and pharmaceuticals. Among the reported techniques, metal-free reactions are of great importance in the development of new technologies for the synthesis of aromatic ketones. Particularly, as an important class of nitrogen-containing heterocyclic aromatic ketones, indol-3-yl aryl ketones are the common building blocks in natural products, biological active compounds and pharmaceuticals, and have showed excellent biological and pharmaceutical activity. Consequently, the construction of indol-3-yl aryl ketones has received increasing attention. The well-known synthetic procedures of indol-3-yl aryl ketones mainly include Friedel-Crafts reactions, Vilsmeier-Haack type reactions, and Grignard reactions. Recently, some promising protocols involving transition-metal-catalyzed acylation of C–H bonds for the synthesis of indol-3-yl aryl ketones has been developed. However, most of these reactions employ acids, bases or transition metals as the catalysts. Given the fact that some functional groups are sensitive to acids or bases, and the price of transition metal is generally high, which makes these reactions limited in use.

Over the last several years, visible-light-induced organic transformation has emerged as a powerful and promising tool, which has become a new research hotspot due to its efficient synthesis with safety and sustainability. However, most of the studies were based on the use of transition metal (usually Ru and Ir) polypyridyl complexes, which, under visible light irradiation, invoke a long-lived charge transfer state and initiate a series of transformations involving a single-electron transfer process with various functional groups. Although there are many advantages for ruthenium and iridium polypyridyl complexes in visible-light photocatalysis, exorbitant price and environmental pollution limit their further application in industrial processes. Besides, the strong coordinating ability of CO and stability of carbonyl complexes of transition-metal reduce the use of such organometallic catalysts in carbonylation.
reaction. Organic dyes have been used as a viable alternative in photoredox catalysis. Recently, Gu and co-workers reported their study on visible-light-induced indol-3-yl aryl ketone synthesis using aryl diazonium salts as a robust aryl radical source. Given the wide availability of arylsulfonyl chlorides, some of them like p-toluenesulfonfyl chloride being industrially produced on ton scale, this compound class appears to be attractive for the formation of aryl radical precursors. Gu reported that arylsulfonyl chlorides could generate aryl radicals with the aid of the excited state [Eosin Y]. In the presence of a certain amount of CO, the intermediate acyl radicals could be easily and efficiently created from aryl radicals, then acyl radicals would be further oxidized to acylium ion by the oxidized dye radical cation. We presumed that indoles might serve as a good nucleophile to attack the acylium ion intermediate. Herein, we describe our preliminary results on the development of visible-light-mediated carbonylation of indoles and arylsulfonyl chlorides for the synthesis of indol-3-yl aryl ketones under transition-metal-free, base-free and acid-free conditions in carbon monoxide atmosphere (Scheme 1).

2. Results and discussion

Initially, we focused our efforts on optimizing the reaction conditions for the carbonylation reaction between benzenesulfonyl chloride 1a and N-methylindole 2a. After a series of trials, treatment of the benzenesulfonyl chloride 1a with 2a and Eosin Y under irradiation with 5 W green LED light and a CO pressure of 80 atm in MeCN at room temperature afforded the desired product 3aa in the highest yield (Table 1, entry 1). Replacing 5 W green LED light with 5 W white LED light had a negative effect (Table 1, entry 2). Screening of the solvents such as DMSO, THF, EtoAc and PhCF₃, revealed that they were less effective than MeCN (Table 1, entries 3–6 versus entry 1). A number of other organic dyes, including Fluorescein, Rhodamine B and Rose Bengal, were subsequently investigated, and they were found to be less effective than Eosin Y (Table 1, entries 7–9 versus entry 1). Lower pressures of CO led to a low conversion (Table 1, entry 10). Furthermore, it was found that both visible-light photoredox catalysts and visible light are indispensable for the reaction to take place (Table 1, entries 11–12).

With a set of optimized conditions in hand, we then investigated the above visible-light photocatalysis protocol to a series of both arylsulfonyl chlorides 1 and indoles 2 to extend the substrate scope. We initially explored the scope of arylsulfonyl chlorides 1 in the presence of substrate 2a, Eosin Y, CO, and 5 W green LED light. As summarized in Table 2, the standard reaction conditions were found to be compatible with a wide range of arylsulfonyl chlorides 1. The good tolerance of functional groups in the reaction makes both electron-donating and -withdrawing arylsulfonyl chlorides successfully converted to the corresponding products in moderate to good yields (Table 2, entries 1–6). In addition, it was observed that the efficiency of the reaction was not affected in the presence of alkyl, ether, and halide groups, as well as the substituent at meta position on the arene group (Table 2, entry 7). However, when using the ortho-substituted arylsulfonyl chloride as the substrate, the yield of corresponding product 3ai was decreased (Table 2, entry 8), which suggested that the efficiency of the reactions was affected by the steric effect. Notably, indol-3-yl naphthyl ketones 3aj could be obtained directly in 51% yield by using the visible-light-induced acylation process (Table 2, entry 9), which is high affinity binding to the cannabinoid CB1 and CB2 receptors. It should be noted that the metal-free protocol can introduce heterocycles into this system, too, which makes this methodology more valuable for the preparation of pharmaceuticals and functional materials (Table 2, entry 10).

We then further investigated the substrate scope by reacting benzenesulfonyl chloride 1a with different indoles. Apart from 2a, 1-ethyl-2-methyl-1H-indole 2b smoothly reacted with 1a, leading to the corresponding product 3ba in 72% yield (Table 3, entry 1). Application of substrates 2c and 2d with electron-withdrawing groups, produced the desired products 3ca and 3da in a moderate yields (Table 3, entries 2–3). N-Methylindoles bearing electron-donating groups, such as methyl and methoxyl, reacted smoothly to provide the corresponding substituted indol-3-yl phenyl ketones 3ea-3ga in moderate to good yields (Table 3, entries 4–6). In addition, 1-methyl-1H-pyrrolo[2,3-b]pyridine 2h could deliver the expected product 3ha in 51% yield (Table 3, entry 7). To our delight, free NH-indoles 2i-2k could be smoothly converted to the expected products in moderate yields (Table 3, entries 8–10).

To gain insights into the mechanism of the reaction, a series of control experiments were conducted. It has been reported that the reaction of arylsulfonyl chlorides with N-methylindoles can deliver 1-methyl-3-(arylsulfonyl)-1H-indoles, but when we investigated our protocol in Tables 1–3, no sulfonylated product or related intermediates were found in our conditions. Recently Zheng have developed a visible light mediated 3-sulfenylation of N-methylindoles with arylsulfonyl chlorides. When 1-methyl-3-(phenylthio)-1H-indole 4 was subjected to the reaction, no desired product was obtained (Scheme 2, equation 1), which might exclude 4 as the intermediate of this redox reaction. Addition of a radical-trapping
reagent, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (1.0 equiv) to the model reaction, no aryl ketone was obtained and the TEMPO trapped intermediates 5 and 6 were detected (Scheme 2, equation 2), indicating that the photoreaction proceeds via a radical pathway. Furthermore, when no photocatalyst was used and/or the reaction was performed under dark conditions, the product yields severely dropped. Even at increased temperature (up to 80 °C) in the dark, no desired product was formed, which means that homolytic bond cleavage of the starting material to an aryl radical under these conditions was excluded.

Based on the control experiments and previous reports, the mechanism of this transformation was hypothesized as shown in Scheme 3. Under visible-light irradiation, the photocatalyst was excited, which resulted in the reduction of the phenyl-sulfonyl chloride through a single-electron transfer process to yield aryl radical A and the dye radical cation [Eosin Y⁺]. The aryl radical A then trapped a CO molecule and delivered the acyl radical B, which was further oxidized by [Eosin Y⁺] to yield acylium C while [Eosin Y⁺] was reduced to the ground state to complete the catalytic cycle. Finally, nucleophilic attack of the

---

Table 2
Scope of arylsulfonyl chlorides 1.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Arylsulfonyl chlorides 1</th>
<th>Products 3</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>59</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>57</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td>68</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td>65</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td>49</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td>51</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td>55</td>
</tr>
</tbody>
</table>

**a** Reaction conditions: 1 (0.3 mmol), 2a (0.4 mmol), Eosin Y (2 mol%), MeCN (3.0 mL), room temperature, CO (80 atm), 5 W green LED light for 8 h.

**b** Isolated yields.
Table 3
Scope of indoles 2.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Indoles 2</th>
<th>Products 3</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Indole 1a" /></td>
<td><img src="image2" alt="Ketone 1a" /></td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Indole 2b" /></td>
<td><img src="image4" alt="Ketone 2b" /></td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Indole 2c" /></td>
<td><img src="image6" alt="Ketone 2c" /></td>
<td>53</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Indole 2d" /></td>
<td><img src="image8" alt="Ketone 2d" /></td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="Indole 2e" /></td>
<td><img src="image10" alt="Ketone 2e" /></td>
<td>57</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="Indole 2f" /></td>
<td><img src="image12" alt="Ketone 2f" /></td>
<td>67</td>
</tr>
<tr>
<td>7</td>
<td><img src="image13" alt="Indole 2g" /></td>
<td><img src="image14" alt="Ketone 2g" /></td>
<td>51</td>
</tr>
<tr>
<td>8</td>
<td><img src="image15" alt="Indole 2h" /></td>
<td><img src="image16" alt="Ketone 2h" /></td>
<td>50</td>
</tr>
<tr>
<td>9</td>
<td><img src="image17" alt="Indole 2i" /></td>
<td><img src="image18" alt="Ketone 2i" /></td>
<td>47</td>
</tr>
<tr>
<td>10</td>
<td><img src="image19" alt="Indole 2j" /></td>
<td><img src="image20" alt="Ketone 2j" /></td>
<td>22</td>
</tr>
</tbody>
</table>

* Reaction conditions: 1a (0.3 mmol), 2 (0.4 mmol), Eosin Y (2 mol%), MeCN (3.0 mL), room temperature, CO (80 atm), 5 W green LED light for 8 h.
* Isolated yields.

3. Conclusion

In conclusion, we have developed a novel and simple visible-light-mediated carbonylation for the direct synthesis of indol-3-yl aryl ketones from commercially available arylsulfonfonyl chlorides and indoles. The utilization of inexpensive, readily available starting materials and catalysts is significantly advantageous, allowing for the increased usefulness of the reaction. In particular, this carbonylation reaction uses the simple and readily available Eosin Y as an efficient organic catalyst, rather than transition-metal complexes. The transition-metal complexes involving additives, alkaline or acidic reaction medium are often high cost with noble metal, and are intractable to be completely removed from products, especially in the pharmaceutical drug production. Further investigation on the practical application of the reaction is underway.

4. Experimental section

4.1. General materials and methods

Reagents were obtained commercially and used as received. Solvents were purified and dried by standard methods. The supplier of the autoclave irradiation set up is YanZheng Co., Ltd., China. All title products were characterized by Infrared (IR), MS, 1H NMR, 13C NMR and High Resolution mass spectrometry (HRMS). IR spectra were recorded in frequency of the absorption (cm\(^{-1}\)). 1H NMR and 13C NMR spectra were recorded on 100 MHz in CDCl3 or DMSO-d6, using trimethylsilane (TMS) as an internal standard. Chemical shift values (\(\delta\)) are given in ppm. Coupling constants (\(J\)) were measured in Hz. GC-MS analyses were performed on a SHIMADZU QP2010 High Resolution mass spectrometer (HRMS) spectra were recorded on a Bruker microTOF-Q II analyzer. 200–300 mesh silica gel was used for column chromatography.

4.2. General procedure for synthesis of indol-3-yl aryl ketones 3

To an 8 mL vial equipped with a magnetic stir bar was charged with 1 (0.3 mmol), 2 (0.4 mmol), Eosin Y (2 mol%) and dry MeCN (3.0 mL). The vial was purged with \(N_2\) in the dark and then transferred into an autoclave with a Quartz window bottom. After the autoclave was flushed three times, 80 atm of CO was slowly filled. The reaction was irradiated with external LEDs at room temperature for 8 h. After the reaction was finished, the gas was carefully released and the vial retrieved, the reaction mixture was diluted with 8 mL H2O, extracted with ethyl acetate (15 mL x 3). The extractions were washed with brine and then dried with Na2SO4. After concentrated in vacuum, the resulting residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1 to 2:1) to give the desired products 3.

(1-Methyl-1H-indol-3-yl)(phenyl)methanone (3aa). \(^{14}\) Yield: 81%, 571 mg; 1H NMR (400 MHz, CDCl3) \(\delta\): 8.37–8.34 (m, 1H), 7.73 (d, \(J = 6.8\) Hz, 2H), 7.73–7.38 (m, 4H), 7.29 (d, \(J = 3.6\) Hz, 1H), 7.19 (d, \(J = 8.4\) Hz, 2H), 7.19–7.23 (m, 3H, \(J = 4.0\) Hz), 7.08 (s, 1H); 13C NMR (100 MHz, CDCl3) \(\delta\): 190.9, 140.9, 137.9, 137.5, 131.1, 128.6, 128.3, 127.1, 123.6, 122.74, 122.73, 115.9, 109.6, 33.6, IR (neat cm\(^{-1}\)) 2923, 2854, 1675 (C=O); LRMS (El 70 ev) \(m/z\) (%): 265 (M\(^+\), 100); HRMS m/z (ESI) calcd for C16H13NNaO (M + Na\(^+\)): 285.0889, found 285.0897.

(4-Methoxyphenyl)(1-methyl-1H-indol-3-yl)methanone (3ab). \(^{14}\) Yield: 74%, 58.8 mg; 1H NMR (400 MHz, CDCl3) \(\delta\): 8.40–8.38 (m, 1H, 7.81 (d, \(J = 8.4\) Hz, 2H), 7.51 (s, 1H), 7.31–7.23 (m, 3H, \(J = 5.0\) Hz), 6.97 (d, \(J = 8.4\) Hz, 2H), 3.88 (s, 3H), 3.81 (s, 3H); 13C NMR (100 MHz, CDCl3) \(\delta\): 191.1, 162.1, 137.2, 137.0, 133.2, 130.4, 127.1, 123.1, 122.2, 122.0, 115.2, 113.2, 109.6, 55.2, 33.4; IR (neat cm\(^{-1}\)): 1643 (C=O); LRMS (El 70 ev) \(m/z\) (%): 255 (M\(^+\), 100); HRMS m/z (ESI) calcd for C16H13NNaO2 (M + Na\(^+\)): 288.0994, found 288.1002.

(1-Methyl-1H-indol-3-yl)p-tolyl)methanone (3ac). \(^{14}\) Yield: 78%, 58.3 mg; 1H NMR (400 MHz, CDCl3) \(\delta\): 8.34–8.31 (m, 1H, 7.77 (d, \(J = 8.0\) Hz, 2H), 7.50 (s, 1H), 7.37–7.34 (m, 3H), 7.30 (d, \(J = 7.2\) Hz, 2H), 3.84 (s, 3H), 2.43 (s, 3H); 13C NMR (100 MHz, CDCl3) \(\delta\): 190.5,
7.49 (s, 1H), 7.39 (d, J = 115.3, 109.8, 33.2; IR (neat cm⁻¹): 149.2, 146.0, 138.2, 137.7, 129.4, 126.9, 124.2, 123.4, 123.0, 122.5, 126.7, 123.8, 122.9, 126.6, 115.1, 109.7, 33.6; IR (neat cm⁻¹): 1664 (C=O); LRMS (EI 70 ev) m/z (%): 269 (M⁺, 100); HRMS m/z (ESI) calcd for C₁₆H₁₂NNaO (M + Na⁺) 292.0500, found 292.0504.

(3-Chloro)-1-methyl-1H-indol-3-yl)methanone (3ah). Yield: 65%, 52.4 mg; ¹H NMR (400 MHz, CDCl₃) δ: 8.42 (d, J = 6.4 Hz, 1H), 7.82 (t, J = 6.6 Hz, 2H), 7.68 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 8.4 Hz, 2H), 7.43–7.37 (m, 3H), 3.85 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 189.0, 142.4, 137.9, 137.5, 134.2, 130.9, 129.6, 128.6, 128.5, 126.7, 123.8, 122.9, 126.6, 115.1, 109.7, 33.6; IR (neat cm⁻¹): 1655 (C=O); LRMS (EI 70 ev) m/z (%): 269 (M⁺, 100); HRMS m/z (ESI) calcd for C₁₆H₁₂NNaO (M + Na⁺) 292.0500, found 292.0508.

(2-Chloro)-1-methyl-1H-indol-3-yl)methanone (3ai). Yield: 49%, 39.5 mg; ¹H NMR (400 MHz, CDCl₃) δ: 8.37 (d, J = 6.6 Hz, 1H), 7.48–7.42 (m, 4H), 7.34–7.30 (m, 1H), 3.70 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 188.8, 140.5, 138.8, 137.7, 130.9, 130.0, 128.6, 126.4, 126.4, 123.8, 123.0, 122.6, 116.4, 109.7, 33.6; IR (neat cm⁻¹): 1649 (C=O); LRMS (EI 70 ev) m/z (%): 269 (M⁺, 100); HRMS m/z (ESI) calcd for C₁₆H₁₂NNaO (M + Na⁺) 292.0500, found 292.0508.

(1-Methyl-1H-indol-3-yl)(naphthalen-3-yl)methanone (3aj). Yield: 57%, 51.8 mg; ¹H NMR (400 MHz, CDCl₃) δ: 8.42 (d, J = 6.4 Hz, 1H), 7.82 (t, J = 6.6 Hz, 2H), 7.74 (s, J = 8.0 Hz, 2H), 7.49 (s, 1H), 7.38 (s, 3H), 3.87 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 183.3, 149.2, 146.0, 138.2, 133.2, 129.4, 126.9, 124.2, 123.4, 123.0, 122.5, 115.3, 109.8, 33.2; IR (neat cm⁻¹): 1657 (C=O); LRMS (EI 70 ev) m/z (%): 280 (M⁺, 100); HRMS m/z (ESI) calcd for C₁₆H₁₂N₂NaO₃ (M + Na⁺) 303.0673, found 303.0679.

(1-Chloro)-1-methyl-1H-indol-3-yl)(4-nitrophenyl)methanone (3ae). Yield: 59%, 46.9 mg; ¹H NMR (400 MHz, CDCl₃) δ: 8.41 (d, J = 6.4 Hz, 1H), 7.88 (d, J = 6.0 Hz, 2H), 7.49 (s, 1H), 7.36 (m, 3H), 7.16–7.12 (m, 2H), 3.84 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ: 189.2, 165.6 (d, J = 258.8 Hz, 3H), 173.5 (d, J = 1.4 Hz, 3H), 131.1 (d, J = 29.5 Hz, 127.1), 127.3, 122.7, 115.2 (d, J = 21.8 Hz, 109.7, 33.5; IR (neat cm⁻¹): 1659 (C=O); LRMS (EI 70 ev) m/z (%): 253 (M⁺, 100); HRMS m/z (ESI) calcd for C₁₆H₁₂ClNNaO (M + Na⁺) 276.0795, found 276.0791.

Scheme 2. Control experiments.
(15-Dimethyl-1H-indol-3-yl)(phenyl)methanone (3a).

Yield: 76%, 56.8 mg; 1H NMR (400 MHz, CDCl3): δ 7.77 (d, J = 6.4 Hz, 2H), 7.51 (d, J = 7.6 Hz, 1H), 7.43 (t, J = 6.4 Hz, 3H), 7.24–7.18 (m, 2H), 3.77 (s, 3H), 2.49 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 190.4, 140.3, 138.1, 135.7, 132.2, 130.6, 128.4, 128.0, 127.2, 125.2, 122.2, 114.5, 109.0, 33.1, 21.2; IR (neat cm⁻¹): 1649 (C=O); LRMS (EI 70 ev) m/z (%): 269 (M⁺, 100); HRMS m/z (ESI) calc for C₁₉H₁₃NNaO (M + Na⁺) 292.0500, found 292.0494.

(4-Methoxy-1-methyl-1H-indol-3-yl)(phenyl)methanone (3a).

Yield: 75%, 45.3 mg; 1H NMR (400 MHz, CDCl3): δ 7.99 (d, J = 7.6 Hz, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.31–7.26 (m, 3H), 7.12 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 8.0 Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 3.72 (s, 3H), 3.63 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 190.5, 143.0, 140.7, 139.1, 135.4, 131.3, 129.7, 127.4, 124.4, 116.6, 116.5, 102.8, 102.1, 55.4, 33.5; IR (neat cm⁻¹): 1649 (C=O); LRMS (EI 70 ev) m/z (%): 249 (M⁺, 100); HRMS m/z (ESI) calc for C₁₇H₁₅NNaO (M + Na⁺) 288.0994, found 288.0999.

(1,7-Dimethyl-indol-3-yl)(phenyl)methanone (3a).

Yield: 67.5%, 50.6 mg; 1H NMR (400 MHz, CDCl3): δ 8.27 (d, J = 7.2 Hz, 1H), 7.76 (d, J = 7.6 Hz, 2H), 7.55–7.51 (m, 1H), 7.45 (t, J = 7.2 Hz, 2H), 7.33 (s, 1H), 7.19 (t, J = 7.2 Hz, 1H), 7.03 (d, J = 7.2 Hz, 1H), 4.03 (s, 3H), 2.74 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 190.5, 140.7, 139.4, 132.6, 130.8, 128.6, 128.0, 126.4, 122.7, 121.5, 120.6, 115.1, 37.5, 19.4; IR (neat cm⁻¹): 1667 (C=O); LRMS (EI 70 ev) m/z (%): 249 (M⁺, 100); HRMS m/z (ESI) calc for C₁₇H₁₅NNaO (M + Na⁺) 292.1046, found 292.1055.

(1-Methyl-1H-pyrrole[2,3-b]pyridin-3-yl)(phenyl)methanone (3a).

Yield: 51%, 36.1 mg; 1H NMR (400 MHz, CDCl3): δ 8.65 (d, J = 7.6 Hz, 1H), 8.44 (dd, J = 4.8 Hz, J = 0.4 Hz, 1H), 7.79 (d, J = 7.2 Hz, 2H), 7.67 (s, 1H), 7.56–7.53 (m, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.29–7.26 (m, 1H), 3.92 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 190.3, 148.0, 144.3, 139.7, 137.2, 131.4, 131.0, 128.8, 128.3, 119.4, 118.2, 113.6, 32.0; IR (neat cm⁻¹): 1641 (C=O); LRMS (EI 70 ev) m/z (%): 236 (M⁺, 100); IR (neat cm⁻¹): 1667 (C=O); LRMS (EI 70 ev) m/z (%): 249 (M⁺, 100); HRMS m/z (ESI) calc for C₁₇H₁₅NNaO (M + Na⁺) 259.0842, found 259.0851.

(1H-indol-3-yl)(phenyl)methanone (3a).

Yield: 50%, 33.2 mg; 1H NMR (400 MHz, DMSO-d₆): δ 12.06 (brs, 1H), 8.26 (t, J = 5.8 Hz, 1H), 7.91 (s, 1H), 7.78 (d, J = 7.2 Hz, 2H), 7.62–7.52 (m, 4H), 7.29 (d, J = 6.0 Hz, J = 6.4 Hz, 2H); 13C NMR (100 MHz, DMSO-d₆): δ 190.6, 140.8, 137.1, 136.3, 131.6, 128.9, 128.8, 126.6, 123.8, 122.5, 121.9, 115.4, 112.8; IR (neat cm⁻¹): 1648 (C=O); LRMS (EI 70 ev) m/z (%): 221 (M⁺, 100); HRMS m/z (ESI) calc for C₁₇H₁₃NNaO (M + Na⁺) 259.0842, found 244.0733, found 244.0740.

(2-Methyl-1H-indol-3-yl)(phenyl)methanone (3a).

Yield: 47%, 33.1 mg; 1H NMR (400 MHz, DMSO-d₆): δ 11.96 (brs, 1H), 7.60 (t, J = 7.2 Hz, 3H), 7.52 (t, J = 7.4 Hz, 2H), 7.40 (d, J = 8.0 Hz), 7.33 (d, J = 8.0 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H); 2.37 (s, 3H); 13C NMR (100 MHz, DMSO-d₆): δ 192.3, 145.0, 142.0, 135.4, 131.5, 128.8, 124.8, 127.7, 122.3, 121.4, 120.4, 112.9, 111.7, 14.6; IR (neat cm⁻¹): 1640 (C=O); LRMS (EI 70 ev) m/z (%): 235 (M⁺, 100); HRMS m/z (ESI) calc for C₁₉H₁₄NNaO (M + Na⁺) 258.0881, found 258.0881.

(6-Fluoro-1H-indol-3-yl)(phenyl)methanone (3a).

Yield: 44%, 31.5 mg; 1H NMR (400 MHz, DMSO-d₆): δ 12.10 (brs, 1H), 8.25 (t, J = 7.2 Hz, 1H), 7.93 (s, 1H), 7.79 (d, J = 7.2 Hz, 2H), 7.61–7.52 (m, 3H), 7.33 (d, J = 6.0 Hz, 1H), 7.13 (t, J = 9.4 Hz, 1H); 13C NMR (100 MHz, DMSO-d₆): δ 190.5, 161.0, 158.7, 140.5, 137.3, 137.1, 136.9, 131.7, 128.9, 128.3, 123.3, 123.0, 115.3, 110.6, 99.1, 98.8; IR (neat cm⁻¹): 1655 (C=O); LRMS (EI 70 ev) m/z (%): 239 (M⁺, 100); HRMS m/z (ESI) calc for C₁₉H₁₄FNNaO (M + Na⁺) 262.0638, found 262.0644.
1535–1538;
2707–2713;
12. (a) Tocco G, Begala M, Esposito F, Caboni P, Cannas V, Tramontano E. Tetra-
hedron Lett. 2013;54:6237–6241;
2016;8:2206–2209.
10445–10447.