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ORIGINAL ARTICLE

Design of a new method for the synthesis of novel 2-aryl/alkyl-3*H*-indol-3-ones

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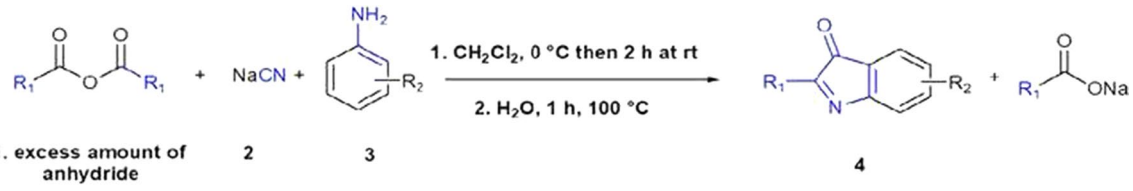
Abstract

In this research, a mild, efficient, and general method has been developed to synthesize the new derivatives of 2-aryl/alkyl-3*H*-indol-3-ones in moderate to excellent yields. This method allowed the syntheses of these compounds via the three-component reaction of anhydride compound, sodium cyanide, and aniline derivatives using acetic anhydride as an organic catalyst in one-pot reactions. The advantages of this method include mild reaction conditions, simple procedures, and easy workup.

Graphical abstract



R_1	R_2	yield	R_1	R_2	yield	R_1	R_2	yield
CH_3	H	85	$CH_2CH_2CH_3$	H	81	p-Tolyl	H	80
CH_3	4-CH_3	88	$CH_2CH_2CH_3$	4-CH_3	81	p-Tolyl	4-CH_3	70
CH_3	4-OCH_3	80	$CH_2CH_2CH_3$	4-OCH_3	77	p-Tolyl	4-Br	78
CH_3	4-F	75	$CH_2CH_2CH_3$	4-F	74	4-CH_3OPh	H	74
CH_2CH_3	H	86	$CH_2CH_2CH_3$	4-CO_2CH_3	73	4-CH_3OPh	4-CH_3	73
			$CH_2CH_2CH_2OCOCH_3$	H	74	4-CH_3OPh	4-Br	70

Keywords Organic catalysis · Heterocycles · Synthetic design · Indol-3-one

Introduction

2-Aryl-3*H*-indol-3-ones were found as one of the most important five-membered ring nitrogen heterocyclic compounds which had a wide range of biological activities such as antimalarial [1], antiplasmodial [2], antibacterial [3, 4], and antifungal [5, 6]. Indol-3-ones were used as a molecular core in the design and synthesis of some new molecules such as imidazoloindolines [7], matemone [8], phalarine [9], difluoroalkylated indolin-3-ones [10], 2,3-dihydro-1*H*-imidazo[1,5-*a*]indol-9(9a*H*)-one derivatives [11], and 3-(2-isocyanoethyl)indoles [12]. Because of these important applications, several methods have been described for the preparation of indol-3-ones derivatives, including oxidation of indoles with TEMPO + BF_4 [13], oxidative activation of o-alkynylanilines [14], dearomative oxyarylation, oxyallylation, and oxycyanation of indoles with TEMPO oxoammonium salt [15], dearomatization–alkoxylation of *N*-Boc indoles with ruthenium-catalyzed oxidative [16], cascade reaction of *o*-nitroalkynes from indoles with gold(I)-catalyzed [17], 2-alkynyl arylazides with palladium catalyzed [18], Michael addition of 1-acetylindolin-3-ones to β,γ-unsaturated α-ketoesters [19], and cyclizations of ortho-nitrochalcones [20]. Although these methods have been widely used in the literature, they suffer from

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Scheme 1 Synthesis of 3*H*-indol-3-ones

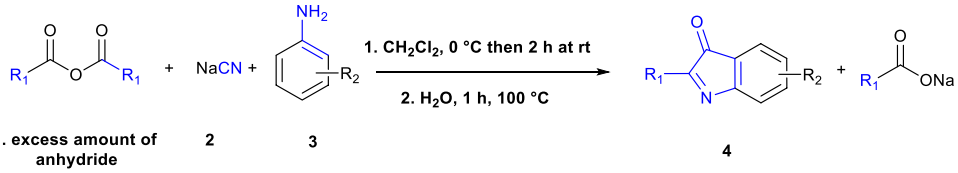
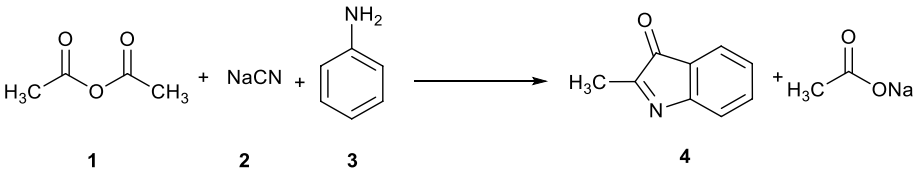


Table 1 Optimization of the reaction conditions for the synthesis of 2-methyl-3*H*-indol-3-one



Entry	Ratio: Aniline/cyanide/acetic anhydride	Solvent	Temperature	Time (h)	Yield[a]
1	1: 1: 1	CH_2Cl_2	r.t	24	[b]trace
2	1: 1: 1	CH_2Cl_2	reflux	24	[b]trace
3	1: 1: ethyl acetate	CH_2Cl_2	r.t	6	[b]0
4	1: 1: 1.5	CH_2Cl_2	r.t	6	60
5	1: 1: 2.1	CH_2Cl_2	r.t	6	80
6	1: 1: 2.5	CH_2Cl_2	r.t	6	82
7	1: 1.1: 2.1	CH_2Cl_2	r.t	6	83
8	1: 1.2: 2.1	CH_2Cl_2	r.t	6	87
9	1: 1.2: 2.1	CH_2Cl_2	r.t	4	87
10	1: 1.2: 2.1	CH_2Cl_2	r.t	2	85
11	1: 1.2: 2.1	CH_2Cl_2	r.t	1	70
12	1: 1.2: 2.1	CHCl3	r.t	6	71
13	1: 1.2: 2.1	*n*-hexane	r.t	6	69
14	1: 1.2: 2.1	benzene	r.t	6	77
15	1: 1.2: 2.1	CCl_4	r.t	6	73
16	1: 1.2: 2.1	methanol	r.t	6	0

[a]The reaction was monitored with TLC

[b]All yields represent the isolated product

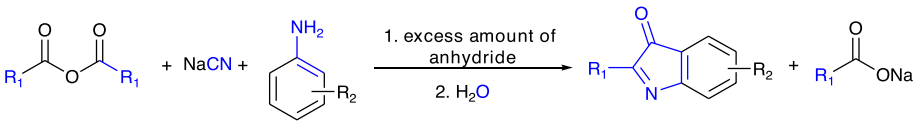
several disadvantages, such as exclusive substrates and catalysts, relatively low performance, hazardous reagents, limited substrate scope, and inconvenient reaction conditions. Therefore, it is desirable to access indol-3-one compounds via multicomponent reactions without transition metal. In the past few years, more transition-metal-free reactions have been developed for organic transformation [21]. Herein, we described a metal-free intermolecular coupling reaction of cyanide with aniline derivatives and excess amounts of organic acid anhydride for the synthesis of 3H-indol-3-ones derivatives under mild reaction conditions. As a continuation of the research, the development of a new multicomponent methodology was applied for the preparation of some 3*H*-indol-3-ones (4) from excess anhydride acetic derivatives (1), sodium cyanide (2), and aniline derivatives (3) with high yields, which are shown in Scheme 1. The applicability of the present method to a large-scale process was examined with 60 mmol sodium cyanide, 50 mmol aniline, and 105 mmol of acetic anhydride, which gave 2-methyl-3*H*-indol-3-one in 85% yield.

Results and discussion

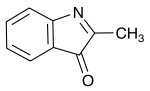
The reaction of anhydride derivatives (1), sodium cyanide (2), and aniline derivatives (3) in CH_2Cl_2 afforded the corresponding 2-aryl/alkyl-3*H*-indol-3-ones (4) by a one-pot procedure in high yields (Table 2).

In our initial study, the reaction of acetic anhydride (1), sodium cyanide (2), and aniline (3) was chosen as a model reaction to optimize the reaction condition including the ratio of substrates, solvent, temperature, and time by

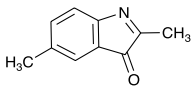
Table 2 Synthesis of 2-aryl/alkyl-3*H*-indol-3-ones via multicomponent reaction in one-pot procedure (The sodium cyanide (12.0 mmol),↑aniline (10.0 mmol), and acetic anhydride (21 mmol) in the presence of 10 mL of anhydrous in CH_2Cl_2 at room temperature, stirred for 2 h, and 10 mL water was added, stirred, and refluxed for 1 h)



1 **2** **3**



3a 85%



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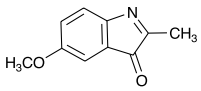

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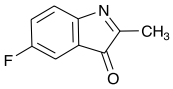
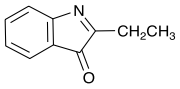


3d 75%



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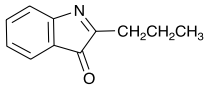
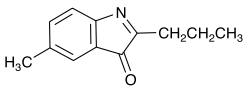
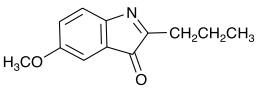


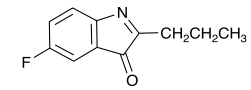
3f 81%



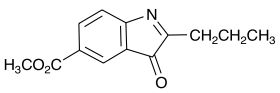
3g 81%



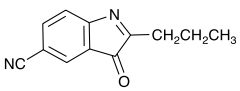
3h 77%



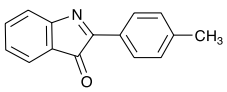
3i 74%



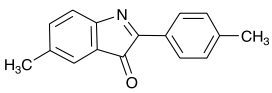
3j 73%



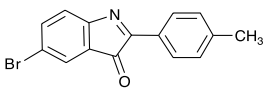
3k 75%



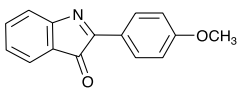
3l 80% (46%)



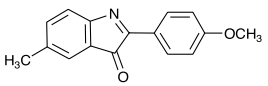
3m 70%



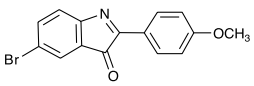
3n 78%



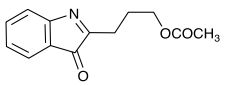
3o 81% (74%,){Najahi, 2014 #145}



3p 73%



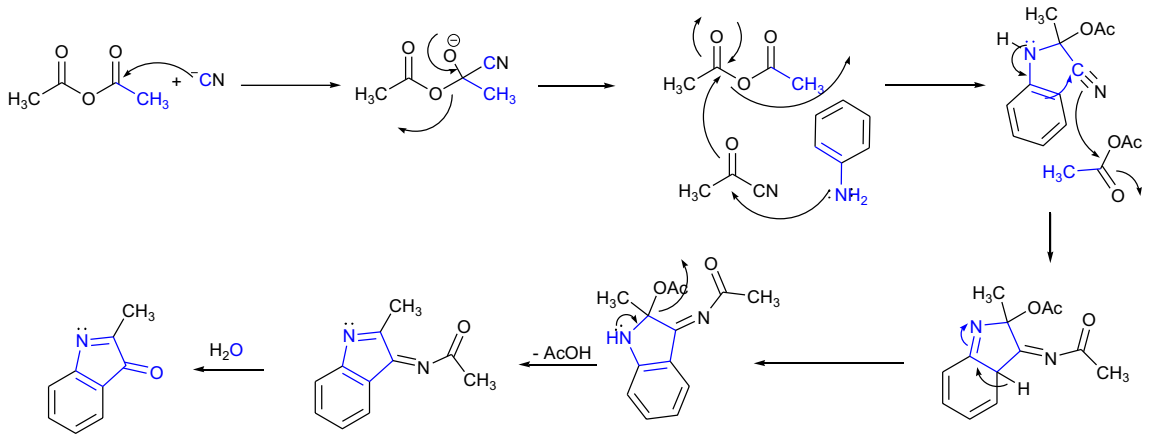
3q 70%



3r 74%

applying the same portion of substrates (acetic anhydride, sodium cyanide, and aniline) (Table 1). Trace amount of product was obtained at room temperature and under reflux conditions (Table 1, entries 1 and 2). It is noted that the yield of the product was increased from 60 to 80% by increasing the molar ratio of acetic anhydride from 1.5 to 2.1, respectively (Table 1, entries 4–5). No significant change to yield of product was shown in the molar ratio of acetic anhydride to 2.5 and excess (Table 1, entry 6). The results in Table 1 (entries 7–8) show that the use of 1.2 molar ratio cyanide is sufficient to promote the reaction. In addition, chloroform, *n*-hexane, benzene, carbon tetrachloride, and methanol were also tested as a solvent. In these cases, product was formed in slightly lower yields (Table 1, entries 13–16). As a result of performed experiments, CH_2Cl_2 (10 mL), and the ratio of acetic anhydride/sodium cyanide/aniline (1:1.2:2.1) at room temperature was chosen as the optimal condition for further studies (Table 1, entry 10).

Under the optimized reaction conditions, various amines reacted with acetic anhydride and cyanide to give 2-aryl/alkyl-3*H*-indol-3-ones in high yields within 2 h, and the results are shown in Table 2. The use of various aryl amines



Scheme 2 The reaction mechanism for the formation of 2-methyl-3*H*-indol-3-one via cyanide, aniline, and acetic anhydride

reveals that aryl amines containing electron-donating groups exhibited a slightly better effect than those with electron-withdrawing substituents. Investigations on some anhydrides with aliphatic and aromatic groups were done by the reaction of amines with aliphatic and aromatic anhydrides. The results showed that even in the presence of aromatic anhydrides, the formation of 3*H*-indol-3-ones is favorable under the reaction conditions (Table 2, entries 3 m, 3p).

The proposed mechanism of the reaction is presented in Scheme 2. Firstly, the cyanide ion reacted with the carbonyl group of acetic anhydride. Acetic acid acetoxy-cyano-methyl-methyl ester intermediate was formed and reacted with aniline. After the cyclization reaction of aniline with alkyl nitrile in the presence of excess acetic anhydride, aromatization was performed and finally with the addition of water the desirable product formed.

Conclusion

In conclusion, a new and efficient method with an easy procedure was described for the synthesis of 3*H*-indol-3-ones for some novel products provided with moderate to good yields. We have developed a one-pot synthesis of 2-aryl/alkyl-3H-indol-3-ones via a three-component reaction between an anhydride compound, sodium cyanide, and aniline derivatives. The structure of all products was confirmed by FT-IR spectroscopy, mass spectrometer, ^{1}H NMR, and ^{13}C NMR spectra.

Experimental

Materials

All chemicals and reagents were obtained from Sigma–Aldrich and used without further purification.

Instruments

The products were characterized by various analyses such as nuclear magnetic resonance (NMR) spectroscopy, mass spectrometer using electrospray ionization (ESI) in positive-ion and Fourier transform infrared (FT-IR) spectroscopy. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker Avance 400 MHz and 100 MHz, respectively, and chemical shifts are expressed in ppm using TMS as an internal standard. FT-IR spectra were obtained on a Bruker, Equinox 55 spectrometer, and mass spectra were obtained using a commercial apparatus (Agilent Technologies, CA, USA).

Procedure for the synthesis of 2-methyl-3*H*-indol-3-one (Table 1, entry 11)

Briefly, 0.62 g of sodium cyanide 95.0% (12 mmol), 0.9 ml of aniline (10 mmol), and 10 mL of anhydrous CH_2Cl_2 were added to a round-bottomed flask (50 ml). The reaction mixture was cooled to 0 °C in an ice bath and placed under a nitrogen atmosphere. Then, 2.0 ml acetic anhydride (21 mmol) was added dropwise to the reaction mixture at 0 °C, allowed to warm up to room temperature, and stirred for another 2 h. The solvent was removed, and then, 10 mL water was added, stirred, and refluxed for

1 h. The reaction was monitored with TLC. After completing the reaction, the reaction mixture was cooled to room temperature, 20 mL of cooled water was added and the product was extracted with CH_2Cl_2 (3 × 10 mL). The eluting organic solvent was evaporated with a vacuum evaporator. The product was dried and purified by recrystallization from ethanol.

2-Methyl-3*H*-indol-3-one (3a)

FT-IR $\nu(cm^{-1})$: 1757, 1724, 1539, 835, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (*s*, 3H), 3.11 (*s*, 3H), 7.24 (dd, *J* = 7.88, 1 Hz, 1H), 7.37 (*d*, *J* = 7.88 Hz, 1H), 7.69 (*s*, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.77, 21.10, 98.05, 116.40, 124.67, 133.39, 134.51, 138.66, 149.93, 195.92; HRMS m/z (ESI): calculated for $C_{10}H_9NO$ $[M+H]^+$ 159.0679, found 159.0677.

2,5-Dimethyl -3*H*-indol-3-one (3b)

FT-IR $\nu(cm^{-1})$: 1757, 1724, 1539, 835, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (*s*, 3H), 3.11 (*s*, 3H), 7.24 (dd, *J* = 7.88, 1 Hz, 1H), 7.37 (*d*, *J* = 7.88 Hz, 1H), 7.69 (*s*, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.77, 21.10, 98.05, 116.40, 124.67, 133.39, 134.51, 138.66, 149.93, 195.92; HRMS m/z (ESI): calculated for $C_{10}H_9NO$ $[M+H]^+$ 159.0679, found 159.0677.

5-Methoxy-2-methyl-3*H*-indol-3-one (3c)

FT-IR $\nu(cm^{-1})$: 1758, 1723, 1539, 835, 763; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.03 (s, 3H), 3.79 (*s*, 3H), 6.98 (dd, *J* = 8.76, 2.76 Hz, 1H), 7.36–7.42 (*m*, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.59, 58.47, 105.49, 116.45, 123.97, 128.20, 157.87, 158.52, 162.29, 191.38; HRMS m/z (ESI): calculated for $C_{10}H_9NO_2$ $[M+H]^+$ 175.0628, found 175.0627.

5-Fluoro-2-methyl-3*H*-indol-3-one (3d)

FT-IR $\nu(cm^{-1})$: 1759, 1724, 1537, 837, 764; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.02 (s, 3H), 7.15–7.22 (*m*, 1H), 7.50 (*d*, *J* = 8.76 Hz, 1H), 7.63 (dd, *J* = 8.28, 2.64 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.74, 99.17, 112.01, 112.28, 115.68, 115.72, 120.18, 120.40, 136.28, 136.36, 159.45, 161.97, 190.08; HRMS m/z (ESI): calculated for C_9H_6FNO $[M+H]^+$ 163.0428, found 163.0431.

2-Ethyl-3*H*-indol-3-one (3e)

FT-IR $\nu(cm^{-1})$: 1759, 1726, 1541, 837, 762; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (*t*, *J* = 7.36 Hz,3H), 3.14 (*q*, *J* = 7.4 Hz,2H), 7.16–7.22 (*m*, 1H), 7.27–7.36 (*m*, 1H), 7.65 (*d*, *J* = 9.12,1H), 7.97(*d*, *J* = 8.76,1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.81, 25.37, 115.93, 119.09, 121.25, 128.44, 131.29, 157.54, 159.67, 190.79; HRMS m/z (ESI): calculated for $C_{10}H_9NO$ $[M+H]^+$ 159.0679, found 159.0678.

2-Propyl-3*H*-indol-3-one (3f)

FT-IR $\nu(cm^{-1})$: 1757, 1721, 1537, 835, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (*t*, *J* = 7.52 Hz, 3H), 2.28–2.39 (*m*, 2H), 3.06 (*t*, *J* = 7.36 Hz, 2H), 7.15–7.21 (*m*, 1H), 7.29–7.36 (*m*, 1H), 7.65(*d*, *J* = 9 Hz, 1H), 7.99(*d*, *J* = 8.88 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.70, 14.91, 22.24, 113.79, 121.38, 123.20, 130.99, 134.36, 140.09, 147.47, 186.73; HRMS m/z (ESI): calculated for $C_{10}H_9NO_2$ $[M+H]^+$ 173.0835, found 173.0831.

5-Methyl-2-propyl-3*H*-indol-3-one (3 g)

FT-IR $\nu(cm^{-1})$: 1764, 1724, 1538, 770, 692; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (*t*, *J* = 7.4 Hz,3H),1.72–1.82 (*m*, 2H), 2.36 (*s*, 3H), 3.06 (*t*, *J* = 7.36 Hz, 2H), 7.02 (*d*, *J* = 8.88 Hz,1H), 7.36 (*s*, 1H), 7.84 (*d*, *J* = 8.88 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.78, 17.12, 22.43, 25.37, 113.33, 118.01, 120.59, 131.96, 141.86, 158.21, 159.32, 190.42; HRMS m/z (ESI): calculated for. $[M+H]^+$ 187.0992, found 187.0990.

5-Methoxy-2-propyl-3*H*-indol-3-one (3 h)

FT-IR $\nu(cm^{-1})$: 1762, 1721,1546, 1249, 1043, 780, 761, 757; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.97 (*t*, *J* = 7.25 Hz, 3H), 1.71–1.81 (*m*, 2H), 3.03 (*t*, *J* = 7.24 Hz, 2H), 3.82 (*s*, 3H), 6.71 (sd, *J* = 1.36 Hz 1H), 6.85 (dd, *J* = 9.4, 2 Hz, 1), 7.82 (dd, *J* = 9.24, 0.88 Hz, 1); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.75, 17.09, 22.65, 55.56, 90.16, 116.13, 121.93, 125.59, 158,92, 158.96, 161.77, 190.49; HRMS m/z (ESI): calculated for $C_{12}H_{13}NO_2$. $[M+H]^+$ 203.0941, found 203.0940.

5-Fluoro-2-propyl-3*H*-indol-3-one (3i)

FT-IR $\nu(cm^{-1})$: 1755, 1724, 1537, 1265, 1221, 834, 762; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (*t*, *J* = 7.36 Hz, 3H), 1.70–1.85 (*m*, 2H), 3.06 (*t*, *J* = 7.12 Hz, 2H), 6.99 (td, *J* = 9.36, 2 Hz, 1H), 7.17–7.21(*m*, 1H), 7.97–8.02(*m*,1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.71, 17.03, 25.36, 98.19, 98.44, 116.76, 121.40, 121.70, 123.88, 123.98, 157.76, 157.89, 160.03, 160.05, 162.52, 190.26; HRMS m/z (ESI): calculated for $C_{11}H_{10}FNO$. $[M+H]^+$ 191.074194, found 191.0739.

2-propyl-3*H*-indol-3-one-5-Carboxylic acid methyl ester (3j)

FT-IR $\nu(cm^{-1})$: 1760, 1751, 1726, 1537, 1283, 1115, 833, 755; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (*t*, $J=7.52$ Hz, 3H), 1.74–1.85 (*m*, 2H), 3.10 (*t*, $J=7.24$ Hz, 2H), 3.92 (*s*, 3H), 7.76 (*d*, $J=9.12$ Hz,1H), 8.04 (*d*, $J=9.12$,1H), 8.44 (*s*,1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.75, 17.05, 22.29, 52.83, 119.66, 119.92, 121.70, 127.56, 133.32, 157.31, 160.43, 165.66, 190.16; HRMS m/z (ESI): calculated for. $[M+H]^+$ 231.0890, found 231.0889.

2-Propyl-3*H*-indole-3-one-5-carbonitrile (3 k)

FT-IR $\nu(cm^{-1})$: 2237, 1755, 1722, 1537, 1437, 967, 835, 760; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.99 (*t*, $J=7.36$ Hz, 3H), 1.74–1.85 (*m*, 2H), 3.11 (*t*, $J=7.24$ Hz, 2H), 7.27 (*d*, $J=9.12$ Hz, 1H), 8.11–8.17 (*m*, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.71, 16.97, 22.64, 115.67, 117.43, 118.85, 123.68, 123.71, 127.72, 155.88, 161.18, 189.98; HRMS m/z (ESI): calculated for $C_{12}H_{10}N_2O$; $[M+H]^+$ 198.0788, found 198.0790.

2-p-Tolyl-3*H*-indol-3-one (3 l)

FT-IR $\nu(cm^{-1})$: 1759, 1722, 1535, 1273, 874, 755; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (*s*, 3H), 7.19 (*d*, $J=8.08$ Hz, 2H), 7.22–7.32 (*m*, 2H), 7.39 (*d*, $J=8.04$, 2H), 7.47 (*t*, $J=7.48$ Hz,1H), 7.56 (*d*, $J=6.96$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.16, 123.66, 124.55, 125.40, 126.65, 127.51, 129.23, 130.7, 138.10, 140.85, 154.20, 167.88, 193.28; HRMS m/z (ESI): calculated for $C_{15}H_{11}NO$. $[M+H]^+$ 221.0835, found 221.0838.

5-Methyl-2-p-tolyl-3*H*-indol-3-one (3 m)

FT-IR $\nu(cm^{-1})$: 1758, 1723, 1536, 1272, 873, 756; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (*s*, 6H), 7.14 (*d*, $J=8.2$ Hz,1H), 7.19 (*d*, $J=8.08$ Hz, 2H), 7.25–7.30 (*m*, 1H), 7.39 (*d*, $J=8.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.00, 21.60, 123.53, 125.67, 126.32, 128.36, 131.10, 133.96, 135.38, 136.04, 136.90, 148.17, 156.62, 193.27; HRMS m/z (ESI): calculated for $C_{16}H_{13}NO$. $[M+H]^+$ 235.0992, found 235.0995.

5-Bromo-2-p-tolyl-3*H*-indol-3-one (3n)

FT-IR $\nu(cm^{-1})$: 1760, 1722, 1536, 1514, 1383, 1250, 831, 757, 650; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (*s*, 3H), 7.12 (*d*, $J=8.56$ Hz,2H), 7.20 (*d*, $J=8.04$ Hz, 2H), 7.38 (*d*, $J=8.04$ Hz,2H), 7.57 (*d*, $J=8.32$ Hz, 1H), 7.68 (*s*, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.20, 118.49, 123.51, 126.11, 126.62, 129.30, 130.34, 131.65, 138.28, 139.89, 153.84, 166.52, 193.38; HRMS m/z (ESI): calculated for $C_{15}H_{10}BrNO$. $[M+H]^+$ 297.9862, found 297.9870.

2-(4-Methoxy-phenyl)-3*H*-indol-3-one (3o)

FT-IR $\nu(cm^{-1})$: 1763, 1725, 1539, 1257, 1045, 833, 758; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84(s,3H), 6.91(*d*, $J=8.92$ Hz, 2H), 7.23–7.29 (*m*, 2H), 7.38–7.61 (*m*, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.36, 113.92, 122.89, 124.55, 125.39, 127.42, 128.01, 131.18, 133.43, 154.20, 159.69, 167.94, 193.99; HRMS m/z (ESI): calculated for $C_{15}H_{11}NO_2$. $[M+H]^+$ 237.0784, found 237.0781.

2-(4-Methoxy-phenyl)-5-methyl-3*H*-indol-3-one (3p)

FT-IR $\nu(cm^{-1})$: 1761, 1723, 1537, 1255, 1043, 830, 759; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (*s*, 3H), 3.84 (*s*, 3H), 6.91 (*d*, $J=8.29$ Hz, 2H), 7.13 (*d*, $J=8.16$, 2H), 7.24–7.29 (*m*, 1H), 7.37 (*s*, 1H) 7.42 (*d*, $J=8.68$, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.77, 55.35, 113.91, 123.03, 124.51, 127.88, 128.02, 129.81, 131.80, 133.50, 138.30, 159.69, 167.98, 193.27; HRMS m/z (ESI): calculated for $C_{16}H_{13}NO_2$. $[M+H]^+$ 251.0941, found 251.0940.

5-Bromo-2-(4-methoxy-phenyl)-3*H*-indol-3-one (3q)

FT-IR $\nu(cm^{-1})$: 1762, 1724, 1538, 1515, 1384,1253, 1043, 831, 756, 652; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (*S*, 3H), 6.91 (*d*, $J=8.8$ Hz, 2H) 7.12 (*d*, $J=8.56$ Hz, 1H), 7.42 (*d*, $J=8.68$ Hz, 2H), 7.57 (*d*, $J=7.84$ Hz, 1H), 7.67 (*s*, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ, 55.35, 114.00, 122.77, 126.13, 127.96, 130.32, 131.70, 133.20, 134.06, 153.85, 159.82, 166.48, 193.33; HRMS m/z (ESI): calculated for $C_{15}H_{10}BrNO2$. $[M+H]^+$ 314.9895, found 314.9891.

Acetic acid 3-(3*H*-indol-3-one-2-yl)-propyl ester (3r)

FT-IR $\nu(cm^{-1})$:1758, 1752, 1720, 1539,1251, 833, 761; ^{1}H NMR (400 MHz, CDCl3): δ 1.96 (*s*, 3H), 2.08–2.15 (*m*, 2H), 3.22 (*t*, $J=7.24$ Hz, 2H), 4.14 (*t*, $J=6.64$ Hz, 2H), 7.18–7.24 (*m*, 1H), 7.31–7.37 (*m*,1H), 7.66 (*d*, $J=9.12$ Hz, 1H), 7.97 (*d*, $J=8.76$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl3): δ 20.90, 22.52, 23.25, 63.40, 116.01, 119.21, 121.13, 128.71, 131.39, 157.59, 159.50, 171.03, 189.10; HRMS m/z (ESI): calculated for $C_{13}H_{13}NO_3$ $[M+H]^+$ 231.0890, found 231.0888.

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Declarations

Conflict of interest There are no conflicts to declare.

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