

Study on the conjugate addition of indole with 1,5-diaryl-1,4-pentadien-3-ones catalyzed by AlCl_3 under ultrasonication

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Received 19 April 2007; accepted (revised) 13 November 2007

The conjugate addition of indoles with 1,5-diaryl-1,4-pentadien-3-ones catalyzed by AlCl_3 affords the corresponding products in moderate yields under ultrasonication at room temperature within 60-170 min.

Keywords: Indole, conjugate addition, 1,5-diaryl-1,4-pentadien-3-one, ultrasonication, aluminium trichloride

The indole framework is widely distributed in compounds with significant biological, agrochemical and pharmacological relevance¹. The development of synthetic methodologies leading to indole derivatives has attracted much attention among organic chemists². The carbon-carbon bond formation at the C-3 of indoles takes advantage of the electron-rich nature of this position, which can be viewed as possessing enamine-like character. Furthermore, 3-substituted indoles are components of many drugs and are commonly found in molecules of pharmaceutical interest in a variety of therapeutic areas³.

The Michael addition reactions involving indole and 1,5-diaryl-1,4-pentadien-3-ones, represents one of the most important carbon-carbon bond-forming reactions at the C-3 position and is a widely investigated process. The resultant β -indolylketones obtained are highly useful building blocks for the synthesis of biologically active compounds and natural products. In particular, this reaction is applied in the total synthesis of bioactive indole alkaloids known as the hapalindoles D 1 (Ref. 4).

In the classical Michael reaction, a conjugate addition reaction of nucleophiles to unsaturated carbonyl compounds requires either basic conditions or acidic catalysts. However, the acid-catalyzed electrophilic substitution of indoles requires careful control of acidity to prevent side reactions such as dimerisation or polymerization⁵. Furthermore, many of these procedures involve expensive reagents, long reaction duration, poor yields of products due to dimerisation of the indole or polymerization of the

vinyl ketones, and cumbersome isolation procedures. Other methods for the synthesis of β -indolylketones involve the conjugate addition of indoles to α,β -enones in the presence of protic⁶ or Lewis acids⁷.

Recently, it has been demonstrated that indium tribromide can mediate the conjugate addition of enones to indoles⁸. However, with less electron-rich indoles, the yields of the products are not satisfactory. Indium trichloride has proved to be very effective. But these reactions require long duration (16-24 hr) using approximately 10 mole percent of the catalyst. In some cases, an external proton source such as isopropyl alcohol is needed for the success of the reaction. Thus, a fast and efficient method is desirable for the conjugate addition of indole to electron-deficient olefins.

The Lewis acid promoted organic reactions were carried out as early as 1890, and they still play important roles in modern organic chemistry⁹. Among them, AlCl_3 can efficiently catalyzed many kinds of organic reactions such as, Friedel-Crafts reaction¹⁰, Diels-Alder reaction¹¹, various rearrangements¹², and several other reactions¹³. But AlCl_3 catalyzed conjugate addition reaction of indole to 1,5-diaryl-1,4-pentadien-3-ones have not been reported so far.

Ultrasound has increasingly been used in organic synthesis in the last three decades. Ultrasonication has been used to enhance the reaction rates for a large number of classical organic reactions¹⁴. Recently, Ji *et al.* reported the conjugate addition accelerated by ultrasound to afford the β -indolylketones in excellent yields within 1.5-4 hr¹⁵. Continuing the investigations

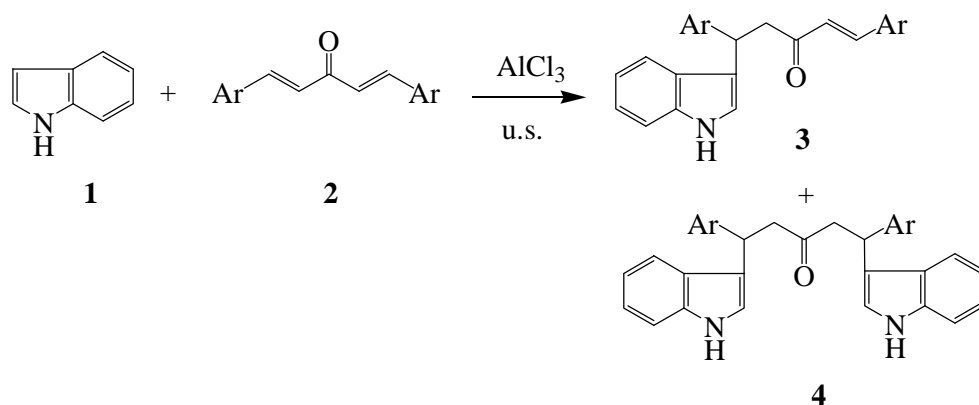
in this area¹⁶, herein is reported the results of the conjugate addition of indole with 1,5-diaryl-1,4-pentadien-3-ones catalyzed by AlCl_3 in ethyl acetate under ultrasonication (**Scheme I**).

Results and Discussion

In a preliminary experiment, the influence of the molar ratio of 1:2 and amount of AlCl_3 on the yield was studied. As shown in **Scheme I** and **Table I**, the conjugate addition catalyzed by AlCl_3 in ethyl acetate under ultrasonication can give mono-addition product

3 and the bis-addition product **4**. It was found that a molar ratio of 1:2: AlCl_3 of 0.7:0.5:1.0 gave the best total yield (97%, Entry i). Experiments were also carried out in which the sequence of addition of indole, dibenzylideneacetone and AlCl_3 were changed. It was found that when indole was added after the addition of AlCl_3 and 1,5-diphenyl-1,4-pentadien-3-one, the total yield was higher (Entry a and b).

In the absence of ultrasonication, the conjugate addition of indole to 1,5-diphenyl-1,4-pentadien-3-



Scheme I

Table I — The effect of the reaction conditions on conjugate addition of indole with 1,5-diphenyl-1,4-pentadien-3-one under ultrasonication

Entry	1:2 (mmole)	Amount of the catalyst, mole%	Frequency (kHz)	Time (min)	Isolated yield (%)		
					Total	3	4
a	0.5:0.5	6	25	75	64 ^a	42	22
b	0.5:0.5	6	25	75	55 ^b	40	15
c	0.5:0.5	25	25	60	65	37	28
d	0.5:0.5	50	25	60	70	31	39
e	0.5:0.5	75	25	60	47	15	32
f	0.5:0.5	100	25	60	61	10	51
g	0.5:0.5	200	25	50	74	44	30
h	0.67:0.5	200	25	50	84	36	48
i	0.7:0.5	200	25	50	97	18	79
j	1.0:0.5	200	25	80	65	57	8
k	1.2:0.5	200	25	90	84	63	21
l	0.7:0.5	200	-	50	75 ^c	40	35
m	0.7:0.5	200	40	50	72	34	38
n	0.7:0.5	200	59	50	69	31	38
o	0.7:0.5	200	25	120	0 ^d	0	0

^a Indole was added after the addition of AlCl_3 and 1,5-diphenyl-1,4-pentadien-3-one.

^b Indole, 1,5-diphenyl-1,4-pentadien-3-one and AlCl_3 were added in one portion.

^c Stirring in the absence of ultrasonication.

^d Without catalyst AlCl_3 .

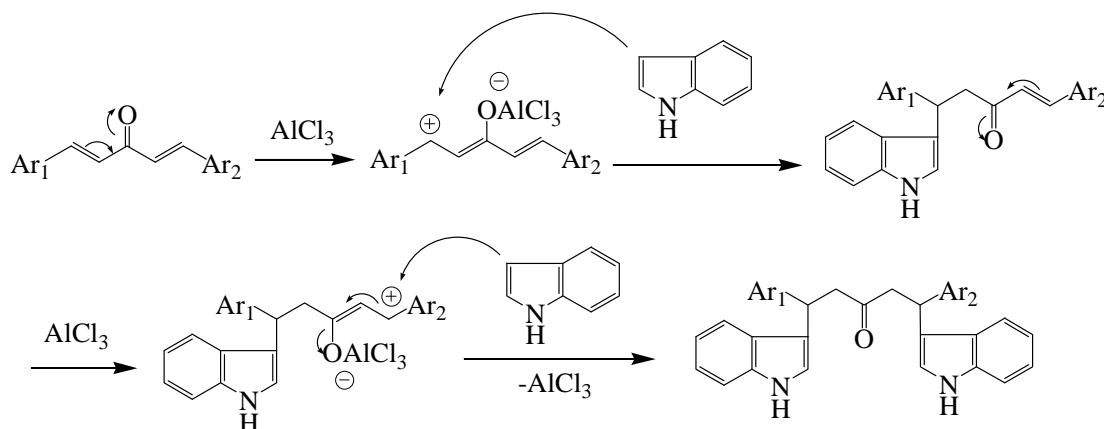
one mediated by AlCl_3 gave only 75% yield in 50 min by stirring alone (Entry l). Under ultrasonication at 25 kHz, the product was obtained in 97% yield within 50 min (Entry i). It is apparent that ultrasonication can accelerate the conjugate addition of indole to 1,5-diphenyl-1,4-pentadien-3-one. When using ultrasonication at 40 kHz and 59 kHz, the reaction was completed in 50 min with 72% and 69% yield respectively (Entry m and n). This indicates that lower frequency ultrasonication improved the yield. Therefore, the reaction was repeated with 25 kHz. In the absence of catalyst, the reaction did not occur at all even after 2 hr (Entry o).

From the above results, the optimum reaction conditions were chosen: indole (0.7 mmole), 1,5-diaryl-1,4-pentadien-3-ones (0.5 mmole), AlCl_3 (200 mole%)/ ethyl acetate (3 mL). Under these conditions, a series of experiments for the conjugate addition of indole to 1,5-diaryl-1,4-pentadien-3-ones under 25 kHz ultrasonication were performed. The results are summarized in **Table II**.

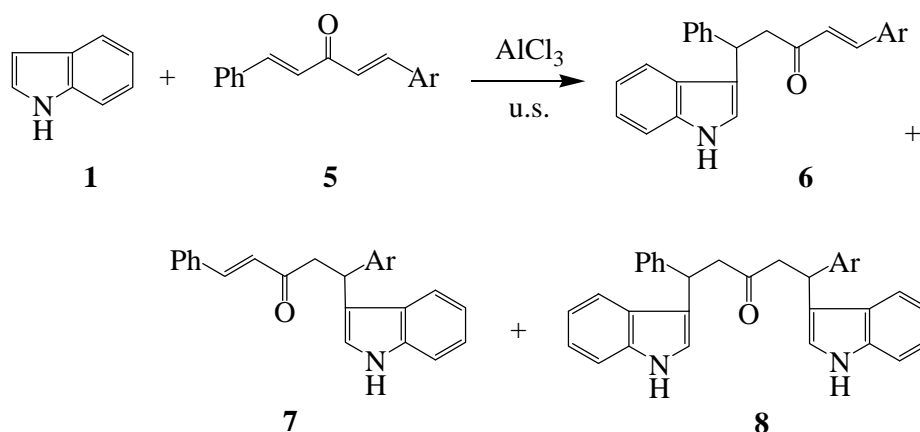
As shown in **Table II**, the conjugate addition of indole to 1,5-diaryl-1,4-pentadien-3-ones was carried out with good yield catalyzed by AlCl_3 under ultrasonication. Reddy *et al.* reported that the conjugate addition of indole to 1,5-dibenzyl-1,4-pentadien-3-one catalyzed by $\text{Bi}(\text{OTf})_3$ gave bis-addition product **4** in 80% yield by stirring for 120 min in CH_3CN (Ref. 17a). Arcadi *et al.* used the expensive reagent $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O}$ to catalyze the conjugate addition^{17b}. Bandini *et al.* reported the conjugate addition by stirring in anhydrous CH_2Cl_2 for 16-24 hr under a nitrogen atmosphere^{8b}. In contrast, the present procedure gave the bis-addition product **4** in 79% yield within 50 min under ultrasonication. The notable advantage of the present method appears to be the negligible formation of side products arising mainly due to the polymerization of olefinic bond and N-alkylation of indole. This important result provided a remarkable departure from similar reactions under palladium catalysis, where N-alkylation was predominant¹⁸.

Table II — The conjugate addition of indole with 1,5-diaryl-1,4-pentadien-3-ones catalyzed by AlCl_3 under ultrasonication

Entry	Ar	Time (min)	Isolated yield (%)		
			Total	3	4
a	C_6H_5	50	97	18	79
b	4- BrC_6H_4	90	99	13	86
c	3- BrC_6H_4	90	98	26	72
d	4- ClC_6H_4	90	97	18	79
e	3- ClC_6H_4	100	95	20	75
f	2- ClC_6H_4	100	96	30	66
g	4- $\text{CH}_3\text{C}_6\text{H}_4$	90	93	29	64
h	4- $\text{CH}_3\text{OC}_6\text{H}_4$	60	90	18	72
i	4- $\text{NO}_2\text{C}_6\text{H}_4$	70	45	12	33



Scheme II



Scheme III

The reaction seems to occur *via* a Friedel-Crafts alkylation pathway (Scheme II)¹⁹. From the data in Table II, 1,5-diaryl-1,4-pentadien-3-ones carrying the electron-withdrawing substituents in the benzene ring show higher reactivity than those carrying electron-donating substituents. The electron-withdrawing substituents can decrease the electronic cloud density on 1,5-position in 1,5-diaryl-1,4-pentadien-3-ones resulting in the increase of electrophilicity at the 3-position of indole. But 1,5-diaryl-1,4-pentadien-3-ones carrying the strong electron-withdrawing substituents such as the nitro group show less reactivity towards conjugate addition (Entry i). At the same time, the selectivity of this conjugate addition certainly has room for improvement.

In addition, a series of experiments for the conjugate addition of indole to asymmetric 1,4-pentadien-3-ones catalyzed by AlCl_3 under ultrasonication were performed (Scheme III). The results are summarized in Table III.

As shown in Scheme III, there are two different active positions in 5, so these reactions produce two mono-addition (Scheme III, 6 and 7) and one bis-addition products (Scheme III, 8). The nucleophilic reagent in the conjugate addition preferentially attacks the position that has the lower electronic cloud density in 1,4-pentadien-3-ones.

Experimental Section

Liquid substrates were distilled prior to use. Melting points are uncorrected. ^1H NMR spectra were recorded on a Bruker Avance 400 (400 MHz) spectrometer using TMS as the internal standard. MS were determined on a Shimadzu GCMS-QP2010 spectrometer (EI, 10-200eV). Elemental analyses

Table III — The conjugate addition of indole with asymmetric 1,4-pentadien-3-ones 5 catalyzed by AlCl_3 under ultrasonication

Entry	Ar	Time (min)	Isolated yield (%)			
			Total	6	7	8
a	4- $\text{CH}_3\text{C}_6\text{H}_4$	120	89	30	14	45
b	4- $\text{CH}_3\text{OC}_6\text{H}_4$	90	76	13	7	56
c	3- ClC_6H_4	95	99	4	30	65

were carried out on a Heraeus (CHNO, Rapid) analyzer. Sonication was performed in Shanghai Branson-CQX ultrasonic cleaner (with a frequency of 25 kHz and a nominal power of 250 W) and SK 250 LH ultrasonic cleaner (with a frequency of 40 kHz, 59 kHz and a nominal power of 250 W; Shanghai Kudos Ultrasonic Instrument Co., Ltd.). The reaction flask was located in the cleaner, where the surface of the reactants was kept slightly lower than the level of the water. The reaction temperature was controlled by addition or removal of water from the ultrasonic bath.

General procedure for the conjugate additions

The preparation of 1,5-diaryl-1,4-pentadien-3-ones were referred to Ref. 20

Typical procedure (3a and 4a): Indole (81.9 mg, 0.7 mmole), 1,5-diphenyl-1,4-pentadien-3-one (117 mg, 0.5 mmole), ethyl acetate (3 mL), AlCl_3 (133 mg, 1.0 mmole), were all mixed in a 50 mL Pyrex flask. The reaction mixture was ultrasonicated in the water bath of an ultrasonic cleaner at RT for 50 min (the progress of reaction was followed by TLC). After the completion of the reaction, the resulting suspension was quenched with 10 mL water. The reaction

mixture was extracted with ethyl acetate (3×15 mL). The combined organic layers were washed with saturated aqueous NaHCO₃ solution and brine, dried over anhydrous magnesium sulfate for 12 hr and filtered. The ethyl acetate was evaporated under reduced pressure to give the crude product, which was separated by column chromatography over silica gel (200-300 mesh), eluted with petroleum ether or a mixture of petroleum ether and diethyl ether.

3a: Solid, m.p. 164-64.5°C; ¹H NMR (DMSO-*d*₆): δ 3.42 (dd, *J*=7.6, 16.0 Hz, 1H), 3.60 (dd, *J*=7.6, 16.2 Hz, 1H), 4.83 (t, *J*=7.6 Hz, 1H), 6.89-7.62 (m, 17H), 10.86 (s, 1H, NH); MS: *m/z* (%) 351 (43), 220 (40), 206 (100), 178 (10), 131 (13), 115 (7), 103 (33), 77 (19). Anal. Calcd. for C₂₅H₂₁NO: C, 85.47; H, 5.98; N, 3.99. Found: C, 85.48; H, 5.99; N, 4.01%.

4a: Solid, m.p. 198-99°C; ¹H NMR (DMSO-*d*₆): δ 3.25 (dd, *J*=7.6, 14.8 Hz, 2H), 3.33 (dd, *J*=7.6, 14.8 Hz, 2H), 4.63 (t, *J*=7.2 Hz, 2H), 6.86-7.33 (m, 20H), 10.81 (s, 2H, NH); MS: *m/z* (%) 468 (34), 351 (6), 262 (26), 219 (25), 206 (100), 178 (14), 143 (5), 130 (23), 115 (6), 103 (11), 77 (6). Anal. Calcd. for C₃₃H₂₈N₂O: C, 84.61; H, 5.98; N, 5.98. Found: C, 84.62; H, 5.99; N, 6.00%.

3b: Solid, m.p. 125-27°C; ¹H NMR (DMSO-*d*₆): δ 3.43 (dd, *J*=8.0, 16.8 Hz, 1H), 3.59 (dd, *J*=7.2, 16.4 Hz, 1H), 4.82 (t, *J*=7.6 Hz, 1H), 6.90-7.67 (m, 15H), 10.91 (s, 1H, NH); MS: *m/z* (%) 392 (12), 204 (3), 130 (3), 115 (4), 102 (100), 76 (22). Anal. Calcd. for C₂₅H₁₉NOBr₂: C, 58.94; H, 3.73; N, 2.75. Found: C, 58.97; H, 3.75; N, 2.78%.

4b: Solid, m.p. 209-11°C; ¹H NMR (Acetone-*d*₆): δ 3.24 (dd, *J*=8.0, 16.8 Hz, 2H), 3.37 (dd, *J*=8.0, 16.8 Hz, 2H), 4.81 (t, *J*=8.0 Hz, 2H), 7.06-7.75 (m, 18H), 10.08 (s, 2H, NH); MS: *m/z* (%) 626 (28), 509 (5), 392 (12), 342 (20), 299 (15), 284 (41), 204 (31), 178 (11), 144 (15), 130 (48), 117 (28), 102 (62), 89 (23), 28 (100). Anal. Calcd. for C₃₃H₂₆N₂OBr₂: C, 63.26; H, 4.15; N, 4.47. Found: C, 63.30; H, 4.18; N, 4.48%.

3c: Viscous liquid; ¹H NMR (DMSO-*d*₆): δ 3.45 (dd, *J*=7.6, 16.4 Hz, 1H), 3.61 (dd, *J*=7.6, 16.2 Hz, 1H), 4.84 (t, *J*=7.6 Hz, 1H), 6.92-7.70 (m, 15H), 10.92 (s, 1H, NH); MS: *m/z* (%) 392 (12), 204 (3), 130 (3), 115 (4), 102 (100), 76 (22). Anal. Calcd. for C₂₅H₁₉NOBr₂: C, 58.94; H, 3.73; N, 2.75. Found: C, 58.96; H, 3.75; N, 2.78%.

4c: Viscous liquid; ¹H NMR (DMSO-*d*₆): δ 3.23 (dd, *J*=7.8, 15.2 Hz, 2H), 3.31 (dd, *J*=7.8, 15.2 Hz, 2H), 4.63 (t, *J*=8.0 Hz, 2H), 6.89-7.61 (m, 18H), 10.88 (s, 2H, NH); MS: *m/z* (%) 626 (21), 509 (3),

340 (29), 299 (32), 284 (100), 204 (59), 178 (12), 143 (15), 130 (55), 115 (10), 102 (11), 89 (2), 77 (3). Anal. Calcd. for C₃₃H₂₆N₂OBr₂: C, 63.26; H, 4.15; N, 4.47. Found: C, 63.29; H, 4.17; N, 4.48%.

3d: Viscous liquid; ¹H NMR (Acetone-*d*₆): δ 3.50 (dd, *J*=8.0, 16.0 Hz, 1H), 3.63 (dd, *J*=7.2, 16.0 Hz, 1H), 4.99 (t, *J*=8.0 Hz, 1H), 6.92-7.70 (m, 15H), 10.11 (s, 1H, NH); MS: *m/z* (%) 421 (65), 419 (100), 356 (5), 254 (45), 240 (89), 204 (25), 178 (17), 165 (24), 137 (77), 115 (54), 102 (99), 89 (24), 77 (38). Anal. Calcd. for C₂₅H₁₉NOCl₂: C, 71.60; H, 4.53; N, 3.34. Found: C, 71.63; H, 4.57; N, 3.37%.

4d: Viscous liquid; ¹H NMR (Acetone-*d*₆): δ 3.24 (dd, *J*=8.0, 16.8 Hz, 2H), 3.36 (dd, *J*=7.6, 16.8 Hz, 2H), 4.83 (t, *J*=8.0 Hz, 2H), 7.06-7.39 (m, 18H), 10.07 (s, 2H, NH); MS: *m/z* (%) 536 (3), 254 (18), 240 (100), 218 (41), 204 (80), 144 (30), 130 (15), 117 (25), 89 (21), 77 (12), 55 (57). Anal. Calcd. for C₃₃H₂₆N₂OCl₂: C, 73.88; H, 4.85; N, 3.34. Found: C, 73.91; H, 4.88; N, 3.36%.

3e: Viscous liquid; ¹H NMR (DMSO-*d*₆): δ 3.45 (dd, *J*=7.6, 16.4 Hz, 1H), 3.62 (dd, *J*=7.6, 16.4 Hz, 1H), 4.86 (t, *J*=7.6 Hz, 1H), 6.92-7.66 (m, 15H), 10.93 (s, 1H, NH); MS: *m/z* (%) 421 (66), 419 (100), 356 (11), 254 (60), 240 (94), 204 (20), 178 (12), 137 (25), 115 (24), 102 (44), 89 (10), 77 (15). Anal. Calcd. for C₂₅H₁₉NOCl₂: C, 71.60; H, 4.53; N, 3.34. Found: C, 71.64; H, 4.56; N, 3.37%.

4e: Viscous liquid; ¹H NMR (DMSO-*d*₆): δ 3.24 (dd, *J*=7.6, 15.2 Hz, 2H), 3.32 (dd, *J*=7.6, 15.2 Hz, 2H), 4.63 (m, 2H), 6.89-7.39 (m, 18H), 10.88 (s, 2H, NH); MS: *m/z* (%) 537 (5), 254 (25), 240 (100), 217 (21), 204 (68), 144 (10), 130 (17), 117 (21), 104 (18), 89 (20), 77 (19). Anal. Calcd. for C₃₃H₂₆N₂OCl₂: C, 73.88; H, 4.85; N, 3.34. Found: C, 73.90; H, 4.87; N, 3.36%.

3f: Solid, m.p. 69-71°C; ¹H NMR (DMSO-*d*₆): δ 3.66 (dd, *J*=8.4, 16.4 Hz, 1H), 4.04 (dd, *J*=8.4, 16.4 Hz, 1H), 5.29 (t, *J*=7.4 Hz, 1H), 7.03-7.84 (m, 15H), 10.94 (s, 1H, NH); MS: *m/z* (%) 421 (65), 419 (96), 356 (9), 254 (72), 240 (100), 218 (15), 204 (34), 189 (5), 143 (11), 137 (43), 117 (37), 101 (67), 89 (16), 77 (26). Anal. Calcd. for C₂₅H₁₉NOCl₂: C, 71.60; H, 4.53; N, 3.34. Found: C, 71.61; H, 4.56; N, 3.35%.

4f: Solid, m.p. 102-04°C; ¹H NMR (DMSO-*d*₆): δ 3.17 (dd, *J*=7.2, 17.6 Hz, 2H), 3.40 (dd, *J*=7.2, 18.2 Hz, 2H), 5.11 (t, *J*=7.4 Hz, 2H), 6.88-7.40 (m, 18H), 10.88 (s, 2H, NH); MS: *m/z* (%) 293 (9), 253 (20), 240 (100), 204 (81), 176 (37), 143 (2), 130 (10), 117

(8), 102 (12), 89 (5), 75 (11). Anal. Calcd. for $C_{33}H_{26}N_2OCl_2$: C, 73.88; H, 4.85; N, 3.34. Found: C, 73.89; H, 4.87; N, 3.36%.

3g: Solid, m.p. 150-52°C; 1H NMR (DMSO- d_6): δ 1.25 (s, 3H), 2.18 (s, 3H), 3.34 (dd, $J=7.6$, 15.8 Hz, 1H), 3.47 (dd, $J=7.6$, 15.8 Hz, 1H), 4.90 (t, $J=7.6$ Hz, 1H), 6.77-7.70 (m, 15H), 10.83 (s, 1H, NH); MS: m/z (%) 379 (98), 234 (39), 220 (100), 204 (15), 178 (8), 145 (24), 130 (8), 117 (65), 102 (4), 77 (5). Anal. Calcd. for $C_{27}H_{25}NO$: C, 85.49; H, 6.60; N, 3.69. Found: C, 85.50; H, 6.63; N, 3.71%.

4g: Solid, m.p. 132-34°C; 1H NMR (DMSO- d_6): δ 2.21 (s, 6H), 3.11 (dd, $J=7.6$, 15.8 Hz, 2H), 3.23 (dd, $J=7.6$, 15.8 Hz, 2H), 4.57-4.62 (q, 2H), 6.86-7.33 (m, 18H), 10.79 (s, 2H, NH); MS: m/z (%) 496 (30), 379 (18), 276 (41), 233 (40), 220 (100), 204 (21), 178 (13), 143 (10), 130 (38), 117 (23), 77 (5). Anal. Calcd. for $C_{34}H_{32}N_2O$: C, 84.30; H, 6.61; N, 5.79. Found: C, 84.32; H, 6.63; N, 5.82%.

3h: Solid, m.p. 156-58°C; 1H NMR (DMSO- d_6): δ 3.35 (dd, $J=7.6$, 15.0 Hz, 1H), 3.51 (dd, $J=7.6$, 15.8 Hz, 1H), 3.68 (s, 3H), 3.81 (s, 3H), 4.78 (t, $J=7.6$ Hz, 1H), 6.79-7.66 (m, 15H), 10.83 (s, 1H, NH); MS: m/z (%) 411 (81), 249 (22), 236 (100), 221 (5), 204 (4), 178 (3), 257 (19), 133 (56), 115 (11), 103 (10), 77 (11). Anal. Calcd. for $C_{27}H_{25}NO_3$: C, 78.83; H, 6.08; N, 3.41. Found: C, 78.85; H, 6.12; N, 3.42%.

4h: Solid, m.p. 150-52°C; 1H NMR (DMSO- d_6): δ 3.11 (dd, $J=8.0$, 13.2 Hz, 2H), 3.19 (dd, $J=7.6$, 12.6 Hz, 2H), 3.68 (s, 6H), 4.57-4.60 (m, 2H), 6.72-7.33 (m, 18H), 10.78 (s, 2H, NH); MS: m/z (%) 293 (3), 236 (55), 204 (17), 192 (30), 176 (2), 165 (22), 133 (15), 117 (10), 102 (2), 77 (6), 43 (57), 39 (100). Anal. Calcd. for $C_{34}H_{32}N_2O_3$: C, 79.07; H, 6.20; N, 5.43. Found: C, 79.10; H, 6.23; N, 5.46%.

3i: Viscous liquid; 1H NMR (Acetone- d_6): δ 3.84 (dd, $J=8.0$, 16.4 Hz, 1H), 3.94 (dd, $J=8.0$, 16.4 Hz, 1H), 5.31 (t, $J=8.0$ Hz, 1H), 7.18-8.36 (m, 15H), 10.25 (s, 1H, NH); MS: m/z (%) 324 (47), 277 (19), 245 (73), 232 (26), 220 (29), 206 (51), 176 (83), 144 (18), 130 (68), 115 (30), 102 (75), 90 (36), 76 (30). Anal. Calcd. for $C_{25}H_{19}N_3O_5$: C, 71.26; H, 4.51; N, 9.98. Found: C, 71.28; H, 4.54; N, 9.99%.

4i: Viscous liquid; 1H NMR (Acetone- d_6): δ 3.68 (dd, $J=8.0$, 16.4 Hz, 2H), 3.78 (dd, $J=7.2$, 16.8 Hz, 2H), 5.15 (t, $J=8.0$ Hz, 2H), 7.05-8.26 (m, 18H), 10.22 (s, 2H, NH); MS: m/z (%) 245 (100), 233 (5), 217 (8), 189 (3), 130 (3), 117 (9), 77 (5). Anal. Calcd.

for $C_{33}H_{26}N_4O_5$: C, 73.60; H, 4.83; N, 10.42. Found: C, 73.62; H, 4.86; N, 10.46%.

3j: Solid, m.p. 128-30°C; 1H NMR (DMSO- d_6): δ 3.46 (dd, $J=7.6$, 16.2 Hz, 1H), 3.56 (dd, $J=7.6$, 16.2 Hz, 1H), 3.73 (s, 3H), 4.83 (t, $J=7.6$ Hz, 1H), 6.91-7.70 (m, 17H); MS: m/z (%) 365 (39), 234 (16), 220 (100), 204 (8), 178 (7), 144 (4), 131 (12), 115 (8), 103 (24), 77 (17). Anal. Calcd. for $C_{26}H_{23}NO$: C, 85.48; H, 6.30; N, 3.84. Found: C, 85.49; H, 6.32; N, 3.85%.

4j: Solid, m.p. 104-06°C; 1H NMR (DMSO- d_6): δ 3.14 (dd, $J=7.2$, 17.0 Hz, 1H), 3.25 (dd, $J=7.2$, 18.4 Hz, 1H), 3.45 (dd, $J=7.6$, 20.8 Hz, 1H), 3.56 (dd, $J=7.6$, 16.4 Hz, 1H), 3.67 (d, $J=8.0$ Hz, 3H), 3.72 (d, $J=8.8$ Hz, 3H), 4.66 (t, $J=7.6$ Hz, 1H), 4.83 (t, $J=7.6$ Hz, 1H), 6.91-7.44 (m, 20H); MS: m/z (%) 496 (100), 276 (78), 233 (40), 144 (31). Anal. Calcd. for $C_{33}H_{32}N_2O$: C, 84.68; H, 6.45; N, 5.65. Found: C, 84.69; H, 6.47; N, 5.68%.

7a: Solid, m.p. 108-10°C; 1H NMR (CDCl₃): δ 2.25 (s, 3H), 3.01-3.16 (m, 2H), 4.71-4.75 (m, 1H), 6.67-7.31 (m, 16H), 8.68-8.75 (m, 1H, NH); MS: m/z (%) 365 (100), 234 (14), 220 (64), 206 (63), 178 (17), 131 (21), 117 (63), 103 (55), 77 (30). Anal. Calcd. for $C_{26}H_{23}NO$: C, 85.48; H, 6.30; N, 3.84. Found: C, 85.50; H, 6.32; N, 3.86%.

8a: Solid, m.p. 145-47°C; 1H NMR (DMSO- d_6): δ 2.34 (s, 3H), 3.34-3.44 (m, 1H), 3.55-3.61 (m, 1H), 4.82-4.85 (m, 1H), 6.86-7.69 (m, 16H), 10.86 (s, 1H, NH); MS: m/z (%) 365 (100), 234 (14), 220 (64), 206 (63), 178 (17), 131 (21), 117 (63), 103 (55), 77 (30). Anal. Calcd. for $C_{26}H_{23}NO$: C, 85.48; H, 6.30; N, 3.84. Found: C, 85.49; H, 6.32; N, 3.86%.

9a: Solid, m.p. 79-81°C; 1H NMR (DMSO- d_6): δ 2.22 (s, 3H), 3.13-3.34 (m, 4H), 4.63-4.68 (q, 2H), 6.89-7.36 (m, 19H), 10.80 (s, 1H, NH), 10.83 (s, 1H, NH); MS: m/z (%) 482 (2), 277 (8), 233 (20), 220 (100), 204 (81), 130 (15), 117 (16), 103 (12), 77 (11). Anal. Calcd. for $C_{34}H_{30}N_2O$: C, 84.65; H, 6.22; N, 5.81. Found: C, 84.69; H, 6.24; N, 5.83%.

7b: Solid, m.p. 87-89°C; 1H NMR (DMSO- d_6): δ 3.39 (dd, $J=7.6$, 16.0 Hz, 1H), 3.56 (dd, $J=7.6$, 16.0 Hz, 1H), 3.81 (s, 3H), 4.82 (t, $J=7.6$ Hz, 1H), 6.78-7.66 (m, 16H), 10.86 (s, 1H, NH); MS: m/z (%) 381 (63), 220 (60), 206 (100), 178 (18), 142 (8), 133 (17), 115 (16), 103 (36), 89 (14), 77 (20). Anal. Calcd. for $C_{26}H_{23}NO_2$: C, 81.89; H, 6.04; N, 3.67. Found: C, 81.92; H, 6.05; N, 3.68%.

8b: Solid, m.p. 166-67°C; 1H NMR (DMSO- d_6): δ 3.38 (dd, $J=8.0$, 16.0 Hz, 1H), 3.55 (dd, $J=7.6$, 15.8 Hz, 1H), 3.67 (s, 3H), 4.78 (t, $J=7.6$ Hz, 1H), 6.79-

7.70 (m, 16H), 10.83 (s, 1H, NH); MS: m/z (%) 381 (63), 220 (60), 206 (100), 178 (18), 142 (8), 133 (17), 115 (16), 103 (36), 89 (14), 77 (20). Anal. Calcd. for $C_{26}H_{23}NO_2$: C, 81.89; H, 6.04; N, 3.67. Found: C, 81.91; H, 6.08; N, 3.68%.

9b: Solid, m.p. 163–64°C; 1H NMR (DMSO- d_6): δ 3.16 (dd, $J=7.6$, 16.2 Hz, 2H), 3.28 (dd, $J=7.6$, 16.2 Hz, 2H), 3.68 (s, 3H), 4.61–4.67 (m, 2H), 6.75 (t, $J=8.0$ Hz, 2H), 6.89 (t, $J=8.0$ Hz, 2H), 7.01–7.35 (m, 15H), 10.79 (s, 1H, NH), 10.82 (s, 1H, NH); MS: m/z (%) 377 (3), 236 (20), 204 (31), 133 (21), 117 (11), 104 (18), 90 (9), 77 (23), 52 (15), 43 (52), 39 (100). Anal. Calcd. for $C_{34}H_{30}N_2O_2$: C, 81.93; H, 6.02; N, 5.62. Found: C, 81.95; H, 6.04; N, 5.63%.

7c: Viscous liquid; 1H NMR (Acetone- d_6): δ 3.48 (dd, $J=8.0$, 16.0 Hz, 1H), 3.58 (dd, $J=8.0$, 16.0 Hz, 1H), 4.96 (t, $J=7.6$ Hz, 1H), 6.83–7.74 (m, 16H), 10.01 (s, 1H, NH); MS: m/z (%) 385 (76), 254 (25), 240 (33), 220 (26), 206 (100), 178 (18), 130 (18), 115 (21), 103 (40), 89 (7), 77 (24). Anal. Calcd. for $C_{25}H_{20}NOCl$: C, 77.92; H, 5.19; N, 3.64. Found: C, 77.95; H, 6.24; N, 3.68%.

8c: Solid, m.p. 70–72°C; 1H NMR (Acetone- d_6): δ 3.49 (dd, $J=8.0$, 16.0 Hz, 1H), 3.59 (dd, $J=8.0$, 16.0 Hz, 1H), 5.00 (t, $J=8.0$ Hz, 1H), 6.83–7.47 (m, 16H), 10.01 (s, 1H, NH); MS: m/z (%) 385 (76), 254 (25), 240 (33), 220 (26), 206 (100), 178 (18), 130 (18), 115 (21), 103 (40), 89 (7), 77 (24). Anal. Calcd. for $C_{25}H_{20}NOCl$: C, 77.92; H, 5.19; N, 3.64. Found: C, 77.96; H, 6.24; N, 3.66%.

9c: Solid, m.p. 78–80°C; 1H NMR (Acetone- d_6): δ 3.30–3.33 (m, 4H), 4.81–4.86 (m, 2H), 6.91–7.79 (m, 19H), 10.01 (s, 1H, NH), 10.04 (s, 1H, NH); MS: m/z (%) 504 (19), 502 (35), 385 (12), 262 (18), 240 (38), 220 (18), 206 (100), 178 (20), 143 (9), 130 (42), 115 (13), 103 (17), 89 (6), 77 (10). Anal. Calcd. for $C_{33}H_{27}N_2OCl$: C, 78.88; H, 5.38; N, 5.58. Found: C, 78.90; H, 5.40; N, 5.59%.

Conclusion

In conclusion, $AlCl_3$ is an efficient catalyst for the regioselective alkylation at the 3-position of indole through conjugated addition type reaction with 1,5-diaryl-1,4-pentadien-3-ones under ultrasonication.

Acknowledgements

The authors thank the Natural Science Foundation of Hebei Province (B2006000969), China, for financial support.

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