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Conjugate Addition of Indoles with 1,5-Diaryl-1,4-pentadien-3-ones Catalyzed by Molecular Iodine under Ultrasound Irradiation

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The conjugate addition of indoles with 1,5-diaryl-1,4-pentadien-3-ones catalyzed by molecular iodine afforded the corresponding products in moderate to good yields under ultrasound irradiation at room temperature within 40-90 min.

Key Words: Conjugate addition, Indole, 1,5-Diaryl-1,4-pentadien-3-one, Ultrasound irradiation.

INTRODUCTION

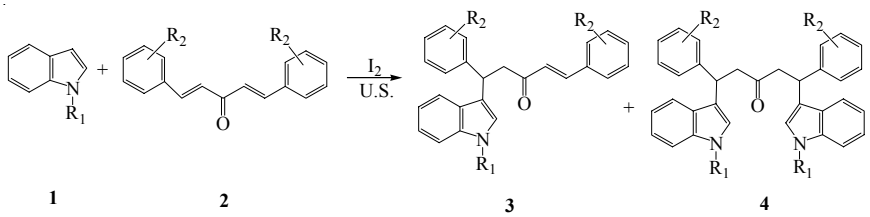
Indole derivatives have received much interest in heterocyclic chemistry because indole fragments are featured in many pharmacologically and biologically active compounds[1]. Since 3-position of indole is the preferred site for electrophilic substitution reaction, 3-alkyl or acyl indoles are versatile intermediates for the synthesis of a wide range of indole derivatives. In particular, the β-indolylketones are highly interesting building blocks for the synthesis of biologically active compounds as well as natural products[2]. Over the past few years, many synthetic methods for preparation of these compounds have been reported. The reactions were occurred in the presence of several kind of catalyst, such as silica sulfuric acid[3], $InBr_3$[4], $InCl_3$[5], SmI_3[6], $NaAuCl_4{\cdot}2H_2O$[7], $Bi(OTf)_3$[8], $Bi(NO)_3$[9], Al(salen)Cl[10], Pd(II) complex[11], $Yb(OTf)_3$[12], $CeCl_3{\cdot}7H_2O$[13] and montmorillonite clay[14].

However, the conjugate addition of indoles with 1,5-diaryl-1,4-pentadien-3-ones have been poorly documented and only one or two reports published by the previous researchers[4-7].

In recent times, the use of molecular iodine has received considerable attention as an inexpensive, nontoxic, readily available catalyst for various organic reactions to afford the corresponding products in excellent yields with high selectivity. The mild Lewis acidity associated with iodine enhanced its usage in organic synthesis[15-18]. Wang *et al.*[19] reported the Michael addition of indoles to α,β-unsaturated ketones catalyzed by iodine at room temperature to afford the β-indolylketones in excellent yields within 4-12 h. Banik *et al.*[20] also reported this reaction catalyzed by iodine

under solvent free condition to afford the β-indolylketones in moderate yields within 0.5 h. Thus in present studies, we have chosen to examine the potential of iodine in view of its remarkable catalytic activity and ready availability in conjugate addition of indoles with 1,5-diaryl-1,4-pentadien-3-ones.

Ultrasound has increasingly been used in organic synthesis in the last three decades. A large number of organic reactions, especially many metal-involved reactions, can be carried out in higher yields, shorter reaction time and milder conditions under ultrasound irradiation[21]. Ji *et al.*[22] published the Michael addition accelerated by ultrasound to afford the β-indolyl-ketones in excellent yields within 1.5-4 h. In continuation of our work in the synthesis of indole derivatives[3,23], herein we wish to report the results of the conjugate addition of indoles with 1,5-diaryl-1,4-pentadien-3-ones catalyzed by iodine in CH_3CN under ultrasound irradiation (**Scheme-I**).



Scheme-I

EXPERIMENTAL

Liquid substrates were distilled prior to use. Melting points were uncorrected. ^{1}H NMR spectra were measured 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 were measured 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 250 W) and SK 250 LH ultrasonic cleaner (with a frequency of 40 kHz, 59 kHz and a nominal power 250 W; Shanghai Kudos Ultrasonic Instrument Co., Ltd.). The reaction flask was located in the cleaner, where the surface of reactants is slightly lower than the level of the water. The reaction temperature was controlled by addition or removal of water from ultrasonic bath.

3a solid, m.p.164-164.5 ºC. ^{1}H NMR (DMSO): 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) ppm. m/z (%): 351 (43), 220 (40), 206 (100), 178 (10), 131 (13), 115 (7), 103 (33), 77 (19). Anal. calcd. for $C_{25}H_{21}NO$: C 85.47, H 5.98, N 3.99; found C 85.48, H 5.99, N 4.01.

4a solid, m.p. 198-199 ºC. ^{1}H NMR (DMSO): 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) ppm. 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 $C_{33}H_{28}N_2O$: C 84.61, H 5.98, N 5.98; found C 84.62, H 5.99, N 6.00.

3b solid, m.p. 125-127 ºC. ^{1}H NMR (DMSO): 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) ppm. m/z (%): 392 (12), 204 (3), 130 (3), 115 (4), 102 (100), 76 (22). Anal. calcd. for $C_{25}H_{19}NOBr_2$: C 58.94, H 3.73, N 2.75; found C 58.97, H 3.75, N 2.78.

4b solid, m.p. 209-211 ºC. ^{1}H 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) ppm. 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 $C_{33}H_{26}N_2OBr_2$: C 63.26, H 4.15, N 4.47; found C 63.30, H 4.18, N 4.48.

3c viscous liquid. ^{1}H NMR (DMSO): 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) ppm. m/z (%): 392 (12), 204 (3), 130 (3), 115 (4), 102 (100), 76 (22). Anal. calcd. for $C_{25}H_{19}NOBr_2$: C 58.94, H 3.73, N 2.75; found C 58.96, H 3.75, N 2.78.

4c viscous liquid. ^{1}H NMR (DMSO): 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) ppm. 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 $C_{33}H_{26}N_2OBr_2$: C 63.26, H 4.15, N 4.47; found C 63.29, H 4.17, N 4.48.

3d viscous liquid. ^{1}H 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) ppm. 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 $C_{25}H_{19}NOCl_2$: C 71.60, H 4.53, N 3.34; found C 71.63, H 4.57, N 3.37.

4d viscous liquid. ^{1}H 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) ppm. m/z (%): 536 (3), 254 (18), 240 (100), 218 (41), 204 (80), 144 (30), 130 (15), 117 (25), 89 (21), 77 (12), 69 (22), 55 (57). Anal. calcd. for $C_{33}H_{26}N_2OCl_2$: C 73.88, H 4.85, N 3.34; found C 73.91, H 4.88, N 3.36.

3e viscous liquid. ^{1}H NMR (DMSO): 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) ppm. 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 $C_{25}H_{19}NOCl_2$: C 71.60, H 4.53, N 3.34; found C 71.64, H 4.56, N 3.37.

4e viscous liquid. ^{1}H NMR (DMSO): 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) ppm. 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 $C_{33}H_{26}N_2OCl_2$: C 73.88, H 4.85, N 3.34; found C 73.90, H 4.87, N 3.36.

3f solid, m.p. 69-71ºC. ^{1}H NMR (DMSO): 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) ppm. 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 $C_{25}H_{19}NOCl_2$: C 71.60, H 4.53, N 3.34; found C 71.61, H 4.56, N 3.35.

4f solid, m.p. 102-104 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 150-152 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 132-134 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 156-158 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 150-152 ºC. ^{1}H NMR (DMSO): 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) ppm. m/z (%): 293 (3), 236 (55),

204 (17), 192 (30), 176 (2), 165 (22), 133 (15), 117 (10), 102 (2), 77 (6), 55 (9), 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. ^{1}H 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) ppm. 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. ^{1}H 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) ppm. 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. 128-130 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 104-106 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 108-110 ºC. ^{1}H NMR ($CDCl_3$): 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) ppm. 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. 145-147 ºC. ^{1}H NMR (DMSO): 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) ppm. 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 ºC. ^{1}H NMR (DMSO): 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) ppm. 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 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 166-167 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. 163-164 ºC. ^{1}H NMR (DMSO): 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) ppm. 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. ^{1}H 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) ppm. 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 ºC. ^{1}H 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) ppm. 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 ºC. ^{1}H 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) ppm. 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.

General procedure for the conjugate addition: The preparation of 1,5-diaryl-1,4-pentadien-3-ones were referred[24]. Indole (**1** or **5**, 0.8 mmol), 1,5-diaryl-1,4-pentadien-3-ones (**2** or **6**, 0.4 mmol), acetonitrile (3 mL), iodine (50 mmol %), were mixed in a 50 mL pyrex flask. The reaction mixture was irradiated in water bath of an ultrasonic cleaner at room temperature for a period as indicated in Tables 4 and 5 (the reaction was followed by TLC). After the completion of the reaction, the resulting

suspension was quenched with 10 mL water. A pinch of sodium bisulfite serves to remove little free iodine liberated in reaction. The reaction mixture was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over anhydrous magnesium sulfate for 12 h and filtered. Ethyl acetate was evaporated under reduced pressure to give the crude product, which was separated by column chromatography on silica (200-300 mesh), eluted with petroleum ether or a mixture of petroleum ether and diethyl ether.

RESULTS AND DISCUSSION

In a preliminary experiment, we studied the influence of the molar radio of **1:2:**I_2 and amount of the catalyst on the reaction yield. As shown in Table-1, the conjugate addition of indoles with 1,5-diphenyl-1,4-pentadien-3-one catalyzed by iodine in CH_3CN under ultrasound irradiation can give mono-additive product **3** as the main products and the *bis*-additive product **4** was isolated as a by-product. Increasing the quantity of the catalyst from 20 to 50 % can improve the yield of mono-additive product **3** from 76.2 to 92.0 % (Entry a, b and c). While increasing the catalyst quantity from 50 to 100 % decreased the yield of mono-additive product **3** from 92.0 to 67.3 % (Entry c and d). In order to higher the conversion of dibenzylidene acetone, we chose the molar radio of **1:2** instead of 2:1.

TABLE-1
EFFECTS OF THE MOLAR RADIO OF **1:2:**I_2 AND AMOUNT OF THE CATALYST ON CONJUGATE ADDITION OF INDOLE TO 1,5-DIPHENYL-1,4-PENTADIEN-3-ONE UNDER ULTRASOUND IRRADIATION*

Entry	**1:2** (mmol)	Amount of the catalyst (mol %)	Time (min)	**3** (%)	**4** (%)
a	0.4:0.4	20	40	76.2	16.5
b	0.8:0.4	20	40	85.5	10.3
c	0.8:0.4	50	40	92.0	7.5
d	0.8:0.4	100	40	67.3	28.3
e	0.5:0.5	100	40	41.3	50.2

*Ultrasound frequency: 25 kHz.

We also carried out the reaction of indole with dibenzylidene acetone in the presence of iodine using different solvents under ultrasound. The results are listed in Table-2. The reaction of indole with dibenzylidene in the presence of iodine (50 %) and CH_2Cl_2 proceeded smoothly under ultrasound irradiation, giving the mono-additive product **3** in 80 % and the *bis*-

additive product **4** in 17 % yield, while **3** in 92 % and **4** in 7.5 % were found in CH_3CN (Entry a and d). It is noteworthy that this reaction can also work in aqueous media (Entry f). While the yield of **3** was lower than in THF only (Entry e). So the study continued to be done using CH_3CN.

TABLE-2
EFFECT OF THE SOLVENT ON CONJUGATE ADDITION OF INDOLE TO 1,5-DIPHENYL-1,4-PENTADIEN-3-ONE UNDER ULTRASOUND IRRADIATION*

Entry	Solvent	Time (min)	**3** (%)	**4** (%)
a	CH_3CN	40	92.0	7.5
b	CH_2Cl_2	40	80.0	17.0
c	Anhyd. EtOH	40	30.6	65.7
d	THF	40	73.3	21.3
e	THF-H_2O = 1:1	40	26.0	22.4

*Indole: 0.8 mmol; 1,5-diphenyl-1,4-pentadien-3-one: 0.4 mmol; iodine: 50 mol %; ultrasound frequency: 25 kHz.

In the absence of ultrasound, the conjugate addition of indole to 1,5-diphenyl-1,4- pentadien-3-one mediated by iodine proceeded in only 78 % yield within 40 min by stirring alone (Table-3, Entry d). The conjugate addition gave **3** in 92 % yield within 40 min under the ultrasonication of 25 kHz (Table-3, Entry a). While under 40 kHz and 59 kHz ultrasound irradiation, the reaction was completed in 40 min with 87 and 86 % yield, respectively (Table-3, Entry b and c). It is apparent that the ultrasound can accelerate the conjugate addition of indole to 1,5-diphenyl-1,4-pentadien-3-one and lower frequency of ultrasound irradiation improves the yield. Therefore, the reaction was carried out with 25 kHz ultrasound irradiation.

TABLE-3
EFFECT OF ULTRASOUND FREQUENCY ON THE CONJUGATE ADDITION OF INDOLE TO 1,5-DIPHENYL-1,4-PENTADIEN-3-ONE IN CH_3CN*

Entry	Ultrasound frequency kHz	Time (min)	**3** (%)	**4** (%)
a	25	40	92.0	7.5
b	40	40	87.0	10.1
c	59	40	86.0	9.6
d	Stiring	40	78.0	11.9
e	25[a]	40	0	0

*Indole: 0.8 mmol; 1,5-diphenyl-1,4-pentadien-3-one: 0.4 mmol; iodine: 50 mol %; [a]The reaction was proceeded in the absence of iodine.

The experiment for the addition of indole to 1,5-diphenyl-1,4-pentadien-3-one in the absence of iodine under ultrasonic irradiation have also been performed. It is noted that no additive product was obtained (Table-3, Entry e).

From the above results, the optimum reaction condition was chosen: indoles (0.8 mmol), 1,5-diaryl-1,4-pentadien-3-ones (0.4 mmol), iodine (50 mol %, 0.2 mmol)/CH_3CN (3 mL). Under this condition, a series of experiments for the conjugate addition of indole to 1,5-diaryl-1,4-pentadien-3-ones under 25 kHz ultrasound irradiation was performed. The results are summarized in Table-4.

TABLE-4
CONJUGATE ADDITION OF INDOLE TO 1,5-DIARYL-1,4-PENTADIEN-3-ONE CATALYZED BY IODINE UNDER ULTRASOUND IRRADIATION

Entry	R_1	R_2	Time (min)	**3** (%)	**4** (%)
a	H	H	40	92.0	7.5
b	H	4-Br	40	76.0	23.0
c	H	3-Br	50	61.0	33.0
d	H	4-Cl	50	69.2	28.9
e	H	3-Cl	50	61.3	34.9
f	H	2-Cl	50	64.1	34.7
g	H	4-CH_3	50	60.1	34.7
h	H	4-CH_3O	90	62.4	29.8
i	H	4-NO_2	70	17.0	33.0
j	CH_3	H	50	96.7	1.3
k	H	-	60	-	66.4[a]

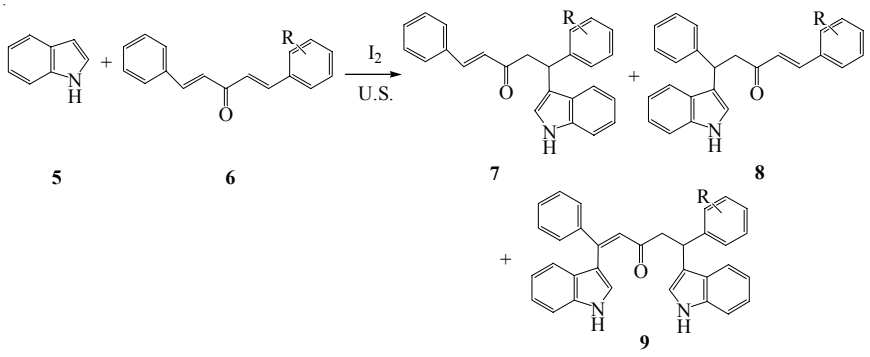
[a]Mono-additive product **3** as the substrate; molar radio of **3** and indole = 1:2; iodine (100 mol %).

As shown in Table-4, the conjugate addition of indole to 1,5-diaryl-1,4-pentadien-3-ones was carried out in moderate to good yield catalyzed by iodine under ultrasonic irradiation. Arcadi *et al.*[7] reported that the conjugate addition of indole to 1,5-dibenzyl-1,4-pentadien-3-one catalyzed by $NaAuCl_4 \cdot 2H_2O$ gave mono-additive product **3** in 65 % yield by stiring within 90 min, the polycyclic indole *b*-annulated with a seven-membered cycle product was isolated as a by-product. While in our system, the iodine-catalyzed reaction was given **3** in 92.0 % yields under ultrasound irradiation within 40 min and no cyclic product was isolated.

If the mono-additive product **3** as the substrates, *bis*-additive product (Table-4, Entry 4j) was obtained in 66.4 % yield catalyzed by iodine (100 mol %) within 1 h under ultrasound irradiation. This result indicated that the conjugate addition gave the mono-additive product **3** first, then the *bis*-additive product.

The reaction seems to occur *via* a classic Friedel-Crafts alkylation pathway[25]. From the data in Table-4, the electron-withdrawing substituents in the benzene ring in 1,5-diaryl-1,4-pentadien-3-ones (**3b-3f**) can increase the rate of reaction. In contrast, electron-donating substituents (**3g-3i**) decrease the reactivity. It is indicated that electron-withdrawing substituents can decrease the electronic cloud density on 1,4-position in 1,5-diaryl-1,4-pentadien-3-ones, then increase the electrophilicity in the conjugate addition. But 1,5-diaryl-1,4-pentadien-3-ones carrying the strong electron-withdrawing substituents such as nitro-group show less reactivity in the conjugate addition (Entry i). On the other hand, it is found that N-methylindole are much more reactive than indole in the conjugate addition (**3a** and **3i**). It may be that electron-donating substituents can increase the electronic cloud density on 3-position in indole, then increase the nucleophilicity in the conjugate addition.

In addition, a series of experiments for the conjugate addition of indole to asymmetry 1,4-pentadien-3-ones catalyzed by iodine under ultrasound irradiation were performed (**Scheme-II**). The results are summarized in Table-5.



Scheme-II

As shown in **Scheme-II**, there are two different active positions in **6**, so these reactions have two mono-additive (**Scheme-II**, **7** and **8**) and one *bis*-additive products (**Scheme-II**, **9**). The nucleophilic reagent in the conjugate addition are preferentially attacked the position that has the lower electronic cloud density in 1,4-pentadien-3-ones. The results were indicated in Table-5.

In conclusion, it is shown that iodine is an efficient catalyst for the regioselective alkylation at the 3-position of 3-unsubstituted indoles through conjugated addition type reaction with 1,5-diaryl-1,4-pentadien-3-ones under ultrasound irradiation.

TABLE-5
CONJUGATE ADDITION OF INDOLE TO ASYMMETRY 1,4-PENTADIEN-3-ONES (**6**) CATALYZED BY IODINE UNDER ULTRASOUND IRRADIATION

Entry	R	Time (min)	**7** (%)	**8** (%)	**9** (%)
a	4-$CH_3C_6H_4$	40	30.1	60.3	5.8
b	4-$CH_3OC_6H_4$	50	28.3	32.5	33.6
c	3-ClC_6H_4	60	39.2	2.7	56.5

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