Photoinduced 1,4-Additions of Indoles to Enones

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General Information. All reactions were performed in air-dried or oven-dried borosilicate tubes. Reactions were either carried out in a Rayonet photoreactor equipped with eight 8W ultraviolet lamps or between two Luzchem exposure panels equipped with four 8W ultraviolet lamps each. UV-A bulbs (~350 nm),^{1,2} UV-B bulbs (~300 nm), and exposure panels were purchased from Luzchem Research, Inc. Purification of reaction products was carried out by flash column chromatography using silica gel (40-63 μ m). Analytical thin layer chromatography was performed on aluminum sheets pre-coated with silica gel 60 F254, cut to size. Visualization was accomplished with UV light and an aqueous vanillin solution followed by heating.

¹H NMR spectra were recorded on a 300 MHz spectrometer at ambient temperature and are reported in ppm using solvent as the internal standard (CDCl₃ at 7.26 ppm or C₆D₆ at 7.15 ppm). Data are reported as: multiplicity (ap = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant(s) in Hz. ¹³C NMR spectra were recorded at 75 MHz. Chemical shifts are reported in ppm from tetramethylsilane, with the solvent resonance employed as the internal standard (CDCl₃ at 77.0 ppm or C₆D₆ at 128.02 ppm). High-resolution mass spectra were obtained from the Ottawa-Carleton Mass Spectrometry Centre.

(1) For specifications, see <http://www.luzchem.com/handbook/LESUVA011.pdf>

(2) Alternatively, this apparatus could be substituted for a medium pressure Hg lamp fitted with a uranium glass filter.

Materials. Dichloromethane was dried by distillation over calcium hydride. Tetrahydrofuran was dried by distillation over sodium/benzophenone ketyl. Diethyl ether was purified by passage through a column of activated alumina under a nitrogen atmosphere.³ Unless otherwise noted, all commercial materials were used without further purification. Cyclohept-2-enone and cyclooct-2-enone were prepared according to literature procedures.^{4,5} 1-Benzylindole and 1-allylindole were prepared according to the procedure of Guida.⁶ 1-Acetylindole was prepared according to the procedure of Nickisch.⁷ *tert*-Butylindole-1-carboxylate was prepared according to the procedure of Vazquez.⁸

General Procedure for Solvent Scan (Table 1). Into each of 10 borosilicate tubes equipped with stirbars was added cyclohept-2-enone (0.033 g, 0.30 mmol) and indole (0.053 g, 0.45 mmol). To each tube was added 2 mL of solvent (Table 1). In the case of volatile solvents, the volume was marked on the tube, and an excess of solvent was added. The tube was capped with a rubber septum and purged with a nitrogen balloon and an outlet while stirring for a minimum of 5 minutes or until the solvent had evaporated to the marked level. The tubes were then placed on a Luzchem rotating carousel equipped with a stirplate and allowed to stir in a Rayonet photoreactor equipped with eight 8W UV-A bulbs for 18 hours. The reactions were monitored by TLC (40% EtOAc/hexanes). The contents of each tube were then transferred to a round-bottom flask, and the solvent was removed under reduced pressure. To each flask was added 1.00 mL of a standardized solution of 1% tetramethylsilane in deuteriochloroform. ¹H NMR spectra of these solutions were recorded, and the % conversion calculated based on the ratio of the tetramethylsilane (12H) resonance at 0.0 ppm to the resonance corresponding to the product's methine proton (1H) at 3.26 ppm. The method is estimated to have an error of approximately $\pm 5\%$.

Table 5. Concentration Scan for the Photoinduced 1,4-Addition of Indole to Cyclohept-2-enone

Entry	[Enone] (mol/L)	% Conversion ^a
1	0.05	Quantitative
2	0.10	Quantitative
3	0.30	74
4	0.50	49

^a Determined by ¹H NMR using TMS as an internal standard

General Procedure for Concentration Scan (Table 5). Into each of 4 borosilicate tubes equipped with stirbars were added cyclohept-2-enone (0.033 g, 0.30 mmol) and indole (0.053 g, 0.45 mmol). To each tube

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(5) Chidambaram, N.; Chandrasekaran, S. *J. Org. Chem.* **1987**, *52*, 5048.

(6) Guida, W. C.; Mathre, D. J. *J. Org. Chem.* **1980**, *45*, 3172.

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was then added either 6.0, 3.0, 1.0, or 0.60 mL of dichloromethane to give concentrations of 0.050, 0.10, 0.30 and 0.50 M, respectively. The volume was marked on the tube, and an excess of solvent was added. The tube was capped with a rubber septum and purged with a nitrogen balloon and an outlet while stirring for a minimum of 5 minutes or until the solvent had evaporated to the marked level. The tubes were then placed on a Luzchem rotating carousel equipped with a stirplate and allowed to stir in a Rayonet photoreactor equipped with eight 8W UV-A bulbs for 18 hours. The contents of each tube were then transferred to a round-bottom flask, and the solvent was removed under reduced pressure. To each flask was added 1.00 mL of a standardized solution of 1% tetramethylsilane in deuteriochloroform. ^1H NMR spectra of these solutions were recorded, and the % conversion calculated based on the ratio of the tetramethylsilane (12H) resonance at 0.0 ppm to the resonance corresponding to the product's methine proton (1H) at 3.26 ppm. The method is estimated to have an error of approximately $\pm 5\%$.

General Procedure for Photoinduced 1,4-Addition of Indoles (Tables 2, 3 and 4).

3-(1H-Indol-3-yl)cycloheptanone (3a)(table 2, entry 4). A borosilicate tube was charged with a stir bar, cyclohept-2-enone (0.105 g, 0.949 mmol) and indole (0.117 g, 0.999 mmol). A volume of 18.0 mL dichloromethane was added to the mixture and the volume was marked on the tube. An excess of 1-2 mL of solvent was then added to the tube. The tube was capped with a septum and was purged with stirring using a nitrogen balloon and an outlet until the solvent evaporated to the volume marked. The reaction mixture was then placed on a stir-plate and allowed to stir between two exposure panels each equipped with four 8W UV-A bulbs for 18 hours to obtain the crude mixture as a dark red liquid.⁹ The reaction was monitored by TLC and the product was found to have TLC R_f 0.51 on silica gel (40% EtOAc/hexanes). The crude mixture was concentrated under reduced pressure to a few milliliters and was purified by flash chromatography using CH_2Cl_2 . The purified product was a clear, colorless oil (0.211 g, 98% yield); ^1H NMR (C_6D_6 , 300 MHz) δ 7.65-7.62 (m, 1H), 7.26-7.17 (m, 2H), 7.12-7.09 (m, 1H), 6.99 (br s, 1H), 6.38 (d, 1H, $J = 2.4$ Hz), 3.05 (tt, 1H, $J = 10.4$ and 2.7 Hz), 2.79 (ddd, 1H, $J = 14.4$, 3.6 and 1.5 Hz), 2.71 (dd, 1H, $J = 14.4$ and 10.5 Hz), 2.29 (ap dd, 2H, $J = 9.2$ and 4.5 Hz), 2.07-2.01 (m, 1H), 1.63-1.43 (m, 3H), 1.36-1.09 (m, 2H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.7, 136.9, 126.5, 122.2, 121.4, 119.6, 119.5, 119.4, 111.5, 50.5, 43.8, 38.2, 34.0, 29.2, 24.4; IR (film): 3411, 3057, 2927, 2856, 1691, 1458, 1339, 1099, 741 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{15}\text{H}_{17}\text{NO}$ $[\text{M}]^+$: 227.1310. Found: 227.1304.

(9) The described transformations were typically accompanied by a change in color from a clear to a red or an amber solution.

Table 2a. Experimental Details for Results in Table 2

Entry	m _{enone} (g)	n _{enone} (mmol)	m _{indole} (g)	n _{indole} (mmol)	V _{solvent} (mL)
1	0.034	0.49	0.080	0.68	10
2	0.033	0.40	0.071	0.61	8.0
3	0.033	0.34	0.060	0.51	7.0
4	0.105	0.949	0.117	0.999	19
5	0.033	0.27	0.047	0.40	5.5

4-(1H-Indol-3-yl)butan-2-one (5)(table 2, entry 1). Isolated 42 mg as white crystals after column chromatography (15% EtOAc/hexanes). Spectral data were found to be in good agreement with those in the literature.¹⁰

3-(1H-Indol-3-yl)cyclopentanone (7)(table 2, entry 2). Isolated 15 mg as a white powder after column chromatography (25% EtOAc/hexanes). Spectral data were found to be in good agreement with those in the literature.¹¹

3-(1H-Indol-3-yl)cyclohexanone (9)(table 2, entry 3). Isolated 10 mg as a clear, colorless oil after column chromatography (30% EtOAc/hexanes). Spectral data were found to be in good agreement with those in the literature.¹²

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3-(1H-Indol-3-yl)cyclooctanone (11)(table 2, entry 5). Isolated 43 mg as a clear, colorless oil after column chromatography (20% EtOAc/hexanes). TLC R_f 0.53 (40% EtOAc/hexanes); ^1H NMR (CDCl_3 , 300 MHz) δ 7.96 (br s, 1H), 7.68 (d, 1H, $J = 7.8$ Hz), 7.36 (d, 1H, $J = 8.1$ Hz), 7.19 (td, 1H, $J = 7.2$ and 1.2 Hz), 7.12 (td, 1H, $J = 7.8$ and 0.9 Hz), 6.98 (d, 1H, $J = 2.4$ Hz), 3.57 (tt, 1H, $J = 12$ and 3.3 Hz), 2.92 (t, 1H, $J = 12.6$ Hz), 2.66 (ddd, 1H, $J = 12.9$, 3.2 and 1.2 Hz), 2.58 (dd, 1H, $J = 12.3$ and 3 Hz), 2.46-2.39 (m, 1H), 2.18-1.42 (m, 8H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 213.9, 136.9, 126.8, 122.4, 121.6, 119.9, 119.7, 119.6, 111.6, 48.3, 42.8, 35.7, 34.5, 27.9, 25.1, 24.6; IR (film): 3410, 3055, 2929, 2857, 1686, 1458, 1339, 740 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{16}\text{H}_{19}\text{NO}[\text{M}]^+$: 241.1467. Found: 241.1487.

Table 3a. Experimental Details for Results in Table 3

Entry	m_{enone} (g)	n_{enone} (mmol)	m_{indole} (g)	n_{indole} (mmol)	V_{solvent} (mL)
1	0.105	0.949	0.117	0.999	19
2	0.100	0.907	0.131	0.998	18
3	0.050	0.45	0.263	1.36	9.0
4	0.033	0.30	0.132	0.906	6.0
5	0.050	0.45	0.178	1.36	9.0
6	0.050	0.45	0.267	1.36	9.0
7	0.050	0.45	0.184	1.36	9.0
8	0.050	0.45	0.239	1.36	9.0
9	0.050	0.45	0.193	1.36	9.0
10	0.050	0.45	0.221	1.36	9.0

3-(2-Methyl-1H-indol-3-yl)cycloheptanone (3b)(table 3, entry 2). Isolated 128 mg as a clear, colorless oil after column chromatography (CH_2Cl_2). TLC R_f 0.35 (25% EtOAc/hexanes); ^1H NMR (C_6D_6 , 300 MHz) δ 7.60-7.57 (m, 1H), 7.21 (ddd, 2H, $J = 13.9$, 7.0, and 1.5 Hz), 7.07-7.04 (m, 1H), 6.46 (br s, 1H), 3.14 (dd, 1H, $J = 13.4$ and 12.1 Hz), 3.05-2.95 (m, 1H), 2.60 (dt, 1H, $J = 13.4$ and 1.9 Hz), 2.34-2.30 (m, 2H), 1.99-1.86 (m, 2H), 1.83 (s, 3H), 1.69-1.47 (m, 2H), 1.44-1.29 (m, 1H), 1.19-1.05 (m, 1H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.5, 135.9, 128.7, 127.4, 121.1, 119.6, 119.4, 116.8, 110.8, 50.6, 43.9, 38.1, 35.2, 29.8, 24.4, 11.6; IR (film): 3357, 3053, 2928, 2856, 1695, 1461, 1264, 739 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{16}\text{H}_{19}\text{NO}[\text{M}]^+$: 241.1467. Found: 241.1473.

3-(2-Phenyl-1H-indol-3-yl)cycloheptanone (3c)(table 3, entry 3). Isolated 69 mg as a clear, colorless oil after column chromatography (15% EtOAc/hexanes). TLC R_f 0.49 (25% EtOAc/hexanes); ^1H NMR (CDCl_3 , 300 MHz) δ 8.10 (br s, 1H), 7.74 (d, 1H, $J = 7.8$ Hz), 7.47-7.37 (m, 6H), 7.22 (ap q, 1H, $J = 7.2$ Hz), 7.14 (ap q, 1H, $J = 7.4$ Hz), 3.50-3.33 (m, 2H), 2.69 (d, 1H, $J = 13.2$ Hz), 2.61-2.56 (m, 2H), 2.34-1.41 (m, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 214.6, 136.6, 133.8, 133.5, 129.3, 129.1, 128.4, 127.3, 122.5, 120.9, 119.9, 118.2, 111.6, 60.0, 44.3, 38.4, 34.9, 30.1, 24.9; IR (film): 3344, 2925, 2853, 1689, 1457, 1275, 764, 749, 699 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{21}\text{H}_{21}\text{NO}[\text{M}]^+$: 303.1623. Found: 303.1629.

3-(5-Methoxy-1H-indol-3-yl)cycloheptanone (3d)(table 3, entry 4). Isolated 58 mg as a clear, colorless oil after column chromatography (30% EtOAc/hexanes). TLC R_f 0.44 (40% EtOAc/hexanes); ^1H NMR (CDCl_3 , 300 MHz) δ 8.15 (br s, 1H), 7.22 (d, 1H, $J = 8.8$ Hz), 7.03 (d, 1H, $J = 2.3$ Hz), 6.89 (d, 1H, $J = 2.3$ Hz), 6.85 (dd, 1H, $J = 8.8$ and 2.4 Hz), 3.86 (s, 3H), 3.19 (tt, 1H, $J = 10.8$ and 2.5 Hz), 2.93 (t, 1H, $J = 12.4$ Hz), 2.83 (dddd, 1H, $J = 14.4$ Hz, $J = 1.6$ Hz, $J = 1.5$ Hz, $J = 1.4$ Hz), 2.63 (q, 2H, $J = 4.4$ Hz), 2.28 (d, 1H, $J = 14.0$ Hz), 2.09-1.95 (m, 2H), 1.83-1.51 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 214.9, 154.2, 132.0, 126.8, 121.5, 121.0, 112.5, 112.4, 101.4, 56.4, 50.9, 44.5, 38.4, 34.3, 29.6, 24.8; IR (film): 3366, 2930, 2855, 1691, 1583, 1485, 1441, 1211, 1052, 796, 749 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_2[\text{M}]^+$: 257.1416. Found: 257.1406.

3-(5-Methyl-1H-indol-3-yl)cycloheptanone (3e)(table 3, entry 5). Isolated 53 mg as a clear, colorless oil after column chromatography (CH_2Cl_2). TLC R_f 0.33 (25% EtOAc/hexanes); ^1H NMR (C_6D_6 , 300 MHz) δ 7.51 (d, 1H, $J = 0.7$ Hz), 7.08 (dd, 1H, $J = 8.4$ and 1.3 Hz), 7.00 (d, 1H, $J = 8.3$ Hz), 6.57 (s, 1H), 6.33 (d, 1H, $J = 2.1$ Hz), 3.08 (tt, 1H, $J = 10.4$ and 2.5 Hz), 2.83 (ddd, 1H, $J = 14.4$, 3.3, and 1.6 Hz), 2.74 (dd, 1H, $J = 14.4$ and 10.9 Hz), 2.44 (s, 3H), 2.31 (dd, 2H, $J = 8.5$ and 4.6 Hz), 2.11-2.03 (m, 1H), 1.67-1.43 (m, 3H), 1.37-1.11 (m, 2H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.5, 135.5, 128.1, 127.2, 124.2, 121.4, 119.9, 119.4, 111.4, 50.8, 44.1, 38.6, 34.4, 29.5, 24.9, 22.0; IR (film): 3367, 2926, 2856, 1698, 1444, 1347, 795 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{16}\text{H}_{19}\text{NO}[\text{M}]^+$: 241.1467. Found: 241.1460.

3-(5-Bromo-1H-indol-3-yl)cycloheptanone (3f)(table 3, entry 6). Isolated 60 mg as a clear, colorless oil after column chromatography (CH_2Cl_2). TLC R_f 0.31 (30% EtOAc:hexanes); ^1H NMR (C_6D_6 , 300 MHz) δ 7.86 (d, 1H, $J = 1.9$ Hz), 7.33 (dd, 1H, $J = 8.7$ and 1.8 Hz), 6.71 (dd, 1H, $J = 8.6$ and 0.4 Hz), 6.67 (br s, 1H), 6.23 (br d, 1H, $J = 2.3$ Hz), 2.87-2.78 (m, 1H), 2.62-2.60 (m, 2H), 2.34-2.17 (m, 2H), 1.89-1.83 (m, 1H), 1.53-1.02 (m, 5H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.2, 135.3, 125.2, 122.1, 121.4, 121.0, 113.01, 112.99, 50.2, 43.8, 38.4, 33.7, 29.1, 24.4; IR (film): 3348, 2926, 2855, 1692, 1459, 1275, 1260, 884, 749 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{15}\text{H}_{16}\text{BrNO}[\text{M}]^+$: 305.0415. Found: 305.0399.

3-(5-Fluoro-1H-indol-3-yl)cycloheptanone (3g)(table 3, entry 7). Isolated 36 mg as a clear, colorless oil after column chromatography (30% EtOAc/hexanes) followed by column chromatography with 1% MeOH/dichloromethane. TLC R_f 0.31 (30% EtOAc:hexanes); ^1H NMR (C_6D_6 , 300 MHz) δ 7.33 (dd, 1H, $J = 9.7$ and 2.3 Hz), 6.97 (td, 1H, $J = 8.9$ and 2.4 Hz), 6.80 (ap dd, 2H, $J = 8.8$ and 4.4 Hz), 6.33 (d, 1H, $J = 2.2$ Hz), 2.91-2.83 (m, 1H), 2.65 (ap d, 2H, $J = 7.6$ Hz), 2.30-2.24 (m, 2H), 1.91 (ap d, 1H, $J = 14.9$ Hz), 1.56-1.29 (m, 5H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.5, 158.2 (d, $J = 234.1$ Hz, C(5)-F), 133.3, 126.8 (d, $J = 9.4$ Hz, C(α)-F), 121.7 (d, $J = 4.8$ Hz, C(3)-F), 121.6, 112.2 (d, $J = 9.6$ Hz, C(7)-F), 110.6 (d, $J = 26.2$ Hz, C(6)-F), 104.5 (d, $J = 23.3$ Hz, C(4)-F), 50.2, 43.8, 38.2, 33.9, 29.1, 24.4; IR (film): 3349, 2928, 2856, 1689, 1581, 1486, 1456, 1347, 1259, 1161, 1100, 938, 850, 796, 763, 749 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{15}\text{H}_{16}\text{FNO}[\text{M}]^+$: 245.1216. Found: 245.1201.

Methyl 3-(3-oxocycloheptyl)-1H-indole-5-carboxylate (3h)(table 3, entry 8). Isolated 28 mg as a clear, colorless oil after column chromatography (40% EtOAc/hexanes). TLC R_f 0.20 (30% EtOAc/hexanes); ^1H NMR (CDCl_3 , 300 MHz) δ 8.34 (br s, 2H), 7.88 (d, 1H, $J = 8.4$ Hz), 7.34 (d, 1H, $J = 8.6$ Hz), 7.00 (s, 1H), 3.92 (s, 3H), 3.30 (br ap t, 1H, $J = 13.1$ Hz), 2.95 (dd, 1H, $J = 14.7$ and 11.4 Hz), 2.82 (d, 1H, $J = 14.5$ Hz), 2.63 (ap dt, 2H, $J = 7.8$ and 3.8 Hz), 2.26 (br d, 1H, $J = 13.4$ Hz), 2.08-1.95 (m, 2H), 1.85-1.58 (m, 3H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.5, 168.0, 139.4, 126.3, 123.9, 123.1, 122.5, 122.1, 121.3, 111.4, 51.5, 50.4, 43.8, 38.6, 33.8, 29.1, 24.4; IR (film): 3339, 2926, 2855, 1697, 1437, 1275, 1260, 1109, 764, 750 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_3[\text{M}]^+$: 285.1365. Found: 285.1369.

Table 4a. Experimental Details for Results in Table 4

Entry	m _{enone} (g)	n _{enone} (mmol)	m _{indole} (g)	n _{indole} (mmol)	V _{solvent} (mL)
1	0.105	0.949	0.117	0.999	19
2	0.050	0.45	0.060	0.45	9.0
3	0.050	0.45	0.071	0.45	9.0
4	0.050	0.45	0.094	0.45	9.0
5	0.050	0.45	0.087	0.55	9.0
6	0.050	0.45	0.118	0.55	9.0

3-(1-Methyl-3-indolyl)-cycloheptanone (3k)(table 4, entry 2). Isolated 56 mg as a clear, colorless oil after column chromatography (20% EtOAc/hexanes). TLC R_f 0.29 (20% EtOAc/hexanes); ^1H NMR (C_6D_6 , 300 MHz) δ 7.67 (d, 1H, $J = 7.9$ Hz), 7.29-7.17 (m, 2H), 7.03 (d, 1H, $J = 7.6$ Hz), 6.27 (s, 1H), 3.10 (apt t, 1H, $J = 10.7$ and 2.9 Hz), 2.94 (s, 3H), 2.82-2.72 (m, 2H), 2.33 (dd, 2H, $J = 9.7$ and 4.7 Hz), 2.11-2.05 (m, 1H), 1.68-1.47 (m, 3H), 1.40-1.14 (m, 2H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.4, 137.9, 127.4, 124.5, 122.2, 120.7, 119.9, 119.4, 109.8, 51.0, 44.1, 38.8, 34.3, 32.0, 29.5, 24.8; IR (film): 3052, 2927, 2855, 1697, 1472, 1326, 1262, 1154, 740 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{16}\text{H}_{19}\text{NO}[\text{M}]^+$: 241.1467. Found: 241.1479.

3-(1-Allyl-3-indolyl)-cycloheptanone (3l)(table 4, entry 3). Isolated 64 mg as a clear, colorless oil after column chromatography (20% hexanes/ CH_2Cl_2). TLC R_f 0.58 (CH_2Cl_2); ^1H NMR (C_6D_6 , 300 MHz) δ 7.78 (dd, 1H, $J = 6.8$ and 1.1 Hz), 7.38-7.29 (m, 4H), 6.56 (s, 1H), 5.65 (ddt, 1H, $J = 17.0$, 10.4 and 5.3 Hz), 4.95 (ddd, 1H, $J = 10.2$, 2.9 and 1.4 Hz), 4.85 (ddd, 1H, $J = 17.1$, 3.1 and 1.6 Hz), 4.16 (dt, 2H, $J = 5.3$ and 1.6 Hz), 3.21 (tt, 1H, $J = 10.6$, 2.7 Hz), 2.94 (ddd, 1H, $J = 14.4$, 3.3, 1.6 Hz), 2.86 (dd, 1H, $J = 14.4$ and 10.9 Hz), 2.44 (dd, 1H, $J = 9.3$ and 4.4 Hz), 2.22-2.16 (m, 1H), 1.79-1.24 (m, 5H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.2, 137.2, 134.0, 127.3, 123.4, 122.1, 121.0, 119.8, 119.4, 116.6, 110.1, 50.7, 48.4, 43.9, 38.5, 34.5, 29.4, 24.5; IR (film): 3052, 2926, 2856, 1697, 1644, 1613, 1466, 1331, 1266, 992, 740 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{18}\text{H}_{21}\text{NO}[\text{M}]^+$: 267.1623. Found: 267.1601.

3-(1-Benzyl-3-indolyl)-cycloheptanone (3m)(table 4, entry 4). Isolated 47 mg as a clear, colorless oil after column chromatography (30% hexanes/ CH_2Cl_2). TLC R_f 0.58 (CH_2Cl_2); ^1H NMR (C_6D_6 , 300 MHz) δ 7.81-7.77 (m, 1H), 7.31-7.29 (m, 4H), 7.21-7.16 (m, 1H), 7.12-7.08 (m, 3H), 6.93-6.90 (m, 2H), 6.57 (s, 1H), 4.79 (s, 2H), 3.21 (ap tt, 1H, $J = 13.7$ and 2.7 Hz), 2.97-2.91 (m, 1H), 2.83 (dd, 1H, $J = 14.3$ and 11.1 Hz), 2.43 (ap dd, 2H, $J = 9.8$ and 4.7 Hz), 2.18 (br d, 1H, $J = 13.9$ Hz), 1.77-1.54 (m, 3H), 1.49-1.22 (m, 2H); ^{13}C NMR (C_6D_6 , 75 MHz) δ 211.0, 138.1, 137.3, 128.7, 127.3, 126.7, 123.7, 122.2, 121.2, 119.7, 119.5, 110.0, 50.6, 49.5, 43.8, 38.3, 34.1, 29.3, 24.4; IR (film): 3055, 3029, 2926, 2856, 1696, 1466, 1453, 1347, 1331, 1264, 1178, 1015, 741 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{22}\text{H}_{23}\text{NO}[\text{M}]^+$: 317.1780. Found: 317.1783.

3-(1H-Pyrrol-2-yl)cycloheptanone (13)(eq 4). A borosilicate tube was charged with a stir bar, cyclohept-2-enone (0.100 g, 0.907 mmol) and pyrrole (0.182 g, 2.72 mmol). A volume of 6.0 mL dichloromethane was added to the mixture and the volume was marked on the tube. An excess of 1-2 mL of solvent was then added to the tube. The tube was capped with a septum and was purged with a nitrogen balloon and an outlet to the volume marked. The reaction mixture was then placed on a stir-plate and allowed to stir between two exposure panels each equipped with four 8W UV-A bulbs for 48 hours to obtain the crude mixture as a dark red liquid. The crude mixture was concentrated under reduced pressure to a few milliliters and was purified by flash chromatography using 25% ethyl acetate in hexanes. The purified product was a clear, colorless oil (0.011 g, 7% yield). TLC R_f 0.39 (30% EtOAc/hexanes); ^1H NMR (CDCl_3 , 300 MHz) δ 8.06 (br s, 1H), 6.68 (dd, 1H, $J = 3.8$ and 2.3 Hz), 6.10 (dd, 1H, $J = 5.8$ and 2.9 Hz), 5.92 (s, 1H), 3.00 (ap t, 1H, $J = 10.4$ and 3.3 Hz), 2.89-2.73 (m, 2H), 2.53 (d, 1H, $J = 4.9$ Hz), 2.50 (d, 1H, $J = 4.4$ Hz), 2.17 (ap br d, 1H, $J = 13.3$ Hz), 2.03-1.87 (m, 2H), 1.82-1.44 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 214.0, 117.1, 108.6, 104.3, 53.83, 50.18, 44.4, 37.6, 35.6, 28.6, 24.4; IR (film): 3374, 2928, 2856, 1692, 1275, 764, 750, 718 cm^{-1} ; HRMS (EI): Exact mass calcd for $\text{C}_{11}\text{H}_{15}\text{NO}$: 177.1154. Found: 177.1156.

Procedure for Attempted Low Temperature Generation/Trapping of (*E*)-cyclooct-2-enone.^{13,14} A borosilicate tube was charged with a stir bar and (*Z*)-cyclooct-2-enone (0.033 g, 0.27 mmol). A volume of 5.4 mL dichloromethane was added and the volume was marked on the tube. An excess of 1-2 mL of solvent was then added to the tube. The tube was capped with a septum and was purged with stirring using a nitrogen

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- (13) For examples of low temperature generation/trapping experiments with (*E*)-cycloalkenones, see: (a) Corey, E. J.; Tada, M.; LaMahieu, R.; Libit, L. *J. Am. Chem. Soc.* **1965**, 87, 2051. (b) Noyori, R.; Watanabe, A.; Katô, M. *Tetrahedron Lett.* **1968**, 52, 5443. (c) Katô, M.; Noyori, R. *Bull. Chem. Soc. Jpn.* **1974**, 47, 1460.
- (14) For examples of low temperature generation/trapping experiments with (*E*)-cycloalkenes, see: (a) Inoue, Y.; Ueoka, T.; Kuroda, T.; Hakushi, T. *J. Chem. Soc., Chem. Commun.* **1981**, 1031. (b) Inoue, Y.; Ueoka, T.; Kuroda, T.; Hakushi, T. *J. Chem. Soc., Perkin Trans. 2* **1983**, 983. (c) Steinmetz, M. G.; Seguin, K. J.; Udayakumar, B. S.; Behnke, J. S. *J. Am. Chem. Soc.* **1990**, 112, 6601.

balloon and an outlet until the solvent evaporated to the volume marked. The solution was cooled to $-75\text{ }^{\circ}\text{C}$ and was then placed on a stir-plate and allowed to stir between two exposure panels each equipped with four 8W UV-A bulbs for 20 minutes, maintaining cooling.¹⁵ Irradiation was then stopped, and a heterogeneous mixture of indole (0.034 g, 0.242 mmol) in 1.0 mL dichloromethane, pre-cooled to $-75\text{ }^{\circ}\text{C}$, was then added to the borosilicate tube. The reaction mixture was then allowed to gradually warm to room temperature while stirring for 45 minutes. No reaction was observed by TLC. The solvent was evaporated under reduced pressure. ^1H NMR of the crude reaction mixture indicated only a mixture of starting materials.

Procedure for Oxygen-Induced Quenching of Enone Triplet. A borosilicate tube was charged with a stir bar, cyclohept-2-enone (0.025 g, 0.23 mmol) and indole (0.029 g, 0.25 mmol). A volume of 4.5 mL dichloromethane was added to the tube and stirred open to the atmosphere for 1 minute. The tube was capped with a septum and was then placed on a stir-plate and allowed to stir between two exposure panels each equipped with four 8W UV-A bulbs for 18 hours. No indole adduct was observed by TLC. The solvent was evaporated under reduced pressure. ^1H NMR of the crude reaction mixture indicated a mixture of starting materials as well as a modest amount of dimers of cyclohept-2-enone.^{13a}

Discussion of Mechanistic Alternatives

Scheme 2. Proposed photoinduced electron transfer mechanism for the 1,4-addition of indoles to enones

We favor the PET mechanism presented in Scheme 2 over a [2+2] cycloaddition/cyclobutane ring opening sequence that could afford the same products. Such a mechanistic scenario is not consistent with the observed electronic effects on the indole moiety. In addition, the regiochemistry observed in enone [2+2] cycloadditions usually favors formation of the cycloadduct in which the carbonyl and the electron rich group are in a head to

(15) The sample was immersed in a 95% ethanol bath contained in a 5L quartz Dewar and cooled to $-75\text{ }^{\circ}\text{C}$ by an FTS Systems cold finger apparatus.

tail configuration, which could not form the formal 1,4-adduct upon cyclobutane ring opening. During the course of these studies, we have not observed formation of [2+2] cycloadducts between indoles and enones.¹⁶

In specific cases, other mechanisms could also be operating. For example, cyclohept-2-enone and cyclooct-2-enone could also afford the observed 1,4-addition product through an *E*-cycloalkenone intermediate.¹³ However, low temperature generation/trapping experiments have been performed with *E*-cyclooct-2-enone and have resulted in recovery of the starting materials,¹³ suggesting *E*-cycloalkenones are not likely intermediates for these substrates. We also speculate that reaction of methyl vinyl ketone (MVK) via a Bauld-Steckhan type cycloaddition mechanism,¹⁷ namely a formal hetero-Diels-Alder reaction of MVK with the indole radical cation (affording the 1,4-adduct upon hydrolysis), is unlikely and not consistent with the substrate scope of the reaction.

(16) For examples of [2+2] cycloadditions between *N*-acylindoles and alkenes, see: Weedon, A. C.; Zhang, B. *Synthesis* **1992**, 95 and references cited therein.

(17) (a) Bauld, N. L.; Bellville, D. J.; Harirchian, B.; Lorenz, K. T.; Pabon, R. A. Jr.; Reynolds, D. W.; Wirth, D. D.; Chiou, H.-S.; Marsh, B. K. *Acc. Chem. Res.* **1987**, 20, 371. (b) Mlcoch, J.; Steckhan, E. *Angew. Chem., Int. Ed. Engl.* **1985**, 24, 412.

Table 2, Entry 4

3a

Table 2, Entry 5
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Table 3, Entry 2

3b

Table 3, Entry 3

3c

Table 3, Entry 4

3d

Table 3, Entry 5
3e

Table 3, Entry 6

3f

Table 3, Entry 7

3g

Table 3, Entry 8

3h

Table 4, Entry 2

3k

Table 4, Entry 3

3I

Table 4, Entry 4

3m

equation 4
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