Total synthesis of the novel antifungal agent (±)-Jesterone

Goverdhan Mehta* and Subhas Chandra Pan

Department of Organic Chemistry, Indian Institute of Science

Bangalore 560 012, India

Email Address gm@orgchem.iisc.ernet.in

Supporting Information

Compound 6

¹H NMR (300 MHz) (CDCl₃) δ 6.76-6.64 (m, 3H), 5.33 (tt, 1H, J = 1.5 Hz, 7.5 Hz), 5.12 (br s, 1H), 3.77 (s, 3H), 3.34 (d, 2H, J = 6.9 Hz), 1.78 (s, 6H)

¹³C NMR (75 MHz) (CDCl₃) δ 153.5, 148.1, 134.5, 128.2, 121.6, 116.1, 115.7, 111.9, 55.7, 29.7, 25.7, 17.8

Compound 7

¹H NMR (300 MHz) (CDCl₃) δ 6.77-6.67 (m, 2H), 6.54-6.52 (m, 1H), 5.17-5.10 (m, 1H), 3.11 (d, 2H, J = 6.6 Hz), 1.75 (s, 3H), 1.63 (s, 3H)

¹³C NMR (75 MHz) (CDCl₃) δ 187.9, 187.5, 148.5, 136.7, 136.5, 136.3, 132.3, 117.8, 27.4, 25.7, 17.7

Compound 8

^1H NMR (300 MHz) (CDCl_3) δ 6.39 (s, 1H), 6.05 (d, 1H, $J = 2.4$ Hz), 6.00 (d, 1H, $J = 2.4$ Hz), 5.07 (t, 1H, $J = 7.2$ Hz), 3.51 (br s, 2H), 3.25-3.23 (m, 2H), 2.98 (d, 2H, $J = 6.9$ Hz), 1.73 (s, 3H), 1.59 (s, 3H), 1.52 (d, 1H, $J = 8.7$ Hz), 1.45 (d, 1H, $J = 9$ Hz)

^{13}C NMR (75 MHz) (CDCl_3) δ 198.8, 198.7, 153.8, 138.0, 135.5, 135.0, 134.5, 117.9, 48.6, 48.5, 48.4, 48.2, 27.4, 25.3, 17.3

HRMS Calcd for $(\text{M} + \text{K})^+$: 281.1167
Found $(\text{M} + \text{K})^+$: 281.1372

Compound 9

^1H NMR (300 MHz) (CDCl_3) δ 6.05 (s, 2H), 4.92 (t, 1H, $J = 7.5$ Hz), 3.50-3.41 (m, 2H), 3.35 (s, 1H), 3.27 (br s, 2H), 2.65 (dd, 1H, $J = 6.9$ Hz, 15.6 Hz), 2.54 (dd, 1H, $J = 8.1$ Hz, 15.9 Hz), 1.68 (s, 3H), 1.59 (s, 3H), 1.48 (d, 1H, $J = 8.7$ Hz), 1.29 (d, 1H, $J = 8.4$ Hz)

^{13}C NMR (75 MHz) (CDCl_3) δ 205.3, 205.2, 137.0, 136.6, 115.2, 66.9, 62.0, 50.5, 50.1, 46.7, 43.3, 43.1, 25.8, 25.7, 18.0

HRMS Calcd for $(\text{M} + \text{Na})^+$: 281.1154
Found $(\text{M} + \text{Na})^+$: 281.1134

Compound 10

^1H NMR (300 MHz) (CDCl_3) δ 6.06 (br s, 2H), 4.90 (t, 1H, $J = 7.5$ Hz), 4.36 (dd, 1H, $J = 3.6$ Hz, 10.8 Hz), 3.80 (dd, 1H, $J = 3.3$ Hz, 11.4 Hz), 3.42 (s, 1H), 3.32-3.28 (m, 2H), 2.87 (d, 1H, $J = 3.6$ Hz), 2.64- 2.55 (m, 2H), 2.17 (br s, 1H), 1.68 (s, 3H), 1.59 (s, 3H), 1.51 (d, 1H, $J = 9.6$ Hz), 1.44 (d, 1H, $J = 9.3$ Hz)

^{13}C NMR (75 MHz) (CDCl_3) δ 205.7, 204.6, 138.1, 137.9, 137.2, 115.0, 68.2, 67.8, 61.8, 61.6, 53.9, 45.9, 44.3, 43.4, 25.8, 25.7, 18.0

HRMS Calcd for $(\text{M} + \text{Na})^+$: 311.1259
Found $(\text{M} + \text{Na})^+$: 311.1250

Compound 11

^1H NMR (300 MHz) (CDCl_3) δ 6.10-6.01 (m, 2H), 4.94-4.88 (m, 1H), 4.46 (d, 1H, $J = 10.5$ Hz), 3.74 (d, 1H, $J = 10.5$ Hz), 3.38 (s, 1H), 3.27 (br s, 1H), 3.23 (br s, 1H), 2.78 (d, 1H, $J = 3.9$ Hz), 2.63 (dd, 1H, $J = 6.6$ Hz, 15.3 Hz), 2.52 (dd, 1H, $J = 7.8$ Hz, 15.6 Hz), 1.68 (s, 3H), 1.59 (s, 3H), 1.53 (d, 1H, $J = 8.7$ Hz), 1.39 (d, 1H, $J = 9.0$ Hz), 0.89 (s, 9H), 0.05 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 205.2, 204.1, 138.7, 137.5, 136.9, 115.2, 67.8, 62.1, 61.7, 54.1, 45.8, 43.8, 43.2, 25.9, 25.8, 25.7, 25.6, 18.2, 18.0, -5.5, -5.6

HRMS Calcd for $(\text{M} + \text{Na})^+$: 425.2124
Found $(\text{M} + \text{Na})^+$: 425.2124

Compound 12

^1H NMR (300 MHz) (CDCl_3) δ 5.96 (s, 2H), 4.82 (t, 1H, $J = 7.2$ Hz), 4.08-3.82 (m, 4H), 3.40 (dd, 1H, $J = 3.0$ Hz, 9.6 Hz), 3.29 (s, 1H), 3.05 (s, 1H), 2.98 (s, 1H), 2.66 (dd, 1H, $J = 7.5$ Hz, 15.3 Hz), 2.40 (dd, 1H, $J = 6.6$ Hz, 15.3 Hz), 1.61 (s, 3H), 1.52 (br s, 4H), 1.23 (d, 1H, $J = 9.3$ Hz), 0.83 (s, 9H), 0.01 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 206.6, 206.3, 138.5, 138.2, 136.6, 115.4, 68.1, 67.6, 66.5, 62.8, 62.7, 61.8, 50.6, 50.1, 42.7, 26.1, 25.7, 25.6, 18.1, 17.9, -5.7, -5.8

HRMS Calcd for $(\text{M} + \text{Na})^+$: 455.2230
Found $(\text{M} + \text{Na})^+$: 455.2205

Compound 13

^1H NMR (300 MHz) (CDCl_3) δ 6.32-6.22 (m, 2H), 5.11 (t, 1H, $J = 6.9$ Hz), 4.60 (d, 1H, $J = 10.5$ Hz), 4.21 (d, 1H, $J = 9.6$ Hz), 3.98 (dd, 1H, $J = 4.8$ Hz, 11.1 Hz), 3.72 (d, 2H, $J = 12.9$ Hz), 3.14 (s, 1H), 3.04 (s, 1H), 2.97 (s, 1H), 2.80 (dd, 1H, $J = 7.8$ Hz, 15.0 Hz), 2.33 (dd, 1H, $J = 6.6$ Hz, 15.0 Hz), 2.13 (t, 1H, $J = 5.1$ Hz), 1.73 (s, 3H), 1.63 (s, 3H), 1.30 (d, 1H, $J = 10.2$ Hz), 1.21 (d, 1H, $J = 10.8$ Hz), 0.87 (s, 9H), 0.03 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 207.2, 136.9, 136.6, 116.6, 70.9, 68.4, 65.9, 65.4, 64.8, 59.9, 56.9, 48.1, 47.9, 44.7, 31.0, 25.8, 25.7, 18.1, 18.0, -5.5, -5.6

HRMS Calcd for $(\text{M} + \text{Na})^+$: 457.2386
Found $(\text{M} + \text{Na})^+$: 457.2408

Compound 14

^1H NMR (300 MHz) (CDCl_3) δ 5.18 (t, 1H, $J = 7.2$ Hz), 4.68 (d, 1H, $J = 5.7$ Hz), 4.56 (dd, 1H, $J = 4.8$ Hz, 14.4 Hz), 4.47-4.37 (m, 3H), 3.55 (br s, 1H), 3.48 (br s, 1H), 3.34 (s, 1H), 2.91 (dd, 1H, $J = 7.8$ Hz, 15.6 Hz), 2.43 (dd, 1H, $J = 7.2$ Hz, 15.3 Hz), 1.73 (s, 3H), 1.65 (s, 3H), 0.85 (s, 9H), 0.06 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 195.2, 154.2, 136.7, 131.7, 116.5, 67.8, 65.1, 62.3, 58.2, 56.1, 28.9, 25.8, 25.7, 18.1, 18.0, -5.4, -5.5

HRMS Calcd for $(\text{M} + \text{Na})^+$: 391.1917
Found $(\text{M} + \text{Na})^+$: 391.1935

Compound 15

^1H NMR (300 MHz) (CDCl_3) δ 10.55 (s, 1H), 5.21 (br s, 1H), 5.14 (s, 1H), 4.82 (d, 1H, $J = 14.4$ Hz), 4.65 (d, 1H, $J = 14.7$ Hz), 3.46 (s, 1H), 2.98 (br s, 1H), 2.48 (br s, 1H), 1.77 (s, 3H), 1.69 (s, 3H), 0.88 (s, 9H), 0.09 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 196.4, 194.5, 143.1, 141.9, 136.3, 115.6, 64.2, 62.8, 57.7, 56.3, 28.3, 25.2, 25.0, 17.4, -6.1, -6.2

HRMS Calcd for $(\text{M} + \text{Na})^+$: 389.1760
Found $(\text{M} + \text{Na})^+$: 389.1746

Compound 16

^1H NMR (300 MHz) (CDCl_3) δ 10.41 (s, 1H), 6.29 (s, 1H), 5.06 (t, 1H, $J = 7.2$ Hz), 4.81 (d, 1H, $J = 14.7$ Hz), 4.62 (d, 1H, $J = 14.7$ Hz), 3.46 (s, 1H), 2.60 (dd, 1H, $J = 6.6$ Hz, 15.3 Hz), 2.49 (dd, 1H, $J = 7.8$ Hz, 15.6 Hz), 2.03 (s, 3H), 1.72 (s, 3H), 1.59 (s, 3H), 0.85 (s, 9H), 0.06 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 197.0, 192.1, 169.2, 144.4, 140.2, 137.1, 115.2, 64.7, 62.6, 57.6, 57.0, 28.7, 25.7, 25.6, 20.6, 18.0, 17.9, -5.5, -5.6

HRMS Calcd for $(\text{M} + \text{Na})^+$: 431.1866
Found $(\text{M} + \text{Na})^+$: 431.1866

Compound 17b

^1H NMR (300 MHz) (CDCl_3) δ 6.65 (dd, 1H, $J = 1.2$ Hz, 15.6 Hz), 6.41- 6.29 (m, 1H), 6.32 (s, 1H), 5.07 (t, 1H, $J = 8.1$ Hz), 4.52 (d, 1H, $J = 12$ Hz), 4.41 (d, 1H, $J = 12$ Hz), 3.38 (s, 1H), 2.57-2.43 (m, 2H), 2.05 (s, 3H), 1.88 (dd, 3H, $J = 1.5$ Hz, 6.6 Hz), 1.72 (s, 3H), 1.59 (s, 3H), 0.85 (s, 9H), 0.04 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 195.5, 169.9, 145.6, 136.6, 135.6, 131.8, 127.5, 115.8, 66.1, 61.7, 57.1, 55.8, 29.0, 25.8, 20.9, 19.6, 18.2, 18.0, -5.2, -5.3

HRMS Calcd for $(\text{M} + \text{Na})^+$: 443.2230
Found $(\text{M} + \text{Na})^+$: 443.2246

Compound 18

^1H NMR (300 MHz) (CDCl_3) δ 6.69 (dd, 1H, $J = 1.5$ Hz, 15.6 Hz), 6.53-6.43 (m, 1H), 5.21 (t, 1H, $J = 7.5$ Hz), 4.90 (d, 1H, $J = 6$ Hz), 4.48 (d, 1H, $J = 11.7$ Hz), 4.39 (d, 1H, $J = 11.7$ Hz), 3.35 (s, 1H), 2.93 (dd, 1H, $J = 7.5$ Hz, 15.6 Hz), 2.52 (dd, 1H, $J = 7.2$ Hz, 15 Hz), 2.18 (d, 1H, $J = 6$ Hz), 1.95 (dd, 3H, $J = 1.5$ Hz, 7.2 Hz), 1.76 (s, 3H), 1.68 (s, 3H), 0.86 (s, 9H), 0.06 (s, 6H)

^{13}C NMR (75 MHz) (CDCl_3) δ 195.7, 149.2, 136.7, 135.9, 129.6, 127.9, 116.6, 65.7, 63.8, 57.9, 55.6, 29.1, 25.9, 25.8, 19.5, 18.2, 18.0, -5.2, -5.3

HRMS Calcd for $(\text{M} + \text{Na})^+$: 401.2124
Found $(\text{M} + \text{Na})^+$: 401.2135

Compound 19

^1H NMR (300 MHz) (CDCl_3) δ 6.71-6.59 (m, 1H), 6.46 (dd, 1H, $J = 1.5$ Hz, 14.7 Hz), 5.01 (t, 1H, $J = 7.2$ Hz), 4.59 (d, 1H, $J = 11.4$ Hz), 4.33 (d, 1H, $J = 11.4$ Hz), 3.66 (s, 1H), 2.85 (dd, 1H, $J = 7.8$ Hz, 15.3 Hz), 2.66 (dd, 1H, $J = 6.9$ Hz, 15.3 Hz), 1.93 (dd, 3H, $J = 1.5$ Hz, 6.6 Hz), 1.71 (s, 3H), 1.65 (s, 3H), 0.87 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H)

^{13}C NMR (75 MHz) (CDCl_3) δ 194.7, 193.6, 142.5, 140.9, 137.1, 136.6, 123.1, 115.4, 61.6, 57.6, 56.4, 25.8, 25.7, 25.6, 20.1, 18.2, 18.0, -5.3, -5.4

HRMS Calcd for $(\text{M} + \text{Na})^+$: 399.1968
Found $(\text{M} + \text{Na})^+$: 399.1973

Compound 20

^1H NMR (300 MHz) (CDCl_3) δ 6.57-6.45 (m, 1H), 6.37-6.30 (m, 1H), 5.04-4.98 (m, 1H), 4.54 (d, 1H, $J = 12\text{ Hz}$), 4.43 (d, 1H, $J = 12\text{ Hz}$), 3.67 (s, 1H), 2.88 (dd, 1H, $J = 8.1\text{ Hz}$, 15.3 Hz), 2.64 (dd, 1H, $J = 7.2\text{ Hz}$, 15.6 Hz), 2.41 (br s, 1H), 1.94 (dd, 3H, $J = 1.8\text{ Hz}$, 6.6 Hz), 1.72 (s, 3H), 1.65 (s, 3H)

^{13}C NMR (75 MHz) (CDCl_3) δ 195.3, 194.0, 142.2, 141.8, 137.3, 136.5, 122.1, 115.2, 61.7, 57.6, 57.4, 25.8, 25.7, 20.0, 18.0

HRMS Calcd for $(\text{M} + \text{Na})^+$: 285.1103
 Found $(\text{M} + \text{Na})^+$: 285.1110

Compound 1

^1H NMR (300 MHz) (CDCl_3) δ 6.09 (d, 1H, $J = 15.9\text{ Hz}$), 5.92-5.81 (m, 1H), 5.06 (t, 1H, $J = 7.2\text{ Hz}$), 4.93 (s, 1H), 4.75 (d, 1H, $J = 14.4\text{ Hz}$), 4.48 (d, 1H, $J = 14.4\text{ Hz}$), 3.67 (d, 1H, $J = 1.8\text{ Hz}$), 3.20 (d, 1H, $J = 3.9\text{ Hz}$), 2.78 (dd, 1H, $J = 8.1\text{ Hz}$, 15.6 Hz), 2.55 (dd, 1H, $J = 6.6\text{ Hz}$, 15.6 Hz), 2.18 (br s, 1H), 1.84 (dd, 3H, $J = 1.5\text{ Hz}$, 6.6 Hz), 1.71 (s, 3H), 1.65 (s, 3H)

^{13}C NMR (75 MHz) (CDCl_3) δ 195.0, 145.5, 136.0, 134.9, 131.5, 122.2, 116.5, 65.3, 63.1, 60.1, 59.5, 26.6, 25.8, 19.2, 18.0

HRMS Calcd for $(\text{M} + \text{Na})^+$: 287.1259
 Found $(\text{M} + \text{Na})^+$: 287.1255