AN EFFICIENT GREEN PROTOCOL FOR THE SYNTHESIS OF NOVEL DIHYDROINDENO[1,2-*b*]PYRROLES

Veerappan Jeyachandran, Muthumani Muthu and Raju Ranjith Kumar*

Department of Organic Chemistry, School of Chemistry, Madurai Kamaraj University,

Madurai – 625021, Tamil Nadu, India

SUPPLEMENTARY INFORMATION

EXPERIMENTAL

General

The melting points were measured in open capillary tubes and are uncorrected. The ^1H , ^{13}C and the 2D NMR spectra were recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as internal standard and CDCl_3 as solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ -scale) and the coupling constants are given in Hertz. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyzer. All the chemicals were purchased from Sigma-Aldrich and used without any further purification. Single crystal X-ray studies of **5a**, **5d** and **5h**, Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT* (Bruker, 2004); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used: *SHELXL97* (Sheldrick, 2008).

General procedure for the synthesis of dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-ones 4 and 5

An equimolar mixture of (*E*)-*N*-methyl-1-(methylthio)-2-nitroethenamine **1** or (*E*)-*N*-(1-(methylthio)-2-nitrovinyl)anilines **2** and ninhydrin **3** were dissolved in ethanol (2–3 mL) and stirred at ambient temperature for 5 min. Completion of the reaction was noted when the product precipitated from the reaction mixture, which was a clear solution at the beginning of the reaction. The precipitate was filtered, washed with water (10 mL) and dried to obtain novel 3a,8b-dihydroxy-1-methyl-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one **4** or 3a,8b-dihydroxy-2-(methylthio)-3-nitro-1-phenyl-1,8b-di-hydroindeno[1,2-*b*]pyrrol-4(3a*H*)-ones **5** in quantitative yields.

3a,8b-Dihydroxy-1-methyl-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (4)

Isolated as pale yellow solid; Yield 99 %; m.p. 195–197 °C; ¹H NMR (300 MHz, CDCl₃) δ_H: 2.48 (s, 3H), 3.36 (s, 3H), 6.03 (s, 1H), 6.49 (s, 1H), 7.47–7.52 (m, 1H), 7.66–7.68 (m, 2H), 7.47–7.52 (m, 1H), 7.76 (d, *J* = 7.5Hz, 1H); C¹³ NMR (75 MHz, CDCl₃) δ_C: 17.0, 29.6, 81.1, 94.8, 120.6, 123.6, 123.8, 130.4, 134.2, 135.5, 145.8, 161.1 and 194.8. Anal. Calcd. for C₁₃H₁₂N₂O₅S: C, 50.65; H, 3.92; N, 9.09%. Found: C, 50.63; H, 3.88; N, 9.04%.

3a,8b-Dihydroxy-2-(methylthio)-3-nitro-1-phenyl-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (5a)

Isolated as pale yellow solid; Yield 94%; m.p. 178–180 °C; ¹H NMR (300 MHz, CDCl₃) δ_H: 1.87 (s, 3H), 6.58 (d, *J* = 7.2Hz, 1H), 7.42–7.55 (m, 6H), 7.87 (d, *J* = 7.8Hz, 1H); C¹³ NMR (75 MHz, CDCl₃) δ_C: 16.8, 80.6, 97.6, 122.3, 124.6, 125.5, 129.3, 129.4, 129.7, 131.1, 134.5, 135.6, 136.7, 145.9, 163.8 and 195.1. Anal. Calcd. for C₁₉H₁₆N₂O₅S: C, 58.37; H, 3.81; N, 7.56%. Found: C, 58.35; H, 3.83; N, 7.54%.

3a,8b-Dihydroxy-2-(methylthio)-3-nitro-1-*o*-tolyl-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (5b)

Isolated as pale yellow solid; Yield 96%; m.p. 200–202 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.34 (s, 3H), 1.87 (s, 3H), 4.94 (s, 1H), 5.97 (s, 1H), 6.49 (d, $J = 7.8\text{Hz}$, 1H), 7.12–7.17 (s, 1H), 7.39–7.58 (m, 4H), 7.77–7.80 (m, 1H), 7.89 (d, $J = 7.5\text{Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 16.0, 17.3, 80.7, 97.7, 120.5, 124.4, 125.1, 127.2, 129.9, 130.9, 131.9, 134.1, 134.9, 135.3, 138.2, 146.3, 163.0 and 195.7. Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_5\text{S}$: C, 59.37; H, 4.20; N, 7.29%. Found: C, 59.35; H, 4.17; N, 7.26%.

3a,8b-Dihydroxy-2-(methylthio)-3-nitro-1-*m*-tolyl-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (5c)

Isolated as pale yellow solid; Yield 96%; m.p. 195–197 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.69 (s, 3H), 1.88 (s, 3H), 4.82 (s, 1H), 5.99 (s, 1H), 6.61 (d, $J = 7.8\text{Hz}$, 1H), 7.31–7.56 (m, 6H), 7.88 (d, $J = 7.5\text{Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 16.7, 21.2, 80.4, 97.1, 122.2, 124.6, 125.4, 126.1, 129.4, 129.5, 130.1, 131.1, 134.5, 135.4, 136.4, 139.9, 145.9, 163.5 and 194.7. Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_5\text{S}$: C, 59.37; H, 4.20; N, 7.29%. Found: C, 59.33; H, 4.17; N, 7.27%.

3a,8b-Dihydroxy-2-(methylthio)-3-nitro-1-*p*-tolyl-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (5d)

Isolated as pale yellow solid; Yield 96%; m.p. 199–201 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.87 (s, 3H), 2.11 (s, 3H), 6.57 (d, $J = 7.8\text{Hz}$, 1H), 7.43–7.56 (m, 6H), 7.89 (d, $J = 7.5\text{Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 16.7, 20.6, 80.5, 97.2, 122.4, 124.6, 125.4, 129.2, 129.3, 129.6, 131.1, 134.5, 135.5, 136.7, 146.0, 163.4, 176.5 and 195.0. Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_5\text{S}$: C, 59.37; H, 4.20; N, 7.29%. Found: C, 59.33; H, 4.18; N, 7.26%.

1-(2,4-Dimethylphenyl)-3a,8b-dihydroxy-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*] pyrrol-4(3a*H*)-one (5e)

Isolated as pale yellow solid; Yield 96%; m.p. 202–204 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.29 (s, 3H), 1.89 (s, 3H), 2.42 (s, 3H), 4.93 (s, 1H), 5.31 (s, 1H), 6.55 (d, $J = 7.5\text{Hz}$, 1H),

7.23 (d, $J = 8.4\text{Hz}$, 1H), 7.45 (t, $J = 7.8\text{Hz}$, 1H), 7.55 (t, $J = 7.5\text{Hz}$, 1H), 7.65 (d, $J = 8.4\text{Hz}$, 1H), 7.89 (d, $J = 7.8\text{Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 16.5, 17.3, 21.3, 79.3, 97.5, 124.7, 125.1, 128.1, 130.6, 131.0, 134.8, 135.5, 137.8, 140.4, 146.0 and 194.9. Anal. Calcd. for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}_5\text{S}$: C, 60.29; H, 4.55; N, 7.03%. Found: C, 60.27; H, 4.51; N, 7.01%.

1-(2,5-Dimethylphenyl)-3a,8b-dihydroxy-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*] pyrrol-4(3a*H*)-one (5f)

Isolated as pale yellow solid; Yield 95%; m.p. 215–217 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.28 (s, 3H), 1.89 (s, 3H), 2.46 (s, 3H), 4.92 (s, 1H), 5.97 (s, 1H), 6.53 (d, $J = 7.5\text{Hz}$, 1H), 7.01 (d, $J = 8.1\text{Hz}$, 1H), 7.23–7.29 (m, 1H), 7.43 (t, $J = 7.8\text{Hz}$), 7.51–7.58 (m, 1H), 7.89 (d, $J = 7.2\text{Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 21.2, 21.6, 84.8, 102.8, 128.9, 130.1, 135.1, 135.6, 135.7, 136.2, 138.6, 139.7, 140.0, 141.2, 141.6, 151.1, 167.9 and 200.6. Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$: C, 60.29; H, 4.55; N, 7.03%. Found: C, 60.27; H, 4.54; N, 7.01%.

3a,8b-Dihydroxy-1-(2-methoxyphenyl)-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*] pyrrol-4(3a*H*)-one (5g)

Isolated as pale yellow solid; Yield 94%; m.p. 209–211 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.98 (s, 3H), 2.22 (s, 3H), 4.78 (s, 1H), 5.77 (s, 1H), 6.57 (d, $J = 7.8\text{Hz}$, 1H), 6.80 (d, $J = 8.4\text{Hz}$, 1H), 7.16 (t, $J = 7.8\text{Hz}$, 1H), 7.40 (t, $J = 7.5\text{Hz}$, 1H), 7.37–7.53 (m, 2H), 7.69 (dd, $J = 1.5\text{Hz}$, $J = 7.8\text{Hz}$, 1H), 7.87 (d, $J = 7.2\text{Hz}$, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 15.8, 54.6, 79.9, 96.9, 110.6, 120.4, 120.9, 123.2, 124.0, 124.4, 129.9, 130.7, 134.2, 146.4, 155.7, 164.1 and 195.5. Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$: C, 56.99; H, 4.03; N, 7.00%. Found: 56.95; H, 4.00; N, 6.99%.

3a,8b-Dihydroxy-1-(4-methoxyphenyl)-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*] pyrrol-4(3a*H*)-one (5h)

Isolated as pale yellow solid; Yield 95%; m.p. 200–202 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.91 (s, 3H), 3.91 (s, 3H), 4.82 (s, 1H), 5.56 (s, 1H), 6.64 (d, $J = 7.5\text{Hz}$, 1H), 6.97–7.0 (m,

3H), 7.45–7.56 (m, 3H), 7.88 (d, $J = 7.5\text{Hz}$, 1H); C^{13} NMR (75 MHz, CDCl_3) δ_{C} : 16.7, 55.5, 80.8, 97.8, 114.5, 122.3, 124.2, 125.6, 128.8, 130.6, 130.8, 134.7, 135.2, 146.3, 159.9, 163.2 and 195.4. Anal. Calcd. for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$: C, 56.99; H, 4.03; N, 7.00%. Found: 56.93; H, 4.01; N, 6.96%.

1-(4-Chlorophenyl)-3a,8b-dihydroxy-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (5i)

Isolated as pale yellow solid; Yield 92%; m.p. 187–189 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.95 (s, 3H), 5.00 (s, 1H), 5.57 (s, 1H), 6.67 (d, $J = 7.5\text{Hz}$, 1H), 7.37–7.59 (m, 6H), 7.89 (d, $J = 7.5\text{Hz}$, 1H); C^{13} NMR (75 MHz, CDCl_3) δ_{C} : 16.9, 80.6, 97.4, 122.6, 124.7, 125.2, 129.8, 130.6, 131.2, 134.5, 135.2, 135.3, 135.7, 145.7, 163.2 and 194.7. Anal. Calcd. for $\text{C}_{18}\text{H}_{13}\text{ClN}_2\text{O}_5\text{S}$: C, 53.41; H, 3.24; N, 6.92%. Found: C, 53.37; H, 3.21; N, 6.90%.

1-(4-Fluorophenyl)-3a,8b-dihydroxy-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (5j)

Isolated as pale yellow solid; Yield 93%; m.p. 182–184 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.94 (s, 3H), 6.62 (d, $J = 7.8\text{Hz}$, 1H), 7.16–7.25 (m, 3H), 7.48–7.59 (m, 3H), 7.88 (d, $J = 7.8\text{Hz}$, 1H); C^{13} NMR (75 MHz, CDCl_3) δ_{C} : 16.81, 80.5, 97.1, 116.7, 122.5, 124.8, 125.3, 131.2, 131.3, 132.6, 134.6, 135.6, 145.9, 162.1 and 194.8. Anal. Calcd. for $\text{C}_{18}\text{H}_{13}\text{FN}_2\text{O}_5\text{S}$: C, 55.67; H, 3.37; N, 7.21%. Found: C, 55.63; H, 3.36; N, 7.18%.

1-(4-Bromophenyl)-3a,8b-dihydroxy-2-(methylthio)-3-nitro-1,8b-dihydroindeno[1,2-*b*]pyrrol-4(3a*H*)-one (5k)

Isolated as pale yellow solid; Yield 93%; m.p. 182–184 °C; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 2.11 (s, 3H), 4.85 (s, 1H), 5.76 (s, 1H), 6.57 (d, $J = 7.5\text{Hz}$, 1H), 7.25–7.27 (m, 2H), 7.49–7.65 (m, 4H), 7.87–7.91 (m, 1H); C^{13} NMR (75 MHz, CDCl_3) δ_{C} : 16.9, 80.6, 97.3, 122.8, 123.4, 124.8, 125.2, 130.7, 131.2, 132.9, 134.5, 135.7, 145.7 and 194.7. Anal. Calcd. for $\text{C}_{18}\text{H}_{13}\text{BrN}_2\text{O}_5\text{S}$: C, 48.12; H, 2.92; N, 6.24%. Found: C, 48.07; H, 2.88; N, 6.21%.

Figure 1. ^1H NMR spectra of **5i**

Figure 2. ^1H NMR spectra of **5i** D_2O exchange

Figure 3. ^{13}C NMR spectra of **5i**

Figure 4. DEPT-135 spectra of **5i**

Figure 5. H,H-COSY spectra of **5i**

Figure 6. HMBC spectra of **5i**

Figure 7. ^1H NMR spectra of **4**

Figure 10. ^{13}C NMR spectra of **5a**

Figure 11. ¹H NMR spectra of **5b**

Figure 12. ^{13}C NMR spectra of **5b**

Figure 13. ^1H NMR spectra of **5c**

Figure 14. ^{13}C NMR spectra of **5c**

Figure 15. ^1H NMR spectra of **5d**

Figure 17. ^1H NMR spectra of **5e**

Figure 18. ^{13}C NMR spectra of **5e**

Figure 19. ^1H NMR spectra of **5f**

Figure 20. ^{13}C NMR spectra of **5f**

Figure 22. ^{13}C NMR spectra of **5g**

Figure 23. ^1H NMR spectra of **5h**

Figure 24. ^{13}C NMR spectra of **5h**

Figure 28. ^{13}C NMR spectra of **5k**