

Experimental Supplement

All melting points were determined in a capillary tube and are uncollected. The Infrared (ir) spectra were recorded in potassium bromide pellets using a JASCO 810 spectrometer and ultraviolet (uv) absorption spectra were determined in 95% ethanol using a Shimadzu UV3100pc spectrometer. Nuclear magnetic resonance (nmr) spectra were obtained using Gemini 300NMR(300 MHz) and JEOL-GX-400(400MHz) spectrometers with tetramethylsilane as the internal standard. Mass(ms) spectra were recorded on JEOL MS-DX303 mass spectrometer. Elemental analyses were performed at the Microanalytical Laboratory of the Center for Instrumental Analysis in Nagasaki University.

Methyl

1-Methyl-4-(pyrrol-2-yl)-2,5-dioxo-1H-pyrrole-3-carbonitrile (3a)

A solution of 2.81 g (12.1 mmol) of pyrrole (**2a**) and 1.82 g (10.0 mmol) of (**1a**) in 12 ml of acetic acid was refluxed for 4 hrs. The color of the reaction mixture changed from orange to yellow in 30 min. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 1.93 g (9.6 mmol, 96%) of reddish needles, mp 199-202°C. IR(KBr) ν_{\max} cm^{-1} : 3325(NH), 3115, 2203(CN), 1760 (C=O), 1685(C=O), 1603, 1522, 1442, 1420, 1362, 1338, 1223, 1140, 1110, 1063, 1040, 1000, 950, 878, 770, 742, 705, 620, 598. UV(EtOH) λ_{\max} nm(log ϵ): 459(4.30), 309(3.75), 263(3.97). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.12(3H, s, NMe), 6.58-6.61(1H, m, 3H), 7.36-7.38(1H, m, 5-H). EI-MS m/z : 202(M^++1 , 12), 201(M^+ , 100), 171(3), 145(6), 116(84), 89(12). *Anal.* Calcd. For $\text{C}_{10}\text{H}_7\text{N}_3\text{O}_2=201.184$: C, 59.70; H, 3.51; N, 20.89. Found: C, 59.67; H, 3.50; N, 20.87.

Methyl

1-Methyl-4-(pyrrol-2-yl)-2,5-dioxo-1H-pyrrole-3-carboxylate (3b)

A solution of 3.23 g (15 mmol) of pyrrole (**2a**) and 1.01 g (15 mmol) of (**1b**) in 15 ml of acetic acid was refluxed for 2 hrs. The color of the reaction mixture changed to red in 10 min. and finally to deep yellow solution. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 2.85 g (12.2 mmol, 81%) of greenish needles, mp 174-179°C. IR(KBr) ν_{\max} cm^{-1} : 3235(NH), 3140, 2948, 1750(C=O), 1702(C=O), 1678 (C=O), 1560-1570(br), 1500, 1438,

1413, 1390, 1345, 1258, 1243, 1200, 1130, 1102, 1041, 998, 955, 878, 802, 775. UV(EtOH) λ_{\max} nm(log ϵ): 456(3.92), 306(3.42), 258(3.52), 220(3.71). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.07(3H, s, NMe), 3.96(3H, s, OMe), 6.52(1H, dd, $J=5.3, 2.3$ Hz, 3-H), 7.37(1H, m, 4-H), 8.03(1H, ddd, $J=4.1, 2.3, 1.4$ Hz, 5-H). $^{13}\text{C-NMR}(\text{CDCl}_3)\delta$: 24.2(NMe), 52.8(OMe), 107.4(3-C), 114.5(3'-C), 124.6(2'-C), 125.3(5'-C), 130.4(4'-C), 137.8(4-C), 165.9(COOMe), 168.1(5-C), 168.4(2-C). EI-MS m/z : 235(M^++1 , 13), 234(M^+ , 100), 203(34), 202(53), 176(11), 118(40), 117(15), 106(15), 91(25), 90(16), 63(10). *Anal.* Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_4=234.213$: C, 56.41; H, 4.30; N, 11.96. Found: C, 56.30; H, 4.26; N, 11.97.

Methyl

1-Methyl-4-(methylpyrrol-2-yl)-2,5-dioxo-1H-pyrrole-3-carbonitrile (3c)

A solution of 0.24 g (3.0 mmol) of *N*-methylpyrrole (**2b**) and 0.37 g (2.0 mmol) of (**1a**) in 10 ml of acetic acid was refluxed for 16 hrs. The color of the reaction mixture changed from orange to deep red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from ethanol to give 0.37 g (1.7 mmol, 78%) of brownish needles, mp 119-122°C. IR(KBr) ν_{\max} cm^{-1} : 3440, 3110, 2210(CN), 1765(C=O), 1710(C=O), 1595, 1510, 1445, 1402, 1385, 1340, 1278, 1260, 1170, 1100, 1070, 1001, 930, 830, 741. UV(EtOH) λ_{\max} nm(log ϵ): 453(4.13), 309(3.56), 258(3.84). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.13(3H, s, NMe), 3.94(3H, s, NMe), 6.43(1H, dd, $J=4.3, 2.5$ Hz, 4-H), 7.20(1H, dd, $J=2.5, 1.6$ Hz, 5-H), 7.41(1H, dd, $J=4.3, 1.6$ Hz, 3-H). EI-MS m/z : 216(M^++1 , 14), 215(M^+ , 100), 214(28), 131(10), 130(78), 129(22), 86(13). *HRms* Calcd. for $\text{C}_{10}\text{H}_9\text{N}_3\text{O}_2=215.0694$. Found: 215.0688.

Methyl

1-Methyl-4-(methylpyrrol-2-yl)-2,5-dioxo-1H-pyrrole-3-carboxylate (3d)

A solution of 0.24 g (3.0 mmol) of *N*-methylpyrrole (**2b**) and 0.43 g (2.0 mmol) of (**1b**) in 10 ml of acetic acid was refluxed for 8 hrs. The color of the reaction mixture changed from yellow to red in 30 min and finally to deep red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from toluene to give 0.26 g (1.0 mmol, 52%) of reddish oil. IR(film) ν_{\max} cm^{-1} : 1730 (C=O), 1705(C=O), 1616, 1440, 1382, 1288, 1200, 1142, 1160, 1078, 1060, 1000, 755. UV(EtOH) λ_{\max} nm(log ϵ): 435(3.96), 282(3.81), 223(4.03).

$^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.16(3H, s, NMe), 3.69(3H, s, NMe), 3.86(3H, s, OMe), 6.30(1H, m, 4'-H), 6.95(1H, dd, $J=4.1, 1.6\text{ Hz}$, 5'-H), .04(1H, m, 3'-H). EI-MS m/z : 249(M^++1 , 14), 248(M^+ , 100), 217(34), 216(44), 215(29), 184(11). *HRms* Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_4=248.0797$: Found: 248.0781.

Methyl

1-Methyl-4-(indol-3-yl)-2,5-dioxo-1H-pyrrole-3-carbonitrile(5a)

A solution of 0.35 g (3.0 mmol) of indole (**4a**) and 0.36 g (2.0 mmol) of (**1a**) in 5 ml of acetic acid was refluxed for 1 hrs. The color of the reaction mixture changed to red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 0.43 g (1.7 mmol, 86%) of reddish needles, mp 308-311°C. IR(KBr) $\nu_{\text{max}} \text{ cm}^{-1}$: 3270(NH), 3150, 2990, 2930, 2210(CN), 1765 (C=O), 1695(C=O), 1590, 1485, 1435, 1390, 1335, 1315, 1255, 1230, 1215, 1135, 1105, 1045, 935, 745, 645, 625, 510. UV(EtOH) $\lambda_{\text{max}} \text{ nm}(\log \epsilon)$: 470(4.28), 323(3.30), 278(4.26), 262(4.20), 210(4.49). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.01(3H, s, NMe), 7.24-7.38(2H, m, 5,6-H), 7.61(1H, d, $J=7.1 \text{ Hz}$, 7-H), 8.25(1H, d, $J=7.5 \text{ Hz}$, 4-H), 8.66(1H, s, 2-H), 12.85(1H, brs, NH). EI-MS m/z : 252(M^++1 , 17), 251(M^+ , 100), 195(5), 166(57), 139(18), 83(12), 44(16). *Anal.* Calcd. for $\text{C}_{14}\text{H}_9\text{N}_3\text{O}_2=251.247$: C, 66.93; H, 3.61; N, 16.72. Found: C, 66.99; H, 3.75; N, 16.78.

Methyl

1-Methyl-4-(2-methylindol-3-yl)-2,5-dioxo-1H-pyrrole-3-carbonitrile(5b)

A solution of 0.39 g (3.0 mmol) of 2-methylindole (**4b**) and 0.36 g (2.0 mmol) of (**1a**) in 5 ml of acetic acid was refluxed for 1 hrs. The color of the reaction mixture changed to red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 0.42 g (1.6 mmol, 78%) of reddish needles, mp 264-266°C. IR(KBr) $\nu_{\text{max}} \text{ cm}^{-1}$: 3295(NH), 2220(CN), 1705 (C=O), 1585, 1575, 1485, 1450, 1430, 1385, 1350, 1215, 1005. UV(EtOH) $\lambda_{\text{max}} \text{ nm}(\log \epsilon)$: 497(4.08), 333(2.99), 278(4.19), 267(4.18), 215(4.56). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 2.66(3H, s, Me), 3.19(3H, s, NMe), 7.25-7.36(4H, m, aromatic-H), 7.73(1H, s, NH). EI-MS m/z : 266(M^++1 , 18), 265(M^+ , 100), 206(4), 180(27), 179(22), 152(4), 133(5), 90(8). *Anal.* Calcd. for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_2=265.274$: C, 67.92; H, 4.18; N, 15.84. Found: C, 67.70; H, 4.33; N, 15.74.

Methyl

1-Methyl-4-(2-phenylindol-3-yl)-2,5-dioxo-1H-pyrrole-3-carbonitrile(5c)

A solution of 0.57 g (3.0 mmol) of 2-phenylindole (**4c**) and 0.36 g (2.0 mmol) of (**1a**) in 10 ml of acetic acid was refluxed for 11 hrs. The color of the reaction mixture changed to dark red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 0.26 g (0.8 mmol, 40%) of dark red needles, mp 326°C. IR(KBr) $\nu_{\text{max}} \text{ cm}^{-1}$: 3060, 3010, 2940-2960(br), 2840, 2775, 2210(CN), 1675(C=O), 1650, 1585, 1545, 1465, 1350, 1305, 1270, 1245, 1200, 1160, 1120, 1060. UV(EtOH) $\lambda_{\text{max}} \text{ nm}(\log \epsilon)$: 504, 289, 233, 205. $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 2.95(3H, s, NMe), 7.24(1H, m, 5-H), 7.31(1H, m, 6-H), 7.45-7.56(3H, m, 3',4',5'-H), 7.56(1H, d, $J=7.4 \text{ Hz}$, 4-H), 7.65-7.68(2H, m, 2',6'-H), 7.72(1H, d, $J=7.4 \text{ Hz}$, 7-H), 12.71(1H, s, NH). EI-MS m/z : 328(M^++1 , 22), 327(M^+ , 100), 243(12), 242(59), 241(22), 214(11), 121(16), 108(10), 44(10). *Anal.* Calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_3\text{O}_2=327.346$: C, 73.39; H, 4.00; N, 12.84. Found: C, 73.40; H, 4.15; N, 12.91.

Methyl

1-Methyl-4-(indol-3-yl)-2,5-dioxo-1H-pyrrole-3-carboxylate(5d)

A solution of 0.35 g (3.0 mmol) of indole (**4a**) and 0.40 g (2.0 mmol) of (**1c**) in 10 ml of acetic acid was refluxed for 8 hrs. The color of the reaction mixture changed to red in 10 min. and finally to dark red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 0.14 g (0.52 mmol, 26%) of reddish needles, mp 281-283°C. IR(KBr) $\nu_{\text{max}} \text{ cm}^{-1}$: 3295(NH), 1760 (C=O), 1705(C=O), 1590, 1495, 1440, 1420, 1335-1345(br), 1320, 1290, 1245, 1190, 1170, 1130, 1065. UV(EtOH) $\lambda_{\text{max}} \text{ nm}(\log \epsilon)$: 444(4.07), 273(4.05), 216(4.53). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.73(3H, s, OMe), 7.15-7.27(3H, m, aromatic-H), 7.53(1H, d, $J=8.3 \text{ Hz}$, 7-H), 8.21(1H, d, $J=3.1 \text{ Hz}$, 2-H), 11.23(1H, s, NH), 12.30(1H, s, NH). EI-MS m/z : 271(M^++1 , 16), 270(M^+ , 100), 256(3), 239(23), 221(6), 199(6), 168(12), 141(15), 84(14), 57(14), 55(11), 44(52), 43(18). *Anal.* Calcd. for $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}_4=270.247$: C, 62.22; H, 3.73; N, 10.37. Found: C, 62.20; H, 3.81; N, 10.37.

Methyl

1-Methyl-4-(indol-3-yl)-2,5-dioxo-1H-pyrrole-3-carboxylate(5e)

A solution of 0.35 g (3.0 mmol) of indole (**4a**) and

0.43 g (2.0 mmol) of (**1b**) in 10 ml of acetic acid was refluxed for 2 hrs. The color of the reaction mixture changed from yellow to red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 0.52 g (1.8 mmol, 91%) of orange needles, mp 250-252°C. IR(KBr) ν_{\max} cm^{-1} : 3275(NH), 2950, 1765 (C=O), 1710(C=O), 1600, 1500, 1440, 1425, 1320, 1290, 1245, 1195, 1170, 1125, 1105, 1040, 1005. UV(EtOH) λ_{\max} nm(log ϵ): 456(4.13), 276(4.17), 257(4.13), 215(4.56). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.14(3H, s, NMe), 3.84(3H, s, OMe), 7.24(1H, m, 5-H), 7.38(1H, m, 4-H), 7.45(1H, m, 7-H), 8.22(1H, d, J=3.2 Hz, 2-H), 8.98(1H, brs, NH). EI-MS m/z : 285(M^++1 , 18), 284(M^+ , 100), 253(35), 226(15), 168(22), 141(18), 140(12), 40(20). *Anal.* Calcd. for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_4=284.274$: C, 63.38; H, 4.25; N, 9.85. Found: C, 63.43; H, 4.36; N, 9.95.

Methyl

1-Methyl-4-(2-methylindol-3-yl)-2,5-dioxo-1H-pyrrole-3-carboxylate(5f)

A solution of 0.39 g (3.0 mmol) of 2-methylindole (**4b**) and 0.43 g (2.0 mmol) of (**1b**) in 10 ml of acetic acid was refluxed for 4 hrs. The color of the reaction mixture changed from yellow to red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 0.38 g (1.3 mmol, 64%) of dark reddish needles, mp 201-204°C. IR(KBr) ν_{\max} cm^{-1} : 3335(NH), 2950, 1765 (C=O), 1725(C=O), 1695(C=O), 1600, 1580, 1460, 1435, 1385, 1365, 1250, 1200, 1145, 1070, 745. UV(EtOH) λ_{\max} nm(log ϵ): 485(3.92), 276(4.11), 263(4.12), 218(4.60). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 2.36(3H, s, Me), 3.79(3H, s, OMe), 7.13-7.33(4H, m, aromatic-H), 8.75(1H, s, NH). EI-MS m/z : 299(M^++1 , 15), 298(M^+ , 79), 267(27), 266(100), 240(20), 182(15), 181(27), 155(20), 154(24), 153(11), 91(13), 69(13), 44(33), 40(70). *Anal.* Calcd. for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_4=298.301$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.56; H, 4.85; N, 9.45.

Methyl

1-Methyl-4-(2-phenylindol-3-yl)-2,5-dioxo-1H-pyrrole-3-carboxylate(5g)

A solution of 0.57 g (3.0 mmol) of 2-phenylindole (**4c**) and 0.43 g (2.0 mmol) of (**1b**) in 15 ml of acetic acid was refluxed for 4 hrs. The color of the reaction mixture changed dark red. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 0.28 g (0.78

mmol, 39%) of dark reddish needles, mp 228-231°C. IR(KBr) ν_{\max} cm^{-1} : 3300(NH), 2945, 1765, 1725 (C=O), 1700(C=O), 1620, 1435, 1375, 1325, 1295, 1240, 1200, 1155, 1145, 1110, 1040, 1010, 985, 840, 750, 695. UV(EtOH) λ_{\max} nm(log ϵ): 493(3.79), 294(4.30), 233(4.49), 204(4.59). $^1\text{H-NMR}(\text{CDCl}_3)\delta$: 3.05(3H, s, Me), 3.52(3H, s, OMe), 7.19-7.26(3H, m, aromatic-H), 7.31-7.47(6H, m, aromatic-H), 8.95(1H, s, NH). EI-MS m/z : 361(M^++1 , 23), 360(M^+ , 100), 329(10), 302(24), 301(70), 300(19), 245(14), 244(71), 217(21), 216(42), 215(16). *Anal.* Calcd. for $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}_4=360.373$: C, 69.99; H, 4.48; N, 7.77. Found: C, 69.83; H, 4.65; N, 7.73.