Supporting Information

Unexpected isocyanide-based three-component bicyclizations for stereoselective synthesis of densely functionalized pyrano[3,4-c]pyrroles

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General Information

$^1$H NMR ($^{13}$C NMR) spectra were measured on a Bruker DPX 400 MHz spectrometer in CDCl$_3$ (DMSO-$d_6$) with chemical shift ($\delta$) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant (Hz)]. HRMS (APCI-TOF) was determined by using microTOF-Q II HRMS/MS instrument (BRUKER). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

Fig 1, X-ray Structure of 4b

Scheme 1. Hydrogen-deuterium exchange experiment
Example for the synthesis of 4a: Dimethyl 2-(tert-butyl)-6-(4-chlorophenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyran[3,4-c]pyrrole-3a,4-dicarboxylate

4-(4-chlorophenyl)-4-oxobut-2-enoic acid (1a, 0.5 mmol), dimethyl but-2-ynedioate 2a (0.6 mmol, 1.2 equiv) and tert-butyl isonitrile 3a (0.6 mmol, 1.2 equiv) were introduced into a 25-mL Schlenk reaction flask, CH₃CN (4.0 mL) was then successively added into this reaction mixture. The reaction system was stirred at 80 °C for 6.0 hours. After completion of the reaction as indicated by TLC, the solvent was removed under vacuum. The residue was separated by column chromatography on silica gel (eluent, petroleum ether/ethyl acetate 10:1 v/v) to afford the pure white solid 4a.
Dimethyl 2-(tert-butyl)-6-(4-chlorophenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4a)

White solid, mp: 147-148 °C.
IR (KBr, v, cm−1): 2977, 2957, 1751, 1707, 1492, 1435, 1357, 1334, 1253, 1225, 1113, 1013, 835, 777.

1H NMR (400 MHz, CDCl3) δ 7.55 (d, J = 8.4 Hz, 2H, ArH), 7.33 (d, J = 8.8 Hz, 2H, ArH), 5.74 (d, J = 4.4 Hz, 1H, CH), 5.30 (s, 1H, CH), 3.88 (s, 3H, CH3), 3.79 (s, 3H, CH3), 3.78 (d, J = 4.0 Hz, 1H, CH), 1.57 (s, 9H, CH3).

13C NMR (100 MHz, CDCl3) δ 174.8, 171.8, 168.3, 167.6, 152.4, 135.4, 131.5, 128.6, 126.5, 94.8, 74.2, 59.5, 57.3, 53.9, 53.0, 43.4, 27.9.

HRMS (APCI): m/z calcd for: C21H22ClNO7, 436.1163 [M+H]+; found: 436.1155.

Dimethyl 2-(tert-butyl)-1,3-dioxo-6-phenyl-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4b)

White solid, mp: 103-104 °C.
IR (KBr, v, cm−1): 2984, 2955, 1784, 1749, 1705, 1496, 1425, 1354, 1335, 1249, 1221, 1163, 1107, 1012, 877, 763, 690.

1H NMR (400 MHz, CDCl3) δ 7.63–7.60 (m, 2H, ArH), 7.37–7.34 (m, 3H, ArH), 5.75 (d, J = 4.4 Hz, 1H, CH), 5.27 (s, 1H, CH), 3.87 (s, 3H, CH3), 3.81 (s, 3H, CH3), 3.81 (s, 3H, CH3), 3.75 (d, J = 4.4 Hz, 1H, CH), 1.57 (s, 9H, CH3).

13C NMR (100 MHz, CDCl3) δ 175.0, 171.9, 168.4, 167.7, 153.5, 131.5, 129.5, 128.4, 125.2, 94.3, 74.2, 59.4, 57.5, 53.9, 52.9, 43.7, 27.9.


Dimethyl 2-(tert-butyl)-6-(4-methoxyphenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4c)

White solid, mp: 155-156 °C.
IR (KBr, v, cm−1): 3008, 2985, 2880, 2847, 1774, 1696, 1610, 1516, 840, 765, 678.

1H NMR (400 MHz, CDCl3) δ 7.55 (d, J = 8.8 Hz, 2H, ArH), 6.87 (d, J = 8.8 Hz, 2H, ArH), 5.60 (d, J = 8.8 Hz, 1H, CH), 5.25 (s, 1H, CH), 3.87 (s, 3H, CH3), 3.82 (s, 3H, CH3), 3.81 (s, 3H, CH3), 3.75 (d, J = 4.4 Hz, 1H, CH), 1.57 (s, 9H, CH3).
$^{13}$C NMR (100 MHz, CDCl$_3$) δ 175.3, 172.0, 168.5, 167.8, 160.6, 153.4, 126.7, 125.7, 113.7, 92.4, 74.2, 59.3, 57.6, 55.3, 53.8, 52.9, 43.7, 28.0.

HRMS (APCI): m/z calcd for: C$_{22}$H$_{25}$NO$_8$, 432.1658[M+H]$^+$; found: 432.1656.

**Dimethyl 2-(tert-butyl)-1,3-dioxo-6-(p-tolyl)-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4d)**

White solid, mp: 139-140 °C.

IR (KBr, v, cm$^{-1}$): 2984, 2957, 1778, 1738, 1705, 1259, 1110, 1052, 860, 827, 798, 765.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.50 (d, J = 8.4 Hz, 2H, ArH), 7.16 (d, J = 8.0 Hz, 2H, ArH), 5.68 (d, J = 4.0 Hz, 1H, CH), 5.25 (s, 1H, CH), 3.87 (s, 3H, CH$_3$), 3.81 (s, 3H, CH$_3$), 3.75 (d, J = 4.4 Hz, 1H, CH), 2.35 (s, 3H, CH$_3$), 1.56 (s, 9H, CH$_3$).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 175.2, 172.0, 168.5, 167.8, 153.6, 139.6, 130.3, 129.1, 125.2, 93.4, 74.1, 59.3, 57.6, 53.8, 52.9, 43.7, 28.0, 21.3.

HRMS (APCI): m/z calcd for: C$_{22}$H$_{25}$NO$_7$, 416.1709[M+H]$^+$; found: 416.1709.

**Diethyl 2-(tert-butyl)-6-(4-chlorophenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4e)**

White solid, mp: 88-89 °C.

IR (KBr, v, cm$^{-1}$): 2982, 2941, 1744, 1706, 1491, 1402, 1371, 1333, 1246, 1218, 1161, 1025, 835, 774.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.57 (d, J = 8.8 Hz, 2H, ArH), 7.32 (d, J = 8.8 Hz, 2H, ArH), 5.75 (d, J = 4.0 Hz, 1H, CH), 5.30 (s, 1H, CH), 4.34-4.29 (m, 2H, CH$_2$), 4.27-4.21 (m, 2H, CH$_2$), 3.77 (d, J = 4.4 Hz, 1H, CH), 1.57 (s, 9H, CH$_3$), 1.33 (t, J = 6.8 Hz, 3H, CH$_3$), 1.22 (t, J = 7.2 Hz, 3H, CH$_3$).
\[ ^{13} \text{C NMR (100 MHz, CDCl}_3 \] \delta 175.0, 171.8, 167.9, 167.0, 152.4, 135.3, 131.7, 128.5, 126.6, 94.9, 74.3, 63.1, 62.2, 59.3, 57.3, 43.4, 27.9, 13.9, 13.9.

HRMS (APCI): m/z calcd for: C_{23}H_{26}ClNO_7, 464.1476 [M+H]^+; found: 464.1469.

**Diethyl 2-(\text{tert}-\text{butyl})-1,3-dioxo-6-phenyl-1,2,3,3a,4,7a-hexahydropyran[3,4-c]pyrrole-3a,4-dicarboxylate (4f)**

![Chemical structure of 4f]

White solid, mp: 81-82 °C.

IR (KBr, \nu, cm\textsuperscript{-1}): 2990, 1767, 1735, 1710, 1345, 1266, 1141, 861, 760, 681.

\[ ^1\text{H NMR (400 MHz, CDCl}_3 \] \delta 7.67–7.60 (m, 2H, ArH), 7.38–7.31 (m, 3H, ArH), 5.76 (d, \( J = 4.0 \) Hz, 1H, CH), 5.28 (s, 1H, CH), 4.35–4.29 (m, 2H, CH\textsubscript{2}), 4.28–4.20 (m, 2H, CH\textsubscript{2}), 3.77 (d, \( J = 4.4 \) Hz, 1H, CH), 1.57 (s, 9H, CH\textsubscript{3}), 1.33 (t, \( J = 6.8 \) Hz, 3H, CH\textsubscript{3}), 1.24 (t, \( J = 7.2 \) Hz, 3H, CH\textsubscript{3}).

\[ ^{13} \text{C NMR (100 MHz, CDCl}_3 \] \delta 175.2, 172.0, 168.0, 167.2, 153.4, 133.2, 129.4, 128.3, 125.3, 94.3, 74.2, 63.1, 62.1, 59.3, 57.4, 43.6, 28.0, 13.9.

HRMS (APCI): m/z calcd for: C_{23}H_{27}NO_7, 430.1866 [M+H]^+; found: 430.1860.

**Diethyl 2-(\text{tert}-\text{butyl})-6-(4-methoxyphenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyran[3,4-c]pyrrole-3a,4-dicarboxylate (4g)**

![Chemical structure of 4g]

White solid, mp: 110-111 °C.

IR (KBr, \nu, cm\textsuperscript{-1}): 2985, 2907, 2879, 2972, 1762, 1740, 1712, 1607, 1515, 1341, 1267, 1242, 1183, 1138, 1026, 841, 682, 637.

\[ ^1\text{H NMR (400 MHz, CDCl}_3 \] \delta 7.49 (d, \( J = 8.8 \) Hz, 2H, ArH), 6.79 (d, \( J = 8.8 \) Hz, 2H, ArH), 5.54 (d, \( J = 4.0 \) Hz, 1H, CH), 5.18 (s, 1H, CH), 4.25–4.22 (m, 2H, CH\textsubscript{2}), 4.20–4.15 (m, 2H, CH\textsubscript{2}), 3.74 (s, 3H, CH\textsubscript{3}), 3.67 (d, \( J = 4.0 \) Hz, 1H, CH), 1.50 (s, 9H, CH\textsubscript{3}), 1.25 (t, \( J = 7.2 \) Hz, 3H, CH\textsubscript{3}), 1.16 (t, \( J = 6.8 \) Hz, 3H, CH\textsubscript{3}).

\[ ^{13} \text{C NMR (100 MHz, CDCl}_3 \] \delta 175.4, 172.0, 168.1, 167.3, 160.6, 153.3, 130.5, 126.8, 113.6, 92.5, 74.2, 63.0, 62.0, 59.2, 57.5, 55.3, 43.6, 27.9, 13.9, 13.9.

HRMS (APCI): m/z calcd for: C_{24}H_{29}NO_8, 460.1971 [M+H]^+; found: 460.1976.

**Dimethyl 6-(4-chlorophenyl)-1,3-dioxo-2-(2,4,4-trimethylpentan-2-yl)-1,2,3,3a,4,7a-hexahydropyran[3,4-c]pyrrole-3a,4-dicarboxylate (4h)**

![Chemical structure of 4h]
White solid, mp: 138-139 °C.
IR (KBr, v, cm⁻¹): 2956, 1763, 1748, 1707, 1491, 1435, 1344, 1257, 1128, 1012, 857, 813, 680.
¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, J = 8.8 Hz, 2H, ArH), 7.32 (d, J = 8.8 Hz, 2H, ArH), 5.68 (d, J = 4.4 Hz, 1H, CH), 5.18 (s, 1H, CH), 3.86 (s, 3H), 3.84 (s, 3H), 3.73 (d, J = 4.4 Hz, 1H, CH), 2.02–1.80 (m, 2H, CH₂), 1.67 (s, 3H, CH₃), 1.63 (s, 3H, CH₃), 0.89 (s, 9H, CH₃).
¹³C NMR (100 MHz, CDCl₃) δ 175.0, 172.3, 168.4, 167.5, 152.7, 135.4, 131.5, 128.6, 126.5, 94.6, 74.1, 63.6, 57.7, 53.7, 53.0, 50.1, 44.0, 31.5, 31.0, 29.0, 29.0.
HRMS (APCI): m/z calcd for: C₂₅H₃₀ClNO₇, 492.1789[M⁺H]⁺; found: 492.1791.

Dimethyl 1,3-dioxo-6-phenyl-2-(2,4,4-trimethylpentan-2-yl)-1,2,3,3a,4,7a-hexahydropyrano [3,4-c]pyrrole-3a,4-dicarboxylate (4i)

White solid, mp: 98-99 °C.
IR (KBr, v, cm⁻¹): 2955, 1761, 1740, 1709, 1433, 1345, 1258, 1227, 1126, 861, 777, 758, 689.
¹H NMR (400 MHz, CDCl₃) δ 7.61–7.57 (m, 2H, ArH), 7.37–7.33 (m, 3H, ArH), 5.69 (d, J = 4.4 Hz, 1H, CH), 5.17 (s, 1H, CH), 3.86 (s, 3H, CH₃), 3.85 (s, 3H, CH₃), 3.73 (d, J = 4.4 Hz, 1H, CH), 2.03–1.80 (m, 2H, CH₂), 1.67 (s, 3H, CH₃), 1.63 (s, 3H, CH₃), 0.89 (s, 9H, CH₃).
¹³C NMR (100 MHz, CDCl₃) δ 175.2, 172.4, 168.5, 167.7, 153.8, 133.1, 129.5, 128.4, 125.2, 94.1, 74.1, 63.5, 57.9, 53.7, 52.9, 50.1, 44.2, 31.5, 31.0, 29.0, 29.0.
HRMS (APCI): m/z calcd for: C₂₅H₃₁NO₇, 458.2179[M⁺H]⁺; found: 458.2180.

Dimethyl 6-(4-methoxyphenyl)-1,3-dioxo-2-(2,4,4-trimethylpentan-2-yl)-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4j)

White solid, mp: 117-118 °C.
IR (KBr, v, cm⁻¹): 2955, 1759, 1747, 1708, 1608, 1512, 1345, 1242, 1175, 1127, 842, 684.
¹H NMR (400 MHz, CDCl₃) δ 7.52 (d, J = 8.8 Hz, 2H, ArH), 6.87 (d, J = 8.8 Hz, 2H, ArH), 5.55
(d, \(J = 4.0\) Hz, 1H, CH), 5.15 (s, 1H, CH), 3.85 (s, 3H, CH₃), 3.84 (s, 3H, CH₃), 3.82 (s, 3H, CH₃),
3.70 (d, \(J = 4.0\) Hz, 1H, CH), 2.02–1.80 (m, 2H, CH₂), 1.67 (s, 3H, CH₃), 1.62 (s, 3H, CH₃), 0.89
(s, 9H, CH₃).
\(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta\) 175.4, 172.5, 168.6, 167.8, 160.6, 153.7, 126.7, 125.7, 113.7, 92.3,
74.1, 63.5, 58.0, 55.3, 53.6, 52.9, 50.1, 44.2, 31.5, 31.0, 29.1, 29.0.
HRMS (APCI): m/z calcd for: C₂₆H₃₃NO₈, 488.2284[M+H]⁺; found: 488.2274.

**Diethyl 6-(4-chlorophenyl)-1,3-dioxo-2-(2,4,4-trimethylpentan-2-yl)-1,2,3,3a,4,7a-
hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4k)**

![Diagram of 4k]

White solid, mp: 124-125 °C.
IR (KBr, \(\nu\), cm⁻¹): 2952, 2938, 1748, 1731, 1704, 1300, 1261, 1220, 1106, 1019, 860, 844, 763.
\(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 7.47 (d, \(J = 8.8\) Hz, 2H, ArH), 7.25 (d, \(J = 8.8\) Hz, 2H, ArH), 5.63
(d, \(J = 4.4\) Hz, 1H, CH), 5.15 (s, 1H, CH), 4.25–4.22 (m, 2H, CH₂), 4.21–4.15 (m, 2H, CH₂), 3.65
(d, \(J = 4.4\) Hz, 1H, CH), 1.98–1.71 (m, 2H, CH₂), 1.61 (s, 3H, CH₃), 1.56 (s, 3H, CH₃), 1.25 (t, \(J =
7.2\) Hz, 3H, CH₃), 1.17 (t, \(J = 7.2\) Hz, 3H, CH₃), 0.83 (s, 9H, CH₃).
\(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta\) 175.2, 172.3, 167.9, 166.9, 152.6, 135.3, 129.4, 128.3, 94.6,
74.2, 63.5, 63.1, 62.1, 57.5, 51.0, 43.8, 31.5, 31.0, 29.0, 28.9, 14.0, 13.9.
HRMS (APCI): m/z calcd for: C₂₇H₃₄ClNO₇, 520.2102[M+H]⁺; found: 520.2098.

**Diethyl 1,3-dioxo-6-phenyl-2-(2,4,4-trimethylpentan-2-yl)-1,2,3,3a,4,7a-
hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4l)**

![Diagram of 4l]

White solid, mp: 110-111 °C.
IR (KBr, \(\nu\), cm⁻¹): 2980, 2952, 1741, 1698, 1339, 1251, 1221, 1098, 1023, 858, 757, 688.
\(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 7.56–7.51 (m, 2H, ArH), 7.30–7.25 (m, 3H, ArH), 5.63 (d, \(J = 4.4\)
Hz, 1H, CH), 5.14 (s, 1H, CH), 4.25–4.22 (m, 2H, CH₂), 4.21–4.15 (m, 2H, CH₂), 3.66 (d, \(J = 4.4\)
Hz, 1H, CH), 1.98–1.72 (m, 2H, CH₂), 1.61 (s, 3H, CH₃), 1.56 (s, 3H, CH₃), 1.25 (t, \(J = 7.2\) Hz,
3H, CH₃), 1.18 (t, \(J = 7.2\) Hz, 3H, CH₃), 0.83 (s, 9H, CH₃).
\(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta\) 175.4, 172.4, 168.0, 167.1, 153.7, 133.2, 129.4, 128.3, 125.2, 94.1,
74.2, 63.4, 63.0, 62.0, 57.7, 50.1, 43.9, 31.5, 31.0, 29.0, 28.9, 14.0, 13.9.
HRMS (APCI): m/z calcd for: C₂₇H₃₅NO₇, 486.2492[M+H]⁺; found: 486.2495.

**Diethyl 6-(4-methoxyphenyl)-1,3-dioxo-2-(2,4,4-trimethylpentan-2-yl)-1,2,3,3a,4,7a-
hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4m)**
hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4m)

White solid, mp: 108-109 °C.
IR (KBr, \( \nu \), cm\(^{-1} \)): 2979, 2953, 1767, 1744, 1707, 1512, 1248, 1176, 1127, 1031, 852, 805, 682, 603.

\(^1\)H NMR (400 MHz, DMSO) \( \delta \) 7.55 – 7.50 (m, 2H, ArH), 6.97 – 6.93 (m, 2H, ArH), 5.62 (d, \( J = 4.4 \) Hz, 1H, CH), 5.15 (s, 1H, CH), 4.24 – 4.14 (m, 4H, CH2), 3.81 (d, \( J = 4.4 \) Hz, 1H, CH), 3.77 (s, 3H, CH3), 1.93 – 1.76 (m, 2H, CH2), 1.59 (s, 3H, CH3), 1.54 (s, 3H, CH3), 1.22 (t, \( J = 7.2 \) Hz, 3H, CH3), 1.17 (t, \( J = 7.2 \) Hz, 3H, CH3), 0.82 (s, 9H, CH3).

\(^{13}\)C NMR (100 MHz, DMSO) \( \delta \) 174.8, 172.5, 167.5, 166.5, 160.0, 152.5, 149.1, 130.4, 128.6, 126.5, 94.8, 74.1, 62.2, 57.4, 53.9, 43.7, 41.3, 38.9, 36.1, 29.7.

HRMS (APCI): m/z calcd for: C\(_{28}\)H\(_{37}\)NO\(_8\), 516.2597[M+H] \(^+\); found: 516.2598.

Dimethyl 2-(adamantan-1-yl)-6-(4-chlorophenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano
[3,4-c]pyrrole-3a,4-dicarboxylate (4n)

White solid, mp: 150-151 °C.
IR (KBr, \( \nu \), cm\(^{-1} \)): 2910, 2849, 1741, 1705, 1491, 1304, 1156, 1112, 1013, 837, 773, 643.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.55 (d, \( J = 8.8 \) Hz, 2H, ArH), 7.33 (d, \( J = 8.8 \) Hz, 2H, ArH), 5.72 (d, \( J = 4.4 \) Hz, 1H, CH), 5.23 (s, 1H, CH), 3.87 (s, 3H, CH3), 3.81 (s, 3H, CH3), 3.73 (d, \( J = 4.4 \) Hz, 1H, CH), 2.38 (d, \( J = 2.4 \) Hz, 6H), 2.11 (s, 3H), 1.76–1.62 (m, 6H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 174.9, 172.0, 168.4, 167.6, 152.4, 135.4, 131.6, 128.6, 126.5, 94.8, 74.1, 62.2, 57.4, 53.9, 53.0, 43.7, 38.9, 36.1, 29.7.

HRMS (APCI): m/z calcd for: C\(_{27}\)H\(_{28}\)ClNO\(_7\), 514.1633[M+H] \(^+\); found: 516.1634.

Dimethyl 2-(adamantan-1-yl)-1,3-dioxo-6-phenyl-1,2,3,3a,4,7a-hexahydropyrano
[3,4-c]pyrrole -3a,4-dicarboxylate (4o)
White solid, mp: 107-108 °C.
IR (KBr, ν, cm⁻¹): 2951, 2901, 2844, 1740, 1708, 1447, 1304, 1232, 1113, 1050, 864, 756, 691.
¹H NMR (400 MHz, CDCl₃) δ 7.67–7.57 (m, 2H, ArH), 7.41–7.31 (m, 3H, ArH), 5.72 (d, J = 4.4 Hz, 1H, CH), 5.20 (s, 1H, CH), 3.87 (s, 3H, CH₃), 3.83 (s, 3H, CH₃), 3.73 (d, J = 4.4 Hz, 1H, CH), 2.38 (d, J = 2.4 Hz, 6H), 2.10 (s, 3H), 1.74–1.63 (m, 6H).
¹³C NMR (100 MHz, CDCl₃) δ 175.1, 172.2, 168.5, 167.8, 153.5, 133.1, 129.5, 128.4, 125.2, 94.3, 74.1, 62.1, 57.5, 53.8, 52.9, 43.9, 38.9, 36.1, 29.7.

**Dimethyl 2-(adamantan-1-yl)-6-(4-methoxyphenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4p)**

White solid, mp: 161-162 °C.
IR (KBr, ν, cm⁻¹): 2903, 2844, 1743, 1699, 1608, 1514, 1335, 1303, 1257, 1183, 1154, 1103, 847, 794, 769, 661.
¹H NMR (400 MHz, CDCl₃) δ 7.55 (d, J = 8.8 Hz, 2H, ArH), 6.87 (d, J = 8.8 Hz, 2H, ArH), 5.58 (d, J = 4.0 Hz, 1H, CH), 5.18 (s, 1H, CH), 3.86 (s, 3H, CH₃), 3.83–3.80 (m, 6H), 3.70 (d, J = 4.0 Hz, 1H, CH), 2.38 (d, J = 2.8 Hz, 6H), 2.10 (s, 3H), 1.73–1.64 (m, 6H).
¹³C NMR (100 MHz, CDCl₃) δ 175.4, 172.3, 168.6, 167.9, 160.6, 153.4, 130.5, 126.7, 113.7, 92.5, 74.1, 62.0, 57.6, 55.3, 53.8, 52.9, 43.9, 38.9, 36.1, 29.7.
HRMS (APCI): m/z calcd for: C₂₈H₃₁NO₈, 510.2128[M+H]⁺; found: 510.2130.

**Dimethyl 2-benzyl-6-(4-chlorophenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4q)**

White solid, mp: 131-132 °C.
IR (KBr, ν, cm⁻¹): 2963, 2873, 1740, 1706, 1492, 1398, 1259, 1092, 1001, 838, 772, 744, 701, 630.
¹H NMR (400 MHz, CDCl₃) δ 7.57–7.49 (m, 2H, ArH), 7.34–7.25 (m, 7H, ArH), 5.74 (d, J = 4.4 Hz, 1H, CH), 5.31 (s, 1H, CH), 4.75–4.62 (m, 2H, CH₂), 3.92 (d, J = 4.0 Hz, 1H, CH), 3.80 (s, 3H, CH₃), 3.72 (s, 3H, CH₃).
¹³C NMR (100 MHz, CDCl₃) δ 173.4, 170.8, 167.8, 167.2, 153.0, 135.6, 134.8, 131.3, 128.6, 128.6, 128.4, 128.0, 126.6, 94.3, 74.4, 57.8, 54.0, 53.0, 43.8, 43.2.
HRMS (APCI): m/z calcd for: C₂₄H₂₀ClNO₇, 470.1007[M+H]⁺; found: 470.1007.
Dimethyl 2-benzyl-1,3-dioxo-6-phenyl-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4r)

White solid, mp: 126-127 °C.
IR (KBr, ν, cm⁻¹): 2955, 1785, 1745, 1716, 1438, 1335, 1273, 1126, 1020, 761, 723, 696.
¹H NMR (400 MHz, CDCl₃) δ 7.57–7.49 (m, 2H, ArH), 7.32–7.26 (m, 3H, ArH), 7.25–7.17 (m, 5H, ArH), 5.68 (d, J = 4.0 Hz, 1H, CH), 5.22 (s, 1H, CH), 4.66–4.56 (m, 2H, CH₂), 3.85 (d, J = 4.4 Hz, 1H, CH), 3.74 (s, 3H, CH₃), 3.68 (s, 3H, CH₃).
¹³C NMR (100 MHz, CDCl₃) δ 173.6, 170.9, 167.9, 167.4, 154.1, 134.8, 132.8, 129.6, 128.6, 128.4, 128.3, 127.9, 125.3, 93.9, 74.3, 58.0, 53.9, 53.0, 44.0, 43.1.
HRMS (APCI): m/z calcd for: C₂₄H₂₁NO₇, 436.1396[M+H]⁺; found: 436.1398.

Dimethyl 2-benzyl-6-(4-methoxyphenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4s)

White solid, mp: 127-128 °C.
IR (KBr, ν, cm⁻¹): 2952, 2894, 1747, 1712, 1610, 1514, 1395, 1259, 1174, 1115, 999, 839, 762, 692, 631.
¹H NMR (400 MHz, DMSO) δ 7.58 – 7.54 (m, 2H, ArH), 7.28 – 7.23 (m, 3H, ArH), 7.21 – 7.16 (m, 2H, ArH), 6.99 – 6.94 (m, 2H, ArH), 5.75 (d, J = 4.8 Hz, 1H, CH), 5.27 (s, 1H, CH), 4.67 – 4.59 (m, 2H, CH₂), 4.16 (d, J = 4.4 Hz, 1H, CH), 3.78 (s, 3H, CH₃), 3.76 (s, 3H, CH₃), 3.68 (s, 3H, CH₃).
¹³C NMR (100 MHz, DMSO) δ 173.4, 171.1, 167.4, 167.4, 154.1, 134.8, 132.8, 129.6, 128.6, 128.4, 126.9, 126.4, 125.1, 113.7, 92.7, 73.8, 57.8, 55.1, 53.5, 52.4, 43.6, 41.8.
HRMS (APCI): m/z calcd for: C₂₅H₂₃NO₈, 466.1502[M+H]⁺; found: 466.1501.

diethyl 2-benzyl-6-(4-chlorophenyl)-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4t)

White solid, mp: 132-133 °C.
IR (KBr, ν, cm⁻¹): 2992, 1751, 1734, 1707, 1400, 1303, 1255, 1221, 1091, 1016, 937, 837, 768, 749, 701, 629.
¹H NMR (400 MHz, DMSO) δ 7.69 – 7.64 (m, 2H, ArH), 7.51 – 7.46 (m, 2H, ArH), 7.31 – 7.24 (m, 3H, ArH), 7.23 – 7.18 (m, 2H, ArH), 5.99 (d, J = 4.4 Hz, 1H, CH), 5.33 (s, 1H, CH), 4.68 – 4.59 (m, 2H, CH₂), 4.24 – 4.18 (m, 3H), 4.18 – 4.12 (m, 2H, CH₂), 1.21 – 1.12 (m, 6H, CH₃).
$^{13}$C NMR (100 MHz, DMSO) $\delta$ 173.2, 171.0, 166.8, 166.2, 151.8, 135.1, 133.9, 131.6, 128.4, 128.4, 127.5, 127.0, 126.6, 95.6, 73.8, 62.6, 61.4, 57.6, 43.4, 41.9, 13.6, 13.5.

HRMS (APCI): m/z calcd for: C$_{26}$H$_{24}$ClNO$_7$, 498.1320[M+H]$^+$; found: 498.1321.

**Dimethyl 6-(4-chlorophenyl)-2-cyclohexyl-1,3-dioxo-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4u)**

White solid, mp: 130-131 ºC.

IR (KBr, $\nu$, cm$^{-1}$): 2957, 2929, 2853, 1779, 1739, 1701, 1492, 1370, 1261, 1187, 1106, 1046, 1000, 851, 776, 641.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.51–7.44 (m, 2H, ArH), 7.30–7.22 (m, 2H, ArH), 5.69 (d, $J$ = 4.0 Hz, 1H, CH), 5.24 (s, 1H, CH), 3.92–3.84 (m, 1H, CH), 3.80 (s, 3H, CH$_3$), 3.76 (d, $J$ = 4.4 Hz, 1H, CH), 3.72 (s, 3H, CH$_3$), 2.07–1.93 (m, 2H), 1.78–1.54 (m, 5H), 1.27–1.08 (m, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.9, 171.1, 168.1, 167.4, 152.7, 135.5, 131.4, 128.6, 126.5, 94.7, 74.3, 57.4, 54.0, 53.0, 52.8, 43.4, 28.6, 28.2, 25.7, 25.0.

HRMS (APCI): m/z calcd for: C$_{23}$H$_{24}$ClNO$_7$, 462.1320[M+H]$^+$; found: 462.1329.

**Dimethyl 2-cyclohexyl-1,3-dioxo-6-phenyl-1,2,3,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4v)**

White solid, mp: 94-95 ºC.

IR (KBr, $\nu$, cm$^{-1}$): 2954, 2855, 1742, 1733, 1704, 1368, 1269, 1106, 999, 896, 764, 694.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.64–7.59 (m, 2H, ArH), 7.37–7.33 (m, 3H, ArH), 5.76 (d, $J$ = 4.4 Hz, 1H, CH), 5.29 (s, 1H, CH), 3.99–3.92 (m, 1H, CH), 3.87 (s, 3H, CH$_3$), 3.83 (d, $J$ = 4.4 Hz, 1H, CH), 3.81 (s, 3H, CH$_3$), 2.14–2.02 (m, 2H), 1.83–1.62 (m, 5H), 1.32–1.17 (m, 3H).
$^{13}$C NMR (100 MHz, CDCl$_3$) δ 174.1, 171.2, 168.2, 167.5, 153.7, 133.0, 129.5, 128.4, 125.2, 94.2, 74.3, 57.5, 53.9, 53.0, 52.7, 43.6, 28.7, 28.2, 25.7, 25.7, 25.0.

HRMS (APCI): m/z calcd for: C$_{28}$H$_{25}$NO$_7$, 428.1709[M+H]$^+$; found: 428.1704.

**Dimethyl 2-(4-bromophenyl)-6-(4-chlorophenyl)-1,3-dioxo-1,2,3a,4,7a-hexahydropyrano[3,4-c]pyrrole-3a,4-dicarboxylate (4w)**

White solid, mp: 175-176 °C.

IR (KBr, ν, cm$^{-1}$): 2953, 2878, 1741, 1716, 1490, 1381, 1255, 1113, 1094, 1046, 1014, 820, 770, 618.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.62–7.57 (m, 4H, ArH), 7.37–7.33 (m, 2H, ArH), 7.28 (s, 1H, ArH), 7.25 (s, 1H, ArH), 5.88 (d, $J$ = 4.0 Hz, 1H, CH), 5.61 (s, 1H, CH), 4.18 (d, $J$ = 4.0 Hz, 1H, CH), 3.94 (s, 3H, CH$_3$), 3.74 (s, 3H, CH$_3$).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 172.8, 169.8, 167.7, 167.4, 153.0, 135.7, 132.4, 131.3, 130.5, 128.7, 128.0, 126.7, 122.9, 94.2, 74.8, 57.4, 54.4, 53.3, 42.6.

HRMS (APCI): m/z calcd for: C$_{23}$H$_{17}$BrClNO$_7$, 533.9955[M+H]$^+$; found: 533.9956.
Copies of $^1$H NMR and $^{13}$C NMR of compounds 4

$^1$H NMR Spectrum of Compound 4a

$^{13}$C NMR Spectrum of Compound 4a
$^{1}$H NMR Spectrum of Compound 4b

$^{13}$C NMR Spectrum of Compound 4b
$^1$H NMR Spectrum of Compound 4c

$^{13}$C NMR Spectrum of Compound 4c
$^{1}$$H$ NMR Spectrum of Compound 4d

$^{13}$$C$ NMR Spectrum of Compound 4d
$^1$H NMR Spectrum of Compound 4e

$^{13}$C NMR Spectrum of Compound 4e
S19

$^{1}H$ NMR Spectrum of Compound 4f

$^{13}C$ NMR Spectrum of Compound 4f

S19
1H NMR Spectrum of Compound 4i

13C NMR Spectrum of Compound 4i
$^{1}H$ NMR Spectrum of Compound 4k

$^{13}C$ NMR Spectrum of Compound 4k
$^1$H NMR Spectrum of Compound 4n

$^{13}$C NMR Spectrum of Compound 4n
$^1$H NMR Spectrum of Compound 4o

$^{13}$C NMR Spectrum of Compound 4o
1H NMR Spectrum of Compound 4r

13C NMR Spectrum of Compound 4r
$^1$H NMR Spectrum of Compound 4s

$^{13}$C NMR Spectrum of Compound 4s
$^1$H NMR Spectrum of Compound 4t

$^{13}$C NMR Spectrum of Compound 4t
1H NMR Spectrum of Compound 4u

13C NMR Spectrum of Compound 4u
$^{1}H$ NMR Spectrum of Compound 4v

$^{13}C$ NMR Spectrum of Compound 4v
$^1$H NMR Spectrum of Compound 4w

$^{13}$C NMR Spectrum of Compound 4w