Supporting Information

Phosphine-Mediated Domino Reactions of Phthalimidomalonates with Allenoates or But-2-ynoate: Facile Entry into Highly Functionalized Pyrroloisoindolinone Derivatives

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1. General Information

All reactions were performed in dry solvents under an N₂ atmosphere and anhydrous conditions. DCM, THF, DMSO, and MeCN etc were freshly distilled over CaH₂ prior to use. All other reagents were used as received from commercial sources. Reactions were monitored through thin layer chromatography (TLC) on 0.25-mm SiliCycle silica gel plates and visualized under UV light. NMR spectra of the new product were recorded using Bruker Avance-300 and Bruker Avance-500 instruments, calibrated to CD(H)Cl₃ as the internal reference (7.26 and 77.0 ppm for ¹H-NMR and ¹³C-NMR spectra, respectively), calibrated to DMSO-d₆ as the internal reference (2.50 and 39.5 ppm for ¹H-NMR and ¹³C-NMR spectra, respectively). ¹H-NMR spectral data are reported in terms of chemical shift (δ, ppm), multiplicity, coupling constant (Hz), and integration. ¹³C-NMR spectral data are reported in terms of chemical shift (δ, ppm) and multiplicity. The following abbreviations indicate the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer. IR spectra were recorded on a Bruker Optics Tensor 37 spectrometer by the KBr pellet method.

2. Substrate Preparation

2.1 Allenoate Preparation

Except for the ethyl 2,3-butadienoate was purchased from TCI Co., other regents: methyl 2,3-butadienoate, benzyl 2,3-butadienoate, were prepared using reported methods.[¹]

\[
\text{O} \\ \text{Br} \\ \text{R}_1 \text{O}
\overset{1)}{\text{PPh}_3, \text{toluene}} \\ \text{2)} \text{NaOH, H₂O} \\ \text{O} \\ \text{R}_1 \text{O}
\]

2.2 Phthalimidomalonates Preparation

2.2.1 Preparation of malonates

Except for the di-tert-butyl malonate and tert-butyl ethyl malonate were purchased from TCI Co. and Aladdin Co., respectively. other dialkyl malonates were prepared by this way below.[²]

\[
\text{HOOC} \overset{\text{COOH}}{+} \text{R-OH} \overset{\text{SOCl}_2}{\text{anhydrous CH}_2\text{Cl}_2} \rightarrow \text{ROOC} \overset{\text{COOR}}{\text{COOH}}
\]

Procedure: malonamic acid (1.041 g, 10 mmol) and R-OH (5 mL) were added to the dried 50mL round-bottom flask, then SOCl₂ (2.19 mL, 30 mmol) in 10 mL anhydrous CH₂Cl₂ was added droplet by funnel. Then saturated Na₂CO₃ solvent was added to treat the surplus acid after overnight. The mixture was washed with 3×20 mL CH₂Cl₂, the combined organic layer was over dried by anhydrous Na₂SO₄. The crude product was obtained by evaporating the solvent after
filtration. It was used directly in the next step without further purifying. (Suitable for: R = Me; Et; n-Pr; i-Pr; n-Bu; Bn.)

2.2.2 Substituted Phthalimide Preparation

Except for the 3-nitrophthalimide, 4-nitrophthalimide and 3,4,5,6-tertachlorophthalimide were purchased from Energy Co., other substituted phthalimide were prepared by this way below.\[3\] (Suitable for: R = 4,5-dichloro and R = 4-Me.)

General Procedure: Typical experimental procedure for synthesis of substituted phthalimide. A mixture of substituted phthalic acid (2 mmol), imidazole (0.264g, 3 mmol) and the suitable urea (4 mmol) were well triturated and placed in a 25 mL bottom-flask followed by the addition of 6 drops of DMF. The mixture was heated at 150 °C in an oil bath for 3h. The crude material was cooled down, triturated and stirred in a 10% v/v aqueous HCl solution for 10 min. The resulting solid residue was filtered-off purified by recrystallization from ethanol or column chromatography with gradient ethyl acetate : n-hexane (1:4) to generate the desired pure products.

General Procedure: Typical experimental procedure for synthesis of phthalimide. A mixture of 1,2,4,5-benzenetetracarboxylic acid (2 mmol), imidazole (0.528g, 6 mmol) and the suitable urea (8 mmol) were well triturated and placed in a 50 mL bottom-flask followed by the addition of 12 drops of DMF. The mixture was heated at 150 °C in an oil bath for 3h. The crude material was cooled down, triturated and stirred in a 10% v/v aqueous HCl solution for 10 min. The resulting solid residue was filtered-off purified by recrystallization from ethanol or column chromatography with gradient ethyl acetate : n-hexane (1:4) to generate the desired pure products.

2.2.3 Substituted Phthalimidomalonates Preparation

General procedure A
General Procedure: General experimental procedure for synthesis of substituted phthalimidomalonates. A mixture of phthalimide (2 mmol), potassium carbonate (6 mmol) and the diethyl bromomalonate (2 mmol) placed in a 50 mL bottom-flask followed by the addition of 20 mL DMF. The mixture was stirred at room temperature for 12 h. The reactant solution was dumped into 100 mL of NaCl saturated solution and extracted with 30 mL ethyl acetate, the organic layer was washed by saturated brines (3 x 100 mL), gathered the organic layer, dried with anhydrous MgSO₄, filtered and distilled under reduced pressure to give the crude material, purified by column chromatography with gradient ethyl acetate : petroleum ether (1:10) to give substituted phthalimidomalonates (>80% yield).[⁴] (Suitable for : R = 3-NO₂, R = 4-NO₂, R = 3,4,5,6-tetrachloro, R = 4,5-dichloro and R = 4-Me.)

General Procedure: A mixture of pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetrone(2 mmol), potassium carbonate (12 mmol) and the diethyl bromomalonate (4 mmol) placed in a 50 mL bottom-flask followed by the addition of 20 mL DMF. The mixture was stirred at room temperature for 12 h. The reactant solution was dumped into 100 mL of NaCl saturated solution and extracted with 30 mL ethyl acetate, the organic layer was washed by saturated brines (3 x 100 mL), gathered the organic layer, dried with anhydrous MgSO₄, filtered and distilled under reduced pressure to give the crude material, purified by column chromatography with gradient ethyl acetate : petroleum ether (1:10) to give substituted phthalimidomalonates (90% yield).

**General procedure B**

General procedure for the preparation of phthalimidomalonates: To a solution of malonates (1.0 mmol) in MeCN (2.0 mL) was added NBP (339.0 mg, 1.5 mmol) and DBU (0.261 mL, 1.8 mmol). The mixture was stirred at room temperature for 20 min. The reaction mixture was poured into water and then extracted with CH₂Cl₂ (3 x 10 mL). The combined organic phase was washed with water (3 x 10 mL), filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (silica gel, petroleum ether: ethyl acetate = 20: 1 as eluent) to give phthalimidomalonates (>90% yield) as colorless solid.[⁵] (Suitable for : R₁ = R₂ = MeO; R₁ = R₂ = EtO; R₁ = R₂ = nPrO; R₁ = R₂ = iPrO; R₁ = R₂ = nBuO; R₁ = R₂ = iBuO; R₁ = R₂ = BnO; R₁ = tBuO, R₂ = EtO; R₁ = R₂ = Me and R₁ = Me, R₂ = EtO).
3. References

4. Synthetic procedures and characterization data
4.1 General procedure for synthesis of 3
To a mixture of phthalimidomalonate derivative 1 (0.2 mmol) and allenate 2 (0.44 mmol) in anhydrous Et₂O (2.0 mL), Ph₂EtP (0.22 mol, 47 mg) was added. The resulting solution was stirred at room temperature for 12 h. After removal of solvent, the product was purified through silica gel to give the desired products 3.

4.2 Characterization data for substituted phthalimidomalonates

**Diethyl 2-(5,6-dichloro-1,3-dioxoisindolin-2-yl)malonate (1i)**

\[ ^1H \text{NMR (300 MHz, CDCl}_3) \delta 7.98 (d, J = 0.7 Hz, 2H), 5.45 (s, 1H), 4.35–4.27 (m, 4H), 1.30 (t, J = 7.1 Hz, 6H); ^13C \text{NMR (75 MHz, CDCl}_3) \delta 164.52 (2C), 163.87 (2C), 139.52 (2C), 130.80 (2C), 125.89 (2C), 62.93 (2C), 54.68, 13.94 (2C). HRMS (ESI-TOF) calcd for C₁₅H₁₃Cl₂N₂O₆ (M+Na⁺) = 396.0120, found 396.0122.**

**Diethyl 2-(4,5,6,7-tetrachloro-1,3-dioxoisindolin-2-yl)malonate (1j)**

\[ ^1H \text{NMR (300 MHz, CDCl}_3) \delta 5.47 (s, 1H), 4.36–4.27 (m, 4H), 1.32 (t, J = 7.1 Hz, 6H); ^13C \text{NMR (75 MHz, CDCl}_3) \delta 163.59 (2C), 161.84 (2C), 140.67 (2C), 130.25 (2C), 63.07 (2C), 54.82, 13.95 (2C). HRMS (ESI-TOF) calcd for C₁₅H₁₁Cl₄NO₆ (M+Na⁺) = 465.9312, found 465.9315.**

**Diethyl 2-(5-methyl-1,3-dioxoisindolin-2-yl)malonate (1k)**

\[ ^1H \text{NMR (300 MHz, CDCl}_3) \delta 7.76 (d, J = 7.7 Hz, 1H), 7.68 (s, 1H), 7.54 (d, J = 7.7 Hz, 1H), 5.45 (s, 1H), 4.35–4.24 (m, 4H), 2.51 (s, 3H), 1.30 (t, J = 7.1 Hz, 6H); ^13C \text{NMR (75 MHz, CDCl}_3) \delta 166.65, 166.52, 164.39 (2C), 145.80, 134.94, 132.14, 129.16, 124.30, 123.71, 62.68 (2C), 54.43, 22.00, 13.94 (2C). HRMS (ESI-TOF) calcd for C₁₆H₁₇NO₆ (M+Na⁺) = 342.1078, found 342.1074.**
Diethyl 2-(4-nitro-1,3-dioxoisindolin-2-yl)malonate (1l)

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.17 (ddd, $J = 7.7$, 3.5, 1.0 Hz, 2H), 7.97 (t, $J = 7.8$ Hz, 1H), 5.50 (s, 1H), 4.37 – 4.27 (m, 4H), 1.31 (t, $J = 7.1$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 164.01, 163.70 (2C), 161.16, 135.83, 133.74, 129.07, 127.59, 123.55, 114.58, 63.05 (2C), 54.85, 13.94 (2C). HRMS (ESI-TOF) calcd for C$_{15}$H$_{14}$N$_2$O$_8$(M+Na$^+$) = 373.0754, found 373.0758.

Diethyl 2-(5-nitro-1,3-dioxoisindolin-2-yl)malonate (1m)

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.70 (dd, $J = 2.0$, 0.6 Hz, 1H), 8.64 (dd, $J = 8.1$, 2.0 Hz, 1H), 8.10 (dd, $J = 8.1$, 0.7 Hz, 1H), 5.50 (s, 1H), 4.38 – 4.27 (m, 4H), 1.31 (t, $J = 7.1$ Hz, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 164.39, 164.12, 163.70 (2C), 151.99, 136.04, 133.11, 129.61, 125.11, 119.23, 63.07 (2C), 54.83, 13.93 (2C). HRMS (ESI-TOF) calcd for C$_{15}$H$_{14}$N$_2$O$_8$(M+Na$^+$) = 373.0754, found 373.0759.

Tetraethyl 2,2'-(1,3,5,7-tetraoxo-5,7-dihydropyrrolo[3,4-f]isoindole-2,6(1H,3H)-diyl)dimalonate (1n)

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.39 (s, 2H), 5.53 (s, 2H), 4.41 – 4.25 (m, 8H), 1.32 (t, $J = 7.2$ Hz, 12H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 164.22 (4C), 163.63 (4C), 137.11 (3C), 119.42 (3C), 63.03 (4C), 54.84 (2C), 13.94 (4C). HRMS (ESI-TOF) calcd for C$_{24}$H$_{24}$N$_2$O$_{12}$(M+Na$^+$) = 555.1329, found 555.1336.

Ethyl 2-(1,3-dioxoisindolin-2-yl)-3-oxobutanoate (1o)

$^1$H NMR (300 MHz, CDCl$_3$) δ 12.74 (s, 1H), 7.92 (dd, $J = 5.5$, 3.1 Hz, 2H), 7.79 (dd, $J = 5.6$, 3.1 Hz, 2H), 4.17 (t, $J = 7.1$ Hz, 2H), 1.96 (s, 3H), 1.17 (d, $J = 7.1$ Hz, 3H); $^{13}$C NMR (75 MHz,
CDCl₃ δ 176.92 (2C), 167.35 (2C), 134.39, 134.34, 131.91, 123.81, 123.74, 114.58, 96.33, 61.38, 18.08, 14.04. HRMS (ESI-TOF) calcd for C_{14}H_{13}NO_{5} (M+Na⁺) = 298.0794, found 298.0797.

2-(2,4-dioxopentan-3-yl)isoindoline-1,3-dione (1p)

1H NMR (300 MHz, CDCl₃) δ 16.19 (s, 1H), 7.95 (dd, J = 5.5, 3.1 Hz, 2H), 7.82 (dd, J = 5.5, 3.1 Hz, 2H), 1.98 (s, 6H); 13C NMR (75 MHz, CDCl₃) δ 191.06 (2C), 167.38 (2C), 134.71, 134.34, 134.26, 131.58, 123.98, 123.55, 106.47, 21.84 (2C). HRMS (ESI-TOF) calcd for C_{13}H_{11}NO_{4} (M+Na⁺) = 268.0691, found 268.0687.

4.3 Characterization data for products

Diethyl (E)-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isoindole-3,3-dicarboxylate (3a)

White solid; mp 100-101 °C. Yield (101.5 mg, 99%). 1H-NMR (300 MHz, DMSO-d_{6}) δ 8.10 (d, J = 7.7 Hz, 1H), 7.82 – 7.69 (m, 2H), 7.63 (t, J = 7.5 Hz, 1H), 6.80 (dd, J = 15.0, 7.9, 6.4 Hz, 1H), 5.94 (d, J = 15.6 Hz, 1H), 4.38 (dd, J = 9.1, 6.2, 1H), 4.25 – 3.98 (m, 8H), 3.71 (d, J = 18.4 Hz, 1H), 3.60 (d, J = 18.0 Hz, 1H), 2.88 – 2.79 (m, 1H), 2.74 – 2.63 (m, 1H), 1.22 – 1.07 (m, 12H); 13C-NMR (75 MHz, DMSO-d_{6}) δ 171.31, 167.64, 167.52, 166.00, 161.62, 145.85, 137.13, 135.63, 133.07, 130.91, 130.07, 124.27, 124.12, 123.97, 115.18, 68.31, 63.26, 63.22, 61.85, 60.56, 46.60, 42.55, 33.02, 14.84, 14.80, 14.64, 14.57. HRMS (ESI-TOF) calcd for C_{27}H_{31}NO_{9} (M+Na⁺) = 536.1891, found 536.1892. IR (KBr) v (cm⁻¹): 3010, 2988, 2879, 2852, 1738, 1736, 1729, 1711, 1672, 1655, 1560, 1508, 1473, 1369, 1342, 1299, 1272, 1244, 1225, 1201, 1178, 1158, 1095, 1043, 1013, 969, 862, 771, 689.

Dimethyl( E)-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isoindole-3,3-dicarboxylate (3b)

3b, 93%, E/Z>99/1
White solid; mp 120-121 °C. Yield (90.2 mg, 93%). \(^1\)H-NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.10 (d, \(J = 7.7\) Hz, 1H), 7.81 – 7.71 (m, 2H), 7.63 (t, \(J = 7.5\) Hz, 1H), 6.80 (ddd, \(J = 15.0, 7.2, 6.2\) Hz, 1H), 5.94 (d, \(J = 15.6\) Hz, 1H), 4.37 (dd, \(J = 8.8, 6.4\) Hz, 1H), 4.16 – 4.09 (m, 2H), 4.04 (d, \(J = 6.7\) Hz, 1H), 3.99 (d, \(J = 7.1\) Hz, 1H), 3.82 – 3.58 (m, 8H), 2.86 – 2.79 (m, 1H), 2.73 – 2.62 (m, 1H), 1.16 – 1.07 (m, 6H); \(^1^3\)C-NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 171.50, 167.21, 167.15, 166.10, 161.28, 145.64, 136.85, 135.26, 132.73, 130.56, 129.68, 123.92, 123.55, 123.40, 114.70, 67.98, 62.87, 62.83, 52.84, 51.64, 46.20, 42.00, 32.69, 14.24, 14.15. HRMS (ESI-TOF) calced for C\(_{25}\)H\(_{47}\)NO\(_9\) (M+Na\(^+\)) = 508.1578, found 508.1580. IR (KBr) v (cm\(^{-1}\)): 3013, 2998, 2955, 1762, 1736, 1727, 1705, 1668, 1655, 1562, 1511, 1474, 1436, 1385, 1343, 1286, 1256, 1226, 1195, 1168, 1140, 1098, 1058, 1041, 997, 961, 933, 864, 767, 689.

Dipropyl (\(E\))-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isoindole-3,3-dicarboxylate (3c)

White solid; mp 85-86 °C. Yield (95.2 mg, 88%). \(^1\)H-NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.10 (d, \(J = 7.7\) Hz, 1H), 7.86 – 7.68 (m, 2H), 7.63 (t, \(J = 7.4\) Hz, 1H), 6.81 (ddd, \(J = 15.0, 7.9, 6.5\) Hz, 1H), 5.91 (d, \(J = 15.4\) Hz, 1H), 4.38 (ddd, \(J = 9.1, 6.1\) Hz, 1H), 4.22 – 3.93 (m, 8H), 3.72 (d, \(J = 18.0\) Hz, 1H), 3.61 (d, \(J = 17.9\) Hz, 1H), 2.90 – 2.76 (m, 1H), 2.74 – 2.63 (m, 1H), 1.58 (hd, \(J = 7.2, 3.6\) Hz, 4H), 1.11 (q, \(J = 7.3\) Hz, 6H), 0.84 (td, \(J = 7.4, 5.5\) Hz, 6H); \(^1^3\)C-NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 171.33, 167.81, 167.69, 166.00, 161.66, 145.85, 137.19, 135.66, 133.06, 130.92, 130.08, 124.25, 124.11, 123.97, 115.11, 68.61, 68.58, 68.37, 61.85, 60.56, 46.73, 42.56, 33.03, 22.22, 22.16, 14.83, 14.78, 10.88, 10.85. HRMS (ESI-TOF) calced for C\(_{26}\)H\(_{49}\)NO\(_{9}\) (M+Na\(^+\)) = 564.2204, found 564.2207. IR (KBr) v (cm\(^{-1}\)): 3085, 2983, 2966, 2943, 2922, 2901, 1745, 1738, 1730, 1715, 1671, 1657, 1625, 1584, 1471, 1452, 1370, 1341, 1292, 1267, 1230, 1200, 1175, 1157, 1144, 1112, 1063, 1045, 1014, 989, 974, 942, 928, 892, 866, 766, 692.

Diisopropyl (\(E\))-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isoindole-3,3-dicarboxylate (3d)

White solid; mp 85-86 °C. Yield (100.6 mg, 93%). \(^1\)H-NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.09 (d, \(J = 7.7\) Hz, 1H), 7.82 – 7.67 (m, 2H), 7.63 (t, \(J = 7.9\) Hz, 1H), 6.80 (ddd, \(J = 15.1, 7.9, 6.4\) Hz, 1H), 5.94 (d, \(J = 15.6\) Hz, 1H), 5.01 (h, \(J = 6.3\) Hz, 2H), 4.38 (ddd, \(J = 9.2, 6.0\) Hz, 1H), 4.15 – 4.10 (m, 2H), 4.00 (q, \(J = 7.1\) Hz, 2H), 3.66 (d, \(J = 18.0\) Hz, 1H), 3.56 (d, \(J = 18.0\) Hz, 1H), 2.90 – 2.75 (m, 1H), 2.76 – 2.63 (m, 1H), 1.25 – 1.14 (m, 12H), 1.18 – 1.06 (m, 6H); \(^1^3\)C-NMR (75 MHz,
Dibutyl (E)-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isoindole-3,3-dicarboxylate (3e)

White solid; mp 80–81 °C. Yield (96.7 mg, 85%). 1H-NMR (300 MHz, DMSO-duc) δ 8.10 (d, J = 7.6 Hz, 1H), 7.81 – 7.71 (m, 2H), 7.63 (t, J = 7.5 Hz, 1H), 6.80 (ddd, J = 15.0, 7.9, 6.5 Hz, 1H), 5.93 (d, J = 15.8 Hz, 1H), 4.38 (dd, J = 9.1, 6.2 Hz, 1H), 4.20 – 3.96 (m, 8H), 3.71 (d, J = 18.0 Hz, 1H), 3.59 (d, J = 18.0 Hz, 1H), 2.90 – 2.77 (m, 1H), 2.75 – 2.62 (m, 1H), 1.54 (dtt, J = 8.7, 6.3, 3.5 Hz, 4H), 1.28 (dtt, J = 14.4, 7.1, 3.7 Hz, 4H), 1.11 (q, J = 7.2 Hz, 6H), 0.83 (td, J = 7.4, 2.0 Hz, 6H); 13C-NMR (126 MHz, DMSO-duc) δ 170.92, 167.37, 167.26, 165.59, 161.28, 145.41, 136.81, 135.30, 132.64, 130.49, 129.69, 123.83, 123.72, 123.55, 114.67, 68.02, 66.43, 66.42, 61.44, 60.15, 46.32, 42.21, 32.65, 30.39 (2C), 30.31 (2C), 18.81, 14.43, 14.38, 13.79. HRMS (ESI-TOF) ced for C31H38NO6 (M+Na+) = 592.2517, found 592.2519. IR (KBr) ν (cm⁻¹): 3056, 2963, 2934, 2847, 1746, 1739, 1727, 1716, 1677, 1656, 1578, 1527, 1471, 1453, 1369, 1343, 1311, 1228, 1198, 1158, 1100, 1062, 1039, 994, 932, 858, 775, 690.

Di-tert-butyl (E)-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isoindole-3,3-dicarboxylate (3f)

Brown oil. Yield (92.2 mg, 81%). 1H-NMR (300 MHz, DMSO-duc) δ 8.08 (d, J = 7.7 Hz, 1H), 7.79 – 7.70 (m, 2H), 7.62 (t, J = 7.5 Hz, 1H), 6.81 (ddd, J = 15.0, 7.2, 6.0 Hz, 1H), 5.95 (d, J = 15.6 Hz, 1H), 4.37 (dd, J = 9.2, 6.0 Hz, 1H), 4.19 – 4.08 (m, 2H), 4.00 (q, J = 7.1 Hz, 2H), 3.60 (d, J = 17.9 Hz, 1H), 3.51 (d, J = 18.0 Hz, 1H), 2.86 – 2.79 (m, 2H), 2.75 – 2.64 (m, 1H), 1.42 (s, 18H), 1.15 – 1.07 (m, 6H); 13C-NMR (126 MHz, DMSO-duc) δ 171.00, 166.26, 166.15, 165.61, 161.19, 145.48, 136.89, 135.54, 132.50, 130.39, 129.66, 123.76, 123.72, 123.45, 114.53, 83.37, 83.36, 69.50, 61.42, 60.13, 45.84, 42.22, 32.58, 27.80 (2C), 27.76 (2C), 27.76 (2C), 14.43, 14.35. HRMS
(ESI-TOF) calcd for C_{31}H_{30}NO_{8} (M+Na') = 592.2517, found 592.2519. IR (KBr) ν (cm⁻¹): 3048, 2987, 2956, 2879, 2832, 1743, 1731, 1720, 1709, 1670, 1655, 1577, 1529, 1474, 1453, 1370, 1334, 1290, 1228, 1198, 1148, 1114, 1042, 1022, 932, 858, 786, 688.

\[ \text{Dibenzyl (E)-1-(1,6-diehtoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-aj]sindole-3,3-dicarboxylate (3g)} \]
Brown oil. Yield (104.6 mg, 82%). \(^1\)H-NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.10 (d, \(J = 7.6\) Hz, 1H), 7.82 – 7.72 (m, 2H), 7.64 (t, \(J = 7.6\) Hz, 1H), 7.33 – 7.29 (m, 10H), 6.81 (ddd, \(J = 15.7, 7.7, 6.5\) Hz, 1H), 5.93 (d, \(J = 15.5\) Hz, 1H), 5.26 – 5.22 (m, 4H), 4.37 (ddd, \(J = 8.6, 6.6\) Hz, 1H), 4.09 – 4.05 (m, 2H), 3.99 (q, \(J = 6.9\) Hz, 2H), 3.78 (d, \(J = 18.0\) Hz, 1H), 3.66 (d, \(J = 18.0\) Hz, 1H), 2.87 – 2.78 (m, 1H), 2.70 – 2.58 (m, 1H), 1.11 – 1.05 (m, 6H); \(^1\)C-NMR (126 MHz, DMSO-\(d_6\)) \(\delta\) 179.47, 167.06, 167.00, 165.63, 161.45, 145.41, 136.76, 135.52, 135.23, 132.76, 130.58, 129.71, 128.82 (5C), 128.62, 128.58, 128.08, 128.05, 128.02, 127.96, 123.93, 123.75, 123.63, 114.87, 68.21, 68.18, 68.04, 61.46, 60.18, 46.45, 42.25, 32.70, 14.44, 14.37. HRMS (ESI-TOF) calcd for C_{37}H_{35}NO_{8} (M+Na') = 660.2205, found 660.2211. IR (KBr) ν (cm⁻¹): 3039, 2994, 2976, 2889, 2842, 1739, 1737, 1730, 1708, 1673, 1655, 1579, 1531, 1473, 1456, 1371, 1297, 1274, 1212, 1198, 1172, 1101, 1042, 1017, 982, 871, 762, 689.

\[ \text{3-(tert-butyl) 3-ethyl (E)-1-(1,6-diehtoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo[2,1-aj]sindole-3,3-dicarboxylate (3h)} \]
Brown oil. Yield (84.5 mg, 78%). \(^1\)H-NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 8.09 (d, \(J = 7.7\) Hz, 1H), 7.78 (d, \(J = 7.7\) Hz, 1H), 7.72 (dd, \(J = 7.6, 1.3\) Hz, 1H), 6.81 (ddd, \(J = 15.6, 7.5, 6.6\) Hz, 1H), 5.95 (dd, \(J = 15.7, 4.3\) Hz, 1H), 4.37 (ddd, \(J = 8.9, 6.1, 2.6\) Hz, 1H), 4.26 – 3.96 (m, 6H), 3.64 (d, \(J = 18.0\) Hz, 1H), 3.59 (d, \(J = 17.9\) Hz, 1H), 2.87 – 2.79 (m, 1H), 2.73 – 2.68 (m, 1H), 1.41 (s, 9H), 1.23 – 1.10 (m, 9H); \(^1\)C-NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) 179.35, 167.92, 166.33, 165.99, 161.63, 145.88, 137.21, 136.66, 135.76, 132.97, 130.84, 130.05, 124.20, 123.90, 115.06, 84.05, 69.08, 63.02, 61.78, 60.18, 46.45, 42.57, 33.00, 28.16 (3C), 14.82, 14.68, 14.62. HRMS (ESI-TOF) calcd for C_{29}H_{33}NO_{8} (M+Na') = 564.2204, found 564.2200. IR (KBr) ν (cm⁻¹): 3045, 3002, 2981, 2889, 2840, 1738, 1735, 1726, 1710, 1675, 1655, 1580, 1536, 1477, 1459, 1370, 1284, 1269, 1214, 1188, 1154, 1101, 1053, 1019, 986, 875, 763, 687.
Diethyl(E)-7,8-dichloro-1-(1,6-dioxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo[2,1-a]isoindole-3,3-dicarboxylate (3i)

Brown oil. Yield (107.6 mg, 93%). 1H-NMR (500 MHz, DMSO-d6) δ 8.53 (s, 1H), 8.03 (s, 1H), 6.84 (dd, J = 15.0, 8.0, 6.5 Hz, 1H), 5.95 (d, J = 15.6 Hz, 1H), 4.55 (dd, J = 9.6, 5.2 Hz, 1H), 4.27 – 4.11 (m, 1H), 3.76 (d, J = 18.4 Hz, 1H), 3.66 (d, J = 18.3 Hz, 1H), 2.88 – 2.83 (m, 1H), 2.73 – 2.67 (m, 1H), 1.23 – 1.15 (m, 12H); 13C-NMR (126 MHz, DMSO-d6) δ 170.71, 166.90, 166.77, 165.58, 159.29, 145.35, 135.90, 135.04, 135.00, 133.51, 129.12, 125.71, 125.69, 123.84, 117.74, 68.10, 63.01, 62.97, 61.53, 61.04, 14.37, 14.19, 14.12, 13.96. HRMS (ESI-TOF) calcd for C27H29Cl2N9O9 (M+H+) = 582.1292, found 582.1300. IR (KBr) ν (cm⁻¹): 3032, 3014, 2987, 2878, 2843, 1742, 1739, 1727, 1717, 1673, 1655, 1579, 1545, 1480, 1447, 1369, 1286, 1270, 1234, 1181, 1156, 1097, 1053, 1027, 970, 879, 763, 687.

Diethyl(E)-6,7,8,9-tetrachloro-1-(1,6-dioxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo[2,1-a]isoindole-3,3-dicarboxylate (3j)

Brown oil. Yield (114.6 mg, 88%). 1H-NMR (300 MHz, CDCl3) δ 6.90 (ddd, J = 14.9, 7.2, 6.0 Hz, 1H), 5.95 (d, J = 15.6 Hz, 1H), 5.04 (t, J = 7.5 Hz, 1H), 4.38 (q, J = 7.1 Hz, 4H), 4.29 – 4.18 (m, 4H), 3.79 (s, 2H), 3.04 – 2.91 (m, 1H), 2.71 – 2.61 (m, 1H), 1.40 – 1.31 (m, 12H); 13C-NMR (75 MHz, CDCl3) δ 170.87, 167.16, 167.10, 166.06, 157.88, 143.61, 137.68, 136.25, 134.80, 132.57, 130.88, 129.82, 126.54, 126.68, 120.30, 67.58, 63.56, 63.48, 62.16, 60.81, 46.89, 44.27, 34.07, 14.53, 14.48, 14.32 (2C). HRMS (ESI-TOF) calcd for C27H27Cl4N9O9 (M+H+) = 652.0489, found 652.0494. IR (KBr) ν (cm⁻¹): 3025, 3007, 2983, 2894, 2852, 1740, 1737, 1724, 1714, 1671, 1655, 1577, 1554, 1487, 1446, 1390, 1368, 1342, 1272, 1234, 1185, 1096, 1044, 1023, 945, 858, 783, 730, 655, 625.
Diethyl(\textit{E})-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-7-methyl-5-oxo-2,5-dihydro-3H-pyrrolo[2,1-a]isooindole-3,3-dicarboxylate (3k) and Diethyl(\textit{E})-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-8-methyl-5-oxo-2,5-dihydro-3H-pyrrolo[2,1-a]isooindole-3,3-dicarboxylate (3k')

Selected data:
Brown oil. Yield (96.0 mg, 91%). $^1$H-NMR (300 MHz, DMSO-$d_6$) $\delta$ 7.99 – 7.93 (m, 1H), 7.65 (d, $J$ = 7.8 Hz, 1H), 7.43 (d, $J$ = 7.9 Hz, 1H), 6.80 (ddd, $J$ = 15.0, 7.2, 6.3 Hz, 1H), 5.94 (dd, $J$ = 15.6, 4.4 Hz, 1H), 4.41 – 4.31 (m, 1H), 4.22 (q, $J$ = 7.1 Hz, 6H), 4.01 (q, $J$ = 6.4 Hz, 2H), 3.67 (d, $J$ = 17.9 Hz, 1H), 3.59 (d, $J$ = 17.9 Hz, 1H), 2.89 – 2.79 (m, 1H), 2.73 – 2.63 (m, 1H), 1.21 – 1.12 (m, 15H); $^{13}$C-NMR (75 MHz, DMSO-$d_6$) $\delta$ 171.34, 167.72, 167.60, 166.00, 161.75, 145.85, 143.49, 141.14, 137.19, 135.93, 133.81, 133.23, 131.69, 130.44, 127.61, 68.29, 63.19, 63.15, 61.80, 60.55, 46.54, 42.53, 33.10, 22.23, 14.79, 14.77, 14.60, 14.54. HRMS (ESI-TOF) calcd for C$_{28}$H$_{33}$NO$_9$ (M+Na$^+$) = 550.2048, found 550.2051. IR (KBr) $\nu$ (cm$^{-1}$): 3025, 2911, 2874, 2831, 1739, 1736, 1726, 1712, 1669, 1655, 1583, 1549, 1487, 1448, 1369, 1297, 1272, 1249, 1183, 1142, 1084, 1054, 1028, 970, 824, 762, 711.

Diethyl (\textit{E})-1-(1,6-diethoxy-1,6-dioxohex-4-en-2-yl)-6-nitro-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isooindole-3,3-dicarboxylate (3l)

Brown oil. Yield (100.5 mg, 90%). $^1$H-NMR (500 MHz, DMSO-$d_6$) $\delta$ 8.46 (d, $J$ = 7.8 Hz, 1H), 8.09 (d, $J$ = 7.9 Hz, 1H), 7.98 (d, $J$ = 7.9 Hz, 1H), 6.82 (ddd, $J$ = 15.0, 8.0, 6.5 Hz, 1H), 5.96 (d, $J$ = 15.6 Hz, 1H), 4.51 (dd, $J$ = 9.1, 6.2 Hz, 1H), 4.30 – 4.22 (m, 4H), 4.18 – 4.12 (m, 2H), 4.03 (q, $J$ = 7.1 Hz, 2H), 3.80 (d, $J$ = 18.4 Hz, 1H), 3.70 (d, $J$ = 18.4 Hz, 1H), 2.91 – 2.85 (m, 1H), 2.77 – 2.70 (m, 1H), 1.22 (t, $J$ = 6.6 Hz, 6H), 1.16 (t, $J$ = 5.5 Hz, 3H), 1.12 (t, $J$ = 5.5 Hz, 3H); $^{13}$C-NMR (126 MHz, DMSO-$d_6$) $\delta$ 170.57, 166.75, 166.60, 165.58, 156.71, 145.97, 145.20, 134.87, 134.23, 131.23, 127.36, 125.07, 124.35, 123.92, 118.90, 68.20, 63.11, 63.07, 61.64, 60.19, 46.38, 42.19, 32.58, 14.42, 14.38, 14.19, 14.13. HRMS (ESI-TOF) calcd for C$_{27}$H$_{30}$N$_2$O$_{11}$ (M+Na$^+$) = 581.1742, found 581.1747. IR (KBr) $\nu$ (cm$^{-1}$): 3030, 3019, 2980, 2940, 2869, 1763, 1742, 1734, 1713, 1677, 1655, 1620, 1578, 1543, 1473, 1369, 1349, 1288, 1237, 1182, 1159, 1098, 1034, 1011, 970, 860, 815, 792, 777, 754, 720, 701.
Diethyl (E)-1-(1,6-dicthoxy-1,6-dioxohex-4-en-2-yl)-7-nitro-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-ajisoindole-3,3-dicarboxylate (3m) and

Diethyl (E)-1-(1,6-dicthoxy-1,6-dioxohex-4-en-2-yl)-8-nitro-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-ajisoindole-3,3-dicarboxylate (3m')

Selected data:
Brown oil. Yield (105.8 mg, 95%). $^1$H-NMR (500 MHz, DMSO-$d_6$) $\delta$ 8.51 – 8.42 (m, 2H), 8.09 (d, $J = 8.6$ Hz, 1H), 6.84 (ddd, $J = 15.0$, 10.8, 6.9 Hz, 1H), 5.97 (d, $J = 15.6$ Hz, 1H), 4.58 (dd, $J = 9.1$, 6.3 Hz, 1H), 4.32 – 4.00 (m, 8H), 3.83 – 3.71 (m, 2H), 2.92 – 2.84 (m, 1H), 2.78 – 2.69 (m, 1H), 1.33 – 1.23 (m, 6H), 1.17 (t, $J = 7.3$ Hz, 3H), 1.12 (dt, $J = 6.9$, 3.5 Hz, 3H). $^{13}$C-NMR (126 MHz, DMSO-$d_6$) $\delta$ 170.72, 170.51, 166.67, 165.60, 159.42, 150.72, 148.74, 145.44, 139.56, 136.04, 135.34, 134.08, 130.05, 123.87, 118.87, 68.22, 63.15, 61.60, 60.55, 60.16, 46.49, 42.04, 32.61, 14.40, 14.36, 14.21, 14.14. HRMS (ESI-TOF) calcd for C$_{27}$H$_{30}$N$_2$O$_{11}$ (M+Na') = 581.1742, found 581.1746. IR (KBr) ν (cm$^{-1}$): 3025, 2938, 2929, 2938, 2865, 1742, 1736, 1723, 1716, 1670, 1655, 1619, 1577, 1533, 1472, 1369, 1349, 1273, 1237, 1184, 1161, 1097, 1037, 1019, 970, 858, 817, 705.

Diethyl (E)-2-(1,3-dicthoxy-1,3-dioxopropan-2-yl)-9-(1,7-dicthoxy-1,7-dioxohept-5-en-3-yl)-1,3,5-trioxo-2,3,5,8-tetrahydrodipyrrlo[2,1-a:3',4'-jisoindole-7,7(1H)-dicarboxylate (3n)

Brown oil. Yield (128.8 mg, 87%). $^1$H-NMR (300 MHz, DMSO-$d_6$) $\delta$ 8.79 (s, 1H), 8.24 (s, 1H), 6.83 (ddd, $J = 15.1$, 8.0, 6.4 Hz, 1H), 5.97 – 5.87 (m, 2H), 4.75 (dd, $J = 9.0$, 6.1 Hz, 1H), 4.29 – 4.19 (m, 8H), 4.16 – 4.10 (m, 2H), 3.97 (q, $J = 7.7$ Hz, 2H), 3.79 (d, $J = 18.0$ Hz, 1H), 3.75 (d, $J = 18.2$ Hz, 1H), 2.93 – 2.82 (m, 1H), 2.78 – 2.65 (m, 1H), 1.25 – 1.16 (m, 12H), 1.16 – 1.11 (m, 3H), 1.09 – 1.04 (m, 3H). $^{13}$C-NMR (75 MHz, DMSO-$d_6$) $\delta$ 170.97, 167.12, 166.99, 166.05, 165.95, 165.74, 164.78 (2C), 159.73, 145.79, 140.78, 136.14, 135.15, 134.79, 132.27, 124.27, 121.66, 120.31, 119.97, 68.67, 63.53, 63.49, 63.19 (2C), 62.01, 60.53, 55.37, 46.81, 42.43, 33.06, 14.78, 14.76, 14.65 (2C), 14.60, 14.53. HRMS (ESI-TOF) calcd for C$_{38}$H$_{44}$N$_4$O$_{15}$ (M+Na') = 763.2324, found 763.2320. IR (KBr) ν (cm$^{-1}$): 3026, 3011, 2989, 2878, 2857, 1785, 1748, 1728, 1715, 1677, 1655, 1601, 1578, 1532, 1508, 1423, 1372, 1341, 1274, 1245, 1218, 1201, 1187, 1160, 1093, 1043, 1013, 975, 862, 762, 692.
Diethyl (E)-1-(1,6-dimethoxy-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo[2,1-a]-isoindole-3,3-dicarboxylate (3q)

White solid; mp 118-119 °C. Yield (86.4 mg, 89%). $^1$H-NMR (500 MHz, DMSO-$d_6$) $\delta$ 8.11 (d, $J = 7.7$ Hz, 1H), 7.81 (d, $J = 7.7$ Hz, 1H), 7.77 (td, $J = 7.6$, 1.2 Hz, 1H), 7.66 (t, $J = 7.6$ Hz, 1H), 6.84 (ddd, $J = 14.9$, 8.0, 6.4 Hz, 1H), 5.98 (d, $J = 15.6$ Hz, 1H), 4.43 (dd, $J = 9.2$, 6.1 Hz, 1H), 4.27 – 4.20 (m, 4H), 3.75 – 3.63 (m, 6H), 3.58 (s, 2H), 2.90 – 2.82 (m, 1H), 2.76 – 2.82 (m, 1H), 1.25 – 1.18 (m, 6H); $^{13}$C-NMR (126 MHz, DMSO-$d_6$) $\delta$ 171.50, 167.21, 167.15, 166.10, 161.28, 145.64, 136.85, 135.26, 132.73, 130.56, 129.68, 123.92, 123.55, 123.40, 114.70, 67.98, 62.87, 62.83, 52.84, 51.64, 46.20, 42.00, 32.69, 14.24, 14.15. HRMS (ESI-TOF) calc for C$_{38}$H$_{29}$NO$_6$ (M$^+$) = 686.1758, found 686.1755. IR (KBr) v (cm$^{-1}$): 3012, 2988, 2957, 1754, 1741, 1729, 1709, 1659, 1655, 1563, 1517, 1475, 1437, 1382, 1339, 1275, 1258, 1227, 1201, 1169, 1151, 1101, 1063, 1039, 998, 962, 931, 863, 760, 687.

Diethyl (E)-1-(1,6-bis(benzyloxy)-1,6-dioxohex-4-en-2-yl)-5-oxo-2,5-dihydro-3H-pyrrolo-[2,1-a]isoindole-3,3-dicarboxylate (3r)

Brown oil. Yield (100.5 mg, 79%). $^1$H-NMR (300 MHz, DMSO-$d_6$) $\delta$ 8.10 (d, $J = 7.6$ Hz, 1H), 7.78 (d, $J = 7.5$ Hz, 1H), 7.68 (t, $J = 7.5$, 1H), 7.61 (t, $J = 7.4$ Hz, 1H), 7.31 – 7.22 (m, 10H), 6.89 (ddd, $J = 14.8$, 7.1, 6.0 Hz, 1H), 6.01 (d, $J = 15.6$ Hz, 1H), 5.16 (d, $J = 4.5$ Hz, 2H), 5.06 (d, $J = 6.8$ Hz, 2H), 4.51 (dd, $J = 9.1$, 6.1 Hz, 1H), 4.23 – 4.11 (m, 4H), 3.73 (d, $J = 18.2$ Hz, 1H), 3.59 (d, $J = 17.7$ Hz, 1H), 2.94 – 2.83 (m, 1H), 2.80 – 2.69 (m, 1H), 1.18 – 1.07 (m, 6H); $^{13}$C-NMR (75 MHz, DMSO-$d_6$) $\delta$ 171.23, 167.56, 167.52, 165.81, 161.73, 146.37, 137.40, 136.88, 136.51, 135.65, 133.01, 130.89, 129.99, 129.44, 129.26, 129.20, 129.19, 128.91, 128.77, 128.68, 128.57 (2C), 128.43, 124.26, 123.97, 123.91, 114.88, 68.30, 67.32, 66.14, 63.23, 63.19, 46.58, 42.50, 33.10, 14.60, 14.51. HRMS (ESI-TOF) calc for C$_{37}$H$_{33}$NO$_6$ (M$^+$Na$^+$) = 660.2204, found 660.2199. IR (KBr) v (cm$^{-1}$): 3027, 3007, 2962, 2873, 2840, 1742, 1738, 1727, 1718, 1671, 1655, 1580, 1532, 1469, 1456, 1378, 1297, 1262, 1216, 1202, 1179, 1101, 1042, 1017, 987, 876, 764, 698.
5. Copies of $^1$H-NMR, $^{13}$C-NMR spectra

5.1 $^1$H-NMR, $^{13}$C-NMR spectra of Substituted Phthalimidomalonates
5.2 $^1$H-NMR, $^{13}$C-NMR spectra of products
6. Copies of HSQC of Compound 3a
7. Copies of HMBC of Compound 3a