A novel approach to isoindolo[2,1-a]indol-6-ones

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Electronic Supplementary Information

Experimental

General details

Melting points were obtained on a Buchi SMP-20 capillary melting point apparatus and are uncorrected. IR spectra were recorded either on a Shimadzu FTIR-8300 or a Perkin Elmer Spectrum 65 FT-IR spectrophotometer and selected bands are reported below. Low resolution mass spectra were obtained using a Bruker Esquire LC mass spectrometer equipped with an electrospray ionisation source or an Agilent GC mass spectrometer equipped with an electron ionisation detector. High resolution mass spectrometry was carried out by the EPSRC facility at Swansea. TLC was performed with a Sigma-Aldrich Ltd. and used as received unless indicated otherwise.

General procedure to prepare the benzoic acid derivatives 13

A mixture of the appropriate anhydride 11 (20 mmol), 2-aminobenzoic acid 12 (20.5 mmol) and glacial acetic acid (25 cm³) was heated at 110 °C for 16 h. The solution was then cooled and the solvent evaporated to leave a solid residue, which was purified as indicated below.

2-(1,3-Dioxoisindolin-2-yl)benzoic acid 13a₁ was prepared from phthalic anhydride and 2-aminobenzoic acid. A pure sample of the acid 13a (2.5 g, 47%) was isolated as a cream coloured solid, mp 221-222 °C [lit. 217 °C (aq EtOH)] by the slow evaporation of an ethanolic solution of the crude product, δ_H(270 MHz, d_6-DMSO) 7.57 (1 H, dd, J 8 and 1, 3-H), 7.65 (1 H, td, J 8 and 1, 5-H), 7.78 (1 H, td, J 8 and 2, 4-H), 7.89-7.95 (2 H, m, 4'/7'-H), 7.96-8.03 (2 H, m, 5'/6'-H), 8.07 (1 H, dd, J 8 and 2, 6-H), 13.13 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 132.5 (x2)(C-4'), 129.3 (C-1), 129.3 (C-5'), 130.7 (C-3), 131.0 (C-6), 131.5 (C-2), 131.8 (x2)(C-3a'/7a'), 133.1 (C-4), 134.9 (x2)(C-5'/6'), 166.2 (CO_2H), 167.2 (x2)(C-1'/3'); v_max/cm⁻¹ (ATM) 3170 br, 3091, 1701, 1603, 1495, 1457, 1384, 1293, 1232, 1219, 1174, 1118, 1085, 1074, 896, 882, 833, 791, 774, 755, 718, 705.

4-Chloro-2-(1,3-dioxo-1,3-dihydro-2H-isindolin-2-yl)benzoic acid 13b was prepared from phthalic anhydride and 2-amino-4-chlorobenzoic acid. The crude product was recrystallised from glacial acetic acid to give the pure acid 13b (4.3 g, 71%) as a white powder, mp 280-281 °C (lit. 1 269-270 °C (AcOH)); δ_H(270 MHz, d_6-DMSO) 7.72 (1 H, dd, J 8 and 2, 5-H), 7.75 (1 H, d, J 2, 3-H), 7.91-7.96 (2 H, m, 5'/6'-H), 7.98-8.02 (2 H, m, 4'/7'-H), 8.07 (1 H, d, J 8, 6-H), 13.37 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 123.7 (x2)(C-4'), 128.3 (C-1), 129.5 (C-5), 130.6 (C-3), 131.8 (x2)(C-3a'/7a'), 132.8 (C-6), 133.0 (C-2), 135.0 (x2)(C-5'/6'), 137.2 (C-4), 165.5 (CO_2H), 166.9 (x2)(C-1'/3'); v_max/cm⁻¹ (ATM) 1707, 1681, 1594, 1492, 1419, 1437, 1276, 1220, 1105, 896, 841, 779, 712, 693, 680; m/z (ESI) 324 (M+Na⁺). C₁₃H₁₂ClNO₂ requires 324.

2-(5,6-Dichloro-1,3-dioxo-1,3-dihydro-2H-isindolin-2-yl)benzoic acid 13c was prepared from 4,5-dichlorophthalic anhydride and 2-aminobenzoic acid. The crude product was recrystallised from a chloroform/methanol (98:2) mixture to give the pure acid 13c (4.2 g, 63%) as a fawn coloured solid, mp 245-246 °C; δ_H(270 MHz, d_6-DMSO) 7.54 (1 H, d, J 7.5, 3-H), 7.63 (1 H, t, J 7.5, 5-H), 7.77 (1 H, t, J 7.5, 6-H), 7.89 (2 H, m, 4'/7'-H), 8.00-8.02 (2 H, m, 5'/6'-H), 8.05 (1 H, d, J 8, 6-H), 13.7 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 123.7 (x2)(C-4'), 128.3 (C-1), 129.5 (C-5), 130.6 (C-3), 131.8 (x2)(C-3a'/7a'), 132.8 (C-6), 133.5 (C-2), 135.0 (x2)(C-5'/6'), 137.2 (C-4), 165.5 (CO_2H), 169.9 (x2)(C-1'/3'); v_max/cm⁻¹ (ATM) 1707, 1681, 1594, 1492, 1419, 1437, 1276, 1220, 1105, 896, 841, 779, 712, 693, 680; m/z (ESI) 324 (M+Na⁺). C₁₃H₁₀Cl₄NO₂ requires 324.
DMF (1 drop) was added to a mixture of the base.

General procedure for the preparation of acid chlorides

DMF (1 drop) was added to a mixture of the benzoic acid derivative 13 (3.0 mmol) and thionyl chloride (10 cm³) and the mixture stirred at room temperature for 16 h. If any solid remained the mixture was then heated under reflux for 5 min. Volatile compounds were removed under reduced pressure (40 °C at 15 mmHg). To ensure the removal of any residual thionyl chloride, the residue was redissolved in warm dry toluene (20 cm³) and the toluene and other volatile compounds were then removed under reduced pressure (55 °C at 15 mmHg) taking care to rigorously exclude moisture from the product. The resulting acid chloride 14 was used without further purification.

2-(3,4-Dichloro-2,5-dioxo-1,4-dihydro-1H-pyrrrol-1-yl)benzoic acid 14c

This compound was prepared from dichloromaleic anhydride and 2-aminobenzoic acid using the procedure previously described for the benzoic acids 13 and purified by recrystallisation from a chloroform/methanol 95:5 mixture. The pure product 31c (3.8 g, 43%) was isolated as a yellow powder, mp 241-242 °C (lit., 170 °C (EtOH)); δ̂N(CH₃) (270 MHz, d₄-DMSO) 7.30 (1 H, d, J 8 and 2, 3-H), 7.59 (1 H, d, J 8 and 2, 3-H), 7.72 (1 H, td, J 8 and 2, 4-H), 8.01 (1 H, dd, J 8 and 2, 6-H), 13.12 (1 H, br s, CO₂H); δ̂N(CH₃) (67.9 MHz, d₄-DMSO) 129.7 (x2)(C-1, C-5), 131.2 (C-3), 131.6 (C-6), 131.7 (C-2), 133.6 (C-4), 162.3 (x2)(C-2',5'), 165.9 (CO₂H), νmax/cm⁻¹ (ATR) 3222, 1718, 1603, 1491, 1453, 1372, 1226, 1122, 1081, 1018, 901, 883, 820, 758, 732, 648.

General procedure for the preparation of acid chlorides

DMF (1 drop) was added to a mixture of the benzoic acid derivative 13 (3.0 mmol) and thionyl chloride (10 cm³) and the mixture stirred at room temperature for 16 h. If any solid remained the mixture was then heated under reflux for 5 min. Volatile compounds were removed under reduced pressure (40 °C at 15 mmHg). To ensure the removal of any residual thionyl chloride, the residue was redissolved in warm dry toluene (20 cm³) and the toluene and other volatile compounds were then removed under reduced pressure (55 °C at 15 mmHg) taking care to rigorously exclude moisture from the product. The resulting acid chloride 14 was used without further purification.

2-(1,3-Dioxoisindolin-2-yl)benzoic acid 14a gave δ̂N(CH₃) (270 MHz, CDCl₃) 7.42 (1 H, dd, J 8 and 1, 3-H), 7.58 (1 H, dd, J 8 and 2, 3-H), 7.74 (1 H, td, J 8 and 1, 4-H), 7.74-7.78 (2 H, m, 5',6'-H), 7.88 (1 H, m, 4',5'-H), 8.27 (1 H, dd, J 8 and 2, 6-H); δ̂N(CH₃) (67.9 MHz, CDCl₃) 124.1 (x2)(C-4',7'), 129.5 (C-5), 130.4 (C-3), 131.1 (C-1), 131.4 (C-2), 131.8 (x2)(C-3a',7a'), 133.8 (C-6), 134.7 (x2)(C-5',6'), 135.3 (C-4), 166.3 (COCl), 166.9 (x2)(C-1',3').
4-Chloro-2-(1,3-dioxoisindolin-2-yl)benzoic acid 31a gave δC(270 MHz, CDCl3) 7.45 (1 H, d, J = 2, 3-H), 7.57 (1 H, dd, J = 8 and 2, 5-H), 7.77-7.82 (2 H, m, 5'/6'-H), 7.90-7.95 (2 H, m, 4'/7'-H), 8.24 (1 H, d, J = 8, 6-H); δH(67.9 MHz, CDCl3) 124.3 (CH2(C'4'/7')), 129.7 (CH2(C'5'')), 129.8 (CH3(C'1')), 130.7 (CH3(C'3')), 131.7 (CH2(C'3'a'/7a')), 132.3 (CH2(C'2'-)), 134.9 (CH2(C'6'-)), 141.5 (CH2(C'5'')), 165.5 (CH2(C'1'')), 165.3 (CH(C=O)).

2-(5,6-Dichloro-1,3-dioxoisindolin-2-yl)benzoic acid 14d gave δH(270 MHz, CDCl3) 7.43 (1 H, d, J = 2, 3-H), 7.58 (1 H, dd, J = 8 and 2, 5-H), 7.98 (2 H, s, 4'/7'-H), 8.24 (1 H, d, J = 8, 6-H); δH(67.9 MHz, CDCl3) 126.3 (CH2(C'4'/7')), 130.0 (CH2(C'5'')), 130.6 (CH3(C'1')), 130.8 (CH3(C'3')), 131.1 (CH2(C'3'a'/7a')), 131.3 (CH2(C'2'-)), 134.4 (CH2(C'6'-)), 135.5 (CH2(C'5'')), 139.9 (CH2(C'5'')), 165.3 (CH2(C'1'')), 166.4 (COCl).

4-Chloro-2-(5,6-dichloro-1,3-dioxoisindolin-2-yl)benzoic acid 14d gave δH(270 MHz, CDCl3) 7.43 (1 H, d, J = 2, 3-H), 7.58 (1 H, dd, J = 8 and 2, 5-H), 7.98 (2 H, s, 4'/7'-H), 8.24 (1 H, d, J = 8, 6-H); δH(67.9 MHz, CDCl3) 126.1 (CH2(C'4'/7')), 128.3 (CH2(C'5'')), 129.9 (CH3(C'1')), 130.6 (CH3(C'3')), 131.7 (CH2(C'3'a'/7a')), 132.7 (CH2(C'2'-)), 135.0 (CH2(C'6'-)), 139.8 (CH2(C'5'')), 141.6 (CH2(C'4'-)), 164.5 (CH2(C'1'')), 165.4 (COCl).

The reaction of 2-(2,5-dioxo-2,5-dihydro-1H-pyrrolo-1-yl)benzoic acid 31a with oxalyl chloride and thionyl chloride

1. Limited reaction with oxalyl chloride
A mixture of the benzoic acid 31a (540 mg, 2.5 mmol), oxalyl chloride (5 cm3) and DMF (1 drop) was stirred for 1 h at room temperature and volatile components were then removed under reduced pressure (40 °C at 15 mmHg). Toluene (15 cm3) was then added and removed under reduced pressure (40 °C at 15 mmHg) to give a brown viscous residue that contained the desired acid chloride 32a [δC(270 MHz, CDCl3) 6.85 (s, =CH2)] as only the minor component (ca. 23%). The major component was the halogenated derivative 41 [δH(270 MHz, CDCl3) 3.05 (1 H, dd, J = 18.8 and 4), 3.48 (1 H, dd, J = 18.8 and 8.5), 4.82 (1 H, dd, J = 8.5 and 4)] (ca. 77%). Since these components could not be readily separated, the mixture was used to investigate their reactions with triethyl phosphite.

2. Reaction with thionyl chloride for a more extended period.
2-(2,5-Dioxo-2,5-dihydro-1H-pyrrolo-1-yl)benzoic acid 31a (1.5 g, 6.9 mmol), thionyl chloride (3 cm3) and dry DMF (15 cm3) were stirred at room temperature for 16 h by which time a dark brown/orange solution had been obtained. The solution was filtered and the filtrate evaporated under reduced pressure (50 °C at 15 mmHg) to leave a viscous residue. Final traces of thionyl chloride were removed by repeatedly adding DMCO (20 cm3) and then evaporating the solution under reduced pressure (50 °C, 15 mmHg). The resulting viscous residue was shown to be 2-(3-chloro-2,5-dioxopyrrolo-1-yl)benzoic acid 41 (1.72 g, 92 %) in a good state of purity and this was used without further purification; δH(270 MHz, CDCl3) 3.05 (1 H, dd, J = 18.5 and 4, 4'-H), 3.45 (1 H, dd, J = 18.5 and 8.5, 4'-H), 4.82 (1 H, dd, J = 8.5 and 4, 3-H), 7.18-7.32 (1 H, br m, 4-H), 7.58 (1 H, t, J = 8, 5-H), 7.71 (1 H, br d, J = 8, 6-H), 8.32 (1 H, d, J = 8, 3-H); δC(67.9 MHz, CDCl3) 39.6 (C'4'), 49.2 (C'3'-), 129.9 (C'3), 130.3 (C'5), 130.9 (C'1), 134.5 (C'6'), 134.9 (C'2), 135.8 (C'4), 166.3 (COCl), 171.8 (C'5'), 172.0 (C'2').
X-Ray crystallography

For all complexes, the crystals were glued to a glass fibre and mounted on the diffractometer head. Intensity data for all crystals were collected at 120 K, using a Bruker-Nomius FR591CCD diffractometer, equipped with a Mo-Kα, rotating anode (λ = 0.71073 Å), monochromated by graphite (15a) or 10 cm confocal focusing mirrors (28, 35c and 37c). The crystals were positioned 30 mm from the CCD and all intensities were measured using a counting time of 20 seconds with 1.0° increments (α and Ω) to fill the Ewald sphere. The unit cell parameters were determined by least-squares refinement of all data automatically centred reflections with setting angles of 2.91 ≤ 2θ ≤ 27.48°.

All intensities were collected using the programs COLLECT\(^5\). Data reductions and refinements were performed using both DENZO\(^6\) and COLLECT according to Lorentz and polarisation effects. Absorption corrections were applied based on multi-scan method and were obtained using SADABS\(^7\). X-ray crystal structures were determined using the DirAx\(^12\) program. The programs ORTEP-3\(^{13}\) and PLATON\(^14\) were used for drawing the molecules. WINGX\(^\text{9}\) was used to prepare material for publication.

All structures were solved by the heavy-atom method using the DIRDIFF99\(^{16}\) program and refined anisotropically (non-hydrogen atoms) by full-matrix least-squares technique against \(F^2\) using the SHELXL-97\(^\text{17}\) program. All H atoms were calculated geometrically and refined by a riding model.

Table 1: Crystallographic data for 15a, 28, 35c and 37c\(^\text{18}\)

<table>
<thead>
<tr>
<th>Compound</th>
<th>15a</th>
<th>28</th>
<th>35c</th>
<th>37c</th>
</tr>
</thead>
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<tr>
<td>Formula</td>
<td>(\text{C}<em>{10}\text{H}</em>{14}\text{NO}_3\text{P})</td>
<td>(\text{C}<em>{23}\text{H}</em>{36}\text{NO}_3\text{P})</td>
<td>(\text{C}<em>{15}\text{H}</em>{14}\text{Cl}_2\text{NO}_3\text{P})</td>
<td>(\text{C}_{11}\text{H}_3\text{Cl}_2\text{NO}_2)</td>
</tr>
<tr>
<td>(M_r) (Da)</td>
<td>371.31</td>
<td>421.37</td>
<td>390.14</td>
<td>254.06</td>
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<tr>
<td>(T) (K)</td>
<td>120 (2)</td>
<td>120 (2)</td>
<td>120 (2)</td>
<td>120 (2)</td>
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<tr>
<td>Crystal system</td>
<td>Triclinic</td>
<td>Monoclinic</td>
<td>Monoclinic</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>(P 1)</td>
<td>(1 2/a)</td>
<td>(P2_1/n)</td>
<td>(P 2_1 n b)</td>
</tr>
<tr>
<td>(a) (Å)</td>
<td>8.5690 (2)</td>
<td>22.2526 (5)</td>
<td>12.4096 (3)</td>
<td>3.7524 (7)</td>
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<tr>
<td>(b) (Å)</td>
<td>8.7336 (2)</td>
<td>7.0132 (2)</td>
<td>9.6934 (2)</td>
<td>12.666 (3)</td>
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<td>(c) (Å)</td>
<td>11.8798 (3)</td>
<td>25.1963 (6)</td>
<td>27.4755 (7)</td>
<td>21.009 (4)</td>
</tr>
<tr>
<td>(\alpha) (°)</td>
<td>81.6460 (10)</td>
<td>90</td>
<td>90</td>
<td>90</td>
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<tr>
<td>(\beta) (°)</td>
<td>85.9310 (10)</td>
<td>106.297 (2)</td>
<td>92.9430 (10)</td>
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<td>(\gamma) (°)</td>
<td>88.264 (2)</td>
<td>90</td>
<td>90</td>
<td>90</td>
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<td>(V) (Å(^3))</td>
<td>877.23 (4)</td>
<td>3774.19 (16)</td>
<td>3300.70 (13)</td>
<td>998.5 (4)</td>
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<tr>
<td>(D_{\text{Calc}}) (Mg/m(^3)) (Z)</td>
<td>1.406 (2)</td>
<td>1.483 (8)</td>
<td>1.570 (8)</td>
<td>1.690 (4)</td>
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<td>(\mu) (mm(^{-1}))</td>
<td>0.187</td>
<td>0.184</td>
<td>0.516</td>
<td>0.629</td>
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<td>Crystal size (mm(^3))</td>
<td>0.32 x 0.27 x 0.17</td>
<td>0.30 x 0.17 x 0.04</td>
<td>0.20 x 0.12 x 0.06</td>
<td>0.30 x 0.06 x 0.03</td>
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<tr>
<td>Index ranges for (h, k, l) &amp; -11/11,-11/11,-15/15 &amp; -28/28,-9/9,-27/32 &amp; -14/16,-12/12,-34/35 &amp; -4/4,-16/16,-26/27</td>
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<tr>
<td>No. of reflections collected</td>
<td>20152</td>
<td>19986</td>
<td>29073</td>
<td>5015</td>
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<tr>
<td>No. of reflections unique ((R_{\text{int}}))</td>
<td>4033 (0.0416)</td>
<td>4293 (0.0538)</td>
<td>7515 (0.0494)</td>
<td>1941 (0.0560)</td>
</tr>
<tr>
<td>No. of reflections observed</td>
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<td>3406</td>
<td>6115</td>
<td>1681</td>
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<td>(T_{\text{max/min}})</td>
<td>0.9688 and 0.9425</td>
<td>0.9927 and 0.9468</td>
<td>0.9697 and 0.9038</td>
<td>0.9814 and 0.8337</td>
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<td>Data/restraints/parameters</td>
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<td>4293 / 0 / 273</td>
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<td>Goodness-of-fit (GOF)</td>
<td>1.052</td>
<td>1.092</td>
<td>1.144</td>
<td>1.078</td>
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<td>(R_1, \text{wR}_2 [I &gt; 2\sigma(I)]) (all data)</td>
<td>0.0408, 0.0982</td>
<td>0.0540, 0.1035</td>
<td>0.0648, 0.1204</td>
<td>0.0842, 0.2141</td>
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<td>(all data)</td>
<td>0.0498, 0.1037</td>
<td>0.0747, 0.1142</td>
<td>0.0838, 0.1298</td>
<td>0.0983, 0.2260</td>
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<td>Largest diff. peak and hole (e/Å(^3))</td>
<td>0.452 and -0.410</td>
<td>0.325 and -0.396</td>
<td>0.407 and -0.435</td>
<td>0.587 and -0.653</td>
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Table 1  Selected bond lengths and angles for compounds 28 and 37c

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<th>Bond lengths (Å)</th>
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<td>O(1)-C(1)</td>
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<td>O(1)-C(1)</td>
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<td>O(5)-C(16)</td>
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<td>N(1)-C(8)</td>
<td>1.420 (3)</td>
<td>N(1)-C(4)</td>
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<td>N(1)-C(16)</td>
<td>1.396 (3)</td>
<td>N(1)-C(7)</td>
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<td>P(1)-O(1)</td>
<td>1.597 (2)</td>
<td>C(1)-C(2)</td>
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<td>C(1)-C(2)</td>
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<td>C(2)-C(3)</td>
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<td>C(1)-C(8)</td>
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<td>C(3)-C(4)</td>
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<td>C(2)-C(3)</td>
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<td>C(4)-C(5)</td>
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<td>C(8)-C(9)</td>
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<td>C(5)-C(6)</td>
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<td>C(9)-C(14)</td>
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<td>C(15)-C(16)</td>
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<td>P(1)-O(1)-C(1)</td>
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<td>N(1)-C(7)-C(6)</td>
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<td>C(1)-C(2)-C(3)</td>
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<td>C(2)-C(3)-N(1)</td>
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<td>C(8)-N(1)-C(16)</td>
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<td>N(1)-C(8)-C(9)</td>
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<tr>
<td>C(8)-C(9)-C(14)</td>
<td>117.4 (2)</td>
<td>C(5)-C(6)-C(7)</td>
</tr>
<tr>
<td>C(9)-C(14)-C(15)</td>
<td>121.6 (2)</td>
<td></td>
</tr>
<tr>
<td>C(14)-C(15)-C(16)</td>
<td>121.3 (2)</td>
<td></td>
</tr>
<tr>
<td>C(15)-C(16)-N(1)</td>
<td>115.1 (2)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2  Selected bond lengths and angles for β-ketophosphonates 15a and 35c (structures A and B)$^\text{a}$

<table>
<thead>
<tr>
<th>Bond lengths ($\AA$)</th>
<th>15a</th>
<th>35c (a)</th>
<th>35c (b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(9)-O(2)</td>
<td>1.215 (2)</td>
<td>1.209 (4)</td>
<td>1.207 (4)</td>
</tr>
<tr>
<td>C(2)-O(1)</td>
<td>1.214 (2)</td>
<td>1.206 (4)</td>
<td>1.206 (4)</td>
</tr>
<tr>
<td>C(1)-P(1)</td>
<td>1.842 (2)</td>
<td>1.858 (3)</td>
<td>1.855 (3)</td>
</tr>
<tr>
<td>C(10)-C(11)</td>
<td>1.393 (2)</td>
<td>1.335 (5)</td>
<td>1.330 (4)</td>
</tr>
<tr>
<td>C(11)-C(1)</td>
<td>1.504 (2)</td>
<td>1.498 (5)</td>
<td>1.498 (4)</td>
</tr>
<tr>
<td>C(1)-C(2)</td>
<td>1.549 (2)</td>
<td>1.555 (5)</td>
<td>1.552 (5)</td>
</tr>
<tr>
<td>C(9)-C(10)</td>
<td>1.479 (2)</td>
<td>1.476 (5)</td>
<td>1.477 (5)</td>
</tr>
<tr>
<td>C(2)-C(3)</td>
<td>1.468 (2)</td>
<td>1.478 (5)</td>
<td>1.473 (5)</td>
</tr>
<tr>
<td>C(3)-C(4)</td>
<td>1.395 (2)</td>
<td>1.390 (5)</td>
<td>1.394 (5)</td>
</tr>
<tr>
<td>N(1)-C(9)</td>
<td>1.409 (2)</td>
<td>1.404 (4)</td>
<td>1.409 (4)</td>
</tr>
<tr>
<td>N(1)-C(1)</td>
<td>1.474 (2)</td>
<td>1.474 (4)</td>
<td>1.474 (4)</td>
</tr>
<tr>
<td>N(1)-C(4)</td>
<td>1.417 (2)</td>
<td>1.421 (4)</td>
<td>1.434 (4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bond angles (°)</th>
<th>15a</th>
<th>35c (a)</th>
<th>35c (b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(2)-C(1)-C(11)</td>
<td>120.31 (12)</td>
<td>119.0 (3)</td>
<td>118.6 (3)</td>
</tr>
<tr>
<td>P(1)-C(1)-N(1)</td>
<td>109.91 (9)</td>
<td>105.7 (2)</td>
<td>105.7 (2)</td>
</tr>
<tr>
<td>C(2)-C(1)-N(1)</td>
<td>104.40 (11)</td>
<td>104.9 (3)</td>
<td>104.9 (3)</td>
</tr>
<tr>
<td>C(11)-C(1)-N(1)</td>
<td>103.48 (11)</td>
<td>102.7 (3)</td>
<td>102.8 (2)</td>
</tr>
<tr>
<td>P(1)-C(1)-C(2)</td>
<td>108.24 (10)</td>
<td>109.2 (2)</td>
<td>109.7 (2)</td>
</tr>
<tr>
<td>P(1)-C(1)-C(11)</td>
<td>108.24 (10)</td>
<td>113.8 (2)</td>
<td>113.6 (2)</td>
</tr>
<tr>
<td>C(1)-C(2)-C(3)</td>
<td>105.24 (12)</td>
<td>104.6 (3)</td>
<td>104.7 (3)</td>
</tr>
<tr>
<td>C(2)-C(3)-C(4)</td>
<td>109.49 (13)</td>
<td>109.7 (3)</td>
<td>109.9 (3)</td>
</tr>
<tr>
<td>C(3)-C(4)-N(1)</td>
<td>110.87 (13)</td>
<td>111.2 (3)</td>
<td>110.6 (3)</td>
</tr>
<tr>
<td>C(4)-N(1)-C(1)</td>
<td>108.87 (11)</td>
<td>108.5 (3)</td>
<td>108.5 (3)</td>
</tr>
<tr>
<td>C(1)-N(1)-C(9)</td>
<td>111.47 (12)</td>
<td>110.8 (3)</td>
<td>110.7 (3)</td>
</tr>
<tr>
<td>N(1)-C(9)-C(10)</td>
<td>106.05 (13)</td>
<td>105.5 (3)</td>
<td>105.3 (3)</td>
</tr>
<tr>
<td>C(9)-C(10)-C(11)</td>
<td>109.50 (14)</td>
<td>110.1 (3)</td>
<td>110.6 (3)</td>
</tr>
<tr>
<td>C(10)-C(11)-C(1)</td>
<td>108.92 (13)</td>
<td>110.3 (3)</td>
<td>110.2 (3)</td>
</tr>
</tbody>
</table>

$^\text{a}$ Values on the same row of the table show the corresponding bond lengths or bond angles in the two compounds.
Further information on NMR spectra provided.

1. $^{31}$P NMR spectrum of 15a in CDCl$_3$ at 109.3 MHz
2. $^{13}$C NMR spectrum of 15a in CDCl$_3$ at 67.9 MHz
3. $^{31}$P NMR spectrum of 16a in CDCl$_3$ at 109.3 MHz
4. $^{13}$C NMR spectrum of 16a in CDCl$_3$ at 67.9 MHz
5. $^{31}$P NMR spectrum of 20a in CDCl$_3$ at 109.3 MHz
6. $^{13}$C NMR spectrum of 20a in CDCl$_3$ at 100.6 MHz
7. $^{13}$C NMR spectrum of 23a in CDCl$_3$ at 67.9 MHz
8. $^{31}$P NMR spectrum of 15b in CDCl$_3$ at 109.3 MHz
9. $^{13}$C NMR spectrum of 15b in CDCl$_3$ at 100.6 MHz
10. $^{31}$P NMR spectrum of 20b in CDCl$_3$ at 109.3 MHz
11. $^{13}$C NMR spectrum of 20b in CDCl$_3$ at 67.9 MHz
12. $^{13}$C NMR spectrum of 23b in CDCl$_3$ at 100.6 MHz
13. $^{13}$C NMR spectrum of 13c in d$_6$-DMSO at 67.9 MHz
14. $^{31}$P NMR spectrum of 15c in CDCl$_3$ at 109.3 MHz
15. $^{13}$C NMR spectrum of 15c in CDCl$_3$ at 100.6 MHz
16. $^{31}$P NMR spectrum of 20c in CDCl$_3$ at 109.3 MHz
17. $^{13}$C NMR spectrum of 20c in CDCl$_3$ at 100.6 MHz
18. $^1$H NMR spectrum of 23c in CCl$_4$ at 270 MHz
19. $^{13}$C NMR spectrum of 13d in d$_6$-DMSO at 67.9 MHz
20. $^{31}$P NMR spectrum of 15d in CDCl$_3$ at 109.3 MHz
21. $^{13}$C NMR spectrum of 15d in CDCl$_3$ at 100.6 MHz
22. $^{31}$P NMR spectrum of 20d in CDCl$_3$ at 109.3 MHz
23. $^{13}$C NMR spectrum of 20d in CDCl$_3$ at 100.6 MHz
24. $^1$H NMR spectrum of 23d in d$_6$-DMSO at 270 MHz
25. $^{31}$P NMR spectrum of 26 in CDCl$_3$ at 109.3 MHz
26. $^{13}$C NMR spectrum of 26 in CDCl$_3$ at 67.9 MHz
27. $^{31}$P NMR spectrum of 27 in CDCl$_3$ at 109.3 MHz
28. $^{13}$C NMR spectrum of 27 in CDCl$_3$ at 100.6 MHz
29. $^{31}$P NMR spectrum of 28 in CDCl$_3$ at 109.3 MHz
30. $^{13}$C NMR spectrum of 28 in CDCl$_3$ at 100.6 MHz
31. $^{13}$C NMR spectrum of 29 in CDCl$_3$ at 100.6 MHz
32. $^{31}$P NMR spectrum of 35a in CDCl$_3$ at 109.3 MHz
33. $^{13}$C NMR spectrum of 35a in CDCl$_3$ at 67.9 MHz
34. $^{31}$P NMR spectrum of 44 in CDCl$_3$ at 109.3 MHz
35. $^{13}$C NMR spectrum of 44 in CDCl$_3$ at 100.6 MHz
36. $^{13}$C NMR spectrum of 50 in CDCl$_3$ at 67.9 MHz
37. $^{31}$P NMR spectrum of 52 in CDCl$_3$ at 109.3 MHz
38. $^{13}$C NMR spectrum of 52 in CDCl$_3$ at 100.6 MHz
39. $^{31}$P NMR spectrum of 35c in CDCl$_3$ at 109.3 MHz
40. $^{13}$C NMR spectrum of 35c in CDCl$_3$ at 67.9 MHz
41. $^{13}$C NMR spectrum of 38c in CDCl$_3$ at 100.6 MHz
42. $^{13}$C NMR spectrum of 40 in CDCl$_3$ at 100.6 MHz
Spectrum 1

15a

(\text{EtO})_2\text{P}
Spectrum 4

$\text{N} \text{O} \text{O}$

$\text{P(OEt)}_2$

$16a$
Spectrum 5

![Diagram of molecule 20a]
Spectrum 6

20a

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Spectrum 10

20b

The journal is © The Royal Society of Chemistry 2012
Spectrum 11

![Spectrum of compound 20b](image)

ESI for Organic & Biomolecular Chemistry
This journal is © The Royal Society of Chemistry 2012
Spectrum 14

\[
\text{Cl} \quad \text{N} \quad \text{Cl} \\
\text{Cl} \quad \text{(EtO)}_2\text{P} \quad \text{O} \quad \text{O} \\
\text{Cl} 
\]
Spectrum 15

\[
\text{Cl} \quad \text{Cl} \\
\text{(EtO)}_2P \\
\text{Cl} \\
\text{O} \\
\text{O} \\
\text{N} \\
\text{O} \\
\text{Cl}
\]
Spectrum 16

![Chemical Structure](image)

20c
Spectrum 17

\[
\begin{align*}
\text{Cl} & \quad \text{O} \\
\text{Cl} & \quad \text{N} \\
\text{Cl} & \quad \text{O} \\
\text{P(\text{OE})_2} & \\
\end{align*}
\]
Spectrum 19

![Chemical Structure](image)

**13d**
Spectrum 20

15d
Spectrum 21

[Chemical structure image]

**Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry**

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Spectrum 22

![Chemical structure diagram](image)
Spectrum 25

\[
\begin{align*}
\text{P(O)(OEt)}_2
\end{align*}
\]
Spectrum 27

\[
\text{(EtO),P}
\]
Spectrum 28

![Chemical Structure](image)
Spectrum 29

![Chemical Structure](image)
Spectrum 30

![Spectrum Image](image_url)
Spectrum 32

(EtO)$_2$P

35a

ppm
Spectrum 34

\[
\text{Cl} \quad \text{(EtO)}_2P \quad \text{O} \quad \text{N} \quad \text{O} \\
\]

13.20 ppm
Spectrum 35

The spectrum shows various peaks at different ppm values. The compound in the spectrum is illustrated with a molecular structure:

![Molecular Structure]

The structure includes a chlorine atom (Cl), a diethylphosphoramide group ((EtO)₂P), and other functional groups represented by N, O, and Cl. The ppm values range from negative to positive, indicating the chemical shifts at different positions in the molecule.
Spectrum 37

(\text{EtO})_2P\text{H} \text{N}

\text{CO}_2\text{H}

52

ppm
Spectrum 38

(EtO)$_2$P

\[ \text{O} \quad \text{O} \quad \text{O} \quad 52 \]
Spectrum 39

\[ \text{Cl} \]
\[ \text{Cl} \]
\[ \text{(EtO)}_2P \]
\[ \text{O} \]
\[ \text{O} \]

35c
Spectrum 40

\[
\begin{align*}
\text{Cl} & \quad \text{O} \\
\text{Cl} & \quad (\text{EtO})_2\text{P} \\
\text{O} & \quad \text{O} \\
35c 
\end{align*}
\]
Spectrum 41

38c
Notes and references

4. The molecular ions showed the expected isotopic ratio pattern.
18. Data have been deposited with the Cambridge Crystallographic Data Centre. For 15a as CCDC 865150, 28 as CCDC 865151, 35c as CCDC 865152, and for 37c as CCDC 865153; they are available free of charge via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).