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Tuning the reaction pathways of phenanthroline-Schiff bases: routes to novel phenanthroline ligands†

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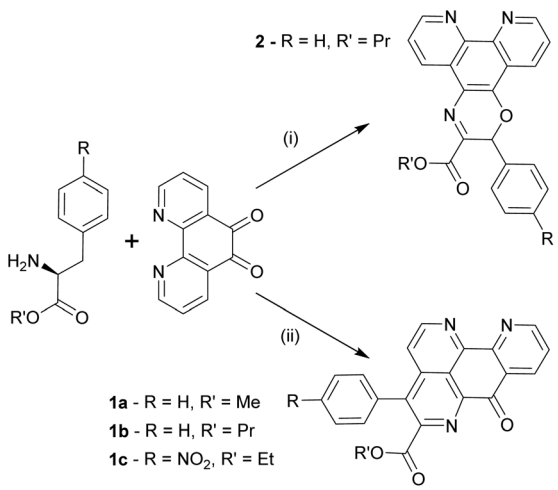
Pyrido-phenanthrolin-7-one compounds are structural analogues of the cytotoxic alkaloid, ascididemin, and would be expected to have interesting biological activities. Synthetic strategies are reported for a novel simple route to form this class of ligand. 1,10-Phenanthrolin-5,6-dione reacts with L-phenylalanine alkyl esters and their *para*-substituted analogues to form both a phenanthroline–oxazine and a pyrido-phenanthrolin-7-one product. The nature of the major product is dependent on the electronic properties of the *para* substituent. Successful metal coordination to the pyrido-phenanthrolin-7-one ligand is also presented.

Introduction

1,10-Phenanthroline, its organic derivatives and their associated metal complexes have been extensively studied for use as optical devices,[1,2] catalysts,[3] chemosensors[4] and in the formation of metal organic frameworks.[5] They have also found use in biological applications as antimicrobial and anticancer agents,[6] and as DNA intercalators.[7] There is significant interest in developing routes to novel phenanthrolines by further derivatisation of functionalised phenanthrolines.[8] One such functionalised phenanthroline, the quinone, 1,10-phenanthrolin-5,6-dione (phendione), has been widely used as the starting material for attaching moieties onto the phenanthroline framework, *via* simple Schiff base condensation reactions with primary amines.[9,10] Previously, members of our group published an unusual reaction of phendione with L-tyrosine methyl ester hydrochloride to produce a phenanthroline–oxazine compound (Scheme 1, Pathway (i) (R = OH, R′ = Me)).[11] It is proposed that the first step of this reaction is a Schiff base condensation, followed by a cyclisation reaction to form a new C–O bond, with a second molecule of phendione acting as the dehydrogenating agent. 1,10-Phenanthrolin-5,6-diol is always observed as side-product of the reaction. In developing this reaction further, we observed that another unusual competing cyclisation reaction could occur, depending on the amino acid ester substrate (Scheme 1, Pathway (ii)), to form pyrido-phenanthrolin-7-one compounds.

The pyrido-phenanthrolin-7-one compounds are synthetic analogues of the marine alkaloid, ascididemin (Fig. 1) which is well-known to have substantial cytotoxic effects against a number of tumour cell lines, including multidrug-resistant cancer cells.[12] Ascididemin can be isolated from natural sources in minute amounts,[13] while routes to its total synthesis require multiple steps and are very challenging.[14] Studies have revealed that some ascididemin synthetic analogues can display greater anti-tumour activity than the natural alkaloid,[15] and there is much interest in developing routes to



Scheme 1 Competing reactions to form phenanthroline–oxazine (pathway (i)) or pyrido-phenanthrolin-7-one (pathway (ii)) ring systems.

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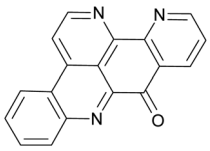


Fig. 1 Structure of ascididemin.

ascididemin analogues.[16] A recent development has been the binding of ascididemin to ruthenium(II) in order to develop metallo-anticancer complexes.[17] In a related context there is substantial interest in developing rhenium(I) tricarbonyl complexes for their anticancer activity.[18–21]

Here we report the novel and simple one-pot route to making ascididemin analogues from readily available starting materials, the full structural characterisation of methyl 7-oxo-4-phenyl-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate (**1a**) and preliminary studies on forming a rhenium(I) tricarbonyl complex with its propyl ester analogue (**1b**). We also give some insights into the factors that control the direction of this unusual reaction to form the pyrido-ligand product.

Results and discussion

Synthesis and characterisation of ligands

Reacting the amino acid ester, 4-nitro-L-phenylalanine ethyl ester hydrochloride, with phendione gives the bright-red pyrido product, ethyl 4-(4-nitrophenyl)-7-oxo-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate (**1c**), in 30% yield as the sole isolated product. Compound **1c** was characterised using HRMS, IR and NMR spectroscopy. Upon changing the amino acid ester to L-phenylalanine methyl ester hydrochloride and L-phenylalanine propyl ester hydrochloride both the phenanthroline–oxazine and the pyrido-phenanthrolin-7-one products were detected in the ^{1}H NMR spectra of the reaction mixtures. Bright-yellow crystals of the pyrido product, methyl 7-oxo-4-phenyl-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate (**1a**) were isolated (7% yield) from the L-phenylalanine methyl ester reaction, whilst yellow crystals of the oxazine product, propyl 2-phenyl-2*H*-[1,4]oxazino[2,3-*f*][1,10]phenanthroline-3-carboxylate (**2**) were isolated (3%) from the L-phenylalanine propyl ester reaction. X-ray crystal structures of **1a** (Fig. 2) and **2** (Fig. 3) were obtained. For **1a** the tetracyclic ring system is nearly planar and the C–C bond lengths are consistent with the aromatic nature of this core. The phenyl ring lies at an angle to the tetracycle (torsional angle C(17)–C(18)–C(19)–C(20) of −60.7(5)°). There is a π ring interaction between adjacent tetracyclic rings with ring C8–N12 centroid-to-centroid distance of 3.619(3) Å (with a shift of 1.533(6) Å). Compound **2** has a stereogenic centre at C9 but is a racemate. The phenyl ring is almost orthogonal to the phenanthroline–oxazine moiety (torsional angle C(8)–C(9)–C(19)–C(24)–77.2(3)°). Packing of the molecule showed π–π interactions between the phenanthroline rings (C12–C17, centroid-to-centroid 3.543(2) Å, shift 0.383(5) Å) and H-bond interactions between adjacent

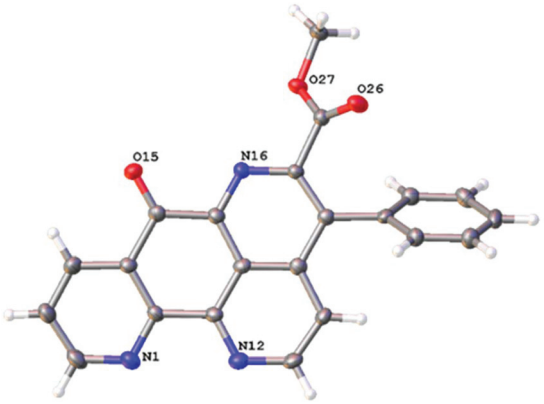


Fig. 2 Molecular structure of **1a** with atomic displacement shown at 50% probability. Only heteroatoms labelled for clarity.

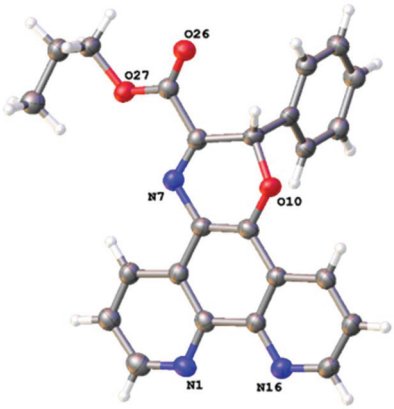


Fig. 3 Molecular structure of **2** with atomic displacement shown at 50% probability. Only heteroatoms labelled for clarity.

molecules for the H atoms on C9 and O(10) (3.383(4) Å), on C13 and O(26) (3.398(4) Å) and on C24 and N1 (3.363(4) Å).

Investigation on product selectivity

To probe the issue of product selectivity, a study using LC-mass spectrometry detection was carried out on the crude reaction mixtures for a series of reactions. In the first instance, the reaction of L-phenylalanine methyl ester with phendione was carried out over a range of temperatures (Table 1). The results clearly show that the two reactions are in competition, with the pyrido-phenanthrolin-7-one product being favoured over the oxazine at higher temperatures. From our initial observations, it appears that product formation is dependent on the nature of the *para* substituent of the phenyl ring borne by the amino acid ester. In this context, the LC-mass spectrometry study was carried out with the reaction held at a fixed temperature (75 °C) on a number of amino acid methyl esters with different substituents at the *para* position of the phenyl ring (Table 2). Formation of the pyrido-phenanthrolin-7-one product was favoured when R was an electron-withdrawing group (*e.g.* NO_2), whilst electron-donating moieties (*e.g.* OMe

Table 1 Product ratio from the reaction of phendione with L-phenylalanine methyl ester hydrochloride[a] over a range of temperatures

Reaction temperature (°C)	Ratio of the pyrido : oxazine products[b]
50	1 : 10
60	1 : 5.3
75	1 : 1.8
90	1 : 0.6

[a] Reactants were heated for 24 h in DMSO in a 1 : 1 mole ratio in the presence of a slight excess of 1 equivalence of *N*-methylmorpholine. [b] Yield ratio of pyrido : oxazine products is based on the intensity ratio of the UV/vis bands at 254 nm in the chromatogram of the LC-MS of the crude reaction mixtures.

Table 2 Product ratio from the reaction of phendione with L-phenylalanine methyl ester hydrochloride and its *para* substituted analogues[a]

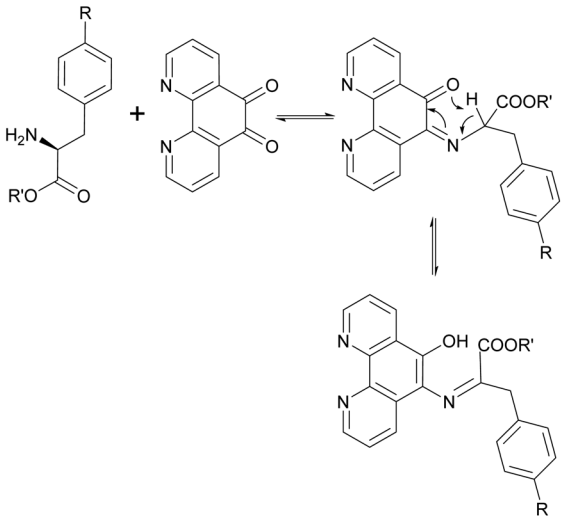
Amino acid ester	*p*-R group	Pyrido : oxazine yield ratio[c]
4-Nitro-L-phenylalanine methyl ester hydrochloride	NO_2	1 : 0.01
4-Nitro-L-phenylalanine methyl ester hydrochloride[b]	NO_2	1 : 0.03
4-Trifluoromethyl-L-phenylalanine methyl ester hydrochloride	CF_3	1 : 0.05
L-Phenylalanine methyl ester hydrochloride	H	1 : 1.8
4-Methoxy-L-phenylalanine methyl ester hydrochloride	OMe	1 : 9
L-Tyrosine methyl ester hydrochloride	OH	1 : 9

[a] Reactants were heated at 75 °C for 24 h in DMSO in a 1 : 1 mole ratio in the presence of a slight excess of 1 equivalence of *N*-methylmorpholine. [b] Same conditions except no *N*-methylmorpholine was added to the reaction. [c] Yield ratio of pyrido : oxazine products is based on the intensity ratio of the UV/vis bands at 254 nm in the chromatogram of the LC-MS of the crude reaction mixtures.

or OH) made the oxazine–phenanthroline the major product. When R = H, there was no significant selectivity for either product at this temperature. Also, no significant effect was observed in the ratio of pyrido : oxazine products in the study upon reducing the amount of base in the reaction. The first step in the reaction will be the formation of the Schiff base which, due to the acidity of the α-H atom, should be in equilibrium with its 1,5-prototropic tautomer (Scheme 2). We postulate this equilibrium as we have previously observed a H-bonding interaction at the same positions in a Schiff base, formed from phendione and a hydrazide, between the N–H of the hydrazide and the carbonyl group on the phenanthroline core.[10a] Moreover the carbonyl group of phendione accepts a H^+ fairly readily as in all our cyclisation reactions 1,10-phenanthrolin-5,6-diol is observed as a side-product.

Metal complexation of pyrido-ligand

The metal coordination ability of the pyrido-phenanthrolin-7-one-ligand, propyl 7-oxo-4-phenyl-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate (**1b**) was investigated by heating the ligand with $[Re(CO)_5Br]$ in toluene for 3 h under N_2. A very



Scheme 2 Formation of the Schiff-base intermediate in the keto–imine and enol–imine forms.

dark-purple precipitate was collected from the solution, using a centrifuge, and washed with toluene. The product was dried under vacuum and assigned to be [(**1b**) $(CO)_3Re(I)Br$] (**3**). Crystals were formed by slow evaporation of solvent from a methanol solution of the complex and the X-ray crystal structure data were obtained (Fig. 4). Complex **3** is a distorted octahedral complex and is shown to be the *facial* isomer and this is consistent with the three intense bands observed in the metal carbonyl stretching region of the IR spectrum.[22] The positions of Br1 and *trans* CO group (C33, O34) are disordered and these were modelled at 95 : 5% occupancy with restraints. See ESI Fig. S14.† There is a halogen–π interaction between Br1 and one ring of the tetracycle (C6, C8, C16, C17, C18) with a Br–centroid distance of 3.266(2) Å. There are several other weaker offset π–π interactions between the tetracycles ranging from 3.4–3.75 Å.

The ^1H NMR spectrum recorded of the complex in DMSO-d_6 would suggest that in solution at room temperature

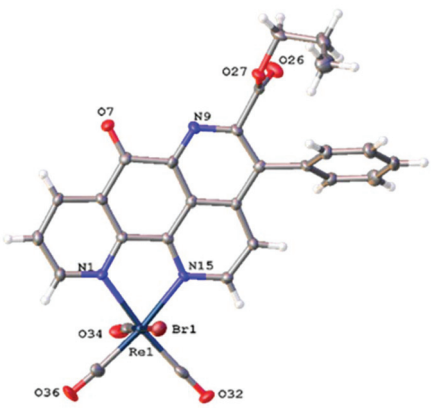


Fig. 4 Major structural moiety of **3** with 95% occupancy. See ESI† for further information. Atomic displacement shown at 50% probability. Heteroatoms labelled only for clarity.

the complex is fluxional as the peaks arising from the phenyl moiety are very broad in comparison to those of the unbound ligand. Preliminary studies indicate that, in contrast to many tricarbonyl rhenium(I) diimine complexes,[23] complex **3** is not luminescent. This may be explained as for **3** the MLCT absorption is shifted to long wavelengths (λ_{max} = 504 nm, MeOH) and previous researchers have proposed that non-luminescent [(diimine)$(CO)_3$Re(I)L] complexes occur due to low energy MLCT states resulting in an increase in probability of non-radiative decay.[24,25] The low energy absorptions of the pyrido-phenanthrol-7-one rhenium complexes may be of interest to researchers attempting to make rhenium complexes for photodynamic therapy which can be activated by red-NIR light.[26,27]

Conclusions

In summary we have developed a simple protocol to form a synthetic analogue of ascididemin from readily available starting materials and in moderate yields. This unusual cyclisation reaction can be promoted by increasing the reaction temperature and by introducing an electron-withdrawing group at the *para* position of the phenyl ring. The reaction has much scope and we intend to a produce a family of novel structural analogues and their rhenium(I) tricarbonyl complexes. It would be expected that the ligands and their complexes should exhibit anti-cancer activity.

Experimental

Materials and methods

All reagents used in chemical syntheses were purchased from Sigma Aldrich or Fluorochem and were used as supplied. NMR (Nuclear Magnetic Resonance) spectra were recorded on a Bruker Avance spectrometer operating at 500 MHz for ^{1}H nucleus and 125 MHz for the ^{13}C nucleus. The probe temperature was maintained at 25 °C. All spectra were referenced to the solvent residual signal. High Resolution Mass Spectrometry (HRMS) analysis was carried out at Maynooth University and University of Bath. In Maynooth University, ESI (electrospray ionization) mass spectra were collected on an Agilent-L 1200 Series coupled to a 6210 Agilent Time-of-Flight (TOF) equipped with both a positive and negative electrospray source. In University of Bath, the HPLC-ESI-TOF analysis was conducted using an electrospray time-of-flight (MicrOTOF) mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany), which was coupled to an Agilent HPLC stack (Agilent, Santa Clara, CA, United States) consisting of Agilent G1312A binary pump with G1329A autosampler and G1316A column oven. Infrared spectra were recorded as KBr discs in the region 4000–400 cm^{-1} or on a ATR-ZnSe crystal 4000–650 cm^{-1} on a PerkinElmer 100 series spectrometer. UV/vis were recorded in a 1 cm pathlength quartz cuvette on a PerkinElmer Lambda 35 spectrometer. The HPLC (High Performance Liquid Chromatography) spectra were extracted from LC-MS studies that were performed on an Agilent Technologies 1200 Series instrument consisting of a G1322A Quaternary pump and a G1314B UV detector (254 nm) coupled to an Advion Expression L Compact Mass spectrometer (ESI) operating in positive mode. Separations were performed on a Waters Xbridge OST 2.5 μm, 4.6 × 50 mm column (C18) operating at a flow rate of 0.2 mL min^{-1}. Separations were performed using a mobile phase of 0.1% formic acid in water (Solvent A) and 0.1% formic acid in acetonitrile (Solvent B) and a linear gradient of 0–100% B over 30 min.

Synthetic procedures

1,10-Phenanthroline-5,6-dione and the esters of the amino acid hydrochloride were synthesised using literature procedures.[28,29] All amino acid ester hydrochlorides used are previously reported compounds. The generalised procedure to synthesise the amino acid esters is as follows: Acetyl chloride (4.352 mL, 60.99 mmol) was added to a cold solution of the required alcohol (1.40 mol). To this, the amino acid (11.04 mmol) was added and the resulting clear colourless solution was refluxed for 3 h. The resulting solution was filtered and then reduced to 10 mL on a rotary evaporator. The product was precipitated *via* addition of 400 mL diethyl ether. The resulting suspension was filtered and washed with 3 × 50 mL portions of diethyl ether and dried under vacuum to yield white solids.

Synthesis of phenanthroline ligands

The appropriate amino acid ester hydrochloride salt (1.00 mmol) was dissolved in DMSO and to this solution, *N*-methylmorpholine (slight excess of 1 eq.) was added. The solution was heated to 75 °C while being constantly stirred and phendione was then added to give a bright yellow solution. After constant stirring at 75 °C for 24 h, a clear bright orange solution was observed and mixed with 125 mL of DCM. The organic layer was washed with 5 × 125 mL portions of H_2O and then dried over $MgSO_4$. The resulting DCM solution was condensed to dryness on a rotary evaporator to give the crude product.

Methyl 7-oxo-4-phenyl-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate (1a). L-Phenylalanine methyl ester hydrochloride (0.215 g, 1.00 mmol), *N*-methylmorpholine (0.121 mL, 1.10 mmol), phendione (0.210 g, 1.00 mmol), DMSO (25 mL), 24 h. A ^{1}H NMR spectrum recorded of the mixture showed signals for the desired product and for the corresponding phenanthroline–oxazine compound. The product mixture was dissolved in MeOH (3 mL) to which EtOAC (5 mL) was added and was left in the freezer (−20 °C) for 72 h. **1a** formed as bright yellow crystals (0.026 g, 7%); **m.p.**: decomp. @ 230 °C; **HRMS (ESI+)**: calculated *m*/*z* for $C_{22}H_{13}N_3O_3$: $(M + Na)^+$ 390.0849; found: $(M + Na)^+$ 390.0863; difference (ppm): 3.59; **LC-MS** rt (23.08 min, 97% purity); **IR (KBr, cm^{-1})** 3434, 1729, 1678, 1578, 1439, 1376, 1280, 1258, 1234, 1202, 1167, 1002, 702, 676, 607. **^{1}H NMR** (DMSO-d_6, 500 MHz): δ 9.12–9.09 (m, 1H, PhenH), 9.02 (d, J = 5.9 Hz, 1H, PhenH), 8.62 (dd, J = 7.9, 1.6 Hz, 1H, PhenH), 7.82 (dd, J = 7.9, 4.6 Hz, 1H, PhenH),

7.69–7.60 (m, 4H, PhenH + 3ArH), 7.51–7.46 (m, 2H, ArH), 3.70 (s, 3H, –OCH_3). **^{13}C NMR** (DMSO-d_6, 125 MHz): δ 181.0 (C═O), 166.7 (C═O), 155.3 (PhenC), 151.7 (PhenC), 150.7 (PhenC), 149.0 (PhenC), 147.5 (αC), 146.4 (PhenC═N), 138.5 (PhenC), 135.9 (PhenC), 135.4 (ArC), 133.5 (βC), 130.2 (ArC), 129.7 (ArC), 129.4 (PhenC), 129.2 (ArC), 126.6 (PhenC), 120.8 (PhenC), 119.8 (PhenC), 53.1 (–OCH_3).

Propyl 7-oxo-4-phenyl-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate (1b). L-Phenylalanine propyl ester hydrochloride salt (0.244 g, 1.00 mmol), *N*-methylmorpholine (0.121 mL, 1.10 mmol), phendione (0.210 g, 1.00 mmol), DMSO (25 mL) 24 h, a clear bright orange solution was observed and mixed with 125 mL of DCM. A ^{1}H NMR spectrum recorded of the mixture showed signals for the desired product and for the corresponding phenanthroline–oxazine compound. The crude product was dissolved in warm diethyl ether. The solution was allowed to cool and **1b** precipitated as a yellow solid and was collected by filtration. (0.073 g, 18%); **m.p.**: decomp. @ 230 °C; **HRMS (ESI+)**: calculated *m*/*z* for $C_{24}H_{17}N_3O_3$: $(M + Na)^+$ 418.1162; found: $(M + Na)^+$ 418.1164; difference (ppm) 0.5; **LC-MS** rt (26.51 min, 91% purity); **IR (KBr, cm^{-1})** 3434, 1728, 1676, 1579, 1441, 1378, 1281, 1259, 1232, 1200, 1169, 1001, 705, 679, 606. **^{1}H NMR** (DMSO-d_6, 500 MHz): δ 9.15–9.14 (m, 1H, PhenH), 9.07 (d, J = 5.9 Hz, 1H, PhenH), 8.66 (dd, J = 7.9, 1.6 Hz, 1H, PhenH), 7.85 (dd, J = 7.9, 4.6 Hz, 1H, PhenH), 7.71–7.62 (m, 4H, PhenH + 3ArH), 7.53–7.47 (m, 2H, ArH), 4.06 (t, J = 6.5 Hz, 2H, –OCH_2), 1.37 (dt, J = 7.3, 6.5 Hz, 2H, CH_2), 0.70 (t, J = 7.3 Hz, 3H, CH_3). **^{13}C NMR** (DMSO-d_6, 125 MHz): δ 181.1 (C═O), 166.5 (C═O), 155.3 (PhenC), 151.8 (PhenC), 150.8 (PhenC), 149.1 (PhenC), 148.0 (αC), 146.6 (PhenC═N), 138.5 (PhenC), 136.0 (PhenC), 135.0 (ArC), 133.6 (βC), 130.3 (ArC), 129.8 (ArC), 129.5 (PhenC), 129.3 (ArC), 126.6 (PhenC), 120.9 (PhenC), 119.8 (PhenC), 67.58 (–OCH_2), 21.6 (CH_2), 10.6 (CH_3).

Ethyl 4-(4-nitrophenyl)-7-oxo-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate (1c). 4-Nitro-L-phenylalanine ethyl ester hydrochloride salt (0.262 g, 1.00 mmol), *N*-methylmorpholine (0.121 mL, 1.10 mmol), phendione (0.210 g, 1.00 mmol), DMSO (25 mL), 24 h. The crude product was dissolved in 10 mL EtOH and allowed to stand overnight. The resulting suspension was filtered, washed with 3 × 10 mL portions of cold EtOH and dried under vacuum to yield a bright red solid (0.132 g, 30%); **m.p.** >250 °C; **HRMS (ESI+)**: calculated *m*/*z* for: $(C_{23}H_{14}N_4O_5 + Na)^+$ $[M + Na]^+$ 449.0856, found: 449.0878, difference (ppm) 4.89; **LC-MS**: rt (24.71 min, 90% purity); **IR (KBr, cm^{-1})** 3429, 2927, 1723, 1683, 1598, 1581, 1505, 1345, 1291, 1204, 1104, 859, 709. **^{1}H NMR** (DMSO-d_6, 500 MHz): δ 9.15 (dd, J = 4.6, 1.8 Hz, 1H, PhenH), 9.07 (d, J = 5.9 Hz, 1H, PhenH), 8.67 (dd, J = 7.9, 1.8 Hz, 1H, PhenH), 8.53–8.45 (m, 2H ArH), 7.86 (dd, J = 7.9, 4.6 Hz, 1H, PhenH), 7.83–7.78 (m, 2H, ArH), 7.61 (d, J = 5.9 Hz, 1H PhenH), 4.19 (q, J = 7.1 Hz, 2H, –OCH_2), 1.04 (t, J = 7.1 Hz, 3H, CH_3). **^{13}C NMR** (DMSO-d_6, 125 MHz): δ 181.1 (C═O), 165.6 (C═O), 155.4 (PhenC), 151.7 (PhenC), 150.8 (PhenC), 149.3 (PhenC), 148.4 (ArC), 147.3 (αC), 146.8 (PhenC═N), 141.0 (ArC), 138.5 (PhenC), 136.1 (PhenC), 134.10 (βC), 131.8 (ArC), 129.5 (PhenC), 126.7 (PhenC), 124.2 (ArC), 120.8 (PhenC), 119.7 (PhenC), 62.3 (–OCH_2), 14.0 (CH_3).

Propyl 2 phenyl-2*H*-[1,4]oxazino[2,3-*f*][1,10]phenanthroline-3-carboxylate (2). L-Phenylalanine propyl ester hydrochloride (0.243 g, 1.00 mmol), *N*-methylmorpholine (0.121 mL, 1.10 mmol), phendione (0.210 g, 1.00 mmol), DMSO (25 mL), 24 h. A ^{1}H NMR recorded of the reaction mixture showed signals which are indicative of the formation of both the phenanthroline–oxazine and the pyrido-phenanthrolin-7-one products. The crude product was dissolved in warm diethyl ether. The solution was allowed to cool and **2** slowly crystallised from the mixture as orange crystals and was collected by filtration. (0.011 g, 3%) **HRMS (ESI+)**: calculated *m*/*z* for: $(C_{24}H_{19}N_3O_3 + H)^+$ $[M + H]^+$ 398.1499, found: 398.1500, difference (ppm) 0.30. **IR (KBr, cm^{-1})** 3429, 2927, 1723, 1683, 1598, 1581, 1505, 1345, 1291, 1204, 1104, 859, 709. **^{1}H NMR** (DMSO-d_6, 500 MHz) δ 9.12 (dd, J = 4.3, 1.8 Hz, 1H, PhenH), 9.02 (dd, J = 4.3, 1.7 Hz, 1H, PhenH), 8.84 (dd, J = 8.3, 1.7 Hz, 1H, PhenH), 8.62 (dd, J = 8.3, 1.8 Hz, 1H, PhenH), 7.83 (dd, J = 8.3, 4.3 Hz, 1H, PhenH), 7.79 (dd, J = 8.3, 4.3 Hz, 1H, PhenH), 7.43–7.37 (m, 2H, ArH), 7.34–7.26 (m, 3H, ArH), 6.70 (s, 1H, βH), 4.27 (m, 2H, OCH_2), 1.75–1.60 (m, 2H, CH_2), 0.91 (t, J = 7.4 Hz, 3H, CH_3). **^{13}C NMR** (DMSO-d_6, 125 MHz): δ 162.5 (C═O), 152.1 (PhenCH), 150.4 (αC), 149.2 (PhenCH), 146.9 (PhenC), 142.8 (PhenC), 138.8 (PhenC), 135.5 (ArC), 131.4 (PhenCH), 130.3 (PhenCH), 130.1 (ArC), 129.6 (ArC), 127.5 (Ar C), 126.4 (PhenC), 124.6 (PhenCH), 124.3(PhenCH), 122.2(PhenC), 121.5 (PhenC), 72.6 (βC), 67.8 (–OCH_2), 21.9 (CH_2), 10.6 (CH_3).

***fac*-Bromotricarbonyl (propyl 7-oxo-4-phenyl-7*H*-pyrido[4,3,2-*de*][1,10]phenanthroline-5-carboxylate) rhenium(I) (3).** $Re(CO)_5Br$ (20 mg, 0.05 mmol) and **1b** (20 mg, 0.05 mmol) were added to a 10 mL pressure tube. Dried degassed toluene (10 mL) was added to the tube and N_2 gas was bubbled slowly through the solution for 30 min. A stirring bead was added to the tube and the tube was sealed and then heated for 3 h at 110 °C with stirring. The solution went very dark purple and the dark purple product was collected using a centrifuge and washed with toluene and the centrifuge collection was repeated. The residual toluene was removed under vacuum (26 mg, 70%). **HRMS (ESI+)**: calculated *m*/*z* for: $(C_{27}H_{17}BrN_3O_6Re + Na)^+$ $[M + Na]^+$ 767.9750, found:767.9724, difference (ppm) 3.4. **IR (ATR, cm^{-1})** 2021 (Re–CO), 1922 (Re–CO), 1900 (Re–CO), 1736 (propyl ester CO), 1690 (phen–CO). **^{1}H NMR** (DMSO-d_6, 500 MHz): δ 9.41 (d, J = 5.5 Hz, 1H, PhenH), 9.15 (d, J = 6.5 Hz, 1H, PhenH), 8.97 (d, J = 7.9, 1H, PhenH), 8.12 (dd, J = 7.9, J = 5.5 1H, PhenH), 7.96 (d, J = 6.5 Hz, 1H, PhenH), 7.67(s(br), 3H, ArH), 7.56 (s(br), 2H, ArH), 4.09 (t, J = 6.4 Hz, 2H, –OCH_2), 1.49–1.28 (m, 2H, CH_2), 0.70 (t, J = 7.4 Hz, 3H, CH_3). **^{13}C NMR** (DMSO-d_6, 125 MHz): δ 197.1 (Re–CO), 196.9 (Re–CO), 187.9 (Re–CO), 178.0 (phen–CO), 166.0 (ester–CO), 157.3 (PhenCH), 154.3 (PhenC), 153.8 (PhenC), 150.4 (PhenCH), 149.6(αC), 146.2 (PhenC═N), 138.2(PhenCH), 138.1 (PhenC), 134.7 (βC), 132.6 (ArC), 132.1 (PhenC), 130.4 (PhenCH), 130.2 (ArC × 3), 129.5(ArC × 2), 124.4 (PhenCH), 121.5 (PhenC), 67.9 (OCH_2), 21.5 (CH_2), 10.5 (CH_3).

Crystallography

X-Ray crystallography: Data for samples **1a**, **2** and **3** were collected on a Bruker D8 Quest ECO (**1a**) using Mo Kα (λ = 0.71073 Å) and a APEX DUO Kappa system (**3** and **2**) using Cu Kα (λ = 1.54184 Å) radiation. Samples were mounted on a MiTeGen microloop and data collected at 100(2) K using an Oxford Instruments Cryostream and Cobra low temperature device. Bruker APEX (Bruker 2016) software was used to collect and reduce data and determine the space group. Structures were solved with the XT[30] structure solution program using Intrinsic Phasing and refined with the XL[31] refinement package using Least Squares minimisation with Olex2.[32] Absorption corrections were applied using SADABS (Bruker 2016/2). Crystal data, details of data collection and refinement are given in Table S1.† In structure **3**, Br1 and *trans* CO groups (C33, O34) were disordered and modelled in two positions with 95 : 5% occupancy with restraints (DFIX, SADI, SIMU). In **2**, the C9 chiral centre is represented as S. As this is a centrosymmetric space group ($P\bar{1}$), the structure is a racemate.

CCDC 1941514–1941516† contains the supplementary crystallographic data for this paper.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

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