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Syntheses, structures and tautomers of 2,5-disubstituted pyrroles

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The preparation of diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (**2**) from diethyl 3,6-dioxooctanedioate (**1**) is detailed, as is the subsequent conversion of **2** into its tautomer, diethyl pyrrole-2,5-diacetate (**3**), by acid catalysis. Alternatively, base hydrolysis of **2** gives pyrrole-2,5-diacetic acid (**4**) in good yield as long as the reaction solution is subsequently acidified to pH = 1 before extraction. In D_2O solution, in the absence of added base, the pyrrole ring C–H protons are rapidly exchanged for deuterons. The X-ray structures of **2** and **4** are reported and confirm the earlier prediction, made primarily on the basis of the ^{1}H NMR data, that **2** is a pyrrolidine tautomer while **4** is a pyrrole tautomer. Hydrogen bonding, intramolecular in the case of **2** and intermolecular in the case of **4**, is a feature of both structurally characterised compounds.

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Introduction

Our interests lie in the development of porphyrin-like polydentate ligands that provide access to *di- and polymetallic first row transition metal* complexes with interesting properties. Whilst in principle the expanded porphyrins, developed by Sessler and co-workers,[1] are capable of binding more than one first row transition metal ion, in practice very few complexes of this type have been prepared and structurally characterised.[2] In an exciting recent development, Furuta and co-workers have extended this concept to the preparation and structural characterisation of a doubly N-confused expanded porphyrin and its dinickel(II) and dicopper(II) complexes.[3] Mertes and co-workers prepared another porphyrin-like macrocycle system in 1984, which they showed could generate catalytically active dimetallic first row transition metal complexes; however, this system has not been fully exploited.[4] All three of these classes of macrocycle are generated using polypyrrole ligand precursors.

Given our experience with Schiff-base ligands,[5] 2,5-diformylpyrrole (**I**, Fig. 1) appears, on first inspection, to be a suitable, non-polypyrrole, ligand precursor. Indeed, in the mid 1980's Fenton and co-workers prepared a series of Schiff-base macrocycles from the condensation of head unit **I** and a variety of α,ω-alkanediamines: use of 1,2-diaminoethane and 1,3-diaminopropane gave mononuclear copper(II) macrocyclic complexes (Fig. 1, **II**) whereas 1,4-diaminobutane, 1,5-diaminopentane and 1,6-diaminohexane gave dinuclear copper(II) macrocyclic complexes (Fig. 1, **III**).[6,7] However, the X-ray crystal structure of the mononuclear copper(II) complex of the macrocycle prepared from **I** and 1,3-diaminopropane illustrates a problem associated with using this particular head unit for coordination to a first row transition metal ion.[6] The single copper(II) ion is coordinated to one side of the macrocycle only; specifically it is coordinated to both of the pyrrole nitrogen atoms and to only two of the four possible imine nitrogen atoms (Fig. 1, **II**, $n = 3$). Both of the potentially tridentate pyrrole diimine head units adopt a mutually *trans* arrangement with only one of the two imine nitrogen atoms bound. Due to the presence of the five-membered pyrrole ring and the five-membered chelate ring formed, the N_{pyrl}–M–N_{imine} binding angles are much less than 90° [79.6(11)° and 84.3(11)° in **II** when $n = 3$]. This probably prevents the pyrrole diimine units from adopting a mutually *cis* arrangement and acting as tridentate donor moieties. Consistent with this, in the proposed structure of the dinuclear copper(II) macrocycles **III** it was suggested that the two imine groups of each pyrrole diimine head unit again adopt a mutually *trans* conformation, and that each of the copper(II) ions is coordinated to a pyrrole nitrogen atom and only one imine nitrogen atom of the pyrrole diimine unit, leaving the other imine nitrogen atom un-coordinated (Fig. 1, **III**), as was the case in the structurally characterised mononuclear copper complex **II**.

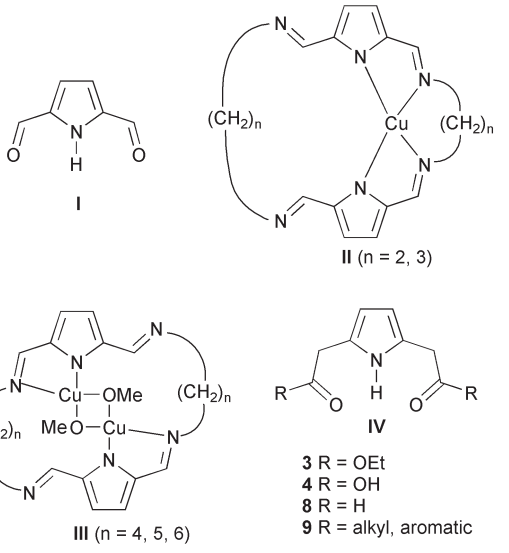

Fig. 1 2,5-Diformylpyrrole **I**, two classes of copper(II) Schiff-base macrocyclic complexes derived from **I**, **II** and **III**, and the class of head unit targeted in this research, **IV**.

Therefore, in order to resolve this problem, which is specific to first row transition metal ions,[8] our interest has focussed on alternative head units of the general type **IV** (Fig. 1),[9] with an extra carbon atom in the arms to increase the resulting N_{pyrl}–M–N_{imine} angle to *ca.* 90°. This should allow the preparation of di- and polymetallic complexes of

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ligands derived from **IV** in which the head unit acts as an all-*cis* tridentate donor.

Ideally, the dialdehyde or diketone head units **8** and **9** (Fig. 1, **IV**), which could in principle be used to synthesise both acyclic and macrocyclic Schiff base ligands and complexes, would be prepared and used, but these compounds are completely unknown in the literature, and may well be rather unstable in any case. Hence our initial targets were instead the literature compounds, the diester **3** and the dicarboxylic acid **4** (Fig. 1, **IV** and Fig. 2). Access to compounds **3** and **4** is *via* compound **2**, the pyrrolidine tautomer of **3** (Fig. 2). Two synthetic routes have been reported for the preparation of diethyl pyrrole-2,5-diacetate (**3**), however, this compound was subsequently reported to be in the pyrrolidine form, diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (**2**), rather than in the pyrrole form, **3** (see below).[9–11]

The shortest route to **2** is the two-step synthesis from pyrrole (**5**), reported by Badger, Elix and Lewis in 1967 (Fig. 2).[9] This route, which is similar to that used for the preparation of diethyl *N*-methylpyrrole-2,5-diacetate,[12] involves the introduction of one ester side chain to pyrrole (**5**), isolation of the resulting ethyl pyrrole-2-acetate and then introduction of the second ester side chain using the same methodology. Both steps require the use of a potentially explosive chemical, ethyl diazoacetate, and this, together with the low overall yield of 8% (36.5% first step[12] and 21% second step[9]), made this method unattractive.

An alternative synthetic route to **2**, involving ring closure of the suitably substituted acyclic precursor diethyl 3,6-dioxooctanedioate, **1**, was outlined by Willstätter and Bommer in 1920,[10] although no experimental details were given, an omission we rectify here. Compound **1** is not commercially available but two syntheses have been reported.[13–15] In 1920 Willstätter and Pfannenstiel[13] developed a four-step preparation of **1** from **6** (Fig. 2), which included an unattractive, low yielding (12%) electrolysis reaction as the final step. In 1982 Johnson *et al.*[14] reported a one-pot reaction for the preparation of dimethyl 3,6-dioxooctanedioate, the methyl analogue of **1**, in 76.5% yield. Subsequently, this route was used by Flitsch and Lüttig[15] to prepare **1** from **7** in 39% overall yield (Fig. 2). An attractive feature of this synthesis of **1** is that mild reaction conditions are employed and the reported overall yield of **1** is acceptable.

Willstätter *et al.*[10] and Badger *et al.*[9] had originally assumed that the product of their respective reactions was the pyrrole tautomer **3**, however, Flitsch and Peters[11] subsequently reported that the product is in fact the pyrrolidine tautomer **2** (Fig. 2). Their comparison of the ^{1}H NMR spectrum and melting point of **2** with the data obtained for **3** gave very clear support for this assertion. Here we confirm this beyond all doubt by reporting the results of the single crystal X-ray structure determination carried out on **2**.

We detail here, for the first time, the synthesis of diethyl pyrrole-2,5-diacetate (**3**). Also, along with the structure of diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (**2**), the structure of pyrrole-2,5-diacetic acid (**4**) and the observed exchange of the C–H protons on the pyrrole ring of **4** with deuterons from D_2O are presented and discussed.

Results and discussion

Synthesis

Diethyl 3,6-dioxooctanedioate (**1**) was synthesised, *via* a slight modification of the reported procedure,[14,15] in an improved yield. The crude product obtained can be used in the following step, ring cyclisation of **1** to form **2**, without further purification; however, if desired, it can be purified by recrystallisation from diethyl ether–pentane.

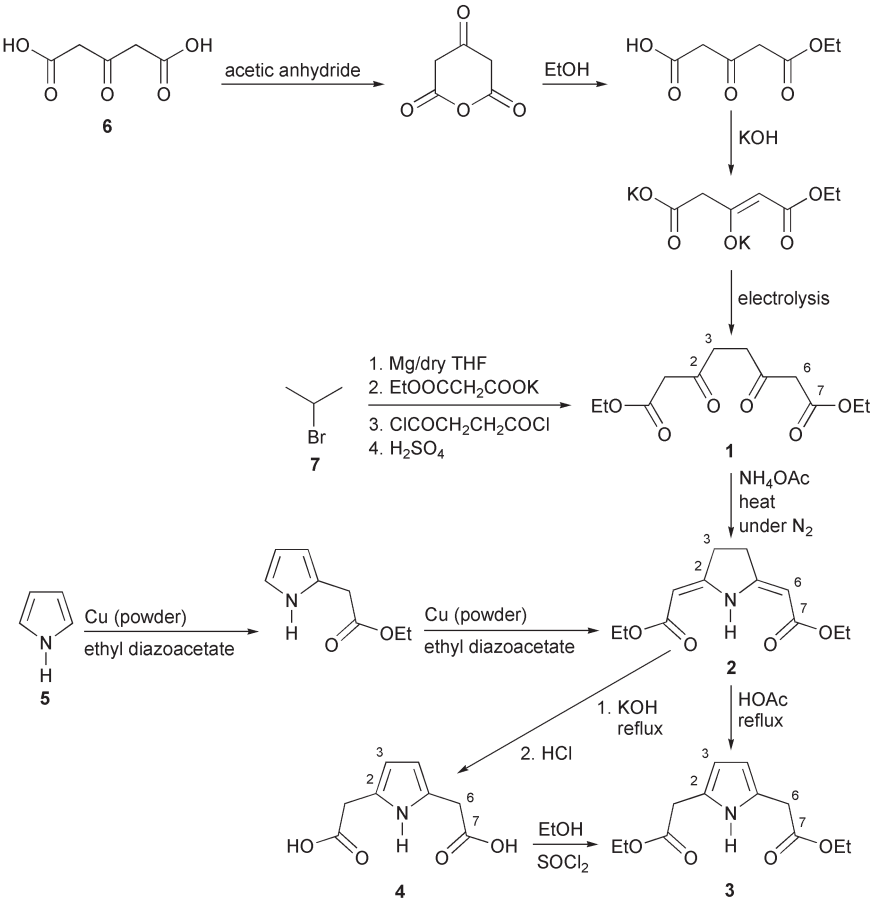

Fig. 2 Synthetic scheme for the preparation of **1**, **2**, **3** and **4**.

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The condensation of the 1,4-diketone **1** with ammonium acetate, as outlined by Willstätter and Bommer,[10] yields **2** (Fig. 2). The necessary synthetic details have now been developed and optimised for this reaction and are described here. A four-fold excess of ammonium acetate is mixed with **1** and the solid mixture ground before it is heated, under nitrogen, at 55 °C for 1 h and then at 85 °C for 40 min. After cooling to room temperature and adding dichloromethane, the excess ammonium acetate was removed by washing with water. Subsequent evaporation of the organic phase gave **2** as a brown solid. Recrystallisation of the crude product from ethanol afforded **2** as colourless crystals in 72% yield.

Diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (**2**) was not expected to react like a typical ester as it is a vinylic ester, which means that there are resonance contributors that reduce the double bond character of the carbonyl group (Fig. 3), which in turn makes nucleophilic substitution difficult. Consistent with this expectation, attempts to form amides, by reacting **2** with several aliphatic amines [including *N*,*N*-dimethylethylenediamine, 2-aminomethylpyridine and 2-(2-aminoethyl)pyridine], were not successful. Therefore, our interest then turned to cleanly converting the pyrrolidine tautomer **2** into the pyrrole tautomer **3** (Fig. 2). Flitsch and Kappenberg[16] had reported that such conversions could be done to produce related N-substituted pyrrole-2,5-disubstituted derivatives, either by heating the solid pyrrolidine tautomer or by acid catalysis, but did not give full experimental details. Both methods were examined. No conversion was observed on directly heating **2** to 150 °C for 2.5 h. Some conversion of **2** to **3** did occur when **2** was dissolved in trifluoroacetic acid and stirred at room temperature, however, a complex mixture of products formed, which made purification of **3** difficult. On further investigation it was found that the utilisation of a weak acid, acetic acid, is central to obtaining a clean conversion reaction: **2** is fully converted into **3**, without the formation of any byproducts, when **2** is dissolved in glacial acetic acid and the resulting solution heated at reflux for 10 min. Evaporation of the acetic acid gives **3** as a pale yellow oil in high yield (93%).

Pyrrole-2,5-diacetic acid (**4**) was prepared *via* a slight modification of the procedure reported by Badger *et al.*[9] Careful base hydrolysis of diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (**2**) gives pure pyrrole-2,5-diacetic acid (**4**) in 85% yield, not 54% as originally reported (Fig. 2). It should be noted that the pH plays a vital role in achieving the improved yield of **4**. When the basic solution is acidified with concentrated hydrochloric acid the pH must be taken down to 1, as any higher pH results in reduced yields. This clean (by microanalysis and NMR spectra) product can be used in the following step, to produce diethyl pyrrole-2,5-diacetate (**3**), without further purification, but if desired it can be recrystallised from diethyl ether–pentane.

As originally reported by Flitsch and Peters,[11] a comparison of the ^{1}H NMR spectra of **2** and **3** clearly shows that the conversion has occurred, the most significant change being the shift of the two singlet signals at 4.91 and 2.73 ppm in the ^{1}H NMR spectrum of **2** to a singlet at 3.62 ppm and a doublet at 5.91 ppm, respectively, in the ^{1}H NMR spectrum of **3** (Table 1). The ^{13}C NMR spectra and the change in state, from solid **2** to oil **3**, are also consistent with a conversion having taken place.

The NMR spectra for dicarboxylic acid **4** were obtained in D_2O in the presence of KOH and were referenced to external DMSO (at 2.71 ppm for ^{1}H NMR and 39.5 ppm for ^{13}C NMR). A comparison of the ^{1}H NMR spectra of **2**, **3** and **4** (Table 1) reveals that this compound is clearly in the pyrrole, as opposed to pyrrolidine, form: the chemical shifts of the C–H ring protons, H_3, and the acetyl protons H_6 ($CH_2C{=}O$) in **4** are similar to those of the corresponding protons on diethyl pyrrole-2,5-diacetate (**3**) but are, as expected, significantly different from those of the corresponding protons in diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (**2**). Interestingly, **4** is the pyrrole tautomer even though it was obtained from the base hydrolysis of the pyrrolidine form of the diester, **2**. This is conclusively proven by the single crystal X-ray structure determination (see below).

When the ^{1}H NMR spectrum of **4** was obtained in D_2O without added KOH a rapid decrease in the relative integration of the H_3 pyrrole ring proton signal at 5.81 ppm (Fig. 4) to that of the H_6 methylene proton signal was observed over time. By analogy with a study carried out on pyrrole-2-acetic acid and its cobalt complex in acid solution, by Sargeson and coworkers,[17] this is believed to be due to these ring protons exchanging with deuterons of the solvent, deuterated water (Fig. 4). After just one hour approximately 95% of the protons had exchanged with deuterons. This was confirmed by the total absence of the H_3 signal from the ^{1}H NMR spectrum obtained immediately after dissolving **4** in acidified (DCl) D_2O. In this case the H_3 ring protons have been extremely rapidly, and fully, exchanged by deuterons. This exchange reaction does not occur in basic solution, hence routine

Table 1 Comparison of the ^{1}H NMR chemical shifts δ_H of **2**, **3** and **4**.

Compound	H_3 (ring)	H_6 (α–$CH_2C{=}O$ or=CHC=O)	Tautomer
2[a]	2.73	4.91	Pyrrolidine
3[a]	5.91	3.62	Pyrrole
4[b]	5.81	3.40	Pyrrole

[a] Run in $CDCl_3$. [b] Run in D_2O/KOH.

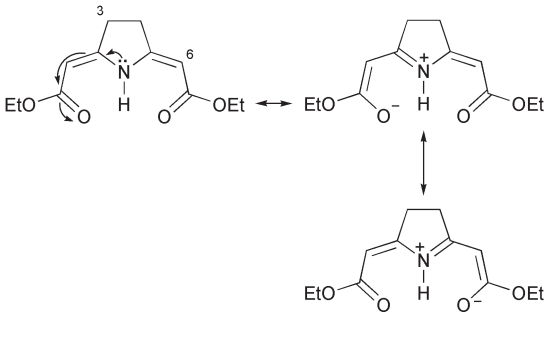

Fig. 3 The resonance contributors of **2**.

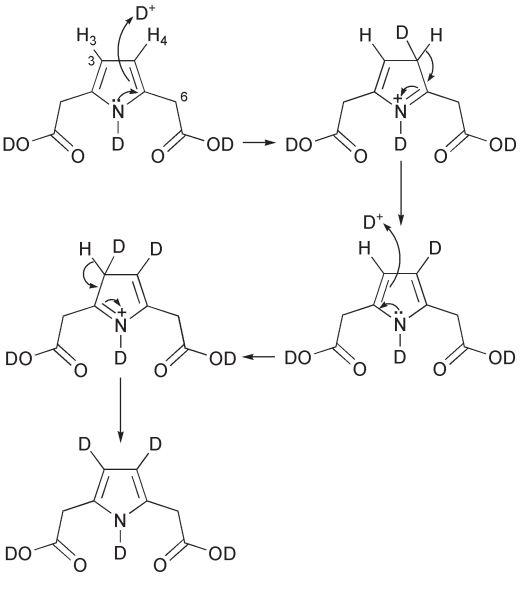

Fig. 4 The exchange of pyrrole ring protons with deuterons in D_2O.

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NMR spectra were obtained in D_2O/KOH. A potentially useful consequence of this observed exchange is that electrophilic substitution reactions, such as the nitration reaction observed for pyrrole-2-acetic acid by Sargeson and co-workers,[17] should be possible for **4**. This could be used in the future to introduce groups at C_3 and C_4, for example electron-withdrawing groups, to fine-tune the properties of this pyrrole derivative and its complexes.

Both NMR studies and microanalysis results confirm that **4** is stable in the solid state for weeks under argon in a refridgerator although it does discolour slowly over this time. For completeness it has been demonstrated that the pyrrole diester **3** can also be obtained by the reaction of pyrrole-2,5-diacetic acid (**4**) with ethanol in the presence of a few drops of thionyl chloride (Fig. 2).

X-Ray crystal structures of 2 and 4

The X-ray crystal structure of **2** has been determined (Fig. 5, Table 2) and confirms beyond all doubt that the heterocyclic ring is in the pyrrolidine, not pyrrole, form. This is clear both from an inspection of the bond lengths and angles of the atoms in the ring and arms and from the fact that appropriate hydrogen atoms were readily located from a difference Fourier map.

The molecule is quite flat, with the maximum deviation from the pyrrolidine ring mean plane, of 0.52 Å, being observed for C(19). The two carbonyl groups adopt a mutually *cis* conformation with respect to the pyrrolidine ring nitrogen atom N(1).

As expected, the bonds to the pyrrolidine nitrogen atom [N(1)–C(2) = 1.3692(14) Å and N(1)–C(5) = 1.3711(14) Å] are significantly shorter in **2** than in pyrrolidines such as *trans*-(2*S*,5*S*)-(1,1-diphenylmethyl)pyrrolidine (1.468 Å),[18] due to the resonance structures of the conjugated N–C=C–(C=O)–O moiety (Fig. 3) leading to each N–C bond in **2** having partial double bond character. Applying the Cruickshank and Sparks treatment[19] (assuming 1.42 Å for the C–N bond involving trigonally hybridised atoms and 1.27 Å for the C=N double bond[20]), the π-bond orders for these two N–C bonds are calculated to be 0.28 for N(1)–C(2) and 0.27 for N(1)–C(5). Similarly, in the mono-substituted analogue of **2**, ethyl 2-(2-pyrrolidineylidene)-acetate,[21] the N–C bond involved in the conjugated structure is short [1.313(4) Å, π-bond order 0.65] compared with the N–C bond that is not involved [N(1)–C(5) = 1.466(5) Å, single bond].

Intramolecular hydrogen bonds are formed between the pyrrolidine N–H and the two C=O groups of the ester (Fig. 5). The hydrogen bond distances, 2.73 Å for N(1)···O(1) and 2.78 Å for N(1)···O(3), are both slightly shorter than the corresponding hydrogen bond distance of 2.81 Å in the pyrrolidine monoester.[21]

The X-ray crystal structure determination carried out on **4** (Fig. 6 and 7, Table 3) confirms that it is a pyrrole tautomer, even though it was obtained from the base hydrolysis of the pyrrolidine form of the diester. Once again this is clear from both an inspection of the bond lengths and angles of the atoms in the ring and arms and from the fact that appropriate hydrogen atoms were located from a difference Fourier map.

Table 2 Bond lengths (Å) and angles (°) for **2**

N(1)–C(2)	1.3692(14)	C(2)–N(1)–C(5)	114.61(9)
N(1)–C(5)	1.3711(14)	C(16)–C(2)–N(1)	125.56(11)
C(2)–C(16)	1.3451(16)	C(16)–C(2)–C(3)	127.03(11)
C(2)–C(3)	1.5048(16)	N(1)–C(2)–C(3)	107.41(10)
C(3)–C(4)	1.5337(17)	C(2)–C(3)–C(4)	104.94(9)
C(4)–C(5)	1.5062(16)	C(5)–C(4)–C(3)	104.29(9)
C(5)–C(6)	1.3449(16)	C(6)–C(5)–N(1)	125.41(10)
C(6)–C(7)	1.4431(16)	C(6)–C(5)–C(4)	126.78(10)
C(7)–O(1)	1.2204(14)	N(1)–C(5)–C(4)	107.80(10)
C(7)–O(2)	1.3490(14)	C(5)–C(6)–C(7)	121.52(10)
O(2)–C(8)	1.4453(15)	O(1)–C(7)–O(2)	121.95(11)
C(8)–C(9)	1.4869(19)	O(1)–C(7)–C(6)	126.17(11)
C(16)–C(17)	1.4451(17)	O(2)–C(7)–C(6)	111.88(10)
C(17)–O(3)	1.2166(14)	C(7)–O(2)–C(8)	115.73(9)
C(17)–O(4)	1.3485(14)	O(2)–C(8)–C(9)	107.11(11)
O(4)–C(18)	1.4425(15)	C(2)–C(16)–C(17)	122.74(10)
C(18)–C(19)	1.5060(17)	O(3)–C(17)–O(4)	122.50(11)
		O(3)–C(17)–C(16)	126.02(11)
		O(4)–C(17)–C(16)	111.48(10)
		C(17)–O(4)–C(18)	116.85(9)
		O(4)–C(18)–C(19)	106.26(10)

The distances and angles observed for the pyrrole ring of **4** correspond closely to those found in pyrrole itself.[22] Consistent with this, the π-bond orders for the C(2)–C(3) and C(4)–C(5) bonds in **4**, 0.78 and 0.76, respectively, are similar to that observed in pyrrole (0.82; these two bonds are constrained to be exactly equivalent by symmetry).

The two carboxylic acid groups adopt a mutually *trans* conformation with respect to the mean plane of the pyrrole ring: one carboxylic acid group [containing C(7)] is above the pyrrole ring whilst the other [containing C(17)] is below it. The C(16)C(17)O(3)O(4) mean plane is almost orthogonal to the pyrrole ring mean plane (dihedral angle of 85.9°). Likewise, the mean plane of the other carboxylic acid group, C(6)C(7)O(1)O(2), makes an angle of 73.2° with the pyrrole ring mean plane.

There are two types of hydrogen bonds in **4** (Fig. 7). Strong double hydrogen bonds, O(2)···O(3) (2.65 Å, 169.5°) and O(1)···O(4) (2.60 Å, 175.0°), are observed between self-complementary carboxylic acid groups of adjacent molecules and this gives rise to zigzag polymeric chains of pyrrole-2,5-diacetic acid molecules. Weaker hydrogen bonds, N···O (3.01 Å, 174.0°), are observed between the pyrrole N–H of one

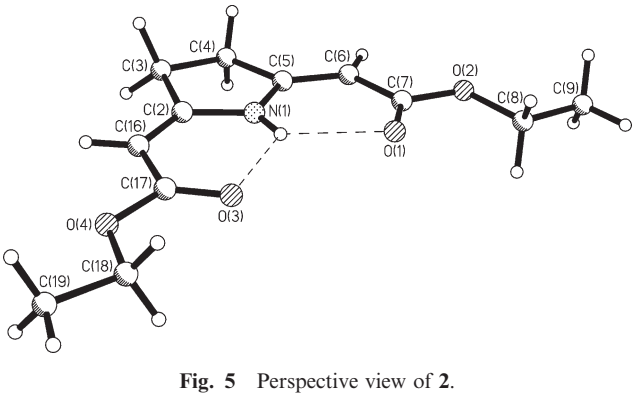

Fig. 5 Perspective view of **2**.

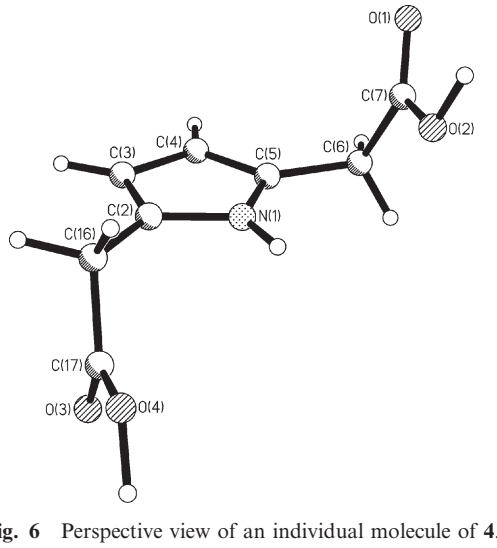

Fig. 6 Perspective view of an individual molecule of **4**.

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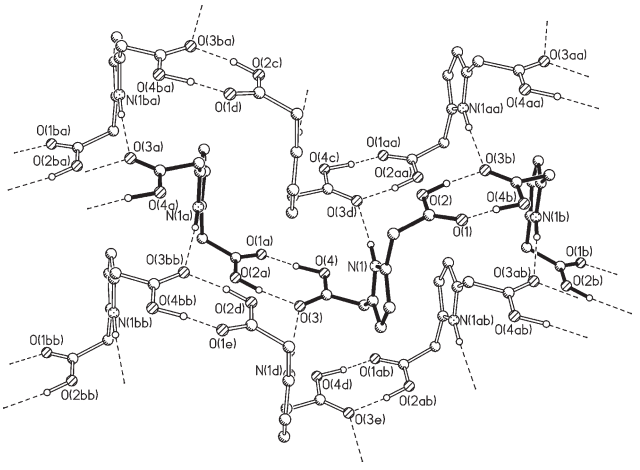

Fig. 7 Perspective view of **4** showing the chains of molecules held together by two types of intermolecular hydrogen bonding.

polymeric chain and the carbonyl oxygen atom [O(3)] of one of the two independent carboxylic acid groups in another chain, providing links between the neighbouring zigzag chains. The O–H···O and N–H···O hydrogen bond distances observed are in the normal ranges for such interactions.[23]

Conclusion

Procedures for the preparation of compounds **2** and **3** have been detailed here for the first time. The pyrrolidine tautomer **2** was cleanly converted to the pyrrole tautomer **3** by acid catalysis. The single crystal X-ray structures of **2** and **4** conclusively confirm that **2** is the pyrrolidine tautomer, not the pyrrole tautomer, while **4** is a pyrrole tautomer even though it was obtained from the base hydrolysis of **2**. The crystal structure of **4** also shows that it is a polymer formed by linking individual molecules together *via* two types of intermolecular N–H···O hydrogen bonds. The observed exchange of protons on the C_3 and C_4 atoms of the pyrrole ring of **4** with deuterons from D_2O is reported. It is noted that in the future this could be used to introduce groups at C_3 and C_4, for example, electron-withdrawing groups, to fine-tune the properties of this pyrrole derivative.

Experimental

General

^{1}H and ^{13}C NMR spectra were recorded on a Varian 500 MHz Inova spectrometer, unless otherwise stated, in which case they were recorded on a 300 MHz Inova NMR spectrometer. ^{1}H and ^{13}C spectra in $CDCl_3$ were referenced to $CHCl_3$ at 7.26 and 77.08 ppm, respectively. Infrared spectra were obtained on a Perkin Elmer Spectrum BX FT-IR System as either pressed KBr discs or as a smear on a KBr plate (oils). MS spectra were collected on an EI/CI/FAB Kratos MS80RFA, or on an ESI/APCI MicroMass LCT coupled to a Waters 2790 LC with a 996 PDA, or on a Shimadzu QP8000 alpha with APCI/ESI probes. Melting points were determined on a Mettler Toledo FP62 melting block or Leica melting point bench and are not corrected. Elemental analyses were carried out by the Campbell Microanalytical Laboratory at the University of Otago. HPLC grade tetrahydrofuran (THF) was used as supplied ($H_2O < 0.05\%$) as dry THF. All other chemicals and solvents were of reagent grade and were used as received.

Table 3 Bond lengths (Å) and angles (°) for **4**.

N(1)–C(5)	1.372(3)	C(5)–N(1)–C(2)	109.18(17)
N(1)–C(2)	1.378(3)	C(3)–C(2)–N(1)	107.66(18)
C(2)–C(3)	1.362(3)	C(3)–C(2)–C(16)	130.92(19)
C(2)–C(16)	1.495(3)	N(1)–C(2)–C(16)	121.38(19)
C(3)–C(4)	1.421(3)	C(2)–C(3)–C(4)	107.83(19)
C(4)–C(5)	1.364(3)	C(5)–C(4)–C(3)	107.18(19)
C(5)–C(6)	1.502(3)	C(4)–C(5)–N(1)	108.14(18)
C(6)–C(7)	1.496(3)	C(4)–C(5)–C(6)	130.3(2)
C(7)–O(1)	1.224(2)	N(1)–C(5)–C(6)	121.40(18)
C(7)–O(2)	1.305(3)	C(7)–C(6)–C(5)	108.88(15)
C(16)–C(17)	1.504(3)	O(1)–C(7)–O(2)	123.14(18)
C(17)–O(3)	1.222(2)	O(1)–C(7)–C(6)	122.8(2)
C(17)–O(4)	1.298(3)	O(2)–C(7)–C(6)	114.02(17)
		C(2)–C(16)–C(17)	113.41(15)
		O(3)–C(17)–O(4)	122.75(18)
		O(3)–C(17)–C(16)	122.36(19)
		O(4)–C(17)–C(16)	114.89(17)

Syntheses

Diethyl 3,6-dioxooctanedioate (1). 1 was prepared according to the literature procedure[14,15] except that distilled water (400–500 mL) was added to dissolve the white solid before extraction of the aqueous phase with diethyl ether. If desired, the crude product can be purified by recrystallisation from diethyl ether–pentane (2:1, v/v). Yield 59–68%. Anal. found: C, 56.09; H, 7.06; calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02%. Mp 46 °C (lit: 46–47 °C[10,15]). IR (KBr disc) ν_{max}/cm^{-1}: 1740, 1707. δ_H ($CDCl_3$): 4.19 ($4H_8$, q, $J = 7.09$), 3.48 ($4H_6$, s), 2.85 ($4H_3$, s), 1.26 ($6H_9$, t, $J = 7.16$). δ_C ($CDCl_3$): 201.1 (C_2), 167.0 (C_7), 61.5 (C_8), 49.3 (C_6), 36.4 (C_3), 14.1 (C_9). EI-MS m/z: 258 $[M]^+$.

Diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (2)[10]. Diethyl 3,6-dioxooctanedioate (**1**; 2.58 g, 10.00 mmol) and ammonium acetate (3.08 g, 40.00 mmol) were mixed together and ground, then placed in a 100 mL round-bottomed flask under nitrogen. The mixture was heated, using a thermostated steam bath, at 55 °C for 1 h and then at 85 °C for 40 min. The steam bath was removed and the resulting mixture was cooled to room temperature. Dichloromethane (100 mL) and distilled water (5 mL) were added and the organic layer was separated. The residual aqueous phase was extracted with dichloromethane (50 mL × 2) and the combined extracts were dried over Na_2SO_4. The drying agent was filtered off and the filtrate evaporated *in vacuo* to yield the product as a brown solid (2.19 g, 91%). Purification of the crude product by recrystallisation from ethanol produced colourless crystals(1.72 g, 72% overall). Anal. found: C, 60.46; H, 7.24; N, 5.89; calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85%. Mp 73.5 °C (lit: 74–75 °C;[10] 73 °C [9]). IR (KBr disc) ν_{max}/cm^{-1}: 3316, 2984, 1672, 1636, 1611. δ_H ($CDCl_3$): 11.72 (1H, N–H, br s), 4.91 ($2H_6$, s), 4.19 ($4H_8$, q, $J = 7.12$), 2.73 ($4H_3$, s), 1.28 ($6H_9$, t, $J = 7.12$). δ_C ($CDCl_3$): 168.4 (C_7), 160.1 (C_2), 87.0 (C_6), 59.6 (C_8), 27.4 (C_3), 14.6 (C_9). EI-MS m/z: 239 $[M]^+$.

Diethyl pyrrole-2,5-diacetate (3). *Method A.* Diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (**2**; 0.1914 g, 0.800 mmol) was dissolved in glacial acetic acid (20 mL) and the resulting solution heated at reflux for 10 min. Evaporation of the acetic acid *in vacuo* gave a pale yellow oil, which was taken up in dichloromethane (100 mL) and washed with saturated sodium bicarbonate solution (30 mL) and saturated NaCl solution (30 mL), and then dried over $MgSO_4$ for 1 h. The drying agent was filtered off and the evaporation of the filtrate *in vacuo* gave diethyl pyrrole-2,5-diacetate, **3**, as a pale yellow oil (0.1781 g, 93%). Anal. found: C, 60.29; H, 7.17; N, 5.91; calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85%. IR (smear) ν_{max}/cm^{-1}: 3373, 3180, 3107, 2982, 2937, 1733, 1591, 1506, 1445, 1404, 1369, 1030, 768. δ_H ($CDCl_3$): 9.04 (1H, N–H, br s),[24] 5.91 ($2H_3$, d, $J = 2.72$), 4.18 ($4H_8$, q, $J = 7.15$), 3.62 ($4H_6$, s), 1.28 ($6H_9$, t, $J = 7.10$). δ_C ($CDCl_3$): 171.1 (C_7), 123.4

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(C_2), 107.4 (C_3), 61.1 (C_8), 33.5 (C_6), 14.2 (C_9). ESI-MS m/z: 240 $[M+H]^+$.

Method B. Pyrrole-2,5-diacetic acid (**4**; 0.043 g, 0.23 mmol) was dissolved in 20 mL ethanol and 10 drops of $SOCl_2$ added. The resulting solution was stirred for 25 h at room temperature. Evaporation of the solvent gave diethyl pyrrole-2,5-diacetate (**3**) as a dark brown oil (0.054 g, 96%). Anal. found: C, 59.48; H, 7.07; N, 5.82; calcd For $C_{12}H_{17}NO_4 \cdot 1/6H_2O$: C, 59.49; H, 7.21; N, 5.78%. δ_H (300 MHz, $CDCl_3$): 9.01 (1H, N–H, br s), 5.91 ($2H_3$, d), 4.18 ($4H_8$, q), 3.63 ($4H_6$, s), 1.28 ($6H_9$, t).

Pyrrole-2,5-diacetic acid (4). **4** was prepared according to literature method.[9] It should be noted that the pH must be taken down to 1 when the basic solution is acidified with concentrated hydrochloric acid. Usually this product was used without further purification but if desired it can be recrystallised from diethyl ether/pentane. **4** is stable for weeks when it is kept under argon in a refridgerator. Anal. found: C, 52.69; H, 5.12; N, 7.64; calcd for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65%. Mp (freshly recrystallised colourless crystals) 122.5 °C (lit:[9] 120.5–121 °C). IR (KBr disc) ν_{max}/cm^{-1}: 3393, 3355, 3016, 2925, 1694, 1593, 1503, 1409. δ_H (D_2O/KOH, external reference to DMSO at 2.71 ppm): 5.81 ($2H_3$, s), 3.40 ($4H_6$, s). δ_C (D_2O/KOH, external reference to DMSO at 39.5 ppm): 180.7 (C_7), 127.5 (C_2), 106.7 (C_3), 36.9 (C_6). ESI-MS m/z: 182 $[M-H]^-$.

X-Ray crystallography

CCDC reference numbers 207581 and 207582. See http://www.rsc.org/suppdata/nj/b3/b303829g/ for crystallographic files in CIF or other electronic format.

Crystal data for diethyl 2,2′-(2,5-pyrrolidinediylidene)bisacetate (2). Colourless block crystals suitable for X-ray diffraction studies were grown by the slow evaporation of a dilute cyclohexane solution of $C_{12}H_{17}NO_4$and the crystal structure determined. $C_{12}H_{17}NO_4$, colourless block, dimensions $0.72 \times 0.63 \times 0.35$ mm, monoclinic, space group $P2(1)/c$, $a = 9.089(3)$, $b = 13.036(4)$, $c = 10.604(3)$ Å, $\beta = 100.047(4)°$, $U = 1237.1(6)$ Å^3, $\mu = 0.096$ mm^{-1}, $Z = 4$, $D_c = 1.285$ g cm^{-3}, $T = 170(2)$ K. Reflections (15 210 total) were collected using a Bruker SMART diffractometer in the range $4.56° < 2\theta < 52.94°$. A semi-empirical absorption correction (SADABS) was applied ($T_{min} = 0.53$, $T_{max} = 1.00$). The 2536 independent reflections were used to solve the structure by direct methods (SHELXS86),[25] which resulted in the location of all non-hydrogen atoms. All non-hydrogen atoms were made anisotropic and the hydrogen atoms on all but the ethyl groups were located from a difference map and fixed. The refinement (SHELXL97)[26] of 156 parameters converged to $R_1 = 0.0362$ [for 2276 reflections having $F > 4\sigma(F)$], $wR_2 = 0.0967$ and goodness-of-fit of 1.046 (for all 2536 F^2 data). Peak/hole 0.179/−0.233 e Å^{-3}.

Crystal data for pyrrole-2,5-diacetic acid (4). Colourless plate crystals suitable for X-ray diffraction studies were grown by the slow diffusion of pentane into a solution of $C_{12}H_{17}NO_4$ in diethyl ether–pentane (1:1) and the crystal structure determined. $C_8H_9NO_4$, colourless plate, dimensions $0.80 \times 0.54 \times 0.02$ mm, monoclinic, space group $P2(1)/c$, $a = 8.333(3)$, $b = 12.671(4)$, $c = 7.960(3)$ Å, $\beta = 91.191(5)°$, $U = 840.3(5)$ Å^3, $\mu = 0.118$ mm^{-1}, $Z = 4$, $D_c = 1.448$ g cm^{-3}, $T = 168(2)$ K. Reflections (5612 total) were collected using a Bruker SMART diffractometer in the range $4.88° < 2\theta < 52.90°$. A semi-empirical absorption correction (SADABS) was applied ($T_{min} = 0.49$, $T_{max} = 1.00$). The 1696 independent reflections were used to solve the structure by direct methods (SHELXS86),[25] which resulted in the location of all non-hydrogen atoms. All non-hydrogen atoms were made anisotropic and all hydrogen atoms were located from a difference map and fixed. The refinement (SHELXL97)[26] of 118 parameters converged to $R_1 = 0.0444$ [for 1205 reflections having $F > 4\sigma(F)$], $wR_2 = 0.1211$ and goodness-of-fit of 1.036 (for all 1696 F^2 data). Peak/hole 0.156/−0.294 e Å^{-3}.

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