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Synthetic studies related to diketopyrrolopyrrole (DPP) pigments. Part 2: The use of esters in place of nitriles in standard DPP syntheses: Claisen-type acylations and furopyrrole intermediates☆

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Abstract—Ethyl 2-aryl-4,5-dihydro-5-oxopyrrole-3-carboxylates react with esters or acyl halides in the presence of a strong base to give 4-acyl derivatives, which exist predominantly as either *E*- or *Z*-enols. These are cyclised, either in solution at temperatures >200 °C or by microwave irradiation, to 3,6-disubstituted 1*H*-furo[3,4-*c*]pyrrolediones which, after *N*-protection, are convertible by reaction with primary amines into novel *N*,*N*′-disubstituted DPP derivatives.
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The synthesis of 3,6-diaryl derivatives of the 2*H*,5*H*-pyrrolo[3,4-*c*]pyrrole-1,4-dione (diketopyrrolopyrrole or DPP) ring system, e.g. **1** (R = Ar), is routinely accomplished by reaction of ethyl 4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate **2** with aromatic nitriles in the presence of a strong base such as sodium *t*-amyloxide,[1,2] and non-aromatic nitriles react similarly with compound **2a** to give analogues of **1** where R = alkyl or cycloalkyl.[3] In Part 1 of this series[1] we have described attempts to use α,β-unsaturated nitriles in these processes: however, the propensity of such nitriles to undergo conjugate rather than 'normal' addition leads initially to the anions **3** and thence to the novel cyclopenta[*c*]pyrrole derivatives **4** (Scheme 1). These products, although highly coloured, appear to be of limited value as pigments, since when incorporated into a PVC film, they show a tendency to migrate out of the latter when it is placed in contact with a second surface.

1. Results and discussion

The corresponding reactions of the pyrrolinecarboxylate ester **2a** with α,β-unsaturated esters were considered worthy of investigation, in the expectation that the analogous products **5** containing an ester group might have potential as pigments. Reaction of the pyrrolinecarboxylate ester **2a** with ethyl cinnamate and sodium *t*-amyloxide under reflux gave a bright orange product, the ^{1}H NMR and infra-red spectra of which confirmed the presence of both ethyl ester and amide functionality. However, the mass spectrum indicated a molecular mass of 361, which was not consistent with the expected product **5** (molecular mass 359), and the ^{1}H NMR spectrum indicated that the alkenic double bond of the cinnamate had been retained in the product. An identical product resulted from reaction of the pyrrolinecarboxylate ester **2a** with *methyl* cinnamate, indicating that the ester group in the product originated in compound **2a** rather than the cinnamate. Structure **6** was therefore proposed for this product, and the overall reaction was recognised as a Claisen-type acylation (Scheme 2). Direct confirmation of the structure **6** was sought using X-ray crystallography, but suitable crystals could not be obtained; it is of course conceivable that this solid consisted of a mixture of crystalline tautomers: not only the keto isomer **6** but also, for example, **6*E*** and **6*Z***. However, in situ methylation of the crude reaction product prior to the final acidification (the

☆ Part 1, see Ref. 1.

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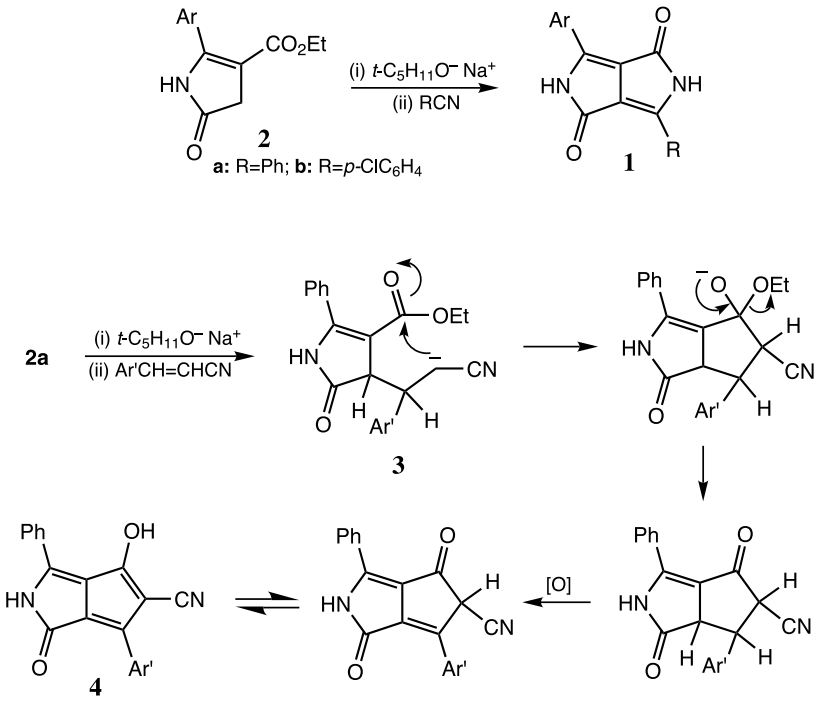


Scheme 1.

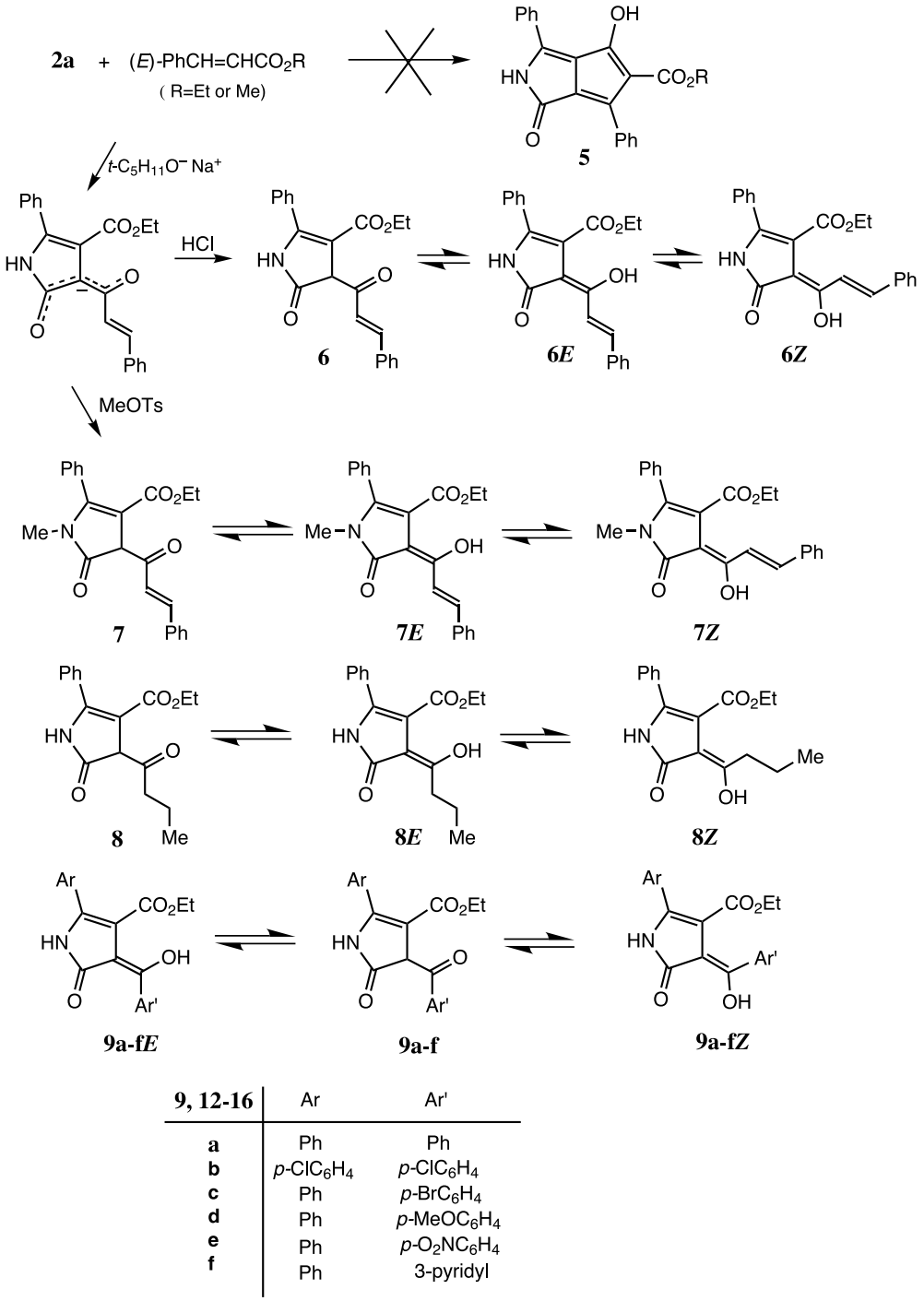
method already described[1] for the methylation of compounds of type **4**) gave an orange *N*-methyl derivative, the structure of which was confirmed as the *E*-enol of **7** by X-ray crystallography (Fig. 1). The coplanarity of the enol and ester functions, and the relatively short distance (2.51 Å) between the enolic and ester carbonyl oxygens is consistent with intramolecular hydrogen bonding between these two functional groups.

Other alkyl and aryl esters react similarly with the pyrrolinecarboxylate ester **2a**. The reaction using ethyl butanoate yielded an almost colourless solid, which was sufficiently crystalline to be identified by X-ray crystallography as the analogous *E*-enol **8*E*** (Fig. 2); and the corresponding reactions of the esters **2a** with ethyl benzoate and sodium *t*-amyloxide gave a beige-coloured enol, the isolated crystal of which was, interestingly, the *Z*-enol **9a*Z*** (Fig. 3); in this molecule hydrogen bonding is apparent (O⋯O distance 2.57 Å) between the enolic hydrogen and the oxygen of the pyrrolinone carbonyl group. Acylations of the esters **2a** and **2b** using various acyl chlorides, with sodium hydride as the base, give broadly similar results: although this process is more convenient in practice, the yields of the acylated products **9a–f** are generally lower. The results are tabulated below (Table 1); the zero yield in several attempted preparations of the *p*-methoxybenzoyl analogue **9d** was unexpected.

The disparity in configuration between the various isolated enols is not immediately explicable. It may be that the keto-isomer and both *E*- and *Z*-enols are all present in solution, and the compound which is isolated in each case is either the most stable, or the least sterically hindered, or merely the one which happens to be the least soluble under these particular conditions. In the case of the benzoyl compound **9a**, the ^{1}H NMR spectrum (in $CDCl_3$) shows the presence of *four* ethoxy-groups, with an approximate integral ratio 70:14:5:11. The main product shows, unusually, the quartet due to the ester methylene group at δ 3.56, with the three other methylene resonances at δ 4.10, 3.75 and 3.45, respectively. In most other cases, the ^{1}H NMR spectrum contains one major and one minor methylene resonance, one with $\delta<4$ and the other with $\delta>4$. Since compounds **6**, **7**, **8** and **9a** are all sharp-melting solids, both by visual observation and (in some cases) by differential scanning calorimetry (DSC), it seems a reasonable supposition that in each case the crystalline isomer isolated is likely to be the principal isomer in solution; and that those with $\delta(CH_2)<4$ are *Z*-enols whereas those with $\delta(CH_2)>4$ have the *E*-configuration.

The fact that some of these Claisen reaction products are obtained in relatively low yield does not necessarily mean a low conversion, but difficulty of isolation: for example the 'one-pot' preparation of the *N*-methyl compound **7** from **2a** by acylation followed by in situ methylation gives a higher overall yield than the two-step sequence in which the intermediate **6** is isolated and purified.

Conversion of these enols into derivatives of DPP requires three further steps. Rubin,[3] Langhals[4] and their co-workers have previously shown that heating of dialkyl 2,3-dibenzoylsuccinates to ca. 300 °C gives diketofurofurans **10**, and that these fused dilactones are converted into *N*,*N*′-diarylated DPPs, **11**, by reaction with a primary aromatic amine in the presence of *N*,*N*′-dicyclohexylcarbodiimide and a catalytic amount of trifluoroacetic acid (Scheme 3(a)). It is now shown that the aroylated pyrrolinone esters **9a–f** may be similarly cyclised to 3,6-diaryl-1*H*-furo[3,4-*c*]-pyrrole-1,4(5*H*)-diones **12a–f** (Scheme 3(b)), a process



9, 12-16	Ar	Ar'
a	Ph	Ph
b	*p*-ClC$_6$H$_4$	*p*-ClC$_6$H$_4$
c	Ph	*p*-BrC$_6$H$_4$
d	Ph	*p*-MeOC$_6$H$_4$
e	Ph	*p*-O$_2$NC$_6$H$_4$
f	Ph	3-pyridyl

Scheme 2.

which presumably involves $Z \rightarrow E$ isomerisation as the first step. Heating to 240 °C in Dowtherm® A for prolonged periods gives moderate yields of the cyclised products, but the yields may be significantly improved and the reaction times greatly reduced when the cyclisations are carried out in the cavity of a microwave reactor. The results are tabulated below (Table 2). Unexpectedly the cinnamoyl and butanoyl compounds **7** and **8**, the principal isomer of which already has the *E*-configuration and might have been expected to undergo cyclisation more readily, underwent only extensive decomposition under similar conditions, and no furopyrrole was isolated. This behaviour is also observable by DSC, where a broad exotherm occurs immediately above the melting temperatures of both compounds.

Conversion of the furopyrroles **12a–f** into DPP derivatives by adaptation of the above literature procedures[3,4] appears to require prior protection of the amido-nitrogen: methylation and benzylation are straightforwardly achieved by standard procedures, and these derivatives (**14** and **13**, respectively) then undergo the ring-opening and

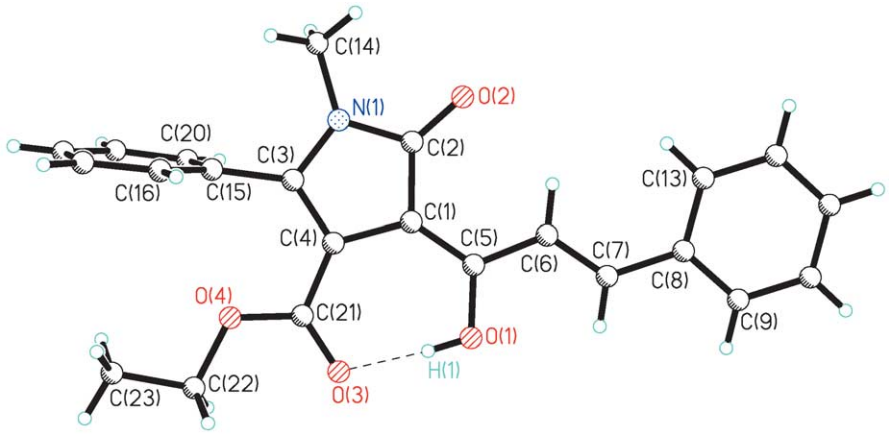


Figure 1. X-ray structure of compound **7**. Selected bond lengths (Å): C(1)–C(5), 1.383(4); C(3)–C(4), 1.370(4); C(5)–C(6), 1.448(5); C(6)–C(7), 1.331(5); C(2)–O(2), 1.235(4); C(5)–O(1), 1.330(4). Selected interbond angles (°): C(4)–C(1)–C(5), 130.2(3); C(1)–C(2)–N, 105.9(3); C(4)–C(3)–N, 109.9(3); C(1)–C(4)–C(21), 128.3(5); C(4)–C(21)–O(3), 124.7(3). Selected torsion angles (°): O(1)–C(5)–C(1)–C(4), 0.6(6); C(1)–C(4)–C(21)–O(3), −2.2(6); C(2)–C(1)–C(5)–O(1), 178.8(3); C(6)–C(7)–C(8)–C(9), −172.8(4); C(4)–(C3)–C(15)– are cts (Å): O(1)···O(3), 2.51; O(3)···H(1), 1.70 (estimated).

ring-closure sequence, leading to the N^5-protected 2,3,6-triaryl-DPP derivatives **16** and **15**.

Langhals et al. had previously shown[4] that the conversion of the furofurans **10** into DPPs **11** required the presence of *N*,*N*′-dicyclohexylcarbodiimide and a catalytic amount of trifluoroacetic acid; in the absence of such reagents the ring-closure step did not apparently occur, and the isolated product[3] from the reaction of **10** with aniline alone was provisionally assigned the structure **17a** or **17b**, although definitive proof of structure was lacking. In our series, however, reaction of the *N*-methylated furopyrrole **14a** with aniline alone led to the enamine **18a**, the structure of which was established by X-ray crystallography (Fig. 4), and the product from the corresponding reaction of **14c** is the analogue **18c**. This suggests that ring-opening of the furopyrroles **14** may involve nucleophilic attack by the amine at C-3 (Scheme 4) rather than at C-1 as implied by the intermediacy of amides such as **17**.

2. X-ray crystallography

In the crystals selected for analysis, the enolic nature of each of compounds **7**, **8** and **9a** is evident from the observed bond lengths (see the data accompanying Figs. 1–3). In each case the length of the carbon–carbon bond joining the acyl group to the pyrroline ring is less than 1.4 Å, indicative of substantial double-bond character, whereas the acyl carbon–oxygen bond lengths (>1.3 Å) are considerably longer than expected for a normal C=O double bond, such as are found in the pyrrolinone carbonyl groups (1.23–1.26 Å). In compounds **7** and **8** the coplanar alignment of the enolic hydroxyl and ester groups, together with the relatively short distance between the enolic and carbonyl oxygen atoms (ca. 2.5 Å; well within the accepted range[5]) is taken as indicative of intramolecular hydrogen bonding between these two functionalities. By similar criteria, the crystal of compound **9a** reveals a structure in which intramolecular hydrogen bonding occurs between the enolic hydrogen and the

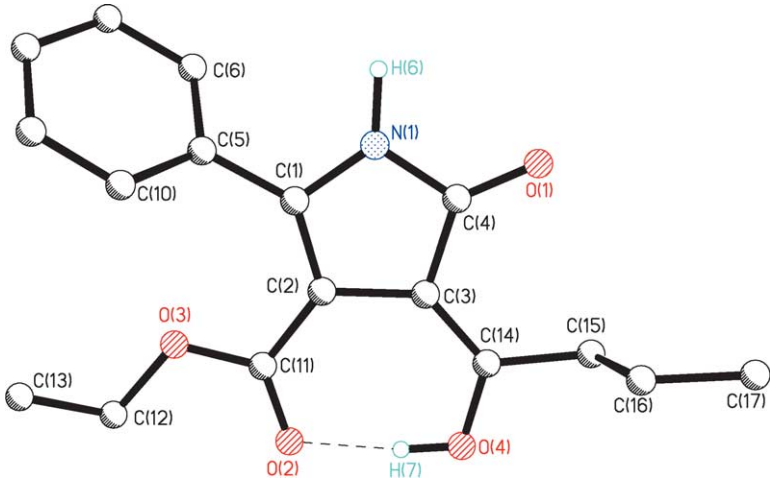


Figure 2. X-ray structure of compound **8**. Selected bond lengths (Å): C(3)–C(14), 1.368(4); C(4)–O(1), 1.243(3); C(14)–O(4), 1.322(3); C(3)–C(4), 1.455(4); C(2)–C(3), 1.477(4); C(1)–C(2), 1.368(4). Selected interbond angles (°): C(2)–C(3)–C(14), 132.2(3); C(3)–C(4)–N, 106.1(2); C(2)–C(1)–N, 109.3(3); C(3)–C(2)–C(11), 125.4(3); C(2)–C(11)–O(2), 125.1(3). Selected torsion angles (°): O(4)–C(14)–C(3)–C(2), 0.0(5); O(2)–C(11)–C(2)–C(3), 4.9(5); C(4)–C(3)–C(14)–O(4), 177.8(3); C(2)–C(1)–C(5)–C(6), −133.7(4). Non-bonded contacts (Å): O(2)···O(4), 2.52; O(2)···H(7), 1.64 (estimated).

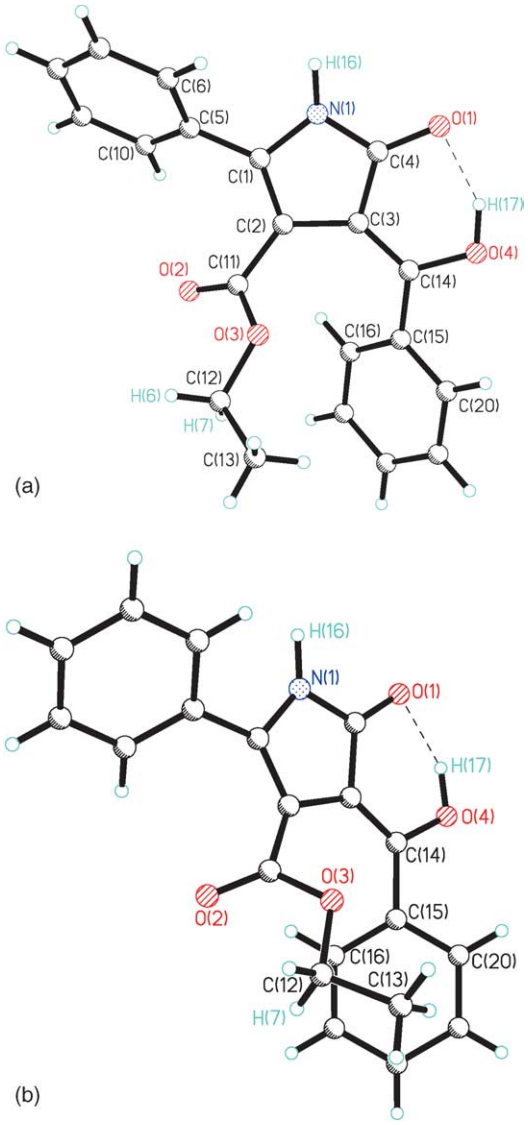


Figure 3. X-ray structure of compound **9a**. [View **3b** shows the close proximity of the ester methylene protons (*ca*. 2.8 Å) to the mean plane of the phenyl ring.] Selected bond lengths (Å): C(3)–C(14), 1.372(4); C(4)–O(1), 1.260(3); C(14)–O(4), 1.342(4); C(3)–C(4), 1.447(4); C(2)–C(3), 1.460(4); C(1)–C(2), 1.357(4). Selected interbond angles (°): C(3)–C(4)–O(1), 127.8(3); C(4)–C(3)–C(14), 119.4(3); C(3)–C(14)–O(4), 118.9(3). Selected torsion angles (°): C(1)–C(2)–C(11)–O(3), 123.4(3); C(3)–C(2)–C(11)–O(2), 141.7(4); C(3)–C(14)–C(15)–C(16), 32.8(5); C(2)–C(1)–C(5)–C(6), 132.5(4); C(4)–C(3)–C(14)–O(4), 6.3(5). Non-bonded contacts (Å): O(1)···O(4), 2.57; O(1)···H(17), 1.70 (estimated).

pyrrolinone oxygen atom; interestingly both the phenyl moiety of the benzoyl substituent and the ester group lie significantly out of the plane of the heterocyclic ring. In the enamine **18a**, there is evidently intramolecular hydrogen bonding between the anilino-NH and the pyrrolinone oxygen.

3. Conclusion

Whereas reaction of the pyrrolinecarboxylate ester **2a** with nitriles leads directly to 3,6-disubstituted DPP derivatives,[1] the corresponding reaction of **2a** with esters proceeds in four distinct stages; (a) *C*-acylation; (b) thermal cyclisation of the acyl compounds, with or without the aid of microwaves, to give furo[3,4-*c*]pyrroles; (c) *N*-protection and (d) ring-opening of the furopyrroles, followed by ring-closure. This sequence constitutes the first reliable general route to N^5-protected 2,3,6-triarylated DPPs.

4. Experimental

4.1. General

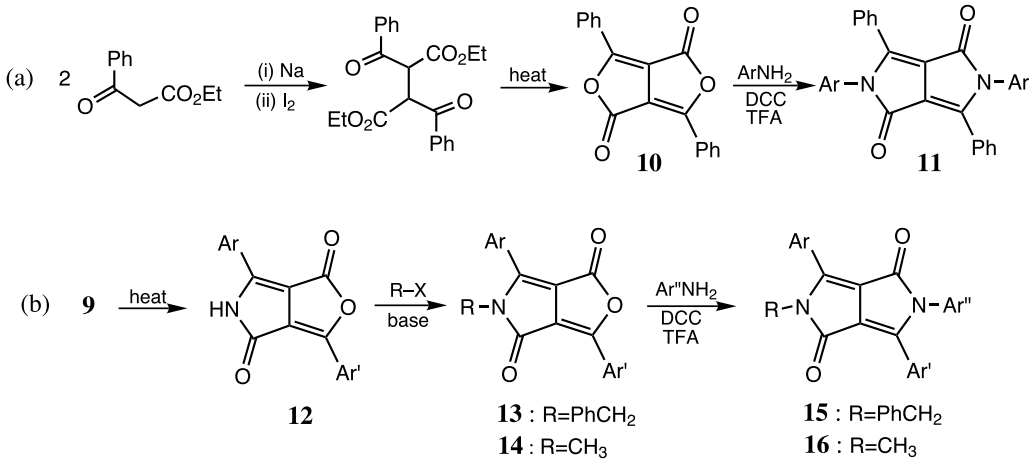
FT-IR spectra were recorded for Nujol mulls; frequencies are expressed in cm^{-1}. Unless otherwise indicated, UV–vis spectra were recorded (wavelengths expressed in nm) for solutions in dimethyl sulfoxide (DMSO), and ^1H and ^{13}C NMR spectra were obtained at 300 and 75.4 MHz, respectively, for solutions in DMSO-d_6 (or, where indicated, $CDCl_3$). Chemical shifts (δ) are expressed relative to $SiMe_4$ ($\delta_H=\delta_C=0$) and coupling constants (J) in Hz. Mass spectra and accurate mass measurements were obtained using electron impact (EI) ionisation at 70 eV, chemical ionisation (CI) using a VG Autospec instrument, or electrospray ionisation (ESI) with a Micromass LCT instrument. The microwave reactor was a CEM Discover™ model, with a circular single mode cavity design and a maximum operating power of 300 W; the samples were contained in sealed glass tubes, whereby the pressure was allowed to increase to a maximum of 2.07 MPa (300 psi).

2-Methylbutan-2-ol (*t*-amyl alcohol) was dried by heating under reflux with sodium metal for several hours followed by distillation on to 4 Å molecular sieves. Sodium *t*-amyloxide solution was obtained by dissolving the appropriate quantity of sodium, cut into small pieces, in boiling *t*-amyl alcohol under nitrogen: this process normally

Table 1. Acylated derivatives of ethyl 2-aryl-4,5-dihydro-5-oxopyrrole-3-carboxylates **2**

Compound	Yield (%), acylating agent		δ_H (OCH_2CH_3)		Isomer ratio (*Z*/*E*)
	RCO_2Et	RCOCl	Major	Minor	
6	59, 40	17	4.00	3.57	<1:10
7			3.97		
8	67	33			
9a	33	10	3.56	4.10	5:1
9b	78	14	3.62	4.19	ca. 2.5:1
9c	—	44	3.63	4.27	2:1
9d	0	0			
9e	—	60	3.62	—	
9f	89	—	3.50	—	

The empty cells in the table indicates that the reaction was not attempted or that the minor isomer was not detected.



Scheme 3.

Table 2. 3,6-Diaryl-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-diones **12** and their derivatives

Compound	Yield (%)		Visible absorption, λ_{max}/nm (log ε in brackets)	
	Conventional heating	Microwave heating	Parent compound **12** (in DMSO)	*N*-Me deriv. **14** (in CH_2Cl_2)
12a	40	86, 70	455, 487 (4.41, 4.45)	453 (4.34)
12b	68	—	463, 495 (4.47, 4.52)	
12c	—	94	461, 493 (4.45, 4.49)	454 (4.20)
12e	—	87	487, 511 (4.38, 4.38)	482 (4.24)
12f	—	19	457, 487 (4.02, 4.03)	

The — in the 'yield' column indicates that the reaction was not attempted.

required several hours but could be accelerated by the addition of a catalytic amount of anhydrous iron(III) chloride.

'Ether' refers to diethyl ether and 'petrol' to the fraction of bp 40–60 °C. Ethyl 4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate **2a** was prepared according to the patented procedure.[6] The *p*-chlorophenyl analogue **2b** was supplied by Ciba Specialty Chemicals Inc. as an off-white solid of mp 198 °C, and was used without further purification. Solutions were dried over anhydrous sodium sulfate or magnesium sulfate.

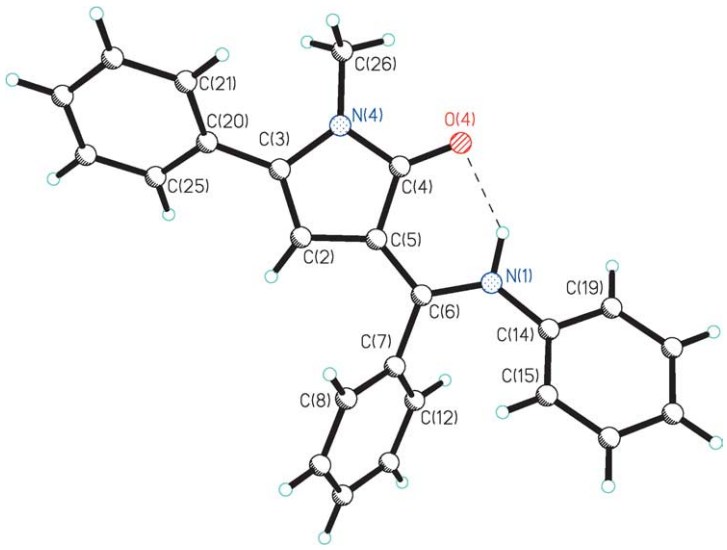
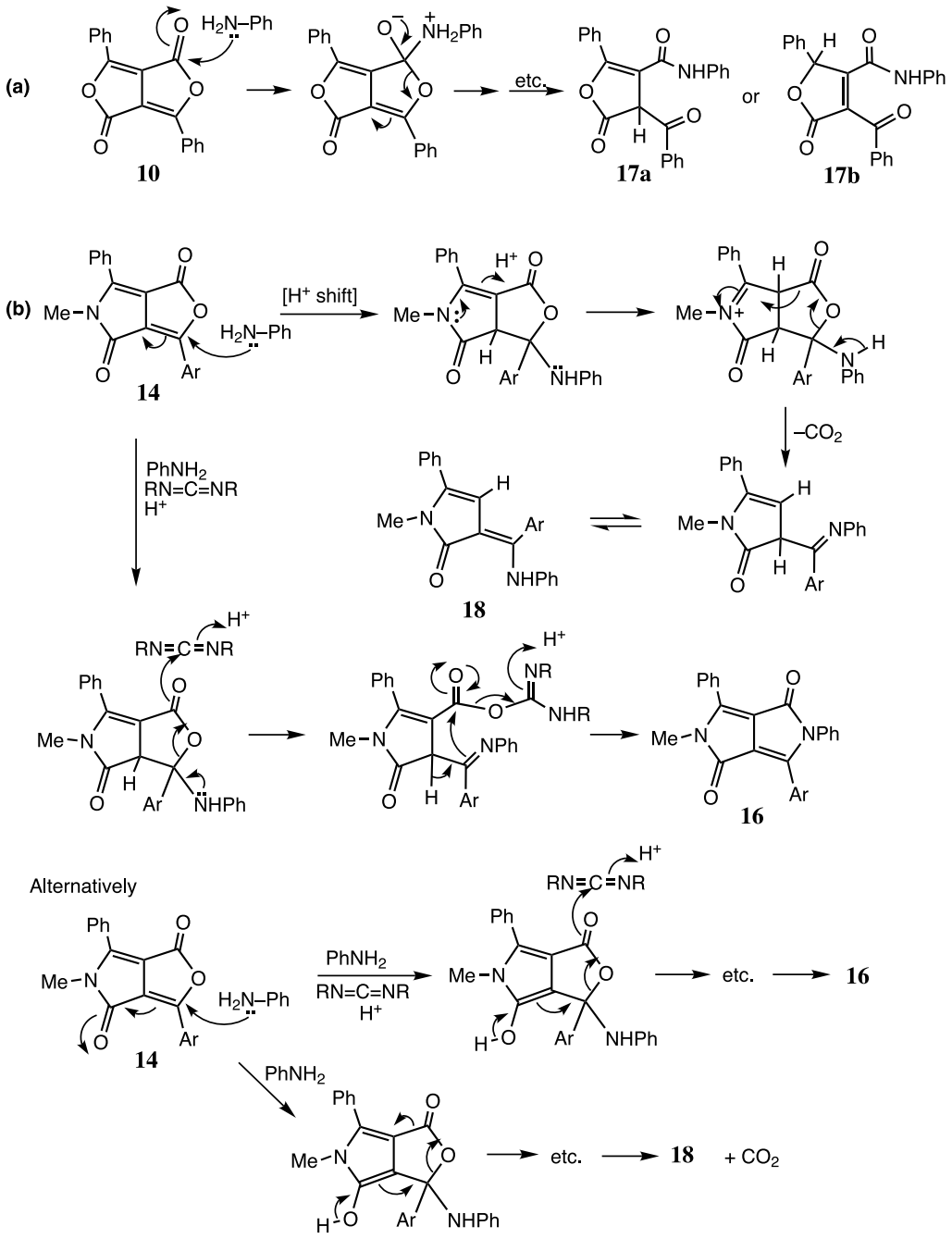


Figure 4. X-ray structure of compound **18a**. Selected bond lengths (Å): C(2)–C(3), 1.356(2); C(4)–C(5), 1.456(2); C(5)–C(6), 1.382(2); C(4)–O, 1.2504(17), C(6)–C(7), 1.481(2); C(6)–N, 1.3573(18); N–C(14), 1.4116(18); C(3)–C(20), 1.4632(19). Selected interbond angles (°): C(2)–C(5)–C(4), 106.39(12); C(4)–C(5)–C(6), 123.25(13); C(3)–C(2)–C(5), 108.46(12); C(5)–C(6)–N, 118.89(13); C(5)–C(4)–O, 128.84(13). Selected torsion angles (°): C(4)–C(5)–C(6)–N, −1.4(2); C(6)–C(5)–C(4)–O, −6.1(2); C(2)–C(3)–C(20)–C(21), 139.92(16); C(5)–C(6)–C(7)–C(8), −56.79(19); C(6)–N–C(14)–C(15), −23.4(2); N–C(6)–C(7)–C(8), 127.70(14); C(5)–C(2)–C(3)–N, 1.14(15). Non-bonded contacts (Å): N···O, 2.7421(16).



14a, 16a, 18a: Ar=Ph; **14c, 16c, 18c**: Ar=*p*-BrC_6H_4

Scheme 4.

4.1.1. Ethyl 4-cinnamoyl-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 6. (a) Sodium (1.21 g, 52.6 mmol) was added, with stirring and under nitrogen, to dried *t*-amyl alcohol (70 cm^3) and the mixture heated to reflux (105–110 °C) until all the sodium dissolved. The solution was cooled to 25 °C, then the pyrrolinecarboxylate ester **2a** (2.00 g, 8.6 mmol) and ethyl cinnamate (2.55 g, 14.5 mmol) were added. The mixture was then heated to reflux for 2 h, during which time an intense orange colour developed. The cooled mixture was then added to an ice-cooled mixture of methanol (20 cm^3) and concentrated hydrochloric acid (5 cm^3) and the bright orange precipitate was filtered off, washed with methanol and dried in vacuo at 40 °C. Yield 3.05 g (59%).

(b) The above method was repeated, using the pyrrolinecarboxylate ester **2a** (2.00 g, 8.6 mmol), sodium *t*-amyloxide [from sodium, (0.60 g, 26.1 mmol)] in dried *t*-amyl alcohol (25 cm^3) and methyl cinnamate (1.40 g, 8.6 mmol); the mixture was heated to reflux for 2.5 h, then cooled and added to an ice-cold mixture of methanol (10 cm^3) and water (20 cm^3), and acidified dropwise with concentrated

hydrochloric acid (3 cm^3). The orange precipitate was filtered off, washed with methanol and water then dried in vacuo. Yield 1.25 g (40%).

Compound **6** had mp 238–240 °C. (Found: C, 72.8; H, 5.3; N, 3.8. $C_{22}H_{19}NO_4$ requires C, 73.1; H, 5.3; N, 3.9%). *m/z* 361 ($M^{+\cdot}$, 100%), 315 (77), 238 (72). δ_H 0.88 (3H, t, J=6.6 Hz, OCH_2CH_3), 4.00 (2H, q, J=6.6 Hz, OCH_2CH_3), 7.43–7.47 (8H, m, Ar-H), 7.59 (1H, d, J=15.7 Hz, CH=CHPh), 7.64–7.67 (2H, m, Ar-H), 8.62 (1H, d, J=15.7 Hz, CH=CHPh), 11.11 (1H, s, NH). A minor signal occurred at δ 3.57 (q, OCH_2).

(c) The pyrrolinone ester **2a** (2.00 g, 8.66 mmol) was added to sodium hydride (1.73 g, 43.25 mmol) THF (200 cm^3), and the mixture was stirred for 30 min. Cinnamoyl chloride (1.44 g, 8.66 mmol) was then added and the mixture stirred at room temperature overnight, acidified (HCl), and extracted with ethyl acetate. The dried extract on concentration gave the enol **6** as an orange solid (523 mg, 17%), mp 247–250 °C, spectroscopically identical with the products from (a) and (b).

4.1.2. Ethyl 4-cinnamoyl-4,5-dihydro-1-methyl-5-oxo-2-phenylpyrrole-3-carboxylate 7. The dianion of the cinnamoyl-pyrrolinecarboxylate ester **6** was prepared as above, from the pyrrolinecarboxylate ester (5.00 g, 21.6 mmol), ethyl cinnamate (3.88 g, 22.0 mmol) and sodium *t*-amyloxide (from sodium, 1.51 g, 65.7 mmol) in *t*-amyl alcohol (25 cm^3). The orange solution was cooled to 25 °C, methyl *p*-toluenesulfonate (15.88 g, 85.3 mmol) was added and the mixture heated under reflux for 1 h, cooled, added to water (30 cm^3), extracted with ethyl acetate, and the extract dried and concentrated. Recrystallisation (propan-2-ol–tetrahydrofuran) gave an orange solid (6.27 g, 77%), mp 190–192 °C. (Found: C, 73.4; H, 5.6; N, 3.7. $C_{23}H_{21}NO_4$ requires C, 73.6; H, 5.6; N, 3.7%). *m/z* 375 ($M^{+\cdot}$, 100%), 329 (98). δ_H ($CDCl_3$) 0.75 (3H, t, J=7.2 Hz, OCH_2CH_3), 2.97 (3H, s, NCH_3), 3.97 (2H, q, J=7.2 Hz, OCH_2CH_3), 7.24–7.48 (8H, m, Ar-H), 7.67–7.76 (3H, m, Ar-H and CH=CHPh), 8.76–8.84 (1H, d, J=15.5 Hz, CH=CHPh).

4.1.3. Ethyl 4-butanoyl-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 8. (a) The pyrrolinecarboxylate ester **2a** (2.00 g, 8.6 mmol) and ethyl butanoate (1.00 g, 8.6 mmol) were added successively, under nitrogen, at 80–90 °C to a stirred solution of sodium *t*-amyloxide, prepared as above from sodium (0.61 g, 26.5 mmol) in *t*-amyl alcohol (25 cm^3). The mixture was heated to reflux for 5 h, then cooled and added to an ice-cold mixture of water (100 cm^3) and methanol (10 cm^3). Dropwise acidificaton (conc. HCl) gave a purple precipitate which was filtered off, washed with methanol then water and decolourised in hot propan-2-ol with charcoal, to yield almost colourless crystals (1.74 g, 67%).

(b) The pyrrolinone ester **2a** (1.00 g, 4.33 mmol) was added to sodium hexamethyldisilazide (1 M solution in THF, 13.4 cm^3), and the mixture was stirred for 30 min. Butanoyl chloride (0.46 g, 0.45 cm^3, 4.33 mmol) was then added and the mixture stirred at room temperature overnight, then acidified (HCl), extracted with ethyl acetate, and the extract dried and concentrated under reduced pressure. Yield 0.43 g (33%).

Compound **8** had mp 173–174 °C. (from ethanol or 1,4-dioxan). (Found: C, 68.1; H, 6.6; N, 4.7. $C_{17}H_{19}NO_4$ requires C, 67.8; H, 6.4; N, 4.7%). δ_H ($CDCl_3$) 0.96 (3H, t, J=7.4 Hz, $CH_2CH_2CH_3$), 1.03 (3H, t, J=7.1 Hz, OCH_2CH_3), 1.65–1.78 (2H, m, $CH_2CH_2CH_3$), 3.04 (2H, br t, J=7.0 Hz, $CH_2CH_2CH_3$), 4.10 (2H, q, J=7.1 Hz, OCH_2CH_3), 7.39–7.42 (5H, m, Ar-H), 8.85 (1H, br s, NH). A minor signal occurred at δ 3.73 (q, OCH_2).

4.1.4. Ethyl 4-benzoyl-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 9a. (a) The pyrrolinecarboxylate ester **2a** (5.03 g, 21.8 mmol) and ethyl benzoate (3.27 g, 21.8 mmol) were added successively at 25 °C to a solution of sodium *t*-amyloxide, prepared as above from sodium (1.50 g, 65.2 mmol) and *t*-amyl alcohol (40 cm^3), and the mixture was then heated to reflux for 5.5 h. The resulting orange solution was cooled and added to an ice-cooled mixture of methanol (10 cm^3) and water (50 cm^3), then acidified dropwise with concentrated hydrochloric acid (3 cm^3) and extracted with tetrahydrofuran/diethyl ether; the extract was dried and concentrated, to give amber-coloured crystals (2.38 g, 33%), mp 156–157 °C. (from ethanol–water).

(b) The pyrrolinone ester **2a** (1.50 g, 6.5 mmol) and benzoyl chloride (0.91 g, 0.75 cm^3, 6.5 mmol) were added successively to sodium hydride (0.55 g, 27.75 mmol) in THF (100 cm^3), and the mixture stirred at room temperature overnight, then added to water, acidified (HCl) and the organic component extracted with ethyl acetate and dried. Recrystallisation from ethanol gave the benzoylpyrrolinone ester (100 mg, 9.5%), mp 157–158 °C, identical to the product of method (a).

Found: C, 71.5; H, 5.2; N, 4.2. $C_{20}H_{17}NO_4$ requires C, 71.6; H, 5.1; N, 4.2%. ν_{max} 3170 (NH), 2720 (H-bonded OH), 1720 (ester C=O), 1630 (lactam C=O), 1610 and 1600 (C=C). δ_H 0.60 (3H, t, J=7.2 Hz, OCH_2CH_3—major), 0.95 (3H, t, J=7.2 Hz, CH_2CH_3—minor), 3.56 (2H, q, J=7.2 Hz, CH_2CH_3—major), 4.10 (2H, q, J=7.2 Hz, CH_2CH_3—minor) 7.42–7.62 (6H, m, *m*/*p*-Ar-H), 7.62–7.80 (4H, m, *o*-Ar-H), 9.52 (1H, br. s, NH). Other minor signals (each OCH_2, q) occur at δ 3.75 and 3.45. δ_C 175.4 (lactam C=O), 170.7 (ester C=O), 165.0 (C=C(OH)Ph), 135.7 (Ph-C=C–CO_2Et), 131.8 (Ar), 130.6 (quat. Ar), 130.2 (quat. Ar), 129.9 (Ar), 129.4 (Ar), 128.9 (2×C, Ar), 128.8 (2×C, Ar), 128.7 (Ar), 128.3 (Ar), 128.0 (Ar), 108.0 (Ph-C=C–CO_2Et), 105.1 (C=C–C=C(OH)Ph), 61.0 (CH_2), and 13.6 (CH_3). *m/z* 335 ($M^{+\cdot}$, 54%), 289 (100), 261 (7), 105 (56).

4.1.5. Ethyl 4-(*p*-chlorobenzoyl)-4,5-dihydro-5-oxo-2-(*p*-chlorophenyl)-pyrrole-3-carboxylate 9b. This compound was prepared similarly to **9a**, from the pyrrolinone ester **2b** (26.29 g, 99 mmol), ethyl *p*-chlorobenzoate (18.27 g, 99 mmol) and sodium *t*-amyloxide [from sodium, 6.82 g (297 mmol) in *t*-amyl alcohol (230 cm^3)], with the reactants being added at 70 °C and the mixture being heated under reflux for 22 h. The product was recrystallised from a mixture of ethanol, propan-2-ol, and water; yield, 31.36 g

(78%). The alternative route, using *p*-chlorobenzoyl chloride and sodium hydride as base, gave **9b** in a yield of only 14%.

Compound **9b** had mp 170–172 °C. (Found: C, 59.4; H, 4.1; N, 3.7; Cl, 17.4. $C_{20}H_{15}Cl_2NO_4$ requires C, 59.4; H, 3.7; N, 3.5; Cl, 17.5%). δ_H ($CDCl_3$) 0.74 (3H, t, $J=7.2$ Hz, CH_2CH_3), 3.62 (2H, q, $J=7.2$ Hz, CH_2CH_3), 7.40, 7.44, 7.55 and 7.59 (each 2H, 2×AA′BB′) and 8.63 (NH). [A minor isomer showed resonances at δ 1.05 (CH_2CH_3) and 4.19 (OCH_2)].

4.1.6. Ethyl 4-(*p*-bromobenzoyl)-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 9c. The pyrrolinone ester **2a** (0.85 g, 3.69 mmol) was added to sodium hydride (0.59 g, 14.75 mmol) in THF (40 cm^3). After stirring for 30 min at room temperature, a solution of freshly prepared *p*-bromobenzoyl chloride (0.81 g, 3.69 mmol) in THF (10 cm^3), and a catalytic amount (a few crystals) of DMAP were added, and the mixture was stirred at room temperature overnight, then acidified (dil. HCl) and extracted with ether. Concentration of the dried extract in vacuo gave the enol as a yellow crystalline solid (0.67 g, 44%), mp 189 °C (from ethanol). (Found: C, 58.4; H, 3.5; N, 3.3. $C_{20}H_{16}BrNO_4$ requires C, 58.0; H, 3.9; N, 3.4%). δ_H 0.76 (3H, t, $J=7.2$ Hz, CH_2CH_3), 3.63 (2H, q, $J=7.2$ Hz, CH_2CH_3), 7.43–7.52 (3H, m, ArH), 7.59–7.66 (4H, m, ArH), 7.74–7.80 (2H, m, ArH) and 11.90 (1H, s, NH). *m/z* (CI) 414/416 [96/100%, $(M+1)^+$] A minor product showed ethoxy-group resonances at δ_H 1.27 (t, CH_2CH_3) and 4.27 (q, OCH_2); the ratio of the two products was ca. 2:1.

4.1.7. Compound 9d. Repeated attempts to prepare ethyl 4-(*p*-methoxybenzoyl)-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate **9d** by either of the above acylation methods were unsuccessful; in every case the only product isolated was *p*-methoxybenzoic acid.

4.1.8. Ethyl 4-(*p*-nitrobenzoyl)-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 9e. The pyrrolinone ester **2a** (6.35 g, 27.5 mmol) was added to a mixture of sodium hydride (2.00 g, 82.5 mmol) and THF (1 dm^3), and this was stirred at room temperature for 15 min. *p*-Nitrobenzoyl chloride (5.50 g, 29.5 mmol) was then added, and the mixture was stirred overnight. Methanol and then water were added, and the mixture acidified (HCl). The organic component was extracted with ether, the extract was dried, the solvent evaporated, and the residue washed with methanol to give the nitro compound as a yellow solid (6.31 g, 60%), mp 254 °C (by DSC). (Found: C, 63.1; H, 4.15; N, 7.3. $C_{20}H_{16}N_2O_6$ requires C, 63.2; H, 4.2; N, 7.4%). δ_H 0.75 (3H, t, $J=6.6$ Hz, OCH_2CH_3), 3.62 (2H, q, $J=6.6$ Hz, OCH_2CH_3), 7.35–7.45 (3H, m, *m*/*p*-Ph-H), 7.50–7.56 (2H, m, *o*-Ph-H), 7.84 and 8.30 (each 2H, AA′BB′, Ar-H), and 11.95 (1H, s, NH); *m/z* (ESI−ve) 380 (22%, $M^{+\cdot}$), 379 [100, $(M-1)]^+$.

4.1.9. Ethyl 4-nicotinyl-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 9f. The pyrrolinone ester **2a** (8.43 g, 36.5 mmol) and methyl nicotinate (5.00 g, 36.5 mmol) were added successively to sodium *t*-amyloxide [from sodium, 2.52 g (0.11 mol) in *t*-amyl alcohol (100 cm^3)], and the mixture heated to reflux overnight. After cooling to room temperature, water was added, and the mixture acidified (HCl). The organic component was extracted with ether, and a precipitate formed in the aqueous layer. This precipitate was filtered off, the remaining aqueous layer was evaporated to dryness and the organic component was extracted with methanol. Evaporation of the methanol gave the nicotinyl compound **9f** as a yellow solid (10.90 g, 89%), mp 194–197 °C (from ethanol). (Found: C, 67.6; H, 4.5; N, 8.2. $C_{19}H_{16}N_2O_4$ requires C, 67.85; H, 4.8; N, 8.3%). δ_H 0.70 (3H, t, $J=6.5$ Hz, OCH_2CH_3), 3.50 (2H, q, $J=6.5$ Hz, OCH_2CH_3), 7.31–7.41 (3H, m, 2× Ar-H+ Py-5-H), 7.43–7.53 (3H, m, Ar-H), 7.93 (1H, br dt, $J=7.9$, 1.5 Hz, Py-4-H), 8.65 (1H, br d, $J=4.8$ Hz, Py-6-H), 8.70 (1H, d, $J=1.5$ Hz, Py-2-H) and 11.89 (1H, s, NH). *m/z* (ESI −ve) 336 (22%, $M^{+\cdot}$), 335 [100, $(M-1)]^+$.

4.1.10. 3,6-Diphenyl-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 12a. (a) A mixture of compound **9a** (10.00 g, 29.9 mmol) and Dowtherm® A (200 cm^3) was heated to 230–240 °C under nitrogen for 64 h. The solution was then cooled to room temperature and added dropwise to petrol (300 cm^3); the fluorescent orange precipitate was filtered off, washed with hexane and dried in vacuo. Yield 3.48 g (40%).

(b) The benzoylpyrrolinone ester **9a** was subjected to flash vacuum pyrolysis (500 °C/8×10^{-3} Torr), on a very small scale (50 mg) for ca. 45 min. The product from this heating gave the desired furopyrrole **12a** as a orange solid.

(c) The benzoylpyrrolinone ester **9a** (100 mg, 0.30 mmol) was irradiated in a microwave reactor, without solvent, heating to 250 °C for 10 min. The crude product was then allowed to cool, methanol was added, and the solid filtered off and washed with further methanol. This gave the furopyrrole **12a** (73 mg, 86%). On a larger scale, irradiation of compound **9a** (643 mg), heating to 180 °C. for 10 min, gave the furopyrrole **12a** (387 mg, 70%).

The benzoylpyrrolinone ester **9a** (100 mg, 0.30 mmol) and toluene (2 cm^3) were irradiated in a microwave reactor, heating up to 250 °C over 40 min. The solution was cooled, and the precipitate filtered off and washed with methanol to give the furopyrrole **12a** as an orange solid (22 mg, 26%), the remainder being unchanged starting material. Extension of the reaction time to 1 h gave **12a** in 48% yield.

Compound **12a** had mp >300 °C (dec.) (broad DSC endotherm at ca. 320 °C). (Found: C, 74.9; H, 4.2; N, 4.8. $C_{18}H_{11}NO_3$ requires C, 74.7; H, 3.8; N, 4.8%). ν_{max} 1760 (ester C=O), 1670 (lactam C=O), 1625 (C=C). δ_H 7.48–7.54 (6H, m, Ar-H), 8.12–8.17 (2H, m, Ar-H), 8.17–8.23 (2H, m, Ar-H) and 11.87 (1H, s, NH); δ_C 161.4 and 159.3 (2×C=O), 152.2 and 148.1 (2×quat.), 132.8, 132.6, 129.1 (2C), 128.0, 127.0 (all Ar-C–H), 126.8, 126.4, 115.8 and 102.8 (4×quat). *m/z* 289 ($M^{+\cdot}$, 100%), 204 (20), 105 (35), 77 (35).

4.1.11. 3,6-Bis-(*p*-chlorophenyl)-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 12b. (a) A mixture of compound **9b** (15.00 g, 37 mmol) and Dowtherm® A (300 cm^3) was heated to 205–210 °C during 48 h, then cooled and added

dropwise to petrol (1 l). The fluorescent purple solid was filtered off, washed with further petrol and dried in vacuo. Yield 8.95 g (68%), mp 387 °C (by DSC). (Found: C, 60.3; H, 2.8; N, 3.9. $C_{18}H_9Cl_2NO_3$ requires C, 60.4; H, 2.5; N, 3.9%). δ_H 7.67, 7.73, 8.25, 8.34 (each 2H, 2×AA′BB′) and 12.25 (1H, br s, NH). *m/z* (EI) 357/359/361 ($M^{+\cdot}$, 95/63/8%), 139/141 (100/35, ClC_6H_4CO), 111/113 (85/26, ClC_6H_4), 75 (35).

(b) The *p*-chlorobenzoylpyrrolinone ester **9b** (58 mg, 0.14 mmol) was irradiated in a microwave reactor, without solvent, heating to 200 °C over 10 min. The crude product was then allowed to cool, methanol was added, and the solid filtered off and washed with further methanol. This gave the furopyrrole as a red solid (42 mg, 82%).

4.1.12. 3-(*p*-Bromophenyl)-6-phenyl-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 12c. The *p*-bromobenzoylpyrrolinone ester **9c** (154 mg, 0.37 mmol) was irradiated with microwave radiation without solvent, heating to 250 °C for 10 min. The crude product was then allowed to cool, methanol was added and the solid filtered off and washed with methanol. This gave the furopyrrole as a red solid (129 mg, 94%), mp 295 °C (subl., dec.) (Found: C, 58.9; H, 2.6; N, 3.7. $C_{18}H_{10}BrNO_3$ requires C, 58.7; H 2.7; N, 3.8%). δ_H 7.43–7.47 (3H, m, Ar-H), 7.66 and 7.98 (each 2H, AA′BB′, *p*-BrC_6H_4), 8.13–8.17 (2H, m, Ar-H) and 11.88 (1H, s, NH). *m/z* (CI) 368/370 [100/94%, $(M+1)^+$].

4.1.13. 3-(*p*-Nitrophenyl)-6-phenyl-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 12e. The *p*-nitrobenzoylpyrrolinone ester **9e** (300 mg, 0.90 mmol) was irradiated with microwave radiation without solvent, heating to 270 °C for 15 min. The crude product was then allowed to cool, methanol was added and the solid filtered off and washed with methanol. This gave the furopyrrole as a red solid (230 mg, 87%), mp 340 °C (by DSC). (Found: C, 64.4; H, 2.9; N, 8.4. $C_{18}H_{10}N_2O_5$ requires C, 64.7; H, 3.0; N, 8.4%). δ_H 7.58–7.69 (3H, m, *m*/*p*-Ph), 8.28–8.34 (2H, m, *o*-Ph), 8.38 (4H, s, *p*-$O_2NC_6H_4$) and 12.15 (1H, s, NH). *m/z* (ESI −ve) 334 (21%, $M^{+\cdot}$), 333 [100%, $(M-1)]^+$.

4.1.14. 6-Phenyl-3-(3-pyridyl)-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 12f. The nicotinylpyrrolinone ester **9f** (100 mg, 0.30 mmol) was irradiated with microwave radiation without solvent, heating to 230 °C for 10 min. The crude product was then allowed to cool, methanol was added and the solid filtered off and washed with methanol. This gave the furopyrrole **12f** as a red solid (16 mg, 19%), the remainder being an intractable black tar. Compound **12f**, mp 333 °C (by DSC), could not be obtained in analytical purity (Found: C, 69.25; H, 3.5; N, 9.8. $C_{17}H_{10}N_2O_3$ requires C, 70.3; H, 3.5; N, 9.65%) but showed the correct ^{1}H NMR and accurate mass: δ_H 7.63–7.74 (5H, m, Ph-H), 8.33–8.39 (1H, m, Py-5-H), 8.56 (1H, dt, J=8.2, 1.9 Hz, Py-4-H), 8.79 (1H, dd, J=1.5, 4.8 Hz, Py-6-H), 9.41 (1H, d, J=1.9 Hz, Py-2-H) and 12.09 (1H, s, NH). *m/z* (ESI −ve) 290 (20%, $M^{+\cdot}$), 289.0618 [100%, $(M-1)^+$; $C_{17}H_9N_2O_3$ requires 289.0613].

4.1.15. 5-Benzyl-3,6-diphenyl-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 13a. Compound **12a** (1.00 g, 3.4 mmol) was added under nitrogen at 25 °C to a suspension of sodium hydride (55–65% dispersion in mineral oil; 0.20 g) in tetrahydrofuran (100 cm^3), and the mixture heated briefly to reflux during 5 min. The solution was cooled to room temperature, benzyl bromide (0.70 g, 4.1 mmol) was added, and the mixture heated under reflux for 19 h, then cooled. Water (50 cm^3) was added and the mixture extracted with a mixture of tetrahydrofuran and ethyl acetate (1:1). The extract was dried and concentrated, and the residue mixed with petrol and immersed in an ultrasonic bath for 20 min. The product **13a** (0.97 g, 74%) was filtered off and dried in vacuo: it had mp (DSC) ca. 213 °C (slow decomp. >150 °C). (Found: C, 78.8; H, 4.9; N, 3.6. $C_{25}H_{17}NO_3$ requires C, 79.1; H, 4.5; N, 3.7%). δ_H 5.09 (2H, s, CH_2), 7.10–7.14 (2H, m, Ar-H), 7.19–7.50 (4H, m, Ar-H), 7.52–7.64 (3H, m, Ar-H), 7.65–7.80 (4H, m, Ar-H) and 8.31–8.40 (2H, m, Ar-H). *m/z* (EI) 379 ($M^{+\cdot}$, 33%), 105 (50), 91 (100).

4.1.16. 2-Benzyl-3,5,6-triphenyl-DPP 15a. A mixture of compound **13a** (10.0 g, 26.4 mmol), *N*,*N*′-dicyclohexylcarbodiimide (13.5 g, 65.5 mmol), and aniline (5.0 g, 53.8 mmol) in dichloromethane (300 cm^3) containing trifluoroacetic acid (3 drops) was stirred under nitrogen at 40 °C for 16 h. Further portions of aniline (15.0 g) and *N*,*N*′-dicyclohexylcarbodiimide (10.0 g) were then added, heating was continued for a further 24 h and finally the solvent was distilled off. The residue was recrystallised from 1,4-dioxan and the fluorescent orange product **15a** washed sequentially with hot propan-2-ol, methanol and water. Yield 1.87 g (16%), mp 270–272 °C. (Found: C, 81.9; H, 4.8; N, 6.2. $C_{31}H_{22}N_2O_2$ requires C, 81.9; H, 4.9; N, 6.2%). δ_H ($CDCl_3$) 5.05 (2H, s, PhCH_2N), 7.16–7.24 (4H, m, Ar-H), 7.27–7.50 (12H, m, Ar-H), 7.66–7.70 (2H, m, Ar-H) and 7.74–7.79 (2H, m, Ar-H). *m/z* (EI) 454 ($M^{+\cdot}$, 100%), 363 (10), 335 (16), 292 (14), 180 (31), 91 (41). λ_{max} (CH_2Cl_2) 468 (log ε 4.26).

4.1.17. 5-Methyl-3,6-diphenyl-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 14a. (a) Sodium hydride (55–65% dispersion in mineral oil: 0.16 g) was added under nitrogen to a stirred mixture of the furopyrrole **12a** (0.99 g, 3.4 mmol) in dry tetrahydrofuran (200 cm^3) and the mixture heated to boiling for ca. 5 min (until hydrogen evolution ceased), then cooled to 25 °C. Iodomethane (1.46 g, 10.3 mmol) was added and the mixture stirred at 25 °C for 16 h. Water (100 cm^3) was added and the mixture extracted several times with a mixture of tetrahydrofuran and ethyl acetate (2:1). The combined extracts were dried and concentrated, the residue was redissolved in DMSO (20 cm^3) and reprecipitated by dropwise addition to water (200 cm^3). The fluorescent orange product was filtered off, washed with water and dried in vacuo.

(b) A mixture of the furopyrrole **12a** (1.19 g, 4.12 mmol), methyl *p*-toluenesulfonate (1.15 g, 6.18 mmol), potassium carbonate (1.14 g, 8.24 mmol) and DMF (40 cm^3) was stirred at room temperature overnight. Water was then added, and the organic component extracted with dichloromethane. The extract was dried and the solvent was removed; washing of the residue with water then methanol

gave the methylated compound **14a** as a red solid (0.85 g, 68%), mp 198–200 °C.

(Found: C, 75.2; H, 4.5; N, 4.6. $C_{19}H_{13}NO_3$ requires C, 75.3; H, 4.3; N, 4.6%). ν_{max} 1755 (ester C=O), 1700 (lactam C=O) and 1625 (C=C). δ_H ($CDCl_3$) 3.46 (3H, s, NCH_3), 7.52–7.62 (6H, m, 2×*m*/*p*-Ph-H), 7.81–7.85 (2H, m, *o*-Ph-H) and 8.39–8.43 (2H, m, *o*-Ph-H).

4.1.18. 3-(*p*-Bromophenyl)-5-methyl-6-phenyl-1*H*-furo[3,4-*c*]pyrrole-1,4(5*H*)-dione 14c. A mixture of the furopyrrole **12c** (1.50 g, 4.08 mmol), methyl *p*-toluenesulfonate (1.14 g, 6.12 mmol), potassium carbonate (1.13 g, 8.16 mmol) and DMF (60 cm^3) was stirred at room temperature overnight. Water was then added, and the organic component extracted with dichloromethane. The extract was dried, the solvent was removed and the residue washed with water then methanol, to give the methylated compound as a red solid (0.83 g, 53%), mp 215–216 °C. (Found: C, 59.6; H, 2.9; N, 3.6. $C_{19}H_{12}BrNO_3$ requires C, 59.7; H, 3.2; N, 3.7%). δ_H ($CDCl_3$) 3.38 (3H, s, NCH_3), 7.50–7.54 (3H, m, *m*/*p*-Ph), 7.61 and 8.19 (each 2H, AA′BB′, *p*-C_6H_4Br), 7.73–7.78 (2H, m, *o*-Ph). *m*/*z* (ESI) 404/406 $(M+Na)^+$.

4.1.19. 5-Methyl-3-(*p*-nitrophenyl)-6-phenyl-1*H*-furo-[3,4-*c*]pyrrole-1,4(5*H*)-dione 14e. A mixture of furopyrrole **12e** (0.90 g, 2.7 mmol), methyl *p*-toluenesulfonate (0.75 g, 4.04 mmol), potassium carbonate (1.00 g, 7.2 mmol) and DMF (40 cm^3) was stirred at room temperature overnight. Water was then added and the organic component extracted with dichloromethane. The extract was dried, solvent was removed and the residue washed with water then methanol, to give the red methylated compound **14e** (0.65 g, 70%), mp 253–255 °C. (Found: C, 65.4; H, 3.3; N, 7.8. $C_{19}H_{12}N_2O_5$ requires C, 65.5; H, 3.5; N, 8.0%). δ_H ($CDCl_3$) 3.49 (3H, s, NCH_3), 7.60–7.65 (3H, m, *m*/*p*-Ph-H), 7.84–7.88 (2H, m, *o*-Ph-H), 8.38 and 8.55 (each 2H, AA′BB′, *p*-$O_2NC_6H_4$). *m*/*z* (ESI) 349 (100%, $[M+1]^+$).

4.1.20. 5-Methyl-2,3,6-triphenyl-DPP 16a. A solution of the furopyrrole **14a** (0.50 g, 1.65 mmol), aniline (1.54 g, 16.5 mmol), *N*,*N*′-di-*i*-propylcarbodiimide (1.04 g, 1.29 cm^3, 8.25 mmol) and trifluoroacetic acid (3 drops) in dichloromethane (100 cm^3) was stirred at room temperature for 8 days. The solvent was distilled off and the residue washed with methanol, to give the orange DPP (0.16 g, 25%), mp 267–269 °C. (Found: C, 79.4; H, 5.0; N, 7.3. $C_{25}H_{18}N_2O_2$ requires C, 79.35; H, 4.8; N, 7.4%). ν_{max} 1675 (C=O). δ_H 3.42 (3H, s, CH_3), 7.15–7.20 (2H, m, Ar-H *o*-Ph-H), 7.28–7.41 (6H, m, Ar-H), 7.51–7.56 (3H, *m*/*p*-Ph-H), 7.62–7.68 (2H, m, Ar) and 7.91–7.95 (2H, m, Ar-H). *m*/*z* (ESI-+ve) 402 $(M+Na+1)^+$, 401 $(M+Na)^+$. λ_{max} (CH_2Cl_2) 468 (log ε 4.11).

4.1.21. 6-(*p*-Bromophenyl)-2-methyl-3,5-diphenyl-DPP 16c. A mixture of furopyrrole **12c** (300 mg, 0.79 mmol), aniline (146 mg, 1.57 mmol), DCC (323 mg, 1.57 mmol), trifluoroacetic acid (2–3 drops) and dichloromethane (100 cm^3) was stirred at room temperature for 6 days. The solvent was removed and washing of the residue with methanol gave the DPP as a red solid (173 mg, 55%), mp 255–256 °C. (Found: C, 65.4; H, 3.7; N, 6.2. $C_{25}H_{17}BrN_2O_2$ requires C, 65.7; H, 3.8; N, 6.1%). δ_H ($CDCl_3$) 3.35 (3H, s, NCH_3), 7.07–7.12 (2H, m, Ar-H), 7.26–7.40 (5H, m, Ar-H), 7.43–7.49 (5H, m, Ar-H) and 7.83–7.88 (2H, m, Ar-H). λ_{max} (CH_2Cl_2) 479 (log ε 4.20).

4.1.22. 2-Methyl-6-(*p*-nitrophenyl)-3,5-diphenyl-DPP 16e. A mixture of furopyrrole **12e** (100 mg, 0.29 mmol), aniline (53 mg, 0.57 mmol), DCC (118 mg, 0.57 mmol), trifluoroacetic acid (2–3 drops) and dichloromethane (25 cm^3) was stirred at room temperature for 72 h. The solvent was removed, and washing of the residue with methanol gave the pyrrolopyrrole as a red solid (63 mg, 52%), mp 233–235 °C. (Found: C, 71.0; H, 3.7; N, 9.7. $C_{25}H_{17}N_3O_4$ requires C, 70.9; H, 4.05; N, 9.9%). δ_H ($CDCl_3$) 3.45 (3H, s, NCH_3), 7.15–7.20 (2H, m, *o*-Ph), 7.36–7.44 (3H, m, *m*/*p*-Ph), 7.55–7.60 (3H, m, *m*/*p*-Ph), 7.81 and 8.16 (each 2H, AA′BB′, *p*-$C_6H_4NO_2$), and 7.93–7.98 (2H, m, *o*-Ph). *m*/*z* (ESI) 447 (28%, $[M+Na+1]^+$), 446 (100%, $[M+Na]^+$). λ_{max} (CH_2Cl_2) 493 (log ε 4.15).

4.1.23. *Z*-1-Methyl-5-phenyl-3-[1-phenyl-1-(phenylamino)methylidene]-2,3-dihydro-pyrrol-2-one 18a. A solution of furopyrrole **14a** (135 mg, 0.38 mmol) and aniline (85 μl, 0.77 mmol) in toluene (3 cm^3) was irradiated at 150 °C for 10 min. The solution was cooled, and the solvent removed under reduced pressure. Recrystallisation from ethanol gave the pyrrolinone as an orange solid (106 mg, 68%), mp 194.5–197.5 °C. (Found: C, 81.6; H, 5.4; N, 7.8. $C_{24}H_{20}N_2O$ requires C, 81.8; H, 5.7; N, 8.0%). δ_H ($CDCl_3$) 3.34 (3H, s, NCH_3), 5.71 (1H, s, CH), 6.72–6.77 (2H, m, *o*-PhN), 6.93–7.00 (1H, m, *p*-PhN), 7.07–7.15 (2H, m, *m*-PhN), 7.28–7.34 (1H, m, Ar-H), 7.34–7.42 (9H, m, Ar-H) and 11.82 (1H, s, NH). *m*/*z* (ESI+ve): 352 (100%, $M^{+\cdot}$), 353 (44%, $[M+1]^+$), 375 (92%, $[M+Na]^+$), 376 (23%, $[M+Na+1]^+$).

4.1.24. *Z*-3-[1-(*p*-Bromophenyl)-1-(phenylamino)methylidene]-1-methyl-5-phenyl-2,3-dihydropyrrol-2-one 18c. This was similarly prepared from furopyrrole **14c** (250 mg, 0.65 mmol) and aniline (119 μl, 1.31 mmol) in toluene (5 cm^3). The orange pyrrolinone (105 mg, 38%) had mp 179.5–181.5 °C. (from ethanol). (Found: C, 67.15; H, 4.2; N, 6.4. $C_{24}H_{19}BrN_2O$ requires C, 66.8; H, 4.4; N, 6.5%). δ_H ($CDCl_3$) 3.36 (3H, s, NCH_3), 5.68 (1H, s, CH), 6.76–6.81 (2H, m, *o*-PhN), 6.97–7.05 (1H, m, *p*-PhN), 7.12–7.18 (2H, m, *m*-PhN), 7.28 and 7.52 (each 2H, AA′BB′, *p*-BrC_6H_4), 7.30–7.45 (5H, m, Ar-H) and 11.80 (1H, s, NH).

4.2. X-ray crystallography

The intensity data for compounds **7**, **8** and **9a** were recorded at 293(1) K with a Rigaku AFC7S diffractometer using graphite-monochromated Mo-Kα radiation (λ=0.7107 Å), and the structures of **8** and **9a** (Figs. 2 and 3) were solved by direct methods using SIR92[7] and refined by full-matrix least squares on *F*, using the TeXsan system 1.[8] In the case of compound **7**, the structure refined with two independent molecules in the asymmetric unit which are chemically identical, and was solved using SHELXS-86.[9] The intensity data for compound **18a** were recorded using a Siemens/Bruker SMART diffractometer, with data being integrated

using the SAINT[10] and SADABS[11] programs, the structure solved by direct methods and refined by full-matrix least-squares against F^2 (SHELXTL[12]).

The systematic absences allowed unique assignment of all the space groups. All hydrogen atoms were located from difference maps, and were included in the refinements as riding atoms in idealised positions with isotropic displacement parameters; all non-hydrogen atoms were refined anisotropically. All data were corrected for Lorentz, polarisation and long-term intensity fluctuations. Absorption effects were corrected on the basis of multiple equivalent reflections or by semi-empirical methods. All hydrogen atoms were assigned isotropic displacement parameters and were constrained to idealised geometries. Crystallographic data (excluding structure factors) for compounds **7**, **8**, **9a** and **18a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 243378, 243379, 243380 and 243381, respectively. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

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