Pergamon

Tetrahedron 58 (2002) 5547–5565

TETRAHEDRON

Synthetic studies related to diketopyrrolopyrrole (DPP) pigments. Part 1: The search for alkenyl-DPPs. Unsaturated nitriles in standard DPP syntheses: a novel cyclopenta[*c*]pyrrolone chromophore☆

Colin J. H. Morton,[a] Ryan Gilmour,[a] David M. Smith,[a,*] Philip Lightfoot,[a] Alexandra M. Z. Slawin[a] and Elizabeth J. MacLean[b]

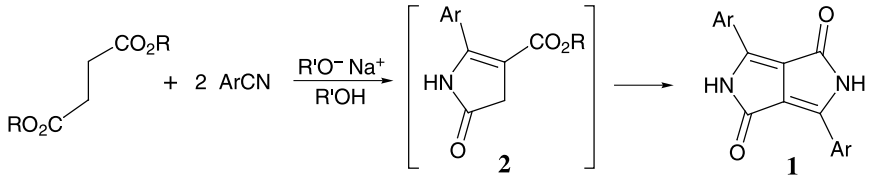
[a]*School of Chemistry, University of St Andrews, Purdie Building, St Andrews, Fife, KY16 9ST Scotland, UK*
[b]*Department of Synchrotron Radiation, Daresbury Laboratory, Daresbury, Warrington, Cheshire, WA4 4AD England, UK*

Received 10 January 2002; revised 25 March 2002; accepted 18 April 2002

Abstract—Reactions of the anion of ethyl 4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate with the Diels–Alder adducts of acrylonitrile and various dienes rarely yield the expected DPP derivatives. The reaction with cyclohex-3-enecarbonitrile provides a noteworthy exception: thermolysis of the resulting cyclohexenyl-DPP gives butadiene and impure 3-ethenyl-6-phenyl-DPP, the latter being thermally unstable. Michael additions predominate when the above anion reacts with α,β-unsaturated nitriles: acrylonitrile and methacrylonitrile give 4,4-bis(cyanoethyl) and 4,4-bis(2-cyanopropyl) derivatives, and cinnamonitrile, substituted cinnamonitriles and 3-(2-thienyl)acrylonitrile give deep red 3-aryl-5-cyano-4-hydroxy-2*H*-cyclopenta[*c*]pyrrol-1-ones. These ambident nucleophiles may undergo *N*- and either *O*- or *C*-alkylation according to the alkylating agent used.

3,6-Disubstituted 2*H*,5*H*-pyrrolo[3,4-*c*]pyrrole-1,4-diones **1**, familiarly known as diketopyrrolopyrroles or DPPs, are currently of considerable commercial importance as 'high-performance' pigments. For example, the 3,6-diaryl compounds are widely used to provide the colouring matter for red automotive paints,[1] and variation of the substituents attached to the aryl rings may serve to modify the precise colour of the pigment.[2] The success of these compounds as pigments relies, in part, on their very low solubility in most common solvents and in the media in which they are dispersed for commercial applications. This lack of solubility is presumed to result from extensive intermolecular hydrogen bonding in the solid,[1–3] and the red colour as well as the low solubility also derive in part from π–π stacking, a phenomenon which is obvious from X-ray crystallography.[3]

DPP derivatives bearing identical 3- and 6-substituents are produced commercially by the reaction of a dialkyl (usually di-*t*-butyl) succinate with 2 molar equiv. of a nitrile in the presence of a strong and sterically hindered base, sodium *t*-amyloxide being the reagent of choice (Scheme 1).[4] The first step in the process is presumed to lead to the pyrroline-carboxylate ester **2**, and the latter (after deprotonation) reacts with a second equivalent of the nitrile to yield the final product **1**. Evidence for the intermediacy of

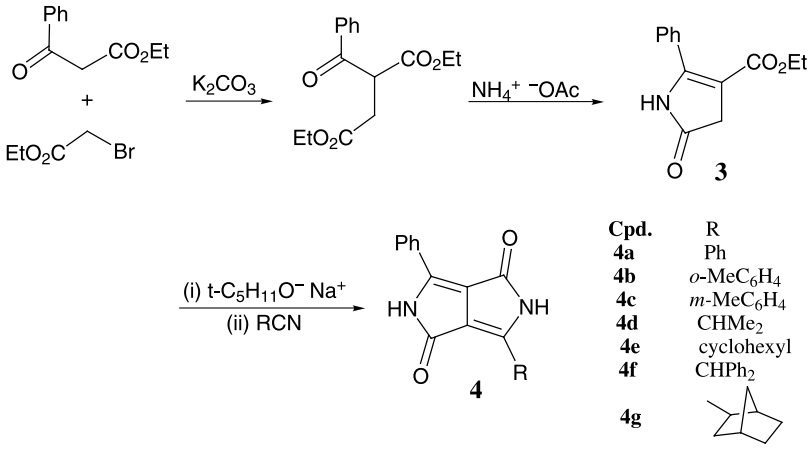


Scheme 1.

☆ Presented, in part, at the 17th International Congress of Heterocyclic Chemistry, Vienna, August 1999.

Keywords: pigments; pyrrolinones; Diels–Alder reactions; Michael reactions; cyclisations.
* Corresponding author; e-mail: dms@st-and.ac.uk

0040–4020/02/$ - see front matter
PII: S0040-4020(02)00443-X



Scheme 2.

compounds of type **2** is provided by the independent synthesis of the ester **3** from ethyl bromoacetate and the anion of ethyl benzoylacetate, followed by ring closure using ammonium acetate (Scheme 2); the ester **3** then reacts further with nitriles to give DPP derivatives **4** in which one of the 3- and 6-substituents is phenyl but the other may vary.[5]

Although many DPP derivatives, both symmetrically and unsymmetrically substituted, have been prepared by one or other of the above methods, to our knowledge there is no literature report to date of a DPP derivative in which the 3- and/or 6-substituent contains an alkenic double bond. Of particular interest to us was the effect on the colour of the pigment of such a double bond, if it were conjugated with the chromophoric π-electron system. In addition, the presence of an alkenic substituent would offer opportunities for further elaboration of this substituent through functional group transformations.

The use of an alkenic nitrile directly in one of the standard DPP syntheses did not at first commend itself to us, for two main reasons:

(i) Acrylonitrile itself is liable to undergo anionic polymerisation in presence of a nucleophilic base,[6] and indeed a preliminary reaction involving acrylonitrile and sodium *t*-amyloxide alone (in the absence of either a succinate or the ester **3**) yielded an intractable colourless solid which is presumed to be an oligomer or polymer.
(ii) α,β-Unsaturated nitriles are excellent Michael acceptors[7]—a fact which we were subsequently able to demonstrate for ourselves (see below).

Accordingly, our initial attempts to synthesize alkenyl-DPPs sought to use as electrophiles some Diels–Alder adducts of acrylonitrile, in the hope that a subsequent retro-Diels–Alder step might release the alkenic functionality after ring closure to the DPP had been achieved.

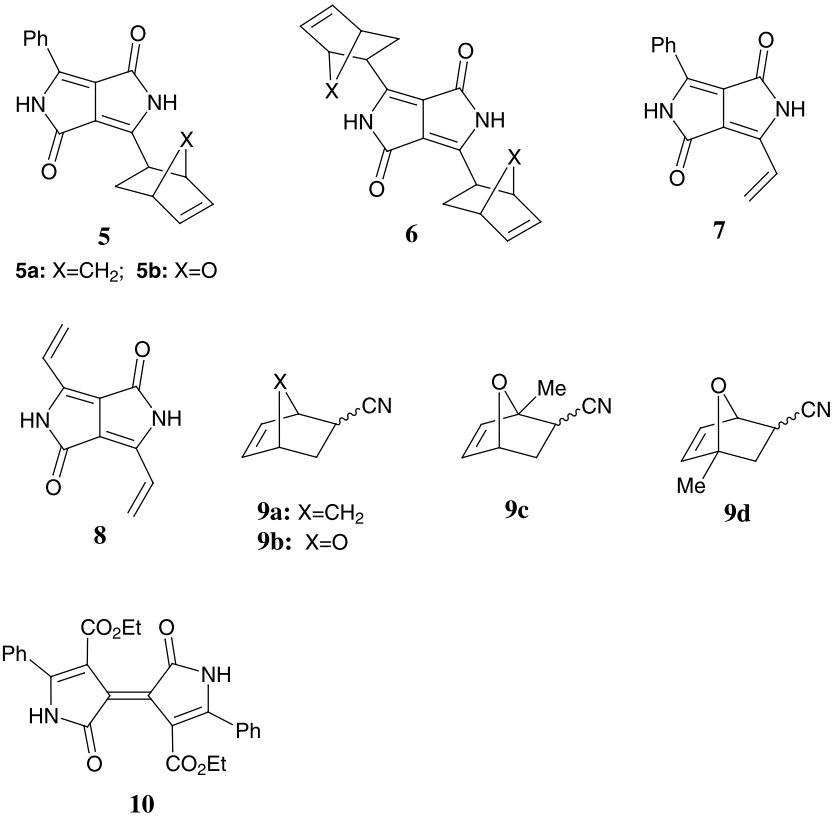
The initial synthetic targets were DPP analogues of the types **5** and **6**, the expectation being that a thermal retro-Diels–Alder procedure might then yield the mono- or di-alkenyl-DPPs **7** and **8**. Of the nitriles required as starting materials for these syntheses, bicyclo[2.2.1]hept-5-ene-2-carbonitrile **9a** (the Diels–Alder adduct of cyclopentadiene and acrylonitrile) is commercially available, and the furan–acrylonitrile adduct **9b** was obtained by the literature procedure;[8] both of these are mixtures of *exo*- and *endo*-isomers. The reaction of 2-methylfuran with acrylonitrile produced a mixture of four isomers, i.e. *exo*- and *endo*-**9c**–**d**.[9] These isomer mixtures were used in standard DPP syntheses with the pyrrolinecarboxylate ester **3** in presence of sodium *t*-amyloxide; however, the reactions were conducted at relatively low temperatures in order to minimise premature retro-Diels–Alder cleavage of the bridged bicyclic moieties.

Reaction of the oxygen-bridged adduct **9b** with the pyrrolinecarboxylate ester **3** and sodium *t*-amyloxide gave a DPP which, surprisingly, was not the expected product **5b** but 3,6-diphenyl-DPP **4a**; the isolated yield was 48%. The corresponding reaction of the mixture **9c** and **9d** with the ester **3** similarly gave, in 46% yield, a mixture of two 3-phenyl-6-tolyl-DPPs (presumably the *o*- and *m*-tolyl isomers **4b** and **4c**). Under similar conditions, the norbornenecarbonitrile **9a** failed altogether to react with the ester **3**, the only product isolated having ^{1}H NMR and mass spectra consistent with the indigoid compound **10**, an expected[10] product of oxidative dimerisation of compound **3**. Reaction of the furan-derived adduct **9b** with diethyl succinate and sodium *t*-amyloxide also led to 3,6-diphenyl-DPP **4a** and benzonitrile, the latter being identified by GC and ^{1}H NMR.

Two important questions arise from these results:

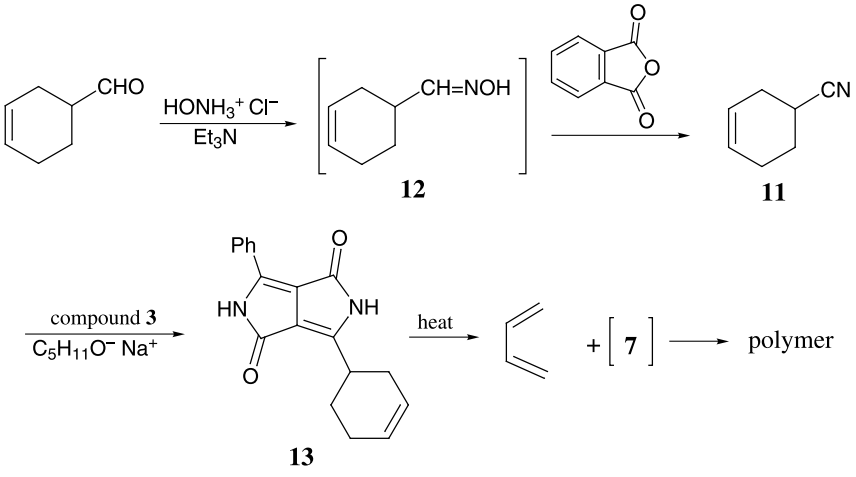
(i) Does the aromatisation of the oxygen-bridged bicyclic system occur prior to, subsequent to, or during, the incorporation of the nitrile into a DPP?
(ii) Why does the methylene-bridged bicyclic nitrile **9a** apparently fail to react with the pyrrolinecarboxylate ester **3**?

(i) The aromatisation of 7-oxabicyclo[2.2.1]heptenes in the presence of base has been recorded in a few cases. It is recorded, for example, that Diels–Alder adducts of furan with fumaronitrile are aromatised to phthalonitriles by reaction with lithium hexamethyldisilazide at −78°C,[11]



and the **9c**–**d** isomer mixture itself is transformed into a mixture of *o*- and *m*-tolunitriles by reaction with potassium *t*-butoxide followed by acidification.[9] The failure of the cyclopentadiene–acrylonitrile adduct **9a** to react with the pyrrolinecarboxylate ester lends weight to the hypothesis that aromatisation of **9b** and **9c**–**d** precedes their reactions with the ester **3**. While, indeed, we have shown that 7-oxabicyclo[2.2.1]hept-5-ene-2-carbonitrile **9b** reacts with sodium *t*-amyloxide alone, in the absence of either the ester **3** or diethyl succinate, to give benzonitrile, the conversion is not quantitative; and it thus appears possible that the aromatisation of the bridged bicyclic system may occur *both* before *and* after reaction of the nitriles with compound **3**.

(ii) Standard DPP syntheses involving aliphatic nitriles appear generally to be lower-yielding than those involving their aromatic counterparts. No reason has evidently been advanced for this difference, although it is conceivable that any nitrile which contains an α-hydrogen may be deprotonated by the action of a strong base, and the electrophilicity of the cyano-carbon thereby reduced. It is also possible that in some branched-chain aliphatic nitriles there may be steric hindrance to nucleophilic attack at the cyano-carbon. Nevertheless we have demonstrated that isobutyronitrile, cyclohexanecarbonitrile, diphenylacetonitrile, and even norbornane-2-carbonitrile react normally with the pyrrolinecarboxylate ester **3** to give the DPP analogues **4d**, **4e**, **4f** and **4g**, respectively, so steric hindrance may be discounted as the reason for the failure of the norbornenecarbonitrile **9a** to produce a

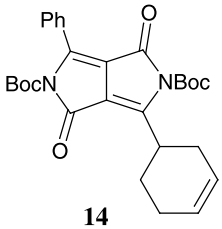


Scheme 3.

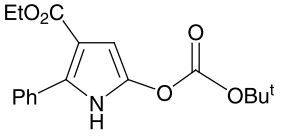
DPP analogue. The possibility of a retro-Diels–Alder process in competition with nucleophilic addition may also be ruled out since the nitrile **9a** is largely recoverable from the reaction mixture. However, the acidity of the α-hydrogen of the nitrile **9a** relative to these other secondary nitriles remains an open question, even although intuitively it appears that diphenylacetonitrile ought to be the most acidic of this whole series.

Cyclohexene-3-carbonitrile **11** (formally the Diels–Alder adduct of butadiene and acrylonitrile) was obtained from the corresponding aldehyde (which is commercially available) by way of the oxime **12** (Scheme 3),[12] and this nitrile also reacts normally with the pyrrolinecarboxylate ester **3** to produce the cyclohex-3-enyl-DPP **13** (Scheme 3). Compound **13**, which was fully characterised as its *N*,*N*′-bis-(*t*-butoxycarbonyl) derivative **14** (see below), is not only an alkenyl-DPP in its own right, and thus the first fully authenticated representative of this class of DPP analogues, but it also undergoes retro-Diels–Alder cleavage on flash vacuum pyrolysis at 700°C, yielding butadiene, identified by ^{1}H NMR, and (presumably) 3-ethenyl-6-phenyl-DPP **7**, although the latter was not obtained pure, possibly because of a tendency to undergo polymerisation at the elevated temperature of the furnace outlet at which it was deposited. Nevertheless, the concept of using a Diels–Alder/retro-Diels–Alder sequence in order to generate alkenyl-DPPs is now established.

A recurring problem in the syntheses of DPP analogues arises as a result of their very low solubility in most common solvents, and impurities trapped within the precipitated solid cannot therefore be removed easily by recrystallisation; for the purposes of complete characterisation conversion of these compounds into *N*,*N*′-diacyl [e.g. bis(*t*-butoxycarbonyl)] derivatives is often necessary.[13] We sought to obviate the synthetic problem by using an *N*-protected pyrrolinone ester as a starting compound in the standard synthetic sequence, since *N*,*N*′-disubstituted DPPs are generally amenable to recrystallisation; but acylation of 2-pyrrolinones tends to occur at oxygen rather than nitrogen, to give 2-acyloxypyrroles,[14] and in accordance with this precedent, reaction of the pyrrolinecarboxylate ester **3** with di-*t*-butyl dicarbonate gave ethyl 5-(*t*-butoxycarbonyloxy)-2-phenylpyrrole-3-carboxylate **15**. The potentially carbanionic centre in the ring is lost on formation of the delocalised 6π-system, and this synthetic approach to DPPs has not therefore been further explored.

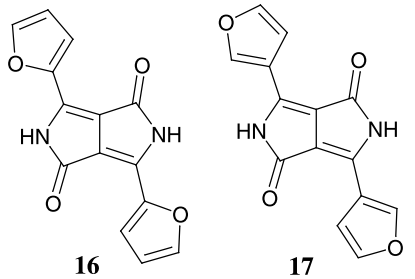


14



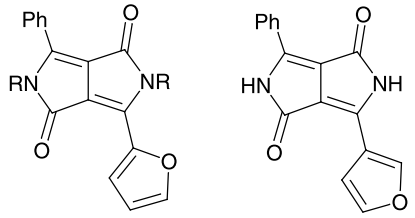
15

A second synthetic approach to alkenyl- and (substituted aryl)-DPPs employing Diels–Alder and retro-Diels–Alder reactions involved the use of furyl-substituted DPPs as intermediates, and their subsequent reactions with dienophiles. 3,6-Di-(2-furyl)-DPP **16** has been mentioned in patent literature,[4a] but details of its preparation and characterisation are lacking; and nothing has hitherto been recorded about the corresponding di-(3-furyl) compound **17**, nor about 3-(2- or 3-furyl)-6-phenyl-DPPs **18a** and **18b**. Compounds **16** and **18a** were obtained by standard DPP syntheses using, respectively, diethyl succinate and the pyrrolinecarboxylate ester **3** in reactions with 2-furonitrile and sodium *t*-amyloxide. The corresponding reactions with 3-furonitrile yielded compounds **17** and **18b**, the 3-furonitrile itself being prepared from 3-furoic acid by reaction with 1,3-dicyanobenzene according to the procedure of Garst and Wilson.[15]



16

17



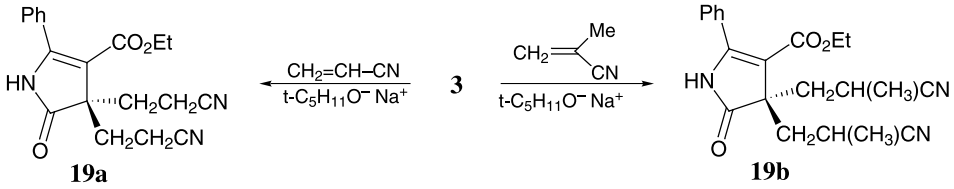
18a: R=H
18c: R=Me

18b

The compounds **16**, **18a** and **18b** were fully characterised as their *N*,*N*′-bis-(*t*-butoxycarbonyl) derivatives, and **18a** was also converted, by reaction with methyl toluene-*p*-sulfonate and base, into its *N*,*N*′-dimethyl derivative **18c** which formed crystals suitable for X-ray analysis (see below).

In the crystals of **18c**, whereas the phenyl substituent is tilted out of this plane by approximately 30°, the furan and DPP ring systems are coplanar. This indicates the possibility of conjugation between the π-electrons of these two systems, although there is no clear evidence for such conjugation in the crystalline state, since the interannular bond is only marginally shorter than that between the phenyl group and the DPP ring (see below); however it is still significantly shorter (by approximately 0.05 Å) than the interannular bond in biphenyl.[16]

Disappointingly none of the four compounds **16**, **17**, **18a** or **18b** showed any tendency to undergo Diels–Alder reactions at atmospheric pressure, either with dimethyl acetylene–dicarboxylate or with phenylacetylene, under a variety of experimental conditions. This is not perhaps entirely surprising in the case of the 2-furyl and di-(2-furyl) compounds, since any conjugation between the adjacent π-electron systems in these compounds would be interrupted by the cycloaddition; and 2-phenylfuran derivatives, where a similar effect may be expected to operate, have been described as 'notoriously poor' dienes in Diels–Alder reactions.[17] In the 3-furyl series, however, the

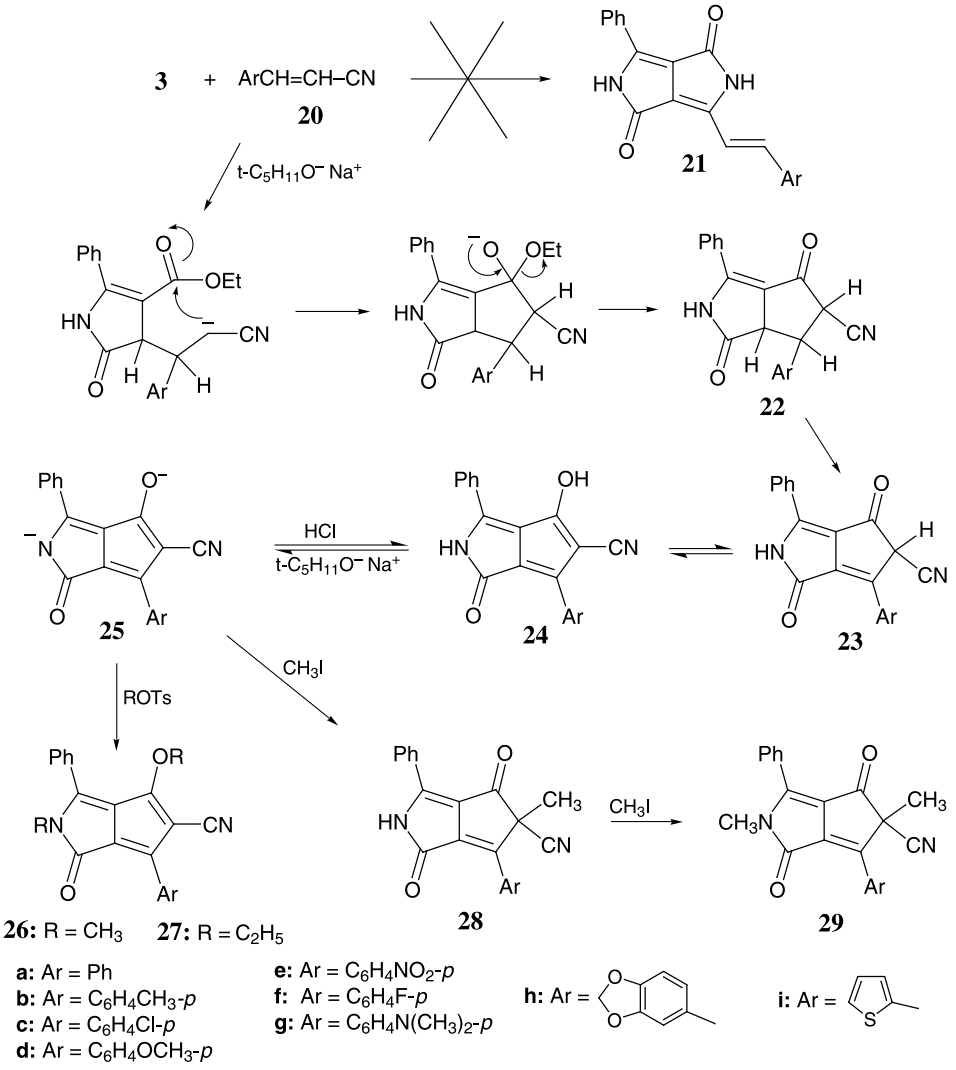


Scheme 4.

formation of a Diels–Alder adduct would still allow a degree of conjugation between the two ring systems, and relative to the 2-furyl series, any steric hindrance to the approach of the diene and dienophile ought also to be reduced.

The limited success of the Diels–Alder/retro-Diels–Alder approach led us to explore the other possible route to these compounds, viz. the direct reaction of ethyl 4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate **3** with α,β-unsaturated nitriles and sodium *t*-amyloxide (cf. Scheme 2), although we recognised the possibility of conjugate addition as a competing process (see above). In the event, the reactions of the anion of compound **3** with acrylonitrile and methacrylonitrile gave 1:2 adducts; the latter was shown by X-ray crystallography (Fig. 4) to have the structure **19b**, and the former was accordingly assigned the corresponding structure **19a** (Scheme 4).

The ^{1}H NMR spectrum of compound **19a** is complicated, on account of the diastereotopicity of the methylene hydrogens: the three signals in the region δ 2–3 (ratio of integrals 1:2:1) all approximate to double triplets. In the case of compound **19b**, the additional complexity observed in the ^{1}H NMR spectrum is consistent (a) with the presence of two diastereomers in unequal proportions, a conclusion which is reinforced by the appearance of 'major' and 'minor' signals in the ^{13}C NMR spectrum, and (b) with the two 2-cyanopropyl substituents being differently oriented in space with respect to the ring, resulting in the non-equivalence of the



Scheme 5.

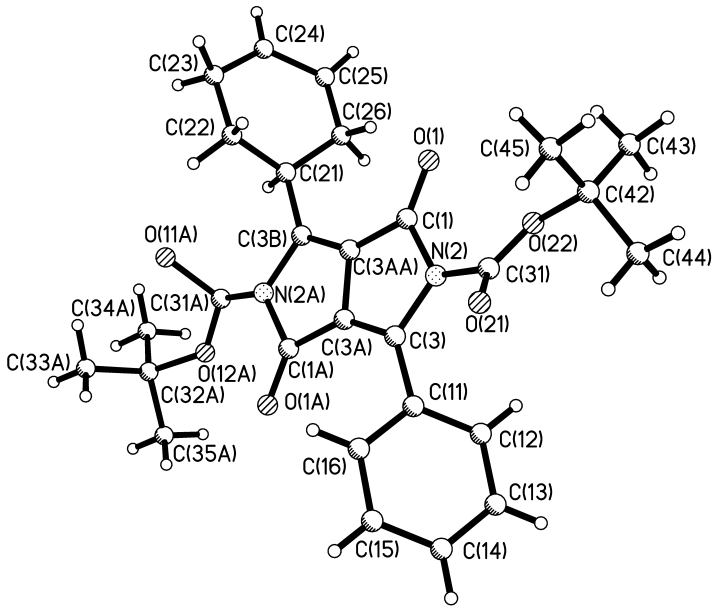


Figure 1. X-ray structure (simplified) of compound **14**.
Selected bond lengths (Å): C(1)-O(1) 1.211(5); C(1)-N(2) 1.446(5); N(2)-C(3) 1.414(5); C(3)-C(3A) 1.352(5); C(3A)-C(3AA) 1.432(6); N(2)-C(31) 1.407(6); C(31)-O(21) 1.291(7); C(21)-C(22) 1.447(11); C(3AA)-C(1) 1.455(6); C(3)-C(11) 1.476(5); C(22)-C(23) 1.46(2); C(23)-C(24) 1.42(2); C(24)-C(25) 1.348(14); C(25)-C(26) 1.481(15).
Selected interbond angles (°): N(2)-C(1)-C(3AA) 102.9(3); C(1)-C(3AA)-C(3A) 108.2(4); C(3)-C(3A)-C(3AA) 110.3(4); N(2)-C(3)-C(3A) 107.3(3); C(1)-N(2)-C(3) 111.1(3); C(21)-C(22)-C(23) 117.8(11); C(22)-C(23)-(C24) 114.8(10); C(23)-C(24)-C(25) 123.3(8); C(24)-C(25)-C(26) 122.2(7); C(25)-C(26)-(C21) 112.8(8); C(26)-C(21)-C(22) 115.8(8).
Selected torsion angles (°): C(1)-C(2)-C(3)-C(3A) 2.0(4); C(1)-C(2)-C(3)-C(11) 177.2(3); C(3A)-C(3)-C(11)-C(12) 126.1(5); C(2)-C(3)-C(11)-C(12) −48.1(6); C(3)-C(2)-C(1)-O(1) 175.0(4); C(21)-C(22)-C(23)-C(24) 23(2); C(22)-C(23)-C(24)-C(25) 2(2); C(23)-C(24)-C(25)-C(26) −7(2); C(24)-C(25)-C(26)-C(21) −13(2); C(26)-C(21)-C(22)-C(23) 43.3(14).

corresponding carbons in these two substituents. The crystal of **19b** selected for X-ray analysis was that of the (racemic) diastereomer in which both 2-cyanopropyl substituents have the same absolute configuration, and the reference molecule shown in Fig. 4 is, arbitrarily, the (*S*,*S*) enantiomer (see below). No cyclised product was detected in these reactions.

The reaction of compound **3** with cinnamonitrile, **20a**, and sodium *t*-amyloxide took a different course. The dark red, highly insoluble, acidic product was clearly not the expected phenyl-styryl-DPP **21a**, since its infra-red spectrum showed retention of the cyano group; nor was it a simple 1:1 adduct, since the ester carbonyl absorption was missing. Furthermore, it was not an isomer of compound **21a** ($C_{20}H_{14}N_2O_2$), since the molecular ion in its mass spectrum corresponds to the formula $C_{20}H_{12}N_2O_2$. The corresponding reactions of the anion of **3** with the substituted cinnamonitriles **20b–d**, **20f** and **20h**, and with 3-(2-thienyl)acrylo-

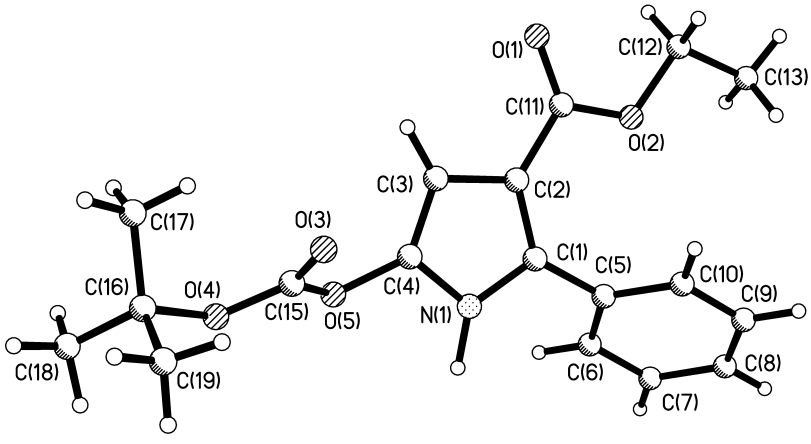


Figure 2. X-ray structure (slightly simplified) of compound **15**.
Selected bond lengths (Å): C(1)-C(2) 1.379(7); C(2)-C(3) 1.423(7); C(3)-C(4) 1.331(8); C(4)-N(1) 1.375(7); N(1)-C(1) 1.371(7); C(2)-C(11) 1.462(7); C(11)-O(1) 1.217(6); C(1)-C(5) 1.479(7); C(4)-O(5) 1.393(6).
Selected interbond angles (°): C(1)-N(1)-C(4) 108.0(5); N(1)-C(4)-C(3) 110.9(5); C(2)-C(3)-C(4) 105.8(5); C(1)-C(2)-C(3) 108.4(5); N(1)-C(1)-C(2) 107.0(5).
Selected torsion angles (°): N(1)-C(1)-C(2)-C(3) 0.0(7); C(2)-C(3)-C(4)-N(1) −0.3(8); N(1)-C(1)-C(2)-C(11) −175.5(6); C(1)-C(2)-C(11)-O(1) −176.9(7); N(1)-C(1)-C(5)-C(6) 47.0(8).

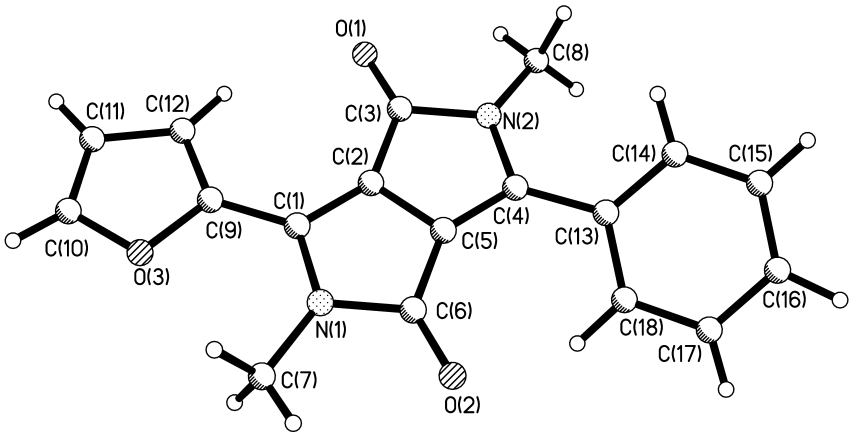


Figure 3. X-ray structure of compound **18c**.
Selected bond lengths (Å): N(1)-C(1) 1.382(5); C(1)-C(2) 1.371(6); C(2)-C(5) 1.405(5); C(5)-C(6) 1.454(6); C(6)-N(1) 1.407(5); C(2)-C(3) 1.450(6); C(3)-N(2) 1.429(5); N(2)-C(4) 1.382(5); C(4)-C(5) 1.366(5); C(4)-C(13) 1.470(6); C(6)-O(2) 1.224(5); C(3)-O(1) 1.208(5); C(1)-C(9) 1.442(6); C(9)-O(3) 1.383(5); O(3)-C(10) 1.367(5); C(10)-C(11) 1.328(7); C(11)-C(12) 1.430(7); C(12)-C(9) 1.355(6).
Selected interbond angles (°): N(1)-C(1)-C(2) 107.8(3); C(1)-C(2)-C(5) 109.2(4); C(2)-C(5)-C(6) 107.7(4); C(5)-C(6)-N(1) 104.0(3); C(6)-N(1)-C(1) 111.2(3); C(2)-C(3)-N(2) 102.8(3); C(3)-N(2)-C(4) 111.7(3); N(2)-C(4)-C(5) 107.4(3); C(4)-C(5)-C(2) 109.5(4); C(5)-C(2)-C(3) 108.6(4).
Selected torsion angles (°): N(1)-C(1)-C(2)-C(5) 0.3(5); C(1)-C(2)-C(5)-C(6) −0.7(5); C(2)-C(5)-C(6)-O(2) 178.6(5); C(2)-C(3)-N(2)-C(4) 0.8(5); C(3)-C(2)-C(5)-C(4) 1.2(5); C(5)-C(2)-C(3)-O(1) −178.3(5); C(5)-C(4)-C(13)-C(14) −147.3(5); C(2)-C(1)-C(9)-C(12) −1.2(8).

nitrile **20i** gave analogous products. The reaction with *p*-(dimethylamino)cinnamonitrile **20g** gave a purple–red product with the expected ^{1}H NMR and mass spectra, but in an impure state and in low yield; and the reaction with *p*-nitrocinnamonitrile **20e** gave only an intractable light brown solid which could not readily be characterised.

Given the retention of the cyano function and the disappearance of the ester group during the reaction, the most plausible course of events was as shown in Scheme 5. Conjugate addition of the anion of **3** to the cinnamonitrile **20** followed by nucleophilic attack on the carbonyl group of the ester would lead to the dihydro-intermediate **22**, and dehydrogenation of the latter, giving **23** and thence its enol tautomer **24**, would result in considerably increased conjugation. In each case the deep red colour of the product, and that of its derived dianion **25**, were consistent with the presence of such a conjugated π-electron system, which is similar to that of diaryl-DPP derivatives. Additionally, the ^{1}H NMR spectra of the compounds were more in accord with the enolic structure **24** than the ketonic tautomer **23**, since no signal corresponding to a tertiary hydrogen at C-5 was discernible.

Although all these new compounds were somewhat more soluble in organic solvents than diaryl-DPP derivatives, and most had measurable melting (decomposition) points and NMR spectra, none could be recrystallised satisfactorily, and as with diaryl-DPPs, it was rarely possible to obtain analytically pure samples. Attempts to form derivatives of **24a** by direct alkylation or acylation, in order to provide definitive proof of its structure, met with little success. However, the dianion **25a**, which is the initially obtained product of the reaction of **3** with **20a**, underwent dimethylation and diethylation in situ by treatment with the appropriate alkyl toluene-*p*-sulfonate, the ^{1}H NMR spectra of the orange–red products being consistent with the *N*,*O*-dialkylated compounds (**26a** and **27a**, respectively). The structure of compound **26d**, obtained in similar fashion by dimethylation of the dianion **25d**, was confirmed by X-ray crystallography (Fig. 5).

When methylation of the dianion **25a** was attempted using iodomethane, however, the alkylation took a different course. This gave first an orange monomethyl derivative, the ^{1}H NMR spectrum of which showed a 3-proton signal

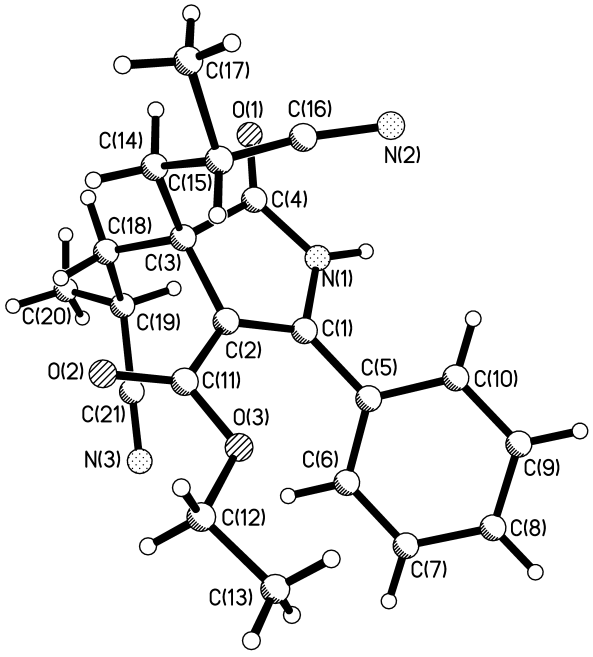


Figure 4. X-ray structure of compound **19b**.
Selected bond lengths (Å): N(1)-C(1) 1.40(1); C(1)-C(2) 1.36(1); C(2)-C(3) 1.51(1); C(3)-C(4) 1.55(1); C(4)-N(1) 1.36(1); C(4)-O(1) 1.21(1); C(2)-C(11) 1.45(1); C(11)-O(2) 1.23(1); C(1)-C(5) 1.44(1); C(3)-C(14) 1.57(1); C(3)-C(18) 1.52(2); C(21)-N(3) 1.14(2).
Selected torsion angles (°): C(2)-C(1)-N(1)-C(4) −1(1); C(1)-C(2)-C(3)-C(4) −5(1); C(2)-C(1)-C(5)-C(10) −130(1); C(1)-C(2)-C(11)-O(3) −11(2); C(1)-C(2)-C(11)-O(2) 170(1); C(2)-C(3)-C(18)-C(19) −56(1); C(2)-C(3)-C(14)-C(15) 32(1).

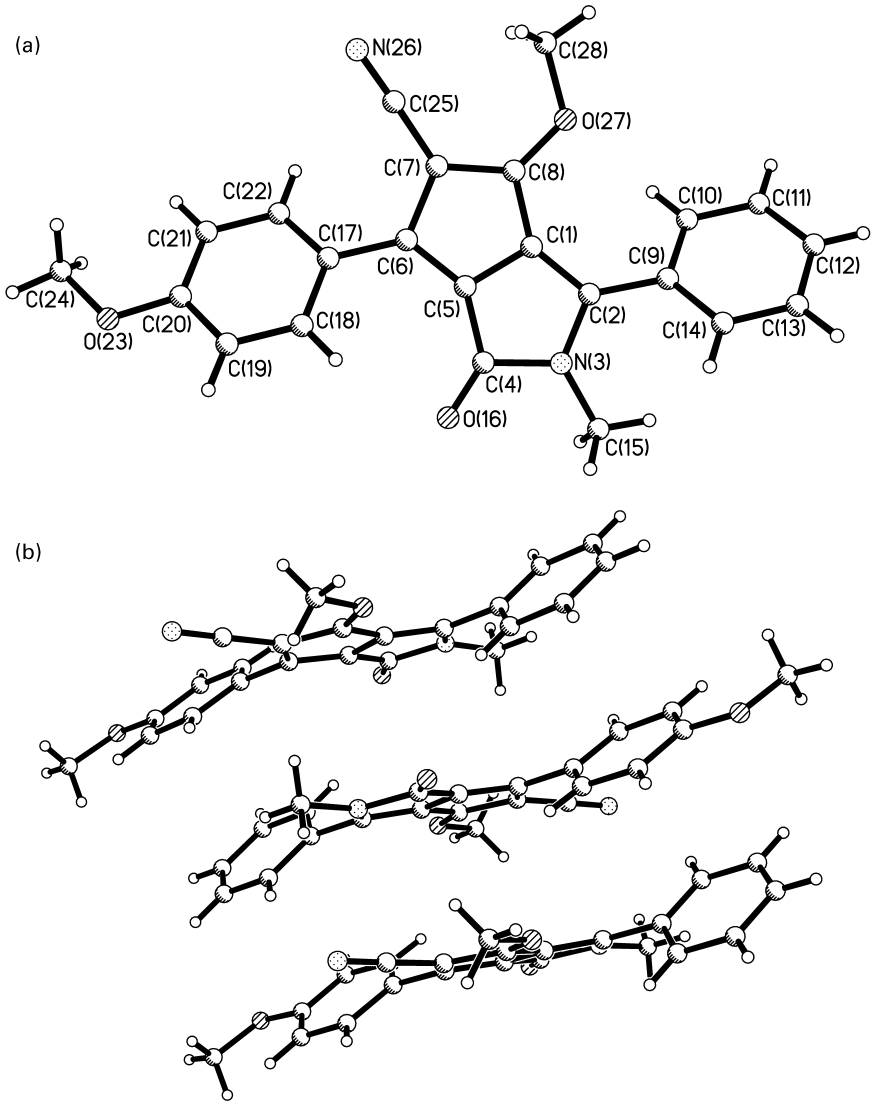


Figure 5. (a) X-ray structure and (b) crystal packing of compound **26d**.
Selected bond lengths (Å): C(1)-C(2) 1.381(4); C(2)-N(3) 1.376(3); N(3)-C(4) 1.435(4); C(4)-C(5) 1.446(4); C(5)-C(6) 1.378(4); C(6)-C(7) 1.454(4); C(7)-C(8) 1.413(4); C(8)-C(1) 1.430(4); C(1)-C(5) 1.419(4); C(4)-O(16) 1.212(3); C(8)-O(27) 1.324(3); C(2)-C(9) 1.471(4); C(6)-C(17) 1.468(4).
Selected interbond angles (°): C(1)-C(2)-N(3) 107.5(2); C(2)-N(3)-C(4) 111.1(2); N(3)-C(4)-C(5) 104.3(2); C(4)-C(5)-C(1) 107.3(3); C(5)-C(1)-C(2) 109.8(2); C(1)-C(5)-C(6) 110.4(2); C(5)-C(6)-C(7) 106.4(2); C(6)-C(7)-C(8) 108.7(3); C(7)-C(8)-C(1) 107.0(2); C(8)-C(1)-C(5) 107.4(2).
Selected torsion angles (°): C(1)-C(2)-N(3)-C(4) 0.2(3); C(2)-N(3)-C(4)-C(5) −1.1(3); C(2)-C(1)-C(5)-C(6) 178.1(2); C(6)-C(7)-C(8)-C(1) −0.8(3); C(1)-C(2)-C9-C(14) 138.4(3); C(5)-C(6)-C(17)-C(18) 33.5(8); C(5)-C(1)-C(8)-O(27) 178.9(3); C(2)-N(3)-C(4)-O(16) 178.8(3); O(16)-C(4)-C(5)-C(6) 2.1(7).

(δ 1.90) which was consistent with the *C*-methyl structure **28a**; prolonged exposure to the methylating agent produced a bright orange dimethyl derivative, with methyl resonances in the ^{1}H NMR spectrum corresponding to those of a *C*,*N*-dimethyl derivative. The structure of this compound, viz. **29a**, was also confirmed by X-ray crystallography (Fig. 6).

1. X-Ray crystallography

Of the six compounds, viz. **14**, **15**, **18c**, **19b**, **26d** and **29a**, the structures of which were determined by X-ray crystallography, analysis of **15** and **18c** is straightforward, despite some disorder in the *t*-butoxycarbonyloxy-substituent in compound **15**. The structures and the most significant data for these compounds are shown in Figs. 2 and 3. The crystal structure of compound **14** (Fig. 1), however, is considerably more complicated, since the spatial requirements of the phenyl and cyclohex-3-enyl groups in the crystal are sufficiently similar that they occupy the same site in the asymmetric unit, and since the *t*-butoxycarbonyl moiety is also disordered unequally over two sites. However, all the disorder may be successfully modelled, and it can be demonstrated that the double bond in the cyclohexenyl moiety has not migrated in the strongly basic medium in which it is formed. The refined structure and the most significant structural data are shown in Fig. 1.

Apart from the coplanarity of the furan and DPP ring systems, the most striking structural feature of compound **18c** is the very short central bond [C(2)–C(5) in Fig. 3]. The same is true of 3,6-diphenyl-DPP **4a** itself and its *N*,*N*′-dimethyl derivative,[3] although apparently this has not previously attracted comment. It implies considerable

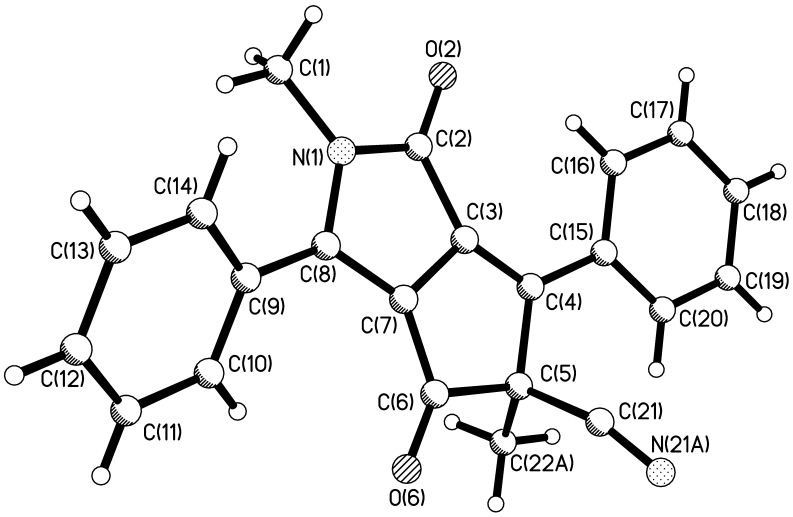


Figure 6. X-ray structure (simplified) of compound **29a**.
Selected bond lengths (Å): N(1)-C(2) 1.414(4); C(2)-C(3) 1.508(4); C(3)-C(4) 1.369(4); C(4)-C(5) 1.506(5); C(5)-C(6) 1.586(4); C(6)-C(7) 1.414(4); C(7)-C(8) 1.397(4); C(8)-N(1) 1.397(4); C(3)-C(7) 1.447(4); C(2)-O(2) 1.232(4); C(6)-O(6) 1.196(4); C(8)-C(9) 1.501(4); C(4)-C(15) 1.474(3).
Selected interbond angles (°): C(8)-N(1)-C(2) 110.7(2); N(1)-C(2)-C(3) 104.9(2); C(2)-C(3)-C(7) 105.5(2); C(3)-C(7)-C(8) 109.2(3); C(7)-C(8)-N(1) 108.5(3); C(3)-C(4)-C(5) 106.1(3); C(4)-C(5)-C(6) 106.7(2); C(5)-C(6)-C(7) 103.5(3); C(6)-C(7)-C(3) 110.5(2); C(7)-C(3)-C(4) 113.1(2).
Selected torsion angles (°): N(1)-C(2)-C(3)-C(7) 8.4(5); C(2)-C(3)-C(7)-C(6) 172.3(4); C(4)-C(3)-C(7)-C(8) −172.0(4); C(3)-C(4)-C(15)-C(16) −2.2(6); C(4)-C(5)-C(6)-C(7) 3.0(5); C(7)-C(8)-C(9)-C(10) −43.1(6); C(1)-N(1)-C(2)-C(3) 179.4(5); O(2)-C(2)-N(1)-C(8) −178.5(5); C(3)-C(7)-C(6)-O(6) −178.3(6); O(6)-C(6)-C(7)-C(8) −9.0(12).

delocalisation within the diene moiety, something which may perhaps be achieved at the expense of conjugation involving the carbonyl groups, since the bonds joining the latter to the diene [C(2)–C(3) and C(5)–C(6)] are in fact the longest within the ring systems.

A view of the structure of compound **19b** is shown in Fig. 4. This shows clearly the spatial non-equivalence of the two 2-cyanopropyl substituents attached to the planar pyrrolinone ring. In the figure, one of the two cyano groups (C(21)–N(3)) appears below, and apparently almost orthogonal to, the carbonyl group of the ester. There is some disorder in the other 2-cyanopropyl group, the cyano group of which [C(16)–N(2)] appears to lie across the pyrrolinone carbonyl group. The torsion angles C(2)–C(3)–C(14)–C(15) and C(2)–C(3)–C(18)–C(19) are also remarkably different [32(1) and 56(1)°, respectively]: whereas the latter represents a normal staggered conformation along the C(3)–C(18) bond, it appears as if the other cyano group is being pulled 'inwards' by the pyrrolinone oxygen, although the C(16)–O(1) distance is still relatively long.

The largest crystals of compound **26d** which could be readily obtained were still too small to be examined by normal X-ray methods. However the structure of **26d** was obtained using the microcrystal diffraction facility at the UK National Synchrotron Radiation Service at the CLRC Laboratory, Daresbury: this showed [Fig. 5(a)] that, as in DPP derivatives, the two aryl substituents are not coplanar with the central heterocyclic ring system, although unlike DPPs, these aryl substituents do not lie in parallel planes. The packing diagram [Fig. 5(b)] shows that the molecules show a degree of π–π stacking in the crystal, although alternate molecules are orientated at 180° to one another, so that the 'stack' is only approximate: the distance between the mean planes of adjacent molecules is approximately 3.6 Å.

In the crystals of compound **29a**, there is some disorder at the tetrahedral carbon, C(5), in the ring; Fig. 6 is a simplified version of the structure showing the major occupancies of the substituents at this carbon. For clarity the minor occupancies, i.e. C(22B) and N(21B), are not shown in this figure. The cyclopentapyrrolone ring system is again essentially planar, although interestingly in this particular case the 6-phenyl substituent [C(15)–C(20) in Fig. 6] also lies in this same plane.

2. Conclusion

In the reaction of the anion of compound **3** with α,β-unsaturated nitriles, conjugate addition occurs in preference to direct attack on the cyano-carbon; the products are either bis-(cyanoalkyl) adducts, or else cyclopenta[*c*]pyrrolones, **24**, and not the expected alkenyl-DPPs. These cyclopentapyrrolones are, however, structurally related to DPPs, and have similar solubilities and chromophoric characteristics. The synthesis of alkenyl-DPPs by a Diels–Alder/retro-Diels–Alder sequence appears to be of very little generality.

3. Experimental

3.1. General

FT-IR spectra of solids were recorded for Nujol mulls, and those of liquids were recorded for thin films, and are expressed in cm^{-1}. Unless otherwise indicated, UV–visible spectra were recorded (wavelengths expressed in nm) for

solutions in acetonitrile or dimethyl sulfoxide, and ^{1}H and ^{13}C NMR spectra were obtained at 300 and 75.4 MHz, respectively, for solutions in d_6-dimethyl sulfoxide. 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 ionisation at 70 eV. Flash chromatography was carried out on silica gel grade H. Organic extracts were dried over sodium sulfate or magnesium sulfate. 'Ether' refers to diethyl ether and 'petrol' to the fraction of bp 40–60°C. 'Boc'=*t*-butoxycarbonyl, $Me_3C–O–CO–$; DMAP=4-(*N*,*N*-dimethylamino)pyridine.

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 required several hours but could be accelerated by the addition of a catalytic amount of anhydrous iron(III) chloride. Ethyl 4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate **3** was obtained, according to the patent procedure,[5] from diethyl benzoylsuccinate[18] (10.0 g, 0.036 mol) and ammonium acetate (28.07 g, 0.36 mol) in acetic acid (50 cm^3) at 70–80°C. Yield 6.35 g (76%), mp 172.5–173.5°C (from propan-2-ol: lit.,[5] 174°C).

Acrylonitrile, methacrylonitrile, cinnamonitrile and *p*-methoxycinnamonitrile were commercial samples, and samples of *p*-fluorocinnamonitrile, 3-(3,4-methylenedioxyphenyl)acrylonitrile and 3-(2-thienyl)acrylonitrile were kindly donated by our colleague Dr R. A. Aitken; these last four were mixtures of *E*- and *Z*-isomers, the former predominating, and were generally used without further purification. These and the other substituted cinnamonitriles may be prepared by a variant of the Horner–Wadsworth–Emmons reaction,[19] from the overnight reaction at room temperature of equimolar quantities of diethyl cyanomethylphosphonate, the appropriate aldehyde and sodium hydride in tetrahydrofuran.

3.1.1. *p*-Methylcinnamonitrile 20b. Yield 92%, mp 71–73°C (lit.,[20] 70–71°C, 71–72°C[21], 73–74°C[22]). δ_H ($CDCl_3$, 200 MHz) *E* isomer: 2.39 (3H, s, Ar-CH_3), 5.82 (1H, d, *J*=16.7 Hz, C*H*CN), 7.21 (2H, d, *J*=8.1 Hz, Ar H-3 and -5), 7.32 (1H, d, C*H*CHCN), 7.37 (2H, d, Ar H-2 and -6). *Z* isomer: 5.36 (1H, d, *J*=12.0 Hz, C*H*CN), 7.08 (1H, d, *J*=12.0 Hz, C*H*CHCN); other resonances obscured by those of the *E*-isomer. *E*/*Z* ratio=10:1. ν_{max} 2215 (C≡N), 1618 (C=C).

3.1.2. *p*-Chlorocinnamonitrile 20c. Yield 66%, mp 85–86°C (from propan-2-ol; lit.,[21] 84–86°C, 84–87°C[23]). δ_H ($CDCl_3$) *E* isomer: 5.86 (1H, d, *J*=16.4 Hz, C*H*CN), 7.36 (1H, d, C*H*CHCN), 7.37–7.46 (4H, m, Ar-H); *Z* isomer: 5.48 (1H, d, *J*=11.8 Hz, C*H*CN), 7.09 (1H, d, *J*=11.8 Hz, C*H*CHCN), 7.45 (2H, d, Ar H-3 and -5), 7.75 (2H, d, *J*=8.0 Hz, Ar H-2 and -6). *E*/*Z* ratio=5:1. ν_{max} 2217 (C≡N), 1625 (C=C), 1591.

3.1.3. *p*-Nitrocinnamonitrile 20e. Yield 56%: recrystallisation gave the *E*-isomer, mp 200–202°C (from ethanol–water; lit.,[22] 197–199°C, 200–201°C[24]). δ_H (isomer mixture: $CDCl_3$, 200 MHz) *E*-isomer: 6.06 (1H, d, *J*=17.5 Hz, C*H*CN), 7.64 (2H, m, *J*=8.8 Hz, Ar-H-2 and -6), 7.48 (1H, d, *J*=17.5 Hz, C*H*CHCN), 8.29 (2H, m, Ar H-3 and -5). *Z* isomer: 5.72 (1H, d, *J*=12.0 Hz, C*H*CN), 7.25 (1H, d, *J*=12.0 Hz, C*H*CHCN), 7.95 (2H, *J*=8.8 Hz, Ar H-2 and -6), 8.32 (2H, d, Ar H-3 and -5). *E*/*Z* ratio=2.5:1. ν_{max} 2218 (C≡N), 1630 (C=C), 1602, 1526 and 1333 (NO_2).

3.1.4. *p*-Fluorocinnamonitrile 20f. As provided, was a semi-solid distillate (bp 110°C/3 mmHg) containing crystals (of the *E*-isomer) with mp 62–66°C (lit.,[21,22] 64–66°C, 64–65°C[25]). δ_H (isomer mixture) ($CDCl_3$; 200 MHz) *E*-isomer: 5.82 (1H, d, *J*=16.7 Hz, C*H*CN), 7.11 (2H, t, *J*=8.6 Hz, Ar H-3 and -5), 7.37 (1H, d, *J*=16.7 Hz, C*H*CHCN), 7.46 (2H, dd, *J*=8.6 (H,H) and 5.4 (H,F) Hz, Ar H-2 and -6). *Z*-isomer: 5.44 (1H, d, *J*=12.0 Hz, C*H*CN), 7.82 (2H, dd, *J*=8.6 and 5.4 Hz, Ar H-2 and -6); other resonances obscured by those of the *E*-isomer. *E*/*Z* ratio=14:1. ν_{max} 2205 (C≡N), 1620 and 1600 (C=C).

3.1.5. *p*-(Dimethylamino)cinnamonitrile 20g. Yield 63%, mp 158–160°C (lit.,[26] 163.5°C) δ_H ($CDCl_3$): *E* isomer: 3.03 [6H, s, $N(CH_3)_2$], 5.58 (1H, d, *J*=17.6 Hz, C*H*CN), 6.66 (2H, d, *J*=8.8 Hz, Ar H-3 and -5), 7.28 (1H, d, C*H*CHCN), 7.32 (2H, d, Ar H-2 and -6); *Z* isomer: 3.04 (6H, s, $N(CH_3)_2$), 5.09 (1H, d, *J*=12.1 Hz, CHCN), 6.68 (2H, d, Ar H-3 and -5), 6.94 (1H, d, *J*=12.1 Hz, C*H*CHCN), 7.75 (2H, d, *J*=9.1 Hz, Ar-H-2 and -6). *E*/*Z* ratio=3.6:1. ν_{max} 2181 (C≡N), 1600 (C=C).

3.1.6. 3-(3,4-Methylenedioxyphenyl)acrylonitrile 20h. As provided, mp 76–89°C (lit.,[21] 91–92°C, 94°C,[23] 88°C[27]). δ_H ($CDCl_3$; 200 MHz) *E*-isomer: 5.67 (1H, d, *J*=16.6 Hz, C*H*CN), 6.03 (2H, s, CH_2), 6.82 (1H, d, *J*=8.4 Hz, Ar H-6), 6.90–7.00 (2H, m, Ar H-2 and -5), 7.28 (1H, d, *J*=16.6 Hz, C*H*CHCN). *Z*-isomer: 5.30 (1H, d, *J*=12.0 Hz, C*H*CN); other resonances obscured by those of the *E*-isomer. *E*/*Z* ratio=9:1. ν_{max} 2220 (C≡N), 1620 and 1600 (C=C).

3.1.7. 3-(2-Thienyl)acrylonitrile 20i. Purified by Kugelrohr distillation, this had bp (bulb temp.) 120°C/0.6 mmHg (lit.,[28] (*E*) 104°C/1 mmHg; (*Z*) 76°C/0.2 mmHg). δ_H ($CDCl_3$; 200 MHz) *E*-isomer: 5.65 (1H, d, *J*=16.3 Hz, C*H*CN), 7.10 (1H, dd, *J*=4.8 and 3.7 Hz, Th H-4), 7.23 (1H, d, *J*=4.7 Hz, Th H-5), 7.43 (1H, d, *J*=3.7 Hz, Th H-3), 7.48 (1H, d, *J*=16.3 Hz, C*H*CHCN); *Z*-isomer: 5.31 (1H, d, *J*=11.7 Hz, C*H*CN), 7.56 (1H, d, *J*=3.9 Hz, Th H-3), other resonances obscured by those of the *E*-isomer. *E*/*Z* ratio=4.5:1. ν_{max} 2215 (C≡N), 1670 and 1605 (C=C).

The other nitriles used in this study were prepared as given below.

3.1.8. 7-Oxabicyclo[2.2.1]hept-5-ene-2-carbonitrile 9b.[8] A mixture of furan (10.05 g, 0.148 mol), acrylonitrile (6.62 g, 0.125 mol) and zinc iodide (2.0 g, 6.3 mmol) was stirred at 40–60°C for 48 h. The light brown mixture was then diluted with ethyl acetate, washed with 0.1 M sodium thiosulfate (2×10 cm^3) and concentrated under reduced pressure. Column chromatography of the residue [silica

gel, 30–70 grade; eluent, petrol/ethyl acetate (2:1)] yielded the adduct **9b** (5.36 g, 35%), bp 110–115°C/0.3 mmHg, as an *exo*/*endo* mixture. ν_{max} 2244 (C≡N). δ_H ($CDCl_3$; assigned with aid of COSY): *exo* adduct: 1.77 (1H, dd, J=8.5 and 11.5 Hz, H-3), 2.14 (1H, m, H-3′), 2.41 (1H, dd, J=4.0 and 8.4 Hz, H-2), 5.19 and 5.24 (1H, m, H-1 or 4), 6.32 (1H, dd, H-5 or 6), 6.44 (1H, dd, $J_{1,6}$=1.7 Hz and $J_{5,6}$=5.8 Hz, H-5 or 6). *endo* Adduct: δ_H 1.56 (1H, dd, J=3.6 and 11.5 Hz, H-3), 2.31 (1H, m, H-3′), 2.94 (1H, dt, J=4.0 and 9.6 Hz, H-2), 5.15 (1H, m, H-1 or 4), 5.24 (1H, m, H-1 or 4), 6.50 (1H, dd, H-5 or 6), 6.58 (1H, dd, $J_{1,6}$=1.7 Hz and $J_{5,6}$=5.8 Hz, H-5 or 6). The *exo:endo* ratio is approximately 4:3, and the spectra are in broad agreement with the published data.[29]

3.1.9. Diels–Alder adducts of 2-methylfuran and acrylonitrile (9c/d).[9] A mixture of 2-methylfuran (10.0 g, 0.122 mol), acrylonitrile (12.93 g, 0.244 mol) and zinc iodide (2.02 g, 0.0063 mol) was stirred at 50°C for 9 h, then at 25°C for 5 days. The light brown mixture was then diluted with ethyl acetate, washed with 0.1 M sodium thiosulfate then water, dried and concentrated under reduced pressure (crude yield 9.86 g, 60%). Column chromatography of a small portion (silica gel; eluent, petrol/ethyl acetate) yielded pure adducts: ν_{max} 2250 (C≡N). The product was a mixture of 2 constitutional isomers **9c** and **9d**, each consisting of an *exo*/*endo* mixture. A complete assignment was not possible due to the complexity of the isomer mixture, but the alkenic protons H-5 and H-6 provided limited information, confirming the presence of 4 isomers: δ_H ($CDCl_3$) 1.61–1.69 (m), 1.76 (s), 1.81 (s), 1.83–1.92 (m), 1.97–2.04 (m), 2.20–2.29 (m), 2.39–2.52 (m), 2.63 (dd, J=3.7 and 9.4 Hz), 3.04–3.10 (m), 5.01–5.07 (m), 5.12–5.14 (m), 6.11 (d), 6.25 (d), 6.30 (d), 6.38 (d, J=5.6 Hz), 6.42 (dd), 6.47 (dd), 6.55 (dd, J=1.6 and 5.8 Hz). The complete ^{1}H NMR spectra are reproduced pictorially in Ref. 9.

3.1.10. Norbornane-2-carbonitrile. Magnesium (5.17 g, 213 mmol) was added to a mixture of 5-norbornene-2-carbonitrile **9a** (5.0 g, 42 mmol), methanol (100 cm^3) and 5% palladium on charcoal (0.4 g). After a brief induction period, the reaction proceeded with brisk evolution of gas. When the magnesium had been consumed, the mixture was added to ice-cooled 30% hydrochloric acid, extracted with an ethyl acetate/ether mixture, dried (Na_2SO_4) then concentrated. Kugelrohr distillation (bulb temp. 90–100°C/1 mmHg) yielded a colourless oil (2.30 g, 45%) which solidified upon standing (lit. bp,[30] 62°C/7 Torr; no mp reported). δ_H ($CDCl_3$) 1.19–2.03 (8H, m), 2.34–2.72 (3H, m).

3.1.11. Cyclohexene-3-carbonitrile 11. The literature method[12] was adapted as follows: Triethylamine (20.70 g, 0.205 mol) was added to a stirred mixture of 1,2,4,6-tetrahydro-benzaldehyde (20.50 g, 0.186 mol), hydroxylamine hydrochloride (19.80 g, 0.285 mol) and dried acetonitrile (160 cm^3) under nitrogen, and the mixture was then heated to reflux (80°C). Phthalic anhydride (30.41 g, 0.205 mol) was then added portionwise during 3 h, heating was continued for a further 2 h, and the mixture was stirred at 25°C for 16 h then evaporated to dryness, extracted with dichloromethane, the colourless precipitate filtered off and the combined filtrates washed with 10% aqueous ammonia and dried (Na_2SO_4). The solution was concentrated to small volume; flash chromatography of the residue (silica gel H; eluent, dichloromethane) yielded a colourless oil (12.74 g, 64%) which was used without further purification. ν_{max} 2240 (C≡N), 1654 (C=C). δ_H ($CDCl_3$; 200 MHz) 1.86–2.30 (4H, m, 2×CH_2), 2.31–2.45 (2H, m, CH_2), 2.76–2.89 (1H, m, C*H*CN), 5.59–5.79 (2H, m, HC=CH).

3.1.12. 3-Furonitrile. A mixture of 3-furoic acid (3.61 g, 32.2 mmol) and 1,3-dicyanobenzene (10.74 g, 83.8 mmol) was heated gradually to 290–300°C in a distillation apparatus fitted with a fractionating column. The colourless distillate [2.47 g, 82%; bp 159–162°C (lit.[31] 151°C)] solidified on standing (mp 23.5–24.5°C). ν_{max} 2247 (C≡N). δ_H ($CDCl_3$) 6.64–6.65 (1H, m, H-4), 7.51–7.52 (1H, m, H-5), 7.97 (1H, d, J=0.8 Hz, H-2).

3.1.13. 3,6-Diphenyl-DPP 4a. (a) Benzonitrile (0.23 g, 2.2 mol) then the pyrrolinecarboxylate ester **3** (0.37 g, 1.6 mmol) were added successively, with stirring and under nitrogen, to a solution of sodium *t*-amyloxide [from sodium (0.14 g, 6.1 mmol)] in dry *t*-amyl alcohol (15 cm^3), whereupon a red precipitate rapidly formed. The mixture was heated under reflux for 2 h, cooled and added portionwise to an ice-cooled mixture of methanol (5 cm^3) and concentrated hydrochloric acid (1 cm^3). The bright red precipitate was filtered off, washed thoroughly with methanol and water then dried in vacuo. Yield 0.24 g (52%).

(b) Benzonitrile (2.24 g, 21.7 mmol) was added, with stirring and under nitrogen, to a solution of sodium *t*-amyloxide [from sodium (0.5 g, 21.7 mmol)] in dry *t*-amyl alcohol (45 cm^3) Diethyl succinate (1.89 g, 10.8 mmol) was then added portionwise over 4 h and heating continued for a further 1 h. The mixture was stirred for 16 h at 25°C, then added to an ice-cooled mixture of concentrated hydrochloric acid (2.2 cm^3) and methanol (20 cm^3). The bright red precipitate was filtered off, washed with methanol and dried in vacuo. Yield 0.11 g (31%). The filtrate was shown by ^{1}H NMR to contain unreacted benzonitrile and diethyl succinate.

ν_{max} 3070 and 3160 (N–H), 1640 (C=O), 1600 (N–H bending or Ar-C=C stretch). m/z 288.0909 ($M^{+\cdot}$, 100%; $C_{18}H_{12}N_2O_2$ requires 288.0899), 258 (25), 230 (41), 104 (72), 77 (63).

The 2,5-bis-(*t*-butoxycarbonyl) derivative[13b] was prepared by stirring a mixture of compound **4a** (0.49 g, 1.7 mmol), tetrahydrofuran (25 cm^3), DMAP (0.08 g, 0.7 mmol) and Boc_2O (1.23 g, 5.6 mmol) at room temperature for 24 h. Further Boc_2O (0.4 g, 1.8 mmol) was then added and stirring continued for 2.5 h. The reaction mixture was concentrated, the residual moist brown solid mixed with methanol (1 cm^3), filtered off and washed with methanol (2 cm^3). The light yellow product (0.69 g, 83%) was dried in vacuo. The product decomposed without melting over the range 185–236°C (by DSC). λ_{max} 424 (ε 10625). δ_H ($CDCl_3$; 200 MHz) 1.38 [18H, s, $C(CH_3)_3$], 7.46–7.51 (6H, m, *m*-/*p*-Ar-H), 7.72–7.76 (4H, m, *o*-Ar-H). δ_C 27.4 ($OC(CH_3)_3$), 85.2 ($OC(CH_3)_3$), 112.3, 112.4 (C-3 and quat. Ar-C), 128.5, 128.6 (*o*-/*m*-Ar-C), 131.6 (*p*-Ar-C), 146.4, 148.2 (C-1 and 3a), 159.5 ($COC(CH_3)_3$).

3.1.14. Reaction of nitrile 9b with the pyrrolinecarboxylate ester 3. The ester **3** (1.57 g, 6.8 mmol) and the nitrile **9b** (0.94 g, 7.8 mmol) were added successively under nitrogen to a solution of sodium *t*-amyloxide [from sodium (0.46 g, 20 mmol)] in dry *t*-amyl alcohol (25 cm^3) at 40°C, and the mixture was stirred at 25°C for 3.5 days. A bright red precipitate gradually formed. The mixture was then added to an ice-cooled mixture of methanol and concentrated hydrochloric acid (2 cm^3). The red precipitate was filtered off, washed with methanol then water, and dried in vacuo, to give 3,6-diphenyl-DPP (1.0 g, 48%), spectroscopically identical with an authentic sample.

3.1.15. Reaction of the nitrile mixture 9c/d with the pyrrolinecarboxylate ester 3. The ester **3** (4.04 g, 17.5 mmol) then the nitrile **9c/d** (3.00 g, 22.2 mmol) were added, at 65–70°C and under nitrogen, to a solution of sodium *t*-amyloxide [from sodium, 1.38 g (60 mmol)] in dry *t*-amyl alcohol (125 cm^3). The mixture was stirred at 85–90°C for 3.5 h, then added to an ice-cooled mixture of methanol (50 cm^3) and concentrated hydrochloric acid (6 cm^3). The bright red precipitate was filtered off, washed with methanol then water, and dried in vacuo. Yield 2.42 g (46%). For the mixture of isomers **4b** and **4c**, δ_H (200 MHz) 2.28 and 2.38 (s, 2×CH_3), 7.34–8.51 (m, Ar-H), 10.90–11.30 (4H, m, NH, removed upon D_2O exchange). *m/z* 302 ($M^{+\cdot}$, 100%), 288 (7), 91 (49).

3.1.16. Reaction of the nitrile 9b with diethyl succinate. A mixture of the nitrile **9b** (1.96 g, 16.2 mmol) and diethyl succinate (2.82 g, 16.2 mmol) was added, portionwise and under nitrogen, over 1 h to a solution of sodium *t*-amyloxide (from sodium, 1.12 g) in dry *t*-amyl alcohol (125 cm^3). Stirring was continued for 2 h at reflux, then for 16 h at 25°C. The mixture was added to an ice-cooled mixture of methanol (30 cm^3) and concentrated hydrochloric acid (4.5 cm^3). The red precipitate was filtered off, washed with methanol then water and dried in vacuo; yield 2.62 g. The product was spectroscopically identical with an authentic sample of **4a**, but elemental analysis indicated traces of inorganic impurity. GC and ^1H NMR analysis of the concentrated filtrate confirmed the presence of benzonitrile.

3.1.17. Reaction of the nitrile 9b with sodium *t*-amyloxide. The nitrile **9b** (1.0 g, 8.3 mmol) was added, under nitrogen, to a boiling solution of sodium *t*-amyloxide (from sodium, 0.56 g) in *t*-amyl alcohol (50 cm^3). A white precipitate quickly formed. Stirring was continued at reflux for 4 h, then the mixture was acidified with concentrated hydrochloric acid (3 cm^3). The light yellow solution containing a white precipitate was concentrated, washed with water (whereupon the precipitate dissolved), extracted with ether, dried and concentrated to give a small amount of white intractable solid and a colourless oil (ca. 50 mg) with the pungent odour of benzonitrile. ^1H and ^{13}C NMR confirmed the presence of benzonitrile and a small amount of nitrile **9b**.

3.1.18. Attempted reaction of the ester 3 with the nitrile 9a. The pyrrolinecarboxylate ester **3** (10.06 g, 43.5 mmol) and 5-norbornene-2-carbonitrile **9a** (7.74 g, 64.9 mmol) were added at 25°C under nitrogen to sodium *t*-amyloxide [from sodium, 3.55 g (154 mmol)] in dried *t*-amyl alcohol (150 cm^3). The mixture was stirred at 25°C for 6 days, then added to a mixture of water (100 cm^3) and methanol (5 cm^3) and acidified dropwise with concentrated hydrochloric acid (15 cm^3). The organic extracts were dried (Na_2SO_4) and concentrated. Flash chromatography (silica gel H; eluent, petrol/ethyl acetate (2/1), then ethyl acetate and methanol) yielded four fractions:

1. yellow oil (5.0 g). ^1H NMR and infra-red spectra showed predominantly nitrile **9a**, with a small amount of alkenic material with δ_H 5.58 (dd, *J*=2.2 and 5.7 Hz).
2. beige solid (0.38 g). The ^1H NMR and mass spectra were consistent with ester **3**.
3. brown solid (4.56 g), with ^1H NMR and mass spectra again consistent with ester **3**.
4. purple solid (3.88 g): ^1H NMR (DMSO-d_6) spectrum was consistent with the structure **10**. δ_H (200 MHz) 1.06 (6H, t, *J*=7.1 Hz, 2×OCH_2CH_3), 3.97 (4H, q, 2×OCH_2CH_3), 7.42–7.45 (6H, m, Ar-H), 7.54–7.59 (4H, m, Ar-H), 10.65 (2H, br. s, NH). *m/z* 458 ($M^{+\cdot}$, 5%), 341 (5), 231 (20), 105 (58), 71 (100).

3.1.19. 3-Isopropyl-6-phenyl-DPP 4d. The pyrrolinecarboxylate ester **3** (2.0 g, 8.6 mmol) and isobutyronitrile (0.69 g, 11.0 mmol) were added successively at 80–90°C under nitrogen, to sodium *t*-amyloxide [from sodium, 0.63 g (27.4 mmol)] in dried *t*-amyl alcohol (30 cm^3). Stirring was continued for 1 h, and the mixture was then heated under reflux for 2 h. Further isobutyronitrile (0.67 g, 9.7 mmol) was added, and stirring continued for 1.5 h at reflux and a further 15 h at 25°C. The mixture was then added to an ice-cooled mixture of methanol (20 cm^3), water (30 cm^3) and concentrated hydrochloric acid (3 cm^3). The yellow precipitate was filtered off, washed with methanol then water, and dried in vacuo. Yield 0.65 g (31%), mp 306–307°C. (Found: C, 71.1; H, 5.5; N, 10.6. $C_{15}H_{14}N_2O_2$ requires C, 70.9, H, 5.6; N, 11.0%). ν_{max} 3140 (N–H), 1654 (C=O). δ_H 1.29 (6H, d, *J*=6.9 Hz, $CH(CH_3)_2$), 2.91 (1H, septet, *J*=6.9 Hz, $CHCH_3$), 7.51–7.53 (3H, m, *m*-/*p*-Ar-H), 8.33–8.37 (2H, m, *o*-Ar-H), 10.59 and 10.85 (each 1H, s, NH, reduced on D_2O exchange). λ_{max} (DMSO) 437 (ε 12872).

The following analogues of **4d** were prepared similarly.

3.1.20. 3-Cyclohexyl-6-phenyl-DPP 4e. This was obtained from the pyrrolinecarboxylate ester **3** (2.0 g, 8.6 mmol), cyclohexanecarbonitrile (1.16 g, 10.6 mmol), and sodium *t*-amyloxide [from sodium, 0.64 g (27.8 mmol)] in dried *t*-amyl alcohol (40 cm^3) at 80–90°C. After 1 h at reflux, further cyclohexanecarbonitrile (1.20 g, 11.0 mmol) was added, and stirring continued at reflux for 2 h, then at 25°C for 14 h. Yellow precipitate, yield 0.28 g (11%); sublimes without melting at >400°C. (Found: C, 72.6; H, 6.0; N, 9.1. $C_{18}H_{18}N_2O_2$ requires C, 73.5, H, 6.2; N, 9.5%). ν_{max} 3143 (N–H), 1648 (C=O), 1609. δ_H 1.10–1.31 (4H, m, cyclohexyl H), 1.65–1.89 (6H, m, cyclohexyl H), 2.50–2.65 (1H, m, H-1′), 7.43–7.56 (3H, m, *m*-/*p*-Ar-H), 8.34–8.37 (2H, m, *o*-Ar-H), 10.56 and 10.87 (each 1H, s, NH, reduced on D_2O exchange). λ_{max} (DMSO) 439 (ε 16006), 460 (15350).

3.1.21. 3-Diphenylmethyl-6-phenyl-DPP 4f. This was prepared from the pyrrolinecarboxylate ester **3** (2.01 g, 8.7 mmol), diphenylacetonitrile (1.73 g, 9.0 mmol), and sodium *t*-amyloxide (from sodium, 0.69 g (30.0 mmol) in dried *t*-amyl alcohol (40 cm^3), the mixture being heated under reflux for 3.5 h, then stirred at 25°C for 18 h. Yellow precipitate, yield 0.95 g (29%), mp 295–296°C. (Found: C, 79.0; H, 4.6; N, 7.4. $C_{25}H_{18}N_2O_2$ requires C, 79.4, H, 4.8; N, 7.4%). ν_{max} 3138 (N–H), 1679 (C=O), 1645. δ_H 5.58 (1H, s, Ar-CH), 7.27–7.40 (10H, m, CH-Ar-*H*), 7.53–7.55 (3H, m, *m*-/*p*-Ar-H), 8.36–8.38 (2H, m, *o*-Ar-H), 10.82 and 10.95 (each 1H, s, NH, reduced on D_2O exchange). λ_{max} (DMSO) 443 (ε 17940), 466 (17284).

3.1.22. 3-(Norborn-2-yl)-6-phenyl-DPP 4g. This was prepared from the pyrrolinecarboxylate ester **3** (3.18 g, 13.8 mmol), norbornane-2-carbonitrile (2.00 g, 16.5 mmol) and sodium *t*-amyloxide (from sodium, 1.16 g (50.4 mmol)) in dried *t*-amyl alcohol (30 cm^3) at 100–110°C for 3 h. Yellow–brown precipitate, yield 0.62 g (15%); subl. >400°C. Elemental analysis shows slight impurity (Found: C, 73.3; H, 5.8; N, 8.6. $C_{19}H_{18}N_2O_2$ requires C, 74.5; H, 5.9; N, 9.1%). δ_H 1.14–1.31 (3H, m, norbornyl H), 1.42–1.60 (4H, m, norbornyl H), 2.28–2.29 (2H, m, norbornyl H), 2.58–2.61 (2H, m, norbornyl H), 7.44–7.51 (3H, m, *m*-/*p*-Ar-H), 8.36–8.37 (2H, m, *o*-Ar-H), 10.60 and 10.91 (each 1H, s, NH, reduced on D_2O exchange). λ_{max} (DMSO) 430 (ε 17381), 449 (17371).

3.1.23. 3-(Cyclohex-3-enyl)-6-phenyl-DPP 13. This was prepared from the pyrrolinecarboxylate ester **3** (5.02 g, 21.7 mmol), cyclohexene-3-carbonitrile **11** (2.33 g, 21.7 mmol), and sodium *t*-amyloxide [from sodium, 1.76 g (77.9 mmol)] in dried *t*-amyl alcohol (35 cm^3), the mixture being heated under reflux for 6.5 h. Yellow-brown precipitate, yield 2.66 g (42%), mp 358–360°C with colour change to orange-red. (Found: C, 73.1; H, 5.3; N, 9.3. $C_{18}H_{16}N_2O_2$ requires C, 74.0; H, 5.5; N, 9.6%). δ_H 1.82–2.89 (7H, m, cyclohexenyl H-1′ and 3×C*H*$_2$), 5.65–5.78 (2H, m, H-3′ and -4′), 7.50–7.53 (3H, m, *m*-/*p*-Ar-H), 8.34–8.36 (2H, m, *o*-Ar-H), 10.61 (1H, s, NH), 10.88 (1H, s, NH).

3.1.24. 2,5-Bis-(*t*-butoxycarbonyl)-3-(cyclohex-3-enyl)-6-phenyl-DPP 14. A mixture of 3-cyclohex-3-enyl-6-phenyl-DPP **13** (0.39 g, 13 mmol), DMAP (0.02 g, 0.16 mmol), di-*t*-butyl dicarbonate (1.02 g, 47 mmol), triethylamine (0.42 g, 42 mmol) and tetrahydrofuran (30 cm^3) was stirred with exclusion of moisture for 8 h, then concentrated to small volume. The residue was mixed with methanol (2 cm^3), the mixture filtered and the fluorescent yellow residue then washed with methanol and dried in vacuo. Yield 0.12 g (19%); decomposes without melting. (Found: C, 68.7; H, 6.8; N, 5.6. $C_{28}H_{32}N_2O_6$ requires C, 68.3; H, 6.6; N, 5.7%). δ_H ($CDCl_3$) 1.38 (9H, s, OC(C*H*$_3$)$_3$), 1.58 (9H, s, OC(C*H*$_3$)$_3$), 1.98–2.10 (1H, m, CH$_2$), 2.19–2.33 (4H, m, 2×CH$_2$), 2.73–2.83 (1H, m, CH$_2$), 3.23–3.32 (1H, m, *H*CCH$_2$), 5.71–5.82 (2H, m, HC=CH), 7.30–7.48 (3H, m, *m*-/*p*-Ar-H), 7.67–7.76 (2H, m, *o*-Ar-H). δ_C (50.3 MHz) 25.1, 26.4, 27.4, 27.8, 29.1 and 34.8 (2×OC(*C*H$_3$)$_3$, C-1′, -2′, -5′ and -6′), 85.0 and 85.4 (O*C*(CH$_3$)$_3$), 110.4 and 111.3 (C-3 and -6), 125.3, 126.4, 128.1, 128.3, 128.4 and 131.1 (Ar-C, C-3′ and -4′), 144.9 (C-3a), 148.1 and 148.5 (C-1 and -4), 157.0 (C-6a), 158.8 and 159.2 (*C*O(CH$_3$)$_3$).

Single crystals suitable for X-ray analysis were prepared by recrystallisation from an ethanol–tetrahydrofuran mixture.

3.1.25. Flash vacuum pyrolysis of 3,6-diphenyl-DPP 4a. 3,6-Diphenyl-DPP **4a** was heated under flash vacuum pyrolysis conditions to a temperature of 700°C under a pressure of 7×10^{-2} Torr. A red solid was collected at the furnace outlet. The infra-red spectrum was identical with that of an authentic sample of diphenyl-DPP **4a**.

3.1.26. Flash vacuum pyrolysis of DPP 13. The DPP derivative **13** was heated under flash vacuum pyrolysis conditions, with a pressure of 8×10^{-3} Torr and a furnace inlet temperature of 300–330°C. In each case a 100 mg sample (±10 mg) was used. The furnace temperature and results were as follows:

Temperature	Products
500 and 600°C	A yellow-orange solid was collected at the furnace outlet. The ^{1}H NMR was identical with that of starting material **13**. The contents of the cold-trap were rinsed out with $CDCl_3$, but no products were detected by ^{1}H NMR other than a trace amount of benzene
700°C	A fluorescent orange solid was collected at the furnace outlet. δ_H (DMSO-d_6) 5.74–5.94 (m, alkenic H), 6.61–6.65 (m, alkenic H), 7.27–7.48 (m, Ar-H), 7.56–7.83 (m, Ar-H), 8.32–8.60 (m, Ar-H), 10.63, 10.93, 10.97, 11.18, 11.19 and 11.36 (s, NH). The contents of the cold-trap, dissolved in $CDCl_3$, contained butadiene: δ_H ($CDCl_3$) 5.07–5.24 (4H, m, C*H*$_2$=CH), 6.23–6.40 (2H, m, CH$_2$=C*H*; identical with the published spectrum[32]), and benzene [trace amount, δ_H 7.34 (s)]

3.1.27. Ethyl 5-*t*-butoxycarbonyloxy-2-phenylpyrrole-3-carboxylate 15. A mixture of the ester **3** (0.37 g, 1.6 mmol), DMAP (0.05 g, 0.4 mmol), Boc_2O (0.39 g, 1.8 mmol) and tetrahydrofuran (25 cm^3) was stirred at 25°C for 24 h and the solvent then evaporated under reduced pressure to give an orange oil. Flash chromatography [silica gel H; eluent petrol/ethyl acetate (2:1)] yielded ester **3** and a colourless solid (0.08 g, 15%), mp 125–126°C (from 70:30 ethanol–water). (Found: C, 65.3; H, 6.5; N, 4.2. $C_{18}H_{21}NO_5$ requires C, 65.3; H, 6.4; N, 4.2%). δ_H ($CDCl_3$) 1.25 (3H, t, J=7.1 Hz, OCH$_2$C*H*$_3$), 1.57 (9H, s, C(C*H*$_3$)$_3$), 4.21 (2H, q, J=7.1 Hz, OC*H*$_2$CH$_3$), 6.30 (1H, s, pyrrole H), 7.35–7.43 (3H, m, *m*-/*p*-Ar-H), 7.58–7.61 (2H, m, *o*-Ar-H), 8.74 (1H, br.s, NH).

3.1.28. 3-(2-Furyl)-6-phenyl-DPP 18a. This was prepared, as described above for compound **4d**, from the pyrrolinecarboxylate ester **3** (1.24 g, 5.4 mmol), 2-furonitrile (0.54 g, 5.8 mol), and sodium *t*-amyloxide [from sodium, 0.39 g (17 mmol)] in boiling dry *t*-amyl alcohol

(30 cm^3) for 3 h at 100–110°C, then for 16 h at 25°C. Red precipitate, yield 1.05 g (70%), mp >400°C. (Found: C, 69.1; H, 3.5; N, 9.8. $C_{16}H_{10}N_2O_3$ requires C, 69.1, H, 3.6; N, 10.1%). δ_H 6.85 (1H, dd, J=1.8 and 3.6 Hz, furyl H-4), 7.52–7.56 (3H, m, *m*-/*p*-Ar-H), 7.75 (1H, d, furyl H-3), 8.08 (1H, d, furyl H-5), 8.40–8.45 (2H, m, *o*-Ar-H), 11.27 (1H, s, NH, reduced on D_2O exchange), 11.32 (1H, s, NH, reduced on D_2O exchange). *m*/*z* 278 ($M^{+\cdot}$, 100%).

The 2,5-bis-*t*-butoxycarbonyl derivative was obtained by stirring a mixture of compound **18a** (0.25 g, 0.9 mmol), Boc_2O (0.59 g, 2.7 mmol), DMAP (0.03 g, 0.2 mmol) and tetrahydrofuran (20 cm^3) at 25°C for 19 h. The solvent was evaporated under reduced pressure, and the residue mixed with methanol (1 cm^3), filtered off and washed with methanol (1 cm^3). The bright orange solid was dried in vacuo. Yield 0.22 g (51%); decomposed without melting. λ_{max} 455 (ε 20842). δ_H ($CDCl_3$) 1.39 (9H, s, $OC(CH_3)_3$), 1.57 (9H, s, $OC(CH_3)_3$), 6.70 (1H, dd, J=1.9 and 3.6 Hz, furyl H-4), 7.45–7.51 (3H, m, *m*-/*p*-Ar-H), 7.62 (1H, d, furyl H-3), 7.70–7.75 (2H, m, *o*-Ar-H), 8.01 (1H, d, furyl H-5). In view of this compound's lack of reactivity in the Diels–Alder reaction (see below) complete characterisation was not attempted.

3.1.29. 2,5-Dimethyl-3-(2-furyl)-6-phenyl-DPP 18c. A mixture of 3-(2-furyl)-6-phenyl-DPP **18a** (1.76 g, 6.3 mmol), potassium carbonate (1.76 g, 12.7 mmol), nitrobenzene (50 cm^3) and methyl toluene-*p*-sulfonate (3.06 g, 16.4 mmol) was stirred at 150°C for 3.5 h, further methyl toluene-*p*-sulfonate (2.36 g, 12.7 mmol) was added and heating continued for 2.5 h. After stirring for a further 15 h at 25°C, the mixture was then added to water, extracted with dichloromethane, dried (Na_2SO_4), concentrated and dried in vacuo at 100°C. Recrystallisation from propan-2-ol-tetrahydrofuran yielded red-orange crystals (1.19 g, 62%), mp 193–194.5°C. (Found: C, 70.9; H, 4.6; N, 9.0. $C_{18}H_{14}N_2O_3$ requires C, 70.6; H, 4.6; N, 9.2%). δ_H ($CDCl_3$) 3.40 (1H, s, NCH_3), 3.58 (1H, s, NCH_3), 6.72 (1H, dd, J=1.6 and 3.6 Hz, furyl H-4), 7.47–7.57 (3H, m, *m*-/*p*-Ar-H), 7.68 (1H, d, furyl H-3), 7.88 (1H, dd, furyl H-5), 8.31 (2H, d, *o*-Ar-H).

3.1.30. 3,6-Di-(2-furyl)-DPP 16. A mixture of 2-furonitrile (0.52 g, 5.6 mmol) and diethyl succinate (0.49 g, 2.8 mmol) was added portionwise over 1.5 h to a solution of sodium *t*-amyloxide (from sodium, 0.22 g, 9.6 mmol) in boiling dry *t*-amyl alcohol (10 cm^3). Stirring was continued for 0.5 h at reflux, and the mixture was then added to an ice-cooled mixture of methanol (35 cm^3) and concentrated hydrochloric acid (1.5 cm^3); the dark purple precipitate was filtered off, washed with methanol and water, then dried in vacuo. Yield 0.46 g (61%). (Found: C, 62.8; H, 2.8; N, 10.2. $C_{14}H_8N_2O_4$ requires C, 62.7; H, 3.0; N, 10.4%). δ_H (200 MHz) 6.83 (2H, dd, J=1.8 and 3.6 Hz, H-4), 7.67 (2H, d, H-3), 8.05 (2H, d, H-5), 11.19 (2H, s, NH). *m*/*z* 268 ($M^{+\cdot}$, 86%).

3.1.31. 3-(3-Furyl)-6-phenyl-DPP 18b. The pyrroline-carboxylate ester **3** (5.30 g, 22.9 mol) in *t*-amyl alcohol (25 cm^3) was added to a solution of sodium *t*-amyloxide (from sodium, 1.64 g, 71.3 mmol) in boiling dry *t*-amyl alcohol (50 cm^3) under nitrogen. 3-Furonitrile (2.14 g, 23.0 mmol) was then added, stirring was continued under reflux for 3 h, then at 25°C for 24 h, during which time a deep purple-red mixture gradually formed. The mixture was added dropwise to a mixture of methanol (90 cm^3) and concentrated hydrochloric acid (8 cm^3) at 0°C and the purple-red solid was filtered off, washed with methanol and water, then dried in vacuo. Yield 4.39 g (69%). This compound was not obtained completely pure (Found: C, 68.7; H, 3.8; N, 9.1. $C_{16}H_{10}N_2O_3$ requires C, 69.1; H, 3.6; N, 10.1%) but gave the correct mass spectrum [*m*/*z* 278 ($M^{+\cdot}$, 6%), 221 (7), 181 (13), 105 (29), 91 (100), 77 (12), 55 (13)] and was converted for full characterisation into its di-Boc derivative (see below). ν_{max} 3138 (N–H), 1706, 1659, 1626 (C=O and N–H bending).

The 2,5-bis-*t*-butoxycarbonyl derivative was obtained by stirring a mixture of compound **18b** (1.5 g, 5.4 mmol), Boc_2O (2.67 g, 12.2 mmol), DMAP (0.13 g, 1.1 mmol), tetrahydrofuran (100 cm^3) and triethylamine (1.25 g, 12.4 mmol) at 25°C for 3 h. Further Boc_2O (1.22 g, 5.6 mmol) was then added, stirring continued for 86 h, then a final portion of Boc_2O (1.26 g, 5.8 mmol) was added and stirring maintained for 7 h more. The solution was then concentrated under reduced pressure, and a light yellow solid precipitated by addition of methanol (2 cm^3); this was filtered off and dried in vacuo. Yield 0.95 g (37%); decomposed without melting. (Found: C, 64.3; H, 5.5; N, 5.6. $C_{26}H_{26}N_2O_7$ requires C, 64.3; H, 5.5; N, 5.85%). δ_H ($CDCl_3$) 1.38 (9H, s, $OC(CH_3)_3$), 1.60 (9H, s, $OC(CH_3)_3$), 6.91 (1H, m, furyl H-4), 7.46–7.52 (3H, m, *m*-/*p*-Ar-H), 7.69–7.80 (3H, m, *o*-Ar-H and furyl H-5), 8.66 (1H, m, furyl H-2).

3.1.32. 3,6-Di-(3-furyl)-DPP 17. To a stirred solution of sodium *t*-amyloxide (from sodium, 0.20 g, 8.7 mmol) in dry *t*-amyl alcohol (15 cm^3), at 95°C and under nitrogen, a mixture of diethyl succinate (0.60 g, 3.4 mmol), 3-furonitrile (0.65 g, 7.0 mmol) and *t*-amyl alcohol (1 cm^3) was added during 10 min; a dark purple precipitate slowly formed in a fluorescent yellow solution. Stirring was continued at 55–60°C for 2 h then the mixture was added to an ice-cooled mixture of methanol (10 cm^3) and concentrated hydrochloric acid (0.5 cm^3). The purple precipitate was filtered off, washed with methanol then water and dried in vacuo. Yield 0.29 g (32%). δ_H 7.34 (2H, m, H-4), 7.87–7.88 (2H, m, H-5), 8.63 (2H, m, H-2), 11.07 (2H, s, NH). *m*/*z* 268.0473 ($M^{+\cdot}$, 100%; $C_{14}H_8N_2O_4$ requires 268.0484).

3.2. Attempted Diels–Alder reactions

Only starting materials were detected (by ^1H NMR) after the following attempted reactions:

(a) 3-(2-Furyl)-6-phenyl-DPP 18a with maleic anhydride (large excess) in acetone at 25°C for 16 h, then at reflux (55–60°C) for 8 h, and in the presence of zinc iodide at 25°C for a further 16 h.
(b) 2,5-Bis-(*t*-butoxycarbonyl)-3-(2-furyl)-6-phenyl-DPP with maleic anhydride (large excess) in acetone in the presence of zinc iodide at 55–60°C for 8 h, then at

25°C for 48 h. [3-(2-Furyl)-6-phenyl-DPP was also detected.]
(c) 3,6-Di-(2-furyl)-DPP 16 with dimethyl acetylenedicarboxylate (large excess) in DMF at 95°C for 4 days.
(d) The 3,6-di-(2-furyl)-DPP dianion with dimethyl acetylenedicarboxylate (4 mol equiv.) in tetrahydrofuran at −78°C for 1.5 h, then under reflux for 2 h and finally at 25°C for 1 week.
(e) 3-(3-Furyl)-6-phenyl-DPP **18b** with phenylacetylene (3 mol equiv.) in 1:1 toluene–DMF at 110°C for 5 h, then 25°C for 2 days, and in the presence of zinc iodide for a further 12 days.
(f) 3,6-Di-(3-furyl)-DPP **17** with phenylacetylene (4.5 mol equiv.) in 1:1 toluene-DMF at 100°C for 39 h in the presence of zinc iodide.

3.2.1. Reaction of acrylonitrile with sodium *t*-amyloxide. Acrylonitrile (10.0 g) was added slowly, under nitrogen, to a stirred solution of sodium *t*-amyloxide (from sodium (1.0 g, 43.5 mmol)) in *t*-amyl alcohol (40 cm^3) at 60–65°C. A white precipitate rapidly formed. Stirring was continued at 30°C for 3 h, and the mixture was then added to a mixture of water (100 cm^3) and concentrated hydrochloric acid (5 cm^3). The white solid was filtered off, washed with water and dried in vacuo. Yield 7.13 g; mp >300°C. ν_{max} 3342 (broad, water O–H), 2245 (C≡N).

3.2.2. Ethyl 4,4-bis-(2-cyanoethyl)-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 19a. The pyrrolinecarboxylate ester **3** (0.76 g, 3.3 mmol) and acrylonitrile (0.20 g, 3.8 mmol) were added successively to a stirred solution of sodium *t*-amyloxide [from sodium (0.23 g, 10 mmol)] in *t*-amyl alcohol (15 cm^3) at 40°C under nitrogen. The mixture was stirred at 25°C for 72 h and was then acidified to pH 5 with dilute (2 M) hydrochloric acid. The solution upon concentration gave a brown solid which was redissolved in dichloromethane, and this solution was washed with water, dried and re-concentrated. Compound **19a** (0.24 g, 37% based on acrylonitrile) formed beige crystals, mp160–161°C. (from propan-2-ol). (Found: C, 67.6; H, 5.5; N, 12.3. $C_{19}H_{19}N_3O_3$ requires C, 67.6; H, 5.7; N 12.5%). ν_{max} 3249 (N–H), 2253 (C≡N), 1735 and 1672 (2×C═O). δ_H ($CDCl_3$) 1.12 (3H, t, J=7.1 Hz, OCH_2CH_3), 2.16 (2H, app. dt, J=13.8 and 6.9 Hz, 2×C$H_A$$CH_2CN$), 2.19–2.34 (4H, m, 2×$CH_2CN$), 2.41 (2H, dt, J=13.8 and 7.1 Hz, 2×C$H_B$$CH_2CN$), 4.12 (2H, q, J=7.1 Hz, OCH_2CH_3), 7.43–7.54 (3H, m, Ar-H), 7.59–7.62 (2H, m, Ar-H), 8.87 (1H, s, NH). δ_C (assigned with the aid of DEPT), 12.7 (CH_2CN), 13.8 (CH_3), 31.3 (CH_2CH_2CN), 54.8 (C-4), 60.4 (OCH_2CH_3), 106.7 (C-3), 118.5 (CN), 128.1 and 128.7 (*o*-/*m*-Ph-C), 129.1 (quat. Ph-C), 130.8 (*p*-Ph-C), 153.7 (C-2), 162.7 (ester C═O), 180.5 (C-5). *m/z* 337 ($M^{+\cdot}$, 37%), 283 (100), 237 (52), 228 (9), 211 (25), 104 (28),77 (20).

3.2.3. Ethyl 4,4-bis-(2-cyanopropyl)-4,5-dihydro-5-oxo-2-phenylpyrrole-3-carboxylate 19b. (a) The pyrrolinecarboxylate ester **3** (4.0 g, 17.3 mmol) and methacrylonitrile (6.0 g, 89.4 mmol) were added successively at 25°C, under nitrogen, to a stirred solution of sodium *t*-amyloxide [from sodium (1.20 g, 52.2 mmol)] in *t*-amyl alcohol (50 cm^3). The mixture was heated under reflux for 3 h, then stirred at 25°C for 16 h. The red-brown solution was then added to an ice-cooled mixture of water (150 cm^3) and concentrated hydrochloric acid (6 cm^3); the beige precipitate was filtered off, recrystallised from propan-2-ol and dried in vacuo at 100°C. Yield 3.22 g (51%).

(b) Sodium hydride (60% w/w mineral oil dispersion, 0.36 g, 9 mmol) was added under nitrogen to a solution of the pyrrolinecarboxylate ester **3** (1.0 g, 4.3 mmol) in tetrahydrofuran (70 cm^3). The mixture was heated briefly to reflux, then cooled to 25°C, whereupon a white precipitate formed. Methacrylonitrile (1.44 g, 21.5 mmol) was then added, the mixture was then briefly reheated to boiling, then stirred at 25°C for 16 h, during which time the precipitate redissolved. The solution was added to ice, extracted with tetrahydrofuran/diethyl ether, the extract dried and the solvent evaporated; the colourless solid residue was dried in vacuo and subjected to flash chromatography (eluent, 5% methanol/dichloromethane then methanol). Yield 1.02 g (65%).

Compound **19b** (mixture of diastereomers) had mp 211–213°C (from propan-2-ol). (Found: C, 69.0; H, 6.5; N, 11.4. $C_{21}H_{23}N_3O_3$ requires C, 69.0; H, 6.3; N, 11.5%). ν_{max} 3222 (N–H), 2238 (C≡N), 1739 and 1656 (2×C═O). δ_H ($CDCl_3$) 1.10 (3H, t, J=7.0 Hz, OCH_2CH_3), 1.29, 1.32 and 1.34 (3 overlapping d, total 6H, J=6.9 Hz, CH_3CHCN), 1.82–1.91, 2.11–2.36, 2.42–2.48 and 2.53–2.72 (4×m, total 6H, CH_2CHCN and CH_2CHCN), 4.00–4.22 (2H, m, OCH_2CH_3), 7.42–7.46 (2H, m, *m*-/*p*-Ar-H), 7.66–7.70 (2H, m, *o*-Ar-H), 7.82 (minor) and 8.07 (major) (2×s, total 1H, NH). δ_H (d_6-DMSO, 40°C) 1.00–1.08 (3H, m, OCH_2CH_3), 1.11–1.23 (6H, m, CH_3CHCN), 1.72–1.85, 1.98–2.15, 2.35–2.50 and 2.58–2.73 (4×m, total 6H, CH_2CHCN and CH_2CHCN), 3.91–4.07 (2H, m, OCH_2CH_3), 7.41–7.47 (3H, m, *m*-/*p*-Ar-H), 7.50–7.64 (2H, m, *o*-Ar-H), 10.94 (minor) and 11.01 (major) (2×s, total 1H, NH). δ_C ($CDCl_3$; provisional assignments, made with the aid of DEPT): 13.7 (OCH_2CH_3); 18.9 and 19.6 (major), 19.1 and 19.4 (minor) (CH_2CHCN); 21.2 and 21.6 (major), 21.3 and 21.4 (minor) ($CHCN$); 40.5 and 40.7 (minor), 40.6 and 41.1 (major) (CH_2CHCN); 54.6 (major) and 55.3 (minor) (C-4); 60.2 (OCH_2CH_3), 107.8 (major) and 108.8 (minor) (C-3); 121.5, 121.7, 122.2 and 122.5 (CN); 128.1 and 128.9 (major) and 128.2 and 128.8 (minor) (*o*-/*m*-Ar-C); 129.8 (major) and 130.5 (minor) (quat. Ar-C); 130.6 (major) and 130.8 (minor) (*p*-Ar-C); 151.9 (minor) and 153.4 (major) (C-2); 163.0 (major) and 163.2 (minor) (ester C═O); 180.8 (major) and 181.0 (minor) (C-5).

3.2.4. 5-Cyano-4-hydroxy-3,6-diphenyl-2*H*-cyclopenta-[*c*]pyrrol-1-one 24a. The pyrrolinecarboxylate ester **3** (17.90 g, 77.4 mmol) was added, under nitrogen, to a boiling solution of sodium *t*-amyloxide (from sodium (5.66 g, 246.2 mmol)) in *t*-amyl alcohol (200 cm^3). Cinnamonitrile **20a** (10.02 g, 77.6 mmol) was then added portionwise over 30 min, during which time a purple-red solution formed. Stirring was continued for 2 h under reflux, then for 15 h at 25°C, and the solution was then added to an ice-cooled mixture of methanol (150 cm^3) and concentrated hydrochloric acid (25 cm^3). The dark red solid was filtered off, washed thoroughly with methanol and water, then dried in vacuo. Yield 7.39 g (31%), mp 273–275°C. (Found: C,

77.1; H, 3.8; N, 8.9; *m/z* 312.1003. $C_{20}H_{12}N_2O_2$ requires C, 76.9; H, 3.9; N, 9.0%; *M*, 312.0899). λ_{max} 457 (ε 3946), 509 (2270). ν_{max} 3114 (strong, N–H or O–H), 2205 (C≡N), 1667 (C=O), 1600. δ_H 7.45–7.57 (6H, m, *m*-/*p*-Ph-H), 8.23 (2H, dd, *J*=1.5 and 8.0 Hz, *o*-Ph(6)-H), 8.33–8.36 (2H, m, *o*-Ph(3)-H), 11.01 (1H, s, NH, reduced on D_2O exchange). *m/z* 312 ($M^{+\cdot}$, 100%), 284 (25), 255 (37), 225 (25), 129 (20), 71 (32).

The following analogues of **24a** were prepared similarly.

3.2.5. 5-Cyano-4-hydroxy-3-phenyl-6-(*p*-tolyl)-2*H*-cyclopenta[*c*]pyrrol-1-one 24b. Dark red, yield 32%, mp 284–287°C (dec.) (Found: C, 77.5; H, 4.4; N, 8.6. $C_{21}H_{14}N_2O_2$ requires C, 77.3; H, 4.3; N, 8.6%). ν_{max} 3114 (weak, N–H or O–H), 2209 (C≡N), 1668 (C=O). δ_H 2.37 (3H, s, CH_3), 7.31 (2H, half of AA′BB′, H-3 and -5 in 4-MeC_6H_4), 7.55–7.57 (3H, m, *m*-/*p*-Ph-H), 8.15 (2H, half of AA′BB′, H-2 and -6 in 4-MeC_6H_4), 8.29–8.32 (2H, m, *o*-Ph-H), 11.04 (1H, s, NH).

3.2.6. 6-(*p*-Chlorophenyl)-5-cyano-4-hydroxy-3-phenyl-2*H*-cyclopenta[*c*]pyrrol-1-one 24c. The reagents were added to the anion of **3** at 75–80°C. Dark red; yield 54%, mp 290–292°C. (Found: C, 69.0; H, 3.3; N, 7.8. $C_{20}H_{11}ClN_2O_2$ requires C, 69.3; H, 3.2; N, 8.1%). ν_{max} 3370 (broad, N–H or O–H), 2208 (C≡N), 1600 (C=O). δ_H 7.51–7.58 (5H, m, Ar-H), 8.25–8.28 (2H, m, Ar-H), 8.33–8.36 (2H, m, Ar-H), 11.04 (1H, s, NH). λ_{max} 461 (ε 14,872), 605 (7907), unaffected by addition of triethylamine (3 drops). *m/z* 346/348 ($M^{+\cdot}$, 100/43%), 318/320 (19/6), 311 (25), 289/291 (25/8), 255 (30), 225 (72), 104 (40), 77 (45).

3.2.7. 5-Cyano-4-hydroxy-6-(*p*-methoxyphenyl)-3-phenyl-2*H*-cyclopenta[*c*]pyrrol-1-one 24d. The reaction time under reflux was extended to 3 h. Purple-red; yield 38%, mp 286–287°C. (Found: C, 73.5; H, 3.9; N, 8.1; *m/z* 342.1009. $C_{21}H_{14}N_2O_3$ requires C, 73.7; H, 4.1; N, 8.2%; *M*, 342.1004). δ_H 3.84 (3H, s, OCH_3), 7.09 (2H, d, *J*=9.0 Hz, half of AA′BB′, H-3 and -5 in 4-$MeOC_6H_4$), 7.55–7.57 (3H, m, *m*- and *p*-Ph-H), 8.43 [4H, coincident *o*-Ph-H (approx. d) and H-2 and -6 of 4-$MeOC_6H_4$ (half of AA′BB′)], 11.13 (1H, s, NH). λ_{max} 460 (ε 13,309), 592 (5927); (+1 drop conc. HCl) 492 (ε 12,876). ν_{max} 3110 (N–H or O–H), 2208 (C≡N), 1673 (C=O), 1611. *m/z* 342 (100%), 314 (13), 285 (10), 121 (14), 77 (9).

3.2.8. 5-Cyano-4-hydroxy-6-(*p*-fluorophenyl)-3-phenyl-2*H*-cyclopenta[*c*]pyrrol-1-one 24f. Obtained (yield, 66%) as for **24d**, was dark red and had mp 274–276°C. (dec., subl.) (Found: C, 71.9; H, 3.1; N, 8.7. $C_{20}H_{11}FN_2O_2$ requires C, 72.7; H, 3.4; N, 8.5%.) δ_H 7.43 (2H, t, *J*=9.0 Hz, Ar-H-3 and -5 in 4-FC_6H_4), 7.5 (1H, br s, OH), 7.55–7.70 (3H, m, *m*-/*p*-PhH), 8.51 (2H, d, *J*=10.0 Hz, *o*-PhH), 8.51 [4H, coincident *o*-Ph (m) and Ar-H-2 and -6 in 4-FC_6H_4 (dd, *J*=9.0 and 5.6 Hz)], 10.73 (1H, s, NH).

3.2.9. 5-Cyano-6-(*p*-dimethylaminophenyl)-4-hydroxy-3-phenyl-2*H*-cyclopenta[*c*]-pyrrol-1-one 24g. The reagents were added to the anion of **3** at 85–90°C and the reaction time under reflux was 1.5 h; purple-red, yield (impure) 0.81 g (20%). ν_{max} 3110 (weak, N–H or O–H), 2202 (C≡N), 1657 (C=O), 1600. (Found: C, 72.5; H, 4.6; N, 11.5. $C_{22}H_{17}N_3O_2$ requires C, 74.4; H, 4.8; N, 11.8%). δ_H 3.05 (6H, s, 2×CH_3), 6.83–6.86 (2H, m, Ar-H), 7.43–7.52 (3H, m, Ar-H), 8.24–8.33 (4H, m, Ar-H), 11.16 (1H, s, NH). *m/z* 355 ($M^{+\cdot}$, 19%), 324 (44), 169 (100), 91 (82), 77 (46), with a trace amount of impurity giving *m/z* 379. λ_{max} 482 (ε 6472), 583 (2829), unaffected by addition of triethylamine (3 drops).

3.2.10. 5-Cyano-4-hydroxy-6-(3,4-methylenedioxyphenyl)-3-phenyl-2*H*-cyclopenta[*c*]-pyrrol-1-one 24h. Obtained as for **24d**, was dark red and had mp 296–298°C.(dec., subl.) (Found: C, 70.5; H, 3.8; N, 7.8. $C_{21}H_{12}N_2O_4$ requires C, 70.8; H, 3.4; N, 7.9%.) δ_H 6.21 (3H, s, CH_2O_2), 7.14 (1H, d, *J*=8.2 Hz, H-5′), 7.58–7.66 (4H, m, *m*- and *p*-Ph-H and OH), 8.07 (1H, dd, *J*=8.2 and 1.8 Hz, H-6′), 8.14 (1H, d, *J*=1.8 Hz, H-2′), 8.46 (2H, d, *J*=8.9 Hz, *o*-Ph-H), 10,80 (1H, s, NH). *m/z* 356 ($M^{+\cdot}$, 88%), 344 (50), 288 (44), 149 (38), 135 (78), 105 (54), 77 (57), 57 (53), 43 (100).

3.2.11. 5-Cyano-4-hydroxy-6-(2-thienyl)-3-phenyl-2*H*-cyclopenta[*c*]pyrrol-1-one 24i. Obtained as for **24d**, was dark red and had mp 285–287°C (dec., subl.) (Found: C, 67.7; H, 3.3; N, 8.5. $C_{18}H_{10}N_2O_2S$ requires C, 67.9; H, 3.2; N, 8.8%.) δ_H 7.40 (1H, dd, *J*=5.0 and 3.8 Hz, Th-H-4), 7.45–7.80 (3H, m, *m*- and *p*-Ph-H), 7.97 (1H, d, *J*=4.6 Hz, Th-H-5), 8.2–8.6 (2H, br, *o*-Ph-H), 8.74 (1H, d, *J*=3.7 Hz, Th-H-3), 11.13 (1H, s, NH). *m/z* 318 ($M^{+\cdot}$, 100%), 290 (29), 261 (32), 153 (98), 105 (37), 81 (55), 55 (40).

Reaction of the pyrrolinecarboxylate ester **3** with *p*-nitrocinnamonitrile **20e** and sodium *t*-amyloxide under the standard conditions produced only a light brown intractable solid which was not sufficiently soluble in DMSO for NMR analysis and which was much less intensely coloured than the other compounds in the series **24a–d** and **24f–i**.

3.2.12. 2,5-Dimethyl-3,6-diphenyl-DPP. The dianion of 3,6-diphenyl-DPP was prepared as described above from the pyrrolinecarboxylate ester **3** (1.02 g, 4.4 mmol), benzonitrile (1.0 g, 9.7 mmol) and sodium *t*-amyloxide [from sodium (0.33 g, 14.4 mmol)] in *t*-amyl alcohol (20 cm^3). After heating under reflux had been maintained for 5 h, the mixture was cooled to 80–90°C, methyl toluene-*p*-sulfonate (9.20 g, 49.4 mmol) was added portionwise, and heating was continued for 45 min, during which time the mixture turned fluorescent yellow. The product was isolated by addition of the mixture to water (50 cm^3) and extraction with ethyl acetate. The orange-red product was finally washed with methanol and dried in vacuo at 60°C; it was identical with the product obtained by the method of Potrawa and Langhals.[33] Yield 0.69 g (50%), mp 228–230°C (from toluene; lit.,[33] 233–234°C).

δ_H (200 MHz) 3.33 (6H, s, 2×CH_3), 7.50–7.54 (6H, m, *m*-/*p*-Ar-H), 7.84–7.89 (4H, m, *o*-Ar-H). δ_C 29.9 (CH_3), 109.6 (C-3a and C-6a), 128.4 (quat. Ar-C), 129.3, 129.5, 131.7 (Ar-C), 149.0 (C-3 and C-6) and 163.0 (C-1 and C-4).

3.2.13. 5-Cyano-4-methoxy-6-(*p*-methoxyphenyl)-2-methyl-3-phenylcyclopenta[*c*]-pyrrol-1-one 26d. The

dianion **25d** was prepared as described above, from the pyrrolinecarboxylate ester **3** (2.56 g, 11.1 mmol), *p*-methoxycinnamonitrile **20d** (2.09 g, 13.1 mmol) and sodium *t*-amyloxide (from sodium (0.79 g, 34.4 mmol)) in *t*-amyl alcohol (25 cm^3). After heating under reflux had been maintained for 4 h, the dark purple solution was cooled to 40°C, and methyl toluene-*p*-sulfonate (20.32 g, 0.1091 mol) was added portionwise during 10 min. Heating under reflux was resumed for 45 min, during which time the colour changed to a bright orange-red. The mixture was cooled, added to water (50 cm^3), extracted with ethyl acetate, and the extract washed with water then concentrated. The orange-red product **26d** was filtered off, washed with methanol then petrol, dried in vacuo, and recrystallised from 1,4-dioxan. Yield 0.97 g (24%), mp 253–255°C. (Found: C, 74.7; H, 4.8; N, 7.4; *m/z* 370.1324. $C_{23}H_{18}N_2O_3$ requires C, 74.6; H, 4.9; N, 7.7%; *M*, 370.1317). ν_{max} 2200 (C≡N), 1701 (C=O), 1607; δ_H 3.19 (3H, s, NCH_3), 3.88 (3H, s, $ArOCH_3$), 4.20 (3H, s, 4-OCH_3), 7.00 (2H, d, *J*=8.8 Hz, H-3 and -5 in 4-$MeOC_6H_4$), 7.54–7.62 (5H, m, Ph-H), 8.33 (2H, d, *J*=8.8 Hz, H-2 and 6 in 4-$MeOC_6H_4$). *m/z* 370 (100%), 355 (39), 314 (6), 185 (8), 118 (13), 77 (8).

3.2.14. 5-Cyano-4-methoxy-2-methyl-3,6-diphenylcyclopenta[*c*]pyrrol-1-one 26a. This was prepared in a similar manner, from the pyrrolinecarboxylate ester **2** (4.0 g, 17.3 mmol), cinnamonitrile **20a** (4.46 g, 34.5 mmol) and sodium *t*-amyloxide (from sodium (1.22 g, 53.1 mmol)) in *t*-amyl alcohol (50 cm^3); after 4 h at the reflux temperature, methyl toluene-*p*-sulfonate (25.22 g, 135.4 mmol) was added at 25°C, and heating under reflux was then resumed for 1 h. The mixture was cooled, added to water (100 cm^3), extracted with ethyl acetate, the extract dried (Na_2SO_4) then concentrated; the orange-red product was purified by dissolution in ethanolic sodium ethoxide solution and, after 18 h, reprecipitation by addition to water and dropwise acidification (conc. HCl). Compound **26a** (1.22 g, 21%) had mp 210–212°C (from propan-2-ol/tetrahydrofuran). (Found: C, 77.3; H, 4.7; N, 8.2. $C_{22}H_{16}N_2O_2$ requires C, 77.6; H, 4.7, N, 8.2%.) ν_{max} 2197 (C≡N), 1703 (C=O), 1677; δ_H 3.18 (3H, s, NCH_3), 4.21 (3H, s, OCH_3), 7.43–7.66 (8H, m, Ar-H), 8.22 (2H, d, *J*=6.6 Hz, Ar-H); *m/z* 340 ($M^{+\cdot}$, 100%), 325 (76), 284 (12), 161 (21), 118 (15), 77 (15), 69 (18).

3.2.15. 5-Cyano-4-ethoxy-2-ethyl-3,6-diphenylcyclopenta[*c*]pyrrol-1-one 27a. This was prepared in a similar manner, from the pyrrolinecarboxylate ester **3** (15.0 g, 64.9 mmol), cinnamonitrile **20a** (8.4 g, 65 mmol) and sodium *t*-amyloxide [from sodium (4.5 g, 0.196 mol)] in *t*-amyl alcohol (80 cm^3); after 1.5 h at the reflux temperature, a solution of ethyl toluene-*p*-sulfonate (52.5 g, 262 mmol) in dimethylformamide (20 cm^3) was added to the purple solution, and heating under reflux continued for a further 1.5 h, during which time the colour changed to orange and a colourless precipitate formed. The mixture was cooled, added to water (250 cm^3), then extracted with ethyl acetate, the organic layer acidified with 10% hydrochloric acid, washed with water, dried and the solvent evaporated. The orange residue was dissolved overnight in ethanolic sodium ethoxide solution, the solution set aside overnight and the product reprecipitated by acidification (10% HCl), filtered off, washed with water and dried in vacuo. Yield 3.07 g (13%), mp 200–202°C. (Found: C, 78.0; H, 5.2; N, 7.8. $C_{24}H_{20}N_2O_2$ requires C, 78.2, H, 5.5; N, 7.6%). ν_{max} 2195 (C≡N), 1694 (C=O), 1655. δ_H (200 MHz) 1.19 (3H, t, *J*=7.1 Hz, CH_2CH_3), 1.29 (3H, t, CH_2CH_3), 3.68 (2H, q, NCH_2CH_3), 4.55 (2H, q, OCH_2CH_3), 7.42–7.67 (8H, m, Ar-H), 8.22 (2H, dd, *J*=2.2 and 8.2 Hz, *o*-Ar-H). *m/z* 368 ($M^{+\cdot}$, 100%), 340 (70), 325 (14), 311 (50), 283 (28), 255 (32), 240 (24), 227 (18), 104 (33), 77 (34).

3.2.16. 5-Cyano-4,5-dihydro-5-methyl-3,6-diphenylcyclopenta[*c*]pyrrole-1,4-dione 28a. The dianion **25a** was prepared as described above, from the pyrrolinecarboxylate ester **2** (2.0 g, 8.6 mmol), cinnamonitrile **20a** (1.19 g, 9.2 mmol) and sodium *t*-amyloxide (from sodium (0.60 g, 26.1 mmol)) in *t*-amyl alcohol (20 cm^3); after 4.5 h at the reflux temperature, the solution was cooled to 55°C and iodomethane (5.5 g, 38.7 mmol) was added. Heating was continued at 40°C for 1 h, then the mixture was added to water, acidified (10% HCl) and extracted with ethyl acetate; the extract was dried (Na_2SO_4) and the solvent evaporated off. Flash chromatography (eluent, petrol/ethyl acetate (2:1)) yielded a bright orange solid (0.76 g, 27%), mp 299–301°C (from propan-2-ol/tetrahydrofuran). (Found: C, 77.3; H, 4.4; N, 8.4. $C_{21}H_{14}N_2O_2$ requires C, 77.3, H, 4.3; N, 8.6%). ν_{max} 3167 (NH), 2365 (C≡N), 1677 (C=O), 1607. δ_H 1.90 (3H, s, CH_3), 7.57–7.65 (6H, m, *m*-/*p*-Ar-H), 8.41–8.51 (4H, m, *o*-Ar-H), 12.22 (1H, s, NH) with trace impurity at 3.32 (≪1H, s, NCH_3). *m/z* 326 ($M^{+\cdot}$, 100%), 340 (14), 297 (13), 283 (4), 269 (9), 255 (95), 118 (10), 105 (12), 77 (14).

3.2.17. 5-Cyano-4,5-dihydro-2,5-dimethyl-3,6-diphenylcyclopenta[*c*]pyrrole-1,4-dione 29a. The dianion **25a** was prepared as described above, from the pyrrolinecarboxylate ester **3** (10.0 g, 43.2 mmol), cinnamonitrile **20a** (5.6 g, 43.4 mmol) and sodium *t*-amyloxide (from sodium (2.97 g, 129.2 mmol)) in *t*-amyl alcohol (80 cm^3). After 3.5 h at reflux temperature and then 2 h at 25°C, iodomethane (25.15 g, 177.2 mmol) was added and the mixture was stirred at 25°C for 6 days; it was then added to water (200 cm^3) and extracted with ethyl acetate. Flash chromatography of the dried (Na_2SO_4) and concentrated extract (eluent, petrol/ethyl acetate (1:1)) afforded a bright orange solid (5.12 g, 35%), mp 199–200°C (from propan-2-ol/tetrahydrofuran). (Found: C, 77.3; H, 4.6; N, 7.9. $C_{22}H_{16}N_2O_2$ requires C, 77.6; H, 4.7; N, 8.2%). ν_{max} 2195 (C≡N), 1694 and 1655 (2×C=O); δ_H 1.87 (3H, s, CCH_3), 3.32 (3H, s, NCH_3), 7.61–7.64 (6H, m, *m*-/*p*-Ar-H), 7.83–7.87 (2H, m, *o*-H in 3-Ph), 8.50–8.53 (2H, *o*-H in 6-Ph). *m/z* 340 ($M^{+\cdot}$, 100%), 325 (3), 312 (17), 311 (17), 283 (10), 254 (6), 240 (6), 156 (9), 127 (6), 118 (280), 105 (80), 91 (5), 77 (13).

3.3. X-Ray crystallography

The intensity data for compounds **14**, **15**, **18c** and **19b** were recorded at 293(1) K with a Rigaku AFC7S diffractometer using graphite-monochromated Mo Kα (λ=0.7107 Å), and the structures in Figs. 2–4 were solved by direct methods using SIR92[34] and refined by full-matrix least squares on F, using the TeXsan system 1.[35] For crystals of compounds **15**, **18c** and **19b** 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. In the case of compound **15**, the structure was disordered at two sites within the *t*-butoxycarbonyloxy group, and for clarity the structure shown (Fig. 2) is simplified to show the sites of maximum occupancy.

In the case of compound **14** (Fig. 1), the original 'triclinic' data set (4696 reflections) gives a very poor R_{int} (16%) on merging to yield a 'monoclinic' data set with 2228 reflections. The space group $P2_1/c$ was chosen as being the best option (two cell angles are 90° and the absences *do* correspond with a monoclinic $P2_1/c$ type cell). The Z value of 2 in the cell demands that the molecule lie about an inversion centre and thus have the phenyl and cyclohexenyl moieties occupying the same site in the asymmetric unit.

The structure solved relatively easily using SHELXS-97.[36] It was apparent at this 'solution' stage that the phenyl/cyclohexenyl site had six peaks, some of which were distended normal to the plane. It was also obvious that the unique *t*-butoxycarbonyl moiety was disordered unequally over two sites. All the disorder was successfully modelled using the available options in SHELXL-97.[36] Using DFIX and Free-variable options, the geometry of the cyclohexenyl ring refined to yield a double-bond location consistent with that anticipated, and the final model has the phenyl and cyclohexenyl rings, each with 0.5 occupancy, occupying the same volume element in the crystal lattice. The *t*-butoxycarbonyl geometry was controlled by the use of various options in SHELXL-97.

For compound **26d**, the intensity data were recorded at 291(2) K with a Siemens/Bruker SMART CCD diffractometer, but with tuneable wavelengths (λ=0.68900 Å) using the microcrystal diffraction facility on station 9.8[37] of the Synchrotron Radiation Source, CLRC Daresbury Laboratory. Processing of the data used the SMART, SAINT and SADABS[38,39] programs, and the structure was solved using SHELXTL.[40] The intensity data for compound **29a** were also recorded using a Siemens/Bruker SMART diffractometer, with data again being integrated using the SAINT and SADABS programs; the structure solved by direct methods and refined by full-matrix least-squares against F^2 (SHELXTL). 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 **14**, **15**, **18c**, **19b**, **26d** and **29a** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 176667, 176668, 176669, 176700, 176701 and 176702, respectively. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

We thank Professor G. Ferguson and Dr C. Glidewell for valuable assistance with the solution of the X-ray crystal structure of compound **14**. For the solution of the structure of compound **26d**, we gratefully acknowledge the provision of time on DARTS, the UK national synchrotron radiation service at the CLRC Daresbury Laboratory. We also thank Professors Abul Iqbal and I. A. Macpherson for helpful discussions, Mrs S. Williamson for the microanalyses, Mr C. Millar for the mass spectra, and Ciba Specialty Chemicals Inc., Basel, for financial support.

References

1. Hao, Z.; Iqbal, A. *Chem. Soc. Rev.* **1997**, *26*, 203–213 and references therein.
2. Iqbal, A.; Jost, M.; Kirchmayr, R.; Pfenninger, J.; Rochat, A.; Wallquist, O. *Bull. Soc. Chim. Belg.* **1988**, *97*, 615–643.
3. Mizuguchi, J.; Grubenmann, A.; Wooden, G.; Rihs, G. *Acta Crystallogr.* **1992**, *B48*, 696–700.
4. (a) Rochat, A. C.; Cassar, L.; Iqbal, A. Eur. Pat. 94,911, 1983. (b) Iqbal, A.; Pfenninger, J.; Rochat, A. C.; Babler, F. Eur. Pat. 181,290, 1986. (c) Surber, W.; Iqbal, A.; Stern, C. Eur. Pat. 302,018, 1989.
5. Pfenninger, J.; Iqbal, A.; Rochat, A. C.; Wallquist, O. US Patent 4,778,899, 1986. Pfenninger, J.; Iqbal, A.; Rochat, A. C. US Patent 4,749,795, 1986.
6. See, for example: Saunders, K. J. *Organic Polymer Chemistry*; 2nd ed; Chapman and Hall: London, 1987; p 16. Stevens, M. P. *Polymer Chemistry: An Introduction*; Oxford University: Oxford, 1990; pp 250–256, and references therein.
7. Bruson, H. A. *Org. React.* **1949**, *5*, 79–135. Bergmann, E. D.; Ginsburg, D.; Pappo, R. *Org. React.* **1959**, *10*, 179–555 and references therein.
8. Brion, F. *Tetrahedron Lett.* **1982**, *23*, 5299–5302.
9. Kienzle, F. *Helv. Chim. Acta* **1975**, *58*, 1180–1183.
10. Iqbal, A. Personal communication.
11. (a) McKeown, N. B.; Chambrier, I.; Cook, M. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1169–1177. (b) Chambrier, I.; Cook, M. J.; Cracknell, S. J.; McMurdo, J. *J. Mater. Chem.* **1993**, *3*, 841–849.
12. Wang, E.-C.; Lin, G.-J. *Tetrahedron Lett.* **1998**, *39*, 4047–4050.
13. (a) Zambounis, J. S.; Hao, Z.; Iqbal, A. *Nature* **1997**, *388*, 131. (b) Eur. Pat. 673,979, 1995.
14. Moon, M. W. *J. Org. Chem.* **1977**, *42*, 2219–2223. San Feliciano, A.; Caballero, E.; Pereira, J. A. P.; Puebla, P. *Tetrahedron* **1989**, *45*, 6553–6562.
15. Garst, J. E.; Wilson, B. J. *J. Agric. Food Chem.* **1984**, *32*, 1083–1087.
16. Charbonneau, G.-P.; Delugeard, Y. *Acta Crystallogr.* **1976**, *B32*, 1420–1423.
17. Bennes, R.; Philp, D.; Spencer, N.; Kariuki, B.; Harris, K. D. M. *Org. Lett.* **1999**, *1*, 1087–1090.
18. Patrick, T. M. *J. Org. Chem.* **1952**, *17*, 1009–1016.
19. Boutagy, G.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87–99.
20. Pastushak, N. O.; Stadniichuk, N. F.; Dombrovskii, A. V. *Zh. Obsh. Khim.* **1963**, *33*, 2950–2952 *Chem. Abstr.* **1963**, *60*, 1639.
21. DiBiase, S. A.; Lipisko, B. A.; Haag, A.; Wolak, R. A.; Gokel, G. W. *J. Org. Chem.* **1979**, *44*, 4640–4649.

22. Butt, G.; Topsom, R. D. *Spectrochim. Acta* **1980**, *36A*, 811–817.
23. Schiemenz, G. P.; Engelhard, H. *Chem. Ber.* **1962**, *95*, 967–970.
24. Koelsch, C. F. *J. Am. Chem. Soc.* **1943**, *65*, 57–58.
25. Claisse, J. A.; Gregory, G. I.; Warburton, W. K. S. Afr. Pat. 68,01861, 1969; *Chem. Abstr.* **1970**, *72*, 21696.
26. Lippert, E.; Lüder, W. *J. Phys. Chem.* **1962**, *66*, 2430–2434.
27. Mendes da Costa, R. *Compt. Rend. Hebd. Acad. Sci.* **1933**, *196*, 1815–1817.
28. Claisse, J. A.; Foxton, M. W.; Gregory, G. I.; Sheppard, A. H.; Tiley, E. P.; Warburtion, W. K.; Wilson, M. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2241–2249.
29. Wah Chan, C.; Fawcett, A. H.; Mulemwa, J. N.; Chao-Eng, Tan *Polymer* **1985**, *26*, 1268–1270.
30. Olah, G. A.; Surya Prakash, G. K.; Arvanaghi, M.; Bruce, M. R. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 92–94.
31. Toland, W. G.; Ferstandig, L. L. *J. Org. Chem.* **1958**, *23*, 1350–1351.
32. Pouchert, C. J.; Behnke, J. *The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*; The Aldrich Chemical: Milwaukee, 1993 Spectrum 1-36B.
33. Potrawa, T.; Langhals, H. *Chem. Ber.* **1987**, *120*, 1075–1078.
34. Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Cryst.* **1993**, *26*, 343–350.
35. TeXsan Crystal Structure Analysis Package, 1985 and 1992: Molecular Structure Corporation, The Woodlands, TX77381, USA.
36. Sheldrick, G. M. University of Göttingen, Germany.
37. Cernik, R. J.; Clegg, W.; Catlow, C. R. A.; Bushnell-Wye, G.; Flaherty, J. V.; Greaves, G. N.; Burrows, I.; Taylor, D. J.; Teat, S. J.; Hamichi, M. *J. Synchrotron Rad.* **1997**, *4*, 279–286.
38. SMART (control) and SAINT (integration) software, version 4, Bruker AXS Inc., Madison, Wisconsin, 1994.
39. Sheldrick, G. M. *SADABS, program for scaling and correcion of area detector data*, University of Gottingen, 1997, based on the method of Blessing, R. H. *Acta Crystallogr., Sect. A* **1995**, *51*, 33.
40. Sheldrick, G. M. *SHELXTL*, version 5; Bruker AXS Inc.: Madison, Wisconsin, 1994.