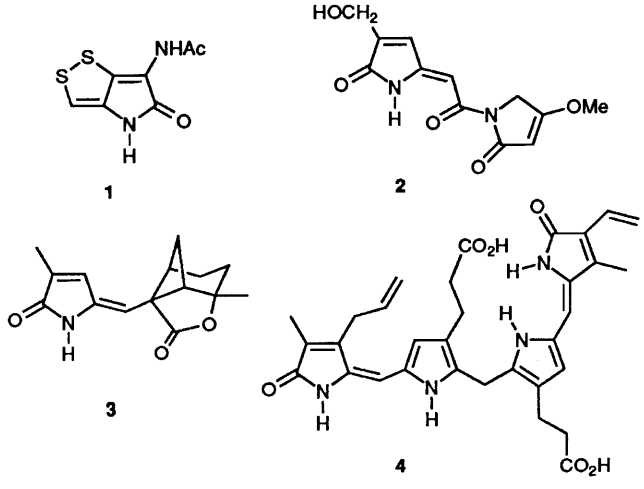
The Synthesis of 5-Ylidenepyrrol-2(5*H*)-ones from Maleimides and from Pyrrol-2-(5*H*)-ones

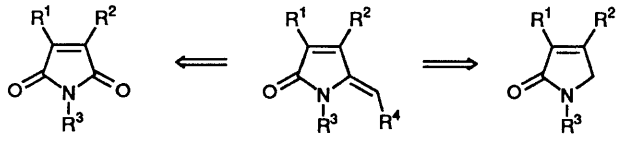
G. Bryon Gill, Gwyn D. James, Karen V. Oates and Gerald Pattenden *
Department of Chemistry, The University, Nottingham NG7 2RD, UK

A series of maleimides **5** have been prepared by reaction of the appropriate maleic anhydrides with either ammonium acetate or methylammonium acetate in boiling acetic acid. The maleimides underwent Wittig-type reactions with stabilised phosphoranes, under moderately forcing conditions, to give 5-ylidenepyrrol-2(5*H*)-ones **6**. The ease of the reaction and the regiochemistry of the addition to unsymmetrical maleimides depended upon the nature of the 3-substituent and on the presence or absence of an *N*-alkyl substituent. Thus, 3-methoxymaleimides reacted exclusively at C-2; the presence of an *N*-methyl substituent required the use of more forcing reaction conditions, but did not alter the preference for C-2 attack. With 3-methylmaleimides, however, the slight preference for reaction at C-2 in **5c** was overturned by the presence of an *N*-methyl substituent as in **5d**. The related reactions of unstabilised phosphoranes or phosphine oxides usually only afforded intractable gums, and with Julia-type reagents only starting materials were recovered. However, the lithium enolate of methyl trimethylsilylacetate (or other Peterson-type reagents) underwent successful addition to *N*-methylmaleimides at −78 °C; the 5-ylidenepyrrolone product distributions were similar to those obtained with the stabilised phosphoranes. Variation of the 5-alkylidene side-chain was achieved through the reactions of *N*-methylmaleimides with alkyl Grignard reagents by dehydrating the first-formed 5-alkyl-5-hydroxypyrrolone. 4-Methoxy-1-methylpyrrol-2(5*H*)-one could be deprotonated exclusively at the 5-position under kinetic control (*i.e.* BuLi, THF, −78 °C), and the anion then quenched with a variety of electrophilic agents to give 5-substituted pyrrolones. These derivatives proved amenable to dehydration or dehydrogenation, as appropriate, to afford the corresponding 5-alkylidenepyrrolones.

The 5-ylidenepyrrol-2(5*H*)-one structural unit **6** is found in a range of biologically important natural products including holomycin **1**,[1] pukeleimide A **2**,[2] isoampullicin **3**,[3] and the bile pigment bilirubin **4**.[4] Although synthetic routes to the corresponding 5-ylidenefuran-2(5*H*)-ones and 4-ylidenetetronic acids are well documented,[5] apart from holomycin **1** and its relatives,[6] very few synthetic studies towards 5-ylidenepyrrol-2(5*H*)-ones have been published. In connection with synthetic studies with the natural products **1**, **2** and **3** we have examined the uses of substituted maleimides **5** and of pyrrolones **7** as starting materials in the elaboration of 5-ylidenepyrrol-2(5*H*)-ones by appropriate carbanion reactions (Scheme 1). In this paper we summarise the outcome of these investigations, and in the accompanying paper we describe the development of the



1 **2** **3** **4**



5 **6** **7**

Scheme 1

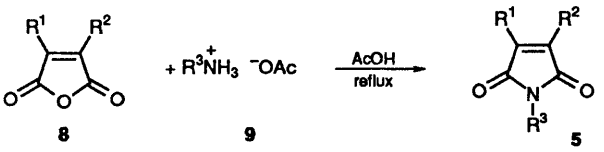
studies in a total synthesis of pukeleimide A **2**, a constituent of the blue green alga *Lyngbya majuscula*.

We began our studies by first examining synthetic routes to a variety of carbon and nitrogen substituted maleimides **5**, and then investigating systematically their reactivity with a range of carbon nucleophiles, particularly those associated with phosphorus (Wittig type), sulfur (Julia reaction), silicon (Peterson) and magnesium (Grignard reaction).

The majority of the methods reported for the synthesis of maleimides are based on the reactions of the corresponding maleic anhydrides **8** with an amine. This affords a half-amide adduct which can be dehydrated and cyclised with, for example, acetic anhydride.[7] However, we found that a one-step method involving the action of the ammonium acetate **9** on the maleic anhydride **8** in boiling acetic acid,[8] to be the most convenient and efficient means for effecting the conversion **8** → **5**. Product yields were usually of the order 60–80% except for the cases where R^3 = H, when yields of 20–50% were obtained.

Reactions of Maleimides with Carbon Nucleophiles

(1) *Phosphoranes.*—The reaction of maleic anhydrides with stabilised phosphoranes leading to 5-ylidenefuran-2-ones is well precedented,[9,10] and has provided the basis for the development of syntheses of the pulvinone, pulvinic acid, and multicolic acid



8 9 5

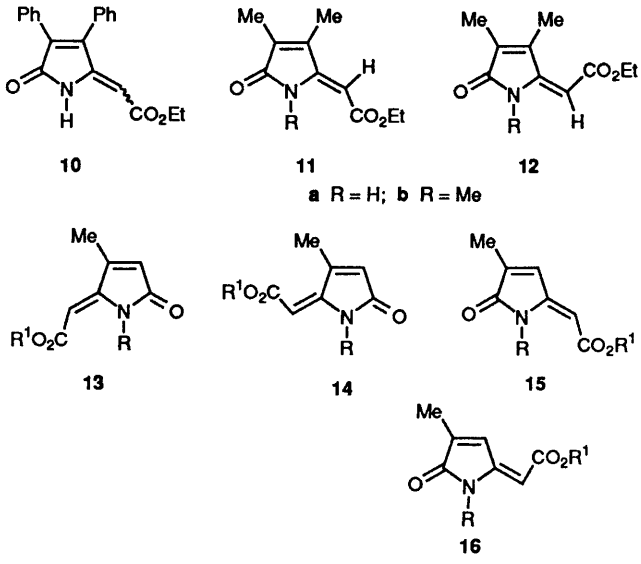
	a	b	c	d	e	f	g	h	i	j
R^1	Me	Me	Me	Me	OMe	OMe	OMe	OMe	SPh	Me
R^2	Me	Me	H	H	H	H	Me	Me	H	H
R^3	H	Me	H	Me	H	Me	H	Me	Me	Bz

groups of natural pigments.[9] The analogous reactions of maleimides have received scant attention despite the fact that the reactions of phosphoranes with both cyclic and acyclic amides are known to give the ylidene derivatives.[11] This lack of interest may, in part, be due to the apparent need for forcing conditions (*e.g.* reaction in the melt or in boiling xylene) and in part to the modest product yields (*ca.* 20–60%). Also, maleimide itself **5** (R^1–R^3 = H) was reported[11] to react by Michael addition to the C=C (to give a 3-phosphoranyl adduct) rather than by nucleophilic attack at the C=O group (to give the 5-ylidenepyrrolone plus Ph_3P=O). However, reaction of 3,4-diphenylmaleimide with ethoxycarbonylmethylene(triphenyl)-phosphorane (CMTP) did afford the product of 1,2 -or Wittig-type addition (**10**; 58%),[10b] but the stereochemistry of the olefination was not specified.

We were interested to discover the influence exerted by the substituent groups R^1–R^3 in the maleimide **5** on reactivity, and on the interplay of steric and electronic factors in dictating the regiochemistry of the nucleophilic attack and the stereochemistry of the 5-ylidene products formed.

The symmetrical maleimides **5a** and **5b** were chosen as suitable substrates for the initial investigations. Both reacted with an excess of CMTP in boiling toluene to afford only products of Wittig addition. From the reaction with **5a** was isolated the *Z*-5-ylidene ester **11a** (71%) and only a trace of the *E*-isomer **12a** could be detected in chromatographically concentrated tail fractions. In contrast, the reaction of the maleimide **5b** gave an inseparable 7:3 mixture of **11b**:**12b** in only 21% yield with recovery of **5b** (55%). Stereochemical assignments are based on ^{1}H NMR chemical shift data and on the results of NOE signal enhancements from double irradiation experiments. Thus, in **12a** the olefinic proton resonates at δ_H 6.02 whereas in **11a** the shift is 5.81 ppm (*i.e.* deshielding by *cis*-*N* of *ca.* 0.2 ppm). The two vinyl methyl signals in **12a** are split by 0.37 ppm, whereas the difference is only 0.09 ppm in **11a**; *i.e.* a *ca.* 0.4 ppm deshielding effect caused by a *cis*-ester carbonyl group. Irradiation of the vinyl methyl groups in **11a** in a NOE double-irradiation experiment caused a 2% enhancement of the olefinic-H signal (see Table 1 in Experimental section), thereby confirming the *Z*-stereochemistry. Likewise, in the **11b**/**12b** mixture the olefinic-H signals at δ_H 5.62 and 5.48 may be assigned, respectively, to **12b** and **11b**. The *N*-Me signals at δ_H 3.40 and 3.13 are assigned to **11b** and **12b**, whereas the C-4 vinyl methyl group in **12b** suffers deshielding relative to that in **11b** by 0.35 ppm.

The unsymmetrical maleimides **5c** and **5d** were appreciably more reactive towards CMTP than were **5a** and **5b**. Both afforded mixtures of olefination products. The major product from 3-methylmaleimide **5c** was the *Z*-ylidenepyrrolone **13a** (30%) while the minor products were the *Z*- and *E*-regioisomers, respectively **15a** (13%) and **16a** (9%). Compound **14a** was not detected among the reaction products. Attack of a phosphorane on the corresponding citraconic anhydride is known to occur predominantly at the less hindered C=O group [C(2):C(5) attack is 1:5][10b] in a relatively fast, presumably kinetically-controlled process. The reaction with the maleimide



10 11 12

a R = H; **b** R = Me

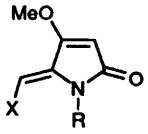
13 14 15 16

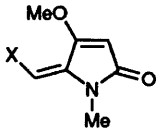
a R = H, R^1 = Et; **b** R = Me, R^1 = Et; **c** R = R^1 = Me

5c requires a six-fold excess of phosphorane and boiling toluene for 21 h to force completion, and it seems likely that these forcing conditions would favour the thermodynamic product (*i.e.* **13a**). The absence of the *E*-isomer **14a** indicates that stereochemistry may be determined by steric factors, and this conclusion is supported by the product distribution in the analogous reaction of 1,3-dimethylmaleimide **5d**. That reaction was somewhat slower, but all four isomeric ylidenepyrrolones were formed: **13b** + **14b** in 4% yield as a 1:1 inseparable mixture, **15b** (2%) and **16b** (29%). In the major product **16b** the ester function is relatively unencumbered being *cis* to a vinylic-H atom. In all of the other products **13b**, **14b** and **15b** the ester moiety is adjacent to a methyl substituent which presumably disrupts planarity, and therefore conjugation. The *Z*-stereochemistry in **13a** and **15a** could also be stabilised by the H-bonding interaction N–H · · · O=C–OEt; however, this may not be a dominant interaction in view of the fact that **16a** is also a significant product. Assignments are again based on ^{1}H NMR shifts and on the results of NOE experiments (see Table 1).

We anticipated that the electronic effect of the 3-methoxy substituent would be particularly marked in the maleimides **5e** and **5f**, and C-2 should be much more susceptible to nucleophilic attack than C-5. Maleimide **5e** reacted with CMTP under relatively mild conditions (1 equiv., benzene, reflux, 26 h), and afforded only the ylidenepyrrolone **17a** (94%). The maleimide **5f** required more forcing conditions (8 equiv., toluene, reflux, 24 h) and gave only the *Z*-alkylidenepyrrolone **17b** (55%). A small quantity of the less hindered regio- and stereo-isomer **20a** (2%) was formed when only 2 equiv. of the phosphorane was employed. This possibly indicates that **20a** is the kinetic product.

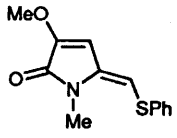
The analogous Wittig addition of CMTP to 3-methoxy-4-methylmaleimide **5g** occurred under relatively mild conditions (2 equiv., toluene, reflux, 24 h). The only ylidenepyrrolone isolated and identified by NOE (Table 1) was the *E*-isomer **22a** (36%), a result that was contrary to expectation based on steric effects and the possibility of H-bonding (*i.e.* **21a** was the predicted major product). On the other hand, the related addition to 1,4-dimethyl-3-methoxymaleimide **5h** required forcing conditions for completion (10 equiv., toluene, reflux, 336 h) and gave **21b** (60%) and **22b** (16%). When the same reaction was repeated, but allowed to run for 552 h, **21b** was again obtained whereas only a trace of **22b** could be detected. It would, therefore, appear that the alkoxycarbonylmethylene



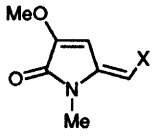


17 **a** R = H X = CO_2Et
b R = Me X = CO_2Et
c R = Me X = CO_2Me
d R = Me X = SPh
e R = Me X = Ph
f R = Me X = C_6H_4OMe-*p*

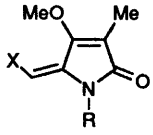
18 **a** X = CO_2Me
b X = SPh
c X = Ph
d X = C_6H_4OMe-*p*
e X = H



19



20a X = CO_2Et
b X = SPh



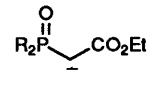
21 **a** R = H X = CO_2Et
b R = Me X = CO_2Et
c R = Me X = CO_2Me
d R = Me X = CO_2Bu^t
e R = Me X = SPh

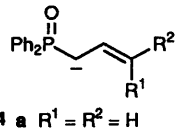
22 **a** R = H X = CO_2 Et
b R = Me X = CO_2Et
c R = Me X = CO_2 Me
d R = Me X = SPh

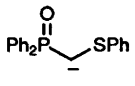
group can be stereomutated, and that **21b** is the thermodynamically more stable isomer of the two.

A few other phosphoranes were examined as substrates for these reactions. The stabilised phosphorane Ph_3P=CH(CO)SEt reacted (3 equiv., toluene, reflux, 243 h) with the maleimide **5a** very sluggishly. Only the thio analogue of **11a** [CO_2Et=C(O)-SEt] was obtained (21%). The maleimide **5e** failed to react with this phosphorane. *N*-Benzyl-3-methylmaleimide **5j** failed to react with 5 equiv. of CMTP in boiling toluene during 100 h, presumably because of steric hindrance. The reactions of semi-stabilised phosphoranylides (*e.g.* Ph_3P=CHCH=CR^1R^2; R^1 = R^2 = H, R^1 = R^2 = Me, or R^1 = H, R^2 = $CHMe_2$) with the maleimide **5d** afforded only intractable gums.

(2) *Anions from Phosphonates and Phosphine Oxides.*—Reactions of the phosphonate anion **23a** or the phosphine oxide anion **23b** with *N*-substituted maleimides afforded highly coloured solutions which, on aqueous work-up, gave only the starting phosphorus species. No starting maleimides or olefination products were ever observed or isolated. Presumably **23a**, **b** are sufficiently basic to deprotonate the maleimide to give a species which is unstable at 0 °C and decomposes. Reaction of 1,3-dimethylmaleimide **5d** with the phosphine oxide anions **24a** or **24b** gave only intractable tars; the maleimide **5h**, however, failed to react with these reagents and 50–75% of the starting materials were recovered. However, stabilisation of the anion by sulfur, as in **25**, proved to be beneficial. Thus, reaction of **25** with the maleimide **5f** at −78 °C gave principally the *Z*-ylidenepyrrolone **17d** (7–9%), a trace of recovered **5f** (2%) and large amounts of starting phosphine oxide (71%).







23 **a** R = OEt
b R = Ph

24 **a** R^1 = R^2 = H
b R^1 = Me,
R^2 = CH_2CH_2CH=CMe_2

25

(3) *α-Sulfone Anions (the Julia Reaction).*—In order to circumvent the problems encountered with unstabilised phosphoranes and the reagents in (2), above, the reactions of the less basic α-sulfone anions were investigated briefly. The addition of 1,3-dimethylmaleimide **5d** or 1,4-dimethyl-3-methoxymaleimide **5h** to a solution of the anion **26a** afforded only starting material on work-up. Similar results were obtained with the anions **26b** or **26c** and **5h**. Although starting material recovery was only moderate, no evidence for addition products was obtained.

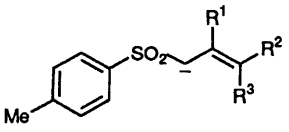
(4) *Peterson Reagents.*—The reactions of the Peterson reagent **27a**, generated from methyl trimethylsilylacetate and lithium diisopropylamide, with *N*-methylmaleimides were more encouraging. Thus, reaction of a slight excess of **27a** with the maleimide **5d** in THF at −78 °C (2 h) afforded, after a hydrolytic work-up and chromatographic purification, an 11:9 mixture (18%) of the *Z*- and *E*-ylidenepyrrolones **13c** and **14c** plus a 1:2 mixture (17%) of the *Z*- and *E*-isomers **15c** and **16c**. In the Wittig reaction the *E*-isomer **16b** was the predominant product, whereas in the Peterson olefination (admittedly using a methyl rather than an ethyl ester), the product distribution was much more even over the four isomers. The Peterson reaction is considerably faster (*i.e.* 2 h at −78 °C *versus* 36 h at 110 °C) and is considered to be under kinetic control; the predominance of **16b** in the Wittig reaction is a reflection of its greater thermodynamic stability among the isomers **13b**–**16b**.

In contrast, reaction of 3-methoxy-1-methylmaleimide **5f** with **27a** at −78 °C (3 h) afforded a 4:1 mixture (40%) of the *Z*- and *E*-alkylidenepyrrolones **17c** and **18a**. The similar reaction of the maleimide **5h** also afforded a 4:1 mixture of *Z*- and *E*-alkylidenepyrrolones **21c** and **22c**; recrystallisation removed the minor isomer to give pure **21c** (51%). On the other hand, reaction of **5h** with the bulky Peterson reagent **27b** at −78 °C (1.5 h) afforded only the *Z*-pyrrolone **21d** (51%). Hence, in the case of alkoxy-substituted maleimides, the Peterson reaction gives good regiochemical and stereochemical control.

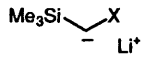
The reaction of 3-methoxy-1-methylmaleimide with the anion derived from phenylthiomethyltrimethylsilane **27c**, however, appears to occur preferentially at the less electrophilic C=O group C-5. Thus, reaction of **27c** with **5f** at −78 °C (2 h) afforded three isomers—**19** (27%), **18b** as a 1:1 mixture (8%) with **19**, and **20b** (25%), plus recovery of phenylthiomethyltrimethylsilane (31%). Structural assignments, which again rely on the results of NOE experiments (Table 1), are somewhat less clear-cut with these particular compounds.

By way of contrast, reaction of the maleimide **5h** with the anion **27c** afforded a 1:1 mixture of the stereoisomers **21e** and **22d** in low yield. The regaining of regioselectivity for attack at the C=O nearest the OMe group, indicates that in the reaction of **5f** with **27c** steric influences override electronic factors. Under similar conditions, the maleimide **5d** reacted with **27c** only to give gummy products. The 3-phenylthiomaleimide **5i** reacted sluggishly with **27c**; after 6 h at −78 °C, 82% of the maleimide was recovered and the olefination products (2.5%) consisted of a mixture of three isomers.

(5) *Aliphatic Grignard Reagents.*—Awad *et al.*,[12] have studied the action of aromatic Grignard reagents on *N*-arylmaleimides. The product formed (*i.e.* β-aroyl-*N*-arylacrylamide[12a] or 1,5-diaryl-5-hydroxypyrrolone)[12b] depended upon the substrate and conditions for the Grignard addition. Clearly, if an aliphatic Grignard reagent were to be employed for the addition, then the hydroxypyrrolone could, in principle, be dehydrated to provide a complementary route to alkylidene pyrrolones. We limited our studies to the reactions of the commercially available butylmagnesium chloride (2 mol dm^{-3} in diethyl ether).

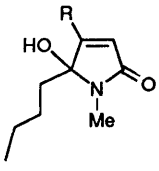


26 **a** $R^1 = R^2 = R^3 = H$
b $R^1 = H$ $R^2 = R^3 = Me$
c $R^1 = R^2 = Me$ $R^3 = H$

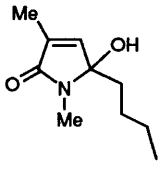


27 **a** $X = CO_2Me$
b $X = CO_2Bu^t$
c X = SPh

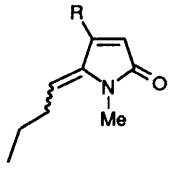
Treatment of 1,3-dimethylmaleimide **5d** with a small excess of butylmagnesium chloride at 0 °C afforded, after hydrolysis and chromatographic purification, the two hydroxypyrrolones **28a** (23%) and **29** (28%). Consistent with these structural assignments were the observation of spectroscopic absorptions characteristic of the OH group: ν_{max} 3560 and 3570 cm^{-1} and δ_H (broad singlets, removed by exchange with D_2O) at 4.75 and 5.20 ppm, respectively. Dehydration of **28a** was achieved under either acidic (pTSA, benzene, reflux) or basic conditions (mesyl chloride, triethylamine) and gave 4:3 mixtures of the *E*- and *Z*-ylidenepyrrolones **30a**. Isomer identification was based solely on the olefinic H-shifts in the ^1H NMR spectrum. In contrast, elimination of water from **29**, by either method, proved to be more selective, affording only one isomer of 5-butylidene-1,3-dimethylpyrrolone **31** (62%). Steric considerations suggest the *E*-stereochemistry, but no definitive assignment could be made on the basis of the data obtained.



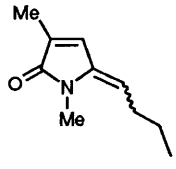
28 **a** R = Me
b R = OMe



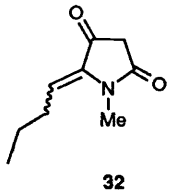
29



30 **a** R = Me
b R = OMe



31



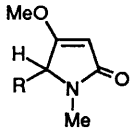
32

Reaction of 3-methoxy-1-methylmaleimide **5f** with 2 equiv. of butylmagnesium chloride (THF, −78 °C) afforded only the hydroxypyrrolone **28b** (98%). Dehydration under the above acidic conditions afforded a mixture of the butylidenepyrrolones **30b** (34%) and a yellow oil (*ca.* 20%). The olefinic H-shifts in the ^1H NMR spectrum of **30b** all occurred in the narrow range δ_H 5.05–5.39; hence, it was not possible to determine the isomer ratio and to assign stereochemistry in this case. The yellow oil was possibly impure **32** since the conversion of enol ethers of the type **30b** into pyrrolidine-2,4-diones under acidic conditions is known.[13]

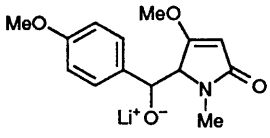
As before, the nucleophilic attack on an alkoxy-substituted maleimide was more selective than with an alkyl-substituted maleimide. The Grignard reaction appears to have potential for the introduction of a variety of side-chains in the preparation of pyrrolones.

Synthesis of 5-Ylidenepyrrolones from the Anions of 5-Unsubstituted Pyrrolones.—The synthesis of 5-ylidenepyrrolones could, in principle, be achieved by a complementary general strategy to those discussed above. Thus, removal of a proton from C-5 of a pyrrol-2-one by a suitable base would afford a nucleophile that could be trapped with a carbon electrophile. Depending upon the electrophilic species employed, the 5-ylidenepyrrolone should then be accessible through the dehydration or dehydrogenation of the intermediate adducts. In our studies the pyrrolone **33a** was chosen as a suitable model system.[13,14]

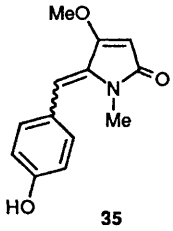
Deprotonation of **33a** under thermodynamic control (1.1 equiv. LDA, THF, −78 °C, 30 min), followed by quenching of the anion with deuteriomethanol (MeOD) afforded the deuterio derivative **33b**. However, the ^1H NMR spectrum indicated contamination (*ca.* 35%) with the 3-deuterio isomer. Deprotonation of **33a** under kinetic conditions (1.4 equiv. BuLi, THF, −78 °C, 45 min), followed by quenching as before, led only to **33b** (> 70%). Confirmation that C-5 deprotonation could be carried out selectively was obtained by performing the kinetic deprotonation and then quenching with an excess of methyl iodide. The pyrrolone **33c** was obtained exclusively in 77–98% yield.



33 **a** R = H
b R = D
c R = Me
d $R = CH_2CO_2Me$
e $R = CH_2C_6H_4OMe$-*p*
f $R = CH_2C_6H_4OH$-*p*



34

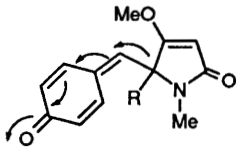


35

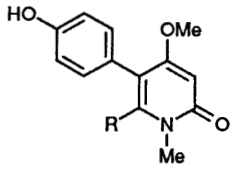
Encouraged by these results, the kinetic anion from **33a** was allowed to react with methyl bromoacetate. The ester **33d** (74%) and a small amount of starting pyrrolone **33a** (8%) were isolated. Dehydrogenation of **33d** with chloranil in boiling benzene afforded an 8:1 mixture of the *Z*- and *E*-ylidenepyrrolones **17c**:**18a**. Chromatographic purification resulted in a partial separation into **17c** (29%) and a 4:1 mixture of **17c**:**18a** (54%).

Reaction of the pyrrolone **33a** with aqueous formaldehyde in methanolic sodium hydroxide resulted in condensation and dehydration to give 4-methoxy-1-methyl-5-methylenepyrrolone **18e** (*ca.* 20%); a similar condensation had been observed with the maleimide **5a**.[15] The related reaction of **33a** with benzaldehyde gave a mixture of the *Z*- and *E*-5-benzylidenepyrrolones **17e** and **18c** in variable (50–80%) yield. It seemed likely that partial hydrolytic ring cleavage occurred under the conditions of the reaction. Pure samples of **17e** (25%) and **18c** (8%) were obtained by chromatography. The condensation of tetramic acids with aromatic aldehydes under acidic alcoholic conditions has been reported previously.[16]

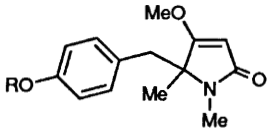
Generation of the anion from **33a** under aprotic conditions, followed by the addition of aryl aldehyde, affords the intermediate adduct rather than the ylidenepyrrolone. The dehydration must then be accomplished in a separate step. Thus, treatment of **33a** first with butyllithium and then with *p*-anisaldehyde gave the salt **34**. Treatment of the salt, without isolation, first with trifluoroacetic anhydride (TFAA) and then with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) effected transformation into a mixture of the ylidenepyrrolones **17f** and **18d**. The isomers were separated by chromatography, and stereochemistry established by ^1H NMR double-resonance experiments (Table 1). A similar sequence of reactions involving **33a** and 4-trimethylsilyloxybenzaldehyde (*i.e.* first BuLi and then TFAA–DBU) gave, after aqueous work-up, the hydroxybenzylidene derivative **35** (8%). The *E*- and *Z*-isomers, although



36a R = H
b R = Me



37a R = H
b R = Me



38a R = Me
b R = H

separable by HPLC, were only obtained as a mixture since isomerization proceeded with some ease.

The benzylidene derivative **35** was also prepared by an alkylation/dehydrogenation route. Thus, treatment of **33a** with BuLi and then 4-methoxybenzyl bromide at −78 °C gave the benzyl derivative **33e** (45%). On reaction with boron tribromide (CH_2Cl_2 solution, 20 °C, 24 h), **33e** underwent regiospecific demethylation to give the phenol **33f** (50%) which, on dehydrogenation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in boiling dioxane (22 h), was converted into the benzylidene derivative **35** (86%). The dehydrogenation could occur in the 1,2-sense (to give **35** directly) or the 1,6-sense to give the quinone methide **36a**. The conversion **36a** → **35** would be expected to occur rapidly through a protonation–deprotonation mechanism, the C-5 hydrogen of the pyrrolone being relatively acidic. We were interested in the generation of quinone methides such as **36a** because of the possibility of using these intermediates to promote the ring expansion of pyrrolones (*e.g.* **36a** arrows) to give pyridones (*e.g.* **37**). However, no evidence for pyridone formation was obtained in the dehydrogenation of **33f**. Hence, in order to block the 1,2-dehydrogenation pathway, **33e** was treated with BuLi at −78 °C, and the anion quenched with an excess of methyl iodide to give a 2:1 mixture (40%) of **38a**:**33e**. Treatment of this mixture with boron tribromide in CH_2Cl_2, as above, and chromatographic purification of the product afforded the phenol **38b** in moderate yield. However, dehydrogenation of **38b** with DDQ afforded much tarry material plus a small quantity (18%) of recovered **38b**. If the quinone methide **36b** was formed, we were unable to detect any products, *e.g.* a pyridone, arising from a 1,2-migration mechanism.

Experimental

General Procedures.—The majority of the organic solvents employed were distilled before use. Tetrahydrofuran (THF) was distilled freshly from sodium under nitrogen. Light petroleum refers to the fraction b.p. 40–60 °C. Organic solutions were dried over anhydrous magnesium sulfate, unless stated otherwise. Ether refers to diethyl ether.

Chromatographic purification was achieved over silica gel [Fluka Kieselgel G or Merck Kieselgel 60 (9385)], and Camlab plastic-backed UV254 silica gel plates were used for TLC analyses. A Reichert Kofler micro hot stage was used for m.p. determinations, and are uncorrected. IR spectra were recorded in a Perkin-Elmer 710B, Pye-Unicam SP3 100 or a Philips PU9706 spectrometer, and were calibrated using a standard polystyrene film. UV spectra were obtained using a Unicam SP700 or SP800 or a Philips PU 8720 spectrophotometer and ε values are expressed in $dm^3\ mol^{-1}\ cm^{-1}$. Unless stated otherwise, solutions in deuteriochloroform were used for the determination of NMR spectra. Shifts are expressed in ppm downfield from Me_4Si as internal standard and J values are expressed in Hz. The ^1H and ^{13}C spectra were recorded on a 90 MHz Perkin-Elmer R32, 90 MHz JEOL FX90Q, 80 MHz Bruker WP80SY, 250 MHz Bruker WM250 or a 400 MHz Bruker AM400 instrument. Signals were singlets unless specified otherwise: *i.e.* d = doublet, dd = double doublet, ddd = double doublet of doublets; dt = double triplet, q = quartet, m = multiplet, br = broad. Assignments in the ^1H spectra were consistent with signal intensities and in the ^{13}C spectra with the results of the DEPT pulse sequence. Mass spectra were by electron impact and were recorded with an AEI MS-902 or VG Micromass 7070E spectrometer. Microanalytical data were obtained on a Perkin-Elmer 240B elemental analyser.

General Procedure for the Preparation of 1H-*Pyrrole*-2,5-*diones* **5a–i**.[8]—A solution of the maleic anhydride and 1.25 equiv. of *either* ammonium acetate **9** (R^3 = H) or methylammonium acetate **9** (R^3 = Me) in glacial acetic acid (*ca.* 1 g substrate/10 cm^3) was heated under reflux for 2 h. The cooled solution was evaporated to dryness, and the residue was then diluted with water and extracted with ethyl acetate. The combined extracts were washed with 2 mol dm^{-3} aqueous sodium hydroxide, dried, filtered and the solvent removed under reduced pressure. The residue thus obtained was then purified by chromatography, distillation or recrystallisation.

3,4-*Dimethyl*-1H-*pyrrole*-2,5-*dione* **5a**.—The pyrroledione was prepared according to the general procedure and the residue was distilled under reduced pressure (b.p. 122–126 °C/10 Torr) to give a white solid. Recrystallisation from hexane–benzene gave the *maleimide* **5a** (53%) as colourless prisms, m.p. 111–113 °C; ν_{max}(KBr)/cm^{-1} 3250, 1770, 1710 and 1670; δ_H 10.55 (NH) and 1.88 (2 × Me); δ_C 172.9 (CO), 138.3 (=C–) and 8.6 (=C*Me*) (Found: *m/z* 125.0476. $C_6H_7NO_2$ requires 125.0477).

1,3,4-*Trimethyl*-1H-*pyrrole*-2,5-*dione* **5b**.—The pyrroledione was prepared according to the general procedure and the residue was distilled under reduced pressure to give the *maleimide* **5b** (78%) as a colourless oil, b.p. 55–65 °C/0.08 Torr; ν_{max}(film)/cm^{-1} 1770 and 1710; δ_H 3.03 (NMe) and 1.99 (2 × Me); δ_C 172.2 (CO), 137.3 (=C–), 23.7 (NMe) and 8.6 (=C*Me*) (Found: C, 60.3; H, 6.8; N, 10.0. $C_7H_9NO_2$ requires C, 60.4; H, 6.5; N, 10.1%).

3-*Methyl*-1H-*pyrrole*-2,5-*dione* **5c**.—The pyrroledione was prepared according to the general procedure and the residue was distilled under reduced pressure and the white solid obtained was then recrystallised from benzene to give citraconimide **5c** (20%), m.p. 103–104 °C (lit.,[17] 103.5–105.5 °C); ν_{max}($CHCl_3$)/cm^{-1} 3270, 1760, 1710 and 1635; δ_H([$^2H_6$]-DMSO) 9.6–9.2 (NH), 6.60 (q, *J* 2, =CH), 2.06 (d, *J* 2, =CHCH_3); δ_C([$^2H_6$]DMSO) 173.3 (CO) 172.4 (CO), 146.2 (=C*Me*), 128.2 (=CH) and 10.3 (=C*Me*) (Found: C, 54.1; H, 4.7; N, 12.6%; M, 111.0327. $C_5H_5NO_2$ requires C, 54.1; H, 4.5; N, 12.6%; *M*, 111.0320).

1,3-*Dimethyl*-1H-*pyrrole*-2,5-*dione* **5d**.—The pyrroledione was prepared according to the general procedure and the residue was distilled under reduced pressure to give the maleimide **5d** (83%) as a colourless oil, b.p. 82–84 °C/10 Torr (lit.,[18] 84–84.5 °C/10 Torr); ν_{max}(film)/cm^{-1} 3100, 1775, 1710 and 1640; δ_H 6.49 (q, *J* 1.8, =CH), 3.08 (NMe), 2.15 (d, *J* 1.8, =CMe); δ_C 171.9 (CO) 170.9 (CO), 145.8 (=C*Me*), 127.4

(=CH), 23.6 (NCH_3) and 10.8 (=C*Me*) (Found: C, 57.6; H, 5.9; N, 11.2%. $C_6H_7NO_2$ requires C, 57.6; H, 5.6; N, 11.2%).

3-*Methoxy*-1H-*pyrrole*-2,5-*dione* **5e**.—The pyrroledione was prepared according to the general procedure and the residue was purified by chromatography (light petroleum–ether, 1:1) to give a yellow solid. Recrystallisation from diisopropyl ether gave fine buff crystals of the maleimide **5e** (30%), m.p. 168.5–169 °C (lit.,[19] 169 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 3230, 1715 and 1640; δ_H 9.6–9.2 (NH), 5.69 (=CH) and 4.02 (OMe); $\delta_C([^2H_6]DMSO)$ 171.3 (CO), 166.7 (CO), 161.0 (=*C*OMe), 97.7 (=CH) and 57.1 (OMe) (Found: *m/z* 127.0273. $C_5H_5NO_3$ requires 127.0269).

3-*Methoxy*-1-*methyl*-1H-*pyrrole*-2,5-*dione* **5f**.—The pyrroledione was prepared according to the general procedure and the residue was purified by chromatography (light petroleum–ether, 1:1) to give a yellow solid. Recrystallisation of this from hexane–benzene afforded soft yellow plates of the *maleimide* **5f** (65%), m.p. 129–130 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3110, 1710 and 1640; δ_H 5.48 (=CH), 3.98 (OMe) and 3.02 (NMe); δ_C 170.2 (CO), 165.7 (CO), 161.2 (=*C*OMe), 96.4 (=CH), 59.0 (OMe) and 23.4 (NMe) (Found: C, 51.3; H, 5.1; N, 9.9%; M, 141. $C_6H_7NO_3$ requires C, 51.1; H, 5.0; N, 9.9%; *M*, 141).

3-*Methoxy*-4-*methyl*-1H-*pyrrole*-2,5-*dione* **5g**.—The pyrroledione was prepared according to the general procedure and the residue was a light brown solid. Recrystallisation from hexane–benzene gave the *maleimide* **5g** (63%) as colourless prisms, m.p. 138–139 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3240, 1715 and 1645; δ_H 8.0–7.5 (br, NH), 4.15 (OMe) and 1.95 (=CMe) (Found: *m/z* 141.0439. $C_6H_7NO_3$ requires 141.0426).

3-*Methoxy*-1,4-*dimethyl*-1H-*pyrrole*-2,5-*dione* **5h**.—The pyrroledione was prepared according to the general procedure and the residue was purified by chromatography (hexane–ether, 3:2). Recrystallisation from benzene–light petroleum (60–80 °C) gave pink monoclinic crystals of the *maleimide* **5h** (62%), m.p. 67–68 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 and 1670; λ_{max}(EtOH)/nm 233; δ_H 4.03 (OMe), 2.85 (NMe), 1.93 (CMe); δ_C 171.9 (CO), 166.7 (CO), 152.7 (=*C*OMe), 109.8 (=*C*Me), 59.2 (OMe), 23.4 (NMe), 6.8 (=C*Me*) (Found: C, 54.3; H, 5.8; N, 9.1. $C_7H_9NO_3$ requires C, 54.2; H, 5.85; N, 9.0%).

1-*Methyl*-3-*phenylthio*-1H-*pyrrole*-2,5-*dione* **5i**.—The pyrroledione was prepared according to the general procedure and the residue was purified by distillation to give the *maleimide* **5i** (61%) as sticky yellow oil, b.p. 165 °C/0.4 Torr; $\nu_{max}(CHCl_3)/cm^{-1}$ 3100, 1765, 1700 and 1560; δ_H 7.7–7.4 (m, 5 × ArH), 5.70 (=CH) and 4.03 (NMe); δ_C 169.9 (CO), 167.9 (CO), 152.5 (quat. C), 134.3 (=CH), 130.4 (=CH), 129.4 (=CH), 129.0 (=CH), 127.5 (quat. C), 119.0 (=CH) and 23.9 (NMe) (Found: C, 60.3; H, 4.2; N, 6.5%; M, 219.0356. $C_{11}H_9NO_2S$ requires C, 60.3; H, 4.1; N, 6.4%; *M*, 219.0354).

Preparation of 1-*Benzyl*-3-*methyl*-1H-*pyrrole*-2,5-*dione* **5j**.—A mixture of citraconimide **5c** (1.11 g, 10 mmol) and freshly prepared silver(I) oxide (1.16 g, 5 mmol) in dry acetonitrile (30 cm^3) was stirred at room temperature in the dark for 22 h. The grey–brown solid was filtered off and then washed with cold acetonitrile (3 × 10 cm^3) and dried to leave a grey solid (1.22 g, 59%); this silver salt was used without further purification. A solution of the citraconimide silver salt (1.22 g, 5.6 mmol) and benzyl chloride (1.43 g, 11.3 mmol) in dry toluene (20 cm^3) was heated under reflux for 20 h. The orange solution was evaporated under reduced pressure to leave a residue which was purified by chromatography (light petroleum–ether, 4:1) to give the *maleimide* **5j** (285 mg, 24%) as a pale yellow oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 1770, 1710 and 1640; δ_H 7.39 (m, 5 × ArH), 6.31 (q, *J* 2, =CH), 4.75 (CH_2Ph) and 2.02 (d, *J* 2, =CMe) (Found: *m/z* 201.0782. $C_{12}H_{11}NO_2$ requires 201.0790).

Reactions with Phosphoranes

(Z)-5-*Ethoxycarbonylmethylene*-3,4-*dimethylpyrrol*-2(5H)-*one* **11a**.—A solution of 3,4-dimethylmaleimide **5a** (371 mg, 2.96 mmol) and ethoxycarbonylmethylene(triphenyl)phosphorane (5.16 g, 14.81 mmol, 5 equiv.) in toluene (40 cm^3) was heated under reflux for 112 h. The solution was evaporated to dryness under reduced pressure and the residue was then purified by chromatography (hexane–ether, 4:1) to give: (i) the *title compound* **11a** (414 mg, 71%) which recrystallised from hexane as pale cream crystals, m.p. 79–80 °C; λ_{max}(EtOH)/nm 275; $\nu_{max}(CHCl_3)/cm^{-1}$ 1790, 1715 and 1660; δ_H 8.95 (NH), 5.81 (=CH), 4.20 (q, *J* 7, $CO_2CH_2CH_3$), 2.00 and 1.91 (2 × Me) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 61.9; H, 6.8; N, 7.2. $C_{10}H_{13}NO_3$ requires C, 61.5; H, 6.7; N, 7.2%) and: (ii) a 2:1 mixture of the Z- and E-*pyrrol*-2(5H)-*ones* **11a** and **12a** (29 mg, 5%) as a yellow solid; λ_{max}(EtOH)/nm 275; $\nu_{max}(CHCl_3)/cm^{-1}$ 1780, 1720 and 1680; *E*-isomer δ_H 6.02 (=CH), 4.26 (q, *J* 7, $CO_2CH_2CH_3$), 2.39 and 2.02 (2 × Me) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 61.7; H, 6.7; N, 7.4. $C_{10}H_{13}NO_3$ requires C, 61.5; H, 6.7; N, 7.2%).

(Z)-5-(*Ethylthio*)*carbonylmethylene*-1H-3,4-*dimethylpyrrol*-2(5H)-*one* **11a** (CO_2Et = COSEt).—A solution of 3,4-dimethylmaleimide **5a** (150 mg, 1.2 mmol) and (ethylthio)carbonylmethylene(triphenyl)phosphorane (1.32 g, 3.62 mmol, 3 equiv.) in toluene (30 cm^3) was heated under reflux for 10 days. The solution was evaporated to dryness under reduced pressure, and the residue purified by chromatography (hexane–ether, 4:1) to give the *Z-ylidenepyrrol*-2(5H)-*one* **11a** (52 mg, 21%) which recrystallised from benzene–hexane as pale green monoclinic crystals, m.p. 92–93 °C; λ_{max}(EtOH)/nm 313; $\nu_{max}(CHCl_3)/cm^{-1}$ 3400, 1715, 1650 and 1610; δ_H 9.2 (NH), 5.63 (=CH), 2.99 (q, *J* 6, $COSCH_2CH_3$), 2.00 and 1.92 (2 × Me) and 1.30 (t, *J* 6, $COSCH_2CH_3$) (Found: C, 56.9; H, 6.3; N, 6.7%; M, 211.0657. $C_{10}H_{13}NO_2S$ requires C, 56.9; H, 6.2; N, 6.6%; *M*, 211.0647).

5-*Ethoxycarbonylmethylene*-1,3,4-*trimethylpyrrol*-2(5H)-*ones* **11b** *and* **12b**.—A solution of 1,3,4-trimethylmaleimide **5b** (230 mg, 1.65 mmol) and ethoxycarbonylmethylene(triphenyl)phosphorane (4.57 g, 13.12 mmol, 8 equiv.) in toluene (40 cm^3) was heated under reflux for 233 h. The cooled solution was evaporated to dryness under reduced pressure and the residue was then purified by chromatography (hexane–ether, 3:2) to give: (i) starting material (126 mg, 55% recovery) and (ii) a 7:3 mixture of Z- and E-*pyrrol*-2(5H)-*ones* **11b** and **12b** (73 mg, 21%), as a yellow oil; λ_{max}(EtOH)/nm 281; $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 and 1625; δ_H 5.62 and 5.48 (=CH), 4.29 (q, *J* 7, $CO_2CH_2CH_3$), 3.13 and 3.40 (NMe), 2.30 and 2.04 (=CMe), 1.95 (2 × =CMe) and 1.33 (t, *J* 7, $CO_2CH_2CH_3$) (Found: *m/z* 209.1046. $C_{11}H_{15}NO_3$ requires 209.1052).

(Z)-5-*Ethoxycarbonylmethylene*-1H-4-*methylpyrrol*-2(5H)-*one* **13a** *and* (Z)-*and* (E)-5-*Ethoxycarbonylmethylene*-3-*methyl*-1H-*pyrrol*-2(5H)-*ones* **15a** *and* **16a**.—A solution of citraconimide **5c** (246 mg, 2.21 mmol) and ethoxycarbonylmethylene(triphenyl)phosphorane (4.95 g, 14.21 mmol, 6.4 equiv.) in toluene (50 cm^3) was heated under reflux for 21 h. The cooled solution was evaporated to dryness under reduced pressure and the residue was then purified by chromatography (hexane–ether, 1:1) to give: (i) the (Z)-*pyrrol*-2(5H)-*one* **15a** (55 mg, 13%) which recrystallised from hexane as pale yellow needles, m.p. 76–76.5 °C; λ_{max}(EtOH)/nm 305inf (ε 12 300) and 283 (16 700); $\nu_{max}(CHCl_3)/cm^{-1}$ 3400, 1720, 1700 and 1655; δ_H

9.22 (NH), 6.77 (=CH), 5.37 (=C*H*CO_2Et), 4.30 (q, *J* 7, $CO_2CH_2CH_3$), 2.04 (d, *J* 1.5, =CMe) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 59.7; H, 6.2; N, 7.9. $C_9H_{13}NO_3$ requires C, 59.7; H, 6.1; N, 7.7%), and (ii) a 3:1 mixture of Z- and E-*pyrrol*-2(5H)-*ones* **13a** and **16a** (178 mg, 39%) which recrystallised from hexane–toluene as yellow plates, m.p. 157–161.5 °C; λ_{max}(EtOH)/nm 315infl. and 278; ν_{max}($CHCl_3$)/cm^{-1} 3400, 1720, 1700 and 1650; δ_H 9.12 and 8.55 (NH), 6.12 and 7.83 (=CH), 5.47 and 5.65 (=C*H*CO_2Et), 4.31 (q, *J* 7, $CO_2CH_2CH_3$), 2.14 and 2.06 (d, *J* 1.5, =CMe) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 59.5; H, 6.2; N, 7.8%. $C_9H_{11}NO_3$ requires C, 59.7; H, 6.1; N, 7.7%).

When the reaction was repeated with 6 equiv. of the phosphorane in boiling chloroform for 5 days, the isomer ratios were altered to the following: (i) starting material **5c** (12%) and **15a** (13%) and (ii) **13a** (41%) and **16a** (11%).

(Z)- *and* (E)-5-*Ethoxycarbonylmethylene*-1,4-*dimethylpyrrol*-2(5H)-*ones* **13b** *and* **14b** *and* (Z)- *and* (E)-5-*Ethoxycarbonylmethylene*-1,3-*dimethylpyrrol*-2(5H)-*ones* **15b** *and* **16b**.—A solution of 1,3-dimethylmaleimide **5d** (240 mg, 1.92 mmol) and ethoxycarbonylmethylene(triphenyl)phosphorane (3.3 g, 9.47 mmol, 5 equiv.) in toluene (40 cm^3) was heated under reflux for 36 h. The solution was concentrated and the residue was then purified by chromatography (hexane–ether, 4:1) to give: (i) (Z)-5-*ethoxycarbonylmethylene*-1,3-*dimethylpyrrol*-2(5H)-*one* **15b** (8 mg, 2%) as a yellow oil; λ_{max}(EtOH)/nm 282; ν_{max}($CHCl_3$)/cm^{-1} 1710 and 1635; δ_H 6.61 (=CH), 5.34 (=C*H*CO_2Et), 4.32 (q, *J* 7, $CO_2CH_2CH_3$), 3.44 (NMe), 2.00 (=CMe) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$); δ_C 172.7 (CO), 164.8 (CO_2), 148.0 (quat. C), 135.5 (quat. C), 134.8 (=CH), 100.0 (=CH), 60.6 (OCH_2), 30.0 (NMe), 14.3 (Me) and 10.8 (Me) (Found: C, 61.6; H, 7.0; N, 7.0%; M, 195.0885. $C_{10}H_{13}NO_3$ requires C, 61.5; H, 6.7; N, 7.2%; *M*, 195.0895); (ii) (E)-5-*ethoxycarbonylmethylene*-1,3-*dimethylpyrrol*-2(5H)-*one* **16b** (108 mg, 29%) which was recrystallised from benzene to give light green needles, m.p. 93–94 °C; λ_{max}(EtOH)/nm 280 (ε 18 500) and 322 (5800); ν_{max}($CHCl_3$)/cm^{-1} 1710, 1670 and 1640; δ_H 7.82 (=CH), 5.51 (=C*H*CO_2Et), 4.34 (q, *J* 7, $CO_2CH_2CH_3$), 3.10 (NMe), 2.02 (=CMe) and 1.34 (t, *J* 7, $CO_2CH_2CH_3$); δ_C 170.7 (CO), 165.9 (CO_2), 151.6 (quat. C), 137.4 (quat. C), 129.2 (=CH), 97.4 (=CH), 60.4 (OCH_2), 25.7 (NMe), 14.3 (Me) and 11.1 (Me) (Found: C, 61.6; H, 6.8; N, 7.1%; M, 195.0898. $C_{10}H_{13}NO_3$ requires C, 61.5; H, 6.7; N, 7.2%; *M*, 195.0895), and (iii) a 3:2 mixture of Z- *and* E-*pyrrol*-2(5H)-*ones* **13b** and **14b** (16 mg, 4%) which was recrystallised from hexane to give an off-white solid, m.p. 67–73 °C; λ_{max}(EtOH)/nm 326infl. and 272; ν_{max}($CHCl_3$)/cm^{-1} 1710 and 1630; δ_H (*E*- and *Z*-, respectively) 6.15 and 6.09 (=CH), 5.60 and 5.50 (=C*H*CO_2Et), 4.33 (q, *J* 7, $CO_2CH_2CH_3$), 3.10 and 3.37 (NMe), 2.39 and 2.14 (=CMe) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 61.2; H, 6.7; N, 7.1%; M, 195.0889. $C_{10}H_{13}NO_3$ requires C, 61.5; H, 6.7; N, 7.2%; *M*, 195.0895).

Similar results were obtained using boiling chlorobenzene as solvent and 1 equiv. of the phosphorane (24 h).

(Z)-5-*Ethoxycarbonylmethylene*-1H-4-*methoxypyrrol*-2(5H)-*one* **17a**.—A solution of 3-methoxy-1*H*-pyrrole-2,5-dione **5e** (91 mg, 0.716 mmol) and ethoxycarbonylmethylene(triphenyl)-phosphorane (249 mg, 0.715 mmol, 1 equiv.) in dry benzene (20 cm^3) was heated under reflux for 26 h. The cooled solution was concentrated, and the residue was then purified by chromatography (light petroleum–ether, 1:1) to give the Z-*ylidenepyrrol*-2(5H)-*one* **17a** (133 mg, 94%) as a white solid, m.p. 120–125 °C; λ_{max}(EtOH)/nm 282 and 262; ν_{max}($CHCl_3$)/cm^{-1} 3300, 1715, 1660 and 1610; δ_H 8.7 (NH), 5.59 (=C*H*CO_2Et), 5.28 (=CH), 4.29 (q, *J* 7, $CO_2CH_2CH_3$), 3.95 (OMe) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 54.6; H, 5.7; N, 7.3%; M, 197.0694. $C_9H_{11}NO_4$ requires C, 54.8; H, 5.6; N, 7.1%; *M*, 197.0688).

Table 1 Results of double irradiation experiments on the 5-ylidenepyrrol-2(5*H*)-one products **11–22**

Compound	Irradiated H*	Observed H*	NOE enhancement (%)
11a	=CCH_3	=CH	2
13b	=CCH_3	=C*H*CO_2Et	14.7
	=CCH_3	=CH (ring)	6
	NCH_3	all other H	0
14b	=CCH_3	=CH (ring)	10.2
	=CCH_3	=C*H*CO_2Et	0
	NCH_3	=C*H*CO_2Et	13.8
15b	=C*H*CO_2Et	NCH_3	0
	NCH_3	all other H	0
16b	=C*H*CO_2Et	NCH_3	7.5
	NCH_3	=C*H*CO_2Et	14
17f	NCH_3	=C*H*Ar	0
	OCH_3	=C(3)H	12.8
	OCH_3	=C*H*Ar	0
18d	NCH_3	=C*H*Ar	16.8
	OCH_3	=C*H*Ar	0
	OCH_3	=C(3)H	14.7
19	OCH_3	=C(3)H	10.7
	NCH_3	all other H	0
20b	OCH_3	=C(4)H	12.2
	NCH_3	=C*H*SPh	14.5
	NCH_3	Aryl-H	−10.9
21b	OCH_3	=C*H*CO_2Et	1.9
	OCH_3	=CCH_3	2.4
	=CCH_3	OCH_3	2.5
22a	OCH_3	all other H	0
	=CCH_3	all other H	0

* See Experimental section for chemical shifts of the irradiated and observed H atoms.

(Z)-5-*Ethoxycarbonylmethylene*-4-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **17b**.—A solution of 3-methoxy-1-methylmaleimide **5f** (177 mg, 1.25 mmol) and ethoxycarbonylmethylene(triphenyl)phosphorane (3.5 g, 10.05 mmol, 8 equiv.) in toluene (40 cm^3) was heated under reflux for 24 h. The solution was evaporated to dryness under reduced pressure and the residue was purified by column chromatography (hexane–ether, 3:2) to give the Z-*ylidenepyrrol*-2(5H)-*one* **17b** (146 mg, 55%), which recrystallised from ether as colourless needles, m.p. 133–134 °C; λ_{max}(EtOH)/nm 280; ν_{max}($CHCl_3$)/cm^{-1} 1720, 1635 and 1620; δ_H 5.68 (=C*H*CO_2Et), 5.23 (=CH), 4.25 (q, *J* 7, $CO_2CH_2CH_3$), 3.91 (OMe), 3.37 (NMe) and 1.30 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 56.7; H, 6.2; N, 6.8%; M, 211.0881. $C_{10}H_{13}NO_4$ requires C, 56.9; H, 6.2; N, 6.6%; *M*, 211.0844).

When the reaction was repeated with 2 equiv. of the stabilised phosphorane in refluxing toluene for 48 h, the reaction products were altered to give: (i) (E)-5-*ethoxycarbonylmethylene*-3-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **20a** (2%) which recrystallised from hexane as pale yellow needles, m.p. 96–98 °C; λ_{max}(EtOH)/nm 293; ν_{max}($CHCl_3$)/cm^{-1} 1735, 1705 and 1635; δ_H 7.00 (=CH), 5.50 (=C*H*CO_2Et), 4.35 (q, *J* 7, $CO_2CH_2CH_3$), 3.92 (OMe), 3.12 (NMe) and 1.38 (t, *J* 7, $CO_2CH_2CH_3$) (Found: C, 56.8; H, 6.1; N, 6.5%; M, 211.0850. $C_{10}H_{13}NO_4$ requires C, 56.9; H, 6.2; N, 6.6%; *M*, 211.0844); (ii) the Z-*ylidenepyrrol*-2(5H)-*one* **17b** (47%), and (iii) recovered starting material **5f** (4%).

(E)-5-*Ethoxycarbonylmethylene*-1H-4-*methoxy*-3-*methylpyrrol*-2(5H)-*one* **22a**.—A solution of 3-methoxy-4-methyl-1*H*-pyrrole-2,5-dione **5g** (0.211 g, 1.5 mmol) and ethoxycarbonylmethylene(triphenyl)phosphorane (1.39 g, 3.99 mmol, 2.66 equiv.) in toluene (35 cm^3) was heated under reflux for 24 h. The toluene was evaporated under reduced pressure

and the residue was then purified by chromatography (hexane–ether, 3:1) to give the E-*alkylidenepyrrol*-2(5H)-*one* **22a** (75 mg, 36%) as a white solid which was recrystallised from benzene–hexane to give fine white crystals, m.p. 89–90 °C; λ_{max}(MeOH)/nm 288 and 325; ν_{max}($CHCl_3$)/cm^{-1} 3410, 1720, 1693, 1660 and 1640; δ_H 8.6 (NH), 5.5 (=CH), 4.2 (q, *J* 7, OCH_2), 4.1 (OCH_3), 2.1 (=CCH_3) and 1.3 (t, *J* 7, CH_3); for NOE data see Table 1; δ_C 171.86 (CO), 167.25 (CO_2), 158.08 (=*C*OMe), 146.37 (quat. C), 105.06 (quat. C), 92.22 (=CH), 60.55 (OCH_2), 58.96 (OMe), 14.29 (Me) and 8.04 (Me) (Found: C, 56.4; H, 6.2; N, 6.4%; M, 211.0860. $C_{10}H_{13}NO_3$ requires C, 56.8; H, 6.2; N, 6.6%; *M*, 211.0844).

(Z)- *and* (E)-5-*Ethoxycarbonylmethylene*-4-*methoxy*-1,3-*dimethylpyrrol*-2(5H)-*ones* **21b** *and* **22b**.—A solution of 3-methoxy-1,4-dimethylmaleimide **5h** (120 mg, 0.77 mmol) and ethoxycarbonylmethylene(triphenyl)phosphorane (2.7 g, 7.75 mmol, 10 equiv.) in toluene (35 cm^3) was heated under reflux for 336 h. The cooled solution was concentrated and the residue was then purified by chromatography (hexane–ether, 3:1) give: (i) the *Z-pyrrol*-2(5H)-*one* **21b** (116 mg, 60%) as a yellow oil which solidified, m.p. 47–48 °C (ether–hexane); λ_{max}(EtOH)/nm 285; ν_{max}($CHCl_3$)/cm^{-1} 1705, 1665 and 1625; δ_H 5.63 (=CH), 4.23 (q, *J* 7, $CO_2CH_2CH_3$), 4.13 (OMe), 3.36 (NMe), 2.07 (=CMe) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$); δ_C 171.7 (CO), 164.0 (CO_2), 157.2 (=*C*OMe), 143.6 (quat. C), 101.4 (quat. C), 93.3 (=CH), 59.4 (OCH_2), 58.1 (OMe), 28.4 (NMe), 13.2 (Me) and 7.2 (Me) (Found: C, 58.4; H, 6.9%; M, 225.0989. $C_{11}H_{15}NO_4$ requires C, 58.7; H, 6.7%; *M*, 225.1001) and (ii) the E-*pyrrol*-2(5H)-*one* **22b** (27 mg, 15%) as a yellow oil; λ_{max}(EtOH)/nm 285; ν_{max}($CHCl_3$)/cm^{-1} 1710, 1665 and 1630; δ_H 5.45 (=CH), 4.24 (q, *J* 7, $CO_2CH_2CH_3$), 4.05 (OMe), 3.13 (NMe), 2.03 (=CMe) and 1.32 (t, *J* 7, $CO_2CH_2CH_3$) (Found: *m*/*z* 225.0982. $C_{11}H_{15}NO_4$ requires 225.1001).

Reactions with the Anions from Phosphonates and Phosphine Oxides

(Z)-4-*Methoxy*-1-*methyl*-5-*phenylthiomethylenepyrrol*-2(5H)-*one* **17d**.—A 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.66 cm^3, 1.06 mmol) was added dropwise over 2 min to a stirred solution of diphenyl(phenylthiomethyl)phosphine oxide[20] (343 mg, 1.06 mmol) in dry THF (15 cm^3) at −78 °C. A yellow colour rapidly developed and after the solution had been stirred for 20 min at −78 °C, 3-methoxy-1-methylmaleimide **5f** (149 mg, 1.06 mmol) in THF (2 cm^3) was added all at once. The solution was stirred at −78 °C for 1 h and then poured into saturated aqueous ammonium chloride. The mixture was extracted with chloroform and then purified by chromatography (ether) to give: (i) impure *Z*-ylidenepyrrol-2(5*H*)-one **17d** (23 mg, 9%) as a yellow solid, and (ii) the starting phosphine oxide (243 mg, 71%).

Reactions with Peterson Reagents

Reaction between 1,3-*Dimethyl*-1H-*pyrrole*-2,5-*dione and Methyl Trimethylsilylacetate; Formation of* **13c**–**16c**.—A solution of methyl trimethylsilylacetate (433 mg, 2.96 mmol) in dry THF (1 cm^3) was added dropwise over 2 min to a stirred solution of LDA (3.11 mmol, 1.05 equiv.) in dry THF (15 cm^3) at −78 °C. The mixture was stirred at −78 °C for 40 min, and then a solution of 1,3-dimethylmaleimide **5d** (363 mg, 2.90 mmol) in dry THF (1 cm^3) was added over 10 min. The solution was stirred at −78 °C for 2 h, and then allowed to warm up to room temperature, when it was quenched with water (20 cm^3) and extracted with chloroform (3 × 15 cm^3). The combined extracts were dried and concentrated under reduced pressure to leave an orange oil which was then purified by chromatography (hexane–ether, 4:1) to give: (i) a 1:2 mixture of (Z)- and (E)-5-*ethoxycarbonylmethylene*-1,3-*dimethylpyrrol*-2-(5H)-*ones* **15c** and **16c** (88 mg, 17%) which recrystallised from hexane as white needles, m.p. 87–92 °C; λ_{max}(EtOH)/nm 314infl. and 279; ν_{max}($CHCl_3$)/cm^{-1} 1715, 1700, 1635 and 1620; δ_H 7.81 and 6.62 (q, *J* 1.5, =CH), 5.52 and 5.31 (=*CH*CO_2Me), 3.83 (OMe), 3.14 and 3.44 (NMe) and 2.04 (=CMe) (Found: C, 59.7; H, 6.3; N, 8.0%; M, 181.0757. $C_9H_{11}NO_3$ requires C, 59.7; H, 6.1; N, 7.7%; *M*, 181.0793) and (ii) an 11:9 mixture of (Z)- and (E)-5-*ethoxycarbonylmethylene*-1,4-*dimethylpyrrol*-2(5H)-*ones* **13c** and **14c** (97 mg, 18%) as a colourless oil; λ_{max}(EtOH)/nm 314infl. and 275; ν_{max}($CHCl_3$)/cm^{-1} 1715, 1705, 1635 and 1615; δ_H 6.12 and 6.07 (q, *J* 1.5, =CH), 5.62 and 5.47 (=*CH*CO_2Me), 3.80 (OMe), 3.08 and 3.35 (NMe), 2.37 and 2.12 (d, *J* 1.5, =CMe) (Found: *m*/*z* 181.0751. $C_9H_{11}NO_3$ requires 181.0739).

(Z)- *and* (E)-4-*Methoxy*-5-*methoxycarbonylmethylene*-1-*methylpyrrol*-2(5H)-*ones* **17c** *and* **18a**.—A solution of methyl trimethylsilylacetate (127 mg, 0.87 mmol) in dry THF (1 cm^3) was added dropwise over 2 min to a stirred solution of LDA (0.87 mmol) in dry THF (15 cm^3) at −78 °C. The mixture was stirred at −78 °C for 35 min, and then 3-methoxy-1-methylmaleimide **5f** (123 mg, 0.87 mmol) was added to it and the solution was stirred at −78 °C for 3 h. The vivid pink solution was quenched with water and then thoroughly extracted with chloroform (4 × 15 cm^3). The combined extracts were dried and evaporated under reduced pressure to leave a 4:1 mixture of the *Z*- and *E*-ylidenepyrrol-2(5H)-*ones* **17c** and **18a** (69 mg, 40%); δ_H 5.70 and 5.57 (=*CH*CO_2Et), 5.27 and 5.33 (=CH) and 3.95 and 3.81 (OMe + CO_2Me). Recrystallisation from benzene–hexane gave the *Z-ylidenepyrrol*-2(5H)-*one* **17c** (54 mg, 30%) as white needles, m.p. 136–138 °C; λ_{max}(EtOH)/nm 280; ν_{max}($CHCl_3$)/cm^{-1} 1720, 1650 and 1620 (Found: C, 55.0; H, 5.8; N, 7.2%. $C_9H_{11}NO_4$ requires C, 54.8; H, 5.6; N, 7.1%).

(Z)- *and* (E)-3-*Methoxy*-1-*methyl*-5-*phenylthiomethylenepyrrol*-2(5H)-*ones* **19** *and* **20b** *and* (E)-4-*Methoxy*-1-*methyl*-5-*phenylthiomethylenepyrrol*-2(5H)-*one* **18b**.—A 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.58 cm^3, 0.9 mmol) was added dropwise over 3 min to a stirred solution of phenylthiomethyltrimethylsilane (164 mg, 0.84 mmol) in dry THF (5 cm^3) at 0 °C. The solution was stirred at 0 °C for 0.5 h, and then cooled to −78 °C when a solution of 3-methoxy-1-methylmaleimide **5f** (114 mg, 0.810 mmol) in dry THF (1 cm^3) was added dropwise to it while the temperature was maintained < −75 °C. The mixture was stirred at −78 °C for 2 h, and then allowed to warm to room temperature during 1 h. Water (30 cm^3) was added to the mixture which was then extracted with ether (4 × 20 cm^3). The combined extracts were washed with saturated brine (20 cm^3), dried, filtered and evaporated under reduced pressure to leave a brown oil. Purification of this chromatography (light petroleum–ether, 1:2 → 1:3) gave: (i) recovered phenylthiomethyl(trimethyl)silane (50 mg, 31%); (ii) the E-*pyrrol*-2(5H)-*one* **20b** (51 mg, 25%) as a colourless oil; λ_{max}(EtOH)/nm 343, 196sh; ν_{max}($CHCl_3$)/cm^{-1} 1703 and 1645; δ_H 7.44–7.20 (m, 5 × ArH), 6.31 (4-H), 5.95 (=*CH*SPh), 3.87 (OMe) and 3.20 (NMe); for NOE data see Table 1; δ_C 153.0 (quat. C), 142.1 (quat. C), 136.7 (quat. C), 136.2 (quat. C), 129.2 (2 × CH), 128.2 (2 × =CH), 126.6 (=CH), 101.0 (=CH), 98.7 (=CH), 57.9 (OMe) and 25.9 (NMe) (Found: *m*/*z* 247.0659. $C_{13}H_{13}NO_2S$ requires 247.0667); (iii) the *pyrrol*-2-(5H)-*one* **19** (55 mg, 27%) as a colourless oil which solidified, m.p. 105–107 °C (from ethyl acetate–light petroleum); λ_{max}(EtOH)/nm 335 and 266sh; ν_{max}($CHCl_3$)/cm^{-1} 1670, 1600 and 1350; δ_H 7.48–7.31 (m, 5 × ArH), 6.25 (=*CH*SPh), 5.12 (4-H), 3.81 (OMe) and 3.42 (NMe); for NOE data see Table 1; δ_C 170.2

(CO), 164.2 (quat. C), 135.0 (quat. C), 133.2 (quat. C), 129.8 (2 × =CH), 129.4 (2 × CH), 127.7 (=CH), 105.5 (=CH), 90.9 (=CH), 58.0 (OMe) and 27.8 (NMe) (Found: C, 63.1; H, 5.6; N, 5.4%; M, 247.0683. $C_{13}H_{13}NO_2S$ requires C, 63.1; H, 5.3; N, 5.7%; *M*, 247.0667) and (iv) a mixture (16 mg, 8%), as an oil, of **19**; (data as above) and the E-*pyrrol*-2(5H)-*one* **18b**; λ_{max}(EtOH)/nm 200; ν_{max}($CHCl_3$)/cm^{-1} 1710sh, 1670 and 1635; δ_H 7.45–7.30 (m, 5 × ArH), 6.05 (d, *J* 1.2, =C*H*SPh), 5.21 (d, *J* 1.2, 3-H), 3.92 (OMe) and 3.06 (NMe) (Found: *m*/*z* 247.0656. $C_{13}H_{13}NO_2S$ requires 247.0667).

(Z)- *and* (E)-4-*Methoxy*-5-*methoxycarbonylmethylene*-1,3-*dimethylpyrrol*-2(5H)-*ones* **21c** *and* **22c**.—A solution of methyl trimethylsilylacetate (0.12 g, 0.82 mmol) in dry THF (1 cm^3) was added dropwise over 3 min to a stirred solution of lithium diisopropylamide (0.82 mmol) in THF at −70 °C. The solution was stirred at −70 °C for 15 min after which a solution of 3-methoxy-1,4-dimethylpyrrole-2,5-dione **5h** (0.127 g, 0.82 mmol) in THF (2 cm^3) was added dropwise to it over 10 min. The resulting yellow solution was stirred at −70 °C for 1 h, and then at room temperature for 1 h. The solution was quenched with water (10 cm^3) and then acidified with 2 mol dm^{-3} hydrochloric acid (5 cm^3) and extracted with ether. The combined organic extracts were washed with water, dried, filtered and evaporated under reduced pressure. The residue was purified by chromatography (ether–hexane, 1:3) to give a 4:1 mixture of the pyrrolones **21c** and **22c**; crystallisation from ether afforded the Z-*ylidenepyrrol*-2(5H)-*one* **21c** (89 mg, 51%) as a white solid, m.p. 64–66 °C; λ_{max}(MeOH)/nm 196, 286; ν_{max}($CHCl_3$)/cm^{-1} 1718, 1705, 1660, 1640 and 1630; δ_H 5.58 (=CH), 4.07 (OMe, ester), 3.74 (OMe), 3.33 (NMe) and 2.05 (=CMe); δ_C 172.7 (CO), 165.5 (CO_2), 158.8 (=*C*OMe), 145.0 (quat. C), 103.5 (quat. C), 93.9 (=CH), 59.3 (OMe), 51.6 (OMe), 29.4 (NMe) and 8.3 (Me) (Found: C, 57.3; H, 6.6; N, 6.2%; M, 211.0857. $C_{10}H_{13}NO_4$ requires C, 56.9; H, 6.2; N, 6.6%; *M*, 211.0845).

(Z)-5-tert-*Butoxycarbonylmethylene*-4-*methoxy*-1,3-*dimethylpyrrol*-2(5H)-*one* **21d**.—A solution of *tert*-butyl trimethylsilylacetate (0.376 g, 2 mmol) in dry THF (2 cm^3) was added dropwise over 2 min to a stirred solution of lithium diisopropylamide (2.1 mmol) in THF (6 cm^3) at −78 °C. The solution was stirred at −78 °C for 20 min, after which a solution of 1,4-dimethyl-3-methoxy-1*H*-pyrrole-2,5-dione **5h** (0.310 g, 2 mmol) in tetrahydrofuran (2 cm^3) was added dropwise to it over 10 min. The mixture was stirred at −78 °C for 1.5 h and then allowed to warm to room temperature over 1 h. The mixture was quenched with 10% aq. ammonium chloride (25 cm^3), the organic phase separated, and the aqueous layer extracted with dichloromethane. The combined organic extracts were then washed with water, dried, filtered and evaporated under reduced pressure to give a dark brown oil. The oil was purified by flash chromatography (methanol–dichloromethane, 3:97) to give the Z-*ylidenepyrrolone* **21d** (0.258 g, 51%) as a brown oil; λ_{max}(MeOH)/nm 282; ν_{max}($CHCl_3$)/cm^{-1} 2980, 1715, 1665 and 1635; δ_H 5.40 (=CH), 3.93 (OMe), 3.16 (NMe) and 1.91 (=CMe); δ_C 172.2 (CO), 164.2 (CO_2), 158.5 (quat. C), 143.1 (quat. C), 102.8 (quat. C), 96.3 (=CH), 88.4 (O*C*Me$_3$), 58.8 (OMe), 28.9 (NMe), 27.9 (3 × Me) and 7.9 (=C*Me*) (Found: C, 60.3; H, 7.6; N, 5.8%; M, 253.1317. $C_{13}H_{13}NO_3$ requires C, 60.2; H, 7.2; N, 5.9%; *M*, 253.1314).

(Z)- *and* (E)-4-*Methoxy*-1,3-*dimethyl*-5-*phenylthiomethylenepyrrol*-2(5H)-*ones* **21e** *and* **22d**.—A 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.62 cm^3, 1 mmol) was added all at once to a solution of phenylthiomethyl(trimethyl)silane (0.196 g, 1 mmol) in dry THF (3 cm^3) at −60 °C. The solution was stirred at −60 °C for 15 min after which a solution of 3-methoxy-1,4-dimethylpyrrole-2,5-dione **3h** (155 mg, 1 mmol) in THF (2 cm^3) was added dropwise to it over 10 min. The orange solution was stirred at −60 °C for 1 h and then warmed to room temperature overnight. The dark orange–brown solution was quenched with water (10 cm^3) and then extracted with ether. The combined organic extracts were washed with water, dried, filtered and evaporated under reduced pressure. The residue was purified by chromatography (ethyl acetate–light petroleum, 3:7) to give the pyrrolone (21 mg, 8%); recrystallisation from ether–ethyl acetate gave a cream solid which was found to be a 1:1 mixture of the *Z*- and *E*-isomers **21e** and **22d**, m.p. 118–127 °C; λ_{max}(MeOH)/nm 234, 265sh and 329; ν_{max}($CHCl_3$)/cm^{-1} 1710, 1675 and 1590; δ_H *Z*-isomer **21e**: 7.49–7.27 (m, 5 × ArH), 6.10 (=CH), 4.02 (OMe), 3.42 (NMe) and 2.06 (=CMe); *E*-isomer **22d**: 7.49–7.27 (m, 5 × ArH), 5.98 (=CH), 4.13 (OMe), 3.06 (NMe) and 2.04 (=CMe); δ_C (*E*/*Z*-mixture) 190.8 (CO), 171.5 (quat. C), 157.0 (quat. C), 136.0 (=CH), 135.5 (quat. C), 129.8 (=CH), 129.2 (=CH), 129.0 (=CH), 128.6 (=CH), 127.2 (=CH), 127.0 (=CH), 107.7 (=CH), 104.8 (=CH), 103.1 (=CH), 58.8 (OMe), 58.6 (OMe), 27.9 (NMe), 25.4 (NMe), 7.8 (=C*Me*) and 7.6 (=C*Me*) (Found: C, 64.5; H, 5.8%; M, 261.0813. $C_{14}H_{15}NO_2S$ requires C, 64.3; H, 5.8%; *M*, 261.0824).

Attempted Preparation of 5-*Phenylthiomethylene*-3/4-*phenylthio*-1-*methylpyrrol*-2(5H)-*one*.—A 1.26 mol dm^{-3} solution of butyllithium in hexane (0.7 cm^3, 0.88 mmol) was added dropwise over 2 min to a stirred solution of phenylthiomethyl(trimethyl)silane (173 mg, 0.88 mmol) in dry THF at −3 °C, and the mixture then stirred at −3 °C for 20 min. The solution was cooled to −78 °C and then added over 30 min by way of a double-ended needle under a positive nitrogen pressure to a stirred solution of 1-methyl-3-phenylthiomaleimide **5j** (193 mg, 0.88 mmol) in THF (10 cm^3) at −78 °C. The mixture was stirred at −78 °C for 6 h and then allowed to warm to room temperature overnight. Saturated brine (30 cm^3) was added to the mixture which was then extracted with ether (3 × 10 cm^3). The combined extracts were washed with water (2 × 20 cm^3), dried, filtered and evaporated under reduced pressure to leave a black oil (0.20 g). The oil was purified by chromatography (light petroleum–ether, 3:1) to give: (i) the starting sulfide (145 mg, 82% recovery) and (ii) 1-*methyl*-5-*phenylthiomethylene*-3/4-*phenylthiopyrrol*-2(5H)-*one* (6.7 mg, 2.5%) as a yellow oil; λ_{max}(EtOH)/nm 363 and 267; ν_{max}($CHCl_3$)/cm^{-1} 1740, 1690 and 1640; δ_H 7.7–7.2 (m, 10 × ArH), 6.65, 6.40, 6.19, 5.96 and 5.61 (=CH) and 3.52, 3.49, 3.20 and 3.12 (NMe)—indicating that it was a mixture of at least three of the possible isomers (Found: *m*/*z* 325.0520. $C_{18}H_{15}NOS_2$ requires 325.0595).

Reactions with Aliphatic Grignard Reagents

5-*Butyl*-5-*hydroxy*-1,4-*dimethylpyrrol*-2(5H)-*one and* 5-*Butyl*-5-*hydroxy*-1,3-*dimethylpyrrol*-2(5H)-*one* **28a** *and* **29**.—A 1.9 mol dm^{-3} solution of butylmagnesium chloride in ether (5.8 cm^3, 11.02 mmol, 1.3 equiv.) was added dropwise over 15 min to a stirred solution of 1,3-dimethylmaleimide **5d** (1.05 g, 8.39 mmol) in dry THF (25 cm^3) at 0 °C (a large exotherm was observed). The cooling bath was removed and the solution was then stirred at room temperature for 1.5 h. Water (30 cm^3) and 2 mol dm^{-3} hydrochloric acid (10 cm^3) were added to the mixture which was then extracted with ethyl acetate (3 × 20 cm^3). The combined extracts were dried, filtered and evaporated under reduced pressure to leave a yellow oil which was purified by chromatography (ether) to give: (i) the *pyrrolone* **29** (429 mg, 28%) as a yellow oil; ν_{max}($CHCl_3$)/cm^{-1} 3570, 3350, 1685 and 1655; δ_H 6.57 (m, =CH), 5.2 (OH), 2.79 (NMe), 2.0–0.8 (m, C_4H_9) and 1.82 (d, *J* 2, =CMe); δ_C 170.3 (CO), 142.4 (=CH), 134.6 (=*C*Me), 90.1 (OCN), 35.0 (CH_2), 25.8 (CH_2), 23.2 (NMe), 22.7 (CH_2), 14.0 (Me) and 10.7 (Me) (Found: *m*/*z* 183.1246. $C_{10}H_{17}NO_2$ requires 183.1233) and (ii) the *pyrrolone* **28a** (356

mg, 23%) as a yellow oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 3560, 3350, 1690 and 1675; δ_H 5.69 (=CH), 4.75 (OH), 2.78 (NMe), 2.0–0.8 (m, C_4H_9) and 1.87 (d, *J* 2, =CMe); δ_C 170.2 (CO), 160.4 (=*C*Me), 121.9 (=CH), 92.7 (OCN), 32.7 (CH_2), 24.9 (CH_2), 23.3 (NMe), 22.4 (CH_2), 13.9 (Me) and 12.1 (Me) (Found: *m/z* 183.1259. $C_{10}H_{17}NO_2$ requires 183.1233).

(Z)- *and* (E)-5-*Butylidene*-1,4-*dimethylpyrrol*-2(5H)-*one* **30a**.—A solution of the hydroxypyrrolone **28a** (108 mg, 0.59 mmol), methanesulfonyl chloride (123 mg, 0.71 mmol, 1.2 equiv.) and pyridine (0.16 cm^3, 3.3 equiv) in dichloromethane (5 cm^3) was stirred at room temperature for 39 h. The solution was evaporated to dryness under reduced pressure and the residue was then purified by chromatography (light petroleum–ether) to give: (i) the Z-*pyrrol*-2(5H)-*one* Z-**30a** (24 mg, 25%), as a yellow oil; λ_{max}(EtOH)/nm 268; $\nu_{max}(CHCl_3)/cm^{-1}$ 1690, 1670 and 1655; δ_H 5.92 (m, =CH), 5.27 (t, *J* 8, =C*H*C_3H_7), 3.37 (NMe), 2.55 (q, *J* 8, =CHC$H_2C_2H_5$), 2.07 (d, *J* 1.5, =CMe) and 1.6–1.0 (m, $CH_2CH_2CH_3$) (Found: *m/z* 165.1144. $C_{10}H_{15}NO$ requires 165.1153) and (ii) the E-*pyrrol*-2(5H)-*one* E-**30a** (32 mg, 33%), as a yellow oil; λ_{max}(EtOH)/nm 269; $\nu_{max}(CHCl_3)/cm^{-1}$ 1685, 1670; δ_H 5.96 (m, =CH), 5.37 (t, *J* 8, =C*H*C_3H_7), 3.35 (NMe), 2.45 (q, *J* 8, =CHC$H_2C_2H_5$), 2.26 (=CMe) and 1.6–0.96 (m, $CH_2CH_2CH_3$) (Found: *m/z* 165.1136. $C_{10}H_{15}NO$ requires 165.1153).

The hydroxypyrrolone **28a** was also dehydrated using toluene-*p*-sulfonic acid in benzene under reflux leading to a similar isomeric ratio, *i.e.* *Z*:*E* = 23:32.

5-*Butylidene*-1,3-*dimethylpyrrol*-2(5H)-*one* **31**.—A solution of the hydroxypyrrolone **29** (198 mg, 1.08 mmol), methanesulfonyl chloride (207 mg, 1.19 mmol, 1.1 equiv.) and pyridine (0.30 cm^3, 3.4 equiv.) in dichloromethane (7 cm^3) was stirred at room temperature for 48 h. The solution was evaporated to dryness under reduced pressure and the residue was then purified by chromatography (light petroleum–ether, 1:1) to give the *butylidenepyrrol*-2(5H)-*one* **31** (111 mg, 62%) as a yellow oil; λ_{max}(EtOH)/nm 272; $\nu_{max}(CHCl_3)/cm^{-1}$ 1750, 1655; δ_H 6.98 (=CH), 5.33 (t, *J* 8, =C*H*C_3H_7), 3.12 (NMe), 2.30 (q, *J* 8, =CHC$H_2C_2H_5$), 2.00 (d, *J* 1.5, =CMe) and 1.6–0.94 (m, $CH_2CH_2CH_3$); δ_C 170.5 (CO), 139.8 (quat. C), 133.8 (quat. C), 126.4 (=CH), 112.0 (=CH), 29.4 (CH_2), 25.5 (NMe), 23.5 (CH_2), 13.6 (Me) and 11.0 (Me) (Found: *m/z* 165.1163. $C_{10}H_{15}NO$ requires 165.1153).

A solution of the hydroxypyrrolone **29** (198 mg, 1.08 mmol) in benzene (40 cm^3) was heated under reflux in the presence of toluene-*p*-sulfonic acid (10 mg) in a Dean and Stark apparatus for 3 h. The solution was concentrated under reduced pressure and the residue was then purified by chromatography as indicated above to give the butylidenepyrrolone **31** (118 mg, 66%).

5-*Butyl*-5-*hydroxy*-4-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **28b**.—A 1.9 mol dm^{-3} solution of butylmagnesium chloride in ether (1.06 cm^3, 2.01 mmol, 2.0 equiv.) was added dropwise over 2 min to a stirred solution of 3-methoxy-1-methylmaleimide **5f** (143 mg, 1.01 mmol) in dry THF (15 cm^3) at −78 °C after which the solution was allowed slowly to warm to 25 °C over 2 h. The excess of reagent was quenched by the addition of water (15 cm^3) and the mixture was then extracted with ethyl acetate (4 × 15 cm^3). The combined organic extracts were dried, filtered and evaporated under reduced pressure to leave a solid residue. The residue was purified by chromatography (ether) to give the *hydroxypyrrol*-2(5H)-*one* **28b** (197 mg, 98%) as a white solid, m.p. 110.5–111 °C; λ_{max}(EtOH)/nm 258 and 209; $\nu_{max}(CHCl_3)/cm^{-1}$ 3400 and 1660; δ_H 5.37 (OH), 4.95 (=CH), 3.90 (OMe), 2.77 (NMe) and 2.0–0.7 (m, C_4H_9) (Found: C, 60.6; H, 8.3; N, 6.8%. $C_{10}H_{17}NO_3$ requires C, 60.3; H, 8.6; N, 7.0%).

5-*Butylidene*-4-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **30b**.—A solution of the hydroxypyrrolone **28b** (190 mg, 0.95 mmol) in toluene (30 cm^3) was heated under reflux in the presence of toluene-*p*-sulfonic acid (10 mg) in a Dean and Stark apparatus for 6 h. The solution was evaporated to dryness under reduced pressure and the residue was then purified by chromatography (light petroleum–ether, 3:7) to give: (i) a mixture of E- and Z-*pyrrol*-2(5H)-*ones* **30b** (59 mg, 34%) as a yellow oil; λ_{max}(EtOH)/nm 267; $\nu_{max}(CHCl_3)/cm^{-1}$ 1670 and 1605; δ_H 5.5–5.1 (m, 2 × =CH), 3.87 (OMe), 3.30 and 3.04 (NMe), 2.7–2.3 (m, =CHC$H_2C_2H_5$) and 1.7–0.8 (m, $CH_2CH_2CH_3$) (Found: *m/z* 181.1118. $C_{10}H_{15}NO_2$ requires 181.1102) and (ii) an unidentified yellow oil (30 mg, ~20%); λ_{max}(EtOH) 300 and 275; $\nu_{max}(CHCl_3)/cm^{-1}$ 3600–2800, 1705 and 1640; δ_H 5.25 (t, *J* 8, =CH), 3.09 (NMe), 2.68 (*ca.* q, *J* 7, ~2 H), 1.52 (m, ~2 H) and 0.96 (t, *J* 7, ~3 H).

Synthesis of 5-*Ylidenepyrrol*-2(5H)-*ones from* **33a**

4-*Methoxy*-1-*methylpyrrol*-2(5H)-*one* **33a**.[13,14]—A solution of ethyl 4-bromo-3-methoxybut-2-enoate (5.2 g, 24.64 mmol) in 40% aq. methylamine (50 cm^3, 581 mmol) was stirred vigorously at room temperature for 12 h. The solution was extracted with chloroform (4 × 30 cm^3) and the combined extracts were dried, filtered and evaporated under reduced pressure to leave a brown solid. Distillation of this gave the *pyrrolone* **33a** (2.31 g, 79%) as a yellow solid, b.p. 190 °C/1.5 Torr, which was recrystallised from benzene–hexane to give colourless prisms, m.p. 86–87 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 1670 and 1635; δ_H 5.19 (=CH), 3.88 (CH_2 + OMe) and 2.98 (NMe); δ_C 173.2 (CO), 172.5 (=CO), 94.4 (=CH), 58.1 (OMe), 52.5 (CH_2) and 28.5 (NMe) (Found: C, 56.6; H, 7.4; N, 11.1%; M, 127.0626. $C_6H_9NO_2$ requires C, 56.7; H, 7.1; N, 11.0%; *M*, 127.0619).

4-*Methoxy*-1-*methyl*[5-^{2}H]*pyrrol*-2(5H)-*one* **33b**.—*Method* (*a*). A solution of the pyrrol-2(5*H*)-one **33a** (110 mg, 0.865 mmol) in dry THF (2 cm^3) was added dropwise over 5 min to a stirred solution of LDA (0.952 mmol) in dry THF (10 cm^3) at −78 °C, after which the solution was stirred at −78 °C for 0.5 h. Methan[^{2}H]ol (0.5 ml^3, 12.3 mmol) was added to the solution which was then allowed to warm to room temperature. The solution was poured into 2 mol dm^{-3} hydrochloric acid (20 cm^3), and the mixture was then extracted with chloroform (2 × 20 cm^3). The combined extracts were dried, filtered and evaporated under reduced pressure to leave a yellow solid (103 mg, 92%). Comparison of ^{1}H NMR signals indicated that complete deuteriation had occurred at C-5 and partial deuteriation (~35%) at C-3; δ_H 5.20 (0.65 H, *i.e.* 35% D, =CH), 3.95 (C*H*D + OMe) (Found: *m/z* 128.0667. $C_6H_8NO_2D$ requires 128.0661).

Method (*b*). A 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.49 cm^3, 0.78 mmol) was added dropwise over 2 min to a stirred solution of the pyrrol-2(5*H*)-one **33a** (79 mg, 0.62 mmol) in dry THF (10 cm^3) at −78 °C for 45 min. Methan[^{2}H]ol (0.5 cm^3, 12.3 mmol) was added to the solution which was then allowed to warm to room temperature. The mixture was worked up in the usual manner to give a yellow solid **33b** (68 mg, 86%). Inspection of the ^{1}H NMR spectrum showed that 70% deuteriation had occurred at C-5; δ_H 5.13 (=CH), 3.87 (m, C*H*D + OMe) and 2.98 (NMe).

4-*Methoxy*-1,5-*dimethylpyrrol*-2(5H)-*one* **33c**.—A 1.6 mol dm^{-3} solution of butyllithium in hexanes (1.58 cm^3, 2.53 mmol) was added dropwise over 5 min to a stirred solution of the pyrrol-2(5*H*)-one **33a** (300 mg, 2.36 mmol) in dry THF (15 cm^3) at −80 °C and the solution was stirred at −80 °C for 45 min. Iodomethane (0.6 cm^3, 9 mmol) was added dropwise over 10 min to the solution, which was stirred for a further 30 min and

then allowed to warm to room temperature over 2 h. Water (25 cm^3) was added to the mixture which was then extracted with dichloromethane (2 × 15 cm^3). The combined extracts were dried, filtered and evaporated under reduced pressure to leave a residue which was purified by chromatography over silica gel (dichloromethane–methanol, 98:2) to give the *pyrrol*-2(5H)-*one* **33c** (290 mg, 98%) as an oil; ν_{max}(film)/cm^{-1} 1772 and 1631; δ_H 4.94 (=CH), 3.87 (q, *J* 7, C*H*CH_3), 3.76 (OMe), 2.84 (NMe) and 1.31 (d, *J* 7, CHCH_3); δ_C 177.7 (CO), 171.7 (=CO), 93.2 (=CH), 58.3 (OMe), 58.0 (NCH), 26.3 (NMe) and 19.4 (Me) (Found: *m*/*z* 141.0778. $C_7H_{11}NO_2$ requires 141.0790).

5-*Methoxycarbonylmethyl*-4-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **33d**.—A 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.74 cm^3, 1.184 mmol) was added dropwise over 3 min to a stirred solution of the pyrrolin-2(5*H*)-one **33a** (130 mg, 1.022 mmol) in dry THF (15 cm^3) at −78 °C and the solution was stirred for −78 °C for 45 min. Methyl bromoacetate (313 mg, 2.046 mmol) was added over 10 min to the solution which was stirred at −78 °C for 30 min and then allowed to warm to room temperature. Water (15 cm^3) was added to the mixture which was then extracted with chloroform (4 × 15 cm^3). The combined extracts were dried, filtered and evaporated under reduced pressure to leave a residue which was purified by chromatography (chloroform–methanol, 99:1) to give: (i) the *pyrrolone ester* **33d** (150 mg, 74%) as a yellow oil; ν_{max}(CHCl$_3$)/cm^{-1} 1735, 1670 and 1630; δ_H 5.11 (=CH), 4.35 (t, *J* 6, NC*H*CH_2), 3.87 and 3.78 (OMe + CO_2Me), 2.93 (NMe) and 2.76 (m, NCHC*H*$_2$) (Found: *m*/*z* 199.0836. $C_9H_{13}NO_4$ requires 199.0845) and (ii) recovered starting material (10 mg, 8%).

Dehydrogenation of the Pyrrol-2(5H)-*one* **33d** *to give* (Z)- *and* (E)-5-*Methoxycarbonylmethylene*-4-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **17c** *and* **18a**.—A solution of the pyrrol-2(5*H*)-one **33d** (98 mg, 0.492 mmol) and *p*-chloranil (260 mg, 1.057 mmol) in benzene (10 cm^3) was heated under reflux for 24 h. The cooled solution was diluted with ether (20 cm^3) and then washed successively with 0.5 mol dm^{-3} aqueous sodium hydroxide, water and saturated brine. The organic layer was dried, filtered and evaporated under reduced pressure to leave a residue which was purified by chromatography (chloroform–methanol, 49:1) to give: (i) the *Z-pyrrol*-2(5H)-*one* **17c** (23 mg, 29%) as a white solid, m.p. 134–137 °C and (ii) a 4:1 mixture of the Z- and E-*ylidenepyrrol*-2(5H)-*ones* **17c** and **18a** (44 mg, 54%) as a white powder, m.p. 124–128 °C. The spectral data were identical with those recorded earlier.

Condensation of the Pyrrolone **33a** *with Benzaldehyde; Formation of* (Z) *and* (E)-4*Methoxy*-1-*methyl*-5-*phenylmethylenepyrrol*-2(5H)-*one* **17e** *and* **18c**.—4 mol dm^{-3} Aqueous sodium hydroxide (60 cm^3) was added to a solution of the pyrrol-2(5*H*)-one **33a** (1.0 g, 7.87 mmol) in methanol (10 cm^3). After 15 min this solution was added to a solution of benzaldehyde (1.0 g, 9.42 mmol) in methanol (10 cm^3). The mixture heated to 100 °C for 10 min and then cooled with ice–water (10 cm^3). The mixture was extracted with chloroform (3 × 10 cm^3), the combined organic layers were dried, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (ethyl acetate–light petroleum, 3:1) to give: (i) the *Z-ylidenepyrrol*-2(5H)-*one* **17e** (0.42 g, 25%) as a cream solid which on recrystallisation from light petroleum–ether gave material of m.p. 130–132 °C; λ_{max}(MeOH)/nm 303; ν_{max}(CHCl$_3$)/cm^{-1} 3400, 1681, 1655 and 1610; δ_H 7.4–7.2 (m, 5 × ArH), 6.50 (*exo* =CH), 5.18 (d, *J* 0.4, 3-H), 3.89 (OMe) and 2.83 (NMe); δ_C 171.9 (CO), 166.7 (=*C*OMe), 135.3 (=CN), 134.1 (=CH), 129.6 (=CH), 128.0 (=CH), 127.5 (=CH), 107.9 (=CH), 91.9 (=CH), 58.1 (OMe) and 29.4 (NMe) (Found: C, 67.0; H, 6.6%; M, 215.0946. $C_{13}H_{13}NO_2 \cdot H_2O$ requires C, 66.9; H, 6.5%; $C_{13}H_{13}NO_2$ requires *M*, 215.0946) and (ii) the E-*isomer* **18c** (0.14 g, 8%) as a brown oil; λ_{max}(MeOH)/nm 301; ν_{max}(film)/cm^{-1} 3420, 1680, 1655sh and 1611; δ_H 7.5–7.2 (m, 5 × ArH), 6.28 (*exo* =CH), 5.24 (d, *J* 1.2, 3-H), 3.72 (OMe) and 3.15 (NMe) (Found: *m*/*z* 215.0918. $C_{13}H_{13}NO_2$ requires 215.0946).

4-*Methoxy*-1-*methyl*-5-*methylenepyrrol*-2(5H)-*one* **18e**.—A 40% aqueous solution of formaldehyde (3 cm^3, 10 mmol) was added to a solution of the pyrrol-2(5*H*)-one **33a** (380 mg, 3 mmol) in 2 mol dm^{-3} aq. sodium hydroxide (1.5 cm^3, 3 mmol). The mixture was stirred at room temperature for 3.5 h, after which time it was acidified with 2 mol dm^{-3} hydrochloric acid to pH 7. The aqueous solution was extracted with dichloromethane and the organic extracts were dried, filtered and evaporated under reduced pressure to give a pale cream solid (160 mg, 38.5%). This solid was purified by chromatography (methanol–dichloromethane, 1:24) to give the *alkene* **18e** (85 mg, 20%) as a white solid. Recrystallisation from ether–hexane afforded material of m.p. 86–88 °C; λ_{max}(MeOH)/nm 194, 258 and 297; λ_{max}(CHCl$_3$)/cm^{-1} 3480, 1690, 1655 and 1610; δ_H 5.11 (d, *J* 1.5, =CH*H*), 4.94 (d, *J* 1.5, 3-H), 4.64 (t, *J* 1.5, =C*H*H), 3.84 (OMe) and 3.03 (NMe); δ_C 169.8 (CO), 165.2 (=*C*OMe), 142.2 (=CN), 92.8 (=CH), 89.9 (=CH_2), 58.0 (OMe) and 24.9 (NMe) (Found: C, 60.5; H, 6.8; N, 9.9%; M, 139.0638. $C_7H_9NO_2$ requires C, 60.4; H, 6.5; N, 10.1%; *M*, 139.0633).

(Z)- *and* (E)-4-*Methoxy*-1-*methyl*-5-(4′-*methoxybenzylidene*)-*pyrrol*-2(5H)-*one* **17f** *and* **18d**.—A solution of the pyrrol-2(5*H*)-one **33a** (127 mg, 1 mmol) in dry THF (1 cm^3) was added to a 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.625 cm^3, 1 mmol) in THF (5 cm^3) at −78 °C. The solution was stirred for 20 min and then *p*-anisaldehyde (136 mg, 1 mmol) was added in one portion. The mixture was stirred at −78 °C for 45 min, and then allowed to warm to room temperature during 1.5 h. Trifluoroacetic anhydride (6 drops) was added to the mixture which was stirred for 5 min and then 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU, 6 drops) was also added to it. The mixture was then stirred for a further 10 min after which it was diluted with water (10 cm^3) and extracted with ether. The combined ether extracts were dried, filtered and evaporated under reduced pressure to give a brown oil, purification of which by flash chromatography (CH_2Cl_2) gave: (i) the E-*isomer* **18d** (11 mg, 5%) as an orange oil; λ_{max}(MeOH)/nm 198, 228sh, 304sh and 332; ν_{max}(CHCl$_3$)/cm^{-1} 3400br, 1705, 1682, 1670, 1635 and 1601; δ_H 7.20 (dd, 4 × ArH), 6.24 (*exo* =CH), 5.24 (d, *J* 1.2, 3-H), 3.84 (OMe), 3.76 (OMe) and 3.14 (NMe); for NOE data see Table 1 (Found: *m*/*z* 245.1047. $C_{14}H_{15}NO_3$ requires 245.1052) and (ii) the Z-*isomer* **17f** (23 mg, 10%) as a yellow oil; λ_{max}(MeOH)/nm 198, 228sh and 329; ν_{max}(CHCl$_3$)/cm^{-1} 3450, 1710, 1685, 1675, 1640 and 1601; δ_H 7.10 (d, *J* 8.8, 2 × ArH), 6.80 (d, *J* 8.8, 2 × ArH), 6.37 (*exo* =CH), 5.09 (3-H), 3.79 (OMe), 3.75 (OMe) and 2.79 (NMe); for NOE data see Table 1; δ_C 171.9 (CO), 166.7 (quat. C), 159.2 (quat. C), 134.5 (quat. C), 130.8 (=CH), 126.2 (quat. C), 113.6 (=CH), 107.9 (=CH), 91.6 (=CH), 57.9 (OMe), 55.2 (OMe) and 29.4 (NMe) (Found: *m*/*z* 245.1045. $C_{14}H_{15}NO_3$ requires 245.1052).

(E)- *and* (Z)-5-(4′-*Hydroxybenzylidene*)-4-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **35**.—A 1.63 mol dm^{-3} solution of butyllithium in hexanes (0.5 cm^3, 0.815 mmol) was added to a cooled solution of the pyrrol-2(5*H*)-one **33a** (118 mg, 0.928 mmol) in dry THF (5 cm^3) at −70 °C, and the mixture was stirred for 15 min. A solution of 4-trimethylsilyloxybenzaldehyde (176 mg, 0.90 mmol) in THF (0.5 cm^3) was then added to it in one portion. The mixture was stirred at −70 °C for 1.5 h and then allowed to warm to room temperature overnight. Trifluoroacetic anhydride (8 drops) followed by DBU (8 drops) were added to

the mixture which was stirred for 10 min and then diluted with water (5 cm^3) followed by 2 mol dm^{-3} hydrochloric acid (10 cm^3). The solution was extracted with ether and the combined extracts were dried, filtered and evaporated under reduced pressure to give an oil. This was purified by flash chromatography (light petroleum–ethyl acetate, 1:1) which afforded a 1:1 mixture of the E- and *Z-olefins* **35** (16 mg, 8%) as a colourless oil; λ_{max}(MeOH)/nm 196, 245, 341 and 479; ν_{max}($CHCl_3$)/cm^{-1} 3275, 1671 and 1604; δ_H 7.37 and 7.15 (d, *J* 8.4, 4 × ArH), 6.80 (m, 4 × ArH), 6.47 and 6.26 (*exo* =CH), 5.18 and 5.26 (3-H), 3.87 and 3.75 (OMe) and 2.88 and 3.15 (NMe), respectively, for *E*-**35** and *Z*-**35**; (Found: *m/z* 231.0879. $C_{13}H_{13}NO_3$ requires 231.0895).

4-*Methoxy*-5-(4′-*methoxybenzyl*)-1-*methylpyrrol*-2(5H)-*one* **33e**.—A 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.64 cm^3, 1.02 mmol) was added in a dropwise manner over 5 min to a solution of the pyrrol-2(5*H*)-one **33a** (127 mg, 1 mmol) in dry THF (2 cm^3) at −78 °C. The solution was stirred at −78 °C *for 15 min after* which a solution of 4-methoxybenzyl bromide (201 mg, 1 mmol) in THF (1 cm^3) was added to it over 10 min. The mixture was stirred at −78 °C for a further 3 h and then at room temperature for 16 h. Water (5 cm^3) was then added to it and the organic layer separated. The aqueous layer was extracted with ether and the combined extracts were dried, filtered and evaporated under reduced pressure. The residue was purified by chromatography (dichloromethane–methanol, 97:3) to give a white solid. Recrystallisation of this from hexane–ethyl acetate afforded the *pyrrolone* **33e** (222 mg, 45%), m.p. 141–143 °C; ν_{max}(MeOH)/nm 200, 213sh and 225; ν_{max}($CHCl_3$)/cm^{-1} 1678, 1665 and 1630; δ_H 6.97 (dd, *J* 1.3, 8.5, 3′-H and 5′-H), 6.77 (dd, *J* 1.5, 8.5, 2′-H and 6′-H), 4.86 (3-H), 4.06 (dd, *J* 4.5, 4.5, 5-H), 3.77 (OMe), 3.76 (OMe), 3.08 (dd, *J* 4.5, 14.4, C*H*H), 2.92 (dd, *J* 4.5, 14.4, CH*H*) and 2.89 (NMe); δ_C 174.7 (CO), 172.0 (quat. C), 158.5 (quat. C), 130.2 (=CH), 127.2 (quat. C), 113.7 (=CH), 94.7 (=CH), 63.0 (NCH), 57.8 (OMe), 55.2 (OMe), 34.5 (CH_2) and 27.4 (NMe) (Found: *m/z* 247.1220. $C_{14}H_{17}NO_3$ requires 247.1208).

5-(4′-*Hydroxybenzyl*)-4-*methoxy*-1-*pyrrol*-2(5H)-*one* **33f**.—A 1% (w/v) solution of boron tribromide in dichloromethane (1.3 cm^3, 0.52 mmol) was added to a solution of the pyrrol-2(5*H*)-one **33e** (61 mg, 0.25 mmol) in dichloromethane (1 cm^3) at room temperature. The reaction mixture was stirred for 24 h and then water (2 cm^3) was added to it. The organic layer was separated and the aqueous layer extracted with ether. The combined organic layers were dried, filtered and evaporated under reduced pressure. The residue was purified by chromatography (dichloromethane–methanol, 97:3) to give the *phenol* **33f** (29 mg, 50%) as a colourless oil; ν_{max}($CHCl_3$)/cm^{-1} 3250, 1665 and 1630; δ_H 6.75 (d, *J* 8.5, 3′-H and 5′-H), 6.65 (d, *J* 8.5, 2′-H and 6′-H), 4.80 (3-H), 4.03 (dd, *J* 3.9, 3.9, 5-H), 3.62 (OMe), 2.98 (m, CH_2) and 2.90 (NMe) (Found: *m/z* 233.1059. $C_{13}H_{15}NO_3$ requires 233.1052).

(E)- *and* (Z)-5-(4′-*Hydroxybenzylidene*)-4-*methoxy*-1-*methylpyrrol*-2(5H)-*one* **35** *by the Dehydrogenation of* **33f**.—A solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ; 15 mg, 0.07 mmol) and the pyrrol-2(5*H*)-one **33f** (14 mg, 0.06 mmol) in dry dioxane (5 cm^3) was boiled under reflux under a nitrogen atmosphere for 22 h and then allowed to cool. Then 2 mol dm^{-3} hydrochloric acid (5 cm^3) was added to it and the organic layer separated. The aqueous layer was extracted with ether and then with dichloromethane. The combined organic phases were dried, filtered and evaporated under reduced pressure to give an oil. Purification of this by chromatography (dichloromethane–methanol, 9:1) afforded a colourless oil (12 mg, 86%) which proved to be identical in all respects with the hydroxybenzylidene compound **35** obtained earlier (see above).

4-*Methoxy*-5-(4′-*methoxybenzyl*)-1,5-*dimethylpyrrol*-2(5H)-*one* **38a**.—A 1.6 mol dm^{-3} solution of butyllithium in hexanes (0.24 cm^3, 0.38 mmol) was added, in a dropwise manner during 5 min, to a solution of the pyrrol-2(5*H*)-one **33e** (74 mg, 0.3 mmol) in dry THF (5 cm^3) at −70 °C. The solution was stirred at −70 °C for 15 min and then methyl iodide (20 mm^3, 0.3 mmol) was added to it. The reaction mixture was stirred for a further 1 h at −70 °C, and then allowed to regain room temperature during 16 h. The mixture was poured into water (5 cm^3) and extracted with ether. The combined organic phases were then dried, filtered and evaporated under reduced pressure. The residue was then filtered through a bed of flash silica gel (dichloromethane–methanol, 19:1) to remove polar impurities. Evaporation of the filtrate afforded an oil which comprised a 1:2 mixture of the starting pyrrolone **33e** and the product **38a** (33 mg, 40%). This mixture was employed in the next stage without further purification: δ_H 6.71 (d, *J* 8.6, 2 × ArH), 6.59 (d, *J* 8.6, 2 × ArH), 4.72 (OMe), 3.66 (OMe), 2.99 (NMe), 2.86 (d, *J* 15, C*H*H), 2.83 (d, *J* 15, CH*H*) and 1.40 (Me) (Found: *m/z* 261.1348. $C_{15}H_{19}NO_3$ requires 261.1365).

5-(4′-*Hydroxybenzyl*)-4-*methoxy*-1,5-*dimethylpyrrol*-2(5H)-*one* **38b**.—A 1% (w/v) solution of boron tribromide in dichloromethane (0.35 cm^3, 0.035 mmol) was added to a solution of the above mixture of **33e** + **38a** (20 mg, 0.08 mmol) in dichloromethane (1 cm^3) at room temperature. The mixture was stirred for 1 h and then quenched by the careful addition of water (2 cm^3). The organic phase was separated and the aqueous phase extracted with dichloromethane. The combined organic phases were dried, filtered and evaporated under reduced pressure. The residue was purified by chromatography (dichloromethane–methanol, 19:1), and the solid thus obtained was then recrystallised from hexane–ethyl acetate to give a buff solid, m.p. 148–150 °C, consisting largely of the phenol **38b** (10 mg, 76%); λ_{max}(MeOH)/nm 220, 226 and 277sh; ν_{max}($CHCl_3$)/cm^{-1} 3300br, 1650, 1630sh and 1615sh; δ_H 8.9 (br, OH), 6.68 (d, *J* 8.7, 2 × ArH), 6.60 (d, *J* 8.7, 2 × ArH), 4.72 (3-H), 3.66 (OMe), 2.99 (NMe), 2.85 (d, *J* 15, C*H*H), 2.82 (d, *J* 15, CH*H*) and 1.40 (CMe) (Found: *m/z* 247.1184. $C_{14}H_{17}NO_3$ requires 247.1208).

Attempted Dehydrogenation of the Pyrrol-2(5H)-*one* **38b** *with DDQ*.—A solution of DDQ (51 mg, 0.23 mmol) and **38b** (56 mg, 0.23 mmol) in benzene (5 cm^3) was boiled under reflux under a nitrogen atmosphere for 46 h and then allowed to cool. Hydrochloric acid (2 mol dm^{-3}; 5 cm^3) was added to it and the organic layer separated. The aqueous layer was extracted with dichloromethane and the combined organic phases were dried, filtered and evaporated under reduced pressure. The oily residue was purified by chromatography (dichloromethane–methanol, 9:1) to give two fractions: (i) recovered starting material **38b** (10 mg, 18%) and an unidentified tar (30 mg). No evidence could be found for the formation of the pyridone **37b**.

Acknowledgements

We thank the SERC for studentships (to G. D. J. and K. V. O.). We also thank ICI Pharmaceuticals, which is part of Zeneca Ltd. (CASE award to G. D. J.) and Pfizer Central Research for financial support, and Dr S. D. Mills (ICI Pharmaceuticals) for his interest.

References

1 W. D. Celmer and I. A. Solomons, *J. Am. Chem. Soc.*, 1955, **77**, 2861 and papers cited therein.
2 C. J. Simmons, F.-J. Marner, J. H. Cardellina II, R. E. Moore and K.

Seff, *Tetrahedron Lett.*, 1979, 2003; J. H. Cardellina II and R. E. Moore, *Tetrahedron Lett.*, 1979, 2007.
3 N. D. Abdullaev, K. Samikov, T. P. Antsupova, M. R. Yagudaev and S. Yu. Yunusov, *Khim. Prir. Soedin.*, 1987, (5), 692 [*Chem. Nat. Compd.* (*Engl. Transl.*)], 1987, **23**, 576.
4 H. Falk, K. Grubmayr, U. Herzig and O. Hofer, *Tetrahedron Lett.*, 1975, 559; D. A. Lightner and Y.-T. Park, *J. Heterocycl. Chem.*, 1977, **14**, 415.
5 See ref. 9 and also G. Pattenden, *Fortschr. Chem. Org. Naturst.*, 1978, **35**, 133; D. W. Knight, *Carboxylic Acids and Derivatives* in *General and Synthetic Methods*, The Royal Society of Chemistry, 1992, vol. 14 and previous volumes in this series.
6 See: I. Dell, C. R. A. Godfrey and D. J. Wadsworth, *Total Synthesis of Naturally Occurring 1,2-Dithiolo*[4,3-b]*pyrrolones and Related Compounds* in *Synthesis and Chemistry of Agrochemicals III*, ACS Symposium Series 1992, **504**, 384.
7 N. B. Mehta, A. P. Phillips, F. Fu Lui and R. E. Brooks, *J. Org. Chem.*, 1960, **25**, 1012.
8 R. A. Earl, F. W. Clough and L. B. Townsend, *J. Heterocycl. Chem.*, 1978, **15**, 1479.
9 M. J. Begley, D. W. Knight and G. Pattenden, *Tetrahedron Lett.*, 1975, 4279; D. W. Knight and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1979, 62.
10 (*a*) C. F. Ingham, R. A. Massy-Westropp, G. D. Reynolds and W. D. Thorpe, *Austral. J. Chem.*, 1975, **28**, 2499; (*b*) R. A. Massy-Westropp and M. F. Price, *Austral. J. Chem.*, 1980, **33**, 333.
11 W. Flitsch and S. R. Schindler, *Synthesis*, 1975, 685.
12 (*a*) W. I. Awad, F. G. Baddar, M. A. Omara and S. M. A. R. Omran, *J. Chem. Soc.*, 1965, 2040; (*b*) W. I. Awad and M. F. Ismail, *U.A.R. J. Chem.*, 1971, **14**, 141 (*Chem. Abstr.*, 1972, **77**, 114300t); W. I. Awad, M. F. Ismail and K. S. Al-Nuaimi, *J. Prakt. Chem.*, 1975, **317**, 29.
13 K. S. Kochhar, H. J. Carson, K. A. Clouser, J. W. Elling, L. A. Gramens, J. L. Parry, H. L. Sherman, K. Braat and H. W. Pinnick, *Tetrahedron Lett.*, 1984, **25**, 1871.
14 K. S. Kochhar and H. W. Pinnick, *J. Org. Chem.*, 1984, **49**, 3222.
15 H. Plieninger and U. Lerch, *Liebigs Ann. Chem.*, 1966, **698**, 191.
16 T. P. C. Mulholland, R. Foster and D. B. Haydock, *J. Chem. Soc., Perkin Trans. 1*, 1972, 2121.
17 W. Flitsch and H. Peters, *Chem. Ber.*, 1970, **103**, 805.
18 T. V. Sheremeteva and T. A. Trushkova, *Doklady Akad. Nauk. S.S.S.R.*, 1958, **122**, 828 (*Chem. Abstr.*, 1959, **53**, 4127h).
19 A. Rothhaas, *Liebigs Ann. Chem.*, 1932, **501**, 295.
20 J. I. Grayson and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1977, 2263.

Paper 3/03243D
Received 7*th June* 1993
Accepted 23*rd June* 1993