Flash vacuum pyrolysis of stabilised phosphorus ylides. Part 7.[1] Cyclisation of amino acid derived α-phthalimidoacyl ylides to give pyrroloisoindolediones

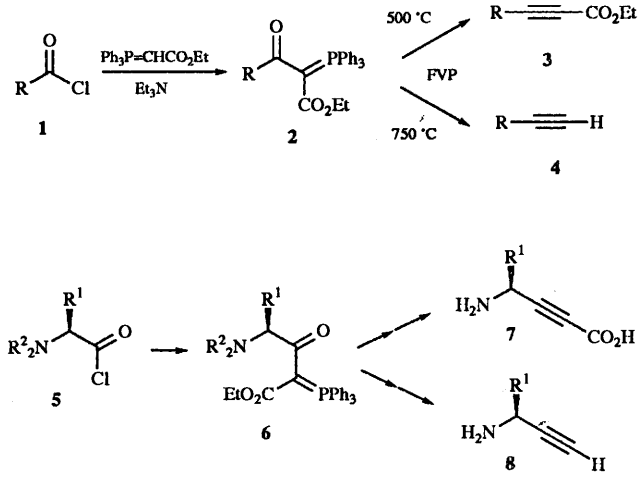
R. Alan Aitken,* Harris R. Cooper and (in part) Amit P. Mehrotra

School of Chemistry, University of St. Andrews, North Haugh, St. Andrews, Fife KY16 9ST, UK

A series of 11 amino acid-derived stabilised ylides 12–14 and 16 have been prepared and characterised. In one case, for compound 17, an X-ray structure determination supports formulation of the compounds as phosphonium enolates. Flash vacuum pyrolysis (FVP) of 12 and 13 at 500 °C results in loss of R^2_3PO between the ylide function and one carbonyl of the phthalimido group to give products characterised spectroscopically as the pyrroloisoindolediones 18. The identity of these is also supported by the results of ^{13}C and ^{15}N labelling experiments, but owing to their high reactivity complete separation from the phosphine oxide was not generally possible even when Bu_3PO rather than Ph_3PO was involved. Chromatographic purification of 29, similarly produced by FVP of 14, led to partial hydrolysis, rearrangement and decarboxylation to give 30. FVP of 12 at 750 °C gave the 1-unsubstituted pyrroloisoindolediones 19 in two cases.

In previous Parts of this series we have described the thermal extrusion of Ph_3PO from suitably substituted β-oxoalkylidenetriphenylphosphoranes using flash vacuum pyrolysis (FVP) as a useful route to a variety of different types of alkynes. In particular, in Part 2,[2] we showed that the ethoxycarbonyl-stabilised ylides **2** may be used to obtain either acetylenic esters **3** or terminal alkynes **4** simply by altering the pyrolysis temperature, thus providing convenient two-step access to either of these products from acid chlorides **1**. In this paper we describe our attempts to extend this method to α-amino acid-derived ylides **6**, which should be readily accessible from the acid chlorides **5** and potentially provide access to derivatives of the α,β-acetylenic γ-amino acids **7** and the prop-2-ynylic amines **8**. Relatively few compounds of these types have been prepared before,[3] but they are of considerable importance as potential mechanism-based inhibitors of medicinally important enzymes.[4] In particular, **7** (R^1 = H) and a number of *N*-substituted analogues have been shown to be effective GABA mimics,[5] and related compounds have been proposed for the therapeutic treatment of alcoholism and as anti-tumour agents.[6] The prop-2-ynylamine **8** [$R^1 = (CH_2)_3NH_2$] and analogues have been shown to be selective irreversible inhibitors of ornithine decarboxylase and thus to have potential anti-tumour activity,[7] while **8** [$R^1 = (CH_2)_2CO_2H$] and related compounds effectively inhibit GABA transaminase and may be used for the treatment of epilepsy.[8] In addition, the relationship between α-amino acids **9** and the analogues **7** extended by insertion of a C≡C unit, a concept recently generalised by Chauvin[9] and termed 'carbomers', makes the latter of interest for the formation of modified peptides.

For the success of this approach, the choice of *N*-protecting group R^2 is clearly important. While our work was in progress, Wasserman and co-workers reported the synthesis of aminoacyl ylides analogous to **6** by carbodiimide-mediated coupling between $Ph_3P{=}CHCO_2CH_2Ph$ and *N*-Cbz- or *N*-Boc-protected amino acids.[10] Bestmann and co-workers also recently described the reaction of $Ph_3P{=}C(SiMe_3)_2$ with unprotected glycine or alanine to give the aminoacyl ylides $Ph_3P{=}CHC(O)CH(R)NH_2$,[11] but this method is not amenable to formation of compounds with an ethoxycarbonyl substituent on the ylide carbon. Bearing in mind the need for a thermally robust *N*-protecting group and the flexibility of access to either **7** or **8** to be gained by having CO_2Et on the ylide carbon, we



decided upon the phthalimidoacyl ylides **12** as our initial target. In this paper we describe the synthesis of these compounds and their behaviour upon FVP which results in the formation of pyrroloisoindolediones.

Results and discussion

A range of α-amino acids **9** were converted into their phthalimido derivatives **10** either by heating with phthalic anhydride in the absence of solvent,[12] or by treatment in basic aqueous solution with *N*-ethoxycarbonylphthalimide in the solid form[13] or as a solution in ethyl acetate.[14] For chiral amino acids the latter methods were found to give less racemisation. The corresponding acid chlorides **11** were then formed from **10** in almost quantitative yield by treatment either with PCl_5 or $SOCl_2$. In this way the phthalimido acid chlorides derived from glycine, (*S*)-alanine, (*S*)-valine, (*S*)-leucine, (*S,S*)-isoleucine and (*S*)-phenylalanine were obtained in reasonable overall yield (see Table 1). The same methods were applied to α-aminoisobutyric acid to obtain the starting material for **14**. The fully assigned ^{13}C NMR spectra for **11b–f** (Table 2), which do not appear to have been recorded before, were of considerable value in interpreting the more complex spectra of the corresponding ylides **12** (*vide infra*).

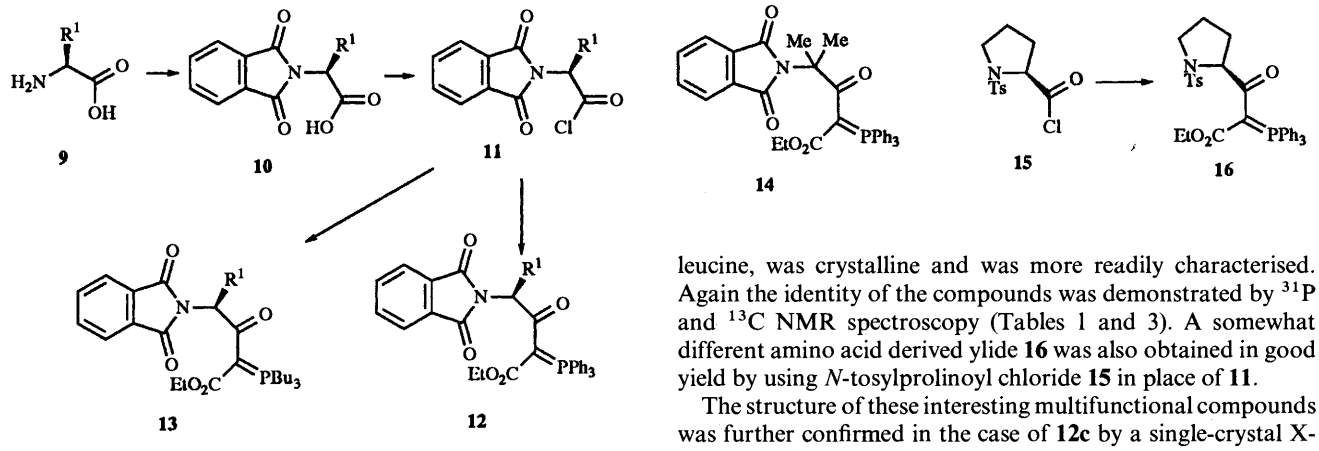
The ylides **12** were prepared in moderate to good yield by

Table 1 Formation of the ylides **12**, **13**, **14** and **16**

	R^1	Yield of **10** from **9** (%)	Yield of **11** from **10** (%)	Yield of **12** from **11** (%)	δ_P	Yield of **13** from **11** (%)	δ_P
a	H	60	98	67	17.2		
b	Me	65	98	45	18.0		
c	Pr^i	71	94	56	18.4	80 (±)	25.9
d	Bu^i	35	96	80	18.1	47	26.2
e	Bu^s	40	94	76	18.4		
f	CH_2Ph	47	98	83	18.1	81 (±)	25.9
14	—	(84)	(98)	(56)	(18.4)		
16	—	—	—	(71)	(16.5)		

Table 2 ^{13}C NMR spectra of phthalimido acid chlorides **11**, δ_C

	R^1	Phthalimido ring CH	Phthalimido 4°	Phthalimido CO	COCl	α-C	R^1 signals
b	Me	134.6, 123.8	131.8	167.1	172.1	55.9	15.4
c	Pr^i	134.7, 124.0	131.4	167.0	169.9	66.4	29.2, 20.4, 19.1
d	Bu^i	134.7, 123.9	131.5	167.0	172.0	59.1	37.3, 25.1, 23.0, 21.0
e	Bu^s	134.8, 124.0	131.4	167.0	169.9	65.8	35.1, 25.5, 16.5, 10.8
f	CH_2Ph	134.6, 123.9	131.2	166.7	171.1	61.4	135.3 (4°), 128.8 and 128.7 (each 2 C), 127.3, 34.7



reaction of **11** with $Ph_3P{=}CHCO_2Et$ (2 equiv.) in boiling THF. The reaction proceeds with transylidation[15] to regenerate one molecule of the conjugate phosphonium salt $Ph_3P^+CH_2CO_2EtCl^-$ which was filtered off at the end of the reaction prior to purification of the ylides by flash chromatography. The ylides **12a–f** and **14** were obtained as colourless crystalline solids which showed the expected analytical and spectroscopic data including ^{31}P NMR signals in the range δ_P +17–19 and highly informative ^{13}C NMR spectra (Table 3) with phosphorus coupling extending throughout the P-phenyl groups, to the ester carbonyl and to the α-carbon of the phthalimidoacyl moiety. As we have found previously,[2] the coupling constant to the keto carbonyl of 4–5 Hz is considerably lower than that of 13–15 Hz to the ester carbonyl. Although the ylides all showed substantial optical rotations, their enantiomeric purity was rather difficult to determine. The NMR spectra of **12c** in the presence of the chiral lanthanide shift reagent $Eu(hfc)_3$ did show splitting and indicated ≥80% ee but this technique failed in the other cases. For **12e** the additional stereogenic centre of the *sec*-butyl group allowed direct estimation of the de from the spectra and this showed that there had been no significant racemisation (≈97% de).

In three cases the corresponding tributylphosphonium ylides **13** were obtained by treatment of **11** with $Bu_3P{=}CHCO_2Et$ (2 equiv.), generated *in situ* by BuLi treatment of the conjugate phosphonium salt. Two of these were prepared using racemic amino acids and were obtained as oils but the third, from (*S*)-leucine, was crystalline and was more readily characterised. Again the identity of the compounds was demonstrated by ^{31}P and ^{13}C NMR spectroscopy (Tables 1 and 3). A somewhat different amino acid derived ylide **16** was also obtained in good yield by using *N*-tosylprolinoyl chloride **15** in place of **11**.

The structure of these interesting multifunctional compounds was further confirmed in the case of **12c** by a single-crystal X-ray diffraction study. The unit cell contained two independent molecules of very similar structure, one of which is shown in Fig. 1. The length of the formal P=C double bond at 1.745 Å is considerably greater than for non-stabilised ylides such as $Ph_3P{=}CH_2$ (1.661 Å),[16] and this feature, together with many other aspects of the structure are in excellent agreement with the structures recently reported for a variety of ylides stabilised by both α-ester and α-keto groups.[17] The bond lengths and angles show clearly that the compound could be best regarded as having the phosphonium enolate structure **17** in which the keto carbonyl is largely in the enolate form with the P and O *syn* and a significant through-space interaction between them, while the ester carbonyl is *anti* to the ylide bond and is not significantly involved in delocalisation.

When the ylides **12** were subjected to FVP at 500 °C, dark-red products were obtained at the furnace exit. Spectroscopic examination of these showed that they consisted of a 1:1 mixture of Ph_3PO and a series of compounds isomeric with the expected acetylenic esters. Their ^{13}C NMR spectra (Table 4) showed that the symmetry of the phthalimido group had been lost and, most significantly, that instead of the expected acetylenic carbon signals there were signals at 105–110 and 190–200 ppm. This initially suggested that an allene structure might have been formed by rearrangement of the acetylenic ester. In order to obtain further information on the nature of these products, a series of isotopically labelled ylides were prepared. Thus, the ^{13}C labelled compounds **20** and **21** as well as the ^{15}N labelled ylide **23** were prepared using the same methods as for

Table 3 ^{13}C NMR spectra of the ylides **12** and **13**, δ_C ($J_{P,C}$)

				CO_2Et				P-Phenyl or butyl					
	R^1	CHR^1CO	P=*C*	CO	CH_2	CH_3	α-CH	C-1	C-2	C-3	C-4	Phthalimido	R^1 signals
12a	H	188.1 (4)	68.7 (112)	167.8 (14)	58.5	13.9	46.4 (9)	125.8 (94)	133.3 (10)	128.6 (13)	131.8 (3)	168.4, 132.7 (4ry) 133.4, 123.0	—
12b	Me	192.5 (4)	68.0 (111)	166.9 (14)	58.5	13.8	54.5 (9)	126.2 (94)	133.1 (10)	128.5 (13)	131.7 (2)	168.7, 132.4 (4ry) 133.3, 122.8	15.7
12c	Pr^i	190.7 (4)	72.1 (109)	167.0 (14)	58.6	13.7	61.7 (8)	126.5 (94)	133.2 (10)	128.3 (13)	131.5 (3)	168.5, 132.2 (4ry) 133.4, 122.9	27.2, 20.4 19.9
12d	Bu^i	192.4 (4)	68.0 (110)	166.7 (14)	58.4	13.9	57.9 (9)	126.3 (94)	133.1 (10)	128.5 (13)	131.6 (2)	168.9, 132.3 (4ry) 133.2, 122.8	37.1, 26.1 23.6, 20.9
12e	Bu^s	190.9 (4)	72.5 (109)	167.0 (15)	58.7	13.8	60.5 (8)	126.5 (94)	133.2 (10)	128.3 (12)	131.5 (2)	168.5, 132.2 (4ry) 133.4, 122.9	32.8, 26.1 16.2, 13.8
12f	Bn	191.3 (4)	68.2 (109)	166.9 (13)	58.6	13.8	60.7 (9)	126.1 (94)	133.1 (9)	128.6 (13)	131.8 (2)	168.8, 132.1 (4ry) 133.2, 122.8	139.2 (4ry) 129.0, 128.2 each (2 C), 126.0, 34.5
13c	Pr^i	191.9 (4)	68.6 (101)	167.7 (15)	58.8	14.6	62.0 (8)	21.6 (55)	24.4 (< 2)	24.0 (16)	13.6	168.5, 132.2 (4ry) 133.6, 122.8	27.2, 20.5 20.0
13d	Bu^i	193.3 (5)	65.6 (102)	167.6 (15)	58.8	14.9	57.8 (8)	21.8 (54)	24.4 (4)	24.0 (15)	13.6	169.1, 132.4 (4ry) 133.4, 123.0	37.9, 26.1 23.5, 20.9
13f	Bn	192.2 (5)	65.6 (101)	167.5 (14)	58.8	14.8	60.4 (8)	21.9 (55)	24.4 (3)	24.0 (16)	13.6	168.9, 132.1 (4ry) 133.3, 122.8	139.2 (4ry) 128.8, 128.1 each (2 C), 126.0, 35.0

Table 4 ^{13}C NMR spectra of the pyrroloisoindolediones **18**, **19** and **29**, δ_C

				CO_2Et							
	R^1	2-CO	5-CO, C-9b	CO	CH_2	CH_3	C-3	C-1	Benzo CH	C-5a, 9a	R^1 signals
18a	H	193.0	162.4, 162.1	169.1	61.3	14.1	50.2	109.0	134.6, 133.7 129.3, 124.4	133.3, 130.3	—
18b	Me	197.0	162.5, 162.3	169.2	61.2	14.3	57.7	107.3	134.5, 133.6 129.2, 124.3	133.2, 130.1	15.7
18c	Pr^i	196.2	162.8, 162.3	170.3	61.2	14.4	67.4	108.7	134.4, 133.6 129.2, 124.4	133.3, 130.1	30.9, 18.5, 16.8
18d	Bu^i	196.7	162.7, 162.3	169.6	61.1	14.3	61.0	107.7	134.4, 133.6 129.1, 124.3	133.3, 130.1	39.9, 24.5, 22.9, 22.3
18e	S-Bu^s	196.6	162.8, 162.2	170.6	61.1	14.3	66.5	108.7	134.4, 133.6 129.1, 124.3	133.2, 130.0	38.0, 26.4, 13.8, 12.1
Diastereo-isomer *		196.3	162.7	170.3			66.4	108.6			37.1, 24.2, 15.0, 12.0
18f	CH_2Ph	196.1	163.0, 162.0	170.1	61.1	14.3	62.5	106.0	134.4, 133.5 129.1, 124.3	133.2, 130.4	134.0 (4ry), 129.5, 128.3 (each 2 C), 127.1, 35.3
29	—	200.2	162.7, 162.5	168.1	61.2	14.3	64.6	106.0	134.4, 133.6 129.3, 124.3	132.8, 130.3	22.6 (2 C)
19a	H	198.9	166.4, 162.0	—	—	—	49.8	103.7	133.4, 132.8 124.4, 124.3	133.3, 130.5	—
19c	Pr^i	202.3	166.3, 162.4	—	—	—	67.2	103.5	133.3, 132.7 124.4, 124.1	133.3, 130.3	30.6, 18.7, 16.7

* Signals as above except where indicated.

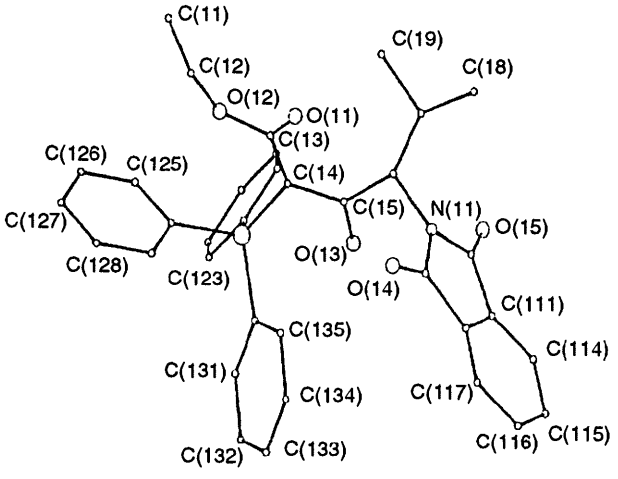
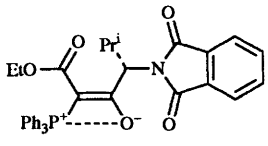


Fig. 1 X-Ray structure of the phthalimidoacyl ylide **12c**. Selected bond lengths and angles; C(14)–P(1) 1.745(9), C(118)–P(1) 1.803(6), C(14)–C(13) 1.455(8), C(13)–O(11) 1.176(12), C(15)–C(14) 1.404(8), C(15)–O(13) 1.253(7) Å; C(118)–P(1)–C(14) 114.0(3), C(13)–C(14)–P(1) 124.2(5), C(14)–C(13)–O(11) 128.1(7), C(14)–C(13)–O(12) 111.4(8), C(15)–C(14)–P(1) 110.1(5), C(15)–C(14)–C(13) 125.2(7), C(14)–C(15)–O(13) 119.4(7)°; dihedral angles P(1)–C(14)–C(15)–O(13) 10.74, P(1)–C(14)–C(13)–O(11) 146.96°; non-bonded distances P(1)–O(12) 3.024, P(1)–O(13) 2.683 Å



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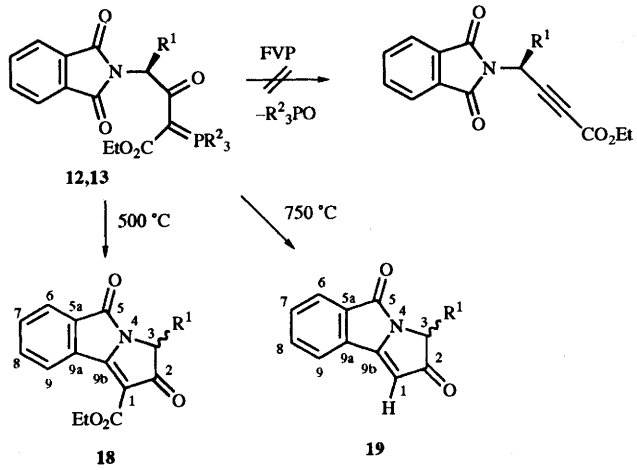
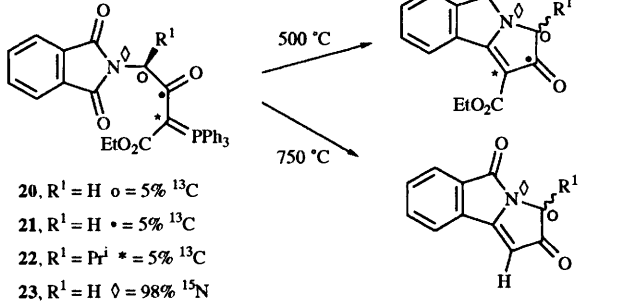
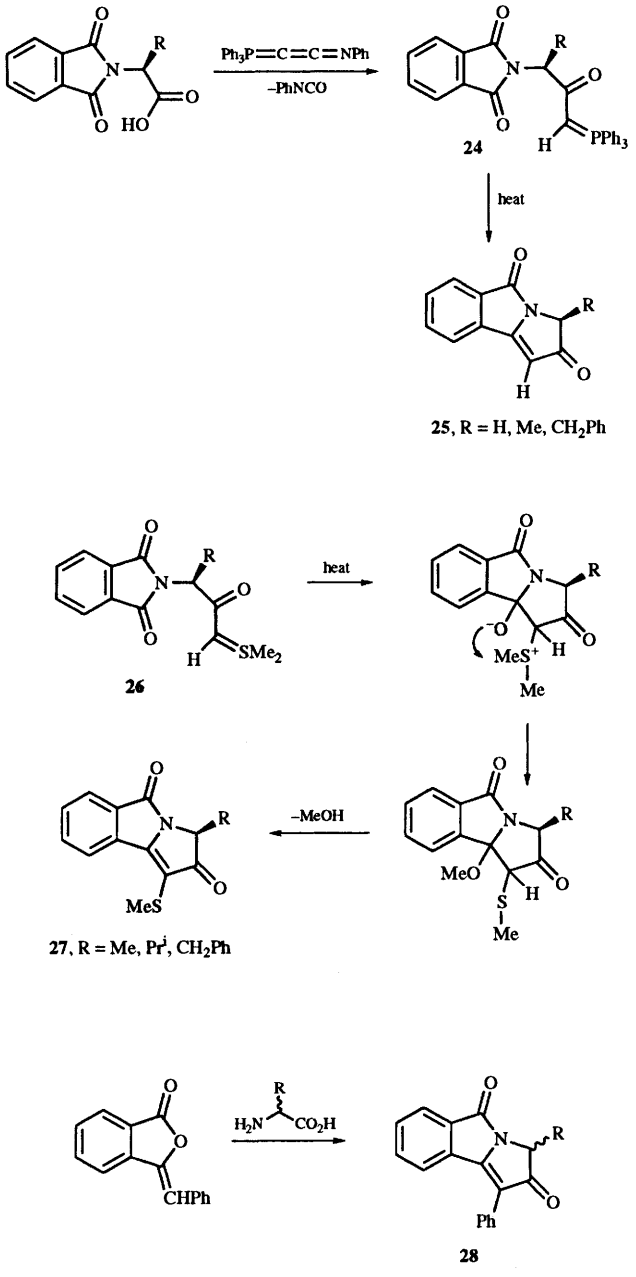
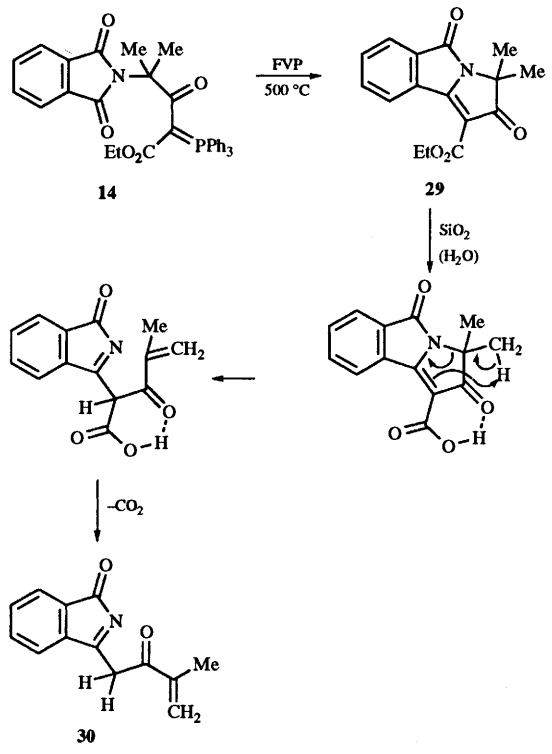




12a but starting from samples of the appropriately labelled glycine. The valine-derived compound **22** labelled at the ylide carbon was similarly obtained by using $Ph_3P{=}^{13}CHCO_2Et$ derived from labelled ethyl bromoacetate. When these were subjected to FVP at 500 °C, the ^{13}C NMR spectra of the products showed that the CHR^1, CO and ylide carbons of the starting ylides were responsible for the signals at 50.2, 193.0 and 108.7, respectively, in the products. The integrity of the phthalimido–CHR^1 fragment had also been preserved as shown by substantial one-bond ^{15}N coupling to the signals at 162.4, 162.1 and 50.2 in the product from **23**.

The structure of the products was finally deduced to be the pyrroloisoindolediones **18** resulting from loss of Ph_3PO between the ylide and one carbonyl of the phthalimido group. The high degree of polarisation in the C(1)–C(9b) double bond, which is to be expected for the β,β-diacylenamine structure, leads to ^{13}C NMR signals for C-9b in the carbonyl region scarcely moved from the position in the precursor, whereas C-1 is highly shielded. Once the structure was clear, the ^{13}C NMR spectra could be readily assigned for the whole range of examples and formed a highly consistent pattern (Table 4). Unfortunately, extensive efforts to isolate the products **18** in pure form were largely unsuccessful and their identity rests largely on spectroscopic data obtained on the 1 : 1 mixtures with Ph_3PO. Only in the case of **18f** was chromatographic separation successful in producing the product free of Ph_3PO. This was





largely due to the reactive nature of the compounds and in other cases chromatography resulted in a series of further reactions leading to complex mixtures of unidentified products. A satisfactory method for estimation of the enantiomeric purity of the products **18** has not been found, but examination of the ^1H and ^{13}C NMR spectra of **18e** showed essentially complete racemisation to have occurred and the very small rotations observed for the other products suggest that they are all racemic. The racemisation which is associated with enolisation at C-3 may have occurred either during the pyrolysis or, perhaps more likely, in solution since the C(3)–H is fairly acidic (δ_H 4.17–4.4).

The formation of **18** from **12** is in excellent agreement with the thermolysis behaviour of the only phthalimido ylides previously studied. Bestmann and co-workers[18] reported the formation of the ylides **24** by reaction of phthalimido acids with the phosphoranylideneketenimine in boiling toluene as shown, and upon simply prolonging the reaction time these were converted into the pyrroloisoindolediones **25**. Wittig reactions of cyclic imides including phthalimides are well known, although intramolecular examples are relatively rare.[19] An interesting variation has been reported for the phthalimido-acylsulfonium ylides **26** for which heating in acetonitrile leads to ring closure as shown, but with subsequent loss of methanol rather than the expected Me_2SO to give the methylsulfanylpyrroloisoindolediones **27**.[20] The closely related phenylpyrroloisoindolediones **28** have also been prepared as shown from amino acids and benzylidenephthalide.[21]

Chromatographic purification of the product **29** from the α-aminoisobutyric acid-derived ylide **14** led to isolation not only of this product but also of a most interesting decomposition product **30**. The formation of this can be explained by assuming initial hydrolysis of the ester function to give the corresponding acid. Although this is a β-oxo acid, it cannot undergo decarboxylation since the normal mechanism would involve formation of an highly strained azacyclopenta-1,2-diene intermediate. To avoid this the compound undergoes a 1,5-hydrogen migration as shown which results in ring opening and formation of an isoindolone. This can then undergo decarboxylation in the normal way to give **30**.

In an attempt to avoid the problems associated with removal of Ph_3PO from the products, the pyrolysis of the corresponding tri-butylphosphonium ylides **13** was examined in the hope that the more volatile Bu_3PO would collect in a separate band in the cold trap. Although the products **18c** and **18d** were formed in good yield by this method they were still obtained as a mixture with the phosphine oxide and separation did not prove to be any easier than before.

When the pyrolysis of **12a** and **12c** was repeated at 750 °C, Ph_3PO was again lost and the products were the corresponding pyrroloisoindolediones **19** resulting from initial cyclisation to **18** and subsequent loss of the whole ethoxycarbonyl group. Compound **19c** was obtained in pure form by chromatographic separation from the Ph_3PO but for **19a** this did not prove possible. The ^{13}C NMR spectra of these compounds (Table 4) are in good agreement with the pattern for **18** and their structure is also supported by the results of FVP of the labelled ylides **20** and **23**. At 750 °C these gave products in which the carbon at δ_C 49.8 was derived from the CHR^1 carbon of the starting material and this, together with the signals at 166.4 and 162.0, showed a one-bond coupling to ^{15}N. In a previous paper,[2] we showed that the similar loss of CO_2Et from acetylenic ethyl esters at 750 °C to give the terminal alkynes might involve either formation of ethene and CO_2 or methane

and 2 CO depending on the mechanism involved. In contrast, the volatile products from the FVP of **12** at 750 °C were mainly ethanol accompanied by a small proportion of acetaldehyde, pointing to the involvement of radical processes in the formation of **19**.

In terms of the original objective of preparing acetylenic compounds **7** and **8**, phthalimido has clearly turned out to be an unsuitable *N*-protecting group, but this method may have some value for preparation of the pyrroloisoindolediones if a way to separate these from the Ph_3PO can be devised. In the mean time we have discovered that *N*-alkoxycarbonyl protected aminoacyl ylides do undergo extrusion of Ph_3PO in the desired sense upon FVP and the results will be reported shortly.

Experimental

Melting points were recorded on a Reichert hot-stage microscope and are uncorrected. IR spectra were recorded for KBr discs or, where indicated, for solutions in CH_2Cl_2 in matched sodium chloride cells of path length 0.1 mm, on a Perkin-Elmer 1420 instrument. NMR spectra were obtained for ^1H at 300 MHz and for ^{13}C at 75 MHz on a Bruker AM300 instrument, and for ^{31}P at 32 MHz using a Varian CFT 20 instrument. All spectra were run on solutions in $CDCl_3$ with internal Me_4Si as reference for ^1H and ^{13}C and external 85% H_3PO_4 as reference for ^{31}P. Chemical shifts are reported in ppm to high frequency of the reference and coupling constants *J* are in Hz. Mass spectra were obtained on a Finnigan Incos 50 instrument and high-resolution measurements were made on an A. E. I. MS-902 spectrometer both using electron impact at 70 eV. Optical rotations were measured on an Optical Activity AA1000 polarimeter and are given in units of 10^{-1} deg cm^2 g^{-1}. Dry THF was freshly distilled from potassium benzophenone ketyl.

Ethoxycarbonylmethylene(triphenyl)phosphorane[22] and ethoxycarbonylmethyl(tributyl)phosphonium bromide[23] were prepared by literature methods. Ethoxycarbonyl[^{13}C]methylene(triphenyl)phosphorane was prepared by the same method as the unlabelled ylide starting from ethyl bromoacetate enriched to 5% ^{13}C at the $BrCH_2$ position.

Preparation of (*S*)-phthalimido acids 10

These compounds were prepared from the corresponding amino acids **9** either by heating an intimate mixture of equimolar quantities of **9** and phthalic anhydride at 120–125 °C for 5 h (Method A),[12] by treatment of an aqueous solution of **9** containing sodium carbonate (1 equiv.) with solid *N*-ethoxycarbonylphthalimide (Method B),[13] or by adding an ethyl acetate solution of *N*-ethoxycarbonylphthalimide to a vigorously stirred solution of **9** containing sodium carbonate (Method C).[14] Using these methods the following were prepared.

Phthalimidoacetic acid **10a** (Method A from glycine, 60%), mp 189–190 °C (lit.,[24] 191–192 °C).

^{13}C-Labelled phthalimidoacetic acids: 5%-[*methylene*-^{13}C]-**10a** (Method A from 5%-[*methylene*-^{13}C]-glycine, 61%) and 5%-[*carbonyl*-^{13}C]-**10a** (Method A from 5%-[*carbonyl*-^{13}C]-glycine, 72%) and ^{15}N-labelled phthalimidoacetic acid 98%-[^{15}N]-**10a** (Method A from 98%-[^{15}N]-glycine, 58%) were similarly prepared.

(2*S*)-2-Phthalimidopropionic acid **10b** [Method A from (*S*)-alanine, 65%], mp 150–151 °C (lit.,[12] 150–151 °C); $[\alpha]_D^{21}$ −22.5 (*c* 1.0 in EtOH) [lit.,[25] −22.0 (*c* 1.0 in EtOH)].

2-Methyl-2-phthalimidopropionic acid (Method A from α-aminoisobutyric acid, 84%), mp 153–154 °C (lit.,[26] 153–154 °C).

(2*S*)-3-Methyl-2-phthalimidobutyric acid **10c** [Method C from (*S*)-valine, 71%], mp 115–116 °C (lit.,[14] 115–116 °C); $[\alpha]_D^{21}$ −67.25 (*c* 2.0 in EtOH) [lit.,[14] −68.0 (*c* 2.0 in EtOH)].

(2*S*)-4-Methyl-2-phthalimidopentanoic acid **10d** [Method B from (*S*)-leucine, 35%], mp 122.5–123.5 °C (lit.,[25] 122–123 °C); $[\alpha]_D^{21}$ −24.75 (*c* 2.0 in EtOH) [lit.,[13] −25.2 (*c* 2.0 in EtOH)].

(2*S*,3*S*)-3-Methyl-2-phthalimidopentanoic acid **10e** [Method B from (*S*,*S*)-isoleucine, 40%], mp 124–124.5 °C (lit.,[14] 123–125 °C); $[\alpha]_D^{21}$ −44.4 (*c* 2.0 in EtOH) [lit.,[14] −45.4 (*c* 2.0 in EtOH)].

(2*S*)-3-Phenyl-2-phthalimidopropionic acid **10f** [Method C from (*S*)-phenylalanine, 47%], mp 186.5–187.5 °C (lit.,[25] 186–187 °C); $[\alpha]_D^{21}$ −184.5 (*c* 1.0 in EtOH) [lit.,[25] −210 (*c* 1.0 in EtOH)].

Preparation of (*S*)-phthalimido acid chlorides 11

These compounds were prepared from the acids **10** either by heating an intimate equimolar mixture of **10** and PCl_5 at 40 °C until evolution of HCl had ceased and removing the $POCl_3$ by distillation (Method D)[27] or by stirring **10** (20 mmol) in an excess of $SOCl_2$ at room temperature for 1 h followed by evaporation (Method E). Using these methods the following were prepared:

Phthalimidoacetyl chloride **11a** (Method D, 98%), mp 81–82 °C (lit.,[28] 84–85 °C).

^{13}C Labelled phthalimidoacetyl chlorides: 5%-[*methylene*-^{13}C]-**11a** (Method D, 96%) and 5%-[*chlorocarbonyl*-^{13}C]-**11a** (Method D, 98%) and [^{15}N]-**11a** (Method D, 98%) were prepared similarly.

(2*S*)-2-Phthalimidopropionyl chloride **11b** (Method E, 98%), mp 60–61 °C (lit.,[27] 73 °C for crude product); δ_C see Table 2.

2-Methyl-2-phthalimidopropionyl chloride (Method D or E, 98%), mp 83–84 °C (lit.,[26] 82–84 °C).

(2*S*)-3-Methyl-2-phthalimidobutyryl chloride **11c** (Method E, 94%), yellow oil; δ_C see Table 2.

(2*S*)-4-Methyl-2-phthalimidopentanoyl chloride **11d** (Method D, 96%), yellow oil; δ_C see Table 2.

(2*S*,3*S*)-3-Methyl-2-phthalimidopentanoyl chloride **11e** (Method E, 94%), colourless oil; δ_C see Table 2.

(2*S*)-3-Phenyl-2-phthalimidopropionyl chloride **11f** (Method E, 98%), mp 122–123 °C [lit.,[29] 131–132 °C for (±)]; δ_C see Table 2.

Preparation of [phthalimidoacyl(ethoxycarbonyl)methylene]-triphenylphosphoranes 12, 14, 16 and 20–23

A solution of ethoxycarbonylmethylene(triphenyl)phosphorane (11.2 g, 32 mmol) in dry THF (100 cm^3) was stirred at room temperature while a solution of the phthalimidoacyl chloride (16 mmol) in dry THF (50 cm^3) was added slowly. After addition the mixture was heated under reflux for 4 h and cooled. The precipitated phosphonium salt was filtered off and the filtrate evaporated to give the crude product as a red solid. This was purified using either flash chromatography or preparative TLC on SiO_2 with EtOAc, or by trituration with EtOAc or Et_2O to give the desired ylide. Using this general method the following were prepared.

Ethyl 3-oxo-4-phthalimido-2-triphenylphosphoranylidenebutyrate **12a** (67%) as colourless crystals, mp 241–242 °C (Found: C, 72.3; H, 5.0; N, 2.5. $C_{32}H_{26}NO_5P$ requires C, 71.8; H, 4.9; N, 2.6%); ν_{max}/cm^{-1} 1770, 1712, 1695, 1590, 1440, 1405, 1370, 1293, 1105, 1090, 950, 747, 720 and 692; δ_H 8.0–7.4 (19 H, m), 5.13 (2 H, d, J_P 2), 3.80 (2 H, q, *J* 8) and 0.73 (3 H, t, *J* 8); δ_C see Table 3; δ_P +17.2; *m*/*z* (M^+ 535 not apparent), 375 (M^+ − $PhthCH_2$, 15%), 303 (8), 278 (30), 277 (50), 262 (16), 257 (M^+ − Ph_3PO, 7), 229 (6), 201 (45), 185 (70), 183 (70), 128 (55) and 77 (100).

Ethyl 5%-[4-^{13}C]-3-oxo-4-phthalimido-2-triphenylphosphoranylidenebutyrate **20** (79%); physical and spectroscopic properties identical with those of **12a** save for 5 × enhancement of δ_C 46.4.

Ethyl 5%-[3-^{13}C]-3-oxo-4-phthalimido-2-triphenylphosphoranylidenebutyrate **21** (51%); physical and spectroscopic properties identical with those of **12a** save for 5 × enhancement of δ_C 188.1.

Ethyl [^{15}N]-3-oxo-4-phthalimido-2-triphenylphosphoranylidenebutyrate **23** (72%); spectroscopic properties identical with those of **12a** save for the ^{13}C NMR signals at δ_C 46.4. (dd, $^3J_{P,C}$ 9, $^1J_{N,C}$ 12) and 168.4 (d, $^1J_{N,C}$ 14).

Ethyl (4*S*)-3-oxo-4-phthalimido-2-triphenylphosphoranylidenepentanoate **12b** (45%) as colourless crystals, mp 141–142 °C (Found: C, 71.7; H, 5.4; N, 2.5. $C_{33}H_{28}NO_5P$ requires C, 72.1; H, 5.1; N, 2.5%); $[\alpha]_D^{21}$ +13.7 (*c* 1.0 in CH_2Cl_2); ν_{max}/cm^{-1} 1770, 1708, 1668, 1568, 1440, 1390, 1312, 1280, 1227, 1108, 1295, 1283, 754, 728 and 692; δ_H 8.0–7.5 (19 H, m), 6.16 (1 H, q of d, *J* 8, 2), 3.80 (2 H, q, *J* 7), 2.01 (3 H, d, *J* 8) and 0.70 (3 H, t, *J* 7); δ_C see Table 3; δ_P +18.0; *m*/*z* 549 (M^+, 0.2%), 504 (1), 376 (21), 375 (100), 347 (7), 303 (16), 277 (60), 199 (25), 183 (22) and 77 (35).

Ethyl (4*S*)-5-methyl-3-oxo-4-phthalimido-2-triphenylphosphoranylidenehexanoate **12c** (56%) as colourless crystals, mp 172–173 °C (Found: C, 73.3; H, 5.65; N, 2.4. $C_{35}H_{32}NO_5P$ requires C, 72.8; H, 5.6; N, 2.4%); $[\alpha]_D^{20.5}$ −60.35 (*c* 1.0 in CH_2Cl_2); ν_{max}/cm^{-1} 1763, 1710, 1660, 1560, 1437, 1380, 1310, 1270, 1216, 1104, 1088, 1070, 888, 780, 755, 720 and 692; δ_H 7.80 (2 H, m), 7.7–7.5 (8 H, m), 7.45–7.3 (9 H, m), 5.65 (1 H, d, *J* 10), 3.68 (2 H, q, *J* 7), 2.95 (1 H, m), 1.05 (3 H, d, *J* 6), 0.90 (3 H, d, *J* 6) and 0.60 (3 H, t, *J* 7); δ_C see Table 3; δ_P +18.4; *m*/*z* (M^+ 577 not apparent), 375 (M^+ − PhthCHPr^i, 100%), 347 (5), 303 (24), 277 (23), 257 (14), 201 (29), 183 (28), 148 (27), 130 (40), 104 (30) and 77 (95).

(±)-Ethyl 5%-[2-^{13}C]-5-methyl-3-oxo-4-phthalimido-2-triphenylphosphoranylidenehexanoate **22** (74%); physical and spectroscopic properties identical with those of (±)-**12c** save for 5 × enhancement of δ_C 72.1.

Ethyl (4*S*)-6-methyl-3-oxo-4-phthalimido-2-triphenylphosphoranylideneheptanoate **12d** (80%) as colourless crystals, mp 172–173 °C (Found: C, 73.3; H, 5.9; N, 2.35. $C_{36}H_{34}NO_5P$ requires C, 73.1; H, 5.8; N, 2.4%); $[\alpha]_D^{20.5}$ +34.5 (*c* 1.0 in CH_2Cl_2); ν_{max}/cm^{-1} 1770, 1710, 1660, 1580, 1468, 1440, 1382, 1300, 1242, 1162, 1105, 1082, 853, 748, 722 and 690; δ_H 7.75–7.4 (19 H, m), 6.13 (1 H, dd, *J* 13, 3), 3.82 (2 H, q, *J* 7), 2.78 (1 H, t of d, *J* 13, 4), 2.18 (1 H, t of d, *J* 13, 4), 1.63 (1 H, m), 1.08 (3 H, d, *J* 6), 1.00 (3 H, d, *J* 6) and 0.73 (3 H, t, *J* 7); δ_C see Table 3; δ_P +18.1.

Ethyl (4*S*,5*S*)-5-methyl-3-oxo-4-phthalimido-2-triphenylphosphoranylideneheptanoate **12e** (76%) as colourless crystals, mp 181–182 °C (Found: C, 73.1; H, 6.0; N, 2.4. $C_{36}H_{34}NO_5P$ requires C, 73.1; H, 5.8; N, 2.4%); $[\alpha]_D^{21}$ −32.6 (*c* 1.1 in CH_2Cl_2); ν_{max}/cm^{-1} 1774, 1714, 1658, 1560, 1440, 1250, 1104, 1282, 1000, 909, 756, 718 and 693; δ_H 8.0–7.4 (19 H, m), 5.95 (1 H, d, *J* 10), 3.81 (2 H, q, *J* 7), 3.0–2.8 (1 H, m), 1.5–1.2 (1 H, m), 1.09 (3 H, d, *J* 6), 1.1–0.7 (4 H, m), 0.71 (3 H, t, *J* 7); δ_C see Table 3; δ_P +18.4; *m*/*z* (M^+ 591 not apparent), 535 (M^+ − C_4H_8, 1%), 375 (87), 347 (6), 303 (16), 277 (40), 257 (16), 211 (23), 183 (25), 160 (22), 130 (25) and 77 (100).

Ethyl (4*S*)-3-oxo-5-phenyl-4-phthalimido-2-triphenylphosphoranylidenepentanoate **12f** (83%) as colourless crystals, mp 116–117 °C (Found: C, 75.0; H, 5.15; N, 2.2. $C_{39}H_{32}NO_5P$ requires C, 74.9; H, 5.2; N, 2.2%); $[\alpha]_D^{19.5}$ +11.75 (*c* 1.0 in CH_2Cl_2); ν_{max}/cm^{-1} 1772, 1710, 1654, 1578, 1437, 1380, 1305, 1270, 1102, 1082, 868, 746, 720 and 690; δ_H 7.7–7.0 (24 H, m), 6.48 (1 H, m), 4.0–3.7 (4 H, m) and 0.69 (3 H, t, *J* 7); δ_C see Table 3; δ_P +18.1; *m*/*z* 625 (M^+, 0.1%), 580 (0.5), 503 (0.4), 434 (0.5), 421 (0.5), 405 (0.5), 376 (50), 375 (100), 347 (M^+ − Ph_3PO, 25), 303 (30), 277 (40), 201 (24) and 183 (40).

Ethyl 4-methyl-3-oxo-4-phthalimido-2-triphenylphosphoranylidenepentanoate **14** (35%) as colourless crystals (slightly impure), mp 152–153 °C; δ_H 7.9–7.3 (19 H, m), 3.2 (2 H, q, *J* 7), 1.87 (6 H, s) and 0.33 (3 H, t, *J* 7); δ_P +17.9; *m*/*z* (M^+ not apparent), 188 (100), 148 (34), 130 (44), 104 (22), 76 (25) and 66 (27). Satisfactory analytical data could not be obtained for this compound since chromatography or recrystallisation were consistently accompanied by partial hydrolysis and/or decomposition to give unidentified impurities of similar R_F and solubility.

(*S*)-*N*-Tosylprolinoylethoxycarbonylmethylene(triphenyl)-phosphorane 16

A reaction as described above but with (*S*)-*N*-tosylprolinoyl chloride **15**[30] in place of the phthalimido acid chloride gave the slightly impure product (71%) as pale yellow crystals, mp 138–139 °C (Found: C, 66.6; H, 5.3; N, 2.4%; M, 399.1393. $C_{34}H_{34}NO_5PS$ requires C, 68.1; H, 5.7; N, 2.3%; *M* − Ts − OEt, 399.1388); $[\alpha]_D^{21}$ −74.7 (*c* 3.86 in CH_2Cl_2); ν_{max}/cm^{-1} 1740, 1646, 1570, 1484, 1440, 1375, 1336, 1300, 1190, 1154, 1103, 1092, 1012, 822, 753, 710, 692 and 660; δ_H 7.75–7.65 (8 H, m), 7.55–7.4 (9 H, m), 7.21 (2 H, half AB pattern, *J* 9), 3.72 (2 H, q, *J* 7), 3.35 (1 H, m), 3.20 (1 H, m), 2.39 (3 H, s), 2.10, 1.92, 1.76, 1.57 and 1.25 (each 1 H, m) and 0.65 (3 H, t, *J* 7); $\delta_C(J_{C,P})$ 194.9 (CO), 167.6 (14, CO_2Et), 142.5 and 136.4 (Ts-4°), 133.3 (10, Ph-C-2), 131.6 (2, Ph-C-4), 129.4 (Ts-CH), 128.5 (13, Ph-C-3), 127.6 (Ts-CH), 126.4 (93, Ph-C-l), 69.5 (110, P=C), 63.5 (9, α-CH), 58.4 (Et-CH_2), 48.9, 31.6 and 24.5 (ring CH_2's), 21.5 (Ts-Me) and 13.7 (Et-CH_3); δ_P +16.5; *m*/*z* (M^+ 599 not apparent), 444 (M^+ − Ts, 2%), 399 (5), 398 (5), 375 (100), 347 (6), 303 (14), 279 (8), 277 (9), 262 (8), 201 (12) and 91 (45).

Preparation of [phthalimidoacyl(ethoxycarbonyl)methylene]-tributylphosphoranes 13

A suspension of ethoxycarbonylmethyl(tributyl)phosphonium bromide (7.4 g, 20 mmol) in dry THF (30 cm^3) was stirred at room temperature under N_2 while a solution of butyllithium in hexane (20 mmol) was added. After 30 min the phthalimido acid chloride (10 mmol) in dry THF (20 cm^3) was added dropwise. After being stirred for 12 h, the mixture was added to water (100 cm^3) and extracted with ethyl acetate (2 × 100 cm^3). The extracts were washed with aqueous $NaHCO_3$ and water and then dried and evaporated to give the product. By this method the following were prepared.

(±)-Ethyl 5-methyl-3-oxo-4-phthalimido-2-tributylphosphoranylidenehexanoate 13c. As a brown oil (80%) (bp not determined owing to decomposition on heating) (Found: M, 517.2998. $C_{29}H_{44}NO_5P$ requires *M*, 517.2957); δ_H 8.0–7.75 (4 H, m), 5.72 (1 H, d, *J* 10), 4.13 (2 H, q, *J* 7), 3.02 (1 H, m), 2.2–2.1 (6 H, m) and 1.75–0.85 (30 H, m); δ_C see Table 3; δ_P +25.9; *m*/*z* 517 (M^+, 1%), 472 (2), 446 (2), 371 (2), 315 (100), 287 (5), 271 (3), 259 (3), 243 (8), 219 (10) and 202 (22).

Ethyl (4*S*)-6-methyl-3-oxo-4-phthalimido-2-tributylphosphoranylideneheptanoate 13d. As colourless crystals, (47%), mp 149–151 °C (Found: C, 67.45; H, 8.8; N, 2.6; M, 531.3093. $C_{30}H_{46}NO_5P$ requires C, 67.8; H, 8.7; N, 2.6%; *M*, 531.3114); δ_H 8.0–7.75 (4 H, m), 6.15 (1 H, dd, *J* 12, 4), 4.26 (2 H, q, *J* 7), 2.62 (1 H, t of d, *J* 13, 3), 2.3–1.7 (7 H, m), 1.6–1.25 (13 H, m), 1.30 (3 H, t, *J* 7) and 1.05–0.8 (15 H, m); δ_C see Table 3; δ_P +26.2; *m*/*z* 531 (M^+, 3%), 486 (2), 475 (8), 419 (3), 315 (100), 287 (8), 259 (10), 243 (16), 219 (24), 160 (52) and 130 (30).

(±)-Ethyl 3-oxo-5-phenyl-4-phthalimido-2-tributylphosphoranylidenepentanoate 13f. As a brown oil (81%) (bp not determined owing to decomposition on heating) (Found: M, 565.2918. $C_{33}H_{44}NO_5P$ requires *M*, 565.2957); δ_H 7.7–7.65 (2 H, m), 7.6–7.5 (2 H, m), 7.4–7.35 (2 H, m), 7.2–7.0 (3 H, m), 6.34 (1 H, dd, *J* 12, 4), 4.22 (2 H, q, *J* 7), 3.83 (1 H, half AB pattern of d, *J* 14, 12), 3.60 (1 H, half AB pattern of d, *J* 14, 4), 2.2–2.1 (6 H, m), 1.5–1.35 (12 H, m), 1.32 (3 H, t, *J* 7) and 0.96 (9 H, t, *J* 6); δ_C see Table 3; δ_P +25.9.

Flash vacuum pyrolysis of the ylides 12–14

The apparatus used was as described previously.[31] All pyrolyses were conducted at pressures in the range 10^{-3}–10^{-2} Torr. Under these conditions the contact time in the hot zone was estimated to be ≈10 ms. In all cases a mixture of the product and Ph_3PO collected at the furnace exit and these were separated by preparative TLC for **18f**, **19c** and **29**, although in

the last case this led to partial hydrolysis and decarboxylation to afford **30**. In the remaining cases attempts at separation failed and the products were analysed spectroscopically as a mixture with Ph_3PO.

Compound 18a. FVP of the ylide **12a** (2.0 g) at 500 °C gave a red gum (1.9 g) at the furnace exit which was shown to consist largely of a 1:1 mixture of Ph_3PO and ethyl 2,5-dioxo-2,3-dihydro-5*H*-pyrrolo[1,2-*a*]isoindole-1-carboxylate **18a**; ν_{max}/cm^{-1} 1730, 1715, 1692 and 1612; δ_H 8.90 (1 H, m), 7.8–7.5 (3 H, m), 4.52 (2 H, q, *J* 7), 4.35 (2 H, s) and 1.45 (3 H, t, *J* 7); δ_C see Table 4.

FVP of the ^{13}C labelled ylide **20** (500 mg) at 500 °C gave a red gum at the furnace exit which had spectroscopic properties identical with those of **18a** save for 5 × enhancement of the ^{13}C NMR signal at δ_C 50.2.

FVP of the ^{13}C labelled ylide **21** (500 mg) at 500 °C gave a red gum at the furnace exit which had spectroscopic properties identical with those of **18a** save for 5 × enhancement of the ^{13}C NMR signal at δ_C 193.0.

FVP of the ^{15}N labelled ylide **23** (100 mg) at 500 °C gave a red gum at the furnace exit which had spectroscopic properties identical with those of **18a** save for the ^{13}C NMR signals at δ_C 162.4 (d, $^1J_{N,C}$ 13), 162.1 (d, $^1J_{N,C}$ 3) and 50.2 (d, $^1J_{N,C}$ 11).

Compound 18b. FVP of the ylide **12b** (120 mg) at 500 °C gave a red gum (104 mg) at the furnace exit which was shown to consist largely of a 1:1 mixture of Ph_3PO and *ethyl* 3-*methyl*-2,5-*dioxo*-2,3-*dihydro*-5H-*pyrrolo*[1,2-a]*isoindole*-1-*carboxylate* **18b** (Found: M, 271.0831. $C_{15}H_{13}NO_4$ requires *M*, 271.0845); ν_{max}/cm^{-1} (CH_2Cl_2) 1730, 1700 and 1600; δ_H 8.90 (1 H, m), 7.9–7.7 (3 H, m), 4.52 (2 H, q, *J* 7), 4.35 (1 H, q, *J* 7), 1.70 (3 H, d, *J* 7) and 1.45 (3 H, t, *J* 7); δ_C see Table 4; *m*/*z* 271 (M$^+$, 9%), 225 (15), 197 (10), 172 (20), 145 (24), 130 (30), 69 (52) and 43 (100).

Compound 18c. FVP of the ylide **12c** (110 mg) at 500 °C gave a red gum (52 mg) at the furnace exit which was shown to consist largely of a 1:1 mixture of Ph_3PO and *ethyl* 3-*isopropyl*-2,5-*dioxo*-2,3-*dihydro*-5H-*pyrrolo*[1,2-a]*isoindole*-1-*carboxylate* **18c** (Found: M, 299.1190. $C_{17}H_{17}NO_4$ requires *M*, 299.1158); ν_{max}/cm^{-1} 1730, 1710, 1690 and 1598; δ_H 8.75 (1 H, m), 7.9–7.7 (3 H, m), 4.44 (2 H, q, *J* 7), 4.29 (1 H, d, *J* 3), 2.73 (1 H, septet of d, *J* 7, 3), 1.45 (3 H, t, *J* 7), 1.12 (3 H, d, *J* 7) and 1.08 (3 H, d, *J* 7); δ_C see Table 4; *m*/*z* 299 (M$^+$, 4%), 244 (34), 172 (48), 145 (18) and 130 (48).

FVP of the ^{13}C labelled ylide **22** (95 mg) at 500 °C gave a red gum (90 mg) at the furnace exit which had spectroscopic properties identical with those of **18c** save for 5 × enhancement of the ^{13}C NMR signal at δ_C 108.7.

Compound 18d. FVP of the ylide **12d** (590 mg) at 500 °C gave a red gum (580 mg) at the furnace exit which was shown to consist largely of a 1:1 mixture of Ph_3PO and ethyl 3-isobutyl-2,5-dioxo-2,3-dihydro-5*H*-pyrrolo[1,2-*a*]isoindole-1-carboxylate **18d**; ν_{max}/cm^{-1} 1730 and 1615; δ_H 8.90 (1 H, m), 7.9–7.7 (3 H, m), 4.52 (2 H, q, *J* 7), 4.40 (1 H, m), 2.66 (1 H, d, *J* 7), 2.00 (1 H, m), 1.48 (3 H, d, *J* 7) and 0.96 (6 H, d, *J* 6); δ_C see Table 4; *m*/*z* 313 (M$^+$, 15%), 278 (22), 277 (100), 244 (22), 224 (30), 172 (25), 145 (28) and 130 (33).

Compound 18e. FVP of the ylide **12e** (505 mg) at 500 °C gave a red gum (472 mg) at the furnace exit which was shown to consist largely of a 1:1 mixture of Ph_3PO and ethyl 3-*sec*-butyl-2,5-dioxo-2,3-dihydro-5*H*-pyrrolo[1,2-*a*]isoindole-1-carboxylate **18e**; ν_{max}/cm^{-1} (CH_2Cl_2) 1720 and 1610; δ_H 8.78 (1 H, m), 7.9–7.7 (3 H, m), 4.42 (2 H, q, *J* 7), 4.34 (1 H, m), 2.53 (1 H, m), 1.7–1.2 (2 H, m), 1.43 (3 H, t, *J* 7) and 1.0–0.85 (6 H, m); δ_C see Table 4; *m*/*z* 313 (M$^+$, 4%), 300 (3), 293 (4), 277 (100), 244 (48), 216 (27), 172 (32), 145 (26) and 130 (50).

Compound 18f. FVP of the ylide **12f** (40 mg) at 500 °C gave a red gum (38 mg) at the furnace exit which was separated by preparative TLC on SiO_2 (EtOAc) to give at R_F 0.5 Ph_3PO and at R_F 0.8 *ethyl* 3-*benzyl*-2,5-*dioxo*-2,3-*dihydro*-5H-*pyrrolo*-[1,2-a]*isoindole*-1-*carboxylate* **18f** (15 mg, 67%) as an oil (bp not determined owing to decomposition on heating) (Found: M, 347.1132. $C_{21}H_{17}NO_4$ requires *M*, 347.1158); ν_{max}/cm^{-1} (CH_2Cl_2) 1740, 1720 and 1604; δ_H 8.62 (1 H, m), 7.95–7.65 (3 H, m), 7.07 (5 H, s), 4.36 (2 H, q, *J* 7), 3.78 and 3.53 (2 H, AB pattern, *J* 20) and 1.38 (3 H, t, *J* 7); δ_C see Table 4; *m*/*z* 347 (M$^+$, 4%), 317 (6), 272 (10), 245 (40), 226 (28), 198 (34), 173 (26), 145 (25), 130 (55), 118 (50) and 91 (100).

Compounds 29 and 30. FVP of the ylide **14** (380 mg) at 500 °C gave a red gum at the furnace exit which was separated by preparative TLC on SiO_2 (Et_2O) to give two components. At R_F 0.8 *ethyl* 3,3-*dimethyl*-2,5-*dioxo*-2,3-*dihydro*-5H-*pyrrolo*[1,2-a]*isoindole*-1-*carboxylate* **29** (105 mg, 55%) as an oil (bp not determined owing to decomposition on heating) (Found: M, 285.1008. $C_{16}H_{15}NO_4$ requires *M*, 285.1001); ν_{max}/cm^{-1}(film) 1730, 1718, 1696, 1610, 1407, 1298, 1240, 1156, 1132, 1028, 872, 778 and 720; δ_H 8.95 (1 H, m), 8.0–7.8 (3 H, m), 4.52 (2 H, q, *J* 7), 1.66 (6 H, s) and 1.46 (3 H, t, *J* 7); δ_C see Table 4; *m*/*z* 285 (M$^+$, 36%), 240 (42), 213 (82), 188 (100), 185 (60), 144 (40), 130 (86), 127 (48), 102 (48) and 76 (47).

At R_F 0.9 3-(3-*methyl*-2-*oxobut*-3-*enyl*)*isoindolone* **30** (34 mg, 24%) as an oil (bp not determined owing to decomposition on heating) (Found: M, 213.0807. $C_{13}H_{11}NO_2$ requires *M*, 213.0790); ν_{max}/cm^{-1}(film) 2960, 2925, 2855, 1728, 1604, 1466, 1376, 1260 and 802; δ_H 8.1–7.8 (4 H, m), 5.46 (1 H, q, *J* 1), 5.24 (1 H, q, *J* 0.5), 2.17 (3 H, m) and 1.87 (2 H, s); *m*/*z* 213 (M$^+$, 40%), 188 (86), 187 (100), 130 (63), 104 (30) and 76 (38).

Compound 18c. FVP of the ylide **13c** (860 mg) at 500 °C gave two fractions: in the cold trap an oil (680 mg) which was largely Bu_3PO, and at the furnace exit a red gum (138 mg) which was mainly **18c**, identical with that obtained from **12c** above, but still significantly contaminated by Bu_3PO.

Compound 18d. FVP of the ylide **13d** (550 mg) at 300 °C resulted in a substantial residue in the inlet tube which proved to be the unchanged ylide. The red gum (220 mg) at the furnace exit was shown to consist largely of a 1:1 mixture of Bu_3PO and **18d** with spectroscopic properties identical with the material produced from **12d**.

Compound 19a. FVP of the ylide **12a** (435 mg) at 750 °C gave a red gum (410 mg) at the furnace exit which was shown to consist largely of a 1:1 mixture of Ph_3PO and 2,3-dihydro-5*H*-pyrrolo[1,2-*a*]isoindole-2,5-dione **19a**; ν_{max}/cm^{-1} 1772, 1722 and 1624; δ_C see Table 4. The fraction in the cold trap consisted mainly of ethanol accompanied by a very small proportion of acetaldehyde.

FVP of the ^{13}C labelled ylide **20** (500 mg) at 750 °C gave a red gum at the furnace exit which had spectroscopic properties identical with those of **19a** save for 5 × enhancement of the ^{13}C NMR signal at δ_C 49.8.

FVP of the ^{15}N labelled ylide **23** (50 mg) at 750 °C gave a red gum at the furnace exit which had spectroscopic properties identical with those of **19a** above save for the ^{13}C NMR signals at δ_C 166.4 (d, $^1J_{N,C}$ 11), 162.0 (d, $^1J_{N,C}$ 15) and 49.8 (d, $^1J_{N,C}$ 10).

Compound 19c. FVP of the ylide **12c** (400 mg) at 750 °C gave a red gum at the furnace exit which was separated by preparative TLC on SiO_2 (Et_2O) to give at R_F 0.8 3-*isopropyl*-2,3-*dihydro*-5H-*pyrrolo*[1,2-a]*isoindole*-2,5-*dione* **19c** (63 mg, 40%) as an oil (bp not determined owing to decomposition on heating) (Found: M, 227.0933. $C_{14}H_{13}NO_2$ requires *M*, 227.0946); ν_{max}/cm^{-1} 1720 and 1625; δ_H 8.1–7.8 (4 H, m), 6.12 (1 H, s), 4.32 (1 H, d, *J* 3), 2.74 (1 H, septet of d, *J* 7, 3), 1.16 (3 H, d, *J* 7) and 1.06 (3 H, d, *J* 7); δ_C see Table 4; *m*/*z* 227 (M$^+$, 10%), 185 (100), 156 (27), 129 (60), 101 (70) and 75 (60).

X-Ray structure determination

Crystal data for **12c**: $C_{35}H_{32}NO_5P$, M = 577.78, triclinic space group $P\bar{1}$; a = 13.428(7), b = 12.200(6), c = 11.650(7) Å, α = 118.51(5), β = 115.70(5), γ = 75.79(4)°, V = 1509.39 Å^3, Z = 2, D_c = 1.31 g cm^{-3}, R = 0.051, final R_g = 0.071 for 4243 data with $I > 4\sigma(I)$ and 750 parameters. Data were recorded at 293 K using Mo-Kα radiation and the structure was solved by direct methods and refined using full-matrix least-squares analysis.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre; for details see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1.

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