# Flash vacuum pyrolysis of stabilised phosphorus ylides. Part 7.<sup>1</sup> Cyclisation of amino acid derived $\alpha$ -phthalimidoacyl ylides to give pyrroloisoindolediones

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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<sup>2</sup><sub>3</sub>PO 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 <sup>13</sup>C and <sup>15</sup>N labelling experiments, but owing to their high reactivity complete separation from the phosphine oxide was not generally possible even when Bu<sub>3</sub>PO rather than Ph<sub>3</sub>PO 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<sub>3</sub>PO 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,<sup>2</sup> 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 aamino acid-derived ylides 6, which should be readily accessible from the acid chlorides 5 and potentially provide access to derivatives of the  $\alpha$ ,  $\beta$ -acetylenic  $\gamma$ -amino acids 7 and the prop-2ynylic amines 8. Relatively few compounds of these types have been prepared before,<sup>3</sup> but they are of considerable importance as potential mechanism-based inhibitors of medicinally important enzymes.<sup>4</sup> In particular, 7 ( $R^1 = H$ ) and a number of N-substituted analogues have been shown to be effective GABA mimics,<sup>5</sup> and related compounds have been proposed for the therapeutic treatment of alcoholism and as anti-tumour agents.<sup>6</sup> 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,<sup>7</sup> 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  $\alpha$ -amino acids 9 and the analogues 7 extended by insertion of a C=C unit, a concept recently generalised by Chauvin<sup>9</sup> 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  $\mathbb{R}^2$  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.<sup>10</sup> 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  $Ph_3P=CHC(O)CH(\mathbb{R})NH_2$ ,<sup>11</sup> 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  $\alpha$ -amino acids 9 were converted into their phthalimido derivatives 10 either by heating with phthalic anhydride in the absence of solvent,<sup>12</sup> or by treatment in basic aqueous solution with N-ethoxycarbonylphthalimide in the solid form<sup>13</sup> or as a solution in ethyl acetate.<sup>14</sup> 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<sub>5</sub> or SOCl<sub>2</sub>. 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  $\alpha$ -aminoisobutyric acid to obtain the starting material for 14. The fully assigned <sup>13</sup>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

	R <sup>1</sup>	Yield of 10 from 9 (%)	Yield of <b>11</b> from <b>10</b> (%)	Yield of <b>12</b> from <b>11</b> (%)	$\delta_{ m P}$	Yield of 13 from 11 (%)	$\delta_{ m P}$
a	Н	60	98	67	17.2		
b	Me	65	98	45	18.0		
с	Pr <sup>i</sup>	71	94	56	18.4	$80(\pm)$	25.9
d	Bu <sup>i</sup>	35	96	80	18.1	47	26.2
e	Bu <sup>s</sup>	40	94	76	18.4		
f	CH <sub>2</sub> Ph	47	98	83	18.1	81 (±)	25.9
14	*	(84)	(98)	(56)	(18.4)	. ,	
16		` <u> </u>	<u> </u>	(71)	(16.5)		

**Table 2** <sup>13</sup>C NMR spectra of phthalimido acid chlorides 11,  $\delta_{\rm C}$ 

	D I	Phthalimido							
	K-	ring CH	4°	СО	COCI	α-C	R <sup>1</sup> signals		
b	Me	134.6, 123.8	131.8	167.1	172.1	55.9	15.4		
с	Pr <sup>i</sup>	134.7, 124.0	131.4	167.0	169.9	66.4	29.2, 20.4, 19.1		
d	Bu <sup>i</sup>	134.7, 123.9	131.5	167.0	172.0	59.1	37.3, 25.1, 23.0, 21.0		
е	Bu <sup>s</sup>	134.8, 124.0	131.4	167.0	169.9	65.8	35.1, 25.5, 16.5, 10.8		
f	CH <sub>2</sub> Ph	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<sub>3</sub>P=CHCO<sub>2</sub>Et (2 equiv.) in boiling THF. The reaction proceeds with transylidation<sup>15</sup> 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 <sup>31</sup>P NMR signals in the range  $\delta_P$  + 17–19 and highly informative <sup>13</sup>C NMR spectra (Table 3) with phosphorus coupling extending throughout the P-phenyl groups, to the ester carbonyl and to the  $\alpha$ -carbon of the phthalimidoacyl moiety. As we have found previously,<sup>2</sup> 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)<sub>3</sub> did show splitting and indicated  $\ge 80\%$  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 ( $\approx 97\%$  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 Xray 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<sub>3</sub>P=CH<sub>2</sub> (1.661 Å),<sup>16</sup> 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  $\alpha$ -ester and  $\alpha$ -keto groups.<sup>17</sup> 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<sub>3</sub>PO and a series of compounds isomeric with the expected acetylenic esters. Their <sup>13</sup>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 <sup>13</sup>C labelled compounds 20 and 21 as well as the <sup>15</sup>N labelled ylide 23 were prepared using the same methods as for Published on 01 January 1996. Downloaded by Northeastern University on 21/01/2014 12:36:22.

**Table 3** <sup>13</sup>C NMR spectra of the ylides **12** and **13**,  $\delta_{\rm C}$  ( $J_{\rm P,C}$ )

				$CO_2Et$				P-Phenyl or	butyl					
	R <sup>1</sup>	CHR <sup>1</sup> CO	P=C	8	CH <sub>2</sub>	CH3	a-CH	C-1	C-2	C-3	C-4	Phthalimido	R <sup>1</sup> signals	
12a	Н	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	$\mathbf{Pr}^{i}$	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 <sup>i</sup>	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 <sup>s</sup>	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	
130	pri	101 0 (4)	(101) 4 89	15177151	58 8	14.6	(8) 0 (8)	21 6 (55)	744(<7)	24.0.016)	13.6	168 5 132 2 (4rv)	each (2 C), 126.0, 34.5 27 2 20 5	
<b>X</b> 1		(+) (-1()	(101) 0.00	((1) /	0.00	0.4	10) 0.70	((()) () 17	(7~) +.+7	(01) 0. <del>1</del> 7	0.01	133.6, 122.8	20.0	
13d	Bu <sup>i</sup>	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	

CO.F

				00220							
	R <sup>1</sup>	2-CO	5-CO, C-9b	СО	CH <sub>2</sub>	CH <sub>3</sub>	C-3	C-1	Benzo CH	C-5a, 9a	R <sup>1</sup> signals
18a	Н	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	133.2, 130.1	15.7
18c	Pr <sup>i</sup>	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 <sup>i</sup>	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 <sup>s</sup>	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 <sub>2</sub> Ph	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	Н	198.9	166.4, 162.0		—		49.8	103.7	133.4, 132.8 124.4, 124.3	133.3, 130.5	_
19c	Pr <sup>i</sup>	202.3	166.3, 162.4	4	—	<u> </u>	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



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 <sup>13</sup>C NMR spectra of the products showed that the CHR<sup>1</sup>, 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<sup>1</sup> fragment had also been preserved as shown by substantial one-bond <sup>15</sup>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<sub>3</sub>PO



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  $\beta$ , $\beta$ -diacylenamine structure, leads to <sup>13</sup>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 <sup>13</sup>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<sub>3</sub>PO. Only in the case of 18f was chromatographic separation successful in producing the product free of Ph<sub>3</sub>PO. 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 <sup>1</sup>H and <sup>13</sup>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  $(\delta_{\rm H} \, 4.17 - 4.4).$ 

-PhNCO

SMe<sub>2</sub>

-MeOH

CO<sub>2</sub>H

н

heat

25, R = H, Me,  $CH_2Ph$ 

( MeS<sup>+</sup> Ъ

MeO

Мe

н

Ġе

Ph

28

24

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<sup>18</sup> 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.<sup>19</sup> An interesting variation has been reported for the phthalimidoacylsulfonium ylides 26 for which heating in acetonitrile leads



to ring closure as shown, but with subsequent loss of methanol rather than the expected Me<sub>2</sub>SO to give the methylsulfanylpyrroloisoindolediones 27.20 The closely related phenylpyrroloisoindolediones 28 have also been prepared as shown from amino acids and benzylidenephthalide.<sup>21</sup>

Chromatographic purification of the product 29 from the  $\alpha$ 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  $\beta$ -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 1,5hydrogen 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<sub>3</sub>PO from the products, the pyrolysis of the corresponding tri-butylphosphonium ylides 13 was examined in the hope that the more volatile Bu<sub>3</sub>PO 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<sub>3</sub>PO 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<sub>3</sub>PO but for 19a this did not prove possible. The <sup>13</sup>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  $\delta_{\rm C}$  49.8 was derived from the CHR<sup>1</sup> carbon of the starting material and this, together with the signals at 166.4 and 162.0, showed a one-bond coupling to <sup>15</sup>N. In a previous paper,<sup>2</sup> we showed that the similar loss of CO<sub>2</sub>Et from acetylenic ethyl esters at 750 °C to give the terminal alkynes might involve either formation of ethene and CO<sub>2</sub> 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<sub>2</sub>Cl<sub>2</sub> in matched sodium chloride cells of path length 0.1 mm, on a Perkin-Elmer 1420 instrument. NMR spectra were obtained for <sup>1</sup>H at 300 MHz and for <sup>13</sup>C at 75 MHz on a Bruker AM300 instrument, and for <sup>31</sup>P at 32 MHz using a Varian CFT 20 instrument. All spectra were run on solutions in CDCl<sub>3</sub> with internal Me<sub>4</sub>Si as reference for <sup>1</sup>H and <sup>13</sup>C and external 85%  $H_3PO_4$  as reference for <sup>31</sup>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  $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$ . Dry THF was freshly distilled from potassium benzophenone ketyl.

Ethoxycarbonylmethylene(triphenyl)phosphorane<sup>22</sup> and ethoxycarbonylmethyl(tributyl)phosphonium bromide<sup>23</sup> were prepared by literature methods. Ethoxycarbonyl[<sup>13</sup>C]methylene(triphenyl)phosphorane was prepared by the same method as the unlabelled ylide starting from ethyl bromoacetate enriched to 5% <sup>13</sup>C at the BrCH<sub>2</sub> 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),<sup>12</sup> by treatment of an aqueous solution of 9 containing sodium carbonate (1 equiv.) with solid *N*-ethoxycarbonylphthalimide (Method B),<sup>13</sup> or by adding an ethyl acetate solution of *N*-ethoxycarbonylphthalimide to a vigorously stirred solution of 9 containing sodium carbonate (Method C).<sup>14</sup> Using these methods the following were prepared.

Phthalimidoacetic acid 10a (Method A from glycine, 60%), mp 189–190 °C (lit.,<sup>24</sup> 191–192 °C).

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

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

2-Methyl-2-phthalimidopropionic acid (Method A from  $\alpha$ -aminoisobutyric acid, 84%), mp 153–154 °C (lit.,<sup>26</sup> 153–154 °C).

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

(2S)-4-Methyl-2-phthalimidopentanoic acid 10d [Method B from (S)-leucine, 35%], mp 122.5-123.5 °C (lit.,<sup>25</sup> 122-

123 °C);  $[\alpha]_D^{21} - 24.75$  (*c* 2.0 in EtOH) [lit.,<sup>13</sup> - 25.2 (*c* 2.0 m<sup>2</sup>) EtOH)].

(2S,3S)-3-Methyl-2-phthalimidopentanoic acid **10e** [Method B from (*S*,*S*)-isoleucine, 40%], mp 124–124.5 °C (lit.,<sup>14</sup> 123–125 °C);  $[\alpha]_D^{21}$  –44.4 (*c* 2.0 in EtOH) [lit.,<sup>14</sup> –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.,<sup>25</sup> 186–187 °C);  $[\alpha]_{D}^{21}$  –184.5 (*c* 1.0 in EtOH) [lit.,<sup>25</sup> –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<sub>5</sub> at 40 °C until evolution of HCl had ceased and removing the POCl<sub>3</sub> by distillation (Method D)<sup>27</sup> or by stirring 10 (20 mmol) in an excess of SOCl<sub>2</sub> 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.,<sup>28</sup> 84–85 °C).

<sup>13</sup>C Labelled phthalimidoacetyl chlorides: 5%-[methylene-<sup>13</sup>C]-11a (Method D, 96%) and 5%-[chlorocarbonyl-<sup>13</sup>C]-11a (Method D, 98%) and [<sup>15</sup>N]-11a (Method D, 98%) were prepared similarly.

(2S)-2-Phthalimidopropionyl chloride 11b (Method E, 98%), mp 60–61 °C (lit.,<sup>27</sup> 73 °C for crude product);  $\delta_{\rm C}$  see Table 2.

2-Methyl-2-phthalimidopropionyl chloride (Method D or E, 98%), mp 83-84 °C (lit.,<sup>26</sup> 82-84 °C).

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

(2S)-4-Methyl-2-phthalimidopentanoyl 'chloride 11d (Method D, 96%), yellow oil;  $\delta_c$  see Table 2.

(2S,3S)-3-Methyl-2-phthalimidopentanoyl chloride 11e (Method E, 94%), colourless oil;  $\delta_{\rm C}$  see Table 2.

(2*S*)-3-Phenyl-2-phthalimidopropionyl chloride 11f (Method E, 98%), mp 122–123 °C [lit.,<sup>29</sup> 131–132 °C for  $(\pm)$ ];  $\delta_c$  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<sup>3</sup>) was stirred at room temperature while a solution of the phthalimidoacyl chloride (16 mmol) in dry THF (50 cm<sup>3</sup>) 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<sub>2</sub> with EtOAc, or by trituration with EtOAc or Et<sub>2</sub>O 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%);  $v_{max}/cm^{-1}$  1770, 1712, 1695, 1590, 1440, 1405, 1370, 1293, 1105, 1090, 950, 747, 720 and 692;  $\delta_H$  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);  $\delta_C$  see Table 3;  $\delta_P$  +17.2; m/z (M<sup>+</sup> 535 not apparent), 375 (M<sup>+</sup> – PhthCH<sub>2</sub>, 15%), 303 (8), 278 (30), 277 (50), 262 (16), 257 (M<sup>+</sup> – Ph<sub>3</sub>PO, 7), 229 (6), 201 (45), 185 (70), 183 (70), 128 (55) and 77 (100).

Ethyl 5%-[4-<sup>13</sup>C]-3-oxo-4-phthalimido-2-triphenylphosphoranylidenebutyrate 20 (79%); physical and spectroscopic properties identical with those of 12a save for 5 × enhancement of  $\delta_c$  46.4.

Ethyl 5%-[3-<sup>13</sup>C]-3-oxo-4-phthalimido-2-triphenylphosphoranylidenebutyrate **21** (51%); physical and spectroscopic properties identical with those of **12a** save for 5 × enhancement of  $\delta_c$  188.1. Ethyl [<sup>15</sup>N]-3-oxo-4-phthalimido-2-triphenylphosphoranylidenebutyrate **23** (72%); spectroscopic properties identical with those of **12a** save for the <sup>13</sup>C NMR signals at  $\delta_{\rm C}$  46.4. (dd, <sup>3</sup>J<sub>P,C</sub> 9, <sup>1</sup>J<sub>N,C</sub> 12) and 168.4 (d, <sup>1</sup>J<sub>N,C</sub> 14).

Ethyl (4S)-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<sub>2</sub>Cl<sub>2</sub>);  $v_{max}$ /cm<sup>-1</sup> 1770, 1708, 1668, 1568, 1440, 1390, 1312, 1280, 1227, 1108, 1295, 1283, 754, 728 and 692;  $\delta_H$  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);  $\delta_C$  see Table 3;  $\delta_P$  +18.0; *m/z* 549 (M<sup>+</sup>, 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<sub>2</sub>Cl<sub>2</sub>);  $\nu_{max}/cm^{-1}$  1763, 1710, 1660, 1560, 1437, 1380, 1310, 1270, 1216, 1104, 1088, 1070, 888, 780, 755, 720 and 692;  $\delta_H$  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);  $\delta_C$  see Table 3;  $\delta_P$  +18.4; *m/z* (M<sup>+</sup> 577 not apparent), 375 (M<sup>+</sup> – PhthCHPr<sup>i</sup>, 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-<sup>13</sup>C]-5-methyl-3-oxo-4-phthalimido-2triphenylphosphoranylidenehexanoate **22** (74%); physical and spectroscopic properties identical with those of (±)-**12c** save for 5 × enhancement of  $\delta_{\rm C}$  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<sub>2</sub>Cl<sub>2</sub>);  $\nu_{max}/cm^{-1}$  1770, 1710, 1660, 1580, 1468, 1440, 1382, 1300, 1242, 1162, 1105, 1082, 853, 748, 722 and 690;  $\delta_H$  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);  $\delta_C$  see Table 3;  $\delta_P$  +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<sub>2</sub>Cl<sub>2</sub>);  $\nu_{max}/cm^{-1}$  1774, 1714, 1658, 1560, 1440, 1250, 1104, 1282, 1000, 909, 756, 718 and 693;  $\delta_H$  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);  $\delta_C$  see Table 3;  $\delta_P$  +18.4; m/z (M<sup>+</sup> 591 not apparent), 535 (M<sup>+</sup> – C<sub>4</sub>H<sub>8</sub>, 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<sub>39</sub>H<sub>32</sub>NO<sub>5</sub>P requires C, 74.9; H, 5.2; N, 2.2%);  $[\alpha]_D^{19.5}$  +11.75 (*c* 1.0 in CH<sub>2</sub>Cl<sub>2</sub>);  $\nu_{max}/cm^{-1}$  1772, 1710, 1654, 1578, 1437, 1380, 1305, 1270, 1102, 1082, 868, 746, 720 and 690;  $\delta_H$  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);  $\delta_C$  see Table 3;  $\delta_P$  +18.1; m/z 625 (M<sup>+</sup>, 0.1%), 580 (0.5), 503 (0.4), 434 (0.5), 421 (0.5), 405 (0.5), 376 (50), 375 (100), 347 (M<sup>+</sup> – Ph<sub>3</sub>PO, 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;  $\delta_{\rm H}$  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);  $\delta_{\rm P}$  +17.9; m/z (M<sup>+</sup> 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  $R_{\rm F}$  and solubility.

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

A reaction as described above but with (S)-N-tosylprolinoyl chloride 15<sup>30</sup> 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<sub>2</sub>Cl<sub>2</sub>);  $v_{max}/cm^{-1}$ 1740, 1646, 1570, 1484, 1440, 1375, 1336, 1300, 1190, 1154, 1103, 1092, 1012, 822, 753, 710, 692 and 660;  $\delta_{\rm H}$  7.75–7.65 (8 H, m), 7.55-7.4 (9 H, m), 7.21 (2 H, half AB pattern, J9), 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);  $\delta_{\rm C}(J_{\rm C,P})$ 194.9 (CO), 167.6 (14, CO2Et), 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, a-CH), 58.4 (Et-CH<sub>2</sub>), 48.9, 31.6 and 24.5 (ring CH<sub>2</sub>'s), 21.5 (Ts-Me) and 13.7 (Et-CH<sub>3</sub>);  $\delta_P$  + 16.5; m/z (M<sup>+</sup> 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<sup>3</sup>) was stirred at room temperature under N<sub>2</sub> 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<sup>3</sup>) was added dropwise. After being stirred for 12 h, the mixture was added to water (100 cm<sup>3</sup>) and extracted with ethyl acetate (2 × 100 cm<sup>3</sup>). The extracts were washed with aqueous NaHCO<sub>3</sub> 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<sub>29</sub>H<sub>44</sub>NO<sub>5</sub>P requires *M*, 517.2957);  $\delta_{\rm H}$  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);  $\delta_{\rm C}$  see Table 3;  $\delta_{\rm P}$  +25.9; *m/z* 517 (M<sup>+</sup>, 1%), 472 (2), 446 (2), 371 (2), 315 (100), 287 (5), 271 (3), 259 (3), 243 (8), 219 (10) and 202 (22).

**Ethyl** (4.5)-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);  $\delta_H$  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);  $\delta_C$  see Table 3;  $\delta_P$ + 26.2; m/z 531 (M<sup>+</sup>, 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);  $\delta_H7.7-7.65$  (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);  $\delta_C$  see Table 3;  $\delta_P$  + 25.9.

### Flash vacuum pyrolysis of the ylides 12-14

The apparatus used was as described previously.<sup>31</sup> 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  $\approx 10$  ms. In all cases a mixture of the product and Ph<sub>3</sub>PO 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<sub>3</sub>PO and ethyl 2,5-dioxo-2,3-dihydro-5*H*-pyrrolo[1,2-*a*]isoindole-1-carboxylate **18a**;  $\nu_{\rm max}/$  cm<sup>-1</sup> 1730, 1715, 1692 and 1612;  $\delta_{\rm H}$  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);  $\delta_{\rm C}$  see Table 4.

FVP of the <sup>13</sup>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 <sup>13</sup>C NMR signal at  $\delta_{\rm C}$  50.2.

FVP of the <sup>13</sup>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 <sup>13</sup>C NMR signal at  $\delta_{\rm C}$  193.0.

FVP of the <sup>15</sup>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 <sup>13</sup>C NMR signals at  $\delta_{\rm C}$  162.4 (d, <sup>1</sup> $J_{\rm N,C}$  13), 162.1 (d, <sup>1</sup> $J_{\rm N,C}$  3) and 50.2 (d, <sup>1</sup> $J_{\rm N,C}$  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<sub>3</sub>PO and *ethyl* 3-methyl-2,5-dioxo-2,3-dihydro-5H-pyrrolo[1,2-a]isoindole-1-carboxylate **18b** (Found: M, 271.0831. C<sub>15</sub>H<sub>13</sub>NO<sub>4</sub> requires M, 271.0845);  $v_{max}/cm^{-1}$  (CH<sub>2</sub>Cl<sub>2</sub>) 1730, 1700 and 1600;  $\delta_{\rm H}$  8.90 (1 H, m), 7.9– 7.7 (3 H, m), 4.52 (2 H, q, J7), 4.35 (1 H, q, J7), 1.70 (3 H, d, J7) and 1.45 (3 H, t, J7);  $\delta_{\rm C}$  see Table 4; m/z 271 (M<sup>+</sup>, 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<sub>3</sub>PO 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);  $v_{max}/cm^{-1}$  1730, 1710, 1690 and 1598;  $\delta_H$  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);  $\delta_C$  see Table 4; m/z 299 (M<sup>+</sup>, 4%), 244 (34), 172 (48), 145 (18) and 130 (48).

FVP of the <sup>13</sup>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 <sup>13</sup>C NMR signal at  $\delta_{\rm C}$  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<sub>3</sub>PO and ethyl 3-isobutyl-2,5-dioxo-2,3-dihydro-5*H*-pyrrolo[1,2-*a*]isoindole-1-carboxylate **18d**;  $v_{max}/cm^{-1}$  1730 and 1615;  $\delta_{H}$  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);  $\delta_{C}$  see Table 4; *m/z* 313 (M<sup>+</sup>, 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<sub>3</sub>PO and ethyl 3-*sec*-butyl-2,5-dioxo-2,3-dihydro-5*H*-pyrrolo[1,2-*a*]isoindole-1-carboxylate **18e**;  $v_{max}/cm^{-1}$  (CH<sub>2</sub>Cl<sub>2</sub>) 1720 and 1610;  $\delta_{\rm H}$  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);  $\delta_{\rm C}$  see Table 4; *m*/*z* 313 (M<sup>+</sup>, 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<sub>2</sub> (EtOAc) to give at  $R_F$  0.5 Ph<sub>3</sub>PO 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:

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M, 347.1132.  $C_{21}H_{17}NO_4$  requires M, 347.1158); w Article Maline (CH<sub>2</sub>Cl<sub>2</sub>) 1740, 1720 and 1604;  $\delta_H$  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);  $\delta_C$  see Table 4; m/z 347 (M<sup>+</sup>, 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<sub>2</sub> (Et<sub>2</sub>O) to give two components. At  $R_{\rm F}$  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<sub>16</sub>H<sub>15</sub>NO<sub>4</sub> requires *M*, 285.1001);  $\nu_{\rm max}/\rm{cm}^{-1}$ (film) 1730, 1718, 1696, 1610, 1407, 1298, 1240, 1156, 1132, 1028, 872, 778 and 720;  $\delta_{\rm H}$  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);  $\delta_{\rm C}$  see Table 4; *m/z* 285 (M<sup>+</sup>, 36%), 240 (42), 213 (82), 188 (100), 185 (60), 144 (40), 130 (86), 127 (48), 102 (48) and 76 (47).

At  $R_{\rm F}$  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<sub>13</sub>H<sub>11</sub>NO<sub>2</sub> requires *M*, 213.0790);  $\nu_{\rm max}$ /cm<sup>-1</sup>(film) 2960, 2925, 2855, 1728, 1604, 1466, 1376, 1260 and 802;  $\delta_{\rm H}$  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<sup>+</sup>, 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<sub>3</sub>PO, 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<sub>3</sub>PO.

**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<sub>3</sub>PO 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<sub>3</sub>PO and 2,3-dihydro-5*H*pyrrolo[1,2-*a*]isoindole-2,5-dione **19a**;  $v_{max}/cm^{-1}$  1772, 1722 and 1624;  $\delta_c$  see Table 4. The fraction in the cold trap consisted mainly of ethanol accompanied by a very small proportion of acetaldehyde.

FVP of the <sup>13</sup>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 <sup>13</sup>C NMR signal at  $\delta_{\rm c}$  49.8.

FVP of the <sup>15</sup>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 <sup>13</sup>C NMR signals at  $\delta_{\rm C}$  166.4 (d, <sup>1</sup> $J_{\rm N,C}$  11), 162.0 (d, <sup>1</sup> $J_{\rm N,C}$  15) and 49.8 (d, <sup>1</sup> $J_{\rm N,C}$  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<sub>2</sub> (Et<sub>2</sub>O) 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<sub>14</sub>H<sub>13</sub>NO<sub>2</sub> requires *M*, 227.0946);  $v_{max}$ /cm<sup>-1</sup> 1720 and 1625;  $\delta_H 8.1$ -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);  $\delta_C$  see Table 4; *m*/*z* 227 (M<sup>+</sup>, 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 P1; a = 13.428(7), b = 12.200(6), c = 11.650(7) Å,  $\alpha = 118.51(5)$ ,  $\beta = 115.70(5)$ ,  $\gamma = 75.79(4)^\circ$ , V = 1509.39 Å<sup>3</sup>, Z = 2,  $D_c = 1.31$  g cm<sup>-3</sup>, 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-K $\alpha$  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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