HETEROCYCLES, Vol. 76, No. 2, 2008, pp. 1401 - 1423. © The Japan Institute of Heterocyclic Chemistry
Received, 19th April, 2008, Accepted, 23rd June, 2008, Published online, 26th June, 2008. COM-08-S(F)12

TRIPHENYLPHOSPHORANYLIDENE SUBSTITUTED HETEROCYCLES AS VERSATILE INTERMEDIATES

Alan R. Katritzky,*[1] Adam S. Vincek,[1] and Peter J. Steel[2]

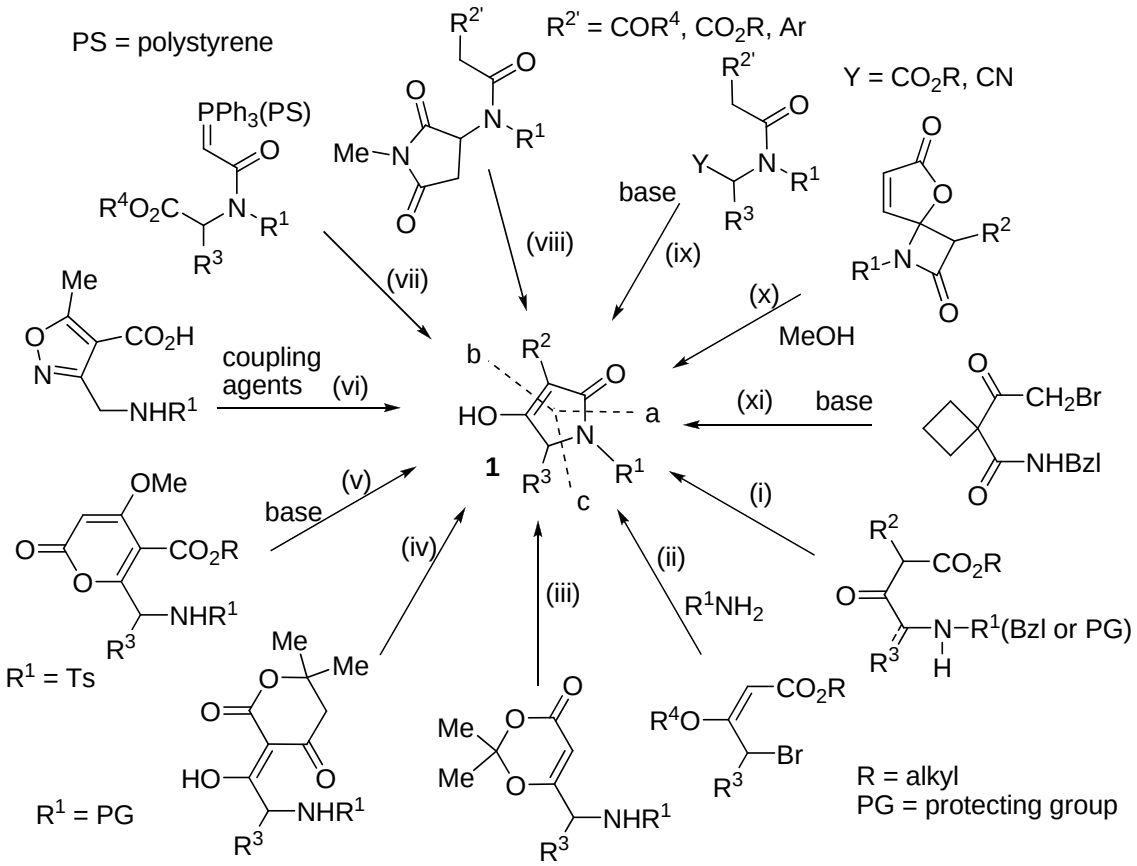
[1]Center for Heterocyclic Compounds, University of Florida, Department of Chemistry, Gainesville, Florida 32611-7200, USA, (E-mail: katritzky@chem.ufl.edu) [2]Department of Chemistry, University of Canterbury, Christchurch, New Zealand

Abstract – *N*-Cbz-(*α*-aminoacyl)benzotriazoles **5a–e** reacted with (stabilized-methylene)triphenylphosphoranes **6** and **13** to give the corresponding esters **7a–e** (66–91%) or nitriles **14a–e** (63–85%). Deprotection of *N*-Cbz-*γ*-amino-*β*-oxo-*α*-triphenylphosphoranylidene esters **7a–d** induced cyclization to form 2,4-dioxo-3-triphenylphosphoranylidene pyrrolidines **9a–c** (20–98%) and 1,3-dioxo-2-triphenylphosphoranylidene tetrahydropyrrolizine **9d** (79%). *N*-Cbz-*δ*-amino-*β*-oxo-*α*-triphenylphosphoranylidene ester **7e** cyclized to form 2,4-dioxo-3-triphenylphosphoranylidene piperidine **9e** (60%). Deprotection of *N*-Cbz-*γ*-amino-*β*-oxo-*α*-triphenylphosphoranylidene nitriles **14a–d** similarly formed 5-amino-4-triphenylphosphonio-2,4-dihydropyrrol-3-one bromides **15a–c** (70–72%) and 3-ammonio-2-triphenylphosphoniotetrahydro-pyrrolizin-1-one dibromide **15d** (66%). *N*-Methyl pyrrolidine **11** was transformed into 3,3-dibromopyrrolidin-2,4-dione **16** (79%), 3,3-dibromo-5-hydroxypyrrolidin-2,4-dione **17** (88%), 4-azido-3-bromopyrrol-2-one **18** (84%), and 4-benzotriazol-1-ylpyrrol-2-one **19** (92%).

INTRODUCTION

The discovery of the occurrence of the tetramic acid ring system, a tautomer of pyrrolidin-2,4-dione, in a number of natural products and pigments coincided with the discovery of their diverse biological activities.[1] Reported syntheses of tetramic acids (Scheme 1) are by the intramolecular formation of bond *a*(i–vi), *b*(vii–ix) or *c*(x, xi). Bond *a* is made by cyclization of (i) *γ*-amino-*β*-keto esters;[2] (ii)

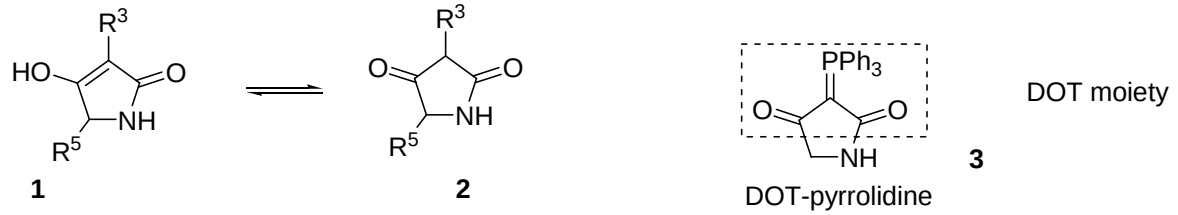
γ-bromoesters;[3] (iii) γ-amino cyclic-enol esters;[4] (iv) 5-(2-amino-1-hydroxyethyliden)-2,2-dimethyl-1,3-dioxan-4,6-diones (Meldrum's acid esters);[5] (v) aminomethyl pyrone esters;[6] or (vi) aminomethyl isoxazole carboxylic acids.[7] Bond *b* is formed by (vii) Wittig olefination,[8] of α-triphenylphosphoranylidene amides with immobilized ylides;[9] (viii) Dieckmann type cyclization of succinimides[10] and (ix) other Dieckmann cyclizations.[11] Bond *c* is closed by (x) alcoholysis of spiro-β-lactams;[12] and (xi) nucleophilic cyclizations of γ-bromo β-keto carboxamides.[13]



Scheme 1. General Tetramic Acid Syntheses by the Formation of Bonds *a*, *b*, or *c*

Natural tetramic acids, exist as enolized lactams **1** of pyrrolidin-2,4-diones **2**.[1] Earlier reports of compounds containing the DOT(dioxotriphenylphosphoranylidene)-moiety as part of the DOT-pyrrolidine substructure **3** include a byproduct during the preparation of showdomycin,[14] a flash vacuum pyrolysis method (FVP, 600–900 °C, 10^2 Torr)[15] accompanied by thermal extrusion of triphenylphosphine oxide to form an alkyne and anomalous "spontaneous"[16] cyclizations at rt,[17] and a byproduct without logical explanation of its formation.[18] The DOT-piperidine substructure was previously synthesized but no further reactions were attempted.[16a,19] We previously reported

stereospecific C-acylations of (carboxymethylene)triphenylphosphorane with *N*-protected peptidic (α-aminoacyl)benzotriazoles to give peptidic α-triphenylphosphoranylidene esters.[20] Attempted hydrogenolysis of *N*-Cbz-γ-amino-β-oxo-α-triphenylphosphoranylidene ester **7b** gave DOT-pyrrolidine **9b** (45%) by cyclization of the expected linear free amine. Crystalline DOT-pyrrolidines are stable to aldehydes,[21] strong bases,[22] and high temperatures,[15] and we now show DOT-pyrrolidines form versatile intermediates. We now report the first convenient synthesis of DOT-pyrrolidines **9a–c**, DOT-tetrahydropyrrolizine **9d**, DOT-piperidine **30**, 5-amino-4-triphenylphosphonio-2,4-dihydropyrrol-3-one bromides **15a–c**, and 3-ammonio-2-triphenylphosphoniotetrahydropyrrolizin-1-one dibromide **15d**.

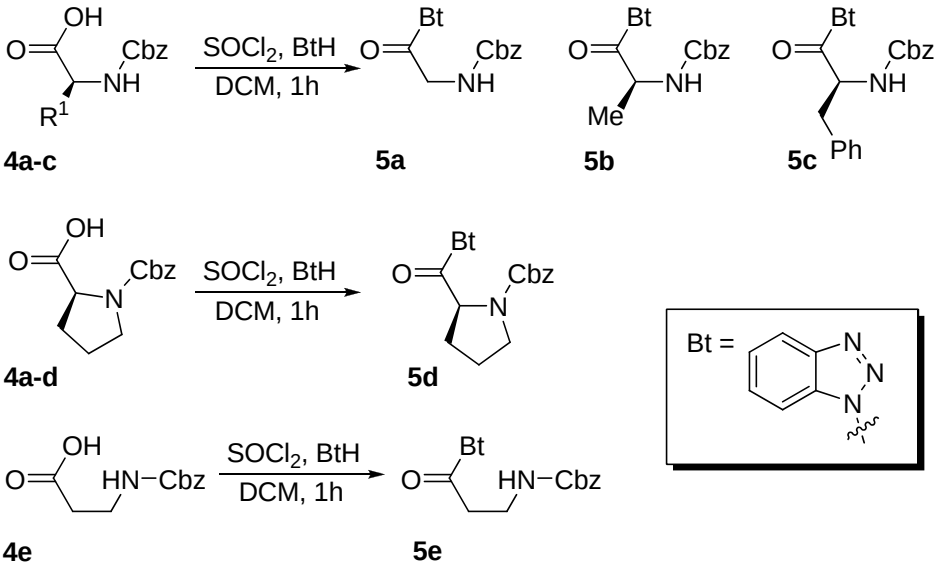


RESULTS AND DISCUSSION

N-Cbz-amino acids **4a–e** were converted by known methodology into *N*-Cbz-aminoacylbenzotriazoles **5a–e** (Scheme 2). *N*-Acylbenzotriazoles have been reported by the Katritzky group as efficient neutral coupling reagents for chiral N-acylation, regioselective C-acylation, and O-acylation of aldehydes. They are sufficiently reactive to form amide bonds at ambient temperature, but stable enough to resist side reactions.[23] N-Protected (α-aminoacyl)benzotriazoles are efficient reagents for acylation of amino amides, amino sulfonamides, amino thiol esters, small peptides with alkyl side chains, small peptides with multi-functional groups , and amino ketones.[23,24]

In the present work, *N*-Cbz-(aminoacyl)benzotriazoles **5a–e** C-acylated (ethoxycarboylmethylene) triphenylphosphorane (**6**) under microwave irradiation (Table 1) to give *N*-Cbz-γ-amino-β-oxo-α-triphenylphosphoranylidene esters **7a–c** (83–91%) (Scheme 3), **7d** (66%) (Scheme 4), and *N*-Cbz-δ-amino-β-oxo-α-triphenylphosphoranylidene ester **7e** (77%) (Scheme 4), following our recently developed procedure.[20] We supported the structures of **7a–c** in that communication. We confirmed by ^{1}H-NMR, ^{13}C-NMR, and elemental analysis structure **7d** suggested by Aitken.[25] The structure of novel

7e was supported by ^{1}H-NMR, ^{13}C-NMR, and elemental analysis. A single cavity microwave synthesizer provides an effective reproducible and safe technique for promoting a variety of reactions and shortening reaction times while reducing pollution by using less solvent.[26] The ^{13}C-NMR chemical shifts and J_{PC} coupling values of the γ-C, β-keto, α-C=P, and ester/amide carbon signals (Table 2) show the P-(*ipso*)Ph, P-(*ortho*)Ph, P-(*meta*)Ph, and P-(*para*)Ph carbon signals remain essentially invariant and the ^{13}C-NMR chemical shifts and J_{PC} values, to be insensitive to changes in solvent and temp,[27] but reflecting local electron densities.[28]



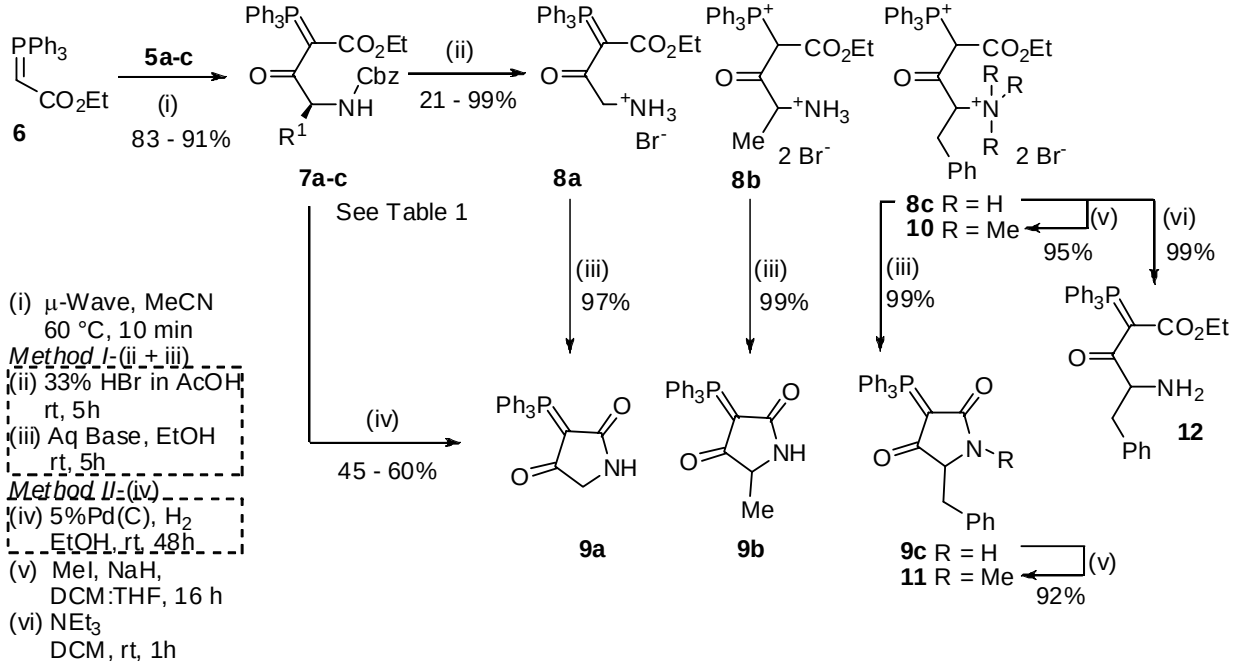
Scheme 2

Hydrobromic acid N-deprotected **7a–e** to give γ-amino-β-oxo-α-triphenylphosphoranylidene ester salts **8a–c** (21–99%), **8d** (90%), and δ-amino-β-oxo-α-triphenylphosphoranylidene ester salt **8e** (92%) for *Method I*.[29] A broad signal around 9 ppm in the ^{1}H-NMR spectra supported P-salt formation. The salt mixtures were isolated by column chromatography (SiO_2). Extension of the stirring time in the 33% hydrobromic acid solution for up to 5h resulted in formation of dibromide salts, which were easily isolated as white powders by filtration from diethyl ether in most cases. In one case the highly hygroscopic dibromide salt resulted in a low yield of achiral monobromide ammonium salt **8a** (21%) due to loss during isolation. Melting points were generally not sharp with initial conversion to amorphous semi-solids typically in the range between 100–200 °C, followed by a session of bubbling and recrystallization, which then melted again above 200 °C probably due to the thermal cyclization involving the loss of ethanol. The structures of novel **8a–e** were supported by ^{1}H-NMR, ^{13}C-NMR, and elemental analysis.

Table 1. Isolated Yields for α-Amino Acid Intermediates and Cyclized Products

Entry	R^1	R^2	*N*-Cbz Amino Acid **4**	**7**	**8**	**9**	**9′**[c]	**14**	**15**
a	H	H	Cbz-Glycine	91	21[a]	20(97)	60	85	71
b	Me	H	Cbz-(L)Alanine	86	99	98(99)	45	79	70
c	CH_2Ph	H	Cbz-(L)Phenylalanine	83	91	90(99)	45	79	72
d	R^1–$(CH_2)_3$–R^2		Cbz-(L)Proline	66	90	79(88[b])	45[b]	64	66[b]

9 yield from *Method I*-(ii + iii), with the yield for step (iii) given in parenthesis. **9′** yield from *Method II*-(iv). [a]Hygroscopic. [b]Tetrahydropyrrolizine. [c]Yield from Recrystallization



Scheme 3

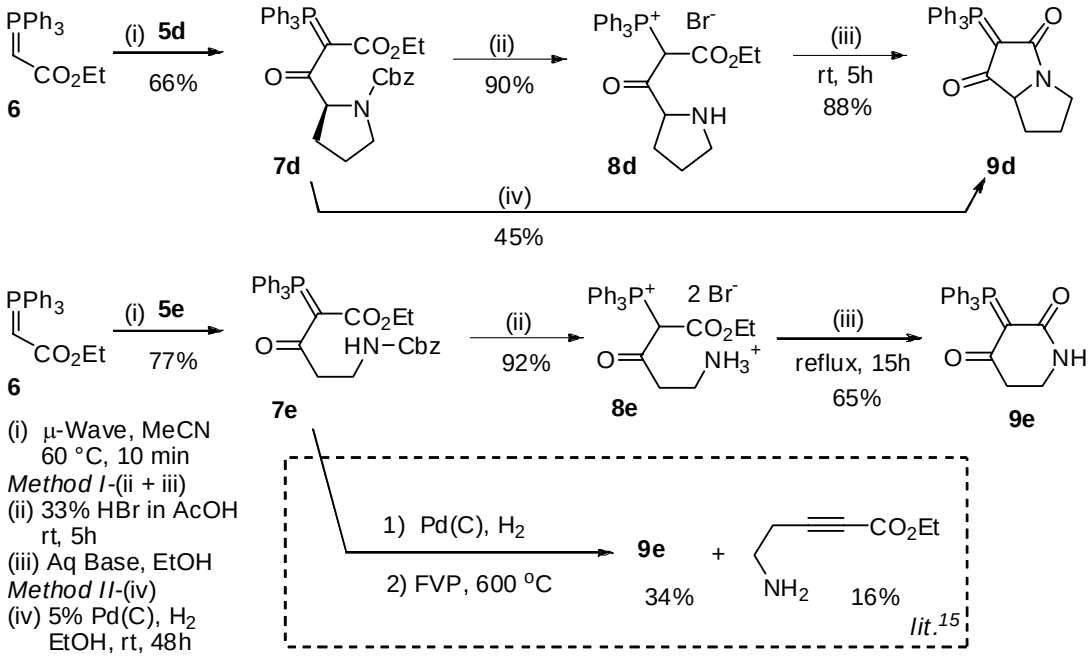
The DOT-pyrrolidines **9a–c** and DOT-pyrrolizines **9d** were prepared by *Method I* (20–98%) and by *Method II* (45–60%) and DOT-piperidine **9e** was prepared by *Method I* (60%). The starting salts **8a–d** were dissolved in ethanol and then aq base was added, which resulted in precipitation of a white solid. Extraction with dichloromethane gave DOT-pyrrolidines **9a–c** (97–99%) and DOT-pyrrolizines **9d** (88%) to complete *Method I*. N-Methylation of **8c** with methyl iodide and sodium hydride gave linear N-trimethylated DOT-salt **10** (95%). N-Methylation of **9c** afforded DOT-pyrrolidine **11** (92%). Treatment of **8c** with triethylamine in dichloromethane cleanly gave the linear free amine **12**. Hydrogenolysis of **7a–d** with palladium on charcoal in ethanol required 48 h and crystallization gave **9b–d** (45%) for *Method II*. To furnish achiral **9a** (60%), with *Method II* conditions, heating under reflux

in ethanol was required. Achiral **8e** was heated under reflux in aq base to afford **9e** (65%). We provide supporting characterization for the structures of compounds **9a,b,d,e** which were previously reported without characterization. The structure of novel **9c** was supported by ^{1}H-NMR, ^{13}C-NMR (Table 2), elemental analysis, and X-ray crystallography.

Table 2. The ^{13}C-NMR Chemical Shifts, δ in ppm (J_{PC} in Hz) **7–9a–e**, **10–12**

Entry	γ-C	β-Keto	α-C=P	Ester/Amide	P-(*ipso*)Ph	P-(*ortho*)Ph	P-(*meta*)Ph	P-(*para*)Ph
7a[b]	49.3 (8.6)	190.3 (<4.0)[a]	68.9 (112.8)	167.3 (14.3)	125.7 (93.3)	133.1 (9.7)	128.6 (12.6)	131.9 (2.9)
7b[b]	52.4 (8.6)	194.7 (<4.0)[a]	68.8 (111.1)	166.7 (14.3)	126.0 (93.3)	133.0 (9.7)	128.5 (12.6)	131.8 (2.9)
7c[b]	56.8 (8.6)	193.5 (<4.0)[a]	70.1 (108.8)	166.9 (14.3)	125.9 (93.9)	133.1 (9.7)	128.5 (12.6)	131.7 (2.9)
7d[c]	62.2 (7.4)	194.8 (2.9)	68.6 (109.9)	167.3 (15.5)	125.9 (93.9)	132.6 (9.7)	128.1 (12.6)	131.2 (2.9)
7d[d]	62.7 (6.3)	195.3 (2.9)	69.0 (111.1)	167.1 (14.3)	126.1 (93.3)	133.0 (9.7)	128.2 (12.0)	131.3 (2.3)
7e	39.6 (6.9)	195.5 (3.4)	71.2 (110.5)	167.5 (14.3)	125.9 (93.3)	132.6 (9.7)	128.2 (12.6)	131.3 (2.3)
8a[f]	45.4 (8.0)	185.3 (5.7)	69.5 (111.1)	166.7 (13.2)	124.1 (93.3)	132.9 (10.3)	128.6 (12.6)	132.1 (2.3)
8b[eh]	51.1 (8.6)	190.5 (4.6)	68.1 (109.4)	166.2 (12.6)	124.9 (92.8)	132.8 (9.7)	129.0 (12.6)	132.3 (2.9)
8c[eh]	55.9 (8.6)	189.0 (4.6)	69.1 (108.2)	166.4 (12.0)	124.8 (92.8)	133.0 (9.7)	129.0 (12.6)	132.3 (<4.0)[a]
8d[g]	63.6 (9.7)	187.7 (5.2)	69.6 (109.9)	166.2 (12.6)	124.2 (93.9)	133.0 (9.7)	128.9 (12.6)	132.5 (2.9)
8e[eh]	37.1 (7.4)	192.4 (4.0)	69.7 (109.4)	166.8 (13.2)	125.7 (92.8)	132.8 (9.7)	128.9 (12.6)	132.1 (<4.0)[a]
9a[j]	52.4 (13.2)	194.8 (8.6)	64.2 (122.6)	177.4 (17.4)	122.8 (93.3)	134.0 (10.9)	128.7 (12.6)	132.9 (2.9)
9b[j]	58.0 (13.7)	197.7 (7.4)	62.8 (122.5)	176.2 (16.6)	122.9 (92.8)	133.9 (10.9)	128.7 (12.6)	132.8 (2.3)
9c	63.5 (13.2)	195.5 (7.4)	64.0 (122.0)	175.9 (16.0)	122.7 (93.3)	133.9 (10.9)	128.7 (13.2)	132.8 (2.9)
9d[j]	69.1 (13.2)	197.6 (8.0)	65.2 (117.4)	179.7 (16.0)	122.6 (92.8)	133.8 (10.9)	128.7 (13.2)	132.8 (2.9)
9e[j]	37.1 (9.2)	191.9 (4.6)	70.0 (115.1)	171.1 (10.9)	125.0 (92.8)	133.3 (10.3)	128.2 (12.6)	131.7 (2.9)
10[k]	71.0 (8.6)	184.4 (6.3)	75.9 (104.2)	166.8 (10.9)	123.1 (93.3)	132.2 (10.3)	128.2 (13.2)	131.9 (2.9)
11	67.6 (13.2)	193.9 (6.9)	64.1 (123.1)	173.8 (16.6)	122.7 (92.8)	133.8 (10.9)	128.6 (12.6)	132.6 (2.9)
12	57.2 (7.4)	198.0 (2.9)	69.3 (108.2)	167.2 (14.3)	126.4 (93.3)	132.9 (9.7)	128.5 (12.6)	131.6 (2.9)

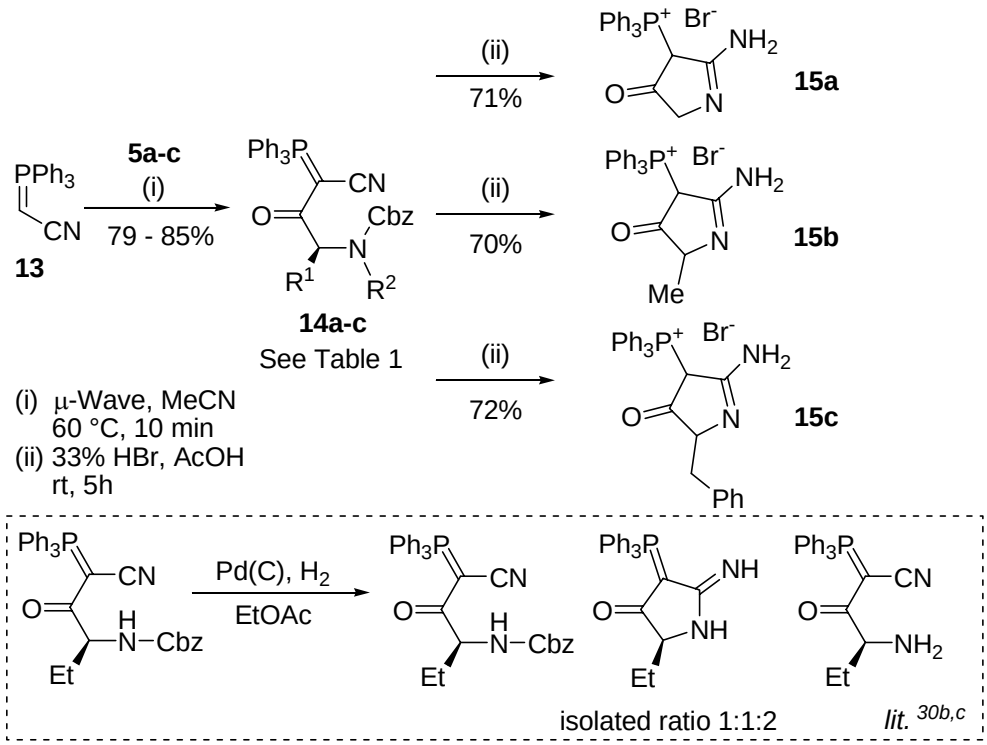
[a]Small couplings not clearly resolved were estimated as less than 4.0 Hz. [b]lit.[20] [c]Rotamer I. [d]Rotamer II. [e]($^{+}$NH$_3$)/($^{+}$PPh$_3$) Dibromide. [f]($^{+}$NH$_3$) Monobromide. [g]($^{+}$PPh$_3$) monobromide. [h]NMR in DMSO-*d*6. [j]*previously reported without characterization.*[lit.15] [k]($^{+}$NMe$_3$)/($^{+}$PPh$_3$) Dibromide



Scheme 4

Transformations similar to those reported above for **5a–e** with **6** converted (triphenylphosphoranylidene)acetonitrile (**13**) into *N*-Cbz-*γ*-amino-*β*-oxo-*α*-triphenylphosphoranylidene nitriles **14a–c** (79–85%) (Scheme 5), **14d** (64%) (Scheme 6), and *N*-Cbz-*δ*-amino-*β*-oxo-*α*-triphenylphosphoranylidene nitrile **14e** (63%) (Scheme 6). Compounds **14b,c** have been reported by Harvey et al.,[29] by Paris et al.,[30a] and by Wasserman et al.[30b] without elemental analysis for the preparation of peptidyl *α*-ketoesters and α-ketoamides.[29,30] The *N*-Cbz-*δ*-amino-*β*-oxo-*α*-triphenylphosphoranylidene nitrile **14e** has been reported, without characterization,[31] as an interesting precursor to *β*-amino-*α*-keto esters,[32] or for the synthesis of enantioselective 3-hydroxypyrrolidin-2-ones. We now report ^{1}H-NMR, ^{13}C-NMR, and elemental analysis to support the structures of **14b,c,e**. The structures of novel **14a,d** were supported by ^{1}H-NMR, ^{13}C-NMR (Table 3), and elemental analysis.

Comparable treatment of nitriles **14a–d** with hydrobromic acid caused simultaneous N-deprotection and cyclization to afford 5-amino-4-triphenylphosphonio-2,4-dihydropyrrol-3-one bromides **15a–c** (70–72%), and 3-ammonio-2-triphenylphosphoniotetrahydropyrrolizin-1-one dibromide **15d** (66%). The same method applied to **14e** gave linear **15e** (35%), possibly due to the extra degrees of freedom associated with this salt. The structures of novel **15a–e** were supported by ^{1}H-NMR, ^{13}C-NMR (Table 3), and elemental analysis.

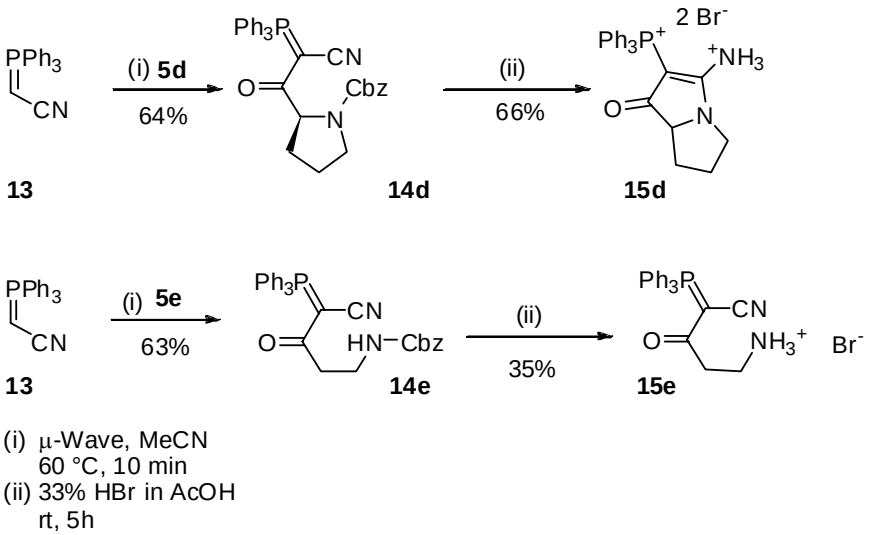


Scheme 5

Table 3. The ^{13}C-NMR Chemical Shifts, δ in ppm (J_{PC} in Hz) **14–15a–e**

Entry	γ-C	β-Keto	α-C=P	Imino/Nitrile	P-(*Ipso*)Ph	P-(*Ortho*)Ph	P-(*Meta*)Ph	P-(*Para*)Ph
14a	47.5 (10.9)	189.9 (<4.0)[a]	46.4 (127.7)	120.6 (14.9)	122.3 (93.3)	133.5 (10.3)	129.2 (13.2)	133.3 (3.4)
14b[b]	52.2 (9.0)	194.3 (3.6)	46.5 (127.5)	120.7 (14.9)	122.3 (93.3)	133.2 (10.3)	129.0 (12.6)	131.7 (4.0)
14c[c]	57.2 (9.0)	192.9 (<4.0)[a]	47.9 (126.0)	121.0 (16.0)	122.4 (93.9)	133.5 (10.3)	129.1 (12.6)	133.2 (3.4)
14d[d]	61.8 (9.1)	194.7 (3.5)	46.2 (126.3)	121.5 (15.4)	122.6 (93.4)	133.2 (10.5)	128.8 (12.6)	132.9 (2.8)
14d[e]	62.4 (9.1)	194.9 (3.5)	46.3 (127.0)	121.3 (14.7)	122.9 (93.4)	133.4 (10.5)	128.9 (12.6)	132.8 (2.8)
14e[f]	38.6 (9.2)	194.9 (<4.0)[a]	49.0 (126.0)	121.8 (16.6)	122.6 (93.9)	133.3 (10.3)	129.0 (13.2)	133.1 (2.9)
15a	52.2 (10.3)	194.5 (6.3)	64.8 (125.4)[h]	170.3 (17.2)	119.7 (93.3)	133.6 (10.9)	130.1 (13.2)	134.6 (2.9)
15b	58.5 (10.3)	197.7 (5.7)	63.1 (124.3)[h]	168.8 (17.2)	120.1 (93.3)	133.6 (10.9)	130.1 (13.1)	134.6 (2.9)
15c	63.3 (10.3)	195.3 (6.3)	64.0 (127.8)[h]	169.3 (16.6)	119.7 (92.8)	133.7 (10.9)	130.0 (12.6)	134.5 (2.9)
15d[g]	70.0 (10.3)	196.2 (5.7)	65.9 (119.1)[h]	170.9 (15.5)	119.4 (92.8)	133.5 (10.9)	130.0 (13.1)	134.6 (2.9)
15e	33.4 (8.0)	195.0 (4.0)	50.4 (124.3)	*120.8 (16.0)*	121.8 (93.3)	133.4 (10.3)	129.3 (13.2)	133.5 (2.3)

[a]Small couplings not clearly resolved were estimated as less than 4.0 Hz. [b]lit.[34] [c]lit.[25] [d]Rotamer I. [e]Rotamer II. [f]lit.[26]
[g]Isolated as $^{+}NH_3/^{+}PPh_3$ dibromide, double bond at C4–C5. [h]α-C–P^{+}.



Scheme 6

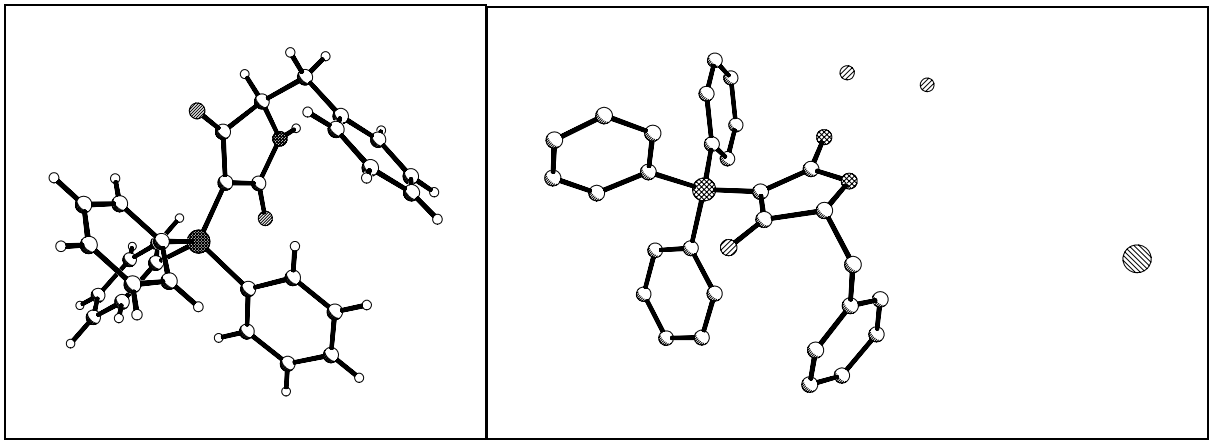
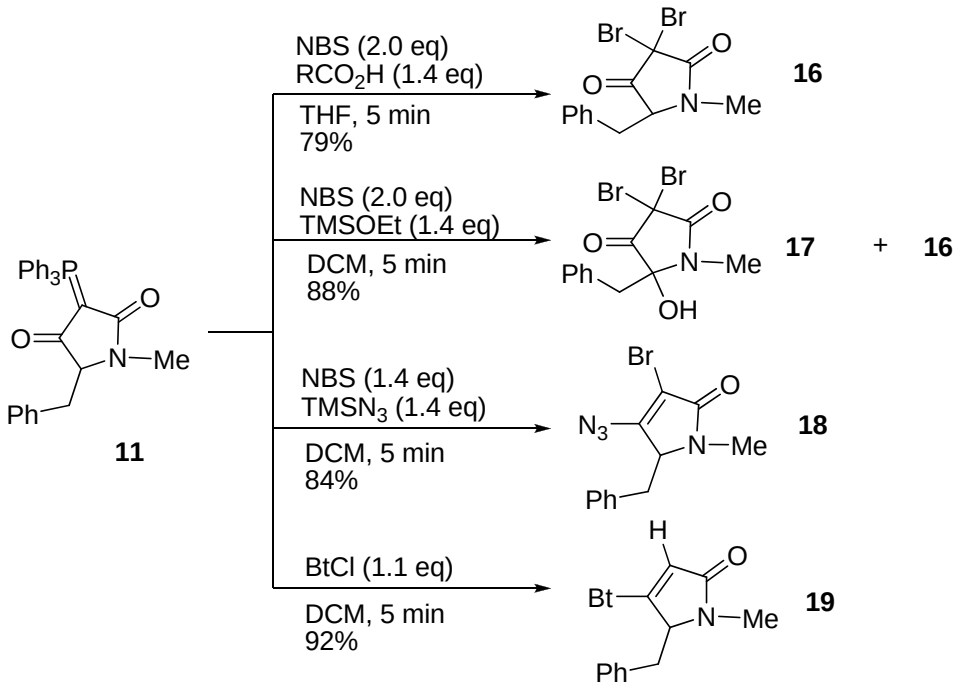


Figure 1. X-Ray Crystal Structure of **9c** (Left), and Preliminary X-ray Crystal Structure of **15c** Showing with Two H_2O Molecules and Br^- Anion (Right)

The structure of **9c** was unambiguously confirmed by X-ray crystallography which showed the O–C–C–(P)–C–O atoms to lie in approximately the same plane, to within 0.003(3) Å (Figure 1). The P=C bond length of 1.732(2) Å and the attached C-C bond lengths (1.422(3) and 1.450(2) Å) and the C=O bond lengths (1.230(2) and 1.253(2) Å) are all very similar to those in the only two other DOT-pyrrolidines to have been crystallographically characterized.[14,18] As is common with amides, the molecules pack in pairs about a crystallographic center of inversion with N-H···O=C hydrogen bonds. In addition a preliminary X-ray crystallographic study on a highly twinned crystal confirmed the structure of (2*RS*)-5-amino-2-benzyl-4-triphenylphosphonio-2,4-dihydropyrrol-3-one bromide hydrate (**15c**). Both **9c** and **15c** are racemic suggesting racemization was caused by the HBr treatment.

Bromination of **11** in the presence of acid gave 3,3-dibromopyrrolidin-2,4-dione **16** (79%) (Scheme 7).

Treatment of **11** with ethoxytrimethylsilane (TMSOEt) and NBS gave **16** (44%) and 3,3-dibromo-5-hydroxypyrrolidin-2,4-dione **17** (44%), the structure of which was confirmed by X-ray crystallography (Figure 2). In **17** the molecules pack in chains with the hydroxy hydrogen atom H-bonded to the carbonyl of an adjacent molecule. Treatment of **11** with azidotrimethylsilane ($TMSN_3$) and NBS gave 4-azido-3-bromopyrrol-2-one **18** (84%). 1-Chlorobenzotriazole (BtCl) transformed **11** into 4-benzotriazolpyrrol-2-one **19** (92%).



Scheme 7

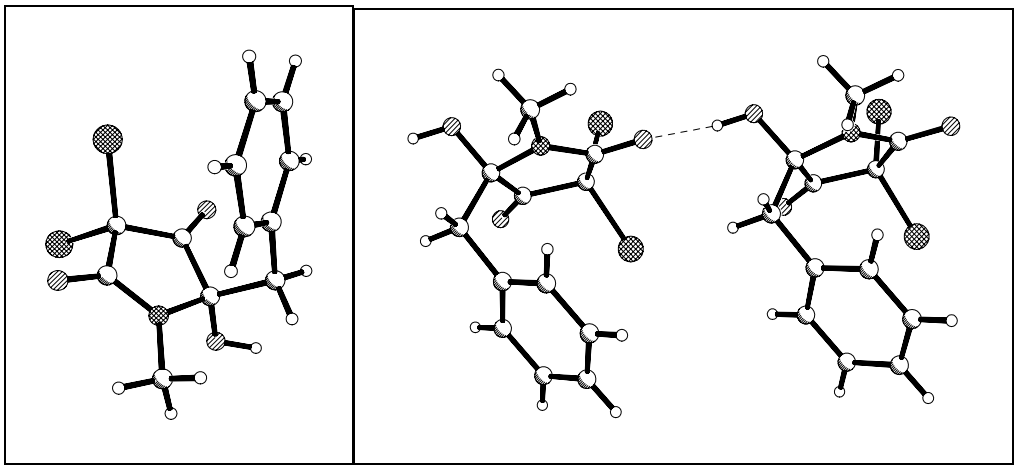


Figure 2. X-Ray Crystal Structure of **17** (Left), and Intermolecular Hydrogen Bonding (Right)

CONCLUSIONS

We now report the first convenient method to 2,4-dioxo-3-triphenylphosphoranylidene pyrrolidines, 1,3-dioxo-2-triphenylphosphoranylidene tetrahydropyrrolizine, 2,4-dioxo-3-triphenylphosphoranylidene piperidine, 5-amino-4-triphenylphosphonio-2,4-dihydropyrrol-3-one bromides, and 3-ammonio-2-triphenylphosphoniotetrahydropyrrolizin-1-one dibromide. In particular, our *Method I* is versatile, inexpensive, reproducible, and high yielding. Racemization was caused by HBr, however the novel linear salts could be cleanly N-methylated, neutralized without cyclization, or cyclized. The ^{13}C-NMR chemical shifts and J_{PC} values provide information for the analysis of distabilized triphenylphosphoranylidene systems, J_{PC} couplings increased with less partial positive character and decreased with more partial positive character on the respective carbons.

We have also developed four novel applications for DOT-pyrrolidines. The first highly versatile[33] 3,3-dibromopyrrolidine-2,4-dione[34] with a racemic stereocenter, was obtained without Lewis acid.[35] The first 3,3-dibromo-5-hydroxypyrrolidine-2,4-dione was obtained and unambiguously identified by X-ray crystallography. 4-Azido-3-bromopyrrol-2-one was obtained, where previously reported in the literature chloro derivatives were used to make β-lactams,[36] and bromo derivatives were trapped with triphenylphosphine to make a Staudinger reagent.[37] The first 4-benzotriazolpyrrol-2-one was obtained. In conclusion the versatile and stable 2,4-dioxo-3-triphenylphosphoranylidene can be easily added synthetically to rings and then easily transformed to provide novel structures.

EXPERIMENTAL

Melting points were determined on a capillary point apparatus equipped with a digital thermometer. NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 with TMS for ^{1}H (300 MHz) and ^{13}C (75 MHz) as the internal reference. The *N*-Cbz-amino acids were purchased from Fluka and were used without further purification. Acetonitrile was freshly distilled from calcium hydride. Microwave heating was carried out with a single mode cavity Discover® Microwave Synthesizer (CEM Corporation, NC), producing continuous irradiation at 2455 MHz.

PREPARATION OF *N*-ACYLBENZOTRIAZOLES 5a–e

The **5a–e** were prepared from the corresponding *N*-protected amino acids (25 mmol) and excess BtH in the presence of thionyl chloride, following recently developed procedures.[23] We confirmed the structure of **5d**, previously reported by the Katritzky group, here with improved resolution of rotamer signals. The structure of novel **5e** was supported by ^{1}H-NMR, ^{13}C-NMR and elemental analysis.

(2*S*)-1-Benzyloxycarbonyl(benzotriazol-1-carbonyl)pyrrolidine (5d). (Two rotameric forms) (6.3 g, 72%) Clear oil. $[\alpha]^{23}_D$ –139.6 (*c* 1.83, DMF).[24e] ^{1}H NMR ($CDCl_3$) δ 1.99–2.14 (m, 2H), 2.15–2.26 (m,

1H), 2.54–2.68 (m, 1H), 3.64–3.88 (m, 2H), 4.95–5.11 (m, 1H), 5.12–5.24 (m, 1H), 5.83–5.88 (m, 1H), 6.97–7.06 (m, 2H), 7.30–7.42 (m, 3H), 7.50–7.56 (m, 1H), 7.65–7.70 (m, 1H), 8.11–8.16 (m, 1H), 8.19–8.31 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 23.7, 24.5, 30.7, 31.6, 46.9, 47.3, 59.2, 60.0, 67.3, 114.3, 114.5, 120.2, 126.4, 127.5, 127.9, 128.1, 128.5, 130.5, 130.6, 145.9, 154.0, 154.9, 171.1, 171.6. Anal. Calcd. for $C_{19}H_{18}N_4O_3$: C, 65.13; H, 5.18; N, 15.99. Found: C, 64.98; H, 5.24; N, 15.77.

3-(Benzotriazol-1-yl)-1-(benzyloxy)carbonylaminopropan-3-one (5e). (7.3 g, 90%) White needles (from Et_2O) mp 111–112 °C. ^{1}H NMR ($CDCl_3$) δ 3.66–3.69 (m, 2H), 3.74–3.80 (m, 2H), 5.09 (s, 2H), 5.47 (br s, 1H), 7.28–7.36 (m, 5H), 7.48–7.53 (m, 1H), 7.62–7.67 (m, 1H), 8.11 (d, J = 8.2 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 35.9, 36.1, 66.8, 114.2, 120.2, 126.3, 128.1, 128.5, 130.5, 130.8, 136.2, 146.1, 156.2, 171.2. Anal. Calcd for $C_{17}H_{16}N_4O_3$: C, 62.95; H, 4.97; N, 17.27. Found: C, 63.19; H, 4.86; N, 17.41.

PREPARATION OF α-TRIPHENYLPHOSPHORANYLIDENE ESTERS 7a–e

Compounds **7a–e** were prepared from the corresponding **5a–e** (1.1 mmol) and **7** (1.0 mmol) in MeCN (1 mL) in a dry 50 mL round bottom flask equipped with a magnetic stir bar and a condenser. The flask containing the reaction mixture was exposed to microwave irradiation (120 W) for 10 min at a temp of 60 °C, and cooled with high-pressure air through an inbuilt system in the instrument until temp fell below 30 °C. The reaction mixture was diluted with ethyl acetate and washed with a saturated aq sodium carbonate. The organic layer was collected, dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to give the crude product, which was purified by column chromatography (SiO_2, hexane:EtOAc = 3:1).

(2*S*)-1-Benzyloxycarbonyl-2-(ethoxycarbonyltriphenylphosphoranylidenacetyl)pyrrolidine (7d). (Two rotameric forms) (0.38 g, 66%) (49%)[25] White microcrystals (from $CHCl_3$ / hexane) mp 129–130 °C. $[\alpha]^{23}_D$ –36.4 (*c* 1.50, CH_2Cl_2) ($[\alpha]^{20}_D$ –45.0 (*c* 1.03, CH_2Cl_2)).[lit.25] ^{1}H NMR ($CDCl_3$) δ 0.66 (t, J = 7.1 Hz, 3H), 1.75 (br s, 2H), 1.98–2.16 (m, 1H), 2.30–2.50 (m, 1H), 3.35–3.56 (m, 2H), 3.62–3.84 (m, 2H) 4.89–5.27 (m, 2H), 5.64–5.76 (m, 1H), 7.20–7.74 (m, 20H). ^{13}C NMR ($CDCl_3$) δ 13.4, 22.7, 23.5, 30.5, 31.5, 46.6, 47.1, 58.0, 58.1, 62.2 (J_{CP} = 7.4 Hz), 62.7 (J_{CP} = 6.3), 65.7, 65.9, 68.7 (J_{CP} = 109.9 Hz), 69.0 (J_{CP} = 111.1 Hz), 125.9 (J_{CP} = 93.9 Hz), 126.1 (J_{CP} = 93.3 Hz), 126.3, 126.9, 127.2, 127.3, 127.9, 128.1 (J_{CP} = 12.6 Hz), 128.2 (J_{CP} = 12.0 Hz), 131.2 (J_{CP} = 2.9 Hz), 131.3 (J_{CP} = 2.3 Hz), 131.6, 131.8, 132.6 (J_{CP} = 9.7 Hz), 133.0 (J_{CP} = 9.7 Hz), 137.1, 137.2, 154.2 (J_{CP} = 4.0 Hz), 167.1 (J_{CP} = 15.5 Hz), 167.3 (J_{CP} = 14.3 Hz), 194.9 (J_{CP} = 2.9 Hz), 195.4 (J_{CP} = 2.9 Hz). Anal. Calcd for $C_{35}H_{34}NO_5P$: C, 72.53; H, 5.91; N, 2.42. Found: C, 72.19; H, 5.90; N, 2.76.

5-(Benzyloxy)carbonylamino-1-ethoxy-2-triphenylphosphoranylidenpentan-1,3-dione (5e). (0.43 g, 77%) Yellowish needles (from Et_2O) mp 88–92 °C. ^{1}H NMR ($CDCl_3$) δ 0.64 (t, J = 7.0 Hz, 3H), 3.15 (t, J

= 5.5 Hz, 2H), 3.40–3.50 (m, 2H), 3.71 (q, *J* = 7.0 Hz, 2H), 5.06 (s, 2H), 5.57 (t, *J* = 5.1Hz, 1H), 7.23–7.52 (m, 15H), 7.59–7.70 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 13.3, 37.2, 39.6 (J_{CP} =6.3 Hz), 58.1, 65.7, 71.2 (J_{CP} =110.5 Hz), 125.9 (J_{CP} = 93.3 Hz), 127.5, 128.0, 128.2 (J_{CP} = 12.6 Hz), 131.3 (J_{CP} = 2.3 Hz), 131.7, 132.6 (J_{CP} = 9.7 Hz), 136.6, 155.9, 167.5 (J_{CP} = 14.3 Hz) 195.5 (J_{CP} = 3.4 Hz). Anal. Calcd for $C_{33}H_{32}NO_5P$: C, 71.60; H, 5.83; N, 2.53. Found: C, 71.57; H, 5.97; N, 2.45.

PREPARATION OF DOT-SALTS 8a–e

Bromide salts **8a–e** were prepared from the corresponding **7a–e**. Compounds **7a–e** (2.0 mmol) were stirred for 5 h in 33% HBr in acetic acid (10 mL). The reaction mixture was diluted with Et_2O (150 mL) and stirred for 12 h. The white precipitated salt **8c** was filtered from the solution and used without further purification.

4-Ammonio-1-ethoxy-2-triphenylphosphoranylidenbutan-1,3-dione Bromide (8a). *Hygroscopic* (0.20 g, 21%) White plates (from CH_2Cl_2 / EtOAc) mp 101–103 °C. ^{1}H NMR ($CDCl_3$) δ 0.67 (t, *J* = 7.0 Hz, 3H), 3.72 (q, *J* = 7.0 Hz, 2H), 4.18 (br s, 2H), 6.83 (br s, 3H), 7.47–7.69 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 13.4, 45.4 (J_{CP} = 8.0 Hz), 49.8, 58.7, 69.5 (J_{CP} = 111.1 Hz), 124.1 (J_{CP} = 93.3 Hz), 128.6 (J_{CP} = 12.6 Hz), 132.1 (J_{CP} = 2.3 Hz), 132.9 (J_{CP} = 10.3 Hz), 166.7 (J_{CP} = 13.2 Hz), 185.3 (J_{CP} = 5.7 Hz). Anal. Calcd for $C_{24}H_{25}BrNO_3P$: C, 59.27; H, 5.18; N, 2.88. Found: C, 58.64; H, 5.29; N, 2.52

(4*RS*)-4-Ammonio-1-ethoxy-2-triphenylphosphoniopentan-1,3-dione Dibromide (8b). (1.15 g, 99%) White microcrystals (from CH_2Cl_2 / EtOAc) mp 147–150 °C. ^{1}H NMR (DMSO-d_6) δ 0.48 (t, *J* = 7.0 Hz, 3H), 1.45 (d, *J* = 6.3 Hz, 3H), 3.50–3.64 (m, 2H), 4.80–4.97 (m, 1H), 7.59–7.69 (m, 15H), 7.80 (br s, 3H), 8.51 (br s, 1H). ^{13}C NMR (DMSO-d_6) δ 13.3, 17.4, 51.1 (J_{CP} = 8.6 Hz), 58.2, 68.1 (J_{CP} = 109.4 Hz), 124.9 (J_{CP} = 92.8 Hz), 129.0 (J_{CP} = 12.6 Hz), 132.3 (J_{CP} = 2.9 Hz), 132.8 (J_{CP} = 9.7 Hz), 166.2 (J_{CP} = 12.6 Hz), 190.5 (J_{CP} = 4.6 Hz). Anal. Calcd for $C_{25}H_{28}Br_2NO_3P$: C, 51.66; H, 4.86; N, 2.41. Found: C, 51.32; H, 4.88; N, 2.35.

(4*RS*)-4-Ammonio-1-ethoxy-5-phenyl-2-triphenylphosphoniopentan-1,3-dione Dibromide (8c). (1.20 g, 91%) White microcrystals (from CH_2Cl_2 / EtOAc) mp 145–147 °C. ^{1}H NMR (DMSO-d_6) δ 0.46 (t, *J* = 7.1 Hz, 3H), 2.80 (dd, *J* = 14.0, 9.2 Hz, 1H), 3.38 (dd, *J* = 14.0, 4.3 Hz, 1H), 3.50–3.66 (m, 2H), 5.18 (br s, 1H), 5.68 (br s, 4H), 7.25–7.45 (m, 5H), 7.56–7.77 (m, 15H). ^{13}C NMR (DMSO-d_6) δ 13.3, 37.4, 55.9 (J_{CP} = 8.6 Hz), 58.3, 69.1 (J_{CP} = 108.2 Hz), 124.8 (J_{CP} = 92.8 Hz), 126.9, 128.5, 129.0 (J_{CP} = 12.6 Hz), 129.6, 132.3, 133.0 (J_{CP} = 9.7 Hz), 136.0, 166.4 (J_{CP} = 12.0 Hz), 188.9 (J_{CP} = 4.6 Hz). Anal. Calcd for $C_{31}H_{32}Br_2NO_3P$: C, 56.64; H, 4.91; N, 2.13. Found: C, 57.09; H, 4.93; N, 2.22.

(2*RS*)-2-(Ethoxycarbonyltriphenylphosphonioacetyl)pyrrolidine Bromide (8d). (0.95 g, 90%) White microcrystals (from CH_2Cl_2 / EtOAc) mp 81–83 °C. ^{1}H NMR ($CDCl_3$) δ 0.69 (t, *J* = 7.3 Hz, 3H), 1.61–1.80 (m, 1H), 2.02–2.20 (m, 2H), 2.65–2.84 (m, 1H), 3.16 (br s, 1H), 3.40–3.60 (m, 1H), 3.73–3.85

(m, 3H), 5.38 (br s, 1H), 7.42–7.71 (m, 15H), 10.70 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 13.6, 24.5, 31.8, 46.5, 59.2, 63.6 (J_{CP} = 9.7 Hz), 69.6 (J_{CP} = 109.9 Hz), 124.2 (J_{CP} = 93.9 Hz), 128.9 (J_{CP} = 12.6 Hz), 132.5 (J_{CP} = 2.9 Hz), 133.0 (J_{CP} = 9.7 Hz), 166.2 (J_{CP} = 12.6 Hz), 187.7 (J_{CP} = 5.2 Hz). Anal. Calcd for $C_{27}H_{29}BrNO_3P$: C, 61.61; H,5.55; N, 2.66. Found: C, 61.28; H, 5.45; N, 3.34.

(5-Ammonio-1-ethoxy-2-triphenylphosphoniopentan-1,3-dione) Dibromide (8e). (1.08 g, 92%) White plates (from CH_2Cl_2 / Et_2O) mp 126–128 °C. ^{1}H NMR (DMSO-d_6) δ 0.50 (t, J = 7.0 Hz, 3H), 2.80–2.95 (m, 2H), 3.22 (t, J = 6.3 Hz, 2H), 3.56 (q, J = 7.0 Hz, 2H), 7.55–7.80 (m, 18H), 9.50 (br s, 1H). ^{13}C NMR (DMSO-d_6) δ 13.4, 35.3, 37.1 (J_{CP} = 7.4 Hz), 55.1, 57.9, 69.7 (J_{CP} = 109.4 Hz), 125.7 (J_{CP} = 92.8 Hz), 128.9 (J_{CP} = 12.6 Hz), 132.1, 132.8 (J_{CP} = 9.7 Hz), 166.8 (J_{CP} = 13.2 Hz), 192.4 (J_{CP} = 4.0 Hz). Anal. Calcd for $C_{25}H_{28}Br_2NO_3P$: C, 51.66; H, 4.86; N, 2.41. Found: C, 51.35; H, 4.88; N, 2.14.

PREPARATION OF DOT-PYRROLIDINES 9a–c, DOT-PYRROLIZINE 9d, AND DOT-PIPERIDINE 9e

Method I: Compounds **9a–e** were prepared from the corresponding **8a–e**. Salts **8a–d** (1.0 mmol) were dissolved in EtOH (1.0 mL) and added to aq sodium hydroxide (10.0 mL, 7.5 M), which precipitated a white solid almost immediately. Extraction with dichloromethane was performed after 5 h. Compound **9e** was prepared from **8e**, following the same procedure with reflux in aq sodium hydroxide (7.5 M) for 15 h.

Method II: Compounds **9a–d** were prepared from the corresponding **7a–d**. A round bottom flask charged with ester **7a–d** (2.0 mmol) and 5% palladium charcoal (2 eq) were stirred vigorously in EtOH, under a hydrogen atmosphere for 48 h. The reaction mixture was filtered through celite and diluted with EtOAc to crystallize **9a–d**.

3-Triphenylphosphoranylidenpyrrolidin-2,4-dione (9a). (0.35 g, 97%) (*Method I* 20%) (*Method II* 0.43 g, 60%) (21%)[15] White needles (from CH_2Cl_2 / EtOAc) mp 222–224 °C. ^{1}H NMR ($CDCl_3$) δ 3.79 (s, 2H), 5.40 (br s, 1H), 7.47–7.56 (m, 6H), 7.58–7.74 (m, 9H). ^{13}C NMR ($CDCl_3$) δ 52.4 (J_{CP} = 13.2 Hz), 64.2 (J_{CP} = 122.6 Hz), 122.8 (J_{CP} = 93.3 Hz), 128.7 (J_{CP} = 12.6), 132.9 (J_{CP} = 2.9 Hz), 134.0 (J_{CP} = 10.9 Hz), 177.4 (J_{CP} = 17.4 Hz), 194.8 (J_{CP} = 8.6 Hz). Anal. Calcd for $C_{22}H_{18}NO_2P$: C, 73.53; H, 5.05; N, 3.90. Found: C, 73.28; H, 4.98; N, 3.88.

(5*RS*)-5-Methyl-3-triphenylphosphoranylidenpyrrolidin-2,4-dione (9b). (0.37 g, 99%) (*Method I* 98%) (*Method II* 0.34 g, 45%) (58%)[15] White needles (from CH_2Cl_2 / EtOAc) mp 210–211 °C. ^{1}H NMR ($CDCl_3$) δ 1.34 (d, J = 6.7 Hz, 3H), 3.87 (q, J = 6.7 Hz, 1H), 5.30 (s, 1H), 7.40–7.80 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 18.5, 58.0 (J_{CP} = 13.7 Hz), 62.8 (J_{CP} = 122.5 Hz), 122.9 (J_{CP} = 92.8 Hz), 128.7 (J_{CP} = 12.6 Hz), 132.8 (J_{CP} = 2.3 Hz), 133.9 (J_{CP} = 10.9 Hz), 176.2 (J_{CP} = 16.6 Hz), 197.7 (J_{CP} = 7.4 Hz). Anal. Calcd for $C_{23}H_{20}NO_2P$: C, 73.98; H, 5.40; N, 3.75. Found: C, 73.72; H, 5.38; N, 3.46. HRMS *m/z* Calcd

for $C_{23}H_{20}NO_2P$ 373.1226 $[M+H]^+$, Found 373.1215.

(5*RS*)-5-Benzyl-3-triphenylphosphoranylidenpyrrolidin-2,4-dione (9c). (0.45 g, 99%) (*Method I* 89%) (*Method II* 0.40 g, 45%) White plates (from CH_2Cl_2 / EtOAc) mp 238–242 °C. ^{1}H NMR ($CDCl_3$) δ 2.82 (dd, *J* = 13.7, 8.1 Hz, 1H), 3.18 (dd, *J* = 13.2, 3.4 Hz, 1H), 4.05–4.08 (m, 1H), 5.17 (s, 1H), 7.20–7.30 (m, 5H), 7.44–7.63 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 38.7, 63.5 (J_{CP} = 13.2 Hz), 64.0 (J_{CP} = 122.0 Hz), 122.7 (J_{CP} = 93.3 Hz), 126.3, 128.2, 128.7 (J_{CP} = 13.2 Hz), 129.6, 132.8 (J_{CP} = 2.9 Hz), 133.9 (J_{CP} = 10.9 Hz), 137.8, 175.9 (J_{CP} = 16.0 Hz), 195.5 (J_{CP} = 7.4 Hz). Anal. Calcd for $C_{29}H_{24}NO_2P$: C, 77.49; H, 5.38; N, 3.12. Found: C, 77.22; H, 5.45; N, 2.76. HRMS *m/z* Calcd for $C_{29}H_{24}NO_2P$ 450.1617 $[M+H]^+$, Found 450.1628.

(2*RS*)-2-(Triphenylphosphoranyliden)tetrahydropyrrolizin-1,3-dione (9d). (0.35 g, 88%) (*Method I* 79%) (*Method II* 0.36 g, 45%) (60%)[15] White needles (from CH_2Cl_2 / EtOAc) mp 211–213 °C. ^{1}H NMR ($CDCl_3$) δ 1.60–1.73 (m, 1H), 1.88–2.18 (m, 3H), 3.04–3.12 (m, 1H), 3.70 (dt, *J* = 11.2, 7.5 Hz, 1H) 3.99 (app t, *J* = 7.7 Hz, 1H), 7.4–7.7 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 27.0, 28.2, 44.6, 65.2 (J_{CP} = 117.4 Hz), 69.1 (J_{CP} = 13.2 Hz), 122.6 (J_{CP} = 92.8 Hz), 128.7 (J_{CP} = 13.2 Hz), 132.8 (J_{CP} = 2.9 Hz), 133.8 (J_{CP} = 10.9 Hz), 179.7 (J_{CP} = 16.0 Hz), 197.6 (J_{CP} = 8.0 Hz). Anal. Calcd for $C_{25}H_{22}NO_2P$: C, 75.18; H, 5.55; N, 3.51. Found: C, 74.96; H, 5.62; N, 3.47.

3-Triphenylphosphoranylidenpiperidin-2,4-dione (9e). (0.29 g, 65%) (*Method I* 60%) (34%)[15] White microcrystals (from CH_2Cl_2 / EtOAc) mp 241–243 °C. ^{1}H NMR ($CDCl_3$) δ 2.42 (t, *J* = 6.3 Hz, 2H), 3.37 (dt, *J* = 6.3, 2.8 Hz, 2H), 5.65 (br s, 1H), 7.39–7.53 (m, 9H), 7.64–7.71 (m, 6H). ^{13}C NMR ($CDCl_3$) δ 37.1 (J_{CP} = 9.2 Hz), 37.9, 70.0 (J_{CP} = 115.1 Hz), 125.0 (J_{CP} = 92.8 Hz), 128.2 (J_{CP} = 12.6 Hz), 131.7 (J_{CP} = 2.9 Hz), 133.3 (J_{CP} = 10.3 Hz), 171.1 (J_{CP} = 10.9 Hz), 191.9 (J_{CP} = 4.6 Hz). Anal. Calcd for $C_{23}H_{20}NO_2P$: C, 73.98; H, 5.40; N, 3.75. Found: C, 74.03; H, 5.55; N, 3.59.

PREPARATION OF DIBROMIDE SALT 10

To a solution of **8c** (1.0 g, 1.52 mmol) dissolved in a solvent mixture (THF:CH_2Cl_2 = v:v = 1:1, 40 mL), sodium hydride 60% on mineral oil (0.610 g, 15.2 mmol) was added and stirred for 1 h. Methyl iodide (1.0 mL, 15.2 mmol) was added dropwise to the reaction mixture with stirring at rt. The reaction mixture was stirred for a further 16 h. The solvent mixture was evacuated and the residue was extracted with CH_2Cl_2. The crude product was filtered and subjected to column chromatography (SiO_2, CH_2Cl_2:MeOH = 98:2).

(4*RS*)-4-Trimethylammonio-1-ethoxy-5-phenyl-2-triphenylphosphoniopentan-1,3-dione Dibromide (10). (1.01 g, 95%) White needles (CH_2Cl_2 / Et_2O) mp 189–191 °C. ^{1}H NMR ($CDCl_3$) δ 0.38 (t, *J* = 7.0 Hz, 3H), 2.43 (s, 1H), 3.04 (t, *J* = 11.9 Hz, 1H), 3.23–3.51 (m, 11H), 6.02 (dd, *J* = 11.2, 3.5 Hz, 1H), 7.08–7.11 (m, 2H), 7.25–7.32 (m, 9H), 7.36–7.52 (m, 7H), 7.48–7.54 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 12.6,

32.6, 52.2, 58.8, 71.0 (J_{CP} = 8.6 Hz), 75.9 (J_{CP} = 104.2 Hz), 123.1 (J_{CP} = 93.3 Hz), 126.7, 128.1, 128.2 (J_{CP} = 13.2 Hz), 128.8, 131.9 (J_{CP} = 2.9 Hz), 132.2 (J_{CP} = 10.3 Hz), 133.3, 166.8 (J_{CP} = 10.9 Hz), 184.4 (J_{CP} = 6.3 Hz). Anal. Calcd for $C_{34}H_{38}Br_2NO_3P$: C, 58.38; H, 5.48; N, 2.00. Found: C, 58.22; H, 5.78; N, 1.98.

PREPARATION OF N-METHYLATED DOT-PYRROLIDINE 11

To a solution of **9c** (1.0 g, 2.2 mmol) dissolved in a solvent mixture (THF:CH_2Cl_2 = v:v = 1:1, 40 mL), sodium hydride 60% on mineral oil (0.890 g, 22.2 mmol) was added. Methyl iodide (1.4 mL, 22.2 mmol) was added dropwise to the reaction mixture and stirred at rt for 16 h. The solvent mixture was evacuated and the residue was extracted with CH_2Cl_2. The crude product was filtered and subjected to column chromatography (SiO_2, CH_2Cl_2:MeOH = 98:2).

(5*RS*)-5-Benzyl-1-methyl-3-triphenylphosphoranylidenpyrrolidin-2,4-dione (11). (0.95 g, 92%) White plates (EtOAc) mp 180–182 °C. ^{1}H NMR ($CDCl_3$) δ 2.94 (s, 3H), 3.13 (d, *J* = 4.1 Hz, 2H), 3.93 (t, *J* = 4.2 Hz, 1H), 7.17–7.25 (m, 5H), 7.36–7.46 (m, 12H), 7.54–7.60 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 27.7, 35.0, 64.1 (J_{CP} = 123.1 Hz), 67.6 (J_{CP} = 13.2 Hz), 122.7 (J_{CP} = 92.8 Hz), 126.0, 127.8, 128.6 (J_{CP} = 12.6 Hz), 130.1, 132.6 (J_{CP} = 2.9 Hz), 133.8 (J_{CP} = 10.9 Hz), 136.7, 173.8 (J_{CP} = 16.6 Hz), 193.9 (J_{CP} = 6.9 Hz). Anal. Calcd for $C_{30}H_{26}NO_2P$: C, 77.74; H, 5.65; N, 2.95. Found: C, 77.45; H, 5.70; N, 2.96.

PREPARATION OF LINEAR FREE AMINE 12

To a solution of **8c** (0.66 g, 1.0 mmol) dissolved in CH_2Cl_2 (10 mL), triethylamine (3.0 eq) was added and stirred for 1 h. The solvent mixture was washed with saturated aq sodium chloride. The organic layer was dried with anhydrous magnesium sulfate, filtered, and removed under vacuum to give **12**.

(4*RS*)-4-amino-1-ethoxy-5-phenyl-2-(triphenylphosphoranyliden)pentan-1,3-dione (12). (0.45 g, quantitative) Clear oil, ^{1}H NMR ($CDCl_3$) δ 0.63 (t, *J* = 7.0 Hz, 3H) 1.53 (br s, 2H), 2.50 (dd, *J* = 12.6, 9.1 Hz, 1H), 3.31 (dd, *J* = 12.6, 4.9 Hz, 1H), 3.62–3.78 (m, 2H), 4.92 (dd, *J* = 9.1, 4.9 Hz, 1H), 7.14–7.31 (m, 5H), 7.40–7.65 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 13.6, 42.4, 57.2 (J_{CP} = 7.4 Hz), 58.4, 69.3 (J_{CP} = 108.2 Hz), 125.8, 126.4 (J_{CP} = 93.3 Hz), 128.1, 128.5 (J_{CP} = 12.6 Hz), 129.6, 131.6 (J_{CP} = 2.9 Hz), 132.9 (J_{CP} = 9.7 Hz), 139.8, 167.2 (J_{CP} = 14.3 Hz), 198.0 (J_{CP} = 2.9 Hz). Anal. Calcd for $C_{30}H_{26}NO_2P$: C, 75.14; H, 6.10; N, 2.83. Found: C, 74.37; H, 6.06; N, 2.97.

PREPARATION OF α-TRIPHENYLPHOSPHORANYLIDENE NITRILES 14a–e

Compounds **14a–e** were prepared from the corresponding **5a–e** (1.1 mmol) and **13** (1.0 mmol), following the procedure developed for **7a–e**.

4-Benzyloxycarbonylamino-3-oxo-2-triphenylphosphoranylidenbutane nitrile (14a). (0.42 g, 85%) White microcrystals (from Et_2O / hexanes) mp 171–173 °C. ^{1}H NMR ($CDCl_3$) δ 4.41 (d, *J* = 4.3 Hz,

2H), 5.09 (s, 2H), 5.59 (br s, 1H), 7.26–7.40 (m, 5H), 7.42–7.72 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 46.4 (J_{CP} = 127.7 Hz), 47.5 (J_{CP} = 10.9 Hz), 66.4, 120.6 (J_{CP} = 14.9 Hz), 122.3 (J_{CP} = 93.3 Hz), 127.8, 128.3, 129.2 (J_{CP} = 13.2 Hz), 133.3 (J_{CP} = 3.4 Hz), 133.5 (J_{CP} = 10.3 Hz), 136.6, 156.0, 189.9. Anal. Calcd for $C_{30}H_{25}N_2O_3P$: C, 73.16; H, 5.12; N, 5.69. Found: C, 72.80; H, 5.08; N, 5.59.

(4*S*)-Benzyloxycarbonylamino-3-oxo-2-triphenylphosphoranylidenpentane nitrile (14b). (0.40 g, 79%) (76%)[30a] (85%)[30b] White microcrystals (from Et_2O / hexanes) mp 73–75 °C. $[\alpha]^{23}_D$ +21.5 (*c* 1.00, CH_2Cl_2) ($[\alpha]^{20}_D$ +18.96 (*c* 1.00, $CHCl_3$))[30b]. ^{1}H NMR ($CDCl_3$) δ 1.53 (d, *J* = 6.7 Hz, 3H), 4.92–5.02 (m, 1H), 5.08 (s, 2H), 5.75 (d, *J* = 6.9 Hz, 1H), 7.22–7.36 (m, 5H), 7.40–7.72 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 19.4, 46.5 (J_{CP} = 127.5 Hz), 52.2, 66.0, 120.7 (J_{CP} = 14.9 Hz), 122.3 (J_{CP} = 93.3 Hz), 127.6, 128.2, 129.0 (J_{CP} = 12.6 Hz), 131.7 (J_{CP} = 4.0 Hz), 131.8, 133.2 (J_{CP} = 10.3 Hz), 136.5, 155.2, 194.3. Anal. Calcd for $C_{31}H_{27}N_2O_3P$: C, 73.51; H, 5.37; N, 5.53. Found: C, 73.13; H, 5.38; N, 5.36.

(4*S*)-Benzyloxycarbonylamino-3-oxo-5-phenyl-2-triphenylphosphoranylidenpentane nitrile (14c). (0.44 g, 79%) (78%)[29] (77%)[30a] White microcrystals (from CH_2Cl_2 / Et_2O) mp 101–103 °C. $[\alpha]^{23}_D$ +7.6 (*c* 1.10, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 3.06 (dd, *J* = 13.9, 7.0 Hz, 1H), 3.34 (dd, *J* = 13.9, 4.9 Hz 1H), 5.03 (s, 2H), 5.16 (q, *J* = 7.0 Hz, 1H), 5.49 (d, *J* = 7.0 Hz, 1H), 7.17–7.30 (m, 10H), 7.40–7.67 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 38.7, 47.9 (J_{CP} = 126.0 Hz), 57.2 (J_{CP} = 9.0 Hz), 66.3, 121.0 (J_{CP} = 16.0 Hz), 122.4 (J_{CP} = 93.9 Hz), 126.4, 127.8. 128.1, 128.3, 129.1 (J_{CP} = 12.6 Hz), 129.7, 133.2 (J_{CP} = 3.4 Hz), 133.5 (J_{CP} = 10.3 Hz), 136.8, 155.5, 192.9. Anal. Calcd for $C_{37}H_{31}N_2O_3P$: C, 76.27; H, 5.36; N, 4.81. Found: C, 76.52; H, 5.38; N, 2.94.

(2S)-1-Benzyloxycarbonyl-(cyanotriphenylphosphoranylidenacetyl)pyrrolidine (14d). (Two rotameric forms) (0.34 g, 64%) White microcrystals (from CH_2Cl_2 / Et_2O) mp 141–143 °C. $[\alpha]^{23}_D$ –12.7 (*c* 1.20, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ 1.79–2.12 (m, 3H), 2.29–2.47 (m, 1H), 3.44–3.58 (m, 2H), 4.99–5.27 (m, 3H), 7.21–7.70 (m, 20H). ^{13}C NMR ($CDCl_3$) δ 23.6, 24.4, 30.4, 31.6, 46.2 (J_{CP} = 126.3 Hz), 46.3 (J_{CP} = 127.0 Hz), 46.8, 47.4, 61.8 (J_{CP} = 9.1 Hz), 62.4 (J_{CP} = 9.1 Hz), 66.4, 121.3 (J_{CP} = 14.7 Hz), 121.5 (J_{CP} = 15.4 Hz), 122.6 (J_{CP} = 93.4 Hz), 122.9 (J_{CP} = 93.4 Hz), 126.9, 127.2, 127.4, 127.4, 128.1, 128.2, 128.4, 128.8 (J_{CP} = 12.6 Hz), 128.9 (J_{CP} = 12.6 Hz), 131.8, 131.9, 132.8 (J_{CP} = 2.8 Hz). 132.9 (J_{CP} = 2.8 Hz), 133.2 (J_{CP} = 10.5 Hz), 133.4 (J_{CP} = 10.5 Hz), 136.9, 137.0, 154.2, 154.4, 194.7 (J_{CP} = 3.5 Hz), 194.9 (J_{CP} = 3.5 Hz). HRMS *m/z* Calcd for $C_{33}H_{29}N_2O_3P$ 533.1989 $[M+H]^+$, Found 533.1995.

5-Benzyloxycarbonylamino-3-oxo-2-triphenylphosphoranylidenpentane nitrile (14e). (0.32 g, 63%) White microcrystals (from Et_2O/hexanes) mp 156–158 °C. ^{1}H NMR ($CDCl_3$) δ 2.95 (t, *J* = 5.9 Hz, 2H), 3.45–3.50 (m, 2H), 5.08 (s, 2H), 5.41 (br s, 1H), 7.24–7.38 (m, 5H), 7.44–7.64 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 36.9, 38.6 (J_{CP} = 9.2 Hz), 49.0 (J_{CP} = 126.0 Hz), 66.1, 121.8 (J_{CP} = 16.6 Hz), 122.6 (J_{CP} = 93.9 Hz), 127.7, 127.8, 128.2, 129.0 (J_{CP} = 13.2 Hz), 133.1 (J_{CP} = 2.9 Hz), 133.3 (J_{CP} = 10.3 Hz), 136.6, 156.0,

195.0. Anal. Calcd for $C_{31}H_{27}N_2O_3P$: C, 73.51; H, 5.37; N, 5.53. Found: C, 73.50; H, 5.37; N, 5.50.

PREPARATION OF 2,4-DIHYDROPYRROL-3-ONE SALTS 15a–c, PYRROLIZIN-1-ONE SALT 15d, AND NITRILE SALT 15e

Compounds **15a–e** were prepared from the corresponding **14a–e** (1.0 mmol) following the procedure developed for salts **8a–e**.

5-Amino-4-triphenylphosphonio-2,4-dihydropyrrol-3-one Bromide (15a). (0.31 g, 71%) White plates (from CH_2Cl_2 / Et_2O) mp 255–258 °C. ^{1}H NMR ($CDCl_3$) δ 3.99 (s, 2H), 7.64–7.71 (m, 12H), 7.74–7.81 (m, 3H), 8.72 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 52.2 (J_{CP} = 10.3 Hz), 64.8 (J_{CP} = 125.4 Hz), 119.7 (J_{CP} = 93.3 Hz), 130.1 (J_{CP} = 13.2 Hz), 133.6 (J_{CP} = 10.9 Hz), 134.6 (J_{CP} = 2.9 Hz), 170.3 (J_{CP} = 17.2 Hz), 194.5 (J_{CP} = 6.3 Hz). Anal. Calcd for $C_{22}H_{20}BrN_2OP$: C, 60.15; H, 4.59; N, 6.38; Found: C, 60.11; H, 4.94; N, 5.59.

(2*RS*)-5-Amino-2-methyl-4-triphenylphosphonio-2,4-dihydropyrrol-3-one Bromide (15b). (0.26 g, 70%) White plates (from CH_2Cl_2 / Et_2O) mp 260–262 °C. ^{1}H NMR ($CDCl_3$) δ 1.45 (d, J = 7.0 Hz, 3H), 1.72 (br s, 2H), 4.03 (q, J = 7.0 Hz, 1H), 7.63–7.69 (m, 12H), 7.75–7.81 (m, 3H), 8.76 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 17.3, 58.5 (J_{CP} = 10.3 Hz), 63.1 (J_{CP} = 124.3 Hz), 120.1 (J_{CP} = 93.3 Hz), 130.1 (J_{CP} = 13.1 Hz), 133.6 (J_{CP} = 10.9 Hz), 134.6 (J_{CP} = 2.9 Hz), 168.8 (J_{CP} = 17.2 Hz), 197.7 (J_{CP} = 5.7 Hz). Anal. Calcd for $C_{23}H_{22}BrN_2OP$: C, 60.94; H, 4.89; N, 6.18. Found: C, 60.58; H, 4.78; N, 5.96.

(2*RS*)-5-Amino-2-benzyl-4-triphenylphosphonio-2,4-dihydropyrrol-3-one Bromide (15c). (0.38 g, 72%) White plates (from CH_2Cl_2 / Et_2O) mp 253–255 °C. ^{1}H NMR ($CDCl_3$) δ 1.69 (s, 2H), 3.11 (dd, J = 14.0, 4.9 Hz, 1H), 3,21 (dd, J = 14.0, 3.5 Hz, 1H), 4.28 (t, J = 4.2 Hz, 1H), 7.32–7.42 (m, 11H), 7.54–7.59 (m, 6H), 7.71–7.76 (m, 3H), 9.06 (br d, J_{HP} = 2.1 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 36.6, 63.3 (J_{CP} = 10.3 Hz), 64.0 (J_{CP} = 127.8 Hz), 119.7 (J_{CP} = 92.8 Hz), 126.8, 128.4, 130.0 (J_{CP} = 12.6 Hz), 130.6, 133.7 (J_{CP} = 10.9 Hz), 134.5 (J_{CP} = 2.9 Hz), 134.9, 169.3 (J_{CP} = 16.6 Hz), 195.3 (J_{CP} = 6.3 Hz). Anal Calcd for $C_{29}H_{26}BrN_2OP + H_2O$: C, 63.63; H, 5.16; N, 5.12. Found: C, 63.21; H, 4.77; N, 4.94.

(4*RS*)-3-Ammonio-2-triphenylphosphonio-tetrahydropyrrolizin-1-one Dibromide (15d). (0.37 g, 66%) White plates (from CH_2Cl_2 / Et_2O) mp 238–240 °C. ^{1}H NMR ($CDCl_3$) δ 1.48–1.59 (m, 1H), 1.93–2.25 (m, 3H), 3.57–3.70 (m, 1H), 3.81–3.88 (m, 1H), 4.02–4.08 (m, 1H), 7.54–7.64 (m, 11H), 7.69–7.79 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 26.7, 27.8, 49.1, 65.9 (J_{CP} = 119.1 Hz), 70.0 (J_{CP} = 10.3 Hz), 119.4 (J_{CP} = 92.8 Hz), 130.0 (J_{CP} = 13.1 Hz), 133.5 (J_{CP} = 10.9 Hz), 134.6 (J_{CP} = 2.9Hz), 170.9 (J_{CP} = 15.5 Hz), 196.2 (J_{CP} = 5.7 Hz). Anal. Calcd for $C_{25}H_{25}Br_2N_2OP$: C, 53.59; H, 4.50; N, 5.00. Found: C, 53.99; H, 4.39; N, 4.52.

1-Ammonio-3-oxo-4-triphenylphosphoranylidenpentan-5-nitrile Bromide (15e). (0.16 g, 35%) White microcrystals (from Et_2O / hexanes) mp 238–244 °C. ^{1}H NMR ($CDCl_3$) δ 3.17–3.24 (m, 4H),

7.42 (br s, 3H), 7.51–7.68 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 33.4 (J_{CP} = 8.0 Hz), 37.0, 50.4 (J_{CP} = 124.3 Hz), 120.8 (J_{CP} = 16.0 Hz), 121.8 (J_{CP} = 93.3 Hz), 129.3 (J_{CP} = 13.2 Hz), 133.4 (J_{CP} = 10.3 Hz), 133.5 (J_{CP} = 2.3 Hz), 195.0 (J_{CP} = 4.0 Hz). Anal. Calcd for $C_{23}H_{24}BrN_2O_2P$: C, 58.61; H, 5.13; N, 5.94. Found: C, 58.63; H, 5.15; N, 5.39.

PREPARATION OF 3,3-DIBROMOPYRROLIDIN-2,4-DIONE 16

4-Chlorobenzoic acid (0.05 g, 0.32 mmol) and **14** (0.13 g, 0.28 mmol) were refluxed in THF (25 mL) for 1 h, no reaction was detected by TLC. Upon the addition of NBS (0.17 g, 0.56 mmol) the reaction was completed after 5 min of stirring at rt. The organic phase was washed with saturated aq sodium chloride. The crude product was subjected to column chromatography (SiO_2, hexane:EtOAc = 4:1).

(5*RS*)-5-Benzyl-3,3-dibromo-1-methylpyrrolidin-2,4-dione (16). (0.08 g, 79%) Yellowish oil. ^{1}H NMR ($CDCl_3$) δ 3.06 (s, 3H), 3.23 (d, *J* = 4.9 Hz, 2H), 4.51 (t, *J* = 4.9 Hz, 1H), 7.07–7.11 (m, 2H), 7.22–7.33 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 29.4, 35.5, 44.7, 66.6, 127.8, 128.9, 129.6, 133.7, 164.8, 194.4. Anal. Calcd for $C_{12}H_{11}Br_2NO_2$: C, 39.92; H, 3.07; N, 3.88. Found: C, 40.45; H, 3.22; N, 3.40.

PREPARATION OF 3,3-DIBROMO-5-HYDROXY-PYRROLIDIN-2,4-DIONE 17

Ethoxytrimethylsilane (0.057 g, 0.5 mmol) and NBS (0.115 g, 0.65 mmol) were combined in CH_2Cl_2 (1 mL) for 2 min and added to **14** (0.15 g, 0.3 mmol) separately dissolved in CH_2Cl_2 (1 mL). The reaction was complete after 5 min stirring at rt. The crude product was subjected to column chromatography (SiO_2, hexane:EtOAc = 4:1) and allowed a mixture (1:1) of **16** (0.05 g, 44%) and **17** (0.05 g, 44%) to be obtained in 88% yield, without workup.

(5*RS*)-5-Benzyl-3,3-dibromo-5-hydroxy-1-methylpyrrolidin-2,4-dione (17). (0.05 g, 44%) White sheets ($CHCl_3$) mp 134–136 °C. ^{1}H NMR ($CDCl_3$) δ 3.13 (s, 3H), 3.21 (d, *J* = 14.0 Hz, 1H), 3.38 (d, *J* = 14.0 Hz, 1H), 4.66 (br s, 1H), 7.05–7.09 (m, 2H), 7.24–7.28 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 25.9, 41.1, 42.6, 90.8, 128.1, 129.0, 130.4, 131.8, 165.1, 194.3. Anal. Calcd for $C_{12}H_{11}Br_2NO_3$ C, 38.23; H, 2.94; N, 3.72. Found: C, 37.48; H, 2.82; N, 3.50.

PREPARATION OF 4-AZIDO-3-BROMOPYRROL-2-ONE 18

N-Bromosuccinimide (0.135 g, 0.76 mmol) and TMS-azide (0.1 mL, 0.76 mmol) were combined in CH_2Cl_2 (5 mL) and added to **14** (0.25 g, 0.54 mmol) dissolved in CH_2Cl_2 (1 mL). The reaction was stirred at rt for 5 min. The crude product was subjected to column chromatography (SiO_2, hexane:EtOAc = 4:1), without workup.

(5*RS*)-4-Azido-5-benzyl-3-bromo-1-methylpyrrol-2-one (18). (0.14 g, 84%) Clear oil. ^{1}H NMR ($CDCl_3$) δ 2.93 (dd, *J* = 14.7, 4.9 Hz, 1H), 2.95 (s, 3H), 3.16 (dd, *J* = 14.7, 4.2 Hz, 1H), 4.08 (t, *J* = 4.9 Hz, 1H), 7.07–7.11 (m, 2H), 7.23–7.31 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 28.7, 35.8, 63.3, 103.1, 127.4, 128.7,

129.0, 134.0, 149.3, 165.8. $C_{12}H_{11}BrN_4O$ HRMS *m/z* Calcd 307.0194, 309.0174 $[M+H]^+$, Found 307.0190, 309.0119.

PREPARATION OF 4-BENZOTRIAZOLPYRROL-2-ONE 19

1-Chlorobenzotriazole (0.7 g, 0.48 mmol) and **14** (0.2 g, 0.43 mmol) were dissolved together in CH_2Cl_2 (1 mL). The reaction was stirred at rt for 5 min. The crude product was subjected directly to column chromatography (SiO_2, hexane:EtOAc = 9:1) without workup.

(5*RS*)-4-(Benzotriazol-1-yl)-5-benzyl-1-methylpyrrol-2-one (19). (0.12 g, 92%) Yellow microcrystals (Et_2O) mp 124–126 °C. ^{1}H NMR ($CDCl_3$) δ (Bt^1:Bt^2 = 1:1) 2.90 (dd, *J* = 14.0, 4.9 Hz, 1H), 3.13–3.30 (m, 7H), 3.37–3.50 (m, 2H), 5.21 (t, *J* = 4.2 Hz, 1H), 5.34 (t, *J* = 4.2 Hz, 1H), 6.47 (s, 1H), 6.49 (s, 1H), 6.65–6.68 (m, 2H), 6.99 (t, *J* = 7.7 Hz, 2H), 7.11–7.14 (m, 4H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.40–7.60 (m, 5H), 7.87–7.98 (m, 3H), 8.16 (d, *J* = 7.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 28.8, 29.0, 35.1, 35.8, 62.0, 62.7, 112.5, 115.0, 116.4, 117.6, 118.6, 120.5, 125.3, 125.7, 127.4, 127.4, 128.5, 128.5, 128.8, 128.8, 128.8, 131.6, 133.0, 133.5, 143.8, 144.7, 145.2, 145.9, 164.6, 164.7. Anal. Calcd for $C_{18}H_{16}N_4O$: C, 71.01; H, 5.30; N, 18.41. Found: C, 68.94; H, 4.96; N, 18.81. Reduced product $C_{18}H_{14}N_4O$ HRMS *m/z* Calcd 303.0120, 325.1060 $[M+H]^+$, $[M+Na]^+$ Found 303.1233, 325.1054, observed ions consistent with M = $C_{18}H_{16}N_4O$.

X-Ray Crystallography

Intensity data were collected with an APEX II CCD area detector using monochromatized Mo Kα (λ = 0.71073 Å) radiation. The intensities were corrected for Lorentz and polarization effects and for absorption. The structures were solved by direct methods and refined on F^2 by full-matrix least-squares procedures. All non-hydrogen atoms were refined with anisotropic displacement coefficients. The positions of hydrogen atoms were refined with isotropic displacement coefficients equal to 1.2 times the isotropic equivalent of their carrier atoms. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC Nos 668264 and 668265). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk.

Crystal data for (9c): $C_{29}H_{24}NO_2P$, MW 449.460, monoclinic, space group $P2_1/n$, *a* = 10.7276(2), *b* = 14.2746(3), *c* = 14.8455(4) Å, *β* = 90.353(1) °, V = 2273.28(9) Å^3, F(000) = 944, Z = 4, T = -180 °C, colorless block, 0.44 x 0.22 x 0.12 mm, μ (MoKα) = 0.148 mm^{-1}, D_{calcd} = 1.313 g.cm^{-3}, $2\theta_{max}$ 50°, $wR(F^2)$ = 0.0997 (all 4022 data), R = 0.0402 (3788 data with I > 2σI).

Crystal data for (17): $C_{12}H_{11}Br_2NO_3$, MW 377.04, monoclinic, space group $P2_1/n$, *a* = 6.8928(5), *b* = 28.975(2), *c* = 7.0527(5) Å, *β* = 110.311(2) °, V = 1320.99(16) Å^3, F(000) = 736, Z = 4, T = -170 °C, colorless plate, 0.53 x 0.26 x 0.14 mm, μ (MoKα) = 6.135 mm^{-1}, D_{calcd} = 1.896 g.cm^{-3}, $2\theta_{max}$ 53°,

$wR(F^2)$ = 0.0754 (all 2540 data), R = 0.0268 (2274 data with $I > 2\sigma I$).

REFERENCES

1. a) H.–G. Henning and A. Gelbin, *Adv. Heterocycl. Chem.*, 1993, **57**, 139. b) S. J. Shimshock and P. DeShong, *Studies Nat. Prod. Chem.*, 1994, **14**, 97. c) B. J. L. Royles, *Chem. Rev.*, 1995, **95**, 1981. d) N. Takahashi, S. Gotohda, Y. Endo, Y. Endo, S. Wakisaka, and Y. Sasama, *Jpn. Pat.*, 2000, 086628. e) G. A. Burdock and W. G. Flamm, *Int. J. Toxicol.*, 2000, **19**, 195. f) J. Markopoulos, A. Detsi, E. Gavrielatos, G. Athanasellis, and O. Igglessi-Markopoulou, *Biomed. Health Res.*, 2002, **55**, 25. g) E. L. Ghisalberti, *Studies Nat. Prod. Chem.*, 2003, **28**, 109. h) H. Poschenrieder, G. Hofner, and H.–D. Stachel, *Arch. Pharm.*, 1999, **332**, 309. i) H. Poschenrieder, H.–D. Stachel, G. Hoefner, and P. Mayer, *Eur. J. Med. Chem.*, 2005, **40**, 391.
2. a) H. Poschenrieder, G. Hoefner, and H.–D. Stachel, *Arch. Pharm.*, 1998, **331**, 389. b) K. Satoh, A. Imura, A. Miyadera, K. Kanai, and Y. Yukimoto, *Chem. Pharm. Bull.*, 1998, **46**, 587. c) N. Toyooka, M. Nishio, H. Shinoda, and T. Momose *Heterocycles*, 1999, **51**, 1427.
3. a) K. S. Kochhar, H. J. Carson, K. A. Clouser, J. W. Elling, L. A. Gramens, J. L. Parry, H. L. Sherman, K. Braat, and H. W. Pinnick, *Tetrahedron Lett.*, 1984, ***25***, 1871. b) R. C. F. Jones and A. D. Bates, *Tetrahedron Lett.*, 1986, **27**, 5285.
4. M. Sato, H. Ogasawara, K. Takayama, and C. Kaneko, *Heterocycles*, 1987, **26**, 2611.
5. a) J.–A. Fehrentz, C. Genu-Dellac, M. Amblard, F. Winternitz, A. Loffet, and J. Martinez, *J. Pept. Sci.*, 1995, **1**, 124. b) J. Svete, *Monatsh. Chem.*, 2004, **135**, 629. c) M. Hosseini, H. Kringelum, A. Murray, and J. E. Tonder, *Org. Lett.*, 2006, **8**, 2103.
6. R. C. F. Jones and J. M. Patience, *Tetrahedron Lett.*, 1989, **30**, 3217.
7. a) R. C. F. Jones, C. E. Dawson, and M. J. O'Mahony, *Synlett*, 1999, 873. b) R. C. F. Jones, G. Bhalay, P. A. Carter, K. A. M. Duller, and S. H. Dunn, *J. Chem. Soc., Perkin Trans. 1*, 1999, 765.
8. a) J. Brennan and P. J. Murphy, *Tetrahedron Lett.*, 1988, **29**, 2063. b) R. Schobert, M. Dietrich, G. Mullen, and J.–M. Urbina-Gonzalez, *Synthesis*, 2006, 3902.
9. a) R. Schobert, C. Jagusch, C. Melanophy, and G. Mullen, *Org. Biomol. Chem.*, 2004, **2**, 3524. b) R. Schobert and C. Jagusch, *Tetrahedron*, 2005, **61**, 2301.
10. a) D. Cartwright, V. J. Lee, and K. L. Rinehart Jr., *J. Am. Chem. Soc.*, 1978, **100**, 4237. b) R. K. Boeckman Jr., J. C. Potenza, and E. J. Enholm, *J. Org. Chem.*, 1987, **57**, 469. c) R. H. Schlessinger and D. D. Graves, *Tetrahedron Lett.*, 1987, **28**, 4385.
11. a) J. A. King and F. H. McMillan, *J. Am. Chem. Soc.*, 1950, **72**, 1236. b) R. N. Lacey, *J. Chem. Soc.*, 1954, 850. c) P. DeShong, J. A. Cipollina, and N. K. Lowmaster, *J. Org. Chem.*, 1988, **53**, 1356. d) T. Iida, K. Hori, K. Nomura, and E. Yoshii, *Heterocycles*, 1994, **38**, 1839. e) B. A. Kulkarni and A. Ganesan, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2454.

12. H.–G. Capraro, T. Winkler, and P. Martin, *Helv. Chim. Acta*, 1983, **66**, 362.
13. A. Miyadera, K. Satoh, and A. Imura, *Chem. Pharm. Bull.*, 2000, **48**, 563.
14. J. C. A. Boeyens, A. J. Brink, and A. Jordaan, *S. Afr. J. Chem.*, 1978, **78**, 7.
15. A. R. Aitken, G. M. Buchanan, N. Karodia, T. Massil, and R. J. Young, *Tetrahedron Lett.*, 2001, **42**, 141.
16. a) C. Baldoli, E. Licandro, S. Maiorana, E. Menta, and A. Papagni, *Synthesis*, 1987, 288. b) A. Detsi, P. Emirtzoglou, K. Prousis, A. N. Nikolopoulos, V. Skouridou, and O. Igglessi-Markopoulou, *Synlett*, 2004, 353. c) K. C. Prousis, A. Detsi, and O. Igglessi-Markopoulou, *Synlett*, 2005, 2763.
17. a) A, R. Aitken, V. Bjørnstad, T. Massil, and J. Skramstad, *Phosphorus Sulfur Silicon Relat. Elem.*, 1999, **144**, 577. b) M. Taillefer and H.–J. Cristau, *Top. Curr. Chem.*, 2003, **229**, 41. c) N. Bricklebank, *Organophosphorus Chem.*, 2003, **33**, 289.
18. Y. Mao, I. Maley, and W. H. Watson, *J. Chem. Crystallogr.*, 2005, **35**, 385.
19. D. T. Connor and M. Von Strandtmann, *J. Org. Chem.*, 1973, **38**, 1047.
20. A. R. Katritzky, A. S. Vincek, and K. Suzuki, *Arkivoc (Arkive for Organic Chemistry)*, 2005, **v**, 116.
21. W. Flitsch and K. Pandl, *Liebigs Ann. Chem.*, 1987, **8**, 649.
22. P. A. Chopard, R. J. G. Searle, and F. H. Devitt, *J. Org. Chem.*, 1965, **30**, 1015.
23. a) A. R. Katritzky, A. A. Shestopalov, and K. Suzuki, *Synthesis*, 2004, 1806. b) A. R. Katritzky, K. Suzuki, and S. K. Singh, *Synthesis*, 2004, 2645.
24. a) A. R. Katritzky, M. Wang, H. Yang, S. Zhang, and N. G. Akhmedov, *Arkivoc (Arkive for Organic Chemistry)*, 2002, **viii**, 134. b) A. R. Katritzky, S. Hoffmann, and K. Suzuki, *Arkivoc (Arkive for Organic Chemistry)*, 2004, **xii**, 14. c) A. R. Katritzky, R. Jiang, and K. Suzuki, *J. Org. Chem.*, 2005, **70**, 4993. d) A. R. Katritzky, P. Angrish, D. Hür, and K. Suzuki, *Synthesis*, 2005, 397. e) A. R. Katritzky, P. Angrish, and K. Suzuki, *Synthesis,* 2006, 411.
25. A. R. Aitken, N. Karodia, T. Massil, and R. J. Young, *J. Chem. Soc., Perkin Trans. 1*, 2002, **4**, 533.
26. a) B. L. Hayes, "*Microwave Synthesis: Chemistry at the Speed of Light"* CEM publishing, North Carolina. 2002. b) A. R. Katritzky and S. K. Singh, *Arkivoc (Arkive for Organic Chemistry)*, 2003, **xiii**, 68.
27. F. Castaneda, G. I. Recabarren, J. Hu, N. D. Gillitt, and C. A. Bunton, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2003, **178**, 2505.
28. M. Schlosser, T. Jenny, and B. Schaub, *Heteroatom Chem.*, 1990, **1**, 151.
29. A. J. Harvey and A. D. Abell, *Tetrahedron*, 2000, **56**, 9763.
30. a) M. Paris, C. Pothion, C. Michalak, J. Martinez, and J. A. Fehrentz, *Tetrahedron Lett.*, 1998, **39**, 6889. b) H. H. Wasserman, A. K. Petersen, and M. Xia, *Tetrahedron*, 2003, **59**, 6771. c) H. H. Wasserman and A. K. Petersen, *Tetrahedron Lett.*, 1997, **38**, 953.

31. G. Gibbs, M. J. Hateley, L. McLaren, M. Welham, and C. L. Willis, *Tetrahedron Lett.*, 1999, **40**, 1069.
32. a) H. H. Wasserman and W.–B. Ho, *J. Org. Chem*., 1994, **59**, 4364. b) A. Papanikos and M, Morten, *J. Comb. Chem.*, 2004, **6**, 181.
33. J.–J. Kim, D.–H. Kweon, S.–D. Cho, H.–K. Kim, S.–G. Lee, and Y.–J. Yoon, *Synlett*, 2006, 194.
34. a) H.–D. Stachel and H. Poschenrieder, *Arch. Pharm.*, 1985, **318**, 311. b) D. J. Wardrop and E. G. Bowen, *Chem. Commun.*, 2005, **40**, 5106.
35. D. Yang, Y.–L. Yan, and B. Lui, *J. Org. Chem.*, 2002, **67**, 7429.
36. a) E. F. V. Scriven and K. Turnbull, *Chem. Rev.*, 1988, **88**, 297. b) H. W. Moore, *Acc. Chem. Res.*, 1979, **12**, 125. c) H. W. Moore, L. Hernandez Jr., and R. Chambers, *J. Am. Chem. Soc.*, 1978, **100**, 2245.
37. M. Augustin, H. J. Milz, and M. Koehler, *Z. Chem.*, 1980, **20**, 54.