The reaction of unstabilised 1,3,4-oxadiazolium-N-methanide 1,3-dipoles with alkenes: N-substituted Δ-2-pyrrolines: contrast with the 1,3,4-thiadiazolium analogue

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Dedicated to Tony McKervey on the occasion of his 65th birthday

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Abstract

Treatment of transient 2,5-diaryl-1,3,4-oxadiazolium-3-methanides, unstabilized 1,3-dipoles, at -60°C with acrylonitrile, methyl acrylate, dimethyl maleate, dimethyl fumarate, chloroacrylonitrile, dimethyl- and diethyl acetylenedicarboxylates, methyl propiolate and butyne-3-one gave in all cases a 1-N-benzamido-substituted pyrrole or pyrroline product. This contrasts with the corresponding 1,3,4- thiadiazolium-methanide 1,3-dipole where the cycloadducts were stable. The reactions involved cycloadditions followed by ring-opening through 1,2- or 1,4-conjugate elimination processes. An X-ray crystal structure is reported on 1-{N-benzoyl-N-[Z-1,2-dimethoxycarbonylvinyl] amino}-2-phenyl-3,4-dimethoxycarbonyl pyrrole, **17**.

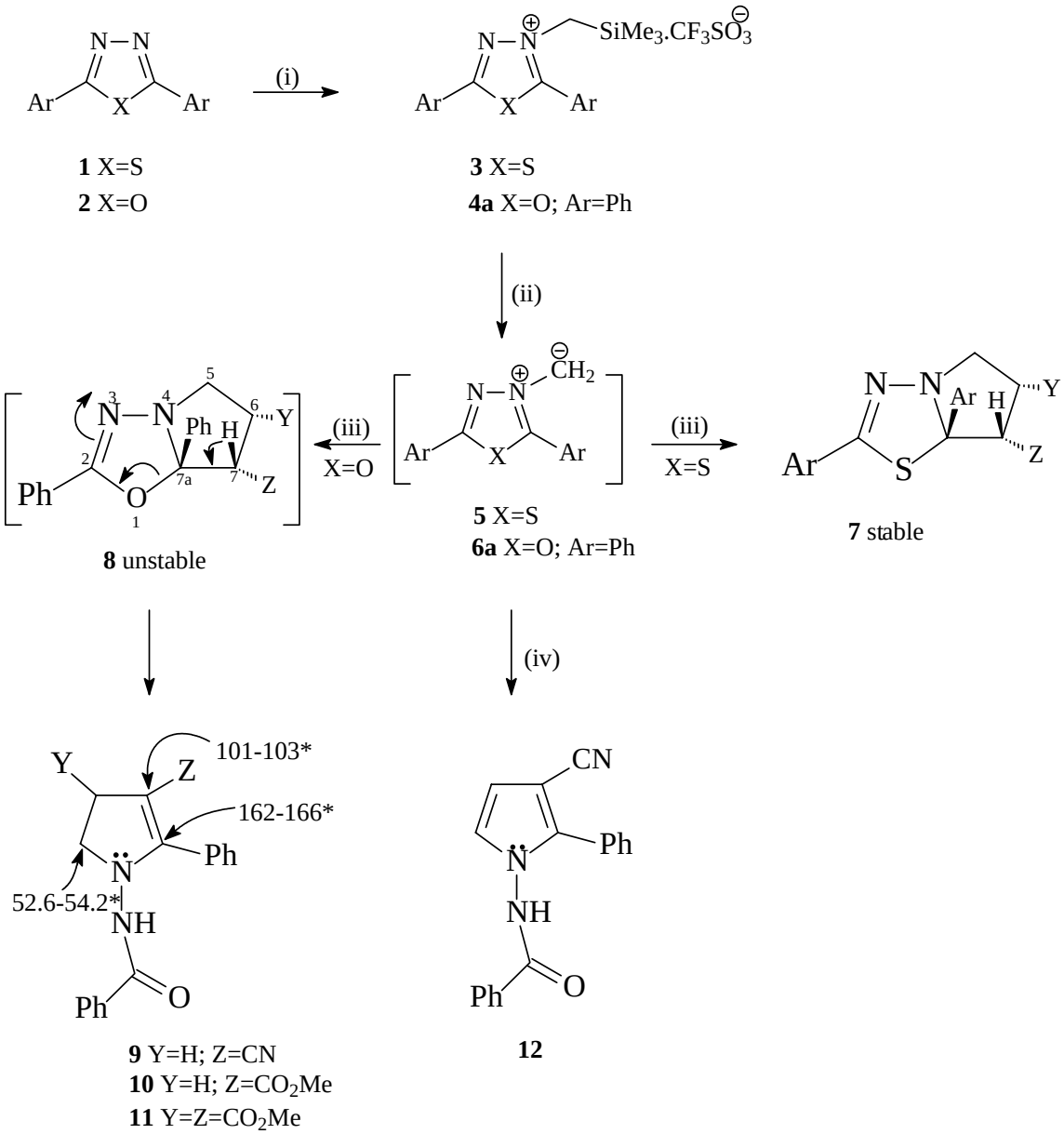
Keywords: 1,3-Dipolar cycloadditions, azolium-*N*-methanide, Δ-2-pyrrolines

Introduction

In our exploration[1] of exocyclic azolium ylide systems as 1,3-dipoles which undergo interesting cycloaddition-rearrangement sequences we have recently established the transient 1,3,4-thiadiazolium-3-methanide species **5** as a synthon for the rare[2] fused pyrrolo [2,1-*b*]-1,3,4-thiadiazole ring system **7** via low-temperature cycloaddition reactions with substituted alkenes.[3] The cycloadducts **7** were stable products. Similar reactions with the oxadiazolium 1,3-dipole **6** should give oxygen analogues **8**.

Results and Discussion

The species **5** was generated at -60°C from the salts **3** by treatment with CsF following a procedure originally developed with quaternised Schiff bases.[4,5] Herein we have similarly generated the 1,3,4-oxadiazolium-3-methanide species **6** at -60°C in methylene chloride in the presence of a number of alkene dipolarophiles. The products of the these reactions were the 1-N-benzamido-4,5-dihydro-pyrroles **9, 10, 11** (Scheme 1, Table) and curiously the bicyclic structure **8** proved labile under the reaction conditions even at -60°C (Scheme 1).



Scheme 1. Reagents: (i) trimethylsilylmethyl trifluoromethanesulfonate; (ii) CsF; (iii) mono- and 1,2-disubstituted alkenes; (iv) 1-chloroacrylonitrile. Some ^{13}C NMR shifts* shown.

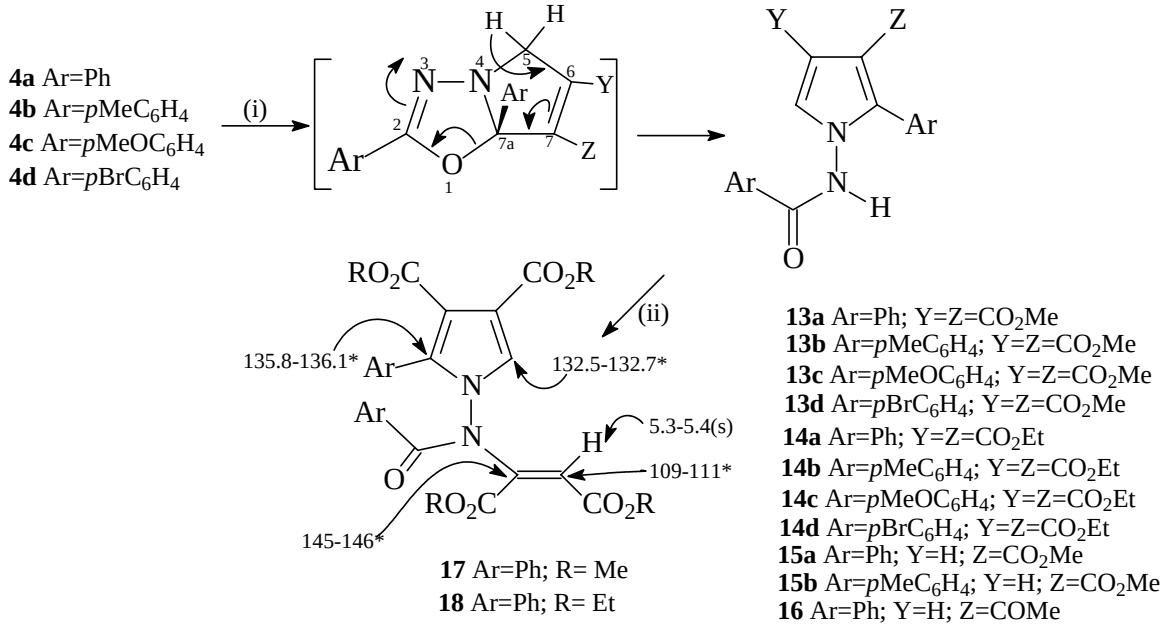
The rearrangement of the cycloadduct involves a 1,2-elimination along the C(7)-C(7a) bond in structure **8** which did not occur in structure **7**. It seems that replacement of the S atom by the electronegative O atom in the fused bicyclic structure **8** has increased the acidity of the 7-C-H bond sufficiently that this 1,2-elimination occurred under the reaction conditions. These conditions may be important and the CsF present could be playing a role in the eliminative ring-opening. In the reactions of the thiadiazolium dipole **5** the stereochemistry of the cycloaddition was predominantly *endo* and the substituent Y and Z in the products **7** were *endo* to the fused bicyclic structure. For the dipoles **6** the stereochemistry is lost *in situ* in the second step and hence the same product is obtained from dimethyl maleate and dimethyl fumarate (Table, entries 3 and 4).

Table. Products from the reactions of 1,3-dipoles **6a-6d**

Entry	Dipolarophile	Ar	Cpd	Y	Z	Yield(%)	Mp/°C[b]
1	Acrylonitrile	Ph	**9**	H	CN	92	178-179
2	Methylacrylate	Ph	**10**	H	CO_2Me	77	gum[c]
3	Dimethyl maleate	Ph	**11**	CO_2Me	CO_2Me	94	131-132
4	Dimethyl fumarate	Ph	**11**	CO_2Me	CO_2Me	85	131-132
5	Chloroacrylonitrile	Ph	**12**	-	-	86	gum[c]
6	DMAD[a]	Ph	**13a**	CO_2Me	CO_2Me	81	184-185
7	DMAD	$pMeC_6H_4$	**13b**	CO_2Me	CO_2Me	67	155-156
8	DMAD	$pMeOC_6H_4$	**13c**	CO_2Me	CO_2Me	56	156-158
9	DMAD	$pBrC_6H_4$	**13d**	CO_2Me	CO_2Me	57	115-117
10	DEAD[a]	Ph	**14a**	CO_2Et	CO_2Et	72	gum[c]
11	DEAD	$pMeC_6H_4$	**14b**	CO_2Et	CO_2Et	60	142-144
12	DEAD	$pMeOC_6H_4$	**14c**	CO_2Et	CO_2Et	53	151-152
13	DEAD	$pBrC_6H_4$	**14d**	CO_2Et	CO_2Et	50	190-191
14	Methyl propiolate	Ph	**15a**	H	CO_2Me	89	130-132
15	Methyl propiolate	$pMeC_6H_4$	**15b**	H	CO_2Me	81	184-186
16	Butyn-3-one	Ph	**16**	H	Ac	76	90-92
17	DMAD[a] (≥ 5mol)	Ph	**17**	-	-	64	186-188
18	DEAD[a] (≥ 5mol)	Ph	**18**	-	-	58	gum[c]

[a] Dimethyl- and Diethyl acetylenedicarboxylate.
[b] Recrystallised from dichloromethane-hexane (2:1 v/v).
[c] Sticky low-melting solids.

Interestingly in the reaction with 1-chloro-1-cyano ethene (chloroacrylonitrile) a double elimination occurred giving the aromatised product **12** (Scheme 1, Table entry 5) . In this case, with Cl atom in place of the H-atom at C-7 of structure **8**, an initial 1,2-elimination of HCl occurred along the C(6)-C(7) bond of **8** followed by a 1,4-conjugate elmination at the 5-C-H and 7a-C-O bonds giving an overall aromatisation. The intermediate from the initial HCl elimination would be the expected cycloadduct from an alkyne dipolarophile. As expected cycloadducts from alkyne dipolorophiles readily aromatised *in situ* giving the products **13a-13d, 14a-14d, 15a-15b and 16** (Scheme 2). When higher than five molar excess of dipolarophile was used in these reactions the amido N-H underwent a further nucleophilic addition across a molecule of the exces alkyne. This addition appears to be a four-centred *cis*-addition since the products had the structure **17** and **18** shown (Scheme 2, Figure 1). In a known stereo-electronic effect nucleophiles adding to triple bonds are expected[6,7] to repel the π-electrons to form a lone pair oriented *trans*- to the incoming nucleophile and the H-atom should ultimately bond at this *trans*-site. The *cis*-addition was confirmed by an X-ray crystal structure of compound **17** (Figure 1).



Scheme 2. Reagents: (i) CsF, alkyne dipolarophiles, (ii) dialkyl acetylenedicarboxylates. Some ^{1}H and $^{13}C^{*}$ NMR shifts shown.

The structures of the products were established from microanalyses, i.r., proton and carbon-13 NMR spectra which showed all of the expected signals and splitting. The enamine unit of the non-aromatic Δ-2 pyrroline structure **9** showed the expected deshielding of the enamine α-carbon (C-2) to 162-166ppm as well as the expected shielding of the enamine β-carbon (C-3) to

101-103ppm (Scheme 1). Similar shielding effects were also present in the exocyclic enamine unit in products **17** and **18** (Scheme 2)**.** When Z was a CN substitutent in compound **9** the pyrroline C-3 was further shielded to 82ppm. The structural assignments and the reaction outlines are further supported by the X-ray crystal structure determination on compound **17** (Figure 1). The regiochemistry of the products indicates an initial HOMO-dipole controlled cycloaddition[8] with the dipole CH_2- terminus bonding to the dipolarophile unsubstituted terminus. The reactions described for the 1,3-dipole species **6a-6d** provide new routes to selectively substituted partially reduced pyrrole derivatives. Despite the range of known routes[9] to the pyrrole ring there is still a need to find controllable new routes to special derivatives and in particular dihydro pyrroles because of the importance of partially reduced pyrroles as intermediates in natural product synthesis.[9,10]

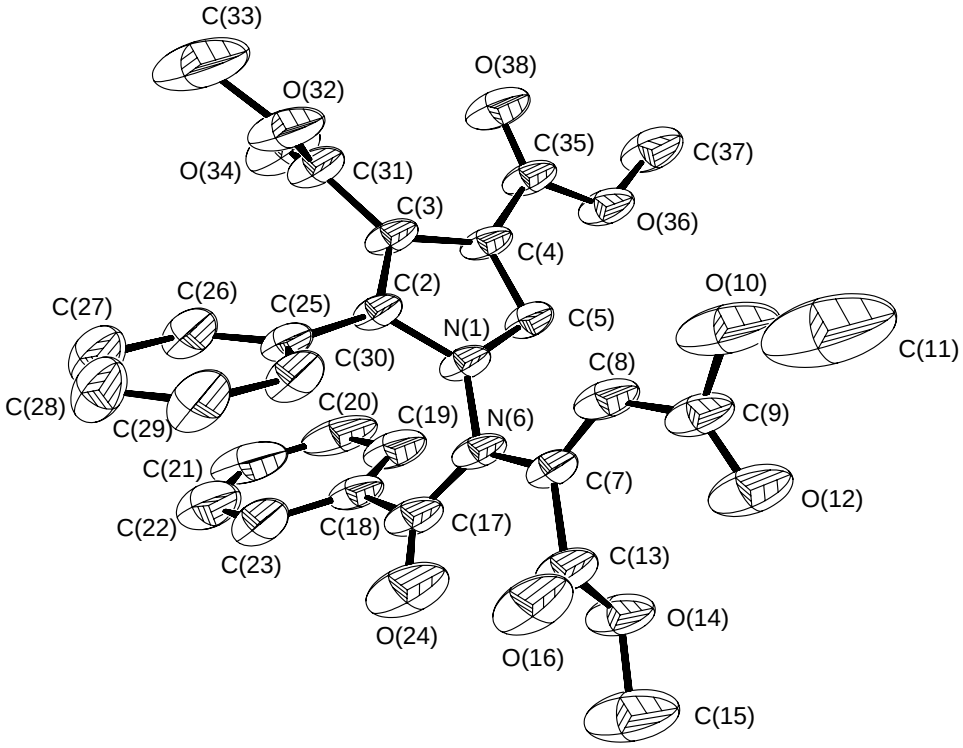


Figure 1. X-Ray crystal structure of compound **17**.

Experimental Section

General Procedures. Melting points were measured on a Stuart Scientific melting point apparatus. IR spectra were measured with a Perkin-Elmer Spectrum 1000 FT-IR spectrometer. NMR spectra were measured on a JEOL LAMBDA 400MHz instrument with tetramethylsilane

as an internal reference and deuteriochloroform as the solvent. *J* values are given in Hz. All carbon-13 NMR assignments were supported by DEPT. Microanalyses were measured on a Perkin-Elmer model 240 CHN analyser. The following chemicals were purchased from Aldrich: acrylonitrile, methyl acrylate, dimethyl fumarate and methyl methacrylate; from Fluka, 1-chloroacrylonitrile; from Lancaster: dimethyl maleate (99%). Dichloromethane was refluxed over CaH_2, followed by distillation onto 4Å molecular sieves.

Synthesis of 2,5-Diphenyl-3-trimethylsilylmethyl-1,3,4-oxadiazolium trifluoromethanesulfonate (4a). A solution of 2,5-diphenyl-1,3,4-oxadiazole **2a** (1.0g, 4.5mmol) and trimethylsilylmethyl trifluoromethanesulfonate (0.99cm^3, 4.95mmol) in dry CH_2Cl_2 (10cm^3) was stirred at 50°C under reflux condenser for 24 hrs., evaporated under reduced pressure and the white residue washed with diethyl ether to give **4a**, m.p. 141-142°C (from CH_2Cl_2/diethyl ether) (2.04g, 99%) (Found: C, 49.7; H, 4.6; N, 6.1. $C_{19}H_{21}F_3N_2O_4SSi$ requires C, 49.7: H, 4.7; N, 6.1%); δ_H ($CDCl_3$) 0.27 (s, 9H, $SiMe_3$), 4.23 (s, 2H, N-CH_2), 7.57-7.82 (m, 6H, $H_{meta,\ para}$), 8.08 (d, 2H, *J* 7.3, H_{ortho} of C-5Ph), 8.17 (d, 2H, *J* 7.3, H_{ortho} of C-2Ph); δ_C ($CDCl_3$) –2.0 ($SiMe_3$), 44.1 (N-CH_2), 120.2, 135.7, 128.0, 130.0 (C-1', C-2', C-3', C-4' of C-2Ph), 117.3, 134.6, 129.6, 130.4 (C-1', C-2', C-3', C-4' of C-5Ph), 162.4 (C-5), 164.1 (C-2).
The salts **4b**-**4d** were similarly prepared.

2,5-Di(4'-methylphenyl)-3-trimethylsilylmethyl-1,3,4-oxadiazolium trifluoromethanesulfonate (4b). M.p. 155-156°C(from CH_2Cl_2-Et_2O)(99%) (Found: C, 51.7; H, 4.9; N, 5.5. $C_{21}H_{25}F_3N_2O_4SSi$ requires C, 51.8; H, 5.1; N, 5.6%); δ_H ($CDCl_3$) 0.25 (s, 9H, $SiMe_3$), 2.45, 2.47 (s, 3H each, 4'-Me), 4.21 (s, 2H, N-CH_2), 7.37, 7.48 (ds, 4H, 3'-CH of *p*-Tolyl rings), 7.96, 8.10 (ds, 4H, 2'-CH of *p*-Tolyl rings); δ_C ($CDCl_3$) –2.1 ($SiMe_3$), 21.7, 21.9 (4-Me), 43.9 (N- CH_2), 114.2, 116.9 (C-1'), 127.7, 130.2, 130.3 (C-2' and C-3' overlap), 145.7, 147.3 (C-4'), 161.9 (C-5), 163.7 (C-2).

2,5-Di(4'-methoxyphenyl)-3-trimethylsilylmethyl-1,3,4-oxadiazolium trifluoromethanesulfonate (4c). M.p. 156-157°C(from CH_2Cl_2-Et_2O)(97%) (Found: C, 48.7; H, 4.7; N, 5.1. $C_{21}H_{25}F_3N_2O_6SSi$ requires C, 48.6; H, 4.8; N, 5.4%); δ_H ($CDCl_3$) 0.27 (s, 9H, $SiMe_3$), 3.89, 3.90 (s, 3H each, 4'-OMe), 4.19 (s, 2H, N-CH_2), 7.05, 7.17 (ds, 4H, 3'-CH of *p*-$MeOC_6H_4$ rings), 8.01, 8.20 (ds, 4H, 2'-CH of *p*- $MeOC_6H_4$ rings); δ_C ($CDCl_3$) –2.2 ($SiMe_3$), 55.6, 55.8 (4'-OMe), 43.8 (N- CH_2), 108.5, 111.7 (C-1'), 129.7, 132.6 (C-2'), 115.0, 115.6 (C-3'), 161.0, 162.9 (C-4'), 164.3 (C-5), 165.4 (C-2).

2,5-Di(4'-bromophenyl)-3-trimethylsilylmethyl-1,3,4-oxadiazolium trifluoromethanesulfonate (4d). Insolubility prevented recrystallisation of the gummy solid (68% yield) and measurment of NMR spectra. The crude sample was used directly to obtain the products **13d** and **14d** which were fully characterised.

(i) Reactions with Substituted Alkenes

1-*N*-Benzamido-2-phenyl-3-cyano -4,5-dihydropyrrole (9). A solution of the salt **4a** (0.28g, 0.61mmol) and acrylonitrile (0.40cm^3, 6.1mmol) in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane (3cm^3) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **9**, m.p. 178-179°C (from 2:1 v/v CH_2Cl_2/ hexane)(92%) (Found: C, 74.4; H, 4.8; N, 14.0. $C_{18}H_{15}N_3O$ requires C, 74.7; H, 5.2; N, 14.5 %); i.r. ν_{max} (nujol mull) cm^{-1} 3304 (NH), 2197 (CN), 1651 amido C=O; δ_H ($CDCl_3$) 2.84 (dd, 2H, *J* 9.4, 9.3, CH_2-4), 3.76 (dd, 2H, CH_2-5), 7.27-7.56 (m, 10H, $H_{aromatic}$), 8.40 (s, 1H, amido NH); δ_C ($CDCl_3$) 28.9 (C-4), 54.2 (C-5), 82.1 (pyrrole C-3), 118.8 (CN), 132.2, 130.4, 127.9, 128.3 (C-1', C-2', C-3', C-4' of phenyl), 131.9, 128.5, 126.9, 128.3 (C-1', C-2', C-3', C-4' of phenyl), 165.2 (pyrrole C-2), 166.8 (amido C=O).

1-*N*-Benzamido-2-phenyl-3-methoxycarbonyl-4,5-dihydropyrrole (10). A solution of the salt **4a** (0.28g, 0.61mmol) and methyl acrylate (0.55cm^3, 6.1mmol) in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane (3cm^3) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **10**, a gum (77%) (recolumned crude sample); i.r. ν_{max} (nujol mull) cm^{-1} 3177 (NH), 1734 ester C=O, 1660 amido C=O; δ_H ($CDCl_3$) 2.81 (dd, 2H, *J* 9.3, 9.5, CH_2-4), 3.50 (s, 3H, OMe), 3.65 (dd, 2H, CH_2-5), 7.14-7.38 (m, 10H, $H_{aromatic}$) 8.55 (s, 1H, amido NH); δ_C ($CDCl_3$) 26.6 (C-4), 50.6 (OMe), 53.4 (C-5), 102.5 (pyrrole C-3), 132.3, 130.5, 127.0, 128.3 (C-1', C-2', C-3', C-4' of phenyl), 131.6, 129.1, 126.9, 127.3 (C-1', C-2', C-3', C-4' of phenyl), 162.2 (pyrrole C-2), 166.0 (ester C=O), 167.1 (amido C=O).

1-*N*-Benzamido-2-phenyl-3,4-dimethoxycarbonyl-4,5-dihydropyrrole (11). A solution of the salt **4a** (0.28g, 0.61mmol) and dimethyl maleate (0.76cm^3, 6.1mmol) or dimethyl fumarate (0.88g, 6.1mmol) from separate reactions in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane (3cm^3) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **11**, m.p. 131-132°C (from 2:1 v/v $CHCl_3$/hexane)(94% from dimethyl maleate, 85% from dimethyl fumarate) (Found: C, 66.3; H, 5.2; N, 7.3. $C_{21}H_{20}N_2O_5$ requires C, 66.3; H, 5.3; N, 7.4 %); i.r. ν_{max} (nujol mull) cm^{-1} 3295 (NH), 1739 ester C=O, 1682 amido C=O; δ_H ($CDCl_3$) 3.33, 3.52 (s, 3H each, OMe), 3.62 (m, 1H, H-4 pyrrole), 3.94 (m, 2H, 5-CH_2 pyrrole), 7.10-7.30 (m, 10H, $H_{aromatic}$) 8.70 (s, 1H, amido NH); δ_C ($CDCl_3$) 45.6 (C-4), 50.6, 52.1 (OMe), 56.2 (C-5), 101.3 (pyrrole C-3), 131.8, 129.4, 126.9, 127.3 (C-1', C-2', C-3', C-4' of phenyl), 129.6, 128.3, 126.9, 129.1 (C-1', C-2', C-3', C-4' of phenyl), 163.6 (pyrrole C-2), 165.1, 167.1 (ester C=O), 174.0 (amido C=O).

1-*N*-Benzamido-2-phenyl-3-cyano pyrrole (12). A solution of the salt **4a** (0.28g, 0.61mmol) and 1-chloro acrylonitrile (0.49cm^3, 6.1mmol) in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated

with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane ($3cm^3$) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **12**, a gum (86%) (Found: C, 74.9; H, 4.2; N, 14.2. $C_{18}H_{13}N_3O$ requires C, 75.2; H, 4.6; N, 14.6 %); i.r. ν_{max} (nujol mull) cm^{-1} 3247 (NH), 2224 (CN), 1671 amido C=O; δ_H ($CDCl_3$) 6.36 (d, 1H, *J* 3.2, H-4 pyrrole ring), 6.49 (d, 1H, H-5 pyrrole ring), 7.22-7.33 (m, 6H, $H_{meta,para}$), 7.48-7.57 (m, 4H, H_{ortho}) 10.27 (s, 1H, amido NH); δ_C ($CDCl_3$) 90.8 (pyrrole C-3), 110.4 (pyrrole C-4), 116.8 (CN), 123.8 (pyrrole C-5), 141.4 (pyrrole C-2), 133.0, 130.4, 127.4, 128.7 (C-1', C-2', C-3', C-4' of phenyl), 131.9, 129.4, 126.8, 128.6 (C-1', C-2', C-3', C-4' of phenyl), 167.2 (amido C=O).

(ii) Reactions with Substituted Alkynes

1-*N*-Benzamido-2-phenyl-3, 4-dimethoxycarbonyl pyrrole (13a). A solution of the salt **4a** (0.28g, 0.61mmol) and dimethyl acetylenedicarboxylate ($0.26cm^3$, 2.14mmol) in CH_2Cl_2 ($10cm^3$) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane ($3cm^3$) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in a 1% (v/v) changing gradient 100:0 to 95:5 gave **13a**, m.p. 184-185°C (from 2:1 v/v CH_2Cl_2/hexane) (81%) (Found: C, 66.5; H, 5.2; N, 7.7. $C_{21}H_{18}N_2O_5$ requires C, 66.6; H, 4.8; N, 7.4 %); i.r. ν_{max} (nujol mull) cm^{-1} 3250 (NH), 1733, 1712 ester C=O, 1661 amido C=O; δ_H ($CDCl_3$) 3.62, 3.65 (s, 3H each, OMe), 7.08 (s, 1H, H-5 pyrrole ring), 7.26-7.52 (m, 6H, H_{meta}, H_{para} of both phenyl rings), 7.70-7.72 (m, 4H, H_{ortho} of both phenyl rings), 10.24 (s, 1H, amido NH); δ_C ($CDCl_3$) 51.6, 52.0 (OMe), 113.3 (pyrrole C-3), 113.6 (pyrrole C-4), 132.8 (pyrrole C-5), 137.0 (pyrrole C-2), 127.5, 128.0, 128.7, 128.9, 129.6, 130.7 (overlapping of C-aromatic signals), 164.3, 166.0 (ester C=O), 166.7 (amido C=O).

Compounds **13b**-**13d** were prepared similarly and showed all the expected NMR signals.

1-*N*-Benzamido-2-phenyl-3, 4-diethoxycarbonyl pyrrole (14a). A solution of the salt **4a** (0.28g, 0.61mmol) and diethyl acetylenedicarboxylate ($0.34cm^3$, 2.14mmol) in CH_2Cl_2 ($10cm^3$) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane ($3cm^3$) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **14a**, a gum (72%) (recolumned crude sample); i.r. ν_{max} (neat) cm^{-1} 3266 (NH), 1721 (br) ester and amido C=O; δ_H ($CDCl_3$) 1.07, 1.19 (t, 3H each, CH_3), 4.04, 4.11 (quartets, 2H each, OCH_2), 7.07 (s, 1H, H-5 pyrrole ring), 7.26-7.52 (m, 8H, $H_{meta, para}$ and H_{ortho} of one phenyl ring), 7.70-7.72 (d, 2H, *J* 7.3 H_{ortho} of phenyl ring), 10.43 (s, 1H, amido NH); δ_C ($CDCl_3$) 13.7, 14.0 (CH_3), 60.5, 61.0 (OCH_2), 113.7 (pyrrole C-3), 113.9 (pyrrole C-4), 132.7 (pyrrole C-5), 136.8 (pyrrole C-2), 130.7, 129.9, 127.8, 128.8 (C-1', C-2', C-3', C-4' of phenyl), 129.7, 129.5, 127.5, 128.3 (C-1', C-2', C-3', C-4' of phenyl), 164.0, 165.4 (ester C=O), 166.6 (amido C=O).

Compounds **14b**-**14d** were prepared similarly and showed all the expected NMR signals.

1-*N*-Benzamido-2-phenyl-3-methoxycarbonyl pyrrole (15a). A solution of the salt **4a** (0.28g, 0.61mmol) and methyl propiolate (0.54cm^3, 6.1mmol) in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane (3cm^3) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **15a**, m.p. 130-132°C (from 2:1 v/v CH_2Cl_2/hexane) (89%) (Found: C, 71.1; H, 4.9; N, 8.3. $C_{19}H_{16}N_2O_3$ requires C, 71.2; H, 5.0; N, 8.7 %); i.r. ν_{max} (nujol mull) cm^{-1} 3243 (NH), 1708 ester C=O, 1649 amido C=O; δ_H ($CDCl_3$) 3.48 (s, 3H, OMe), 6.44 (d, 1H, *J* 2.9, H-4 pyrrole ring), 6.52 (d, 1H, H-5 pyrrole ring), 7.13-7.40 (m, 10H, $H_{aromatic}$), 9.81 (s, 1H, amido NH); δ_C($CDCl_3$) 51.0 (OMe), 109.2 (pyrrole C-4), 111.8 (pyrrole C-3), 132.5 (pyrrole C-5), 138.7 (pyrrole C-2), 131.0, 129.4, 122.4, 128.5 (C-1', C-2', C-3', C-4' of phenyl), 130.2, 128.6, 127.4, 127.6 (C-1', C-2', C-3', C-4' of phenyl), 165.1 (ester C=O), 167.3 (amido C=O).

Compound **15b** was prepared similarly and showed all the expected NMR signals.

1-*N*-Benzamido-2-phenyl-3-acetyl pyrrole (16). A solution of the salt **4a** (0.28g, 0.61mmol) and 3-butyn-2-one (0.48cm^3, 6.1mmol) in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane (3cm^3) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **16**, m.p. 90-92°C (from 2:1 v/v CH_2Cl_2/hexane) (76%) (recolumned crude sample); i.r. ν_{max} (nujol mull) cm^{-1} 3454 (NH), 1657 amido C=O; δ_H ($CDCl_3$) 1.86 (s, 3H, CH_3), 6.51 (m, 2H, H-4 and H-5 pyrrole ring), 7.13-7.19 (m, 8H, $H_{meta,para}$ of both phenyls, H_{ortho} of one phenyl), 7.43 (d, 2H, *J* 7.8, H_{ortho}) 10.35 (s, 1H, amido NH); δ_C ($CDCl_3$) 28.5 (CH_3), 106.4 (pyrrole C-3), 108.4 (pyrrole C-4), 132.4 (pyrrole C-5), 138.6 (pyrrole C-2), 130.3, 129.9, 127.4, 128.0 (C-1', C-2', C-3', C-4' of phenyl), 131.0, 128.9, 127.5, 128.5 (C-1', C-2', C-3', C-4' of phenyl), 167.3 (amido C=O), 194.9 (C=O).

1-{*N*-Benzoyl-*N*-[*Z*-1,2-dimethoxycarbonylvinyl] amino}-2-phenyl-3,4-dimethoxycarbonyl pyrrole 17 (reaction from 5 molar excess of DMAD). A solution of the salt **4a** (0.28g, 0.61mmol) and dimethyl acetylenedicarboxylate (0.37cm^3, 3.05mmol) in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane (3cm^3) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave **17**, m.p. 186-188°C (from 2:1 v/v CH_2Cl_2/hexane) (64%) (Found: C, 62.2; H, 4.5; N, 5.7. $C_{27}H_{24}N_2O_9$ requires C, 62.3; H, 4.6; N, 5.4%); i.r. ν_{max} (nujol mull) cm^{-1} 1719 (br) ester C=O, 1655 amido C=O; δ_H ($CDCl_3$) 3.67, 3.73, 3.76, 3.86 (s, 3H each, OMe), 5.38 (s, 1H, H-β), 7.05-7.38 (m,10H, $H_{aromatic}$), 7.56 (s, 1H, H-5 pyrrole ring); δ_C($CDCl_3$) 51.9, 52.1, 52.3, 53.3 (OMe), 109.8 (C-β), 114.9 (pyrrole C-4), 115.7 (pyrrole C-3), 132.7 (pyrrole C-5), 136.1 (pyrrole C-2), 145.6 (C-α), 130.6, 129.4, 125.8, 128.3 (C-1', C-2', C-3', C-4' of phenyl), 129.8,

128.6, 126.8, 128.6 (C-1', C-2', C-3', C-4' of phenyl), 162.1, 162.9, 164.4, 164.4 (ester C=O), 167.5 (amido C=O).

1-{*N*-Benzoyl-*N*-[*Z*-1,2-diethoxycarbonylvinyl] amino}-2-phenyl-3,4-diethoxycarbonyl pyrrole 18 (reaction with a 5 molar excess of DEAD). A solution of the salt **4a** (0.28g, 0.61mmol) and diethyl acetylenedicarboxylate (0.49cm^3, 3.05mmol) in CH_2Cl_2 (10cm^3) was cooled to -60°C, treated with CsF (0.19g, 1.22mmol), stirred at -60°C for 5 days, warmed to ambient temperatures, filtered to remove salts, evaporated under reduced pressure and the residue in dichloromethane (3cm^3) placed on a silica gel-60 column (230-400 mesh ASTM). Elution with a gradient mixture of dichloromethane and diethyl ether in the gradient 100:0 to 95:5 gave compound **18**, a sticky gum (58%) (recolumned crude sample); i.r. ν_{max} (nujol mull) cm^{-1} 1724 (br) ester C=O; δ_H ($CDCl_3$) 1.21-1.43 (m, 12H, 4 x CH_3), 4.15-4.38 (m, 8H, 4 x OCH_2), 5.47 (s, 1H, H-β), 7.14-7.59 (m,10H, $H_{aromatic}$), 7.61 (s, 1H, H-5 pyrrole ring); δ_C ($CDCl_3$) 13.4, 13.6, 13.8, 14.1 (4 x CH_3), 60.2, 60.6, 60.9, 61.2 (4 x OCH_2), 111.1 (C-β), 114.0 (pyrrole C-3), 115.1 (pyrrole C-4), 132.5 (pyrrole C-5), 135.8 (pyrrole C-2), 145.0 (C-α), 132.0, 130.5, 127.0, 128.2 (C-1', C-2', C-3', C-4' of phenyl), 130.7, 129.5, 125.7, 128.1 (C-1', C-2', C-3', C-4' of phenyl), 161.4, 162.3, 163.9, 176.4 (ester C=O), 168.9 (amido C=O). Compound **14a** (25%) was also recovered.

X-Ray Crystal structure data for compound (17)

The crystals were grown form dichloromethane/hexane (2:1 v/v) by slow evaporation to the atmosphere. The crystal used for data collection had the approximate dimensions 0.66 x 0.44 x 0.25 mm. The crystal was triclinic with the space group P-1 and had unit cell parameters *a* = 11.092(5), *b* = 11.205(3), *c* = 13.054(4) Å, α = 64.83(3), *β* = 65.75(3), γ = 69.92(3)°. Reflections were collected on an Enraf-Nonius CAD4F four circle diffractometer, using graphite monochromated Mo-Kα radiation, λ = 0.71069Å. The criterion which qualified a reflection for observation was $I > 2\sigma(I)$ and 2245 reflections satisfied this condition. The calculated density was 1.319Mg/m^3 and Z = 2. The absorption coefficient was 0.100 mm^{-1} and the theta range for data collection was 1.81 to 20.86°. The total number on independent reflections was 2512 [*R*(int) = 0.0243]. The structure was solved by direct methods SHELXS-86[11], and refined by full matrix least squares using SHELXS-97[12]. SHELX operations were automated using ORTEX which was also used to obtain the drawings[13]. Data were corrected for Lorentz and polarisation effects but not for absorption. Hydrogen atoms were included in calculated positions with thermal parameters 30% larger than the atom to which they were attached. The non-hydrogen atoms were refined anisotropically. After full matrix refinement the final *R* indices [$I > 2\sigma(I)$] were R_1 = 4.49% and wR_2 = 12.14% and *R* indices (all data) were R_1 = 5.01% and wR_2 = 12.77% > the maximum and minimum excursions in the final $F_o - F_c$ difference map were 0.233 and –0.337 eÅ^{-3}. All calculations were performed on a Pentium PC.

References

1. A review: Butler, R.N.; O'Shea, D.F. *Heterocycles* **1994**, 37, 571.
2. (a) Mühlstadt, M.; Weber, L.; Birner, P. *J. Chem. Soc. Perkin Trans. 2* **1988**, 821 (b) Evans, D.M.; Hill, L.; Taylor, D.R.; Myers, M. *J. Chem. Soc. Perkin Trans. 1* **1986**, 1499.
3. (a) Butler, R.N.; Smyth, G.M.; Cloonan, M.O.; McArdle, P.; Cunningham, D. *Chem. Commun.* **2001**, 1950 (b) Butler, R.N.; Smyth, G.M.; McAardle, P.; Cunningham, D. *J. Chem. Soc. Perkin Trans. 1* **2002**, p. 2851.
4. Vedejs, E.; Larsen, S.; West, F.G. *J. Org. Chem*. **1985**, 50, 2170.
5. Jones, R.C.F.; Nichols, J.R.; Cox, M.T. *Tetrahedron Lett*. **1990**, 31, 2333.
6. Deslongchamps, P. In Stereoelectronic Effects in Organic Chemistry, Pergamon Press: Oxford 1983; pp 291-300.
7. A review: Hegarty, A.F., *Acc. Chem. Res*. **1980**, 13, 448.
8. (a) Lown, W. In *1,3-Dipolar Cycloaddition Chemistry*, Padura, A., Ed.; Wiley Interscience: New York, 1984; Vol. 1, 653 (b) Vedejs, E. *Adv. In Cycloaddition*, Curran, D.P., Ed.; JAI Press Inc.: London, England, 1988; Vol. 1, p. 33.
9. (a) Sundbery, R.J. In *Comprehensive Heterocyclic Chemistry II*, Katritzky, A.R.; Rees, C.W.;Scriven, E.F.V. Eds; Pergamon: Oxford, 1996; Vol. 2 (Volume ed., C.W. Bird), pp. 119-206.
10. Pavri, N.P.; Trudell, M.L. *J. Org. Chem*. **1997**, 62, 2649.
11. Sheldrick, G.M. *Acta. Crystallogr., Sect. A, Fundam, Crystallogr.* **1990**, 46, 467.
12. Sheldrick, G.M. SHELX-97 a computer program for crystal structure determination, University of Göttingen, 1997.
13. McArdle, P. *J. Appl. Crystallogr.* **1995**, 28, 65.