Substituted 1-(2¹-Aminovinyl)pyrroles and Pyrrolo[1,2-*a*]pyrazines from the Reaction of a Pyrazolium Methanide 1,3-Dipole with Dialkyl Acetylenedicarboxylates: A 1,2-Carbon to Nitrogen Rearrangement in the Pyrazole System

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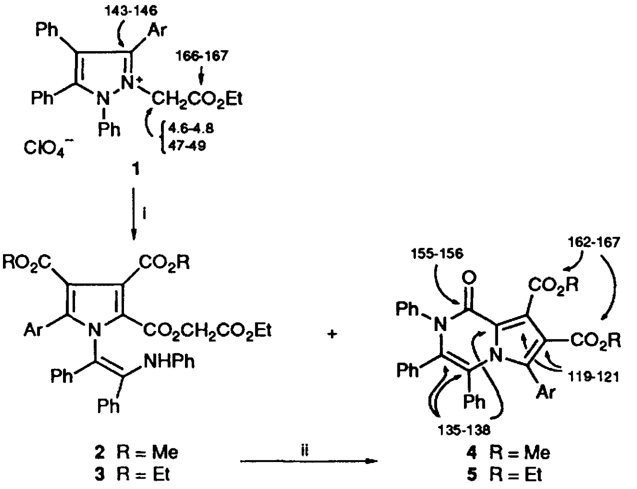
Treatment of 1-ethoxycarbonylmethyl-2,3,4,5-tetraarylpyrazolium salts with base in the presence of dialkyl acetylenedicarboxylates provides a new route to substituted 1-(2¹-aminovinyl)pyrroles and pyrrolo[1,2-*a*]pyrazines.

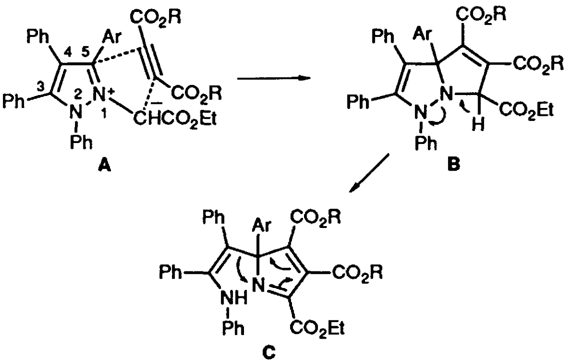
Azolium 1,3-dipoles in which two of the 1,3-dipole 4π-electrons are part of an aromatic sextet are interesting because loss of the azole aromaticity in fused cycloadducts derived from them may lead to unexpected rearrangements. Such behaviour giving interesting new products has been observed with 1,3-dipoles incorporating imidazole,[1] thiazole,[2] 1,2,3-triazole[3,4] and 1,2,5-oxadiazole[5,6] systems. Herein we report a new synthetic route to the *N*-vinylpyrrole and fused pyrrolo[1,2-*a*]pyrazine (7-azaindolizine) systems *via* a substituted pyrazolium methanide 1,3-dipole.

The pyrazolium salts **1** (prepared by quaternisations of the pyrazole with ethyl bromoacetate) when heated with K_2CO_3 or Et_3N in toluene at 100 °C containing dialkyl acetylenedicarboxylate gave the 1-(2¹-aminovinyl)pyrroles **2** or **3** along with the pyrrolo[1,2-*a*]pyrazines **4** and **5** (Table 1, Scheme 1). Separate heating of the products **2** and **3** with the same bases in toluene gave high yields of the products **4** and **5**, and in the main reaction with the salts **1** the products **4** and **5** were formed from subsequent cyclisations of the first formed products **2** and **3**. The reaction could be controlled to produce **2** or **3** only by using temperatures < 50 °C in CH_2Cl_2 as solvent but in such cases the extent of the conversion was low (< 20%) and much of the substrates **1** were recovered.



Scheme 1 *Reagents*: i, K_2CO_3, PhMe, $RO_2C-C\equiv C-CO_2R$; ii, K_2CO_3, PhMe. Ar = **a** Ph; **b** *p*-ClC_6H_4; **c** *p*-MeC_6H_4; **d** *p*-$MeOC_6H_4$. Some proton and ^{13}C NMR shift ranges shown.

The key process in this unexpected reaction is a cycloaddition of the dialkylacetylene dicarboxylate with the pyrazolium methanide 1,3-dipole as in **A**, to give the precursor **B** to the pyrrole moiety of the products **2** or **3**. A base-induced 1,2-elimination in **B** would give the intermediate **C** which could give **2** or **3** by a 1,5-sigmatropic rearrangement driven, no doubt, by the aromatisation to the pyrrole ring. The reaction also involves a second molecule of dialkyl acetylenedicarboxylate and the formation of the side chain at the pyrrole 2-position is a complicated process which is under further investigation.



The structures of the products were established from microanalyses, IR and ^1H and ^{13}C NMR spectroscopy which showed all of the expected signals. An X-ray crystal structure determination for compound **2b** was also carried out (Fig. 1). As well as establishing the rearranged structure it shows the *Z* nature of the enamine moiety which is consistent with the mechanism depicted. The X-ray structure also shows interesting steric effects as a result of substituent crowding in the penta-substituted pyrrole ring with the following torsional angle between the pyrrole ring-plane and the plane of the three atoms immediately bonded: 1-(2¹-aminovinyl) group (69.8°); 2-(*p*-chlorophenyl) (57.2°); 3-methoxycarbonyl (27.0°); 4-methoxycarbonyl (59.1°); 5-ethoxycarbonylmethoxycarbonyl (37.2°).

Experimental

The substrates **1** were prepared by heating the pyrazoles in ethyl bromoacetate as solvent followed by exchanging the bromide with sodium perchlorate in ethanol. The products **2**–**5** were readily prepared by the following typical procedures. (i) A solution of **1a** (1.8 g, 3.22 mmol) in dry toluene (60 cm^3) was treated with K_2CO_3 (0.9 g, 6.44 mmol) and dimethyl acetylenedicarboxylate (0.47 cm^3, 3.86 mmol) and the mixture heated at 100 °C under a reflux condenser for 48 h; it was then cooled, filtered to remove salts, and evaporated under reduced pressure. Treatment of the residue with diethyl ether (50 cm^3) gave compound **4a** (45%), m.p. 282–284 °C (from EtOH) (Found: C, 76.1; H, 4.5; N, 4.9. $C_{35}H_{26}N_2O_5$ requires: C, 75.8; H, 4.7; N, 5.05%); ν_{max}(Nujol)/cm^{-1} 1745 and 1720 (ester C=O)

Table 1

	Substrate		Products						
No.	Compd.	M.p. (°C)[a]	Compd.	M.p. (°C)[b]	Yield (%)	Compd.	M.p. (°C)	From **1**: yield (%)	From **2**: yield (%)
1	**1a**	212–214	**2a**	148–150	41	**4a**	282–284	45	89
2	**1b**	198–200	**2b**	170–172	44	**4b**	281–283	31	86
3	**1c**	202–204	**2c**	174–176	41	**4c**	274–276	45	95
4	**1d**	196–198	**2d**	207–209	36	**4d**	277–279	50	—
5	**1a**	212–214	**3a**	202–204	56	**5a**	225–226	9	94
6	**1b**	198–200	**3b**	128–130	14	**5b**	288–290	53	—
7	**1c**	202–204	**3c**	163–165	3[c]	**5c**	278–280	78	—

[a] Recrystallised from EtOH. [b] From MeOH. [c] Compound **3c** could be obtained exclusively by using CH_2Cl_2 as solvent at temperatures < 50 °C; however the extent of conversion was only 11%, the remainder being recovered **1c**.

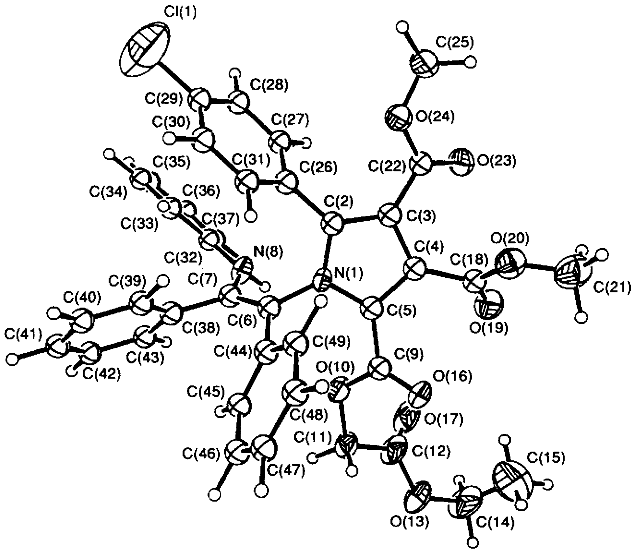


Fig. 1 X-ray crystal structure of **2b**

and 1671 (amido C=O); $\delta_H(CDCl_3)$ 3.6 (s, 3 H, OMe), 4.01 (s, 3 H, OMe) and 6.6–7.2 (m, ArH); δ_C 51.5 and 53.8 (MeO), 166.3 and 162.8 (ester C=O), 155.2 (amide C=O) and 119.65, 120.25, 126.3, 136.0 and 137.0 (quaternary C), 126–132 remaining aromatic signals. The ethereal filtrate was concentrated to 5 cm^3 placed on a column of silica gel (Merck Silica gel 60, 70–230 mesh) eluted with ether–light petroleum (b.p. 40–60 °C) (1:1 v/v) to give compound **2a** (41%), m.p. 148–150 °C (from MeOH) (Found: C, 70.8; H, 5.4; N, 4.25%; M, isopiestic, 680. $C_{39}H_{34}N_2O_8$ requires C, 71.1; H, 5.2; N, 4.25%; *M*, 658); ν_{max}(Nujol)/cm^{-1} 3374 (NH) and 1742–1726br (ester C=O); $\delta_H(CDCl_3)$ 3.62 (s, 3 H, OMe), 3.96 (s, 3 H, OMe), 1.20 (t) and 4.17 (q) (CO_2Et), 4.53 (s, OCH_2CO_2), 5.93 (br, NH) and 6.18–7.4 (m, ArH); δ_C 51.6 and 52.9 (MeO), 14.1 and 60.65 (OEt), 61.5 (OCH_2CO_2), 167.0, 166.5, 163.0 and 158.0 (C=O), 143.1, 140.4 and 137.3 (quaternary C), 118–134.4 remaining aromatic signals.

(ii) A solution of **2a** (150 mg, 0.243 mmol) in dry toluene (30 cm^3) together with K_2CO_3 (70 mg, 0.486 mmol) was heated under reflux for 48 h and then cooled and the solvent removed under reduced pressure. A solution of the residue in water (20 cm^3) was extracted with $CHCl_3$ (3 × 20 cm^3) and the combined extracts were evaporated to give **4a**, m.p. 282–284 °C (83%).

Crystal data for $C_{39}H_{33}ClN_2O_8$ **2b**. Triclinic, a = 10.470(1), b = 12.438(1), c = 14.356(2) Å; Z = 2; space group $P\bar{1}$, 4784 reflections observed with $I > 3\sigma I$ using a CAD4F diffractometer and Mo-Kα radiation; $2\theta_{max}$ = 48°. The structure was solved by SHELX 86[7] and refined with 292 variable parameters using SHELX 76.[8] After full matrix refinement; R = 8.84 and R_w = 8.84%. The maximum and minimum excursions in the final F_o-F_c difference map were 0.21 and −0.21 and −0.28 e/Å.[3] The ORTEP program was used to obtain the drawings.[9] Atomic co-ordinates and bond lengths and angles have been deposited at the Cambridge Crystallography Data Centre.*

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* For details see Instructions for Authors (1993), *J. Chem. Soc., Perkin Trans. 1*, 1993, Issue 1.

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