The Reaction of 1-Phenyl-4-vinylpyrazole with Diethyl Azodicarboxylate. *X*-Ray Molecular Structure of 1,2-Bisethoxycarbonyl-1-[2-hydroxy-2-(1-phenylpyrazol-4-yl)ethyl]hydrazine

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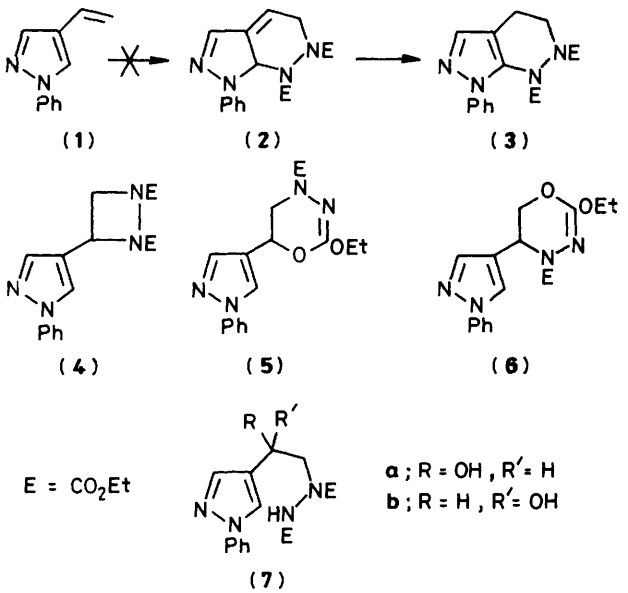
1-Phenyl-4-vinylpyrazole does not undergo cycloaddition reactions with alkenes or alkynes, but a dihydro-oxadiazine is formed *via* a ($_{\pi}4$ + $_{\pi}2$) cycloaddition reaction with diethyl azodicarboxylate under completely anhydrous conditions. In the presence of water the dihydro-oxadiazine undergoes a ready ring-opening reaction to produce a (2-hydroxyethyl)hydrazine derivative, the structure of which was confirmed by *X*-ray crystallographic analysis. The analysis of a single twin of the chiral crystals showed a disorder ratio of 65:35 due to inversion at the chiral C(6) centre.

As an extension of our studies of the reaction of vinylpyrroles with dienophiles,[1-3] we have prepared 1-phenyl-4-vinylpyrazole (**1**) and examined its reactivity with a range of electron-rich and electron-deficient alkenes and alkynes. In contrast with the high reactivity shown by the vinylpyrroles in their reaction with the electron-deficient dienophiles in which ($_{\pi}4$ + $_{\pi}2$) cycloadducts are formed under mild conditions,[1] it was found that the vinylpyrazole could be recovered unchanged from comparable reactions. Similarly, no reaction was observed with electron-rich dienophiles. However, the reaction of diethyl azodicarboxylate (DEAD) with the vinylpyrazole proceeded smoothly in acetonitrile at *ca.* 80 °C to yield a product (**A**) which was shown by elemental analysis and by high-resolution mass spectral data to be a 1:1 adduct incorporating a covalently bound molecule of water. Repetition of the reaction under completely anhydrous conditions produced a compound (**B**), $C_{17}H_{20}N_4O_4$, resulting from a 1:1 addition of the two reagents. Chromatography on silica or recrystallisation from 'wet' solvents resulted in the conversion of (**B**) into (**A**).

Previous work has established that DEAD is an extremely reactive dienophile and is capable of reacting with 'unreactive' dienes.[4] It has also been shown that ethenes react with DEAD to give either an ene product or undergo 1,2- or 1,4-cycloaddition reactions to yield, respectively, 1,2-azetidines or dihydro-1,3,4-oxadiazines.[4,5]

Styrene,[6] vinylpyridines,[7] and 2-vinylthiophene[7] react with DEAD in a manner which is analogous to the reaction of the vinylpyrroles with dimethyl acetylenedicarboxylate[1] to give annulated 1,2,3,4-tetrahydropyridazines in which re-aromatisation of the initially formed Diels–Alder adduct occurs *via* a 1,3-hydrogen shift. The ^{1}H and ^{13}C n.m.r. spectra of compound (**B**) were totally inconsistent, however, with the corresponding ($_{\pi}4$ + $_{\pi}2$) cycloaddition reaction between DEAD and the vinylpyrazole, which would have led to the formation of (**3**). In particular, the series of double doublets at δ 3.62 (*J* 13.2 and 7.8 Hz), 4.30 (*J* 13.2 and 3.0 Hz), and 5.42 (*J* 7.8 and 3.0 Hz), which were well resolved from the ester methylene signals at 400 MHz, together with the ^{13}C signals at δ_C 44.8 and 70.2 p.p.m., which appeared as a triplet and doublet, respectively, in the off-resonance proton-coupled spectrum, were indicative of a >CH·CH$_2$– system. The initial Diels–Alder adduct structure (**2**) could not be completely excluded for compound (**B**) by the above n.m.r. data, but the singlet ^{1}H resonance signals at δ 7.74 and 7.98 provided good evidence that the addition product was a 1,4-disubstituted pyrazole.



It is unusual for electron-deficient alkenes to form 1,2-azetidines[4] and structure (**4**) for compound (**B**) was eliminated on the basis of the observed chemical shifts and coupling constants for the >CH·CH$_2$– group, as the J_{AB}, J_{BX}, and J_{BX} coupling constants for the azetidine systems generally have values of *ca.* 10, 6, and 5 Hz, respectively.[8] On the available spectral evidence, it was not possible, however, to distinguish unequivocally between the isomeric ($_{\pi}4$ + $_{\pi}2$) cycloadducts (**5**) and (**6**). Hindered rotation about the N–CO$_2$Et bond[9] was indicated by the broadened ^{1}H resonance signals observed when the 400 MHz spectrum of the adduct in C_6D_6 was measured at 20 °C, but was not apparent when a $CDCl_3$ solution of the adduct was measured at the same temperature.

Spectral analysis of compound (**A**), derived from (**B**) through the addition of water, indicated that it also was a 1,4-disubstituted pyrazole. *X*-Ray crystallographic analysis of a single twin of the chiral crystals showed the compound to have structure (**7**) (Figure), thereby establishing (**5**) as the structure

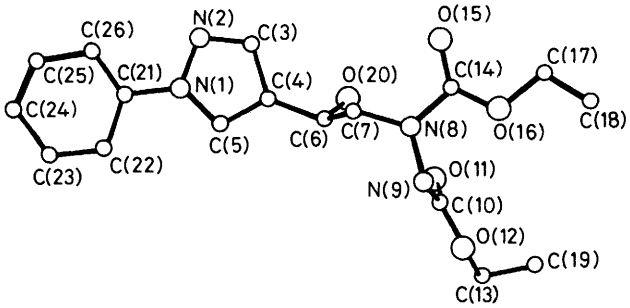


Figure. Computer-drawn molecular structure of the hydrazine (**7**) from *X*-ray data

for compound (**B**). The crystal lattice of the single crystal, which comprised both stereoisomers (**7a**) and (**7b**), showed a disorder ratio of 65:35 due to inversion at the chiral C(6) centre. The data presented in Tables 1—3 relate to the major stereoisomer. The relatively large e.s.d. values and temperature parameters for the methyl carbon atoms of the ethyl esters, C(18) and C(19), also indicate some disorder.

Experimental

I.r. spectra were measured for Nujol mulls using a Perkin-Elmer 297 spectrophotometer. ^{1}H and ^{13}C N.m.r. spectra for *ca.* 30% solutions in $CDCl_3$ were recorded at 100 MHz and at 25.05 MHz, respectively, using a JEOL FX100 spectrometer. 400 MHz ^{1}H N.m.r. spectra of the cycloadduct (**5**) were recorded using a Bruker WH-400 spectrometer by the S.E.R.C. high-resolution n.m.r. service at the University of Warwick. All chemical shifts are reported downfield from the internal standard (Me_4Si). Accurate mass measurements were recorded by the Food Research Institute Mass Spectrometry Unit, Norwich, using an AEI MS902 spectrometer.

1-*Phenyl*-4-*vinylpyrazole* (**1**).—A solution of 4-formyl-1-phenylpyrazole (3.4 g, 0.02 mol) in THF (40 ml) was added under nitrogen at room temperature to a stirred solution of methylenetriphenylphosphorane, obtained from methyltriphenylphosphonium bromide (8.0 g, 0.022 mol) and sodium hydride (0.75 g), in tetrahydrofuran (65 ml). The reaction mixture was heated under reflux for 3 h and then cooled and kept at 20 °C for 12 h. The liquid phase was decanted from the solid and the residue was washed with hexane (4 × 25 ml). Evaporation of the combined organic solutions and distillation of the residual oil at 118 °C/2 mmHg gave 1-phenyl-4-vinylpyrazole (**1**) (2.71 g, 81%), which solidified, m.p. 40 °C (lit.,[10] 39—40 °C).

Reaction of 1-*Phenyl*-4-*vinylpyrazole with Diethyl Azodicarboxylate* (*DEAD*).—(*a*) A solution of DEAD (0.4 g, 2.6 mmol) in *dry* acetonitrile (10 ml) was added to a solution of 1-phenyl-4-vinylpyrazole (0.4 g, 2.4 mmol) in *dry* acetonitrile (10 ml) under nitrogen. The reaction mixture was heated under reflux for 4 h. Evaporation of the solvent and preparative t.l.c. (p.l.c.) purification of the reaction product on Kieselgel HF_{254}, using *dry* diethyl ether as the eluant, followed by recrystallisation from light petroleum (b.p. 60—80 °C) gave 2-*ethoxy*-4-*ethoxycarbonyl*-5,6-*dihydro*-6-(1-*phenylpyrazol*-4-*yl*)-4H-1,3,4-*oxadiazine* (**5**) (0.4 g, 50%), m.p. 92—94 °C (Found: C, 59.0; H, 5.9; N, 16.0%; M^+, 344.1459. $C_{17}H_{20}N_4O_4$ requires C, 59.3; H, 5.8; N, 16.3%; *M*, 344.1480); $\nu_{max.}$ 1 680 cm^{-1}; δ_H (400 MHz; $CDCl_3$; 20 °C) 1.33 (3 H, t, *J* 7.1 Hz), 1.34 (3 H, t, *J* 7.1 Hz), 3.62 (1 H, dd, *J* 13.2 and 7.8 Hz), 4.25 (2 H, q, *J* 7.1 Hz), 4.27 (2 H, q, *J* 7.1 Hz), 4.30 (1 H, dd, *J* 13.2 and 3.0 Hz), 5.42 (1 H, dd, *J* 7.8 and 3.0 Hz), 7.31 (1 H, tt, *J* 7.5 and 1.2 Hz), 7.45 (2 H, tt, *J* 7.5 and 1.0 Hz), 7.66 (2 H, dt, *J* 7.5 and 1.0 Hz), 7.74 (1 H, s), and 7.98 (1 H, s); δ_H (400 MHz; C_6H_6; 50 °C) 1.14 (3 H, t, *J* 7.0 Hz), 1.20 (3 H, t, *J* 7.0 Hz), 3.35 (1 H, dd, *J* 13.2 and 7.7 Hz), 4.14 (1 H, dd, *J* 13.2 and 3.05 Hz), 4.26 (2 H, q, *J* 7.0 Hz), 4.27 (2 H, q, *J* 7.0 Hz), 4.82 (1 H, dd, *J* 7.7 and 3.05 Hz), 6.96 (1 H, tt, *J* 7.4 and 1.0 Hz), 7.09 (2 H, tt, *J* 7.5 and 1.0 Hz), 7.41 (1 H, s), 7.51 (2 H, dt, *J* 7.5 and 1.0 Hz), and 7.55 (1 H, s); δ_C (20 °C) 14.21 (q), 14.68 (q), 44.79 (t), 62.23 (t), 64.46 (t), 70.22 (d), 119.36 (d), 125.40 (d), 126.99 (d), 129.45 (d), 139.02 (d), 129.96 (s), 149.59 (s), and 153.64 p.p.m. (s).

(*b*) A solution of DEAD (0.4 g, 0.026 mol) in 'wet' acetonitrile (10 ml) was heated under reflux with 1-phenyl-4-vinylpyrazole (0.4 g, 0.024 mol) for 4 h. Evaporation of the solvent and purification of the residual oil by p.l.c. on Kieselgel HF_{254} using ethyl acetate–toluene (3:2) as the eluant, followed by recrystallisation from toluene, gave 1,2-*bisethoxycarbonyl*-1-[2-*hydroxy*-2-(1-*phenylpyrazol*-4-*yl*)*ethyl*]*hydrazine* (**7**) (0.71 g, 82%), m.p. 107 °C (Found: C, 56.5; H, 6.1; N, 15.4%; M^+, 362.1712. $C_{17}H_{22}N_4O_5$ requires C, 56.3; H, 6.1; N, 15.5%; *M*, 362.1589); δ_H (20 °C) 1.25 (3 H, t, *J* 7.0 Hz), 1.26 (3 H, t, *J* 7.0 Hz), 3.74 (2 H, br d), 4.18 (2 H, q, *J* 7.0 Hz), 4.22 (2 H, q, *J* 7.0 Hz), 4.71 (1 H, br s), 5.03 (1 H, br d), 7.20—7.60 (5 H, m), 7.67 (1 H, s), and 7.96 (1 H, s); δ_C (20 °C) 14.38 (q), 58.30 (t), 62.53 (t), 62.88 (t), 64.17 (d), 119.06 (d), 124.11 (s), 124.88 (d), 126.40 (d), 129.34 (d), 138.90 (d), 140.14 (s), and 156.40 p.p.m. (s).

Conversion of 2-*Ethoxy*-4-*ethoxycarbonyl*-5,6-*dihydro*-6-(1-*phenylpyrazol*-4-*yl*)-4H-1,3,4-*oxadiazine* (**5**) *into* 1,2-*Bisethoxycarbonyl*-1-[2-*hydroxy*-2-(1-*phenylpyrazol*-4-*yl*)*ethyl*]*hydrazine*. (**7**).—Water (0.02 g, 1 mmol) was added to a solution of the dihydro-oxadiazine (**5**) (0.2 g, 0.6 mmol) in dry acetonitrile (10 ml) and the solution was heated under reflux for 4 h. Evaporation of the solvent, followed by p.l.c. purification of the residue on Kieselgel HF_{254}, using ethyl acetate–toluene (3:2) as the eluant, gave the hydrazine (**7**) (0.2 g, 95%).

Crystal and Molecular Structure of the Hydrazine (**7**).—*Crystal data*. $C_{17}H_{22}N_4O_5$, *M* = 362.37, triclinic, *a* = 5.639(1),

Table 1. Atomic co-ordinates for C, N, and O atoms

	x/*a*	*y*/*b*	*z*/*c*
N(1)	0.187 3(6)	0.912 7(4)	0.367 6(2)
N(2)	0.426 9(6)	0.822 2(5)	0.372 9(2)
C(3)	0.455 7(9)	0.698 7(6)	0.335 0(3)
C(4)	0.241 6(9)	0.702 9(6)	0.305 2(2)
C(5)	0.072 9(8)	0.842 9(6)	0.328 1(2)
C(6)	0.209(1)	0.586 0(6)	0.258 2(3)
C(7)	0.193 7(7)	0.423 7(6)	0.293 7(2)
N(8)	0.194 4(6)	0.299 2(4)	0.248 3(2)
N(9)	−0.020 8(6)	0.314 8(5)	0.217 2(2)
C(10)	−0.025 9(8)	0.365 7(6)	0.151 9(3)
O(11)	0.117 1(6)	0.434 2(4)	0.119 6(2)
O(12)	−0.216 4(6)	0.333 6(4)	0.128 1(2)
C(13)	−0.256(1)	0.384 0(8)	0.059 4(3)
C(14)	0.399 5(8)	0.170 2(5)	0.234 6(2)
O(15)	0.591 8(5)	0.149 8(4)	0.261 1(2)
O(16)	0.366 4(5)	0.077 9(4)	0.190 2(2)
C(17)	0.579(1)	−0.059 9(6)	0.170 9(3)
C(18)	0.530(2)	−0.122 4(9)	0.111 3(4)
C(19)	−0.140(2)	0.254(1)	0.017 8(4)
O(20)	0.374(1)	0.577 8(7)	0.206 0(3)
C(21)	0.087 4(7)	1.054 6(5)	0.404 6(2)
C(22)	−0.154 0(7)	1.151 5(6)	0.397 6(2)
C(23)	−0.252 0(8)	1 286 1(6)	0.435 9(2)
C(24)	−0.113 6(9)	1 326 2(6)	0.480 1(3)
C(25)	0.128 9(9)	1.228 5(6)	0.485 9(2)
C(26)	0.228 8(8)	1.094 5(5)	0.448 1(2)

Table 2. Bond lengths (Å) (standard deviations in parentheses)

N(1)–N(2)	1.359(5)	C(10)–O(12)	1.329(5)
N(1)–C(5)	1.351(5)	O(12)–C(13)	1.435(6)
N(1)–C(21)	1.414(5)	C(13)–C(19)	1.407(9)
N(2)–C(3)	1.315(6)	C(14)–O(15)	1.224(5)
C(3)–C(4)	1.399(6)	C(14)–O(16)	1.305(5)
C(4)–C(5)	1.370(6)	O(16)–C(17)	1.457(6)
C(4)–C(6)	1.493(6)	C(17)–C(18)	1.446(9)
C(6)–C(7)	1.499(7)	C(21)–C(22)	1.388(5)
C(6)–O(20)	1.319(7)	C(21)–C(26)	1.376(5)
C(7)–N(8)	1.458(5)	C(22)–C(23)	1.381(6)
N(8)–N(9)	1.396(4)	C(23)–C(24)	1.374(6)
N(8)–C(14)	1.365(5)	C(24)–C(25)	1.391(6)
N(9)–C(10)	1.350(6)	C(25)–C(26)	1.374(6)
C(10–O(11)	1.217(5)		

Table 3. Bond angles (°) (standard deviations in parentheses)

N(2)–N(1)–C(5)	111.5(4)	N(9)–C(10)–O(12)	109.5(4)
N(2)–N(1)–C(21)	119.4(3)	O(11)–C(10)–O(12)	124.7(5)
C(5)–N(1)–C(21)	129.0(3)	C(10)–O(12)–C(13)	117.5(4)
N(1)–N(2)–C(3)	103.7(4)	O(12)–C(13)–C(19)	111.6(5)
N(2)–C(3)–C(4)	113.8(4)	N(8)–C(14)–O(15)	121.9(4)
C(3)–C(4)–C(5)	103.0(4)	N(8)–C(14)–O(16)	112.6(3)
C(3)–C(4)–C(6)	128.1(5)	O(15)–C(14)–O(16)	125.5(4)
C(5)–C(4)–C(6)	128.9(4)	C(14)–O(16)–C(17)	116.4(4)
N(1)–C(5)–C(4)	108.0(4)	O(16)–C(17)–C(18)	108.5(5)
C(4)–C(6)–C(7)	111.6(4)	N(1)–C(21)–C(22)	120.0(4)
C(4)–C(6)–O(20)	110.2(5)	N(1)–C(21)–C(26)	119.8(4)
C(7)–C(6)–O(20)	116.5(5)	C(22)–C(21)–C(26)	120.2(4)
C(6)–C(7)–N(8)	113.0(4)	C(21)–C(22)–C(23)	119.3(4)
C(7)–N(8)–N(9)	118.6(3)	C(22)–C(23)–C(24)	121.1(4)
C(7)–N(8)–C(14)	122.0(3)	C(23)–C(24)–C(25)	118.9(4)
N(9)–N(8)–C(14)	119.4(3)	C(24)–C(25)–C(26)	120.6(4)
N(8)–N(9)–C(10)	118.9(4)	C(21)–C(26)–C(25)	119.9(4)
N(9)–C(10)–O(11)	125.8(4)		

$b = 8.410(1)$, $c = 20.238(3)$ Å, $\alpha = 84.32(1)$, $\beta = 83.56(1)$, $\gamma = 73.45(1)°$, $U = 911.74$ Å^3, $D_c = 1.32$ g cm^{-3}, $Z = 2$, space group $P\bar{1}$. The structure was solved by direct methods using 2 275 reflections and the SHELX programme, co-ordinates for 24 of the 'heavy atoms' being determined. The remaining atoms were found from an electron-difference map using the CRYSTALS package (1 688 observed reflections). The structure was found to be disordered with two alternative sites for O(20) in the ratio 65:35. The trial structure was refined using isotropic and anisotropic temperature factors to a R value of 8.48%. A Fourier difference map detected many of the hydrogen atoms and these were all included in subsequent calculations to give a final R value of 6.13%.

Atomic co-ordinates, bond lengths, and bond angles for non-hydrogen atoms are listed in Tables 1—3, respectively. Observed and calculated structure factors and thermal parameters, together with atomic co-ordinates and thermal parameters for hydrogen atoms, are listed in Supplementary Publication No. SUP 23925 (21 pp.).*

* For details of the Supplementary Publications Scheme, see Instructions for Authors (1984) in *J. Chem. Soc., Perkin Trans 1*, 1984, Issue 1.

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