Diversity of Reaction of Azoalkenes in Cycloadditions

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Reactions of the azoalkenes (*E,E*)-4-methyl-*N*-phenyl-2,3-diazapenta-2,4-diene-5-carboxamide **2** and methyl (*E,Z*)-3-methyl-4-phenylcarbamoyl-1,2-diazabuta-1,3-diene-1-carboxylate **3**, having respectively an electron-rich and an electron-poor group on nitrogen, are described. Compound **2**, is a stable compound and its stereochemistry was established as *E,E* by X-ray crystallography; compound **3** is much less stable and was assigned the *E,Z* stereochemistry on the basis of its ^{1}H NMR spectrum and the crystal structure of a derivative **17**.

Of a wide variety of substrates, only azo esters react with **2**, which behaves as a heterodiene. The 1,2,3,6-tetrahydro-1,2,3,4-tetrazine **7** obtained from **2** by reaction with dimethyl azodicarboxylate is unstable and on work up yields a 4,5-dihydro-1*H*-1,2,3-triazole **9a** (whose structure was established by X-ray crystallography). This isomerisation is probably acid catalysed since, by inclusion of acid, **7** tautomerises to a 1,2,3,4-tetrahydro-1,2,3,4-tetrazine **8** which then ring contracts to **9a**, followed by a decarboxylative elimination of methyl carbamate to yield the 1,2,3-triazole **10**.

The azoalkene **3** is unreactive to electron-poor substrates, but reacts with cyclopentadiene both as a heterodiene and as a dienophile (at C=C) to give as Diels–Alder adducts the tetrahydro-1*H*-cyclopenta[*c*]pyridazine **16** and the bicyclo[2.2.1]hept-2-ene **17** respectively. With ethyl vinyl ether **3** gave the ethoxytetrahydropyridazine **18** which eliminated EtOH in acid to the dihydro tautomers **19** and **20** which on basic hydrolysis and oxidation give the pyridazine **21**.

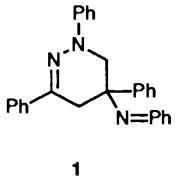
Conjugated azoalkenes are reactive species both as acceptors in Michael reactions and as components in cycloadditions. Michael additions to give hydrazones are observed with a wide variety of nucleophilic species, including activated methylene compounds (cyanoacetates, malononitrile, malonic esters, β-diketones, β-keto esters, β-keto amides and β-sulphonyl ketones),[1,5] thiols,[1–4] amines,[4,6–8] phenylhydrazine,[9] Wittig reagents,[10] and Grignard reagents.[11] Some of these products can be cyclised to pyrroles, with or without Cu^{2+} catalysis.[2,3,5,12] The products derived from β-chloro azoalkenes can eliminate HCl and add a second equivalent of nucleophile to give further hydrazones which are capable of cyclising to pyrroles.[4] β,β-Dichloro azoalkenes can undergo a double sequence of addition and elimination with amines to give stable β,β-diamino azoalkenes.[6] These and other nucleophilic reactions have been reviewed.[13]

In cycloaddition of azoalkenes 4-, 5- and 6-membered heterocycles are produced. 1,2-Diazetidinones are formed from ketene by [2 + 2] additions at the azo link, in competition with [4 + 2] additions.[14] As well as the route to pyrroles by cyclisation of the Michael adducts described above, azoalkenes can be directly converted into pyrroles by [3 + 2] additions, without isolation or detection of an intermediate. Thus enamines[12,15] and enol ethers[15] add across the C=CN termini of the azoalkene, although [4 + 2] addition sometimes competes. [3 + 2] Addition across the CN=N termini to give pyrazolines is also observed with tosylazocyclohexene and a variety of dipolarophiles.[16] Five-membered rings are also formed by insertion, in a [1 + 4] sense, of phosphorus to give 1,2,3-diazaphosphole 3-oxides from a variety of P^{III} species,[17] or of carbon, in the case of phenylazohexenopyranosides, to give pyrazolines using dimethyl sulphoxonium methylide.[18,19] Cyclopropanation may compete in this reaction,[18,19] and is also observed with diazomethane,[19] these being examples of [1 + 2] addition to the carbon–carbon double bond.

The Diels–Alder reaction in which the azoalkene is the 4-component is by far the most commonly encountered cycloaddition. With alkenes tetrahydropyridazines are formed and details can be found in review articles.[13,20] Other dienophiles which have been used are sulphinilimines[21] and carbonylazo compounds[22] to give 1,2,3,6-thiatriazine 1-oxides and 1,2,3,4-tetrazines respectively.

Azoalkenes vary greatly in stability but many have been isolated pure.[4,6,23–27] These contain a variety of substituent types, although they do not usually have conjugatively electron withdrawing groups on nitrogen, which appear to be destabilising. In the condensed state, or in solution, complex decomposition often occurs, but simple dimerisation is occasionally observed and a number of dimers have been isolated and characterized,[25,28,29] the first example being the pyridazine **1** from α-phenylazostyrene.[28] The generality of dimerisation has not been established, but most examples appear to involve azoalkenes in which the alkene group is terminally unsubstituted.

Here we describe and contrast the reactions with a variety of substrates of two azoalkenes, **2** and **3**, differing only in having



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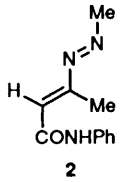

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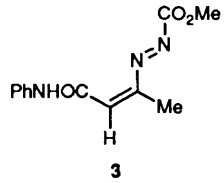


3

an electron releasing and an electron withdrawing group on nitrogen. Novel reactions observed are dihydro-1,2,3-triazole synthesis from **2** with azo esters, and the competing addition of **3** to cyclopentadiene both as a diene and as a dienophile; in the latter role **3** reacts at the carbon–carbon double bond, the first example of this mode of action in an azoalkene, except for the dimerisations described above.

Table 1 Molecular dimensions for **2**

Bond lengths (Å)		Bond angles (°)	
O(8)–C(7)	1.225(3)	N(3)–N(2)–C(1)	113.0(3)
N(2)–N(3)	1.220(3)	N(2)–N(3)–C(4)	115.2(2)
N(2)–C(1)	1.465(4)	C(7)–N(9)–C(11)	128.2(2)
N(3)–C(4)	1.432(3)	N(3)–C(4)–C(5)	119.5(2)
N(9)–C(7)	1.350(3)	N(3)–C(4)–C(6)	112.8(2)
N(9)–C(11)	1.413(3)	C(5)–C(4)–C(6)	127.6(2)
C(4)–C(5)	1.484(4)	C(4)–C(6)–C(7)	127.3(2)
C(4)–C(6)	1.324(3)	O(8)–C(7)–N(9)	122.9(2)
C(6)–C(7)	1.479(3)	O(8)–C(7)–C(6)	123.9(2)
C(11)–C(12)	1.386(3)	N(9)–C(7)–C(6)	113.2(2)
C(11)–C(16)	1.381(4)	N(9)–C(11)–C(12)	122.9(2)
C(12)–C(13)	1.382(4)	N(9)–C(11)–C(16)	117.5(2)
C(13)–C(14)	1.362(5)	C(12)–C(11)–C(16)	119.6(2)
C(14)–C(15)	1.371(5)	C(11)–C(12)–C(13)	118.9(3)
C(15)–C(16)	1.379(4)	C(12)–C(13)–C(14)	121.3(3)
		C(13)–C(14)–C(15)	120.0(3)
		C(14)–C(15)–C(16)	119.6(3)
		C(11)–C(16)–C(15)	120.5(3)

Hydrogen bond distances

Distance (Å)		Angle (°)	
HN(9)–O(8)	1.93	N(9)–HN(9)–O(8)	175.1
N(9)–O(8)	2.8979(2)		

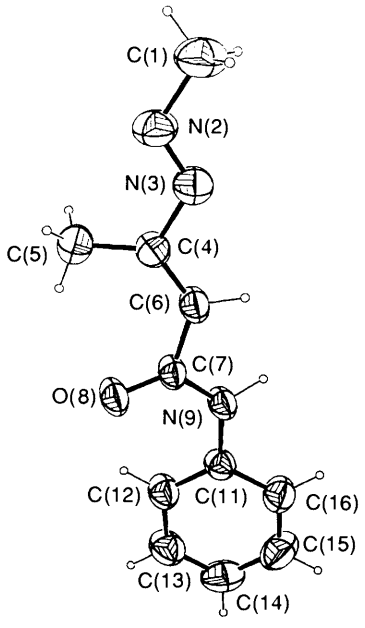


Fig. 1 A view of molecule **2** with the crystallographic numbering scheme; thermal ellipsoids are at the 50% level except for H atoms which are shown as small spheres of an arbitrary size

Azoalkene **2**.—The azoalkene **2** has been used by Sommer with dimethyl azodicarboxylate (see above),[22] and with *N*-sulphinyl compounds[21] in cycloadditions. It was prepared in a reported yield of 44% [m.p. of 131–133 °C (decomp.)],[22] but without details of its synthesis being provided. Following the recommended route[23] we obtained **2** from α-chloroacetoacetanilide[30] and 2 equiv. of methylhydrazine, no effort being made to isolate the α-chloro hydrazone which is the presumed intermediate. Column chromatography gave yellow crystalline **2** (44%; m.p. of 148–149 °C). Its ^{1}H NMR spectrum showed it to be stereochemically pure. Since four diastereoisomers can arise from the two double bonds in the azoalkene we did an X-ray crystallographic analysis of the yellow solid which showed

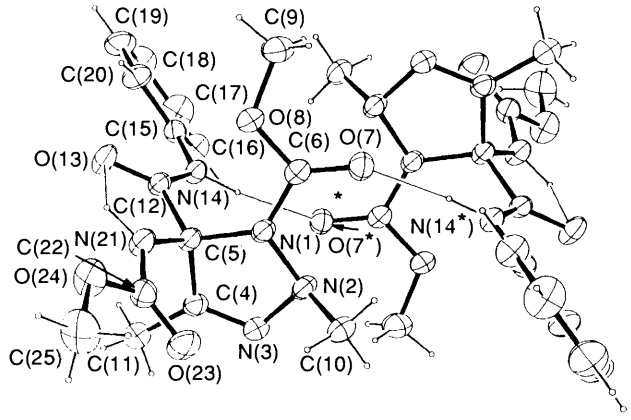


Fig. 2 A view of the centrosymmetric hydrogen-bonded dimer formed by molecule **9a** and the crystallographic numbering scheme; thermal ellipsoids for non-hydrogen atoms are at the 25% level. The * denotes the inversion centre at the dimer centre.

it to have the transoid conformation in the *E,E* configuration (Fig. 1). Bond lengths and angles are shown in Table 1.

Only three X-ray structure determinations* of azoalkenes have been reported, for compounds **4**–**6**.[31–33] Like compound **2** these also ail have the transoid arrangement in the *E,E* configuration. All three have arylazo groups, unlike **2** which has an alkylazo group. The adjacent sp^3 carbon atom causes a much shorter N–N bond in **2** [1.220(3) Å] than those observed for **4**–**6** [**4**, 1.279(8): **5**, 1.245(5), 1.258(5); **6**, 1.262(4) Å]. The molecule is maximally extended and is slightly twisted from a planar conformation; the phenyl ring plane [atoms C(11)–C(16)] and the plane of atoms N(3), C(4), C(5), C(6) are inclined at 23.5 and 24.6° respectively to the plane of atoms C(6), C(7), O(8), N(9). In the chain C(1), N(2), N(3), C(4), C(6), C(7) the maximum deviation of a torsion angle from the maximally extended value of 180° is only 1.8°. The molecules are linked into infinite chains along the crystallographic α-direction by NH · · · O hydrogen bonds between N-9 and O-8 of an adjacent molecule [N · · · O 2.879(2) Å].

The reaction of **2** with dimethyl azodicarboxylate has been described by Sommer as giving the 1,2,3,4-tetrahydrotetrazine **7**, the structure being fully supported by spectroscopic assignments and by an X-ray structure determination on a related azo ester adduct.[22]

We also obtained **7** as the initial and major product of the reaction, the spectrum of the reaction residue showing all the required[22] ^{1}H NMR signals. All efforts to purify this compound, however, failed in our hands. Chromatography on silica gel or attempts at direct crystallization caused its complete transformation to an isomer lacking the lowfield 6-H signal at δ 5.22,[22] and having a second exchangeable NH signal. We initially assumed the isomer, m.p. 154–155 °C, to be the tautomeric tetrazine **8** but our X-ray structure determination in fact showed that ring contraction had occurred through N–N bond cleavage resulting in the 5-amino-Δ^3-triazoline **9a** (Fig. 2).

Dimensions are in Table 2 and serve to establish the structure. In the crystals, **9a** molecules are linked to form centrosymmetric dimers by NH · · · O hydrogen bond formation between the N(14)–H and carbonyl O(7) of an adjacent molecule [N · · · O 2.912(2) Å]; in this way a 14-membered centrosymmetric ring is formed. The conformation adopted by the groups on C-5 is dictated by an NH · · · O bond between N(21)–H and O(13) [N · · · O 2.555(3) Å] which results in the C(12)–C(5)–N(21) bond angle being reduced from the normal tetrahedral value to 104.4(2)°. The triazoline ring is planar (deviations −0.011 to

* Cambridge data bank search to August, 1990.

Table 2 Molecular dimensions for **9a**

Bond lengths (Å)			
N(1)–N(2)	1.453(3)		
N(1)–C(5)	1.451(3)		
N(1)–C(6)	1.352(3)		
N(2)–N(3)	1.402(3)		
N(2)–C(10)	1.469(4)		
N(3)–C(4)	1.276(3)		
C(4)–C(5)	1.515(3)		
C(4)–C(11)	1.472(4)		
C(5)–C(12)	1.560(3)		
C(5)–N(21)	1.442(2)		
C(6)–O(7)	1.203(3)		
C(6)–O(8)	1.335(3)		
O(8)–C(9)	1.431(3)		
C(12)–O(13)	1.208(3)		
C(12)–N(14)	1.343(2)		
N(14)–C(15)	1.424(3)		
C(15)–C(16)	1.375(3)		
C(15)–C(20)	1.382(4)		
C(16)–C(17)	1.385(5)		
C(17)–C(18)	1.375(6)		
C(18)–C(19)	1.347(4)		
C(19)–C(20)	1.378(4)		
N(21)–C(22)	1.351(3)		
C(22)–O(23)	1.191(4)		
C(22)–O(24)	1.339(3)		
O(24)–C(25)	1.432(4)		
Bond angles ( )			
N(2)–N(1)–C(5)	111.0(2)	C(6)–O(8)–C(9)	116.9(2)
N(2)–N(1)–C(6)	118.3(2)	C(5)–C(12)–O(13)	120.1(2)
C(5)–N(1)–C(6)	127.6(2)	C(5)–C(12)–N(14)	114.7(2)
N(1)–N(2)–N(3)	105.2(2)	O(13)–C(12)–N(14)	125.0(2)
N(1)–N(2)–C(10)	112.3(2)	C(12)–N(14)–C(15)	124.3(2)
N(3)–N(2)–C(10)	108.5(2)	N(14)–C(15)–C(16)	117.5(2)
N(2)–N(3)–C(4)	111.2(2)	N(14)–C(15)–C(20)	122.8(2)
N(3)–C(4)–C(5)	113.7(2)	C(16)–C(15)–C(20)	119.8(2)
N(3)–C(4)–C(11)	123.6(2)	C(15)–C(16)–C(17)	119.7(3)
C(5)–C(4)–C(11)	122.6(2)	C(16)–C(17)–C(18)	120.3(2)
N(1)–C(5)–C(4)	98.9(2)	C(17)–C(18)–C(19)	119.4(3)
N(1)–C(5)–C(12)	114.7(2)	C(18)–C(19)–C(20)	121.8(3)
N(1)–C(5)–N(21)	114.6(2)	C(15)–C(20)–C(19)	119.1(2)
C(4)–C(5)–C(12)	110.1(2)	C(5)–N(21)–C(22)	125.2(2)
C(4)–C(5)–N(21)	114.4(2)	N(21)–C(22)–O(23)	126.5(2)
C(12)–C(5)–N(21)	104.4(2)	N(21)–C(22)–O(24)	108.6(2)
N(1)–C(6)–O(7)	124.8(2)	O(23)–C(22)–O(24)	124.9(2)
N(1)–C(6)–O(8)	109.8(2)	C(22)–O(24)–C(25)	116.2(3)
O(7)–C(6)–O(8)	125.3(2)		

Hydrogen bond dimensions

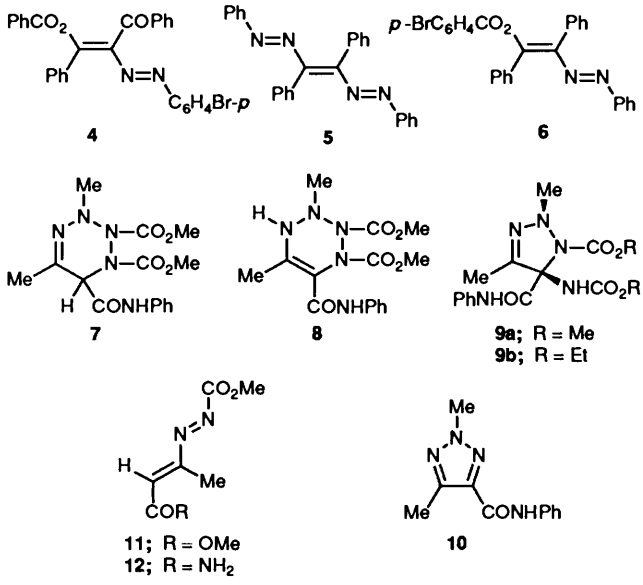
Distances (Å)		Angles (°)	
HN(14)–O(7)(I)	1.997	N(14)–HN(14)–O(7)(I)[a]	161.4
HN(21)–O(13)	2.094	N(21)–HN(21)–O(13)	108.2
N(21)–O(13)	2.555(3)		
N(14)–O(7)(I)	2.912(2)		

[a] The roman numeral (I) refers to the molecule at equivalent position $-x, -y, -z$.

0.009 Å) and the plane of the methoxycarbonyl atoms [N(1), C(6), O(7), O(8), C(9)] is inclined at 19.0° to it. Nitrogen N-2 in the triazoline ring is markedly pyramidal, with C-10 1.214(3) Å from the triazoline plane; carboxyl carbon C-6 (bonded to N-1) is 0.405 Å from the triazoline plane in the opposite direction to C-10.

The triazoline **9b** was similarly prepared from **2** and diethyl azodicarboxylate. Again the tetrazine, related to **7**, could be detected as the initial product.

The isomerisation of **7** to **9a** could be followed by NMR spectroscopy. Reaction of **2** with a slight excess of dimethyl azodicarboxylate in $CDCl_3$ at ambient temperature over 12 h gave **7** as the initial product which was slowly converted into **9a** (*ca.* 50% conversion in 1 week). NMR spectroscopy tube experiments were carried out to determine the effect of added base or acid at the stage when the Diels–Alder reaction was complete and the isomerisation to **9a** had already begun.



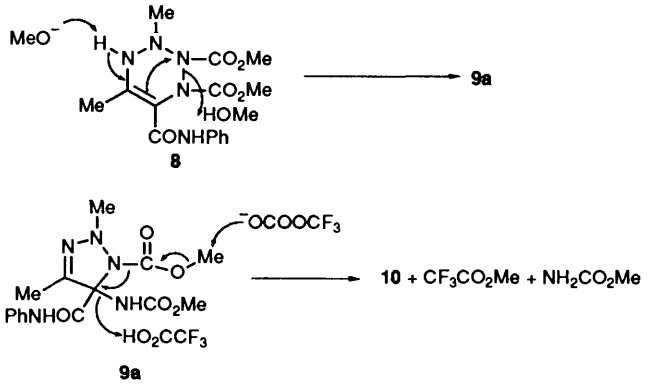
Pyridine had no influence on the reaction but trifluoroacetic acid (TFA) gave a rapid and unexpected result. There was immediate conversion of **7** into a compound judged to be the tautomer **8** by the absence of the methine resonance at δ 5.22. The proportion of **9a** remained fairly constant at first, as **8** reacted, and a new product was formed. In the late stages complete disappearance of **8** followed by that of **9a** were observed.

The new product, formed in nearly quantitative yield, was also cleanly obtained when **9a** alone was treated with TFA (trifluoroacetic acid) under the same conditions, no **8** being observed. Although the spectrum showed four new methyl peaks (C–Me, N–Me, and two O–Me), both methoxy peaks were absent from the product obtained when the reaction mixture was subjected to an aqueous acid or hydrogen carbonate work-up. Loss of both ester groups occurred before the aqueous work-up since the two methoxy peaks in the spectrum were readily attributable to methyl trifluoroacetate and methyl carbamate, by the successive addition of these esters to the NMR tube.

The product was identified as the 2-methyl-1,2,3-triazole **10**, by its elemental and mass spectrometric analyses, and by the deshielded *N*-methyl proton signal at δ 4.18, typical of this ring system.[34]

The NMR tube experiments strongly suggest that **8** is the precursor to **9a** and that the latter is the sole precursor to **10**. Mechanisms for the ring contraction to **9a**, and the solvolysis and deamination of the latter are suggested in Scheme 1.

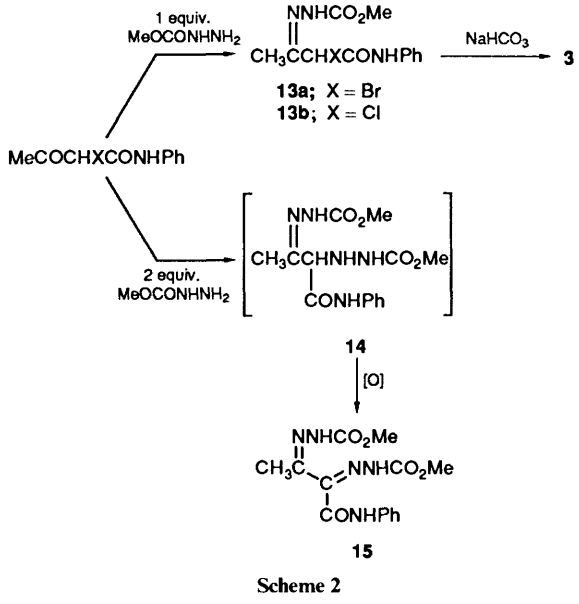
Despite its efficient reaction with azo esters we could not induce any other cycloadditions between compound **2** and any of a wide variety of substrates. A number of electron poor dienophiles proved inert, specifically methyl vinyl ketone, and dimethyl acetylenedicarboxylate. The cyclic azo compound, 4-phenyl-1,2,4-triazolinedione reacted rapidly but not by cycloaddition. Complex products were obtained, likely involving initial attack of nitrogen in **2** on the cyclic compound.[35] Electron rich double bonds were also unreactive in the case of ethyl vinyl ether and vinyl acetate (reactions with enamines were not attempted). Conjugatively unsaturated systems which also proved inert were cyclopentadiene and nitrosocarbonylmethane (MeCONO, from oxidation of acetohydroxamic acid).



Scheme 1

Azoalkene **3**.—This compound has not been described previously, although related examples **11** and **12**, derived from methyl acetoacetate and acetoacetamide have.[36] *E,E* Configurations were assigned to these, as shown, although in the case of **11** about 10% of the carbon–carbon *Z* isomer was also observed.

Compound **3** was prepared by reaction of α-chloro- or α-bromo-acetoacetanilide with 1 equiv. of methyl carbazate, followed by dehydrohalogenation of the hydrazone **13** with aq. sodium hydrogen carbonate (Scheme 2). Alternatively, **3** could



Scheme 2

be generated and treated *in situ* by treatment of solutions of **13** with solid Na_2CO_3. If 2 equiv. of methyl carbazate were used **3** was not formed (*cf.* synthesis of **2**), halogen displacement occurring instead in the second step leading to a product $C_{14}H_{17}N_5O_5$ identified as the bishydrazone **15**. We assume aerial oxidation was responsible for its formation from the intermediate hydrazinohydrazone **14**.

The spectrum of a freshly prepared solution of azo ester showed the presence of one azo compound which slowly isomerized (*ca.* 20% in 2 d) to another. We have assigned the former the *E,Z* stereochemistry shown for **3**, while the latter must be its *E,E* isomer. Our evidence is the downfield shift of the C–Me (δ 2.10 → 2.34) in the isomerisation, due to the deshielding by the phenyl group in the product. The upfield shift in the O–Me group (δ 4.16 → 4.06) is also consistent with this. The *E,Z* assignment to the initial isomer is fully

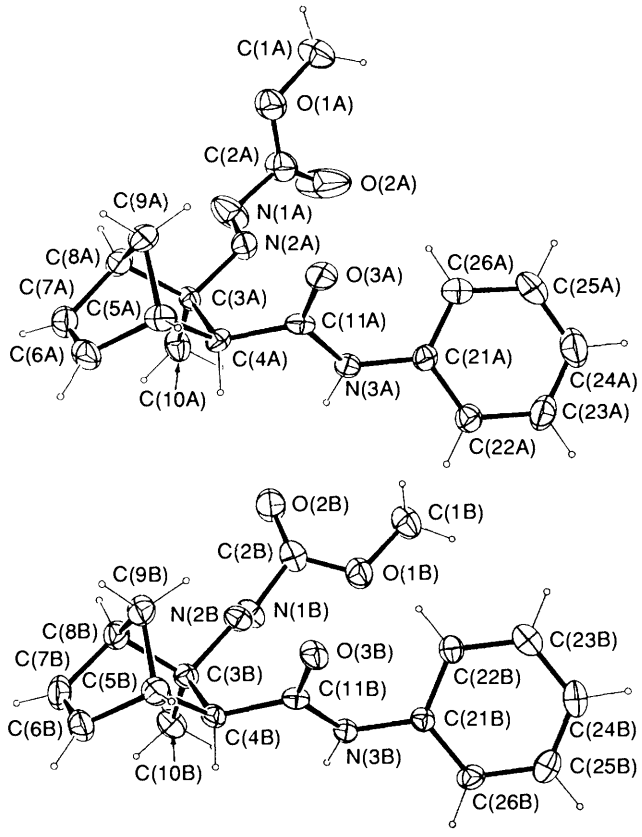
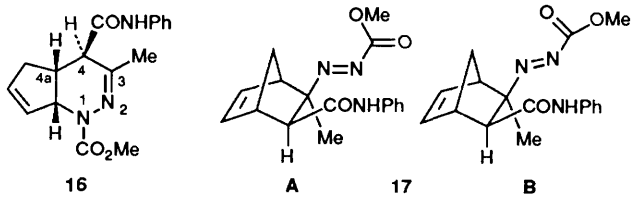


Fig. 3 Views of the two independent molecules **A** and **B** of **17** with the crystallographic numbering scheme showing the two different conformation adopted by azo-ester side chain. Thermal ellipsoids for non-hydrogen atoms are at the 25% level

supported by the Diels–Alder reaction described below. The azo ester forms polymer over long periods of time.

Generation of **3** in CH_2Cl_2 in the presence of cyclopentadiene lead to an approximately 1:1 mixture of two adducts separable by chromatography. One was the tetrahydropyridazine **16**, m.p. 185 °C (decomp.), the product of the expected mode of addition of cyclopentadiene to an azoalkene.[13,20] The stereochemistry shown for **16** is that which would arise from the *E,Z*



configuration of **3** reacting through an *endo* transition state. The coupling constant of 4.2 Hz for the 4,4a protons does not allow us to confirm or reject the *trans* relationship assigned to them. Related cyclopentene-fused pyridazines both with *cis*[25] and with *trans*[37] 4,4a protons have been described having coupling constants which are considerably larger.

The second adduct, m.p. 147–148 °C, had the proton resonance patterns in its NMR spectrum typical of a 1,4-adduct of cyclopentadiene, and thus was the product of addition to **3** at its N=N or C=C bond. The latter was the case, as established by our X-ray crystallographic study of **17**, and, assuming a concerted cycloaddition, the stereochemistry of the original azoalkene **3** is thus established. The product **17** exists in the crystal in two conformational variations **A** and **B** (Fig. 3). **A** and **B** differ primarily in respect to rotation round the

Table 3 Molecular dimensions for **17**

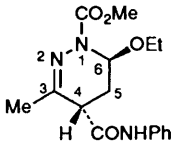
	Bond lengths (Å)		
O(1A)–C(1A)	1.444(7)	O(1B)–C(1B)	1.439(7)
O(1A)–C(2A)	1.255(7)	O(1B)–C(2B)	1.312(6)
O(2A)–C(2A)	1.158(7)	O(2B)–C(2B)	1.170(6)
O(3A)–C(11A)	1.232(5)	O(3B)–C(11B)	1.224(5)
N(1A)–N(2A)	1.148(6)	N(1B)–N(2B)	1.220(5)
N(1A)–C(2A)	1.417(7)	N(1B)–C(2B)	1.438(6)
N(2A)–C(3A)	1.491(6)	N(2B)–C(3B)	1.486(6)
N(3A)–C(11A)	1.345(6)	N(3B)–C(11B)	1.342(5)
N(3A)–C(21A)	1.413(6)	N(3B)–C(21B)	1.412(6)
C(3A)–C(4A)	1.572(6)	C(3B)–C(4B)	1.565(6)
C(3A)–C(3A)	1.548(7)	C(3B)–C(8B)	1.561(7)
C(3A)–C(10A)	1.511(6)	C(3B)–C(10B)	1.523(6)
C(4A)–C(5A)	1.540(7)	C(4B)–C(5B)	1.551(6)
C(4A)–C(11A)	1.508(6)	C(4B)–C(11B)	1.525(6)
C(5A)–C(6A)	1.509(7)	C(5B)–C(6B)	1.496(7)
C(5A)–C(9A)	1.532(7)	C(5B)–C(9B)	1.509(7)
C(6A)–C(7A)	1.314(8)	C(6B)–C(7B)	1.304(7)
C(7A)–C(8A)	1.495(7)	C(7B)–C(8B)	1.502(7)
C(8A)–C(9A)	1.519(7)	C(8B)–C(9B)	1.525(7)
C(21A)–C(22A)	1.369(7)	C(21B)–C(22B)	1.384(6)
C(21A)–C(26A)	1.369(7)	C(21B)–C(26B)	1.383(6)
C(22A)–C(23A)	1.375(8)	C(22B)–C(23B)	1.373(7)
C(23A)–C(24A)	1.351(9)	C(23B)–C(24B)	1.371(7)
C(24A)–C(25A)	1.346(9)	C(24B)–C(25B)	1.368(8)
C(25A)–C(26A)	1.376(9)	C(25B)–C(26B)	1.378(7)
	Bond angles (°)		
C(1A)–O(1A)–C(2A)	118.4(4)	C(1B)–O(1B)–C(2B)	116.1(4)
N(2A)–N(1A)–C(2A)	115.0(5)	N(2B)–N(1B)–C(2B)	111.6(4)
N(1A)–N(2A)–C(3A)	116.1(4)	N(1B)–N(2B)–C(3B)	114.6(4)
C(11A)–N(3A)–C(21A)	127.2(4)	C(11B)–N(3B)–C(21B)	124.6(4)
O(1A)–C(2A)–O(2A)	124.2(5)	O(1B)–C(2B)–O(2B)	126.6(5)
O(1A)–C(2A)–N(1A)	113.4(5)	O(1B)–C(2B)–N(1B)	110.4(4)
O(2A)–C(2A)–N(1A)	121.9(6)	O(2B)–C(2B)–N(1B)	122.8(5)
N(2A)–C(3A)–C(4A)	107.7(3)	N(2B)–C(3B)–C(4B)	107.4(3)
N(2A)–C(3A)–C(8A)	110.3(4)	N(2B)–C(3B)–C(8B)	104.5(3)
N(2A)–C(3A)–C(10A)	109.4(4)	N(2B–C(3B)–C(10B)	114.0(4)
C(4A)–C(3A)–C(8A)	101.1(3)	C(4B)–C(3B)–C(8B)	101.2(4)
C(4A)–C(3A)–C(10A)	113.5(4)	C(4B)–C(3B)–C(10B)	114.2(4)
C(8A)–C(3A)–C(10A)	114.5(4)	C(8B)–C(3B)–C(10B)	114.3(4)
C(3A)–C(4A)–C(5A)	103.1(3)	C(3B)–C(4B)–C(5B)	103.1(4)
C(3A)–C(4A)–C(11A)	112.9(4)	C(3B)–C(4B)–C(11B)	113.8(4)
C(5A)–C(4A)–C(11A)	115.0(4)	C(5B)–C(4B)–C(11B)	112.9(4)
C(4A)–C(5A)–C(6A)	106.0(4)	C(4B)–C(5B)–C(6B)	106.3(4)
C(4A)–C(5A)–C(9A)	101.0(4)	C(4B)–C(5B)–C(9B)	100.8(4)
C(6A)–C(5A)–C(9A)	99.3(4)	C(6B)–C(5B)–C(9B)	99.9(4)
C(5A)–C(6A)–C(7A)	107.4(4)	C(5B)–C(6B)–C(7B)	108.1(5)
C(6A)–C(7A)–C(8A)	107.7(5)	C(6B)–C(7B)–C(8B)	107.5(5)
C(3A)–C(8A)–C(7A)	107.2(4)	C(3B)–C(8B)–C(7B)	107.2(4)
C(3A)–C(8A)–C(9A)	100.8(4)	C(3B)–C(8B)–C(9B)	100.6(4)
C(7A)–C(8A)–C(9A)	100.8(4)	C(7B)–C(8B)–C(9B)	99.7(4)
C(5A)–C(9A)–C(8A)	93.5(4)	C(5B)–C(9B)–C(8B)	94.0(4)
O(3A)–C(11A)–N(3A)	123.2(4)	O(3B)–C(11B)–N(3B)	123.3(4)
O(3A)–C(11A)–C(4A)	122.4(4)	O(3B)–C(11B)–C(4B)	121.5(4)
N(3A)–C(11A)–C(4A)	114.4(4)	N(3B)–C(11B)–C(4B)	115.2(4)
N(3A)–C(21A)–C(22A)	119.1(4)	N(3B)–C(21B)–C(22B)	120.8(4)
N(3A)–C(21A)–C(26A)	121.6(4)	N(3B)–C(21B)–C(26B)	119.8(4)
C(22A–C(21A)–C(26A)	119.2(5)	C(22B)–C(21B)–C(26B)	119.4(4)
C(21A)–C(22A)–C(23A)	120.5(5)	C(21B)–C(22B)–C(23B)	119.6(4)
C(22A)–C(23A)–C(24A)	120.3(5)	C(22B)–C(23B)–C(24B)	121.3(5)
C(23A)–C(24A)–C(25A)	119.0(6)	C(23B)–C(24B)–C(25B)	118.9(5)
C(24A)–C(25A)–C(26A)	122.2(6)	C(24B)–C(25B)–C(26B)	121.1(5)
C(21A)–C(26A)–C(25A)	118.8(5)	C(21B)–C(26B)–C(25B)	119.6(4)
	Hydrogen bond dimensions		
Distances[a] (Å)		Angle (°)	
O(3A)–N(3B)(I)	2.931(4)	N(3A)–HN(3A)···O(38)(II)	153.2
O(3A)–HN(3B)(I)	2.099	O(3A)(I)···HN(3B)–N(3B)	145.3
N(3A)–O(3B)(II)	2.942(4)		
O(3B)–HN(3A)(II)	2.063		

[a] The roman numerals refer to the following equivalent positions; (I), $-x, -y, -z$; (II), $1-x, -y, -z$.

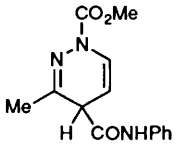
N(1)–C(2) and N(2)–C(3) s-bonds in molecules **A** and **B** [*e.g.* torsion angles N(2)–N(1)–C(2)–O(1) −101.0° (**A**) and +87.5° (**B**), and N(1)–N(2) C(3)–C(4) −177.6° (**A**) and 138.9° (**B**)]. Dimensions are in Table 3 and serve to establish the structure. In the crystal lattice, the molecules are linked into infinite chains by N(3)–H ··· O(3) hydrogen bonds in the a-direction with **A** and **B** molecules alternating in the chain (N(3B) ··· O(3A) 2.931(4), N(3A) ··· O(3B) 2.942(4) Å).

The proportions of the adducts **16** and **17** were not noticeably solvent dependent, the cycloaddition in acetonitrile also giving approximately equal amounts of the products.

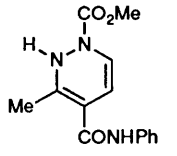
Compound **3** is unreactive to electron poor substrates, for example dimethyl and diethyl azodicarboxylates, and dimethyl acetylenedicarboxylate but it reacts in low yield with ethyl vinyl ether to give the ethoxytetrahydropyridazine **18**. The regiochemistry is in agreement with that of similar enol ether adducts.[15,36] The ring carbon stereochemistry is likely *trans* as shown. In the most stable, half-chair, arrangement 4-H must be axial (or pseudo axial) since it shows a large coupling constant to one 5-H (*J* 10.1 Hz; ax–ax), but 6-H must be equatorial since both its coupling constants to 5-H are small (*J* 2.2, 3.5 Hz; one *eq-ax* and one *eq-eq*). Thus the OEt group in **18** is *trans* to the anilide group and occupies the axial position which minimises its steric interaction with the adjacent NCO_2Me group. When **18** was treated with trifluoroacetic acid rapid elimination of EtOH occurred giving mainly the unconjugated dihydropyridazine **19**, along with some of the conjugated tautomer **20**.



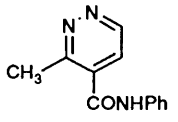
18



19



20



21

When **19** was refluxed in K_2CO_3–MeOH the previously unknown pyridazine **21** was obtained, through hydrolysis, decarboxylation, and (presumably aerial) oxidation. Compound **20** behaved similarly, but more rapidly.

Experimental

The following spectrometers were used: for IR, a Perkin-Elmer 983, using Nujol mulls or $CHCl_3$ solutions; for NMR, Bruker WP 80, AC 200 or AM 250 instruments, $CDCl_3$ being used as solvent (*J* values in Hz); for mass spectra a Varian MATCH7 or VG-7070F. Column chromatography was carried out on silica gel, 230–400 mesh. M.p.s are uncorrected.

(E,E)-4-*Methyl*-N-*phenyl*-2,3-*diazapenta*-2,4-*diene*-5-*carboxamide* **2**.—To a stirred solution of methylhydrazine (2.34 g, 0.052 mol) in methylene dichloride (30 cm^3) in the presence of anhydrous Na_2SO_4 was slowly added a solution of α-chloroacetoacetanilide (5.50 g, 0.026 mol) in methylene dichloride (50 cm^3). After the addition was complete the reaction mixture was stirred for 1 additional hour. Filtration to remove the Na_2SO_4, followed by chromatography and crystallization from hexane–ethyl acetate, gave the azoalkene **2** (2.35 g, 45%) as yellow crystals, m.p. 148–149 °C; ν_{max}/cm^{-1} 3427, 1677, 1640, 1598, 1517, 1498 and 1438; δ_H(200 MHz) 2.28 (d, *J* 1, 1 H) 3.99 (s, 3 H), 6.66 (d, *J* 1, 1 H), 7.1–7.6 (m, 5 H) and 7.41 (br s, NH).

Methyl 5-*Methoxycarbonylamino*-2,4-*dimethyl*-5-*phenylcarbamoyl*-2,5-*dihydro*-1H-1,2,3-*triazole*-1-*carboxylate* **9a**.—A solution of azoalkene **2** (2.035 g, 0.01 mol) and dimethyl azodicarboxylate (1.463 g, 0.01 mol) in benzene (5 cm^3) was stirred at room temperature for 12 h. Removal of solvent followed by column chromatography on silica gel with ethyl acetate–hexane (1:4) gave the *adduct* **9a** (2.63 g, 75%), m.p. 154–155 °C (CH_2Cl_2–hexane): ν_{max}(Nujol)/cm^{-1} 3393, 3261, 1743, 1714, 1691 and 1600; δ_H(200 MHz) 1.95 (s, 3 H) 3.26 (s, 3 H), 3.71 (s, 3 H), 3.74 (br s, 1 H), 6.79 (br s, 1 H), 7.14–7.42 (m, 5 H) and 7.19 (br s, 1 H); *m/z* 349 (M^+, 0.3%), 274 (13), 229 (30), 185 (24), 153 (19) and 124 (100) (Found: C, 51.6; H, 5.4; N, 20.2. $C_{15}H_{19}N_5O_5$ requires C, 51.6; H, 5.5; N, 20.1%).

Detection of **7** *as Precursor to* **9a**.—Reaction of **2** with a slight excess of the azo ester in $CDCl_3$ in an NMR tube showed that formation of **7** was complete within 12 h, as judged by the observation of the published values of the chemical shifts.[22] Evaporation of the solution gave a residue which still showed the NMR signals for **7** which was present before the silica gel chromatography was performed. If the NMR experiment was continued beyond 12 h, slow isomerisation of **7** to **9a** was observed, conversion being about 50% in 1 week.

Ethyl 2,5-*Dihydro*-1H-1,2,3-*triazole*-1-*carboxylate* **9b**. This was prepared exactly as for **9a** using the azoalkene **2** and diethyl azodicarboxylate, and with a similar work-up. *Compound* **9b** had m.p. 146–147 °C (ether), ν_{max}(Nujol)/cm^{-1} 3390, 3293, 1737, 1716, 1690 and 1598; δ_H(200 MHz) 1.60 (br t, 3 H, *J* 6.5), 1.28 (t, 3 H, *J* 7.1) 1.94 (s, 3 H), 3.26 (s, 3 H), 4.16 (m, 6 H), 6.70 (br s, 1 H), 7.16–7.43 (m, 5 H) and 7.18 (br s, 1 H); *m/z* 377 (M^+, 1%), 288 (6), 257 (34), 213 (30), 185 (96) and 139 (100) (Found: M^+, 377.1690. $C_{17}H_{23}N_5O_5$ requires *M*, 377.1701).

Conversion of **9a** *into* **10**.—A solution of compound **9a** (0.104 g, 0.3 mmol) in CH_2Cl_2 (15 cm^3) was stirred with trifluoroacetic acid (TFA) (0.50 cm^3) at room temperature for 6 h. Aqueous work-up, followed by recrystallisation from ether, gave 2,5-*dimethyl*-N-*phenyl*-2H-*triazole*-4-*carboxamide* **10** (0.052 g, 80%) as colourless crystals, m.p. 126–127 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3401, 1686, 1596 and 1536; δ_H(250 MHz) 2.59 (s, 3 H), 4.18 (s, 3 H), 7.10–7.67 (m, 5 H) and 8.47 (br s, 1 H); *m/z* 216 (M^+, 38%) and 124 (100) (Found: C, 60.9; H, 5.7; N, 26.0. $C_{11}H_{12}N_4O$ requires C, 61.1; H, 5.6; N, 25.9%).

NMR Examination of Conversion of **7** *into* **10**.—A $CDCl_3$ solution of **2** and dimethyl azodicarboxylate was allowed to react to the point where the formation of **7** was complete and conversion into **9a** had become detectable. Two drops of TFA were added. There was rapid replacement of **7** by a product judged to be the tautomer **8** mainly because of the absence of a methine proton. The methyl singlets were slightly shifted from those of **7**, but they were slowly lost at the expense of the final product **10**, methyl trifluoroacetate and methyl carbamate. The proportion of **9a** remained almost constant until **8** had reacted completely, after which it too disappeared. The identity of the two methyl esters was confirmed by sequential inclusion of authentic samples in the NMR tube. When pyridine was used in a further run in place of TFA no effect was observed.

Bromohydrazone **13a**.—A solution of α-bromoacetoacetanilide (1.16 g, 5 mmol) and methyl carbazate (0.45 g, 5 mmol) in MeOH (25 cm^3) containing a few drops of phosphoric acid was kept for 12 h at room temperature and poured into water. The crude 1-*bromo*-1-*phenylcarbamoylpropan*-2-*one methoxycarbonylhydrazone* was recrystallised from CH_2Cl_2–hexane as

colourless crystals (1.4 g, 84%), m.p. 141–142 °C; ν_{max}(CHCl$_3$)/cm^{-1} 3384, 3256, 1745, 1684 and 1600; δ_H(200 MHz) 2.04 (s, 3 H), 3.86 (s, 3 H), 5.23 (s, 1 H), 7.15–7.59 (m, 5 H), 7.85 (br s, 1 H) and 8.82 (br s, 1 H) (Found: C, 43.8; H, 4.3; N, 12.6. $C_{12}H_{14}BrO_3N_3$ requires C, 43.9; H, 4.3; N, 12.8%).

Chlorohydrazone **13b**.—This was prepared from α-chloroacetoacetanilide, exactly as for the bromo analogue, and was recrystallised from CH_2Cl_2–hexane to give 1-*chloro*-1-*phenylcarbamoylpropan*-2-*one methoxycarbonylhydrazone*, m.p. 140–141 C; ν_{max}(CHCl$_3$)/cm^{-1} 3397, 3279, 1747, 1690 and 1601; δ_H(250 MHz) 1.98 (s, 3 H), 3.85 (s, 3 H), 5.23 (s, 1 H), 7.13–7.57 (m, 5 H), 7.90 (br s, 1 H) and 8.42 (br s, 1 H); *m/z* (^{35}Cl) 283 (M$^+$, 7%), 247 (8), 218 (7), 164 (79) and 120 (100) (Found: C, 50.9; H, 5.1; N, 14.9. $C_{12}H_{14}ClO_3N_3$ requires C, 50.8; H, 5.0: N, 14.8%).

The bishydrazone **15**.—A solution of α-bromoacetoacetanilide (1.16 g, 5 mmol) and methyl carbazate (0.90 g, 10 mmol) in MeOH (25 cm^3) containing a few drops of phosphoric acid was stirred for 12 h. Work-up as for **13a** followed by crystallisation from CH_2Cl_2–MeOH gave the 1-*phenylcarbamoylpropane*-1,2-*dione* 1,2-*bis*(*methoxycarbonylhydrazone*) **15** (1.45 g, 86%) as light yellow crystals, m.p. 214–215 °C; ν_{max}(Nujol)/cm^{-1} 3238, 3146, 1749, 1700, 1639, 1618 and 1595; δ_H(250 MHz) 2.24 (s, 3 H), 3.88 (s, 3 H), 3.92 (s, 3 H) 7.12–7.81 (m, 5 H), 8.07 (br s, 1 H), 12.35 (br s, 1 H) and 13.74 (br s, 1 H); *m/z* 335 (M$^+$, 72%), 276 (65), 261 (15), 160 (67) and 93 (100) (Found: C, 50.1; H, 5.1; N, 20.9. $C_{14}H_{17}N_5O_5$ requires C, 50.2; H, 5.1; N, 20.9%).

Methyl(E,Z)-3-*Methyl*-4-*phenylcarbamoyl*-1,2-*diazabuta*-1,3-*diene*-1-*carboxylate* **3**.—A solution of the chloro hydrazone **13b** (5 mg) in $CDCl_3$ (1 cm^3) was shaken with saturated aq. $NaHCO_3$ (2 cm^3) for 3 min. The organic layer was dried and half of it analysed by ^{1}H NMR spectroscopy. Peaks from the *E,Z*-isomer dominated the spectrum: δ_H(250 MHz) 2.10 (d, 3 H, *J* 1.0, C-Me), 4.16 (s, 3 H, OMe), 6.74 (q, *J* 1.0, vinyl-H), 7.1–7.7 (m, 5 H) and 10.00 (NH). After 2 days peaks attributable to the *E,E*-isomer (about 20% of the total) were present: 2.34 (d, 3 H, *J* 0.8, C-Me), 4.06 (s, 3 H, OMe), vinyl-H in Ph region. Peaks due to polymeric material (see below) were also detectable.

The other half of the original solution was immediately evaporated to give an oily residue which was kept for 2 days and then redissolved in $CDCl_3$. Its spectrum showed only broad C-Me and OMe absorption due to polymeric material along with peaks from a trace of the *E,E*-isomer, but none from the *E,Z*-isomer.

Methyl 3-*Methyl*-4-*phenylcarbamoyl*-4,4a,5,7a-*tetrahydro*-1H-*cyclopenta*[c]*pyridazine*-1-*carboxylate* **16** *and Methyl* exo-cis-2-*Methyl*-3-*phenylcarbamoylbicyclo*[2.2.1]*hept*-5-*ene*-2-*diazocarboxylate* **17**.—To the bromo hydrazone **13a** (2 g, 6 mmol) in CH_2Cl_2 (25 cm^3) was added cyclopentadiene (5 cm^3), followed by Na_2CO_3 (3.2 g, 30 mmol), and the mixture was stirred at room temperature for 24 h. The reaction mixture was filtered and the solvent was removed under reduced pressure to leave an oil. This was chromatographed on silica gel with ethyl acetate–hexane (1:4) to give two products **17** and **16**, in order of elution. Recrystallisation of the latter from CH_2Cl_2–hexane gave *compound* **16** (0.530, 28%) as a solid, m.p. 185 °C (decomp.); ν_{max}(Nujol)/cm^{-1} 3317, 1703, 1687, 1619 and 1609; δ_H(250 MHz) 2.19 (s, 3 H), 2.56, 2.63 [dd, 1 H, 5-H (*endo*)], 2.69, 2.77 [dq, 1 H, 5-H (*exo*)], 3.24 (d, 1 H, 4-H), 3.35 (m, 1 H, 4a-H), 3.86 (s, 3 H), 5.14 (d, 1 H, 7a-H), 5.79 (m, 1 H, 6-H) 5.89 (br d, 1 H, 7-H) and 7.1–7.6 (m, 5 H). The following coupling constants were obtained by decoupling experiments: $J_{5exo,4a}$ 8.2, J_{5gem} 18, $J_{5endo,4a}$ 4.8, $J_{5exo,6}$ 2.3, $J_{4,4a}$ 4.8 and $J_{7a,4a}$ 9.7; *m/z* 313 (M$^+$, 20%), 221 (6) and 194 (100) (Found: C, 65.0; H, 6.3; N, 13.3. $C_{17}H_{19}N_3O_3$ requires C, 65.2; H, 6.1; N, 13.4%).

Recrystallisation of the minor product from CH_2Cl_2–hexane afforded *compound* **17** (0.26 g, 14%) as yellow needles, m.p. 147–148 °C; ν_{max}(CHCl$_3$)/cm^{-1} 3430, 1761, 1690 and 1599; δ_H(250 MHz) 1.28 (s, 3 H), 1.69, 1.74 (dd, *J* 1.6 and 9.1, 1 H, 7-H), 2.41 (d, *J* 2.1, 1 H, 6-H), 2.57 (d, *J* 9.1, 1 H, 7-H), 2.76 (br s, 1 H, 4-H) 3.38 (br s, 1 H, 1-H), 3.79 (s, 3 H), 6.31, 6.34 (dd, *J* 3.1 and 5.6, 1 H, 3-H), 6.50, 6.53 (dd, *J* 3.1 and 5.6, 1 H, 2-H) 6.97 (br s, 1 H, NH) and 7.0–7.4 (m, 5 H); *m/z* 313 (M$^+$, 49%), 226 (100) and 221 (14) (Found: C, 65.4; H, 6.3; N, 13.6. $C_{17}H_{19}N_3O_3$ requires C, 65.2; H, 6.1; N, 13.4%). The proportions of the adducts **16** and **17** were about the same when the reaction was performed in acetonitrile as solvent.

Methyl 6-*Ethoxy*-3-*methyl*-4-*phenylcarbamoyl*-1,4,5,6-*tetrahydropyridazine*-1-*carboxylate* **18**.—To a solution of chlorohydrazone **13b** (0.50 g, 1.82 mmol) in CH_2Cl_2 (25 cm^3) were added Na_2CO_3 (0.95 g, 9 mmol) and an excess of ethyl vinyl ether. After the reaction mixture had been stirred at room temperature for 12 h, the solvent was removed and the residue was chromatographed on silica gel using ethyl acetate–hexane (1:1) to give the adduct **18** (0.15 g, 25%), m.p. 171–172 °C (ether–hexane); ν_{max}(CHCl$_3$)/cm^{-1} 3309, 1705, 1679 and 1600; δ_H(200 MHz) 1.28 (t, 3 H, CH_2CH_3), 2.20 (s, 3 H, CH_3) 2.27, 2.34 (dq, 1 H, 5a-H), 2.55, 2.56 (dd, 1 H, 5e-H), 3.22 (br d, 1 H, 4a-H), 3.74 (q, 2 H, CH_2CH_3), 3.91 (s, 3 H, OCH_3), 5.85 (br s, 1 H, 6e-H) 7.06–7.50 (m, 5 H) and 9.33 (br s, 1 H, NH), $J_{4a,5a}$ 10.1, $J_{4a,5e}$ 1.0, $J_{5a,5e}$ 15, $J_{5e,6e}$ 2.2, $J_{5a,6e}$ 3.5; *m/z* 319 (M$^+$, 1.5%), 273 (52) and 153 (100) (Found: C, 60.4; H, 6.4; N, 13.0. $C_{16}H_{21}N_3O_4$ requires C, 60.2; H, 6.6; N, 13.2%).

Preparation of Dihydropyridazines **19** *and* **20**.—To a stirred solution of compound **18** (250 mg, 0.78 mmol) in CH_2Cl_2 (10 cm^3) were added a few drops of trifluoroacetic acid, and the reaction mixture was stirred for 2 h at room temperature. Evaporation followed by chromatography on silica gel with ethyl acetate–hexane (3:7) gave two products **20** and **19**, in order of elution. Recrystallisation of the major constituent from CH_2Cl_2–hexane gave *methyl* 3-*methyl*-4-*phenylcarbamoyl*-1,4-*dihydropyridazine*-1-*carboxylate* **19** (0.13 g, 61%) as a colourless solid, m.p. 127–128 °C (CH_2Cl_2–hexane): ν_{max}/cm^{-1} 3333, 1720 and 1687; δ_H(250 MHz) 2.24 (s, 3 H), 3.89 (d, *J* 4.7, 1 H), 3.95 (s, 3 H), 5.15, 5.18 (dd, *J* 4.7 and 8.0, 1 H), 7.1–7.5 (m, 5 H), 7.42 (d, *J* 8.0, 1 H) and 7.45 (br s, 1 H); *m/z* 273 (M$^+$, 2%), 213 (2), 200 (1.5), 173 (1.5) and 153 (100) (Found: C, 61.5; H, 5.6; N, 15.1. $C_{14}H_{15}N_3O_3$ requires C, 61.5; H, 5.5; N, 5.4%)

The *methyl* 3-*methyl*-4-*phenylcarbamoyl*-1,2-*dihydropyridazine*-1-*carboxylate* **20** (0.03 g, 14%) did not crystallise. It had ν_{max}(CHCl$_3$)/cm^{-1} 3405, 3267, 1739 and 1665; δ_H(250 MHz) 2.25 (s, 3 H), 3.79 (s, 3 H), 6.29 (d, *J* 3.4, 1 H) 6.58 (d, *J* 3.4, 1 H), 7.1–7.7 (m, 5 H), 8.21 (br s, 1 H) and 13.72 (br s, 1 H), *m/z* 273 (M$^+$, 14%), 215 (10), 200 (14) 181 (54), 153 (66) and 84 (100).

Preparation of Pyridazine **21**.—Compound **19** (0.09 g, 0.3 mmol) was dissolved in MeOH (10 cm^3) and refluxed with K_2CO_3 (0.2 g, 1.5 mmol) for 12 h. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue was acidified and extracted with CH_2Cl_2. Removal of CH_2Cl_2, followed by column chromatography with ethyl acetate–hexane (8:2) afforded 3-*methyl*-N-*phenylpyridazine*-4-*carboxamide* **21** (0.048 g, 68%) as needles, m.p. 167–168 °C; ν_{max}(CHCl$_3$)/cm^{-1} 3680 and 1677; δ_H(250 MHz) 2.78 (s, 3 H), 7.23 (m, 1 H), 7.38 (m, 2 H), 7.49 (d, *J* 4.9, 1 H), 7.67 (d, *J* 8.2, 2 H) and 8.93 (d, *J* 4.9, 1 H), *m/z* 213 (M$^+$, 78%), 149 (72), 121 (34), 91 (37) and 65 (100) (Found: C,

Table 4 Additional crystallographic data

Compound	2	9a	17
Colour and shape	Yellow needles	Yellow plates	Yellow needles
Crystal dimensions (mm)	0.35 × 0.38 × 0.50	0.21 × 0.36 × 0.42	0.10 × 0.23 × 0.63
$2\theta_{max}$(°)	54	54	50
Unique reflections	1283	3810	4477
Reflections with $I > 3\sigma(I)$	859	2099	1857
Number of variables	135	227	416
R	0.032	0.043	0.043
R_w	0.044	0.062	0.055
p in weighting scheme	0.060	0.055	0.060
Goodness of fit	1.22	1.75	1.36
Extinction coeff.	—	5.4×10^{-7}	5.3×10^{-8}
Residual density (eÅ^{-3})	+0.12	+0.16	+0.30

Table 5 Positional parameters and their esd's for **2**

Atom	x	y	z
O(8)	−0.1460(2)	0.161	0.2437(2)
N(2)	0.0322(3)	0.3266(3)	0.6583(2)
N(3)	0.0779(2)	0.2650(3)	0.5734(2)
N(9)	0.0724(2)	0.1297(3)	0.1756(2)
C(1)	0.1258(4)	0.3292(4)	0.7626(3)
C(4)	−0.0109(3)	0.2578(3)	0.4697(2)
C(5)	−0.1451(3)	0.3269(4)	0.4705(3)
C(6)	0.0433(2)	0.1901(3)	0.3802(2)
C(7)	−0.0209(2)	0.1602(3)	0.2619(2)
C(11)	0.0471(2)	0.0864(2)	0.0564(2)
C(12)	−0.0728(3)	0.1153(3)	−0.0068(3)
C(13)	−0.0898(3)	0.0667(4)	−0.1223(2)
C(14)	0.0100(4)	−0.0065(3)	−0.1753(2)
C(15)	0.1306(4)	−0.0323(3)	−0.1144(3)
C(16)	0.1491(3)	0.0143(3)	0.0014(3)

Table 6 Positional parameters and their esd's for **9a**

Atom	x	y	z
N(1)	0.2178(2)	0.1135(2)	0.1841(2)
N(2)	0.2587(2)	0.0628(2)	0.0619(2)
N(3)	0.3582(2)	−0.0299(2)	0.0842(2)
C(4)	0.3792(3)	−0.0387(3)	0.2004(2)
C(5)	0.2953(2)	0.0541(2)	0.2824(2)
C(6)	0.0878(3)	0.1691(2)	0.1763(2)
O(7)	0.0211(2)	0.2070(2)	0.0862(2)
O(8)	0.0505(2)	0.1831(2)	0.2872(1)
C(9)	−0.0944(3)	0.2267(3)	0.2886(3)
C(10)	0.3484(3)	0.1820(3)	0.0436(2)
C(11)	0.4758(3)	−0.1300(3)	0.2512(3)
C(12)	0.1777(2)	−0.0422(2)	0.3163(2)
O(13)	0.2017(2)	−0.0266(2)	0.4343(1)
N(14)	0.0613(2)	−0.1462(2)	0.2057(2)
C(15)	−0.0480(2)	−0.2562(2)	0.2118(2)
C(16)	−0.1024(3)	−0.3890(3)	0.1035(3)
C(17)	−0.2083(4)	−0.4999(3)	0.1048(3)
C(18)	−0.2597(4)	−0.4774(3)	0.2134(3)
C(19)	−0.2075(3)	−0.3460(3)	0.3178(3)
C(20)	−0.1018(3)	−0.2335(3)	0.3199(2)
N(21)	0.4010(2)	0.1613(2)	0.4148(2)
C(22)	0.5341(3)	0.2580(3)	0.4371(2)
O(23)	0.5878(2)	0.2665(2)	0.3532(2)
O(24)	0.5973(2)	0.3447(2)	0.5711(2)
C(25)	0.7416(4)	0.4533(4)	0.6139(4)

Table 7 Positional parameters and their esd's for **17**

Atom	x	y	z
O(1A)	0.3384(4)	0.0739(1)	0.4862(4)
O(2A)	0.5108(6)	0.0468(1)	0.3921(6)
O(3A)	0.3240(3)	0.1615(1)	0.0953(3)
N(1A)	0.5106(5)	0.1161(1)	0.4273(5)
N(2A)	0.4934(4)	0.1342(1)	0.3345(4)
N(3A)	0.5417(4)	0.1425(1)	0.0392(3)
C(1A)	0.2744(6)	0.0337(2)	0.5035(6)
C(2A)	0.4513(6)	0.0757(2)	0.4286(5)
C(3A)	0.5612(5)	0.1759(1)	0.3278(4)
C(4A)	0.5192(5)	0.1959(1)	0.1965(4)
C(5A)	0.4265(5)	0.2329(2)	0.2339(5)
C(6A)	0.5224(5)	0.2639(2)	0.2983(5)
C(7A)	0.5634(6)	0.2477(2)	0.4071(5)
C(8A)	0.4919(5)	0.2066(2)	0.4205(5)
C(9A)	0.3550(5)	0.2152(2)	0.3505(5)
C(10A)	0.7167(5)	0.1711(2)	0.3477(5)
C(11A)	0.4515(4)	0.1652(1)	0.1063(4)
C(21A)	0.5101(5)	0.1087(2)	−0.0422(4)
C(22A)	0.5847(5)	0.1037(2)	−0.1502(5)
C(23A)	0.5621(6)	0.0698(2)	−0.2275(5)
C(24A)	0.4672(7)	0.0407(2)	−0.1967(6)
C(25A)	0.3931(7)	0.0458(2)	−0.0910(7)
C(26A)	0.4127(6)	0.0794(2)	−0.0118(5)
O(1B)	0.0459(4)	−0.0380(1)	0.1508(3)
O(2B)	0.0917(5)	−0.0392(1)	0.3577(3)
O(3B)	0.1754(3)	−0.1699(1)	0.0228(3)
N(1B)	−0.0479(4)	−0.0895(1)	0.2673(4)
N(2B)	0.0166(4)	−0.1212(1)	0.2433(4)
N(3B)	−0.0309(4)	−0.1419(1)	−0.0394(3)
C(1B)	0.1264(6)	−0.0005(2)	0.1370(6)
C(2B)	0.0406(5)	−0.0534(2)	0.2658(5)
C(3B)	−0.0653(5)	−0.1603(1)	0.2546(4)
C(4B)	−0.0268(5)	−0.1889(1)	0.1405(4)
C(5B)	0.0626(5)	−0.2236(2)	0.2041(5)
C(6B)	−0.0341(5)	−0.2481(2)	0.2847(5)
C(7B)	−0.0685(5)	−0.2249(2)	0.3804(5)
C(8B)	0.0060(5)	−0.1840(2)	0.3674(5)
C(9B)	0.1391(5)	−0.1990(2)	0.3055(5)
C(10B)	−0.2212(5)	−0.1533(2)	0.2688(5)
C(11B)	0.0495(4)	−0.1662(1)	0.0357(4)
C(21B)	0.0193(5)	−0.1165(1)	−0.1374(4)
C(22B)	0.1344(5)	−0.0912(1)	−0.1174(4)
C(23B)	0.1835(5)	−0.0676(2)	−0.2153(5)
C(24B)	0.1181(6)	−0.0676(2)	−0.3320(5)
C(25B)	0.0019(6)	−0.0917(2)	−0.3503(5)
C(26B)	−0.0491(5)	−0.1159(2)	−0.2540(4)

67.4; H, 5.3; N, 19.7 $C_{12}H_{11}N_3O$ requires C, 67.6; H, 5.2; N, 19.7%).

X-ray Crystallography.—*Crystal data.* **2**. $C_{11}H_{13}N_3O$, M = 203.3, orthorhombic, a = 9.654(3), b = 10.466(2), c = 11.039(2) Å, U = 1115(1) Å^3, Z = 4, D_c = 1.21 g cm^{-3}, μ(Mo-K_α) = 0.8 cm^{-1}, λ = 0.710 73 Å, F(000) = 432, space group $Pn2_1a$ or $Pnma$ from systematic absences ($0kl$ absent if $k + l = 2n + 1$; $hk0$ absent if $h = 2n + 1$); $Pn2_1a$ indicated by the E-statistics and confirmed by the analysis.

9a. $C_{15}H_{19}N_5O_5$, M = 349.4, triclinic, a = 9.014(2), b = 10.082(2), c = 11.059(2) Å, α = 109.36(2), β = 107.53(2), γ = 97.05(2)°, U = 876.1(9) Å^3, Z = 2, D_c = 1.32 g cm^{-3},

μ(Mo-$K\alpha$) = 1.0 cm^{-1}, λ = 0.710 73 Å, F(000) = 368, space group $P\bar{1}$ or $P1$; $P\bar{1}$ chosen and confirmed by the analysis.

17. $C_{17}H_{19}N_3O_3$, M = 313.4, monoclinic, a = 9.591(3), b = 32.117(6), c = 10.557(2) Å, β = 91.18(2)°, U = 3251(2) Å^3, Z = 8, D_c = 1.28 g cm^{-3}, μ(Mo-$K\alpha$) = 0.8 cm^{-1}, λ = 0.710 73 Å, F(000) = 1328, space group $P2_1/c$ uniquely from the systematic absences ($h0l$ absent if $l = 2n + 1$; $0k0$ absent if $k = 2n + 1$).

Data collection, structure solution and refinement. All three compounds were treated in a similar manner; pertinent parameters for the data collection and refinement are collected in Table 4. Cell dimensions and crystal orientation matrices were determined by a least-squares refinement of 25 reflections with θ in the range 8 to 15°. Data were collected at 21 °C using a CAD4 diffractometer with graphite monochromated Mo-$K\alpha$ radiation in the $\omega/2\theta$ scan mode; the ω scan width was $(0.60 \pm 0.35 \tan\theta)°$. Analysis of standard reflections monitored throughout the course of the data collections showed that there was no decay in the X-ray beam. Data were corrected for Lorentz and polarisation effects. The structures were solved by direct methods[38] and refined by full-matrix least-squares calculations. The differentiation between carbon and nitrogen atoms in the structures was unequivocally made from consideration of bond lengths, isotropic thermal parameters, difference maps and the location of all relevant H atoms. In the final rounds of calculations, all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were visible in difference maps and were included as riding atoms with d(C–H) and d(N–H) 0.95 Å. For **2** the methyl hydrogens at C-1 and C-5 appeared to be disordered; they were allowed for by placing six hydrogens with 0.5 occupancy in a torus around the carbon atoms. Crystals of **17** have two independent molecules in the asymmetric unit and these differ principally in the orientation of the terminal carboxymethyl moieties. Final difference maps were calculated after convergence was achieved (with all shift/error ratios less than 0.07) and were chemically featureless. Scattering factor data were taken from ref. 39. The weighting scheme used in the refinements was of the form $w = 1/[\sigma^2 F_o + p(F_o^2)]$. All calculations were performed with SDP-Plus.[40]

Final refined atom coordinates for the three structures are given in Tables 5, 6 and 7. Tables with the calculated hydrogen coordinates, anisotropic thermal parameters, mean plane data and torsion angles have been deposited at the CCDC.*

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* For details of the Cambridge Crystallographic Data Centre deposition scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1991, issue 1.

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