Intramolecular Cycloaddition of Azoalkenes Derived from Terminal Alkenoic and Alkynoic Acids

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The azoalkenes (**1**) derived from terminal alkenoic acids $H_2C{=}CH(CH_2)_nCO_2H$ (n = 1, 3, and 4) have been generated in order to determine whether intramolecular cycloaddition would take place. The azoalkenes derived from hex-5-enoic acid (n = 3) underwent intramolecular cycloaddition and four cycloadducts, the pyridopyridazines (**6**), have been isolated in moderate yield. The azoalkenes derived from but-3-enoic acid (n = 1) and from hept-6-enoic acid (n = 4) did not undergo intramolecular cycloaddition: the intermolecular cycloadduct (**5**) was formed when the chlorohydrazone (**2a**) was dehydrochlorinated in the presence of cyclopentadiene.

The intramolecular cycloadducts (**8**) and (**10**) have also been isolated from reactions of the hydrazones (**7**) and (**9**), derived from cyclopent-2-enylacetic acid and pent-4-ynoic acid, respectively, with sodium carbonate. The adducts (**10**) are formed by cycloaddition to an unactivated triple bond, a reaction which has not previously been observed with azoalkenes. Compounds (**10**) are unstable in air, and a long-lived radical, which has been formulated as compound (**11**), has been detected as an oxidation product of the dihydropyridazine (**10c**).

Conjugated axoalkenes can participate in the Diels–Alder reaction as the diene components, and the reaction with alkenes provides a usful route to 1,4,5,6-tetrahydropyridazines. Most cycloaddition reactions of this type are 'inverse electron demand' processes in which alkenes bearing electron-donating substituents add to electron-deficient axoalkenes;[1] there are also a few examples of 'normal electron demand' reactions in which azoalkenes act as the donor components.[2] In either case it is necessary to have a combination of an electrophilic and a nucleophilic partner in order to achieve efficient cycloaddition. Most azoalkenes used in such reactions are transient intermediates which cyclodimerise or react with precursors if no suitable partners for cycloaddition are present. Simple alkenes, unsubstituted by conjugating or strongly electron-releasing groups, give, at best, low yields of cycloadducts. With the exception of an ynamine addition,[3] no reactions have been reported in which triple-bonded dienophiles have been used.

In a preliminary study[4] we found that intramolecular Diels–Alder reactions took place with azoalkenes of the general structure (**1**) (n = 2). In contrast to the intermolecular

$$H_2C{=}CH(CH_2)_nCON{=}NC(R^2){=}CHR^1$$

(**1**)

cycloadditions, these reactions did not require activation of the dienophile, nor of the azoalkene, other than that provided by the carbonyl group. This feature of the intramolecular Diels–Alder reaction, and the steric control which the reaction often provides, are well recognised in other cases.[5] When used to construct heterocycles with weak heteroatom-to-heteroatom bonds, this type of reaction is potentially useful for the controlled introduction of functional groups, as has recently been demonstrated in an investigation of intramolecular nitroalkene cycloaddition.[6] We have now investigated the intramolecular azoalkene addition further, with the aims of determining (a) the effects of varying the length of the alkyl chain linking the diene and dienophile and (b) whether a terminal alkyne function would act as a dienophile.

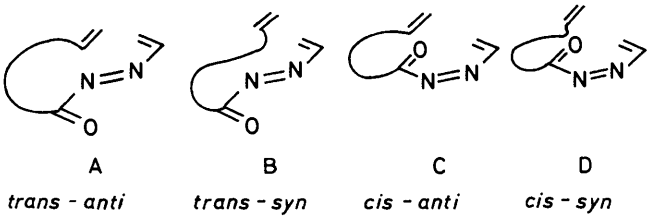


Figure.

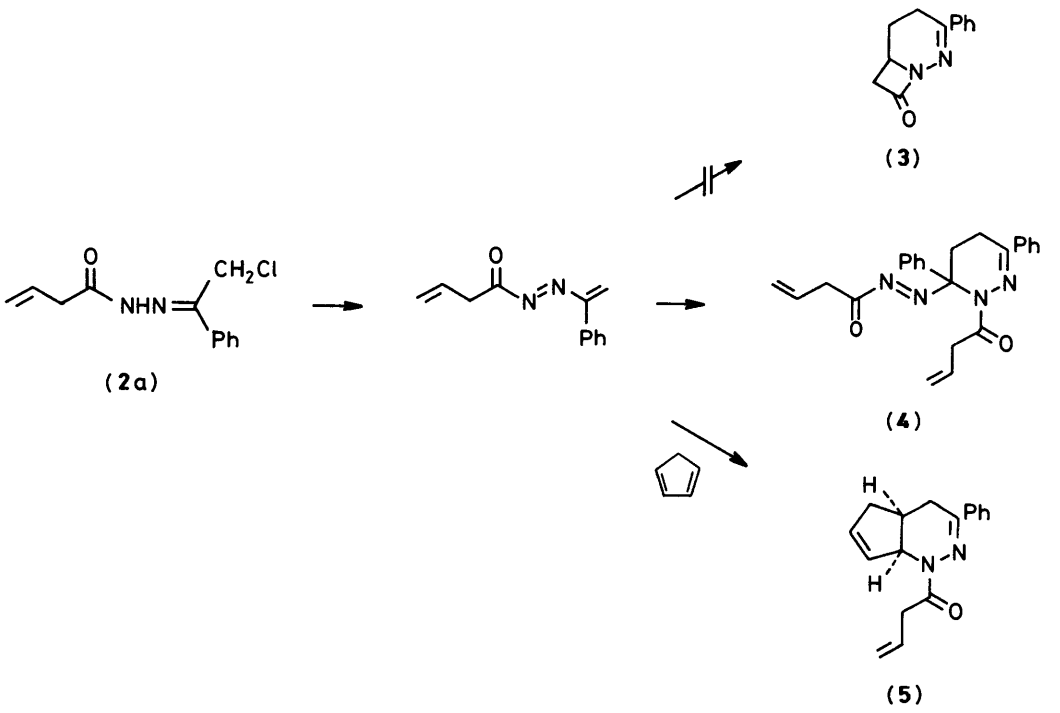
There are, in principle, four possible transition states for intramolecular cycloadditions of this type (Figure). Following the descriptions used by Ciganek,[5] we have designated these as *trans* or *cis* with respect to the diene component and as *anti* or *syn* with respect to the mode of approach of the dienophile to the diene. On the basis of molecular models, it appeared that all four transition states would be too strained for the azoalkenes (**1**) where n = 1 and that transition state A was preferred for cycloaddition where n = 2. Transition state A also appeared to be the least strained for n = 3, since the alkyl chain could adopt a chair-like conformation. In the case of the hept-6-enoic acid derivative (n = 4) both the *trans-anti* transition state A and the *trans-syn* transition state B appeared to be accessible. In none of the azoalkenes was a *cis* transition state attainable without severe twisting of the carbonyl group out of the plane of the azoalkene.

In the preliminary study of the reaction we generated the azoalkenes (**1**; n = 2) from the corresponding halogen-substituted hydrazones (**2**). These hydrazones were obtained by the reaction of halogeno ketones with the hydrazide of pent-4-enoic acid. By using the same method, other members of the homologous series of hydrazones (**2**; n = 1, 3, and 4) have now been prepared and the azoalkenes (**1**) have been generated from them. We have also prepared the hydrazones (**7**) and (**9**) in order to investigate whether alkyl substitution of the double bond would affect the cycloaddition, and whether a triple bond could act as the dienophile.

Table. Hydrazones (**2**), (**7**), and (**9**)

Compound	*n* In (**2**)	Acid hydrazide	Halogeno ketone	R^1	R^2	X
(**2a**)	1	But-3-enoic	Phenacyl chloride	H	Ph	Cl[a]
(**2b**)	3	Hex-5-enoic	Phenacyl chloride	H	Ph	Cl[a]
(**2c**)	4	Hept-6-enoic	Phenacyl chloride	H	Ph	Cl[a]
(**2d**)	3	Hex-5-enoic	Ethyl bromopyruvate	H	CO_2Et	Br[b]
(**2e**)	3	Hex-5-enoic	Chloroacetone	H	Me	Cl[b]
(**2f**)	3	Hex-5-enoic	2-Chlorocyclohexanone	$-(CH_2)_4-$		Cl[b]
(**7a**)		Cyclopent-2-enylacetic	Phenacyl chloride	H	Ph	Cl[a]
(**7b**)		Cyclopent-2-enylacetic	Ethyl bromopyruvate	H	CO_2Et	Br[b]
(**9a**)		Pent-4-ynoic	Phenacyl chloride	H	Ph	Cl[a]
(**9b**)		Pent-4-ynoic	Ethyl bromopyruvate	H	CO_2Et	Br[b]
(**9c**)		Pent-4-ynoic	Ethyl 3-oxo-2-chlorobutanoate	CO_2Et	Me	Cl[a]

[a] Compound isolated and characterised (see Experimental section). [b] Compound generated *in situ*.



Scheme 1.

The hydrazides of hex-5-enoic acid and of cyclopent-2-enylacetic acid have been reported previously: they were prepared from the corresponding methyl or ethyl esters and hydrazine hydrate. The previously unknown hydrazides of but-3-enoic, hept-6-enoic, and pent-4-ynoic acids were prepared in the same way. This seemingly routine ester to hydrazide conversion can prove troublesome unless precautions are taken to exclude oxygen. If this is not done, di-imide can be generated[7] and the multiple bonds of the terminally unsaturated acid derivatives can be reduced. The hydrazides of the corresponding saturated acids then occur as significant impurities when the alkenoic esters are the starting materials. We found that the side-reaction could be avoided by carrying out the conversion in boiling methanol or ethanol under nitrogen, the solvent having been de-gassed before addition of the hydrazine.

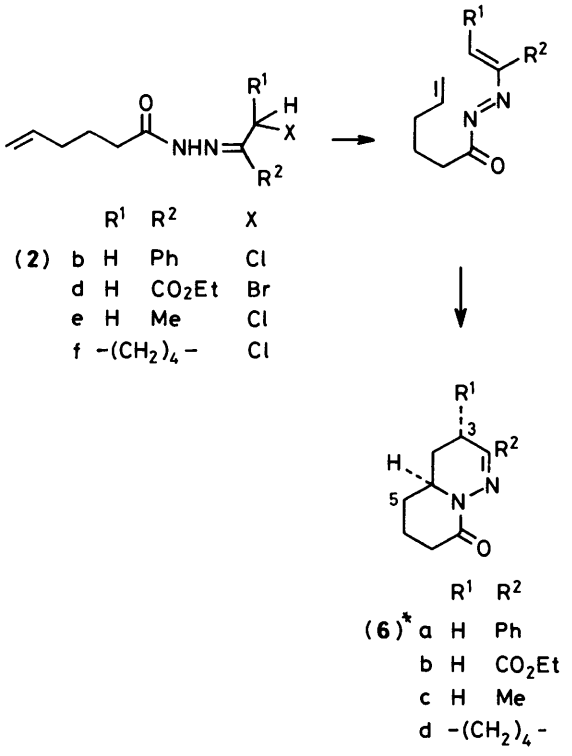
A range of halogeno-ketones bearing functional groups of different types was used to prepare the hydrazones, namely phenacyl chloride, ethyl bromopyruvate, ethyl 2-chloro-3-oxobutanoate, chloroacetone, and 2-chlorocyclohexanone. The derivatives formed from phenacyl chloride and from ethyl 2-chloro-3-oxobutanoate were sufficiently stable to allow their isolation and characterisation. The hydrazones derived from phenacyl chloride were usually isolated as mixtures of *syn* and *anti* isomers. By analogy with related oximes,[8] the isomers with the hydrazone function *syn* to the CH_2Cl group are expected to show the lower field signal for the CH_2 group in the ^1H n.m.r. spectra.

The hydrazones derived from the other halogeno ketones could not, in general, be isolated and purified without considerable loss of material. The formation of these compounds was therefore monitored by t.l.c. and the products were converted directly into the azoalkenes without further purification (see below). The hydrazones which have been isolated or generated in this investigation are listed in the Table.

The azoalkenes were generated from the hydrazones (**2**), (**7**), and (**9**) by the action of anhydrous sodium carbonate in dichloromethane at room temperature. The hydrazone (**2a**) gave, after 24 h, a single unstable product which was clearly not the cycloadduct (**3**). The n.m.r. spectrum showed the presence of

vinylic hydrogen atoms and, by analogy with the reactions of other hydrazones of this type,[1] the product is tentatively formulated as the dimer (**4**). In the presence of an excess of cyclopentadiene, the intermolecular cycloadduct (**5**) was formed in high yield (Scheme 1). It is apparent that the side-chain is too short to permit intramolecular cycloaddition. This has also been found to be the case when other intramolecular Diels–Alder reactions have been attempted with *trans*-fused dienes and a connecting chain of less than three atoms between the diene and dienophile.[5]

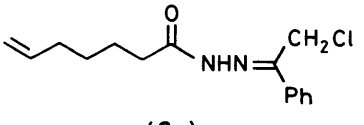
The hydrazones (**2b**), (**2d**), (**2e**), and (**2f**) derived from hex-5-enoic acid all gave intramolecular cycloadducts (Scheme 2). The



Scheme 2.* Numbering shown applies to (**6a**)—(**6c**) only

pyridopyridazines (**6**) were isolated in moderate yield. The compounds all show carbonyl stretching absorptions in the range 1 660—1 680 cm^{-1}, as expected for six-membered lactams, and the bridgehead hydrogens give signals in the n.m.r. spectra in the range δ 3.3—3.5, which is a characteristic of such fused pyridazines. In each of the cycloadducts (**6**), the signal for the bridgehead hydrogen atom appears as a triplet (J 11—12 Hz) which shows further splitting. This is to be expected if the hydrogen atom occupies a pseudo-axial position and is strongly coupled to a hydrogen atom on each of the two vicinal CH_2 groups. Another characteristic of these compounds is a strong fragment ion in the mass spectra equivalent to the loss of the fragment $C_4H_5O^{\bullet}$.

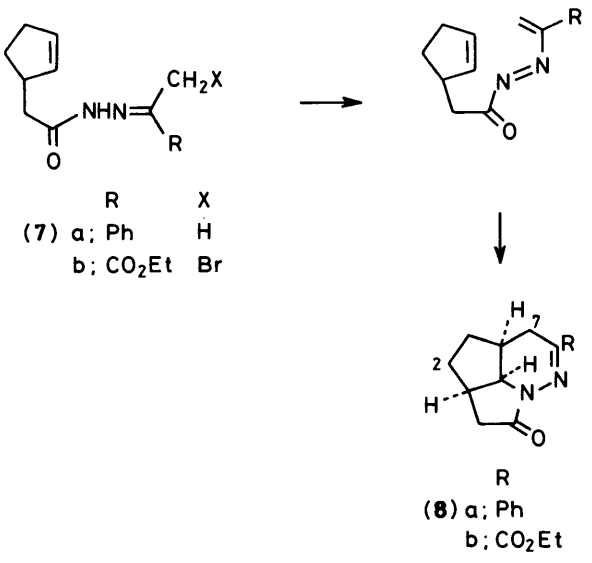
The reactions of these hydrazones are thus analogous to those of the hydrazones derived from pent-4-enoic acid. On the other hand, the hydrazone (**2c**) derived from hept-6-enoic acid



(**2c**)

failed to give any characterisable product on dehydrochlorination. This is consistent with other findings that the connecting chain of five atoms makes the intramolecular cycloaddition no more favourable than the intermolecular equivalent.[5]

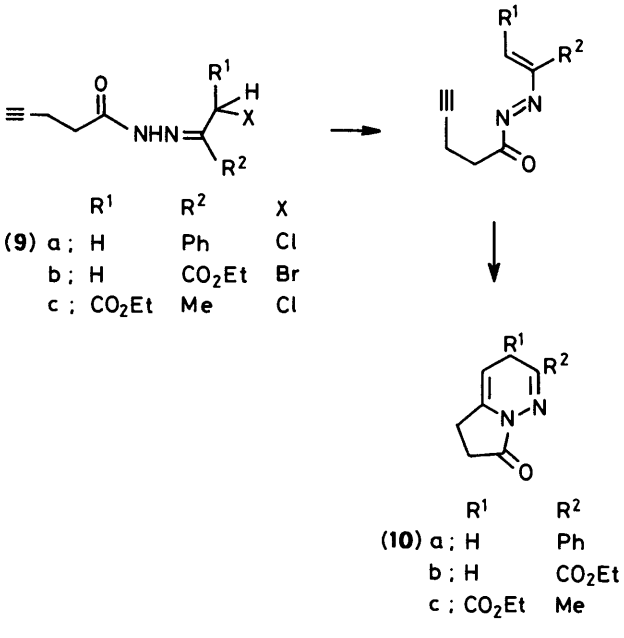
The two hydrazones (**1a**) and (**1b**) derived from cyclopent-2-enylacetic acid each gave a single product on dehydrohalogenation. These were formulated as the all-*cis* cycloadducts (**8a**) and (**8b**) (Scheme 3). As with other intramolecular



Scheme 3.

additions to cyclopentenes,[9] the all-*cis* geometry of the cycloadducts is a consequence of the rigidity of the transition state.

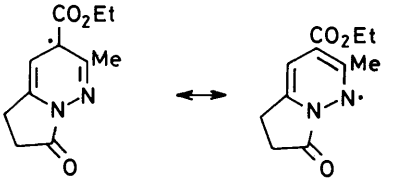
The hydrazones (**9**) derived from pent-4-ynoic acid all reacted with sodium carbonate to give single products, which were formulated as the pyrrolopyridazines (**10**) (Scheme 4). These reactions are the first examples of the addition of azoalkenes to



Scheme 4.

unactivated triple bonds and they provide an alternative to the known methods of synthesis of 1,4-dihydropyridazines.

We found that the pyrrolopyridazines (**10**) were unstable in air; in particular, solutions of compound (**10c**) rapidly developed a deep purple colouration when they were exposed to air. These solutions gave a well defined e.s.r. spectrum which was consistent with the presence of a long-lived nitrogen-centred radical. Although we could not assign a structure to the radical unambiguously on the basis of the spectrum, we suggest structure (**11**) as the most likely. There have been very few



(**11**)

investigations of the chemistry of 1,4-dihydropyridazines,[10] but some such compounds have been shown to react readily with oxygen to form hydroperoxides.[11] The radical (**11**) could be formed by hydrogen atom abstraction from the 3-position of compound (**10c**).

In summary, we have extended the earlier study of intramolecular azoalkene additions and have shown that this is generally a successful reaction for compounds with three or four carbon atoms linking the diene and dienophile, but not for those with shorter or longer chains. We have also shown that a triple bond can act as the dienophile in these reactions.

Experimental

I.r. spectra were recorded for KBr discs (solids) or for films (oils) on a Perkin-Elmer 125 spectrophotometer. ^{1}H N.m.r. spectra were recorded using a Perkin-Elmer R34 spectrometer, operating at 220 MHz, or a Bruker WM250 spectrometer, operating at 250 MHz, and with deuteriochloroform as the solvent, unless otherwise indicated. ^{13}C N.m.r. spectra were recorded on a Varian XL100A instrument operating at 25.2 MHz. E.s.r. spectra were recorded at 22 °C with a Varian E-4 spectrometer. Microwave powers of less than 0.15 mw were used as the sample saturated easily. Spectra were digitised using a Data Dynamics 1 183 paper-tape punch and the tapes were processed on the University of Liverpool ICL 1906s computer. Each spectrum was digitised into 5 088 segments and the spectra could be presented as second derivatives with automatic measurement of line positions. Spectra were simulated using a program written by Dr. W. R. McIlwaine for use on the 1906s computer. Flash column chromatography was performed by the method described by Still *et al.*[12] with Kieselgel 60 (2340—400 mesh) as the stationary phase. Light petroleum refers to the fraction with b.p. 60—80 °C.

But-3-enoic acid, cyclopent-2-enylacetic acid, hept-6-enoic acid, and pent-4-ynoic acid were commercially available and were used as supplied. Hex-5-enoic acid was prepared from tetrahydro-2-furylmethanol by the method of Ansell and Brown.[13]

Acid Hydrazides: General Procedure.—The ethyl or methyl ester of the acid was heated under reflux in ethanol or methanol under nitrogen for 1 h to remove any dissolved oxygen. Hydrazine hydrate (1.0—1.2 equiv.) was then added and the solution was heated for 18 h. The solvent was evaporated off and the residue was re-dissolved in dichloromethane. The solution was dried (sodium sulphate) and evaporated. The residue was purified by crystallisation where indicated.

(a) *But-3-enohydrazide.* Ethyl but-3-enoate (13.0 g, 112 mmol) and hydrazine hydrate (6.2 g, 124 mmol) in ethanol (50 ml) gave the hydrazide (6.84 g, 65%) as an oil which partly solidified with time: it was not purified further (Found: *m/z* 100.0626. $C_4H_8N_2O$ requires *m/z* 100.0637); δ (220 MHz) 3.02 (2 H, d, *J* 7.3 Hz), 4.00 (2 H, br, exchangeable, NH_2), 5.16—5.31 (2 H, m), 5.81—6.15 (1 H, m), and 7.50—8.10 (1 H, br, exchangeable, NH).

(b) *Hex-5-enohydrazide.* Methyl hex-5-enoate (5.0 g, 39 mmol) and hydrazine hydrate (2.0 g, 40 mmol) in methanol (25 ml) gave the hydrazide (3.6 g, 72%) as a solid, m.p. 48 °C (from dichloromethane–hexane) (lit.,[14] 46.5—47.5 °C; δ (220 MHz) 1.41—2.41 (6 H, m), 4.10 (2 H, br, NH_2), 4.89—5.09 (2 H, m), 5.66—5.87 (1 H, m), and 8.45 (1 H, br, NH).

(c) *Hept-6-enohydrazide.* Ethyl hept-6-enoate (6.0 g, 25.6 mmol) and hydrazine hydrate (1.6 g, 31 mmol) in ethanol (50 ml) gave the *hydrazide* (2.8 g, 87%), m.p. 58 °C (from dichloromethane–hexane) (Found: C, 59.0; H, 10.1; N, 20.0. $C_7H_{14}N_2O$ requires C, 59.1; H, 9.9; N, 19.7%); $\nu_{max.}$(KBr) 3 420, 3 310 (NH), and 1 670 cm^{-1} (CO); δ (220 MHz) 1.35—1.54 (2 H, m), 1.60—1.70 (2 H, m), 2.06—2.31 (4 H, m), 4.00 (2 H, br, NH_2), 4.96—5.14 (2 H, m), 5.72—5.92 (1 , m), and 7.80 (1 H, br, NH).

(d) *Cyclopent-2-enylacetohydrazide.* Ethyl cyclopent-2-enylacetate (14.7 g, 94.5 mmol) and hydrazine hydrate (5.8 g, 115 mmol) in ethanol (50 ml) gave the hydrazide (11.4 g, 85%), m.p. 72—74 °C (from dichloromethane–hexane) (lit.,[15] 75—76 °C); δ (220 MHz) 2.01—2.47 (6 H, m), 3.05—3.22 (1 H, m), 3.95 (2 H, br, NH_2), 5.62—5.71 (1 H, m), 5.76—5.86 (1 H, m), and 7.10 (1 H, br, NH).

(e) *Pent-4-ynohydrazide.* Methyl pent-4-ynoate (3.25 g, 29 mmol) and hydrazine hydrate (1.75 g, 35 mmol) gave the *hydrazide* (3.23 g, 99%), m.p. 60—63 °C (from dichloromethane–hexane) (Found: C, 53.7; H, 7.1; N, 24.7. $C_5H_8N_2O$ requires C, 53.55; H, 7.2; N, 25.0%); $\nu_{max.}$ 3 315, 3 290 (NH), and 1 675 cm^{-1} (CO); δ (220 MHz) 2.00 (1 H, t, *J* 3.5 Hz), 2.32—2.47 (2 H, m), 2.48—2.60 (2 H, m), 3.85 (2 H, br, NH_2), and 8.15 (1 H, br, NH).

Hydrazones Derived from Phenacyl Chloride: General Procedure.—The carbohydrazide and an equimolar amount of phenacyl chloride were dissolved in the minimum volume of ethanol at room temperature. Hydrochloric acid (1—2 drops) was added and the reaction mixture was stirred at room temperature for 0.5—2 h, during which time the hydrazone was precipitated. It was filtered off and recrystallised.

(a) *But-3-enoylhydrazone* (**2a**). But-3-enohydrazide (0.10 g, 1.0 mmol) and phenacyl chloride (0.15 g, 1.0 mmol) gave the *hydrazone* (**2a**) (0.18 g, 76%), m.p. 102—103 °C (after three recrystallisations from ethanol) (Found: C, 60.9; H, 5.7; N, 11.5. $C_{12}H_{13}ClN_2O$ requires C, 60.9; H, 5.5; N, 11.8%); δ (220 MHz) (*syn* isomer) 3.50 (2 H, d, *J* 8 Hz), 4.53 (2 H), 5.15—5.32 (2 H, m), 5.95—6.19 (1 H, m), 7.30—7.50 (3 H, m), 7.68—7.83 (2 H, m), and 10.00 (1 H, NH); *m/z* 236 and 238 (M^+). Material obtained after a single recrystallisation from ethanol was a 2:3 mixture of *syn* and *anti* isomers by n.m.r.

(b) *Hex-5-enoylhydrazone* (**2b**). Hex-5-enohydrazide (0.20 g, 1.6 mmol) and phenacyl chloride (0.25 g, 1.6 mmol) gave the *hydrazone* (**2b**) (0.38 g, 92%), m.p. 85 °C (from ethanol) (Found: C, 63.6; H, 6.7; N, 10.5. $C_{14}H_{17}ClN_2O$ requires C, 63.5; H, 6.5; N, 10.6%); $\nu_{max.}$(KBr) 3 190 (NH) and 1 660 cm^{-1} (CO); δ (220 MHz) (1:1 mixture of *syn* and *anti* isomers) 1.55—1.84 (2 H, m), 2.01—2.18 (2 H, m), 2.57—2.81 (2 H, m), 4.35 and 4.49 (together, 2 H), 4.89—5.08 (2 H, m), 5.70—5.91 (1 H, m), 7.20—7.57 (3 H, m), 7.68—7.80 (2 H, m), and 8.40 and 9.85 (together, 1 H, NH); *m/z* 264 and 266 (M^+).

(c) *Hept-6-enoylhydrazone* (**2c**). Hept-6-enohydrazide (0.14 g, 1.0 mmol) and phenacyl chloride (0.15 g, 1.0 mmol) gave the *hydrazone* (**2c**) (0.19 g, 69%), m.p. 72—74 °C (from ethanol)

(Found: C, 64.65; H, 7.0; N, 10.2. $C_{15}H_{19}ClN_2O$ requires C, 64.6; H, 6.9; N, 10.05%); $\nu_{max.}$(KBr) 3 150—2 820br (NH) and 1 680 cm^{-1} (CO); δ (220 MHz) (1:3 mixture of *syn* and *anti* isomers) 1.35—1.81 (4 H, m), 1.95—2.16 (2 H, m), 2.63—2.85 (2 H, m), 4.38 and 4.47 (together, 2 H), 4.96—5.10 (2 H, m), 5.70—5.92 (1 H, m), 7.21—7.58 (3 H, m), 7.68—7.82 (2 H, m), and 8.37 and 9.41 (together, 1 H); *m/z* 278 and 280 (M^+).

(d) *Cyclopent-2-enylacetylhydrazone* (**7a**). Cyclopent-2-enylacetohydrazide (0.50 g, 3.6 mmol) and phenacyl chloride (0.55 g, 3.6 mmol) gave the *hydrazone* (**7a**) (0.62 g, 63%), m.p. 147—150 °C (from ethanol) (Found: C, 64.85; H, 6.5; N, 10.2. $C_{15}H_{17}ClN_2O$ requires C, 65.1; H, 6.2; N, 10.1%); $\nu_{max.}$(KBr) 3 190 (NH) and 1 660 cm^{-1} (CO); δ (220 MHz) (2:3 mixture of *syn* and *anti* isomers) 1.40—2.50 (4 H, m), 2.77—2.88 (2 H, m), 3.07—3.21 (1 H, m), 4.38 and 4.45 (together, 2 H), 5.63—5.85 (2 H, m), 7.22—7.80 (5 H, m), and 8.37 and 9.20 (together, 1 H); *m/z* 276 and 278 (M^+).

(e) *Pent-4-enoylhydrazone* (**9a**). Pent-4-ynohydrazide (0.50 g, 4.5 mmol) and phenacyl chloride (0.69 g, 4.5 mmol) gave the *hydrazone* (**9a**) (0.82 g, 74%), m.p. 125 °C (from dichloromethane–hexane) (Found: C, 62.8; H, 5.3; N, 11.5. $C_{13}H_{13}ClN_2O$ requires C, 62.8; H, 5.3; N, 11.3%); $\nu_{max.}$(KBr) 3 270 (NH), 2 100 (C≡C), and 1 680 cm^{-1} (CO); δ (220 MHz) (2:3 mixture of *syn* and *anti* isomers) 1.54 (1 H, t), 2.16—2.45 (2 H, m), 2.58—2.79 (2 H, m), 4.04 and 4.14 (together, 2 H), 6.88—7.20 (3 H, m), 7.37—7.47 (2 H, m), and 8.10 and 9.26 (together, 1 H); *m/z* 199 ($M^+ - CH_2Cl$).

Ethyl 2-Chloro-3-oxobutanoate Pent-4-ynoylhydrazone (**9c**).—A solution of ethyl 2-chloro-3-oxobutanoate (0.22 g, 1.3 mmol) and pent-4-ynohydrazide (0.15 g, 1.3 mmol) in ether (10 ml) was kept at 20 °C for 2 h. The solvent was evaporated off to leave a colourless solid. Crystallisation gave the *hydrazone* (**9c**) (0.17 g, 50%), m.p. 95 °C (from dichloromethane–hexane) (Found: C, 50.8; H, 5.9; N, 10.9. $C_{11}H_{15}ClN_2O_3$ requires C, 51.05; H, 5.8; N, 10.8%); $\nu_{max.}$(KBr) 3 300 (NH), 2 100 (C≡C), 1 740, and 1 690 cm^{-1} (CO); δ (220 MHz) 1.38 (3 H, t, *J* 7 Hz), 2.02 (1 H, t, *J* 3 Hz), 2.08 (3 H), 2.55—2.60 (2 H, m), 2.95 (2 H, t, *J* 7 Hz), 4.36 (2 H, q, *J* 7 Hz), 5.06 (1 H), and 9.50 (1 H); *m/z* 226 and 228 (M^+).

1-*But-3-enoyl-3-phenyl*-4,4a,5,7a-*tetrahydro*-1H-*cyclopenta*[c]*pyridazine* (**5**).—The hydrazone (**2a**) (0.56 g, 2.5 mmol) and cyclopentadiene (2 ml) were dissolved in dichloromethane (70 ml) and the solution was stirred with anhydrous sodium carbonate (1.0 g, 9.5 mmol) at 20 °C for 24 h. More cyclopentadiene (2 ml) was added and the mixture was stirred for a further 24 h. The mixture was filtered through Celite and the filtrate was evaporated to leave an oil which gave by layer chromatography (silica; ether–hexane, 1:1) the *cyclopentapyridazine* (**5**) (0.63 g, 96%), m.p. 59—63 °C (from pentane) (Found: C, 76.25; H, 7.0; N, 10.6. $C_{17}H_{18}N_2O$ requires C, 76.65; H, 6.8; N, 10.5%); $\nu_{max.}$(KBr) 1 665 cm^{-1} (CO); δ (220 MHz) 2.10—2.28 (2 H, m), 2.47—2.77 (3 H, m), 3.66 (2 H, d, *J* 7 Hz), 5.12—5.31 (3 H, m), 5.82—6.23 (3 H, m), 7.35—7.49 (3 H, m), and 7.70—7.85 (2 H, m), *m/z* 266 (M^+).

3,4,4a,5,6,7-*Hexahydro*-2-*phenylpyrido*[1,2-b]*pyridazin*-8-*one* (**6a**).—The hydrazone (**2b**) (0.85 g, 3.2 mmol) was dissolved in dichloromethane (300 ml) and the solution was stirred with sodium carbonate (5 g) for 24 h. The reaction mixture was filtered through Celite and the filtrate was evaporated to give the *pyridazine* (**6a**) (0.47 g, 65%), m.p. 190—191 °C (from ether–dichloromethane) (Found: C, 73.4; H, 6.9; N, 12.4. $C_{14}H_{16}N_2O$ requires C, 73.65; H, 7.1; N, 12.3%); $\nu_{max.}$(KBr) 1 660 cm^{-1} (CO); δ (250 MHz) 1.56—2.20 (6 H, m, 4-, 5-, and 6-H), 2.49—2.87 (4 H, m, 3- and 7-H), 3.50 (1 H, tdd, *J* 11.2, 3.7, and 2.7 Hz, 4a-H), 7.34—7.42 (3 H, m), and 7.82—7.89 (2 H, m); *m/z* 228 (M^+) and 159 ($M^+ - C_4H_5O$).

Ethyl 3,4,4a,5,6,7-*Hexahydro*-8-*oxopyrido*[1,2-b]*pyridazine*-2-*carboxylate* (**6b**).—A solution of ethyl 3-bromo-2-oxopropanoate (4.57 g, 23 mmol) and hex-5-enohydrazide (3.0 g, 23 mmol) in ether (50 ml) was stirred for 2 h at 20 °C. The ether was evaporated off and the viscous residue was re-dissolved in dichloromethane (300 ml). Sodium carbonate (10 g) was added and the mixture was stirred for 48 h. After removal of the inorganic solids and the solvent, the product was subjected to flash chromatography, which gave (with dichloromethane–ethyl acetate, 1:1) the *pyridazine* (**6b**) (2.3 g, 44%), m.p. 125—127 °C (from dichloromethane–hexane) (Found: C, 58.9; H, 7.1; N, 12.3. $C_{11}H_{16}N_2O_3$ requires C, 58.9; H, 7.2; N, 12.5%); $\nu_{max.}$(KBr) 1 705 and 1 680 cm^{-1} (CO); δ (250 MHz) 1.36 (3 H, t, *J* 7 Hz), 1.53—2.08 (4 H, m), 2.11—2.17 (2 H, m), 2.34—2.63 (2 H, m), 2.69—2.84 (2 H, m), 3.46 (1 H, tt, *J* 11.3 and 3.0 Hz, 4a-H), and 4.26—4.39 (2 H, m, OCH_2Me); *m/z* 224 (M^+), 155 ($M^+ - C_4H_5O$), and 123 (base).

3,4,4a,5,6,7-*Hexahydro*-2-*methylpyrido*[1,2-b]*pyridazin*-8-*one* (**6c**).—A solution of chloroacetone (0.93 g, 10 mmol) and hex-5-enohydrazide (1.28 g, 10 mmol) in ether (10 ml) was kept at 20 °C for 4 h. The solvent was evaporated off and the residue, an oil, was immediately re-dissolved in dichloromethane (300 ml). Sodium carbonate (5 g) was added and the reaction mixture was stirred for 24 h. It was then filtered through Celite and the filtrate evaporated. Sublimation followed by crystallisation gave the pyridazine (**6c**) (0.66 g, 40%), m.p. 38—41 °C (from ether–hexane) (Found: *m/z* 166.1106. $C_9H_{14}N_2O$ requires *m/z* 166.1106); $\nu_{max.}$(film) 1 660 (CO) and 1 640 cm^{-1}; δ (250 MHz) 1.49—2.70 (10 H, m), 2.07 (3 H), and 3.39 (1 H, t, *J* 11 Hz, showing further unresolved splitting, 4a-H); *m/z* 166 (M^+) and 97 ($M^+ - C_4H_5O$, base).

10a,11a-trans-1,2,3,4,8,9,10,10a,11,11a-*Decahydropyrido*[1,2-b]*cinnolin*-7-*one* (**6d**).—A solution of 2-chlorocyclohexanone (1.1 g, 8.3 mmol) and hex-5-enohydrazide (1.05 g, 8.2 mmol) in ether (10 ml) was kept at 20 °C for 2 h. The solvent was evaporated off and the residue was dissolved in dichloromethane (300 ml). Sodium carbonate (3 g) was added and the mixture was stirred for 48 h. Flash chromatography gave (with dichloromethane) the *cinnoline* (**6d**) (0.62 g, 37%), m.p. 88—91 °C (from ether–pentane) (Found: C, 69.6; H, 9.0; N, 13.6. $C_{12}H_{18}N_2O$ requires C, 69.85; H, 8.8; N, 13.6%); $\nu_{max.}$(KBr) 1 665 cm^{-1} (CO); δ (250 MHz) 1.29—2.25 (13 H, m), 2.40—2.70 (4 H, m), and 3.36 (1 H, t, *J* 11.5 Hz, showing further unresolved splitting, 10a-H); *m/z* 206 (M^+) and 137 ($M^+ - C_4H_5O$).

1,2,2a,7,7a,7b-*Hexahydro*-6-*phenyl*-4a,5-*diazacyclopent*[c,d]-*inden*-4(3H)-*one* (**8a**).—A solution of the hydrazone (**7a**) 0.60 g, 2.2 mmol) in dichloromethane (150 ml) was stirred with sodium carbonate (1 g) for 24 h. The mixture was filtered through Celite and the filtrate was evaporated to leave a solid. Crystallisation gave the *pyridazine* (**8a**) (0.35 g, 67%), m.p. 183—184 °C (from dichloromethane–ether) (Found: C, 74.8; H, 6.8; N, 11.4. $C_{15}H_{16}N_2O$ requires C, 75.0; H, 6.7; N, 11.7%); $\nu_{max.}$(KBr) 1 695 cm^{-1} (CO); δ (250 MHz) 1.10—1.40 (1 H, m), 1.42—1.58 (1 H, m), 1.78—1.93 (1 H, m), 2.02—2.21 (1 H, m), 2.28 (1 H, d, *J* 16.0 Hz), 2.39—2.56 (1 H, m), 2.61—2.93 (4 H, m), 3.84 (1 H, t, *J* 4.0 Hz, 7b-H), 7.30—7.42 (3 H, m), and 7.79—7.91 (2 H, m); *m/z* 240 (M^+).

Ethyl 1,2,2a,3,4,7,7a,7b-*Octahydro*-4-*oxo*-4a,5-*diazacyclopenta*[c,d]indene-6-*carboxylate* (**8b**).—A solution of ethyl 3-bromo-2-oxopropanoate (2.0 g, 10 mmol) in ether (20 ml) was stirred with cyclopent-2-enylacetohydrazide (1.26 g, 9 mmol) for 4 h. The solvent was evaporated off and the residue, an oil, was immediately re-dissolved in dichloromethane (300 ml). Sodium carbonate (5 g) was added and the mixture was stirred for 48 h.

Flash chromatography gave (with ethyl acetate) the *pyridazine* (**8b**) (0.51 g, 24%), m.p. 58—60 °C (from ether–pentane) (Found: C, 60.9; H, 6.75; N, 11.9. $C_{12}H_{16}N_2O_3$ requires C, 61.0; H, 6.8; N, 11.9%); $\nu_{max.}$(KBr) 1 730 and 1 710 cm^{-1} (CO); δ (250 MHz) 1.08—1.26 (1 H, m), 1.33—1.39 (3 H, t, *J* 7 Hz), 1.50—1.61 (1 H, m), 1.85—1.95 (1 H, m), 2.07—2.26 (1 H, m), 2.32 (1 H, d, *J* 17.2 Hz), 2.42—2.55 (1 H, m), 2.57—2.70 (2 H, m), 2.76—2.92 (2 H, m), 3.81 (1 H, t, *J* 4.4 Hz, 7b-H), and 4.23—4.43 (2 H, m); *m/z* 236 (M^+).

5,6-*Dihydro*-2-*phenylpyrrolo*[1,2-b]*pyridazin*-7(3H)-*one* (**10a**).—A solution of the hydrazone (**9a**) (1.4 g, 5.6 mmol) in dichloromethane (300 ml) was stirred with sodium carbonate (3 g) at 20 °C for 24 h. Flash chromatography (ethyl acetate) gave the *pyridazine* (**10a**) (0.65 g, 55%), m.p. 164—165 °C (from dichloromethane–ether) (Found: C, 73.4; H, 5.45; N, 13.0. $C_{13}H_{12}N_2O$ requires C, 73.6; H, 5.7; N, 13.2%); $\nu_{max.}$(KBr) 1 730 and 1 700 cm^{-1} (CO); δ_H (250 MHz) 2.56—2.72 (4 H, m, 5- and 6-H), 3.38—3.40 (2 H, m, 3-H), 4.81 (1 H, tt, *J* 3.3 and 1.7 Hz, 4-H), 7.39—7.42 (3 H, m), and 7.86—7.90 (2 H, m); δ_C (25.2 MHz) 20.16 (5-C), 24.20 (6-C), 27.89 (3-C), 93.42 (4-C), 126.21, 128.14, 130.32, and 135.54 (Ph), 134.36 (4a-C), 150.21 (2-C), and 169.99 (7-C); *m/z* 212 (M^+). The compound darkened when stored in contact with air.

Ethyl 3,5,6,7-*Tetrahydro*-7-*oxopyrrolo*[1,2-b]*pyridazine*-2-*carboxylate* (**10b**).—A solution of ethyl 3-bromo-2-oxopropanoate (0.77 g, 3.9 mmol) in ether (5 ml) was stirred with pent-4-ynohydrazide (0.40 g, 3.6 mmol) and conc. HCl (1 drop) for 2 h. The solvent was evaporated off and the solid residue was dissolved in dichloromethane (150 ml). Sodium carbonate (2 g) was added and the mixture was stirred for 24 h. Flash chromatography gave (with ethyl acetate) the *pyridazine* (**10b**) (0.30 g, 40%), m.p. 112—116 °C (from ethanol) (Found: C, 57.7; H, 5.9; N, 13.7. $C_{10}H_{12}N_2O_3$ requires C, 57.7; H, 5.8; N, 13.5%); $\nu_{max.}$(KBr) 1 750 and 1 710 cm^{-1} (CO); δ (220 MHz) 1.31—1.44 (3 H, t, *J* 7 Hz), 2.50—2.60 (4 H, m, 5- and 6-H), 3.24—3.32 (2 H, m, 3-H), 4.37 (2 H, q, *J* 7 Hz), and 4.82—4.90 (1 H, m, 4-H); *m/z* 208 (M^+).

Ethyl 3,5,6,7-*Tetrahydro*-2-*methyl*-7-*oxopyrrolo*[1,2-b]*pyridazine*-3-*carboxylate* (**10c**).—A solution of the hydrazone (**9c**) (0.17 g, 0.74 mmol) in dichloromethane (200 ml) was stirred with sodium carbonate (1 g) for 24 h. Flash chromatography (with ethyl acetate) gave the pyridazine (**10c**) (0.10 g, 71%) as a colourless oil which rapidly decomposed on exposure to air; δ (220 MHz) 1.29 (3 H, t, *J* 7 Hz), 2.10 (3 H, 2-Me), 2.50—2.80 (4 H, m, 5- and 6-H), 2.87—2.95 (1 H, m, 3-H), 4.21 (2 H, q, *J* 7 Hz), and 4.77—4.81 (1 H, m, 4-H). The compound was not further characterised, but a solution of the compound after exposure to air gave a complex well resolved e.s.r. signal. The second derivative spectrum consists of eight groups of lines. Although a detailed analysis is not possible a computer simulation indicates that there are two equivalent nitrogen nuclei having a^N = 0.543 mT, three equivalent protons having a^H_{Me} = 0.543 mT, and two sets of equivalent pairs of protons having $a^H_{CH_2}$ = 0.128 mT and $a^H_{CH_2}$ = 0.064 mT: a line width of 0.030 mT was used in this simulation. This analysis is consistent with the structure (**11**).

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