Competing [4 + 2] and [3 + 2] Cycloaddition in the Reactions of Nucleophilic Olefins with Ethyl 3-(Toluene-*p*-sulphonylazo)but-2-enoate

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The title azo-olefin (4) has been isolated as an unstable oil and its cycloaddition reactions with several enol ethers, an enamine, and two alkyl-substituted indoles have been studied. With ethyl vinyl ether the product is the tetrahydropyridazine (5) but with 2-methoxypropene the product is a pyrrole derivative, (7a). Reaction with α-methoxystyrene similarly gives the pyrrole (7b). 2,3-Dihydrofuran adds to give a tetrahydropyridazine, (8), whereas the product from 4,5-dihydro-2-methylfuran is formulated as a dihydropyrrole, (10). 2-Methyl-1-pyrrolidin-1-ylpropene and 1,3-dimethylindole give mixtures of products arising from both [4 + 2] and [3 + 2] cycloaddition, with *N*-methyltetrahydrocarbazole, only the product (13) of [3 + 2] cycloaddition is detected. The cycloaddition to ethyl vinyl ether is not accelerated in a more polar solvent, but the addition to 2-methoxypropene is 9.5 times faster in [$^2H_3$]acetonitrile than in tetrachloromethane at 298 K.

These reactions are interpreted as involving (i) concerted [4 + 2] cycloadditions which are subject to retardation by substituents on the nucleophilic olefins, and (ii) [3 + 2] additions through highly unsymmetrical transition states.

Three types of cycloaddition reaction are known to occur between conjugated azo-olefins and compounds containing carbon–carbon double bonds: (i) [4 + 2] addition, (ii) [3 + 2] addition, and (iii) [2 + 2] addition to the azo group. The first mode of addition is the most common, and examples of addition of azo-olefins to both electrophilic and nucleophilic double bonds are known.[1,2] The [3 + 2] mode of addition of azo-olefins has been observed in some reactions with enamines.

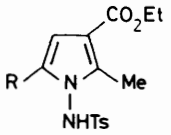
The primary products of [3 + 2] addition are azomethine imides (1) and these have been isolated in a few cases.[3] *N*-Aminodihydropyrroles (2) and *N*-aminopyrroles (3) have also been isolated from reactions of enamines with azo-olefins [3,4] and such compounds can be derived from the adducts (1) by rearrangement and aromatisation. The [2 + 2] mode of cycloaddition of azo-olefins is so far limited to their reaction with ketenes.[5]

We wished to investigate what factors controlled the preference for [4 + 2] or for [3 + 2] addition of azo-olefins to electron-rich double bonds. In a related study of the cycloaddition of α-nitrosostyrene to double bonds we found two cases, with 2-methoxypropene [6] and with *N*-methyltetrahydrocarbazole,[7] in which both [4 + 2] and [3 + 2] adducts were formed in the same reaction. Because α-nitrosostyrene is a transient species, mechanistic investigations of these reactions were limited. It seemed likely that analogous reactions of an isolable azo-olefin would be more fruitful. The more reactive azo-olefins are transient species and therefore suffer from the same limitations as α-nitrosostyrene. Many of the isolable azo-olefins are too unreactive to be useful. After a preliminary investigation we selected the azo-olefin (4) as a suitable species for detailed study. This compound is readily prepared in solution by reaction of the tosylhydrazone of ethyl 2-chloroacetoacetate with sodium hydrogen carbonate. It can be isolated in a pure form as a red oil by rapid chromatography but decomposes within a few hours at room temperature. The ^{1}H n.m.r. spectrum indicates that it is a single isomer; the (*E*)-configuration is assumed. It was found to react at an acceptable rate at room temperature or below with several electron-rich olefins.

Reaction of the Azo-olefin (4) *with Ethyl Vinyl Ether.*—Reaction with ethyl vinyl ether gave, as the only detectable product, a 1 : 1 adduct which was formulated as the tetrahydropyridazine (5). This was isolated (78%) by column chromatography. When a solution of the adduct in deuteriochloroform was allowed to stand at room temperature, an epimeric product was detected by ^{1}H n.m.r. spectroscopy. After 48 h *ca.* 50% of the adduct (5) had epimerised, but the adducts decomposed when the solution was stored for a longer period or when an acidic catalyst was added. The epimer could not be isolated in a pure state, but from the ^{1}H n.m.r. spectrum of the mixture it was assigned structure (6).

The ^{1}H n.m.r. data on which these structural assignments are based are as follows (only the signals for the ring hydrogen atoms being listed). For (5): δ 4-H = 2.83, 5ax-H = 1.50, 5eq-H = 2.65, and 6-H = 5.43; *J* (Hz) 4-H—5ax-H = 7.3, 4-H—5eq-H = 1.0, 5ax-H—5eq-H = 13.7, 5ax-H—6-H = 2.2, and 5eq-H—6-H = 2.2. For (6): δ 4-H = 2.23, 5ax-H = 1.81, 5eq-H = 3.29, and 6-H = 5.50; *J* (Hz) 4-H—5ax-H = 13.1, 4-H—5eq-H = 6.1, 5ax-H—5eq-H = 13.8, 5ax-H—6.H = 3 (approx), and 5eq-H—6-H = 2 (approx). If the rings adopt a half-chair conformation the 6-ethoxy substituent can be assigned to an axial position in both isomers. This preference for an axial 6-ethoxy group has also been observed with the related 6-ethoxy-5,6-dihydro-4*H*-1,2-oxazines,[8] and shows the operation of the anomeric effect in these ring systems.

In comparing the remaining signals for the ring hydrogen atoms, it can be seen that the signal for 4-H in isomer (6) is at higher field than in (5), and shows a large coupling of 13.1 Hz which is absent in the corresponding signal in the



(7)

a; R = Me

b; R = Ph

spectrum of (5a). On this basis, 4-H in (6) is assigned to an axial position, and the ethoxycarbonyl group to an equatorial position. The opposite arrangement is assumed for (5), which thus has the ethoxycarbonyl group *cis* to the 6-ethoxy substituent. The experimental evidence indicates that isomer (5) is the kinetic product.

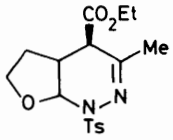
Compound (5) is the product to be expected from a [4 + 2] cycloaddition in which the *endo* transition state is strongly preferred. The preference for *endo*-addition has been observed in several other [4 + 2] cycloadditions of azo-olefins.[1,2,9]

The rates of the cycloaddition in two solvents of different dielectric constant, tetrachloromethane and [$^2H_3$]acetonitrile, were compared. Solutions each containing the same amount of the freshly prepared azo-olefin and a known excess of ethyl vinyl ether in the appropriate solvent were placed in the probe of the n.m.r. spectrometer at 0 °C and the changes in the spectra were monitored. The course of the reactions could be followed most conveniently from the integrals of well-separated methyl group signals in the reactant and the product. The progress of the reaction in each solvent was plotted graphically according to the expression for a second-order reaction,[10] and from the slopes of the straight-line plots the rate constants were determined as 9.3×10^{-5} mol^{-1} l s^{-1} in tetrachloromethane at 273 K and 8.0×10^{-5} mol^{-1} l s^{-1} in [$^2H_3$]acetonitrile at 273 K. Thus there is very little solvent effect on the rate, the reaction being slightly slower (0.86 : 1) in the more polar solvent, [$^2H_3$]acetonitrile.

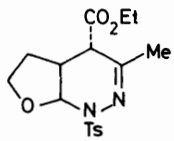
Reaction with 2-Methoxypropene.—The reaction with 2-methoxypropene also gave a single product, which was isolated by column chromatography in 44% yield. The starting azo-olefin was consumed but no other adducts could be detected by t.l.c. The product was identified, from analytical and spectral data, as the aminopyrrole (7a): in contrast to the pyridazine (5) obtained from ethyl vinyl ether it showed an NH stretching absorption ($\nu_{max.}$ 3 120 cm^{-1}) and a conjugated ester carbonyl absorption ($\nu_{max.}$ 1 675 cm^{-1}) in the i.r. spectrum, and an aromatic proton signal at δ 6.13 in the n.m.r. spectrum.

The course of the reaction was followed by carrying it out in the probe of the n.m.r. spectrometer. No intermediate, and no significant side products, were detectable: the olefinic signal of the azo-olefin was smoothly replaced by the hetero-aromatic signal of the pyrrole at δ 6.13 as the reaction proceeded. Since the structure of the product requires the loss of methanol, there must be at least one intermediate in the reaction (and there are probably at least two), but the later steps must be fast relative to the initial addition.

The data were not adequate for a kinetic analysis but the effect of change of solvent was determined semi-quantitatively by measuring the times taken from the reactions to proceed to 50% completion. Two solutions containing equal amounts of the azo-olefin and a measured excess of 2-methoxypropene were made up, one with tetrachloromethane as solvent and the other with [$^2H_3$]acetonitrile. The times taken for the reactions to proceed to 50% completion were determined by following them in the probe of the n.m.r. spectrometer at



(8)



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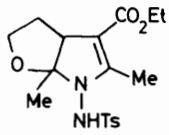

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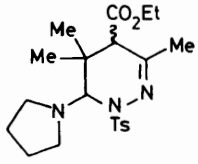

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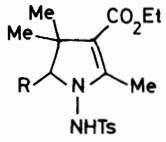


(12)

a; R = OH

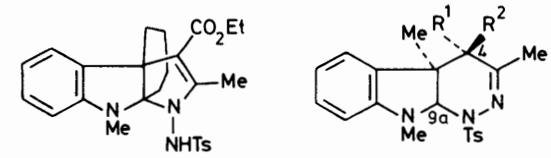
b; R = pyrrolidinyl

298 K. The times taken were in the ratio $CCl_4 : CD_3CN$ = 1 : 9.5. Thus, in contrast to the reaction of ethyl vinyl ether, that of 2-methoxypropene is considerably faster in the more polar solvent. It was also possible to deduce qualitatively that the reaction of the azo-olefin with 2-methoxypropene was slower than with ethyl vinyl ether, even in the more polar solvent.

Reactions with Other Nucleophilic Olefins.—Because of the surprising contrast in the reactions of ethyl vinyl ether and of 2-methoxypropene with the azo-olefin, the reactions of some other nucleophilic olefins were investigated. α-Methoxystyrene gave the pyrrole (7b) (34%) in a reaction analogous to that of 2-methoxypropene. The reactions of two cyclic enol ethers, 2,3-dihydrofuran and 4,5-dihydro-2-methylfuran, with the azo-alkene were then compared. Both were slower than the reaction with ethyl vinyl ether, and both reaction mixtures were more complex than in the earlier experiments. The major product formed initially with dihydrofuran was an adduct to which the pyridazine structure (8) is assigned, but this epimerised during the course of the addition and during chromatographic separation to the *exo*-isomer (9), which was isolated (31%) and characterised. This reaction thus appears to follow predominantly the same course as that of ethyl vinyl ether.

The reaction of 2-methyl-4,5-dihydropyran also gave a mixture of products, from which one major component was isolated as an oil but which was not completely purified. The n.m.r. spectrum showed a signal for an exchangeable hydrogen atom and the data were consistent with the formation of the structure as the dihydropyrrole (10).

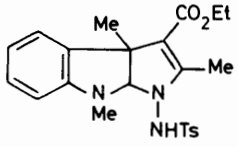
The reaction of the azo-olefin with an aldehyde-derived enamine, 2-methyl-1-pyrrolidin-1-ylpropene, was then examined. The crude product mixture was complex (by n.m.r. and t.l.c.). The mixture was subjected to chromatography and two components were isolated, though neither could be obtained completely free from impurities. A non-polar product, isolated as an amorphous solid in 5% yield, was assigned the pyridazine structure (11) on the basis of its n.m.r. and i.r. spectrum. The compound was also detectable in the n.m.r. of the crude reaction mixture as *ca.* 15% of the total crude product. Only one epimer was present but it is not possible to decide whether it is *cis* or *trans* from the available data. The other product isolated (40%) was assigned the dihydropyrrole structure (12a) on the basis of its n.m.r. spectrum. This is not present in the crude reaction mixture and is a hydrolysis product, presumably of the adduct (12b), for which n.m.r. signals can be seen in the initial product mixture.



(13)

(14) $R^1 = H$, $R^2 = CO_2Et$

(15) $R^1 = CO_2Et$, $R^2 = H$



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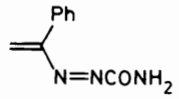

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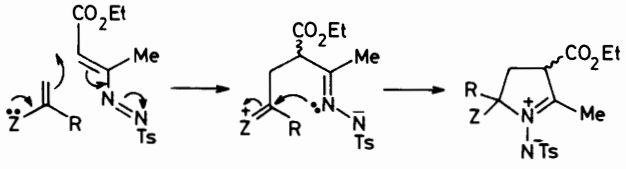

Scheme.

The reactions of the azo-olefin with two indoles, one with a free 2-position and the other with a 2-alkyl-substituent, were then investigated. *N*-Methyltetrahydrocarbazole gave one major product, which was isolated (53%) by chromatography and which was assigned the dihydropyrrole structure (13). 1,3-Dimethylindole gave a mixture from which three components were separated and characterised. Two of these were formulated as pyridazines, and were isolated in a combined yield of 55%, based on the amount of indole consumed. The less polar isomer is tentatively formulated as the product (14) to be expected of *endo*-addition, and the other pyridazine as its epimer (15). The third product, which was isolated in 34% yield, is assigned the dihydropyrrole structure (16).

Conclusions.—The reactions in this series represent the borderline between [4 + 2] and [3 + 2] addition: there are examples in which one or the other type of adduct is formed exclusively, and others in which both are formed. [3 + 2] Cycloaddition is the only reaction observed when the enol ether or enamine has an additional alkyl group at the carbon bearing the heteroatom. [4 + 2] Cycloaddition is the only detectable reaction of the two enol ethers derived from aldehydes. [3 + 2] and [4 + 2] Addition reactions are both observed with the aldehyde-derived enamine and with the α-free indole: [3 + 2] addition is the major reaction of the enamine, but [4 + 2] addition predominates with the indole. [3 + 2] Addition thus appears to be promoted by α-alkyl substitution in the nucleophilic olefin, and by increasing nucleophilicity of the olefin.

These generalisations also apply to the literature examples of the reactions of isolable azo-olefins with enol ethers and enamines.[2-4] On the other hand, the transient and highly reactive azo-styrene (17) is reported to add in a [4 + 2] mode to enamines, indoles, and pyrroles.[11]

The [4 + 2] addition is most simply rationalised as a concerted hetero-Diels-Alder reaction. It shows high *endo* selectivity and there is no evidence, from the solvent effect on the rate, for the existence of a dipolar intermediate. The reaction requires that the azo-olefin is in a *cisoid* conformation, and the presence of additional substituents on the nucleophilic olefin is likely to slow down the reaction because of steric hindrance. In cases where the bulky olefin is also highly nucleophilic, as with these enol ethers and enamines, the [3 + 2] mode of addition becomes competitive. This type of reaction does not require the azo-olefin to adopt a *cisoid* conformation, and it is therefore likely to be less susceptible to steric inhibition.

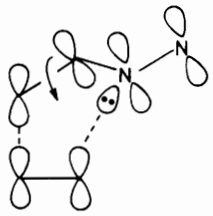

Figure. The proposed transition state for [3 + 2] cycloaddition, showing the rotation about the C–C bond of the azo-olefin

One extreme mechanism which can be envisaged for the [3 + 2] addition is shown in the Scheme. In this, the nucleophilic olefin adds to the azo-olefin, which is in a *transoid* conformation, to give a zwitterion, which then collapses to the azomethine imide. The dihydropyrroles and pyrroles can then be derived from these intermediates by proton transfer and elimination.

Since the reaction of 2-methoxypropene shows only a moderate rate increase when carried out in a solvent of high dielectric constant, it is unlikely that the transition state in the rate-determining step is very much more polar than the reactants. A discrete zwitterionic intermediate, formed in the slow step of the sequence shown in the Scheme, would require such a build-up of charge, and this stepwise mechanism therefore seems unlikely. On the other hand, the nucleophilicity of the olefin is clearly an important factor in promoting this mode of addition and it is probable that the formation of the carbon–carbon bond is more advanced than that of the carbon–nitrogen bond in the transition state. We suggest that the reaction is initiated by the attack of the nucleophile on the *transoid* azo-olefin, as in the Scheme, but that as the reaction proceeds, the C⋯N⋯N fragment of the azo-olefin twists out of the plane, so as to align the lone pair on the central nitrogen with the developing electrophilic centre, the α-carbon atom of the nucleophile (Figure). This represents a concerted, but highly unsymmetrical, mode of addition. In this way, the integrity of the azomethine imide 4π-electron system is preserved throughout the reaction.

Besides these examples and the examples of [3 + 2] addition of nitroso-olefins[6,7] referred to earlier, there are a few other reactions in which heterodienes can behave as formal 1,3-dipoles in cycloadditions. Sommer has pointed this out in an earlier paper.[3] The most important of these are the 'criss-cross' additions of azines to olefins. The reactions represent a small but growing new class of cycloadditions.

Experimental

^{1}H N.m.r. spectra were recorded on a Perkin-Elmer R34 instrument, operating at 220 MHz; $CDCl_3$ was used as solvent, except for the kinetic experiments. I.r. spectra were recorded as mulls in liquid paraffin. Flash chromatography was carried out using silica gel 80—100 mesh (Whatman). 2,3-Dihydrofuran and 4,5-dihydro-2-methylfuran were supplied by the Aldrich Chemical Co. Ltd. 1,3-Dimethylindole and 1,2,3,4-tetrahydrocarbazole were prepared by a modification[7] of the general method described by Gale and Wilt-

shire.[12] 2-Methyl-1-pyrrolidin-1-ylpropene was prepared by a literature procedure [13] and distilled, and its purity checked by n.m.r., immediately before use.

Ethyl 2-Chloroacetoacetate Toluene-p-sulphonylhydrazone.—This was prepared (79%) from ethyl 2-chloroacetoacetate and *p*-tolylsulphonylhydrazine in tetrahydrofuran and had m.p. 116—117 °C (from acetone–ether) (Found: C, 46.7; H, 5.1; N, 8.3. $C_{13}H_{17}ClN_2O_4S$ requires C, 46.9; H, 5.15; N, 8.4%); δ 1.22 (3 H, t), 1.91 (3 H), 2.43 (3 H), 4.18 (2 H, q), 4.93 (1 H), 7.31 (2 H, d), 7.79 (1 H, d), and 8.39 (1 H, NH).

(E)-*Ethyl* 3-(p-*Tolylsulphonylazo*)*but*-2-*enoate* (4).—A suspension of the above toluene-*p*-sulphonylhydrazone (1.66 g, 5.0 mmol) in diethyl ether (25 cm³) was stirred vigorously at room temperature for 0.5 h with aqueous sodium hydrogen carbonate (10%, 12.5 cm³). The ethereal phase was separated, dried over sodium sulphate, and filtered. The filtrate was evaporated to leave the crude azoalkene as a red oil. This material was substantially pure (by n.m.r.) but could be further purified by flash column chromatography (silica) to give, with ethyl acetate–light petroleum (3 : 7), the azoalkene with *ca.* 30% recovery; δ 1.25 (3 H, t, *J* 7.3 Hz), 2.20 (3 H), 2.42 (3 H), 4.23 2 H, q, *J* 7.3 Hz), 6.69 (1 H), 7.37 (2 H, d), and 7.76 (2 H, d). The liquid azo-olefin starts to decompose within a few hours at room temperature but can be kept in dilute solution without appreciable decomposition for 2—3 days.

cis-6-*Ethoxy*-4-*ethoxycarbonyl*-3-*methyl*-1-(p-*tolylsulphonyl*)-1,4,5,6-*tetrahydropyridazine* (5) *and its* trans-*Isomer* (6).—The azo-olefin (4) was freshly prepared (without chromatographic purification) from the toluene-*p*-sulphonylhydrazone (1.66 g, 5.0 mmol). It was dissolved in dry dichloromethane (20 cm³) and ethyl vinyl ether (0.720 g, 10.0 mmol) was added. The solution was kept at 20 °C for 18 h and the solvent was then distilled off. Column chromatography of the residue (silica; ethyl acetate–light petroleum) gave the *pyridazine* (5) (1.44 g, 78%), m.p. 93—95 °C (from ether) (Found: C, 55.1; H, 6.5; N, 7.5. $C_{17}H_{24}N_2O_5S$ requires C, 55.4; H, 6.6; N, 7.6%); $\nu_{max.}$ 1 735 cm⁻¹; δ 0.98 (3 H, t, *J* 7.1 Hz), 1.13 (3 H, t, *J* 7.1 Hz), 1.50 (1 H, ddd), 2.03 (3 H), 2.34 (3 H), 2.65 (1 H, ddd), 2.83 (1 H, m), 3.4—3.7 (2 H, m), 3.9—4.2 (2 H, m), 5.43 (1 H, m), 7.26 (2 H, d), and 7.75 (2 H, d). Assignments and couplings are given in the text. After 48 h at room temperature the solution contained a second component (*ca.* 50%) which showed δ 1.10 (3 H, t, *J* 7.1 Hz), 1.21 (3 H, t, *J* 7.1 Hz); 1.81 (1 H, m), 1.90 (3 H), 2.23 (1 H, m), 2.35 (3 H), 3.29 (1 H, m), 3.4—3.8 (2 H, m), 3.9—4.2 (2 H, m), 5.50 (1 H, m), 7.26 (2 H, d), and 7.75 (2 H, d). These signals were assigned to the *trans*-isomer (6) (see text).

Effect of Solvent on Rate of Formation of (5).—Freshly prepared azo-olefin (4) (purified by chromatography) (0.160 g, 0.54 mmol) and ethyl vinyl ether (0.120 g, 1.67 mmol) were dissolved in tetrachloromethane (0.250 cm³) containing a drop of tetramethylsilane and the solution was immediately cooled. It was transferred to the probe of the n.m.r. spectrometer maintained at 273 K and spectra were recorded at 10 min intervals for 70 min (8 spectra), after which period the reaction had proceeded to *ca.* 75% completion. The extent of reaction in each spectrum was estimated from the integrals of the signals at δ 2.18 (Me of azo-olefin) and δ 1.97 (Me of pyridazine). The results were plotted graphically against time using the standard equation [10] for a second-order reaction. From the slopes of the straight-line plot the value $k = 9.3 \times 10^{-5}$ mol⁻¹ l s⁻¹ was determined. The reaction was repeated with the same quantities of reagents and [$^2H_3$]-acetonitrile as solvent; from the graph the value $k = 8.0 \times 10^{-5}$ mol⁻¹ s⁻¹ was determined.

Ethyl 2,5-*Dimethyl*-1-*toluene*-p-*sulphonamidopyrrole*-3-*carboxylate* (7a).—A solution of the azoalkene (4) (derived from 5.0 mmol chlorohydrazone) and 2-methoxypropene (0.720 g, 10.0 mmol) in dry dichloromethane (20 cm³) was kept at 20 °C for 18 h. The solvent was removed and the residue was subjected to column chromatography (silica) which gave (with ethyl acetate–light petroleum) the *pyrrole* (7a) (0.742 g, 44%), m.p. 98—100 °C (from ethyl acetate–hexane) (Found: C, 57.3; H, 6.1; N, 8.2. $C_{16}H_{20}N_2O_4S$ requires C, 57.1; H, 5.95; N, 8.3%); $\nu_{max.}$ 3 120br and 1 675 cm⁻¹; δ 1.25 (3 H, t, *J* 7.3 Hz), 1.79 (3 H), 2.02 (3 H), 2.41 (3 H), 4.19 (2 H, q, *J* 7.3 Hz) 6.13 (1 H), 7.30 (2 H, d), 7.65 (2 H, d), and 8.18br (1 H).

Effect of Solvent on Rate of Formation of (7a).—Freshly prepared azo-olefin (4) (0.190 g, 0.64 mmol) and 2-methoxypropene (0.120 g, 1.67 mmol) were dissolved in tetrachloromethane (0.250 cm³) containing a drop of tetramethylsilane, and the solution placed in the n.m.r. probe at 298 K. The formation of the product was monitored by the disappearance of the vinylic hydrogen signal of the azo-olefin (δ 6.69) and the appearance of the signal due to 4-H of the pyrrole (δ 6.13). No intermediates were detected. The time taken for the reaction to proceed to 50% completion was determined as 160 min. The experiment was repeated with [$^2H_3$]acetonitrile as solvent; the time for 50% reaction was determined as 17 min.

Ethyl 2-*Methyl*-5-*phenyl*-1-*toluene*-p-*sulphonamidopyrrole*-3-*carboxylate* (7b).—A solution containing the azoalkene (4) (derived from 5.0 mmol chlorohydrazone) and α-methoxystyrene (1.340 g, 10.0 mmol) in tetrachloromethane (20 cm³) was allowed to stand at 20 °C for 18 h. The solvent was removed. Chromatography gave, besides α-methoxystyrene, a single product which was identified as the *pyrrole* (7b) (0.668 g, 34%), m.p. 172—173 °C (from dichloromethane–hexane) (Found: C, 63.1; H, 5.6; N, 7.2. $C_{21}H_{22}N_2O_4S$ requires C, 63.3; H, 5.5; N, 7.0%); $\nu_{max.}$ 3 160br and 1 670 cm⁻¹; δ 1.32 (3 H, t, *J* 7.3 Hz), 2.26 (3 H), 2.63 (3 H), 4.29 (2 H, q, *J* 7.3 Hz), 6.46 (1 H), 6.8—7.2 (9 H, m), and 8.40 (1 H).

cis-4-*Ethoxycarbonyl*-1,4,4a,5,6,7a-*hexahydro*-3-*methyl*-1-(p-*tolylsulphonyl*)*furo*[2,3-c]*pyridazine* (8) *and its* trans-*Isomer* (9).—The azoalkene (5.0 mmol), 2,3-dihydrofuran (1.050 g, 15.0 mmol), and dichloromethane (20 cm³) were kept at 20 °C for 18 h and the solvent and the excess of the furan were then distilled off. The ^1H n.m.r. spectrum of the residue showed two doublets at δ 5.86 and 6.11 (ratio 2 : 5), characteristic of the pyridazines. The products were distinguishable by t.l.c. but were interconverted during column chromatography of the mixture. The less polar isomer, initially present as the major component, was isolated from the column as the minor component. It was a yellow oil (0.150 g, 8%) and was assigned structure (8): δ 1.27 (3 H, t, *J* 7.3 Hz), 1.56—1.75 (1 H, m), 2.05—2.25 (1 H, m), 2.08 (3 H), 2.40 (3 H), 3.14—3.30 (2 H), 3.36 (1 H, d, *J* 4.8 Hz, 4-H), 3.48—3.60 (1 H, m), 4.22 (2 H, q, *J* 7.3 Hz), 6.11 (1 H, d, *J* 7.2 Hz, 7a-H), 7.26 (2 H, d), and 7.94 (2 H, d). The compound epimerised (*ca.* 50%) when allowed to stand in solution at 20 °C for 24 h; it was not purified further.

The more polar component was isolated as a yellow oil (0.774 g) which after crystallisation gave the *furopyridazine* (9) (0.574 g, 31%), m.p. 96—98 °C (from dichloromethane–hexane) (Found: C, 55.7; H, 6.0; N, 7.5. $C_{17}H_{22}N_2O_5S$ requires C, 55.7; H, 6.0; N, 7.65%); $\nu_{max.}$ 1 730 cm⁻¹; δ 1.21 (3 H, t, *J*

7.3 Hz), 1.48—1.62 (1 H, m), 2.06 (3 H), 2.05—2.25 (1 H, m), 2.38 (3 H), 2.95 (1 H, d, *J* 5.3 Hz, 4-H), 3.08—3.22 (1 H, m), 3.50—3.75 (2 H, m), 4.15 (2 H, q, *J* 7.3 Hz), 5.86 (1 H, d, *J* 6.8 Hz, 7a-H), 7.25 (2 H, d), and 7.89 (2 H, d).

There were also several minor products of this reaction but none was obtained in a sufficiently pure state to allow characterisation.

Reaction of the Azo-olefin (4) *with* 4,5-*Dihydro*-2-*methylfuran*.—The azo-olefin (5.0 mmol) and 4,5-dihydro-2-methylfuran in dichloromethane (20 cm^3) were kept at 20 °C for 18 h and the solvent was then removed. Column chromatography of the complex mixture gave a brown oil (0.680 g) as a single component (t.l.c.): δ 1.26 (3 H, t, *J* 7.3 Hz), 1.66 (3 H), 1.99 (3 H), 2.40 (3 H), 2.60—2.95 (2 H, m), 3.50—3.80 (2 H, m), 4.19 (2 H, q, *J* 7.3 Hz) 7.29 (2 H, d), 7.62 (2 H, d), and 9.24 (1 H, exchangeable). This product was tentatively assigned the furopyrrole structure (10) but was not purified further.

Reaction with 2-*Methyl*-1-*pyrrolidin*-1-*ylpropene*—The azo-olefin (4) (3.52 mmol) was dissolved in dry ether. The enamine was added dropwise and reacted immediately. After 0.440 g (3.5 mmol) had been added, the colour of the solution had changed to pale yellow. The solvent was removed and the residue was examined by n.m.r. spectroscopy which showed signals at δ 4.56 and 3.25 (ratio *ca.* 1 : 4), and a complex pattern of signals in the 1—3 region. Column chromatography using gradient elution with ethyl acetate–petroleum mixtures gave (i) a yellow amorphous solid (0.078 g, 5%) which was tentatively identified as the pyridazine (11); $\nu_{max.}$ 1 730 cm^{-1}; δ 0.55 (3 H), 1.04 (3 H), 1.22 (3 H, t, *J* 7.3 Hz), 1.60—1.75 (4 H, m), 1,89 (3 H), 2.37 (3 H), 2.63—2.81 (4 H, m), 3.06 (1 H, 4-H), 4.16 (2 H, q, *J* 7.3 Hz), 4.55 (1 H, 6-H), 7.27 (2 H, d), and 7.79 (2 H, d). This compound was present in the reaction mixture before chromatography (by n.m.r.) as 15—20% of the total product. It was not characterised further. (ii) Further elution gave a brown oily solid (0.520 g, 40%) which was assigned the structure (12a): δ 0.99 (3 H), 1.11 (3 H), 1.20 (3 H, t, *J* 7.3 Hz), 1.91 (3 H), 2.40 (3 H), 3.2—3.7br (1 H, exchangeable), 3.91 (1 H), 4.07 (2 H, q, *J* 7.3 Hz), 7.0—7.5br (1 H, exchangeable), 7.34 (2 H, d), and 7.79 (2 H, d). This compound decomposed on attempted crystallisation.

Reaction with 1-*Methyltetrahydrocarbazole*.—The azo-olefin (4) (5.0 mmol) and 1-methyltetrahydrocarbazole (0.907 g, 4.9 mmol) were dissolved in dichloromethane (20 cm^3). The solution was kept at 20 °C for 18 h and the solvent was removed. One major product was detected by t.l.c. and this was isolated by column chromatography (ethyl acetate–petroleum). It was identified as the *pyrrolo*[2,3-b]*indole* (13) (0.250 g, 53%), m.p. 165—166 °C (from dichloromethane–hexane) (Found: C, 64.7; H, 6.5; N, 8.5. $C_{26}H_{31}N_3O_4S$ requires C, 64.9; H, 6.45, N, 8.7%); $\nu_{max.}$ 3 140 and 1 655 cm^{-1}; δ 0.95—1.84 (6 H, m), 1.22 (3 H, t, *J* 7.3 Hz), 1.60 (3 H), 2.13—2.26 (1 H, m), 2.36—2.55 (1 H, m), 2.41 (3 H), 2.80 (3 H), 4.17 (2 H, q, *J* 7.3 Hz), 6.31—6.37 (1 H, m), 6.67—6.76 (1 H, m), 6.83 (1 H, exchangeable), 7.00—7.10 (1 H, m), 7.25—7.41 (3 H, m), and 7.74—7.82 (2 H, d).

Reaction with 1,3-*Dimethylindole*.—The azo-olefin (10.0 mmol) and 1,3-dimethylindole (1.450 g, 10.0 mmol) were dissolved in ether (50 cm^3) and the solution was kept at 20 °C for 48 h. The solvent was removed and the residue was examined by n.m.r. spectroscopy, which showed two signals at δ 4.75—4.80 and 4.91 (ratio *ca.* 3 : 1). Column chromatography using gradient elution (ethyl acetate–petroleum mixtures) gave (i) 1,3-dimethylindole (0.702 g, 48%); (ii) a solid which was tentatively identified as the *pyridazino*-[3,4-b]*indole* (14) (0.276 g, 12% based on 1,3-dimethylindole consumed), m.p. 181—182 °C (decomp.) (from dichloromethane–ether) (Found: C, 62.3; H, 6.1; N, 9.3. $C_{23}H_{27}N_3O_4S$ requires C, 62.6; H, 6.1; N, 9.5%); $\nu_{max.}$ 1 738 cm^{-1}; δ 0.75 (3 H), 1.07 (3 H, t, *J* 7.3 Hz), 1.97 (3 H), 2.39 (3 H), 2.89 (3 H), 3.16 (1 H, 4-H), 4.01 (2 H, q, *J* 7.3 Hz), 4.79 (1 H, 9a-H), and 6.54—7.85 (8 H, m); (iii) the *pyrrolo*[2.3-b]*indole* (16) (0.776 g, 34%), m.p. 158—162 °C (decomp.) (from ether–hexane) (Found: C, 62.3; H, 6.3; N, 9.4. $C_{23}H_{27}N_3O_4S$ requires C, 62.6; H, 6.1; N, 9.5%); $\nu_{max.}$ 3 160 and 1 658 cm^{-1}; δ 1.22 (3 H, t, *J* 7.3 Hz), 1.60 (3 H), 1.70 (3 H), 2.40 (3 H), 2.92 (3 H), 4.01 (2 H, q, *J* 7.3 Hz), 4.76 (1 H), 6.45—7.90 (8 H, m), and 7.05 (1 H, exchangeable); and (iv) the *pyridazino*[3,4-b]*indole* (15) (0.978 g, 43%), m.p. 159—161 °C (decomp.) (from dichloromethane–ether) (Found: C, 62.3; H, 6.2; N, 9.4. $C_{23}H_{27}N_3O_4S$ requires C, 62.6; H, 6.1; N, 9.5%); $\nu_{max.}$ 1 730 cm^{-1}; δ 0.89 (3 H), 0.90 (3 H, t, *J* 7.3 Hz), 1.96 (3 H), 2.40 (3 H), 2.79 (1 H, 4-H), 2.80 (3 H), 3.55—3.85 (2 H, m), 4.89 (1 H, 9a-H), and 6.42—7.86 (8 H, m).

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