A Route to 3*H*-1,2-Diazepines by the 1,7-Electrocyclisation of α,β;γ,δ-Unsaturated Diazo-compounds

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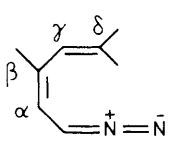
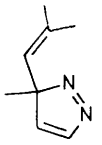
In the thermal cyclisation of α,β;γ,δ-unsaturated diazo-compounds the type (**6**) with a *cis* hydrogen atom at the terminal carbon atom undergo 1,7 ring closure to give 3*H*-1,2-diazepines while those (**9**) with a methyl group at that position take an alternative reaction path to give pyrazoles *via* 1,5 cyclisation.

This communication is concerned with the reactions of α,β;-γ,δ-unsaturated diazo-compounds of type (**1**). This system could in principle react *via* several plausible pathways: (i) by either or both of the two competing modes (1,5 or 1,7) of electrocyclisation giving respectively (**2**) or (**3**); (ii) by a 1,1-cycloaddition[1,2] to give (**4**); (iii) *via* loss of nitrogen to give carbene-derived products. Previous work in this area has shown that compounds analogous to (**1**) but with an 'aromatic' α,β-double bond cyclise exclusively by the 1,7-mode to give 1*H*-2,3-benzodiazepines[3,4] while those with an 'aromatic' γ,δ-double bond generally favour 1,5-electrocyclisation although they can be manipulated *via* stereochemical adjustment so that the 1,7-mode becomes competitive.[5,6] In both these cases it is clear that the periselectivity of the electrocyclisation is much affected by the presence and position of an aromatic double bond in the conjugated system and so it was of interest to determine the preferred mode of cyclisation



(1)



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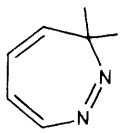

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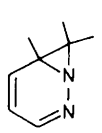
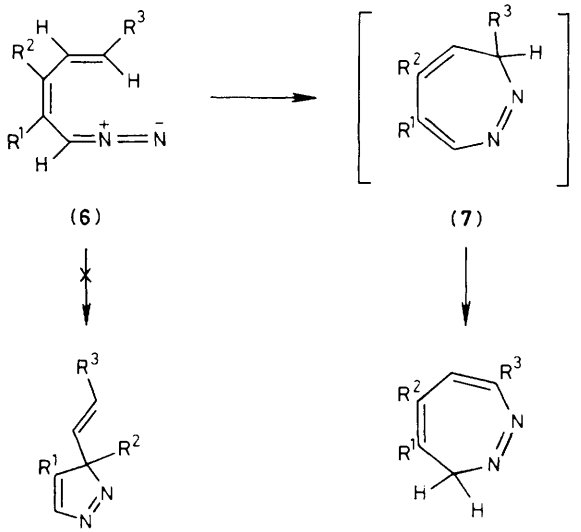


(4)

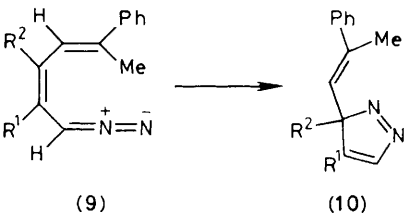
in the system (**1**) with only olefinic unsaturation. In particular it was hoped that the cyclisation of (**1**) would provide a viable route to the interesting 3*H*-1,2-diazepine system (**3**) hitherto only accessible by a base-induced elimination of toluene-*p*-sulphinic acid from 3,4-dihydro-2-tosyl-1,2-diazepines.[7]



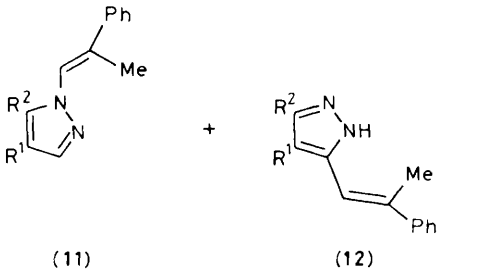
(6) (7) (5) (8)

	R^1	R^2	R^3	% Yield of (**8**)
a	$-[CH_2]_3-$		Me	65
b	$-[CH_2]_4-$		Ph	93
c	Me	Ph	Ph	71

Scheme 1



(9) (10)



(11) (12)

	R^1	R^2	% Yield (**10**)	(**11**)	(**12**)
a	$-[CH_2]_4-$		42	6	—
b	Me	Ph		37	29

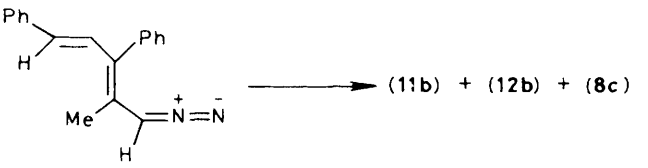
Scheme 2

As in the earlier work the diazo-compounds were generated *in situ* in aprotic solvents at *ca.* 80 °C from the sodium or lithium salts of tosylhydrazones. The results of the thermal reactions were clear-cut and are shown in Schemes 1—3. The systems shown in Scheme 1, *i.e.* those with the required *Z* stereochemistry for the α,β-double bond *and* having a *cis* hydrogen atom at the terminus of the unsaturated system, gave 3*H*-1,2-diazepines (**8**) in good to excellent yields, and in no case was any of the 3*H*-pyrazole (**5**) obtained or any other pyrazoles derived from it by rearrangement. It is notable that in all these cyclisations the primary product (**7**) was not isolated but rearranged by a 1,5 hydrogen shift to give (**8**). Such hydrogen migrations in these systems are known to be fast[7] and confer increased stability by bringing R^3 into conjugation and also in some cases by moving exocyclic double bonds to the more stable endocyclic positions.

Similar reactants (**9**) (Scheme 2) in which the terminal hydrogen atom was replaced by a methyl group did not give diazepines but cyclised by the alternative 1,5-mode to give the 3-vinyl-3*H*-pyrazoles (**10**) and/or the rearranged pyrazoles (**11**) and (**12**) as the only isolated heterocyclic products. Reactants with an *E* α,β-double bond, for example (**13**) (Scheme 3), as expected gave predominantly pyrazoles (**11b**) and (**12b**), but also a low yield of the diazepine (**8c**). The formation of the last is most likely accounted for by postulating some reversibility for the 1,5 cyclisation step; *i.e.* (**13**) cyclises to give (**5c**) which reopens to generate both (**13**) and (**6c**) thus leading to (**8c**) in low yield.

These results therefore show that 1,7 cyclisation is very strongly favoured over 1,5 in systems of type (**6**) but that the activation energy for the 1,7 process is raised so much by the presence of a *cis* methyl at the cyclisation site that the 1,5 mode is then preferred. The latter parallels a similar observation in the cyclisations of *o*-alkenylaryldiazoalkanes[8] but there the reaction path was diverted from 1,7 cyclisation to give only carbene-derived products.

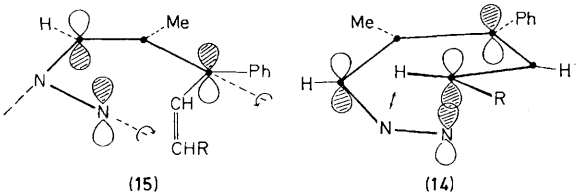
These observations can be accommodated by a transition state geometry for 1,7 cyclisation as shown in (**14**). This brings the terminal atoms into a bonding overlap and requires only the minimum angular distortion of the diazo group from its preferred linear geometry (see below). In this transition state the steric interaction [⟷ in (**14**)] between the *cis* hydrogen atom and N-2 of the diazo group is small; however



(13) → (11b) + (12b) + (8c)

T/°C	% Yield (**11b**)	(**12b**)	(**8c**)
80	32	20	13
110	3	61	6

Scheme 3



(15) (14)

models show that a methyl group at that position comes into a significant steric interaction with N-2 which would either severely inhibit orbital overlap between the termini of the system or would so twist the terminal carbon atom that the conjugation required for an electrocyclisation process would be lost.

The mechanism of the 1,5-electrocyclisation of α,β-unsaturated diazo-compounds has been discussed recently by Huisgen[9] and we suggest that the lack of effective competition from this mode of cyclisation in (**6**) reflects the much greater degree of bending† required in the diazo-group, as shown in (**15**), before disrotation would result in enough orbital overlap to stabilise the transition state. This result contrasts with the cyclisation of carbonyl ylides with extended conjugation analogous to (**6**) which react by both 1,5- and 1,7-ring closure.[12]

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† Calculations show a substantial energy barrier to in-plane bending of the CNN angle for diazomethane.[10,11]

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