Solvent Effect on Product Distribution in the Thermolysis of Dihydropyrazoles

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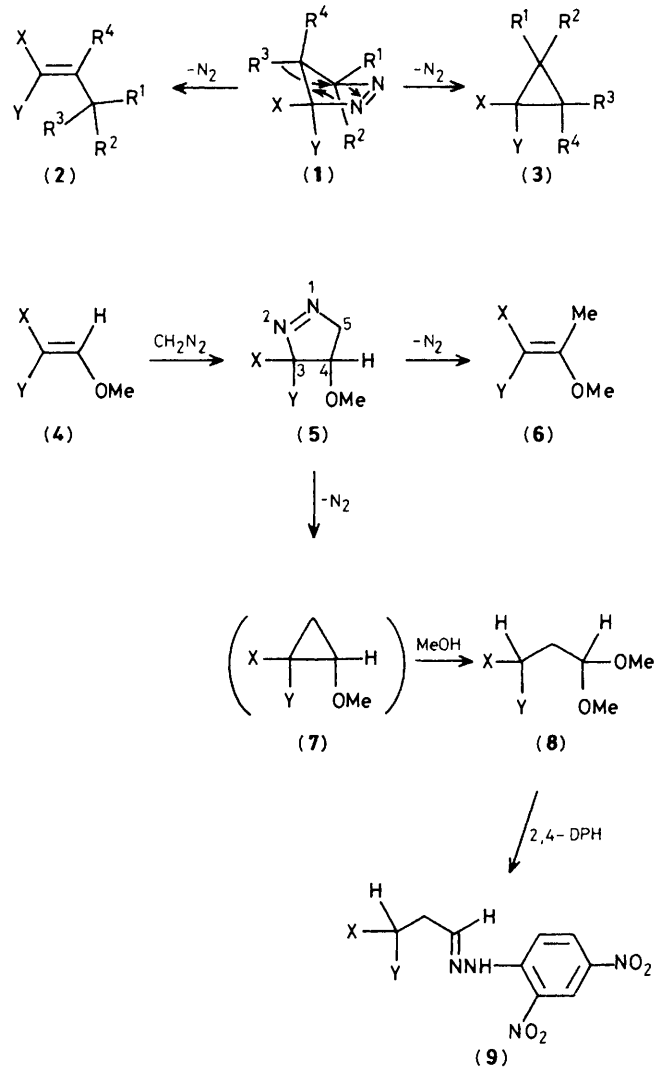
Solvent dependence of products in the thermal decomposition of 4-methoxy-4,5-dihydro-3*H*-pyrazoles bearing two electronegative groups at C-3 was observed; nonpolar solvents gave predominantly alkenes, whereas polar solvents gave predominantly cyclopropanes.

Thermolysis of the dihydropyrazoles (**1**) with two electronegative substituents at position 3 is known to give the alkenes (**2**), often accompanied by the cyclopropanes (**3**),[1] and an explanation is required of how formation of the particular product (alkene *vs.* cyclopropane) is determined. It is likely that the formation of the alkenes is determined by conformational factors as indicated in structure (**1**).[2] However, the mechanism of cyclopropane formation is a complex problem because it must explain why some reactions giving cyclopropanes are highly stereospecific, others only partly so, and yet others are not at all; many mechanisms have been presented.[2]

We have studied the decomposition of 4-heteroatom substituted dihydropyrazoles bearing two electron-withdrawing groups at C-3, in which the reaction modes are dependent upon a heteroatom substituent on C-4. The dihydropyrazoles bearing a sulphur[3] or selenium[4] substituent



a; X = Y = CO_2Me
b; X = CO_2Me, Y = CN
c; X = Y = CN

Scheme 1

at C-4 predominantly undergo migration of sulphur or selenium to C-5 with elimination of nitrogen under mild conditions, whereas 4-alkoxydihydropyrazoles exclusively gave hydrogen migration products in nonpolar solvents[5].

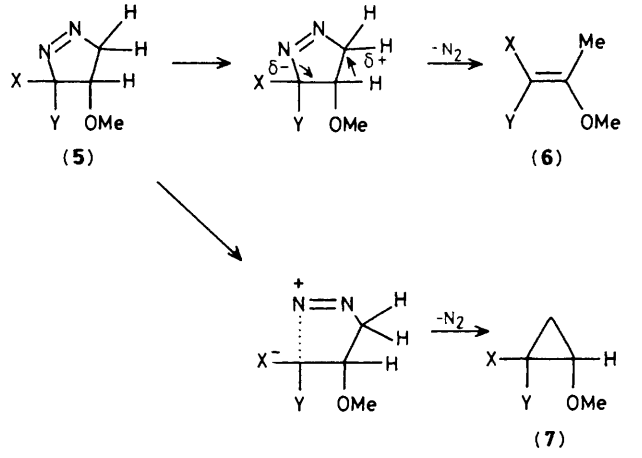
We show now that the thermal decomposition products of dihydropyrazoles strongly depend on the polarity of the solvent. Compound (**5a**) with two methoxycarbonyl groups at C-3 decomposed in xylene at 140 °C to give the alkene (**6a**) exclusively, which was formed by 4-hydrogen migration to C-5 with loss of nitrogen. Although (**5a**) is stable in refluxing benzene, in refluxing methanol it decomposed to give the acetal (**8a**), quantitatively [^{1}H n.m.r.: δ 2.21 (dd, 2H, *J* 5.4, 7.2 Hz), 3.31 (s, 6H), 3.51 (t, 1H, *J* 7.2 Hz), 3.73 (s, 6H), and 4.39 (t, 1H, *J* 5.4 Hz)]. Decomposition of (**5a**) in ethanol gave the corresponding acetal, quantitatively. The formation of the acetals can be explained by cyclopropanation and successive ring opening by alcohols as shown in Scheme 1. Thus, the change of pyrolysis solvent caused a dramatic change in reaction course and product.

As compound (**5b**), substituted by a methoxycarbonyl and a more electronegative cyano group at the 3 position, is unstable

Table 1. Product distribution (**6**:**7**) in the decomposition of (**5**) in various solvents.

		Products from (**5b**)		Products from (**5c**)	
Solvent	ε[a]	(**6b**)	(**7b**)	(**6c**)	(**7c**)
C_6H_6	2.3	100	0	100	0
Et_2O	4.3	100	0	100	0
CH_2Cl_2	9.1	100	0	72	28
AcOEt	6.0	50	50	14	86
Me_2CO	20.7	27	73	12	88
MeCN	37.5	10	90	0	100
MeOH	32.6	0	100	0	100

[a] Solvent dielectric constant.



Scheme 2

at room temperature, it was formed *in situ* by the reaction of the alkene (**4b**) with diazomethane in various solvents. Compound (**5b**) gave exclusively the hydrogen migration product (**6b**) in nonpolar solvents such as benzene, ether, and dichloromethane. However, (**5b**) in polar solvents strongly favours the cyclopropane formation, in methanol giving the acetal (**8b**), quantitatively. The reaction of (**4b**) with diazomethane in polar solvents such as ethyl acetate, acetone, and acetonitrile gave the cyclopropane (**7b**), which reacted with methanol† to form the acetal (**8b**).

Compound (**5c**) bearing two geminal cyano groups at C-3 gave very similar results. The formation of the cyclopropane (**7c**) was confirmed by treatment of the reaction mixture with methanol after completion of the reaction to give the acetal (**8c**). The reaction of (**8a**), (**8b**), and (**8c**) with 2,4-dinitrophenylhydrazine (2,4-DPH) afforded the corresponding hydrazones (**9a**), (**9b**), and (**9c**), respectively. It seems likely that solvent polarity is strongly correlated with product distribution. Nonpolar solvents favour the hydrogen migration reaction and in polar solvents the cyclopropanation is favoured. In solvents of intermediate polarity such as dichloromethane, ethyl acetate, and acetone, both reactions occurred competitively. Product distribution in such solvents indicates that the system bearing two cyano groups at C-3 favours the cyclopropanation more than the system bearing a cyano and a methoxycarbonyl group at C-3.

During the decomposition, polarization of the N(2)–C(3) bond occurs, resulting in development of a negative charge on

† As the cyclopropanes (**7b**) and (**7c**) polymerized on concentration, their structures were confirmed as the acetals (**8b**) and (**8c**).

C-3 which is presumably delocalized into the electron-withdrawing groups attached to C-3, and in nonpolar solvent the developing anion at C-3 can force a hydride on C-4 to C-5, at which a positive charge is developing, with elimination of nitrogen. These processes proceed in a concerted manner as shown in Scheme 2. However, in polar solvents the developing anion can be stabilized by the solvents as well as strongly electron-withdrawing groups, resulting in suppression of the hydrogen migration process and subsequent greater polarization of the N(2)–C(3) bond, which allows an alternative path, the cyclopropanation.

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