4,5-Dihydroisoxazole-5-spirocyclopropanes. Synthesis and Thermolytic Rearrangement to 5,6-Dihydro-4-pyridones

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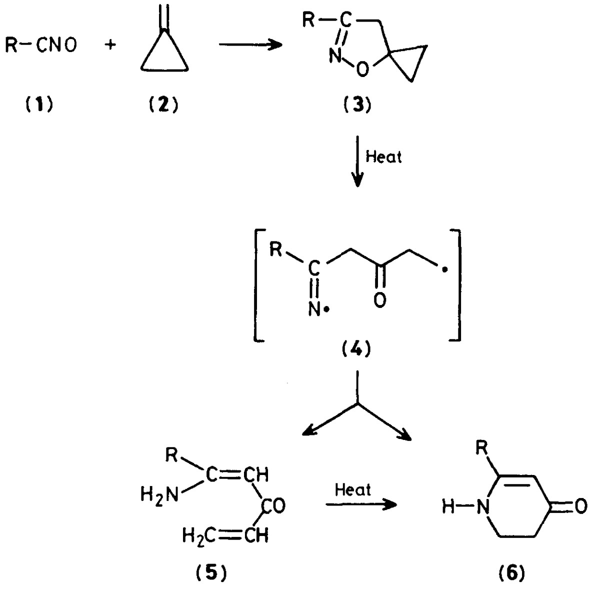
4,5-Dihydroisoxazole-5-spirocyclopropanes (**3**), prepared by cycloaddition of nitrile oxides (**1**) to methylenecyclopropane (**2**), undergo thermolysis affording aminodivinylketone (**5**) and 5,6-dihydro-4-pyridone (**6**) derivatives.

The strain of a small ring can be a source of new reaction pathways (with selectivity enhancement) when this ring is adjacent to reacting sites; many examples are known illustrating this principle.[1,2] In view of the well known synthetic potential of isoxazole derivatives,[3—5] this concept is applied now to isoxazole chemistry. To this end, the 4,5-dihydroisoxazole-5-spirocyclopropanes (**3**) were prepared by cycloaddition of the nitrile oxides (**1**) to methylenecyclo-

Table 1. Rearrangement of 4,5-dihydroisoxazole-5-spirocyclopropanes (**3**).

Comp.	Method[a]	Conc./ M	Solvent	Reaction time/h	% Yield (**5**)[b]	% Yield (**6**)[b]	(**6**) : (**5**) mol. ratio
(**3a**)	T	0.22	C_6H_6	0.5	26	55	2.1 : 1
	T	0.2	MeCN	0.5	16	24	1.5 : 1
(**3b**)	T	0.19	C_6H_6	1	37	45	1.2 : 1
	T	0.2	MeCN	1	38	59	1.5 : 1
	P	0.5	MeCN	24	41	45	1.1 : 1
(**3c**)	T	0.2	MeCN	0.5	15	50	3.3 : 1

[a] T = thermolysis at 200 °C in sealed tube; P = photolysis in solution (Philips 40 W low-pressure mercury lamp). [b] Products isolated by flash-column chromatography.



a; R = Me, 60% yield of (**3a**)
b; R = Ph, 65% yield of (**3b**)
c; R = $PhCH_2$, 35% yield of (**3c**)

propane (**2**); the regioisomers (**3**) predominated [3% of the other regioisomer being detected only in the reaction of (**1a**)]. A similar regioselectivity was observed in the sole previously reported cycloaddition to methylenecyclopropane (with phenylazide)[6] and in the cycloaddition of nitrile oxides to other methylenecycloalkanes.[7,8]

The heterospiranes (**3**) indeed undergo thermolysis more easily and more selectively than known monocyclic 4,5-dihydroisoxazoles; these are known to be stable at 200 °C[9]† and, on thermal or photochemical decomposition, lead in general to several products, mainly arising from 1–2 and 3–4 or 1–2 and 4–5 bond fission.[9,11] By contrast, the heterospiranes (**3**) rearrange completely within 0.5–1 h on heating at 200 °C in a sealed tube (0.2 M solutions); two main products are formed: the enaminones (**5**) and the dihydropyridones (**6**) in molar ratios depending on the substituent R and on the reaction conditions (starting concentration, solvent, heating time) (Table 1).

Thermal conversion of the enaminones (**5**) into the corresponding dihydropyridones (**6**) has been shown to occur in all cases. However, only a slight increase in the (**6**) : (**5**) ratio was observed during the thermolysis of (**3**), and the dihydropyridones (**6**) were produced faster from the heterospiranes (**3**) than from the isolated ketones (**5**) on thermolysis under the same conditions. Therefore, the two isomers (**5**) and (**6**) are produced from (**3**) mainly *via* parallel, rather than consecutive rearrangements. Their formation can reasonably be assumed to involve a common intermediate, possibly the diradical (**4**) or its polar equivalent, by analogy with previous reports concerning thermolysis[9] or photolysis[10] of 4,5-dihydroisoxazoles.

Photolysis of compound (**3b**) gave a similar result to its thermolysis, the main difference being a lower (**6**) : (**5**) ratio, explained by the lack of cyclisation of (**5**) to give (**6**) under the photolysis conditions.

Received, 15th July 1985; Com. 1014

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† 4,5-Dihydro-3-methylisoxazole-4-spirocyclopropane, the regioisomer of compound (**3a**), is also stable at 200 °C.