1,3-DIPOLAR ADDITION REACTIONS WITH VINYLPYRROLES[1]

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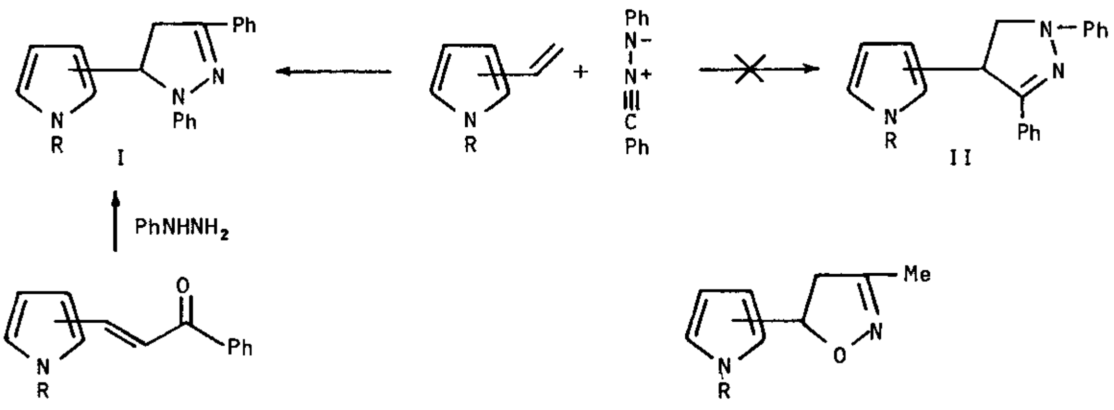
Diphenylnitrilimine and methyl nitrile oxide add regioselectively to 1-substituted vinylpyrroles to give 5-substituted-4,5-dihydropyrazoles and 4,5-dihydroisoxazoles, respectively. These reactions and the corresponding cycloadditions involving p-chlorophenyl sydnone and C-phenyl-N-phenylnitrone are LUMO(dipole) controlled.

The 1,3-dipolar cycloaddition of diphenylnitrilimine, prepared in situ from α-chlorobenzaldehyde phenylhydrazone, with 1-substituted vinylpyrroles proceeds rapidly at 80°C to give the 5-substituted-4,5-dihydropyrazoles (I) in high yield to the complete exclusion of the 4-isomer (II).[2] The unequivocal identification of the adducts was achieved by mixed mp and by comparison of their ir and nmr spectra with those of the products obtained from the reaction of 1-phenyl-3-(1-substituted pyrrolyl)prop-2-en-1-one (III) with phenylhydrazine. Further confirmation was provided by analysis of the ^1H nmr chemical shifts and the spin-spin coupling constants for the ABX system of the dihydropyrazole ring (Table 1).



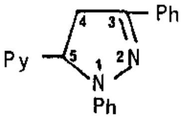
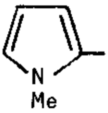
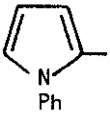
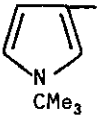
I

II

III

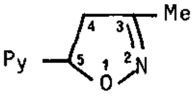
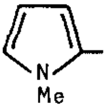
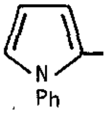
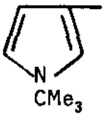
IV

Table 1. ^{1}H Resonance Signals for the 4,5-Dihydropyrazole Ring.

 Py =			
		δ (ppm)	
4a-H	3.65 dd	3.62 dd	3.58 dd
4b-H	3.22 dd	3.08 dd	3.08 dd
5-H	5.20 dd	5.09 dd	5.06 dd
		J (Hz)	
$J_{4a,5}$	13	12	12
$J_{4b,5}$	9	8	7
$J_{4a,4b}$	17	17	17

The corresponding 1,3-dipolar cycloaddition reactions with methyl nitrile oxide, prepared *in situ* from nitroethane, were also regioselective and gave 3-methyl-5-*(1-substituted pyrrolyl)-4,5-dihydroisoxazoles (IV).*[2] *However, unlike the dihydro*pyrazoles, the resonance signals for the 4,5-protons showed the simpler splitting pattern characteristic of an A_2X system (*cf.* ref. 3) with an additional long range coupling between the 3-Me group and the 4-CH_2 group (Table 2).

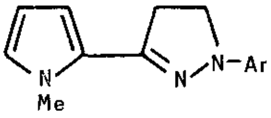
Table 2. ^{1}H Resonance Signals for the 4,5-Dihydroisoxazole Ring.

 Py =			
		δ (ppm)	
4-H	3.15 d×q	2.88 d×q	3.10 m
5-H	5.53 t	5.14 t	5.50 t
		J (Hz)	
$J_{4,5}$	10	10	10
$J_{4a,4b}$	—	—	6
$J_{4,Me}$	1	0.5	1

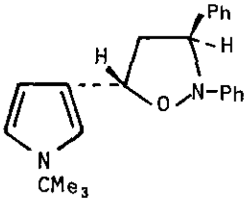
No identifiable stable products were isolated from the reaction of 2-vinylpyrrole with either of the 1,3-dipolar reagents.

Diphenylnitrilimine and methyl nitrile oxide are classified as Type II 1,3-dipolar reagents,[4] i.e. cycloaddition may occur with equal probability with either the HOMO or LUMO levels of the reagent. The observed regioselectivity to yield only isomers (I) and (IV) confirms that the cycloadditions are HOMO(alkene) controlled, as predicted by MO calculations of orbital energies and coefficients,[5] and are compatible with earlier observations of the corresponding reactions of styrene.[6]

The cycloadducts (V) and (VI) were isolated in low yield from reactions of 1-methyl-2-vinylpyrrole with p-chlorophenyl sydnone and 1-tert-butyl-3-vinylpyrrole with C-phenyl-N-phenylnitrone, respectively. The structure of (V) was established on the basis of the nmr signals at 3.22 (m,2H) and 3.71 ppm (m,2H),which are characteristic of the 4- and 5-CH_2 groups of the dihydropyrazole ring. Similarly, the identity of compound (VI) was confirmed by the chemical shifts and coupling constants of the tetrahydroisoxazole signals assigned to the 3-H at 4.85 ppm ($J_{3,4a}$ = 7.5 Hz; $J_{3,4b}$ = 7.5 Hz), the 5-H at 5.07 ppm ($J_{5,4a}$ = 5 Hz; $J_{5,4b}$ = 10 Hz) and the 4-CH_2 group at 3.00 and 2.49 ppm ($J_{4a,4b}$ = 12 Hz). The orientation of both of these reaction products is compatible with MO calculations of the orbital coefficients[5] for a LUMO(dipole) controlled cycloaddition with "large/large" and "small/small" orbital interactions. Secondary orbital effects[7] producing favourable bonding overlaps appear to govern the reaction involving the nitrone such that only one stereoisomer (VI) is formed.



V



VI

The 4,5-dihydropyrazoles and 4,5-dihydroisoxazoles were readily converted into the corresponding pyrazoles and isoxazoles by reaction with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

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Received, 28th November, 1979