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X=Y-ZH SYSTEMS AS POTENTIAL 1,3-DIPOLES

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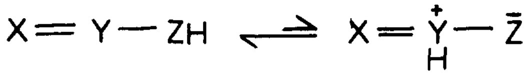
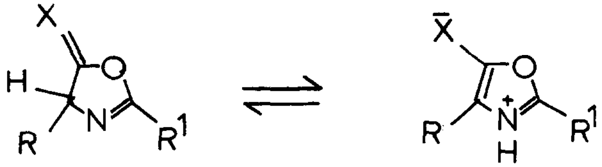
1,3-Dipolar cycloaddition reactions provide the most versatile synthesis of 5-membered heterocycles.[1] Evidence is now presented for a new class of potential 1,3-dipoles involving the tautomeric equilibrium ($1 \rightleftharpoons 2$)[2] which further extends the scope of the cycloaddition reaction.

The oxazolines (3a,b) undergo 1,3-dipolar cycloaddition reactions via their mesoionic oxazolium tautomers (4a,b).[3] The cyclic dipolar species (4) are favoured by the aromatic nature of the oxazolium species whereas the acyclic species (2) do not possess this special stability. Nevertheless we have recently shown that the imines (5) undergo a wide range of 1,3-dipolar cyclo addition reactions via their azomethine ylid tautomers (2; X = CHAr, Y=N, Z = $C(R)CO_2Me$.[4] We now report that arylhydrazones undergo similar cycloaddition reactions and suggest that they are a further example of the tautomeric equilibrium ($1 \rightleftharpoons 2$) where X = CHAr, Y = N, ZH = NHAr. Furthermore we find the cycloaddition can accommodate a range of functional groups. Two earlier reports of reactions of phenyl hydrazones with dimethyl acetylenedicarboxylate (ADE) reported low yields and mixtures of products[5] and interpreted their results in a different way. We find that the arylhydrazones (6a,b) react with N-phenyl maleimide in degassed xylene at ~ 150° to give the corresponding pyrazolidines (7a; 84%) and (7b; 87%). Reaction of (6a, c, and d) with N-phenylmaleimide in the presence of air gave the corresponding pyrazolines (8a; 48%), (8c; 26%) and (8d; 49%), whilst the pyridine derivative (9) gave (10; 13%). The instability of pyrazolidines and phenylhydrazones to aerial oxidation is illustrated by the conversion of (7a) to (8a) on keeping in chloroform solution at room temperature and the reported isolation of a phenylhydrazone radical dimer, from the reaction

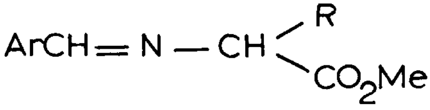


(1) (2)



(3) a. X = O
b. X = S

(4)



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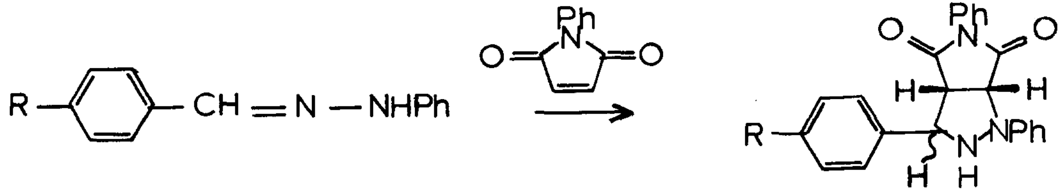
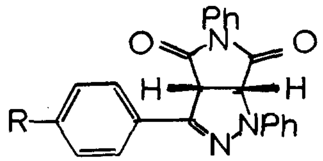
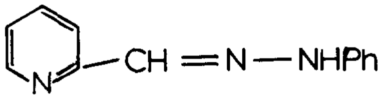


(6) a. R = H
b. R = OMe
c R = NMe_2
d. R = NO_2

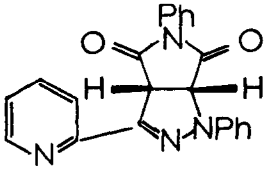
(7)



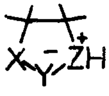
(8)



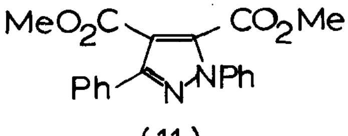
(9)



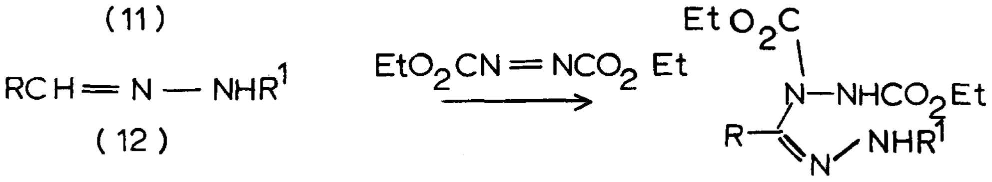
(10)



(14)



(11)



(12) (13)

of p-chlorobenzaldehyde phenylhydrazone with ADE in boiling methanol.[5] We find that reaction of (6a) with ADE in boiling xylene in the presence of air leads directly to the pyrazole (11; 27%). This is a significant improvement on the yield reported previously.[5] An analogous 1,3-dipolar cycloaddition might precede ring opening-rearrangement in the reaction of hydrazones with azodicarboxylic acid esters (12 → 13).[6] An example of tautomerism (1 ⇌ 2) leading to 1,3-dipolar cycloaddition has been observed for 1(2H)-phthalazinone, a cyclic hydrazone,[7] and a related tautomerism is probably involved in cyclo additions to 3-pyridinols.[7]

Two reports of very low yield cycloadditions involving tautomeric equilibration of oximes with the corresponding nitrones (1 ⇌ 2; $X = CH_2$ $Y = N$, $ZH = OH$) have appeared. Thus three variations of X, Y and Z in (1) have been identified and work is proceeding on testing the scope of (1 ⇌ 2) as a means of achieving cycloaddition reactions.[9]

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2. Equilibria involving a number of other neutral and charged species are also possible but are ignored for the sake of brevity.
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9. It should be noted that X = Y - ZH systems where Z is an atom possessing a lone pair of electrons could also undergo cycloadditions in the neutral state, initially producing a charged product (14), which on proton transfer would give the observed neutral species. However the 1,3-dipole, though only expected to be present in very low concentration, will be enormously more reactive.