A PERICYCLIC CASCADE IN THE ADDITION OF DIPHENYL NITRILE IMINE TO PYRIDINE#

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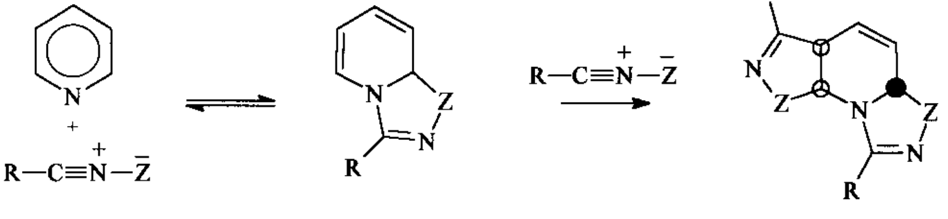
Abstract - On refluxing in benzene in the presence of excess pyridine the monocycloadduct of diphenyl nitrile imine to pyridine smoothly undergoes a [1,5] sigmatropic shift and a subsequent electrocyclic opening to afford 1,2,4-triazole derivatives.

Nitrile oxides add to pyridine to afford the isolable biscycloadducts (**B**) in fair yields.[1,2] The monocycloadducts (**M**) are labile intermediates in equilibrium with the reactants and are unstable towards cycloreversion.

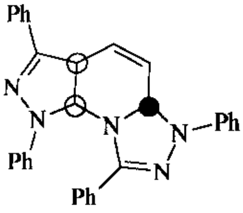


Z = O, NPh **M** **B**

#- Dedicated to Professor Rolf Huisgen on the occasion of his 75th birthday.

On the other hand diaryl nitrile imines afford isolable monocycloadducts which revert to the reactants upon heating.[3-5] The monocycloadducts show only a poor dipolarophilic activity towards nitrile imines and the formation of a bisadduct of type (**B**) in a very low yield was reported in a single case.[5]

We found that the generation of 2 equivalents of diphenyl nitrile imine (DPNI) from *N*-phenylbenzhydrazonoyl chloride and triethylamine in the presence of pyridine in refluxing benzene (Δ, 2 days) afforded a mixture of bisadduct (**1**), mp 207-209 °C, and the rearranged bisadduct (**2**), mp 173-174 °C, which could be isolated by column chromatography with 18 and 43% yields, respectively.



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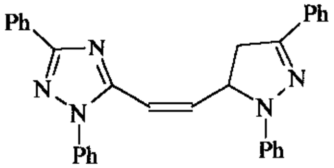

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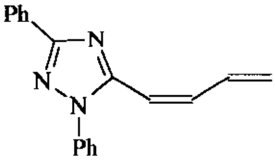

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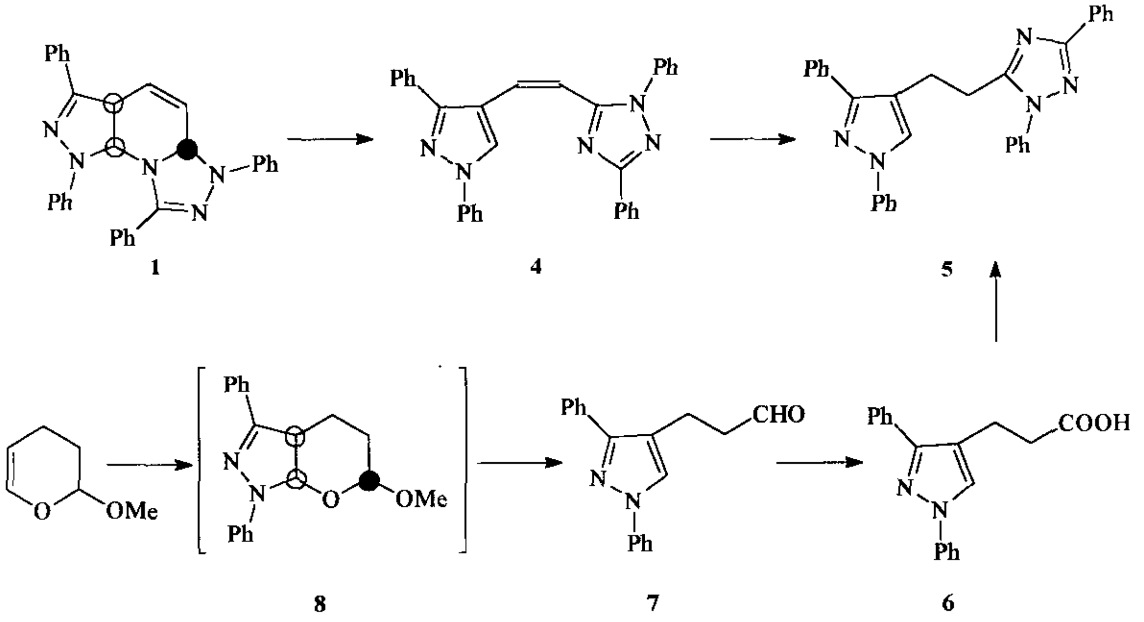
The product distribution is dramatically affected by changes in the ratio of the reactants. When performing the reaction with a higher hydrazonoyl chloride / pyridine molar ratio (4 : 1) bisadduct (**1**) becomes the major product in the mixture (nmr, tlc), while in reactions performed with lower ratio (1 : 1 or 1 : 2) it virtually disappears. With a larger excess of pyridine, increasing amounts of the diene (**3**) are formed along with the rearranged bisadduct (**2**). The diene (**3**), a formally rearranged monocycloadduct, becomes finally the major product in reactions performed in the presence of a very large excess of pyridine (100 equivalents) or even in pyridine itself (Δ, 1 day) and could be isolated from these runs in fair yields (50%) as an oil by column chromatography, along with some bisadduct (**2**) (2 - 5%).

The structures (**2**) and (**3**) of the rearranged adducts are based on spectroscopic[6] as well as on chemical evidence. Diene (**3**) adds DPNI (benzene, Δ, 6 h) to afford **2** (78%), while catalytic hydrogenation of **3** (ethanol, 10% Pd/C) affords the saturated 1,3-diphenyl-5-butyl-1,2,4-triazole, colorless oil, bp 190-200 °C (bath)/0.01 mm Hg, identical with a sample obtained by cycloaddition of DPNI to excess valeronitrile (benzene, Δ, 2 days, 73%).

The spectroscopic data of bisadduct (**1**) closely correspond to those reported by Grubert *et al.*[5] We obtained further structural evidence for bisadduct (**1**) as shown in the Scheme 1. As in the case of the bisadducts of benzonitrile oxide to pyridine,[2] bisadduct (**1**) is easily oxidized (iodine in benzene, exposure to Jones reagent or even standing in solvents) with opening of the pyridine ring to afford the Z-alkene (**4**),[7] mp 171-172 °C. Catalytic hydrogenation (ethanol, 10% Pd/C) of **4** provides the saturated derivative (**5**), mp 137-138 °C, identical with a sample obtained from the acid (**6**) through a classical 1,2,4-triazole synthesis by condensation of the acid chloride with the appropriate amidrazone.[8] The acid (**6**), mp 142-144 °C, is readily available by Jones oxidation of the oily aldehyde (**7**) which is the main product of the cycloaddition of DPNI to excess 3,4-dihydro-2-methoxy-2*H*-pyran (benzene, Δ, 2 days) and derives from the hydrolysis of cycloadduct (**8**) during the chromatographic separation.

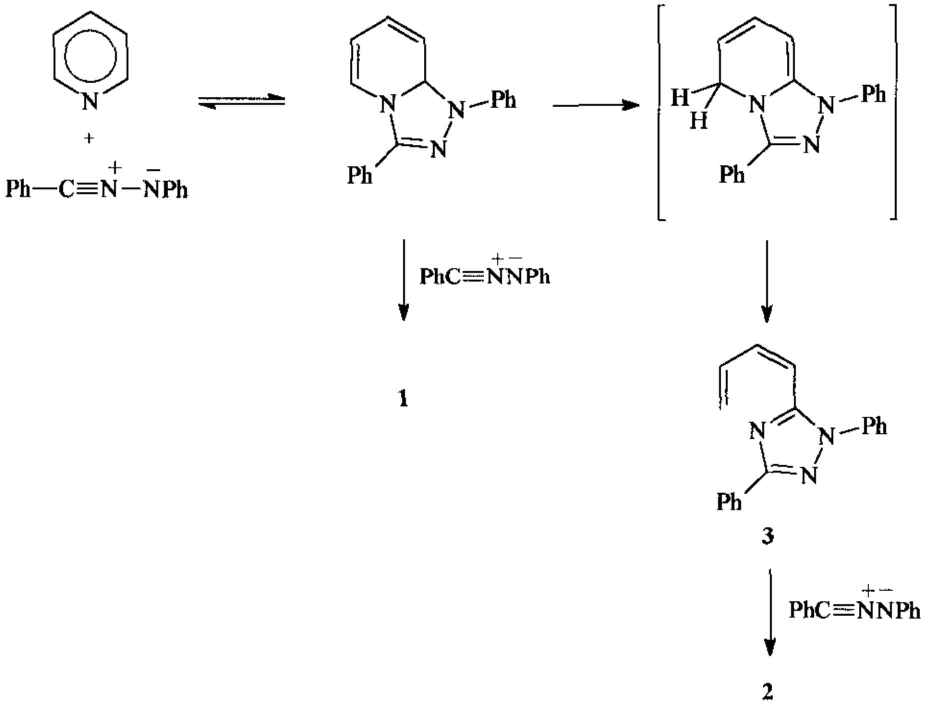
Scheme 1



The results discussed above clearly show that the formation of the "regular" bisadduct (**1**) is favoured by the availability of nitrile imine while the presence of excess pyridine drives the reaction towards the rearranged products. A reasonable rationalization is outlined in Scheme 2.

The first cycloaddition step in Scheme 2 is reversible at 80 °C. The adducts of nitrile imines to pyridine cyclorevert by heating in benzene affording the free nitrile imines, which can be trapped with dipolarophiles, and this technique of generation of nitrile imines has been occasionally used for preparative purposes.[3,9] In the presence of excess pyridine the equilibrium between the reactants and the monocycloadduct is clearly shifted to the right. Thus excess pyridine scavenges the nitrile imine and prevents the formation of bisadduct (1). Under these conditions, in which cycloreversion and further cycloaddition are disfavoured, the monocycloadduct enters the rearrangement route. A thermally allowed [1,5] suprafacial sigmatropic shift followed by an electrocyclic opening leads to diene (3).

Scheme 2



In the presence of only a moderate excess of pyridine, there is still enough free nitrile imine to add to the highly reactive diene system of **3** affording the rearranged bisadduct (**2**). With a large excess of pyridine the stationary concentration of nitrile imine becomes too low and the reaction stops at the diene stage.

The [1,5] sigmatropic shift takes place under relatively mild conditions, the same which can be found in the case of cycloheptatrienes:[10] they are, in fact, isoelectronic with our dihydropyridine system. The electrocyclic ring opening of dihydropyridine derivatives is well documented[11,12] and is presumably facilitated in our case by the formation of the aromatic 1,2,4-triazole ring.

ACKNOWLEDGEMENTS

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6 Bisadduct (**2**), ^{1}H-nmr ($CDCl_3$): δ 3.15 (dd, J = 17 and 6.8 Hz) and 4.00 (dd, J = 17 and 11.5 Hz, 4-pyrazolinic Hs); 6.20 (dd, J = 11.5 and 8.5 Hz) and 6.42 (dd, J = 11.5 and 1.2 Hz, olefinic Hs); 6.45 (m, J = 11.5, 8.5, 6.8 and 1.2 Hz, 5-pyrazolinic H); 6.8 - 8.4 (m, 20 aromatic Hs) ppm.
Diene (**3**), ^{1}H-nmr ($CDCl_3$): δ 5.53 (dd, J = 11 and 2 Hz) and 5.56 (J = 17 and 2 Hz, terminal $=CH_2$); 6.16 (dd, J = 11 and 1 Hz) and 6.49 (t, J = 11 Hz, 1- and 2-butadienyl Hs); 7.4 - 7.6 (m, 8 aromatic Hs); 8.10 (m, J = 17, 11, 11 and 1 Hz, 3-butadienyl H); 8.2 - 8.3 (m, 2 aromatic Hs) ppm.

7 Z-alkene (**4**), ^{1}H-nmr ($CDCl_3$): δ 6.25 (d, J = 13 Hz) and 6.80 (d, J = 13 Hz, olefinic Hs); 7.25 - 7.7 (m, 20 aromatic Hs); 10.21 (s, 5-pyrazolinic H) ppm.

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