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EVIDENCE OF A 1,4-DIPOLE INTERMEDIATE IN THE REACTION OF 1-PHENYL-4-VINYLPYRAZOLE WITH PTAD

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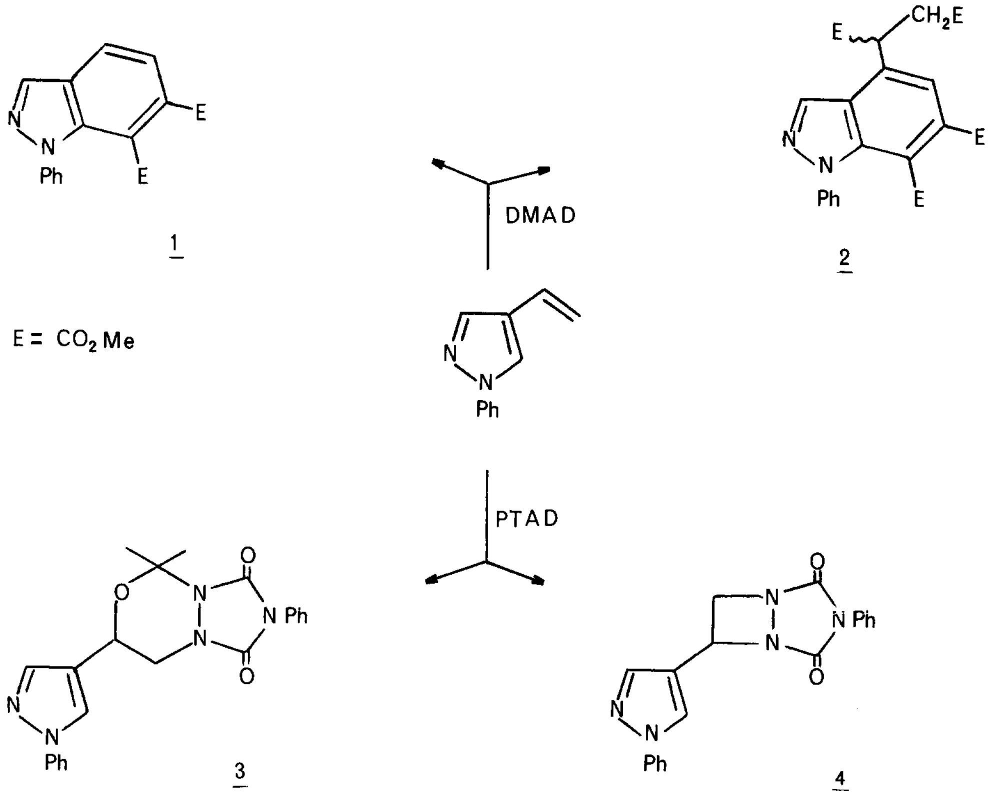
Abstract: 1-Phenyl-4-vinylpyrazole reacts with 1-phenyl-1,2,4-triazoline-3,5-dione in methylene chloride to form an unstable azetidine (4). An intermediate 1,4-dipole is probably involved since, when the reaction is conducted in acetone, a 1:1:1 adduct (3) is isolated.

In a previous publication[1] we reported that 1-phenyl-4-vinylpyrazole reacted with dimethyl acetylenedicarboxylate (DMAD) in dichloromethane at 150°C under a pressure of 8-10 atmospheres to yield the indazole (1) and, in the absence of the solvent, a 1:2 adduct (2).

Although, in theory, the pyrazole or ethenylpyrazoles can react with dienophiles to give the Diels-Alder adducts, the reaction destroys the "aromaticity" of the pyrazole ring and, for this reason, this type of reaction is almost unknown.[2]

The preparation of the indazole (1) is the first example of a Diels-Alder reaction involving this heterocyclic ring so we considered it would be of interest to study the reactivity of 1-phenyl-4-vinylpyrazole with 4-phenyl-1,2,4-triazoline-3,5-dione(PTAD). This reagent is a stronger dienophile than the acetylenic ester,[3] so we would expect a more facile formation of the Diels-Alder adduct and, more importantly, it cannot behave as a diene in its reaction with alkenes, as observed in analogous reactions involving diethyl azodicarboxylate,[4] thereby excluding the formation of dihydro-oxadiazines.

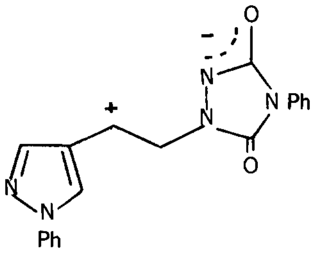
In the present work we have found that 1-phenyl-4-vinylpyrazole reacts with PTAD at -60°C in acetone to give, as the major product, 2,2-dimethyl-4(1-phenylpyrazol-4-yl)-8-phenyl-1,6,8-triaza-3-oxabicyclo(4,3,0)nona-7,9-dione (3), a new tetrahydro-oxadiazine that could be isolated, as a thermally stable white crystalline compound (m.p. 225°C), by column chromatography using a mixture of hexane-ethyl acetate (2:3) in a total yield of 40%.[5] When the same reaction was carried out in dichloromethane an unstable product was obtained, which was difficult to characterize. However, the available evidence, in particular the appearance of a multiplet of signals in the 'H NMR spectrum between δ3.8 and 4.5 integrating for three protons, suggests that the azetidine (4) is formed.



It has been postulated that azetidines arise from 1,4 dipolar intermediates[6,7] and there are only three known examples where the zwitterionic species could be trapped with an external trap (water[8] and acetone[9,10]). The isolation of the tetrahydro-oxadiazine (3) indicates that the unusually stable 1,4-dipolar species (5) is formed as a reactive intermediate via the initial reaction of the nitrogen double bond of PTAD with the olefinic double bond of the vinylpyrazole. The reactivity of the 1,4-dipoles is quite sensitive to stabilization of its positive centre and it has been reported that, in the reaction of PTAD with vinyl ethers, stronger carbonium ion-stabilizing substituents increase the yields of the oxadiazine[9] and higher reaction rates were observed.[10] The reactivity of the 1,4-dipole must be critical to add across the weak dipolarophilic carbonyl group of alkyl ketones and various authors have examined olefins, other than vinyl ethers, in order to test whether this long-lived intermediate intervenes in similar reactions but they have failed to obtain sound evidence in all cases.[11,12]

Measurement of the C=O stretching vibration of acyl derivatives has been used to estimate the electron character of heteroaromatic rings, compared with the benzene nucleus. The pyrazole ring is more electron-donating than the phenyl ring and the highest electron releasing capacity appears to occur at the 4-position.[13] The isolation of the tetrahydro-oxadiazine in relatively high yield suggests that the 1,4-dipole (5) is a long-lived intermediate stabilized by the pyrazole ring and is the first example involving an ethenyl heterocyclic compound.

In spite of the strong dienophilic character of the PTAD no Diels-Alder adducts were detected and the pyrazole ring again shows its poor reactivity to undergo cycloaddition reactions.



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5. Recrystallised from carbon tetrachloride:chloroform (9:1). Found: C, 65.6; H, 5.2; N, 17.6. $C_{22}H_{21}N_5O_3$ requires C, 65.5; H, 5.2; N, 17.4% ν_{max} 1750 cm^{-1}; δ_H (60 mHz, $CDCl_3$) 1.65 (s, 3H), 1.95 (s, 3H), 3.3 (dd. J 12 and 11Hz, 1H), 4.15 (dd. J 12 and 4Hz, 1H) 5.0 (dd. J 11 and 4Hz, 1H) 7.25 (m, 8H), 7.5 (s, 1H), 7.7 (s, 1H); δC, 19.63(q), 27.34(q). 48.13(t), 63.97(d), 89.98(s), 119.27(d), 120.22(s), 125.14(d), 125.47(d), 126.79(d), 128.05(d), 128.57(d), 129.38(d), 131.17(s), 134.04(s), 138.85(d), 150.67(s), 151.20(s).
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