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EXTENDED DIPOLAR CYCLOADDITION REACTIONS OF 3-DIAZOPYRAZOLES WITH ELECTRON RICH OLEFINS

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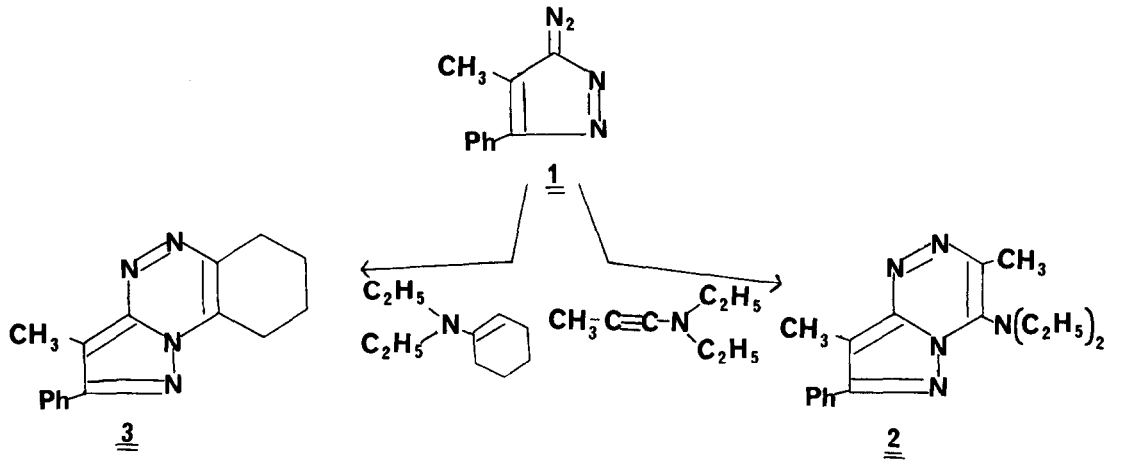
Abstract: 3-Diazo-4-methyl-5-phenylpyrazole readily adds to electron rich olefins to give 1,7-cycloadducts. The mechanism of the reaction consists of an initial 1,3-dipolar cycloaddition followed by a subsequent rearrangement.

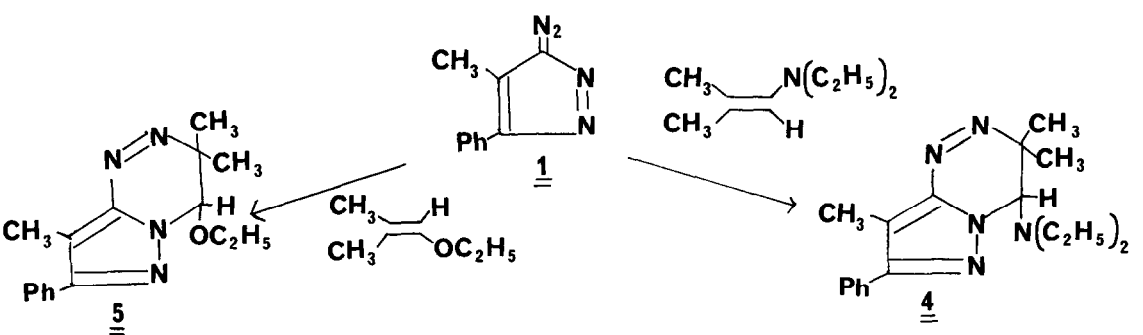
1,3-Dipolar cycloadditions have been shown to be an astonishingly fruitful synthetic method for the preparation of five-ring heterocycles.[1-3] Numerous possibilities for variation are available by changing the structure of both the dipolarophile and dipole. The additions of diazoalkanes to olefins are among the most thoroughly studied 1,3-dipolar cycloadditions.[4] The cycloadditions of simple diazoalkanes are HO(1,3-dipole)-LU(dipolarophile) controlled.[5-7] The use of extended diazoalkanes with six or more π-electrons in cycloadditions has received only a minimum amount of attention despite the considerable synthetic and theoretical interest associated with such processes.[8-11] We became interested in the reactions of heterocyclic diazo compounds with added dipolarophiles in connection with our studies of extended dipolar cycloadditions. In this communication we report on our work with 3-diazopyrazoles which undergo ready dipolar cycloaddition with electron-rich olefins.

3-Diazo-4-methyl-5-phenylpyrazole (1) was prepared by diazotization of the corresponding amine with nitrous acid in hydrochloric acid followed by neutralization with aqueous sodium carbonate.[12] The cycloaddition of 1 with various electron rich olefins was performed in methylene chloride solutions, the reaction mixture being stirred in the dark at room temperature. The end of the reaction was judged by the disappearance of the diazo compound according to ir and tlc analysis. The reaction times varied from a few hours to several days. The products obtained from the reaction of 1 with N,N-diethylaminopropyne and N,N-diethylaminocyclohexene were identified as pyrazolo[5,1-c]triazines 2 and 3. The cycloadducts were isolated in high yield and gave satisfactory elemental analyses. The spectroscopic properties of the cycloadducts were in excellent agreement with the proposed structures. The formation of 3 can be rationalized by elimination of diethylamine from an initially

formed 1,7-cycloadduct.

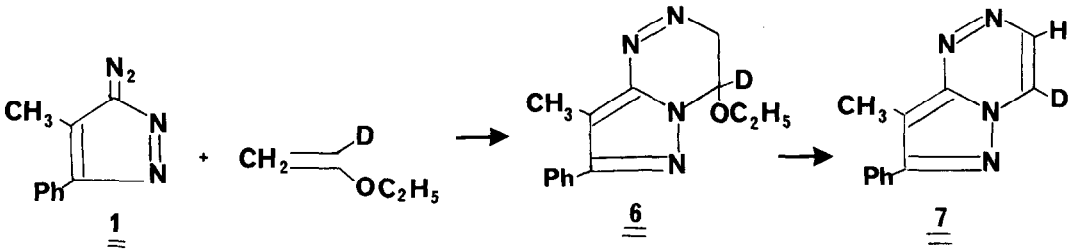


Analogous cycloadditions were observed with related dipolarophiles. The reaction of 3-diazopyrazole 1 with N,N-diethylamino-2-methyl-1-propene at room temperature for 12 hr gave the 1,7-cycloadduct 4 in high yield; NMR ($CDCl_3$,90 MHz) δ 0.93 (t, 6H, J=6.0 Hz), 1.12 (s, 3H), 1.81 (s, 3H), 2.34 (q, 4H, J=6.0 Hz), 2.63 (s, 3H), 4.83 (s, 1H) and 7.3-7.9 (m, 5H). A similar [7+2]-cycloaddition occurs on treatment of 1-ethoxy-2-methyl-1-propene with diazopyrazole 1. The exclusive regioisomer formed was identified as dihydropyrazolotriazine 5; NMR ($CDCl_3$,90 MHz) δ 1.05 (s, 3H), 1.08 (t, 3H, J=6.0 Hz), 1.92 (s, 3H), 2.65 (s, 3H), 3.59 (q, 2H, J=6.0 Hz), 5.02 (s, 1H) and 7.2-7.9 (m, 5H).

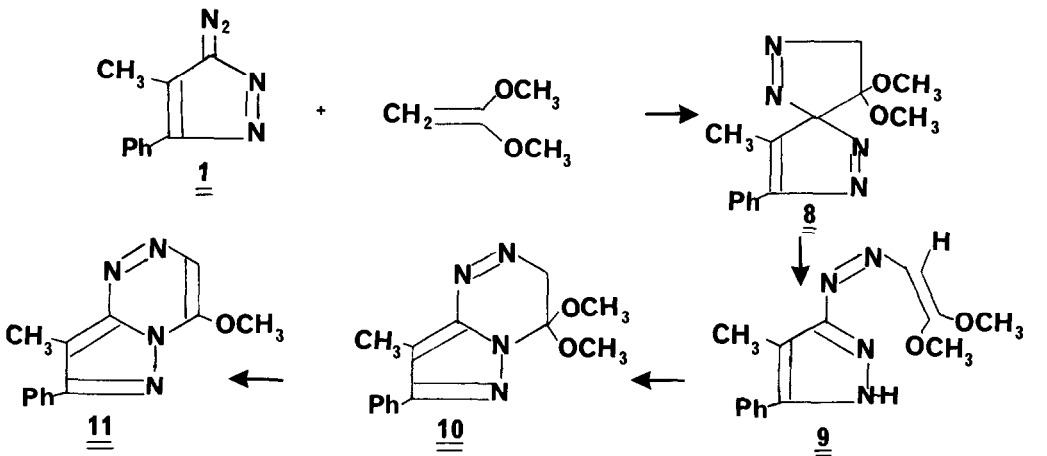


Reaction of 1 with ethyl vinyl ether gave 7-phenyl-8-methylpyrazolo[5,1-c]triazine 7 as a yellow crystalline solid, mp 180-180°C; NMR ($CDCl_3$,60 MHz) δ 2.77 (s, 3H), 7.3-7.9 (m,

5H), 8.38 (d, 1H, J=5.0 Hz) and 8.63 (d, 1H, J=5.0 Hz). When the reaction was carried out using 1-deuterio ethyl vinyl ether, the deuterium atom was found to be located exclusively in the 4-position of the triazine ring.



Formation of the above cycloadducts can be rationalized in terms of a novel 1,7-dipolar cycloaddition. Such a [8π + 2π] addition is an orbital symmetry allowed process. A reasonable alternative to the concerted 1,7-cycloaddition is a two-step mechanism consisting of an initial 1,3-dipolar cycloaddition followed by a subsequent rearrangement. We have obtained evidence that the formation of the pyrazolotriazine ring occurs by the stepwise process. Thus, treatment of 1 with 1,1-dimethoxyethene at 25°C for 2 days gave pyrazolotriazine 11; NMR ($CDCl_3$,90 MHz) δ 2.71 (s, 3H), 4.31 (s, 3H), 7.4-8.0 (m, 5H) and 8.42 (s, 1H). A study of product formation as a function of time established the presence of two intermediates in this transformation which could be isolated and fully characterized. At short periods of



time, 1,3-dipolar cycloadduct 8 was isolated in high yield; NMR ($CDCl_3$,90 MHz) δ 2.61 (s, 3H), 3.36 (s, 6H), 4.51 (s, 2H) and 7.4-8.0 (m, 5H). This material was slowly converted to pyrazole 9 [(NMR,$CDCl_3$) δ 2.11 (s, 3H), 3.31 (s, 6H), 6.53 (s, 1H), 7.1-7.7 (m, 5H) and 9.69 (s, 1H)] which, in turn, rearranged to 11 upon standing at room temperature. The conversion of 9 to 11 most likely proceeds by the elimination of methanol from structure 10.

In conclusion, the 1,7-dipolar cycloadducts isolated from the reaction of 3-diazopyrazole with various electron rich dipolarophiles are the result of a concerted [3+2]-cycloaddition followed by a subsequent reorganization.

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