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# A NOVEL SYNTHESIS OF PYRIDAZINES: INVERSE ELECTRON DEMAND DIELS-ALDER REACTION OF TETRAZINES WITH ACYCLIC DIENAMINES

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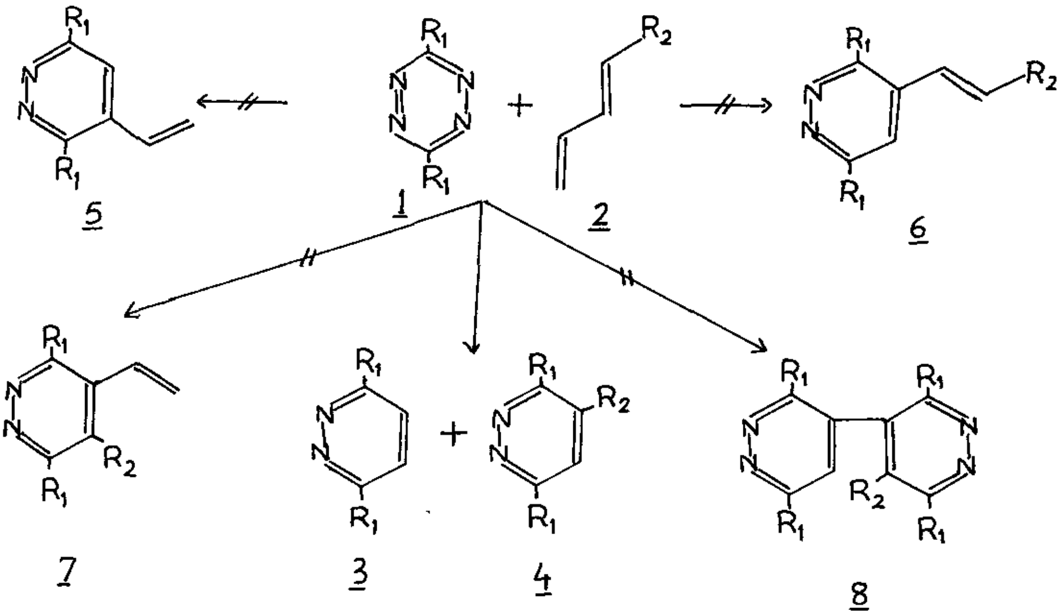
Abstract - Tetrazines (1) when reacted with dienamines (2) furnished, pyridazines (3) and (4) in good yields. This appears to be the first case wherein the intermediate bipyridazines (8) have fragmented to (3) and (4) prefering rupture of carbon-carbon bond.

Cycloaddition reactions have been of great value in organic synthesis and there does not appear to be any other single reaction which could parellel to this strategy[1]. The Diels-Alder reaction though discovered several years ago continues to be the central theme in the synthesis of complex organic molecules[2]. Inverse electron demand Diels-Alder reaction is relatively of much more intensive interest and is the subject of latest investigations because of its recent recognition[3]. Tetrazines are reported to react with a variety of simple electron rich double bonds[4] with the extrusion of nitrogen. The reaction of dienamines with tetrazines does not appear to have been investigated systematically and in case of cyclic dienamines there are conflicting reports on this subject[5]. Here we describe our results of reaction of tetrazines (1) with simple acyclic dienamines (2) produced in situ as well as isolated in purified from and then reacted to obtain pyridazines (3) and (4) in good yields.

Reaction between 3,6-dianisyl 1,2,4,5-tetrazine (1a) and N,N-diethyl 1,3-butadienylamine (2a)[6] was carried out by dissolving their equimolar quantities in dry ether and stirring the reaction mixture at room temperature for 40 h. During this period the red colour of 3,6-dianisyl 1,2,4,5-tetrazine disappeared and a white crystalline solid separated was filtered, washed with ether and recrystallised from acetic acid to obtain the pyridazine (3a) mp. 235°C in 50% yield (based on $\underline{1a}$). The structure of ($\underline{3a}$) is fully corroborated by its spectral and elemental analysis. The mass spectrum of ($\underline{3a}$) showed molecular ion at m/z

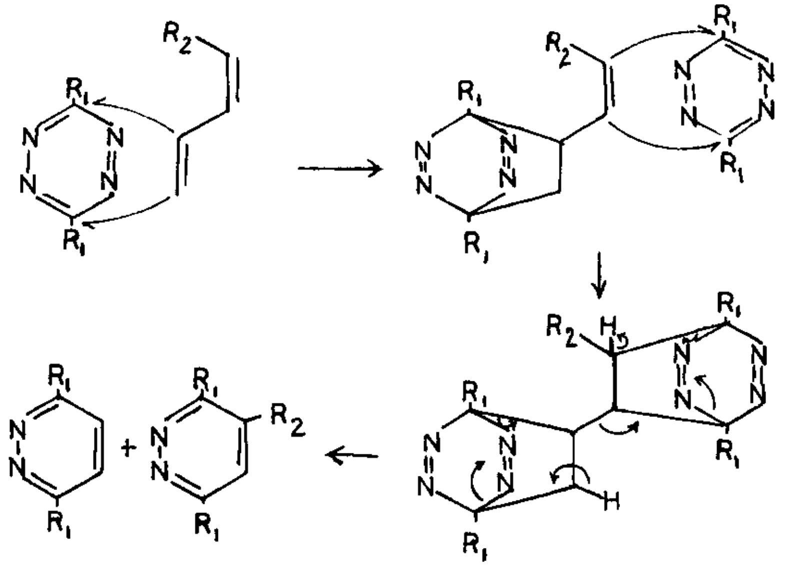


| | $R_1$ | $R_2$ | Yields $\underline{1}:\underline{2}$ = 1:1 | | $\underline{1}:\underline{2}$ = 2:1 | |
|---|---|---|---|---|---|---|
| | | | $\underline{3}$ | $\underline{4}$ | $\underline{3}$ | $\underline{4}$ |
| a | $C_6H_4OCH_3(p)$ | $NEt_2$ | 50% | 30% | 45% | 30% |
| b | $C_6H_4OCH_3(p)$ | $NMe_2$ | 40% | 25% | 40% | 24% |
| c | $C_6H_5$ | $NEt_2$ | 50% | 40% | 48% | 35% |
| d | $C_6H_5$ | $NMe_2$ | 41% | 25% | 40% | 25%. |

292 ($M^+$). $^1H$ NMR ($CDCl_3$) $\delta$ : 3.90 (6H, s, $OCH_3$), 7.06-8.11 (10H, m). Anal. calcd. for $C_{18}H_{16}O_2N_2$ : C, 73.97 ; H, 5.47 ; N, 9.58 ; Found : C, 73.83 ; H, 5.31 ; N, 9.69.

Usual work up of the mother liquor of this reaction mixture gave an oily material on concentration, which was purified by preparative tlc to obtain a thick oily liquid in 30% yield (based on $\underline{1a}$) and is assigned the structure ($\underline{4a}$). The structure ($\underline{4a}$) is also confirmed by elemental and spectral analysis. $^1H$ NMR ($CDCl_3$) $\delta$ : 3.88 (6H, s, $OCH_3$), 0.75 (6H, t), 2.41 (4H, q), 6.65-7.40 (9H, m) ; m/z 363 ($M^+$). Anal. calcd. for $C_{22}H_{25}N_3O_2$ : C, 72.72 ; H, 6.88 ; N, 11.57 ; Found : C, 72.60 ; H, 6.73 ; N, 11.63.

Similarly were prepared pyridazines (<u>3b - d</u>) in satisfactory yields. In each case (<u>3b - d</u>) were isolated and confirmed by comparison with an authentic sample[7]



as well as spectral analyses. The formation of (<u>4b - d</u>) in each case was established vide tlc and these oily materials were proportionate to (<u>3</u>). Regarding the mechanism of this reaction a plausible scheme is depicted above[8].

As indicated in the scheme it appears that one mole of the tetrazine first attacked the terminal double bond of the dienamine followed by the attack of second mole on the enamine double bond. If enamine double bond would have reacted first vinyl pyridazines (<u>5</u>) or (<u>7</u>) would have been the product instead of (<u>3</u>) and (<u>4</u>), which is not observed here. The product (<u>6</u>) would have the sole product if the reaction would have stopped by reacting at the terminal bond of the dienamines. It is also interesting to note here, even under so mild conditions carbon-carbon rupture has occurred rather than the formation of bipyridazines (<u>8</u>). When two moles of tetrazine were used in the above reactions proportionately higher yields of pyridazines were obtained thereby confirming the postulate that two moles of (<u>1</u>) react with one mole of (<u>2</u>). Further scope and details of this reactions are under investigations.

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   b) The new pyridazines encountered in this investigation gave satisfactory spectral as well as microanalyses.
8. We thank one of the referees for his comment on the mechanism and for making the suggestion in favour of ionic and stepwise process ; which would be very useful to us in our further investigations on this aspect of this reaction.

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