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# Synthesis of Aryl- and Hetarylpyrazoles

## Short Communication

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Hetaryldieneamines (**1**) react with sulfonyl azides to give 3-hetarylpyrazoles (**5**). Similarly, N,N-dimethyl-4-phenyldieneamine-2-carboxylic acid methyl ester (**6**) affords 3-phenylpyrazole-5-carboxylic acid methyl ester (**7**).

*(Keywords: Cycloaddition; Dieneamine; Ring closure)*

*Synthese von Aryl- und Hetarylpyrazolen (Kurze Mitteilung)*

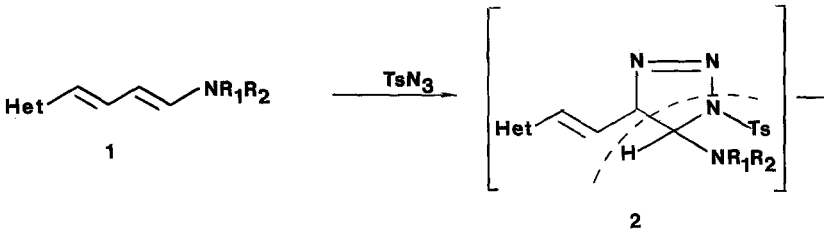
Reaktion von Hetaryldienaminen (**1**) mit Sulfonylaziden führt zu 3-Hetarylpyrazolen (**5**). N,N-Dimethyl-4-phenyldienamin-2-carbonsäure-methylester liefert dabei 3-Phenylpyrazol-5-carbonsäure-methylester.

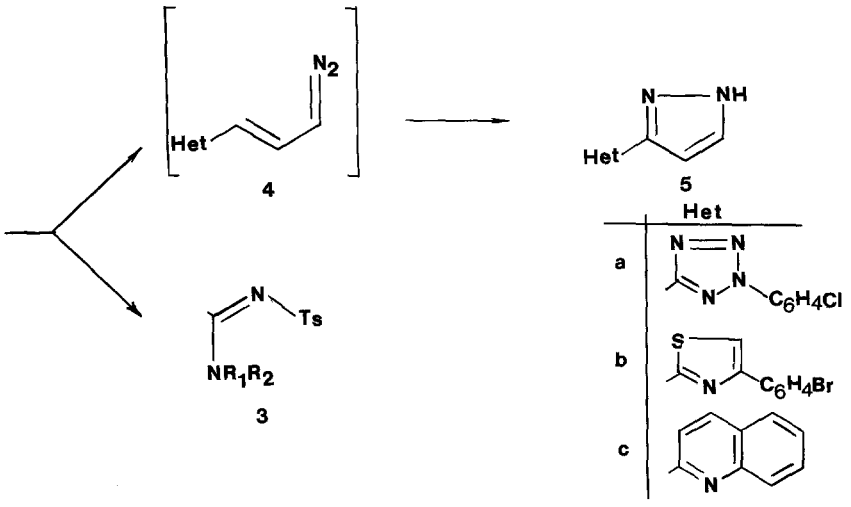
Recently we have reported [1, 2] that hetaryldieneamines available from fused azolium and azinium salts by nucleophilic treatment undergo various cycloaddition reactions to yield ring closed products bearing hetaryl substituents; e.g., reactions with arylazides lead [2] to hetaryl substituted v-triazoles.

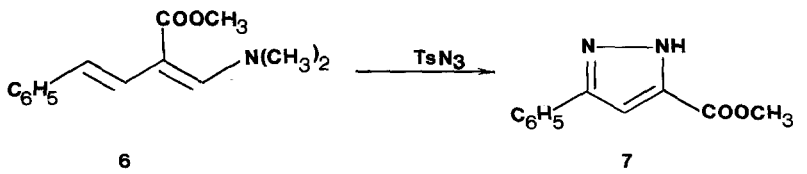
Some literature data concerning enamine chemistry [3–5] indicated that arylazides and sulfonyl azides can react in considerably different ways. Earlier papers reported [6] that simple dieneamines undergo cycloaddition with sulfonylazides and result in pyrazoles. This literature background prompted us to investigate this reactivity of hetaryldieneamines in detail.

We found that hetaryldieneamine **1a** reacted with tosylazide under mild conditions (compared to reactions with arylazides) and 3-tetrazolylpyrazole **5a** could be prepared in moderate yield. This reaction can

be interpreted by supposition of formation of intermediate **2** undergoing fragmentation to give formamidine derivative **3** and diazo compound **4**. Diazoalkenes such as **4** prepared by an independent route were earlier found [7] to undergo cyclization to pyrazoles. In an analogous way, intermediate **4** afforded the pyrazole compound **5 a**. Careful work-up of the crude product by appropriate crystallization allowed isolation of the



supposed by-product **3** ($NR_1R_2$ = morpholino), an evidence supporting the proposed mechanism.

This reaction could be successfully extended for different hetaryldieneamines. Thus, thiazolylpyrazole **5 b** and pyrazolylquinoline **5 c** were also prepared in acceptable yields.

Similarly to hetaryl dieneamines, aryldieneamines were also found to react in an analogous manner. Thus, dieneamine **6** prepared by the procedure of *Gompper* et al. [8] gave 3-phenylpyrazole-5-carboxylic acid methyl ester (**7**) obtained earlier by an independent synthesis [9]).

The authors believe that this reaction seems to be a convenient approach to hitherto unknown aryl and hetaryl pyrazoles.

## Experimental Part

The nmr spectra were obtained on a Varian XL-100 equipment, the ir spectra on a Specord 75 apparatus. Melting points are uncorrected.

Hetaryldieneamines (**1 a**, **b** [1], **1 c** [10]) were prepared according to the literature.

*Reaction of Dieneamine* **1 a** *with Tosyl Azide*

To a solution of dieneamine **1 a** (0.63 g, 2 mmol) in tetrahydrofurane (10 ml), a solution of tosyl azide in benzene (0.7 molar solution, 3.0 ml, 2.1 mmol) was added and the mixture was allowed to stand in a refrigerator (5 °C) for 24 h. The resulting yellow mixture containing few crystals was evaporated to a volume of 5 ml and the precipitate was filtered. Recrystallization from acetonitrile afforded 0.24 g (45%) of 2-(4-chlorophenyl)-5-(3-pyrazolyl)-tetrazole (**5 a**), m.p. 212–213 °C. An additional quantity (0.05 g, 9%) could be recovered from the mother liquour by chromatography on silica using ether as eluent ($R_f = 0.9$).

Anal. calcd. for $C_{10}H_7ClN_6$ (246.67): C 48.69, H 2.86, N 34.07. Found: C 48.71, H 3.16, N 33.75. MS: 246 ($M^+$), 218 (*M*-28), 125, 100, 90. $^1$H-NMR ($CDCl_3$ – *DMSO-d*$_6$): 12.3 (s, 1 H, NH), 7.59 (d, 1 H, H-4 pyrazole, $J = 1.4$ Hz), 7.55 and 6.99 (AA'BB', 4 H, H-*Ar*), 6.91 ppm (d, 1 H, H-5 pyrazole). $^{13}$C-NMR (*DMSO-d*$_6$): 110 (d, C-4), 121 and 131 (2 C doublets, C-*Ar*), 135 ppm (d, C-3).

The mother liquor obtained after separation of compound **5 a** was evaporated *in vacuo* and the residue was treated with ether to give 0.22 g of precipitate which was recrystallized from acetonitrile and then from toluene: N-tosyl-formiminomorpholine (**3**) was obtained in 25% yield (0.132 g).

Anal. calcd. for $C_{12}H_{16}N_2O_3S$ (268.34): C 53.71, H 6.01, S 11.95. Found: C 53.78, H 6.21, S 11.65. MS: 268 ($M^+$), 155, 113, 91, 86. $^1$H-NMR (*DMSO-d*$_6$ – $CDCl_3$): 8.20 (s, 1 H, H-iminoformyl), 7.79 and 7.28 (AA'BB', 4 H, H-Ar), 3.84 and 3.62 (m, 8 H, H-morpholino), 2.49 (s, 3 H, $CH_3$) ppm.

According to the above procedure, the following products were also obtained starting from the appropriate dieneamines (**1 b**, **1 c** and **6**):

*3-[4-(4-Bromophenyl)thiazolyl-2]-pyrazole* (**5 b**)

Yield: 32%, m.p.: 154–156 °C. Anal. calcd. for $C_{12}H_8N_3BrS$ (306.11): C 47.06, H 2.61, N 13.73. Found: C 46.97, H 2.72, N 13.75. $^1$H-NMR (acetonitrile-$d_3$): 6.87

(d, 1 H, H-pyrazole, $J = 2.5$ Hz), 7.52 (d, 1 H, H-pyrazole, $J = 2.5$ Hz), 7.64 (s, 1 H, H-thiazolyl), 7.5–8.0 (AA'BB', 4 H, H-aryl).

*3-(2-Quinolyl)-pyrazole* (**5c**)

Yield: 48%, m.p. 159–160 °C. Anal. calcd. for $C_{12}H_9N_3$ (195.23): C 73.85, H 4.62, N 21.54. Found: C 73.95, H 4.62, N 21.45. $^1$H-NMR (acetonitrile-$d_3$): 7.06 (d, 1 H, H-4, $J = 2.2$ Hz), 7.73 (d, 1 H, H-5, $J = 2.2$ Hz).

*3-Phenylpyrazole-5-carboxylic acid methyl ester* (**7**)

Yield: 35%, m.p. 180–181 °C (Lit. m.p. 180–181 °C [9]).

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