

mit Calciumchlorid bei 0° getrocknet, filtriert und 2 Std. unter Rückfluss gekocht. Dann dampft man das Benzol ab und destilliert das Produkt bei 59°/0,15 Torr: 70 g **5c** (80%). n_D^{20} : 1,5200. IR. (fl.): 4,35, 14,03. UV. (C_6H_{12}): 2650 (4200). NMR. ($CDCl_3$): 1,53/s gem. CH_3 -; 2,34/d, $J = 7,1$ CH_2 -7; 5,24–5,48/m CH -6; 6,05–6,30/m CH -2 und CH -5; 6,53/m CH -3 und CH -4.

$C_{11}H_{13}NO$ (175,2) Ber. C 75,40 H 7,48 N 7,99% Gef. C 75,31 H 7,55 N 7,87%

2-(1-Cycloheptatrienyl)-isopropylamin (**5d**). Eine Suspension von 52,5 g (0,3 Mol) 2-(1-Cycloheptatrienyl)-isopropylisocyanat in 200 ml konzentrierter Salzsäure wird unter Rühren auf 40° erwärmt. Es entwickelt sich CO_2 und die Temperatur steigt auf 52° an (Kühlung). Man hält etwa 10 Min. auf 45°, bis die CO_2 -Entwicklung beendet ist, giesst dann die Lösung in 600 ml Eiswasser und extrahiert viermal mit Äther. Das Wasser und die Salzsäure werden im rotierenden Verdampfer bei höchstens 60° Badtemperatur im Vakuum abgedampft, bis ein dickes Öl und wenig Wasser zurückbleiben. Man gibt 400 ml 2 N Natronlauge hinzu, extrahiert viermal mit Äther und trocknet die ätherische Lösung mit Magnesiumsulfat. Dann dampft man das Lösungsmittel ab und destilliert das Amin bei 46°/0,4 Torr: 39,6 g **5d** (88,6%). n_D^{20} : 1,5327. IR. (fl.): 14,03. UV. (C_6H_{12}): 2670 (4000). NMR. ($CDCl_3$): 1,27/s gem. CH_3 -; 1,32/s $-NH_2$; 2,30/d, $J = 7,0$ CH_2 -7; 5,21–5,45/m CH -6; 6,03–6,28/m CH -2 und CH -5; 6,50/m CH -3 und CH -4.

$C_{10}H_{15}N$ (149,2) Ber. C 80,49 H 10,09 N 9,39% Gef. C 80,44 H 10,21 N 9,59%

LITERATURVERZEICHNIS

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59. Hetarylnitrenes V.¹⁾ Reactions of Tetrazolopyrazine Ring Contraction of Nitrenodiazines in Solution

Preliminary communication²⁾

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(3 I 72)

Summary. Thermolysis of tetrazolopyrazine (**1**) in organic solvents gives pyrazinylnitrene (**2**) which undergoes ring contraction to 1-cyanoimidazole (**3**). 7-Methyl-5-methylthio-tetrazolo[1,5-*c*]-pyrimidine (**4**) likewise gives 1-cyano-2-methylthio-4-methyl-imidazole (**6**). The two tetrazoles also undergo ring contraction to 1-cyanoimidazoles by gas chromatography, and **1** gives a low yield of **3** by photolysis. Thermolysis of **1** and **4** in cyclohexane gives aminopyrazine (**7**) and 6-amino-4-methyl-2-methylthio-pyrimidine (**8**), respectively. Tetrazolo[1,5-*a*]pyrimidines (**9**) give only 2-aminopyrimidines (**10**).

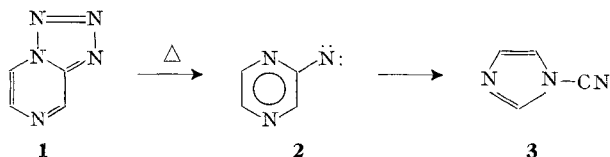
1-Cyanoimidazole, formed by thermolysis of **1** in acetic acid, reacts further to give 1-acetyl-imidazole, which with more acetic acid gives imidazole and acetic anhydride. An earlier report [2] of ring expansion of pyrazinylnitrene in acetic acid is discredited.

In protic deuteriated solvents (D_2O , CH_3OD), tetrazolopyrazine reacts as an enamine, specifically exchanging H—C(6) for deuterium.

¹⁾ Part IV: see [1].

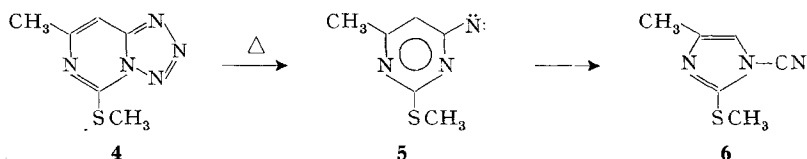
²⁾ A full paper will be submitted to *Helv.*

Aromatic and heteroaromatic nitrenes undergo ring contraction in the gas-phase [1] [3] [4], *e.g.*



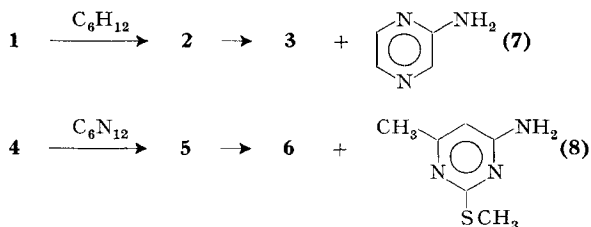
In some cases the formation of amines by hydrogen abstraction confirms the existence of nitrene intermediates [3] [4], but when the reaction is clean it is difficult or impossible to prove that a nitrene is involved. We now report the first examples of nitrene ring contraction in solution, which allow a closer inspection of the reacting species and investigation of the kinetics of its formation.

Thermolyses of tetrazolodiazines in solution (35–45 mg/ml) were performed in sealed NMR. tubes, and the progress of reaction followed by NMR. After reaction was complete the tubes were opened, the content extracted with CHCl_3 , filtered from insoluble polymer, the filtrate evaporated, and the composition of the product checked by IR., gas chromatography, and mass spectrometry. Results are presented in the Table. Tetrazolopyrazine (1) and 7-methyl-5-methylthio-tetrazolo[1,5-*c*]pyrimidine (4) gave 1-cyanoimidazoles 3 and 6, respectively.



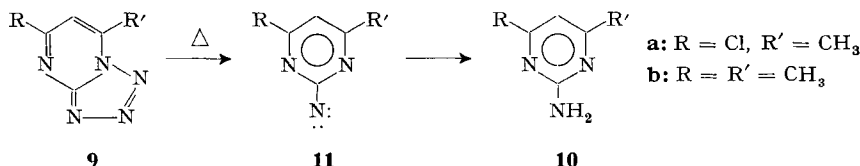
The same two products resulted from gas chromatography of 1 and 4, respectively, above 200° (see Table and [3]). By direct photolysis of 1, ring contraction occurred in low yield (see Table), but the main product was a yellow, insoluble compound (mp. $> 330^\circ$) which showed IR.-bands at $1700\text{--}1600$ and $3400\text{--}3200\text{ cm}^{-1}$, and presumably is formed by poly-condensation of the nitrene 2. It was insufficiently volatile for a mass spectrum to be obtained with a direct insertion probe at 250° .

Evidence for the involvement of nitrenes 2 and 5 was found by thermolysis in cyclohexane, which gave both the cyanoimidazoles 3 and 6, and the amines 7 and 8.



The yields were low in this reaction because the products (*e.g.* 3 and 7) react with each other, as was established by separate experiments, although no definite secondary products have been isolated. Insertion of pyrazinyl nitrene (2) into a C–H bond of

cyclohexane to give 2-cyclohexylamino-pyrazine was not observed. It is noteworthy that gas-phase thermolysis of **1** and **4** did not give detectable amounts of amines **7** and **8**, thus making it uncertain that nitrenes were actually involved [3].



Solution thermolysis of tetrazolo[1,5-*a*]pyrimidines (**9**) (**9a** is the most easily tautomerized into the azido-form [5]) gave only the amino-pyrimidines **10** (cf. [6]); by gas-phase thermolysis of tetrazolo[1,5-*a*]pyrimidines the aminopyrimidines are also predominant, besides 1-cyanopyrazoles [3]. Formation of **10b** from **9b** in CDCl₃ was accompanied by formation of **10-d**₂ and CHCl₃, indicating D-abstraction by the nitrene **11**, giving rise to CCl₃ radicals, which with a proton source gave CHCl₃.

Sasaki *et al.* reported recently [2] that thermolysis of 5,6-diphenyl-tetrazolo[1,5-*a*]pyrazine (**12**) in acetic acid resulted in the corresponding imidazole (**15**) and 1-acetylimidazole (**16**), for which they postulated *ring expansion* of the nitrene

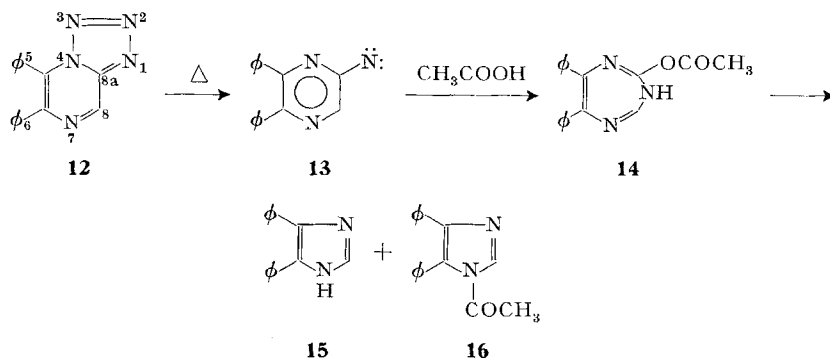
Thermolyses and Photolyses of Tetrazolodiazines

Compound	Reaction conditions			Solvent	Products (yield %)
1	Δ	125°	112 h	CDCl ₃	3 (4), 1 (12)
1	Δ	180°	6 h	C ₆ H ₆	3 (40)
1	Δ	125°	96 h	C ₆ H ₁₂	3 (trace), 7 (8), 1 (25)
1	$h\nu^a$	20°	36 h	CDCl ₃	3 (1), 1 (67), polymer (32 by weight)
1	$h\nu$	20°	48 h	C ₆ H ₆	3 (1), 1 (74), polymer (25 by weight)
1	GC. ^{b)}	300°			3 (50), 1 (50)
1	Δ	125°	120 h	CH ₃ COOH	19 (30), (CH ₃ CO) ₂ O (30), 1 (70)
1	Δ	125°	48 h	CH ₃ OD	20 (99+)
1	Δ	110°	16 h	D ₂ O	20 (99+)
4	Δ	125°	70 h	CDCl ₃	6 (40), 4 (55)
4	Δ	125°	48 h	C ₆ H ₆	6 (50)
4	Δ	125°	72 h	C ₆ H ₁₂	6 (trace), 8 (10)
4	GC.	300°			6 (100) [3]
9a	Δ	190°	168 h	CDCl ₃	10a (10), 9a (25), HCl
9b	Δ	190°	72 h	CDCl ₃	10b (60), 9b (6)

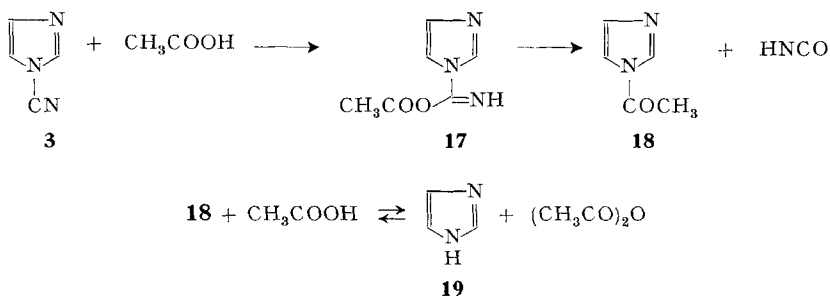
^{a)} $h\nu$: 75 W high-pressure Hg-lamp, Wycor glass.

^{b)} Gas chromatography on 20% carbowax on Chromosorb W, column temp. 180°; injection port temp. stated.

13 to a triazepine (e.g. **14**). We have shown that this postulate is not valid: the products are readily explained by primary *ring contraction* to 1-cyanoimidazole, as in the reaction **1** → **3**. Thermolysis of tetrazolopyrazine (**1**) in acetic acid gave imidazole and acetic anhydride (see Table). When 1-cyanoimidazole (**3**) (50 mg) was dissolved in acetic acid (1 ml), and the reaction monitored by NMR., a rapid transformation



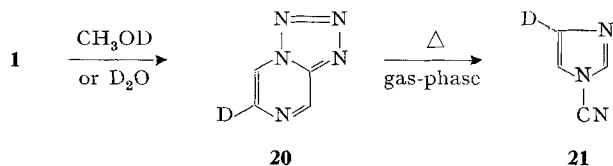
into 1-acetylimidazole (**18**) was observed ($t_{1/2}$ (40°) ≤ 30 s); **18** (50 mg) in acetic acid (1 ml) was further transformed into imidazole (**19**) and acetic anhydride ($t_{1/2}^{\text{initial}}$ (40°) $\simeq 4$ min) (cf. [7]):



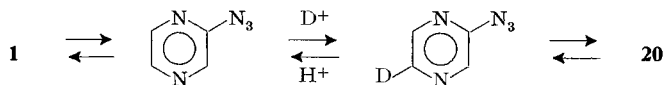
The rate of this latter reaction slowed down as reaction progressed, and it was still not complete after heating at 125° for 24 h. This is because the reaction is reversible [8] and the concentration of **18** thus depends on the concentration of acetic acid, in accord with the observations of Sasaki *et al.* [2] for the formation of **15** and **16** from **12**.

When equivalent amounts of **3** and acetic acid were reacted in CCl_4 at 60 – 65° for $22\frac{1}{2}$ h, NMR. of the soluble fraction showed that it consisted of **18** ($\geq 98\%$) with little acetic anhydride ($\leq 1.5\%$). HNCO was isolated in the form of its trimer, isocyanuric acid, by expelling it from the solution by a stream of N_2 during reaction. The reaction is formulated as passing through an intermediate isoimide (**17**), by analogy with a scheme put forward [9] for the reaction of aminonitriles with carboxylic acids. Our reaction differs from the latter, however, in that the isoimide **17** does not react with acid to give an N-carboxamide and acid anhydride.

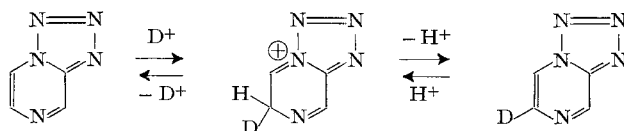
An attempt to thermolyse **1** in CH_3OD resulted in complete and specific exchange of H-C(6):



The reaction was faster in D_2O , and proceeded at temperatures where the product **20** does not decompose (see Table). It is generally accepted that an annelated tetrazole ring is electron withdrawing, while the tautomeric azido group is electron donating [10] [11]. It might therefore be assumed that the formation of **20** proceeds *via* the azido-form in analogy with the exchange of *o*,*p*-protons in anilines [12]:



This mechanism was ruled out, however, since aminopyrazine failed to exchange on heating with D_2O at 135° for 7 days (the amino group is a stronger electron donator than the azido group, *cf.* [11]). The exchange must therefore be a reaction of the tetrazole, reacting as an enamine:



It was reported recently that enamines exchange with acetone- d_6 [13]. **1** did not exchange noticeably with acetone- d_6 at 135° , and can therefore be qualitatively classed as a very weak enamine.

20 was identified by comparison of its IR., NMR., and mass spectra with those of **1** [5], and by the reversal to **1** on treatment with H_2O . Gas-phase thermolysis of **20** (*cf.* [3]) gave 1-cyanoimidazole-4-d (**21**).

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