a [crotyl bromide]/[3-bromo-1-butene] ratio greater than 15 were employed in metal-catalyzed reactions with ethyl diazoacetate. Reactions were performed as previously described for allyl halides. Direct analyses of the crotyl bromide content of product mixtures was performed following complete reaction, usually 24 h. At temperatures at or below 25 °C reactant isomerization was not observed, but at 50 °C isomerization to the equilibrium mixture of [crotyl bromide]/[3-bromo-1-butene] equal to 4.5 occurred during the course of the catalytic reaction. Product isolation and analyses were performed as previously described. GC analyses were performed by using 4-m 5% ethylene glycol adipate columns. The averaged results from duplicate and triplicate experiments are reported in Tables IV and V.

Ethyl 2-bromo-3-methyl-4-pentenoate (9): ^{1}H NMR ($CDCl_3$) of major isomer from $Rh_2(OAc)_4$-catalyzed reactions at or below 25 °C δ 5.72 (ddd, J_{trans} = 17.0 Hz, J_{cis} = 9.7 Hz, J_{vic} = 7.5 Hz, CH=), 5.11 (dd, J_{trans} = 17.0 Hz, J_{gem} = 0.9 Hz, 1 H), 5.09 (dd, J_{cis} = 9.7 Hz, J_{gem} = 0.9 Hz, 1 H), 4.20 (q, J = 7.1 Hz, CH_2O), 4.07 (d, J = 8.6 Hz, CHBr), 3.04-2.55 (sextet m, $CHCH_3$), 1.28 (t, J = 7.1 Hz, CH_3CH_2O), 1.21 (d, J = 6.7 Hz, CH_3CH); ^{1}H NMR ($CDCl_3$) for minor isomer δ 5.80 (ddd, J_{trans} = 17.0 Hz, J_{cis} = 9.6 Hz, J_{vic} = 7.5 Hz, CH=), 5.14 (dd, J_{trans} = 17.0 Hz, J_{gem} = 0.9 Hz, 1 H), 5.13 (dd, J_{cis} = 9.6 Hz, J_{gem} = 0.9 Hz, 1 H), 4.24 (q, J = 7.1 Hz, CH_2O), 4.11 (d, J = 8.4 Hz, CHBr), 3.04-2.55 (sextet m, $CHCH_3$), 1.29 (t, J = 7.1 Hz, CH_3CH_2O), 1.24 (d, J = 6.8 Hz, CH_3CH).

Anal. Calcd for $C_8H_{13}BrO_2$: C, 43.45; H, 5.94. Found: C, 43.62; H, 6.11.

Ethyl *trans*-2-bromo-4-hexenoate (10): ^{1}H NMR ($CDCl_3$) δ 5.84-5.14 (m, 2 H), 4.22 (q, J = 7.1 Hz, CH_2O), 4.16 (t, J = 7.4 Hz, CHBr), 3.00-2.40 (m, 2 H), 1.65 (ddt, J = 5.8, 2.2, 1.2 Hz, CH_3CH=), 1.29 (t, J = 7.1 Hz, CH_3CH_2O).

Anal. Calcd for $C_8H_{13}BrO_2$: C, 43.45; H, 5.94. Found: C, 43.58; H, 6.17.

Ethyl 2-(bromomethyl)-3-methylcyclopropanecarboxylate (*trans*-11): ^{1}H NMR ($CDCl_3$) δ 4.16 (q, J = 7.1 Hz, CH_2O), 3.91-3.43 (m, CH_2Br), 1.86-1.23 (m, 3 H), 1.28 (t, J = 7.1 Hz, CH_3CH_2O), 1.14 (d, J = 5.0 Hz, CH_3CH).

Anal. Calcd for $C_8H_{13}BrO_2$: C, 43.45; H, 5.94; Br, 36.14. Found: C, 43.63; H, 6.01; Br, 36.32.

Ethyl 2-(bromomethyl)-3-methylcyclopropanecarboxylate (*cis*-11): ^{1}H NMR ($CDCl_3$) δ 4.15 (q, J = 7.1 Hz, CH_2O), 3.35 (d, J = 7.2 Hz, CH_2Br), 1.95-1.60 (m, 2 H), 1.50-1.28 (m, 1 H), 1.26 (t, J = 7.1 Hz, CH_3CH_2O), 1.23 (m, CH_3CH).

Ethyl 2-(1-bromoethyl)cyclopropanecarboxylate was isolated from the reaction mixture obtained by treatment of combination of crotyl bromide and 3-bromo-1-butene (molar ratio 1.63) with ethyl diazoacetate and a catalytic amount of $Rh_2(OAc)_4$. Geometrical isomers were not separable by GC analyses: ^{1}H NMR ($CDCl_3$) δ 4.15 and 4.13 (q, J = 7.1 Hz, CH_2O), 3.87-3.43 (quintet, CHBr), 1.78 and 1.76 (d, J = 6.7 Hz, $CHCH_3$), 1.81-0.60 (m, 4 H), 1.26 and 1.25 (t, J = 7.1 Hz, CH_3CH_2O). The isomer ratio of the isolated product was 1.2.

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Registry No. 4a, 10152-76-8; **4b**, 2155-94-4; **4c**, 2588-79-6; (*E*)-**4d**, 51752-08-0; (*E*)-**4e**, 42817-44-7; **5a**, 71031-93-1; **5b**, 66917-63-3; **5c**, 66917-65-5; **5d** (isomer 1), 79373-05-0; **5d** (isomer 2), 79373-06-1; **5e** (isomer 1), 79357-14-5; **5e** (isomer 2), 79357-15-6; **5** (X = I), 79357-16-7; **5** (X = Br), 39149-86-5; **5** (X = Cl), 29119-70-8; *cis*-**6** (X = Br), 79357-17-8; *trans*-**6** (X = Br), 38506-15-9; *cis*-**6** (X = Cl), 79357-18-9; *trans*-**6** (X = Cl), 79357-19-0; **7** (X = Br), 78331-59-6; **8** (X = Br), 79357-20-3; **8** (X = Cl), 79357-21-4; **9** (isomer 1), 79357-22-5; **9** (isomer 2), 79357-23-6; (*E*)-**10**, 79357-24-7; *trans*-**11**, 79357-25-8; *cis*-**11**, 79390-68-4; ethyl diazoacetate, 623-73-4; allyl iodide, 556-56-9; allyl bromide, 106-95-6; allyl chloride, 107-05-1; diethyl diazomalonate, 5256-74-6; (*E*)-crotyl bromide, 29576-14-5; ethyl 2-(1-bromoethyl)-cyclopropanecarboxylate, 79357-26-9; 3-bromo-1-butene, 22037-73-6; $Rh_6(CO)_{16}$, 28407-51-4; $Rh_2(OAc)_4$, 15956-28-2; $CuCl{\cdot}P(O\text{-}i\text{-}Pr)_3$, 78955-42-7; $Cu(acac)_2$, 13395-16-9.

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Occurrence of the S_N(ANRORC) Mechanism in the Hydrazination of 1,2,4,5-Tetrazines[1-3]

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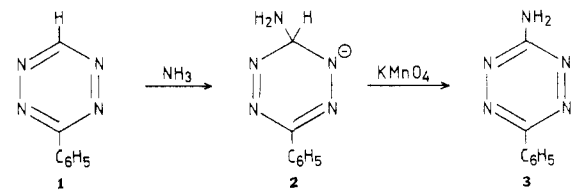
3-Alkyl(aryl)-1,2,4,5-tetrazines (**7**) when treated with hydrazine hydrate were found to undergo a Chichibabin hydrazination into 3-alkyl(aryl)-6-hydrazino-1,2,4,5-tetrazines (**8**) according to an S_N(ANRORC) mechanism. ^{1}H and ^{13}C NMR measurements indicate that the first step in this reaction sequence is the formation of a homoaromatic σ adduct anion, due to attack at C_6, and that the second step is the formation of an open-chain intermediate. With ^{15}N-labeled hydrazine, part of the label is found in the 1,2,4,5-tetrazine ring of the 6-hydrazino compounds **8***. NMR evidence is obtained which shows that the hydrazino compounds with the ^{15}N-label in the ring (**8*II**) and with the ^{15}N-label in the hydrazino group (**8*I**) are formed according to the S_N(ANRORC) mechanism. Treatment of 6-amino- or 6-halogeno-1,2,4,5-tetrazines with hydrazine leads to introduction of a hydrazino group at position 6. During this hydrazino deamination and hydrazino dehalogenation part of the molecules were found to react according to the S_N(ANRORC) mechanism, the other part followed the S_N(AE) pathway.

In a preceding paper[1] we obtained firm evidence that the anion of 6-amino-1,6-dihydro-3-phenyl-1,2,4,5-tetrazine (**2**), formed upon addition of ammonia to 3-phenyl-1,2,4,5-tetrazine (**1**, Scheme I), is homoaromatic. This σ adduct is in the homotetrazole conformation, containing 6 π electrons in the tetrazole ring and holding the amino group in the exo position and the hydrogen at the sp^3

Scheme I



1 2 3

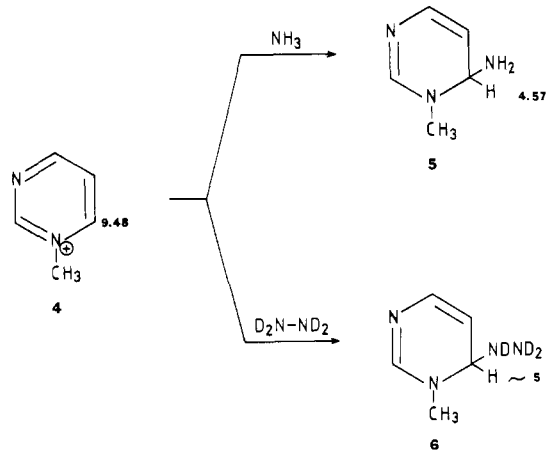
(1) Part 5 on 1,2,4,5-tetrazine and its derivatives. For part 4 see: Counotte-Potman, A.; van der Plas, H. C.; van Veldhuizen, A. *J. Org. Chem.*, in press.

(2) Part 30 on NMR investigations of σ adducts of heterocyclic systems with nucleophiles. For part 29 see: van den Haak, H. J. W.; van der Plas, H. C.; van Veldhuizen, A. accepted for publication in *J. Heterocycl. Chem.*

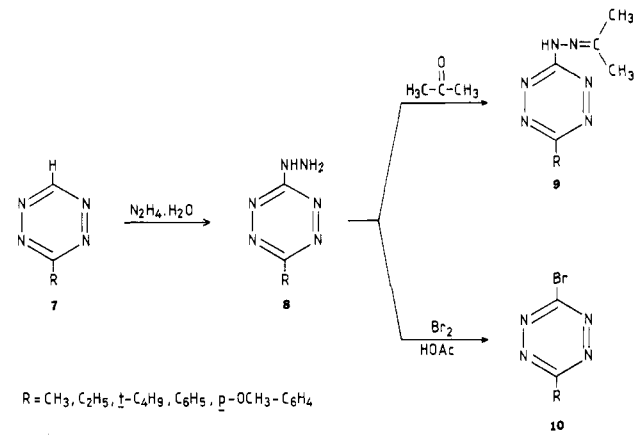
(3) Part 28 on the S_N(ANRORC) mechanism. For part 27 see: Kos, N. J.; van der Plas, H. C. *J. Org. Chem.* **1980**, *45*, 2942.

0022-3263/81/1946-5102$01.25/0

Scheme II



Scheme III



carbon atom above the ring. This hydrogen is located in the shielding region, resulting in a chemical shift at high field (δ 1.51).

In the literature it is described[4] that addition of ammonia to the C_6–N_1 bond in 1-methylpyrimidinium iodide (**4**, Scheme II) is accompanied by an upfield shift of H_6 ($\Delta\delta$ = 4.91 ppm)[4]. Addition of hydrazine hydrate gave about the same upfield shift ($\Delta\delta$ = 4.5–5 ppm),[5] from which it was concluded that hydrazine gave an analogous σ adduct, i.e., 6-hydrazino-1-methyl-1,6-dihydropyrimidine (**6**).

From the σ adduct **2** was obtained 6-amino-3-phenyl-1,2,4,5-tetrazine (**3**) upon oxidation with potassium permanganate;[6] the reaction of **1**→**3** can be considered as a Chichibabin amination.[7] It has been published that the Chichibabin amination of 4-phenylpyrimidine[8] and phenyl-1,3,5-triazine[9] occurs according to the S_N(ANRORC) mechanism,[10] describing a reaction sequence involving Addition of the Nucleophile to the heterocycle, Ring Opening, and Ring Closure.

In an extension of our studies on the amination of 1,2,4,5-tetrazines by liquid ammonia, we became interested whether 1,2,4,5-tetrazines are also appropriate systems for Chichibabin hydrazination by hydrazine hydrate. The use of sodium hydrazide in the Chichibabin hydrazination of some azaaromatic systems has been reported.[11] We were particularly interested whether the hydrazination, if it occurs, is accompanied by the intermediate formation of a 1:1 σ adduct having homoaromatic (and anionic) properties and whether the hydrazination would occur according to the S_N(ANRORC) process.

In a previous paper[12] we already presented some evidence that in the hydrazinolysis of 6-amino- and 6-bromo-3-methyl-1,2,4,5-tetrazine an S_N(ANRORC) mechanism is operative. In this paper we present an extension of these hydrazino deamination and hydrazino dehalogenation reactions and especially the results of our study with ^{15}N-labeled hydrazine and the NMR spectroscopy of the intermediates in the hydrazination involved.

Table I. ^{15}N Excess in Acetone-Hydrazones 9* and in the 6-Bromo Compounds 10*[a]

R	% ^{15}N 9*	% ^{15}N 10*	% ANRORC[b]	av of ANRORC
CH_3	6.5, 24.6	1.70, 5.7	26.2, 23.0	24.6
C_2H_5	5.7, 6.3	1.60, 1.82	28.0, 28.9	28.5
t-C_4H_9	8.0, 20.7	0, 0	0, 0	0
C_6H_5	10.6, 9.3	0.44, 0.27	4.2, 2.9	3.5
SD_{av}[c]	0.4	0.15	2.6	2.6

[a] The percentage of ^{15}N label in 9* is a measure for the ^{15}N enrichment in the ^{15}N doubly labeled hydrazine used for the reaction. This label is incorporated either on the 1,2-position of the 1,2,4,5-tetrazine ring or in the exocyclic hydrazine group, depending on the position of addition of the hydrazine. The percentage of ^{15}N label in 10* is a measure for the molecules in which the label is only present in the 1,2,4,5-tetrazine ring. [b] The percentage ANRORC refers to the percentage of molecules 8* which have been formed by route II (Scheme IV). [c] The standard deviations (SDs) were determined as follows. The ratio of peak heights of the M + 2 and M peaks were determined at high resolving power. The average and standard deviation were determined from 6–10 values. If the value of the SD was <0.15, 0.15 was taken as the value because this is the accuracy of the apparatus. To determine the SD in the percentage of ANRORC we used the formula $(S_z/z)^2 = (S_x/x)^2 + (S_y/y)^2$ (z = % ANRORC, x = % ^{15}N in 9*, y = % ^{15}N in 10*). Then the SDs of the % ^{15}N of 9* and 19*, of the % ^{15}N of 10*, 20*, and 21*, and of the % ANRORC were averaged; e.g., for the % ^{15}N of 9* and 19* we obtained an SD_{av} = 0.32 ± 0.11, resulting in 0.4.

Results and Discussion

(A) Chichibabin Hydrazination of 1,2,4,5-Tetrazines. On treatment of 1 equiv of the 1,2,4,5-tetrazines **7** with 3 equiv of hydrazine hydrate in ethanol at 298 K the corresponding hydrazino compound **8** is formed (Scheme III; yields between 9% and 15%) together with a number of unidentified colored (not red) and colorless products; 10–15% of starting material **7** is retrieved (Table VI). To facilitate separation of the hydrazino compounds **8**, we converted them into the more stable acetone hydrazones **9** (see Experimental Section).

To investigate whether in the formation of **8** the S_N(ANRORC) mechanism is operative, we carried out the hydrazinations with ^{15}N doubly labeled hydrazine. If an S_N(ANRORC) process occurs, addition of hydrazine takes place at C_3, followed by ring opening and ring closure leading to the incorporation of ^{15}N into the 1,2,4,5-tetrazine ring; if not, the label will only be present in the exocyclic

(4) Oostveen, E. A.; van der Plas, H. C.; Jongejan, H. *Recl. Trav. Chim. Pays-Bas* **1974**, *93*, 114.
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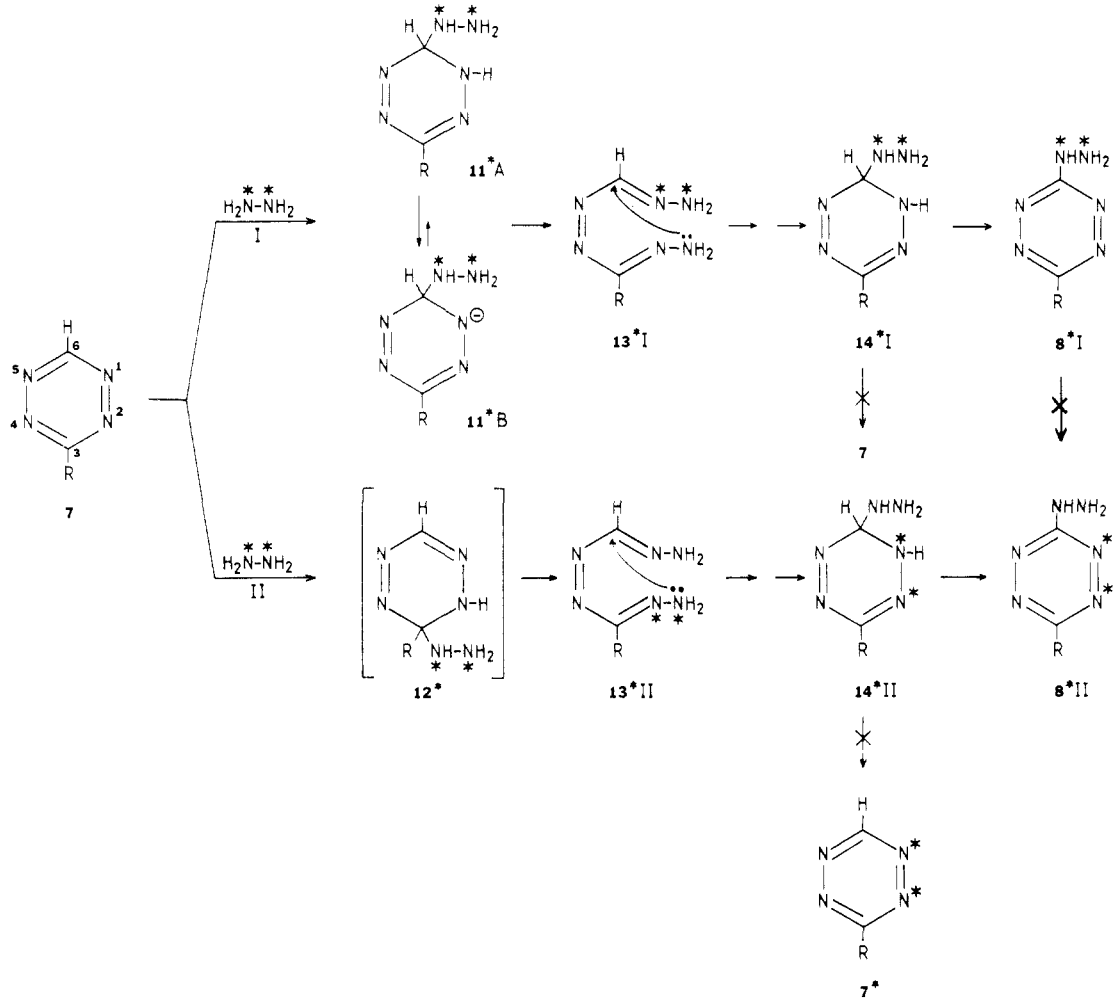
Scheme IV



nitrogens of the hydrazino group due to an addition–elimination process at C_6. To establish the percentages of the ^{15}N label present in the tetrazine ring and in the hydrazino group of the hydrazino compound 8*[13] we measured the excess of ^{15}N label in the acetone hydrazones 9* and in the corresponding bromo compounds 10*, obtained by oxidation of 8* with bromine in acetic acid.[14] The mass spectrometric measurements were carried out at high resolving power.[15] The results are given in Table I. No label was found in the recovered starting material 7.

From the data in Table I it is evident that during the formation of the hydrazino compounds 8* (R = CH_3, C_2H_5) at least part of the ^{15}N label of hydrazine is incorporated into the 1,2,4,5-tetrazine ring. In order to obtain additional evidence for the reaction mechanism, we tried to establish by ^1H and ^{13}C NMR spectroscopy which intermediary species are present during the reaction. We obtained some unexpected results.

Comparison of the proton chemical shifts of 1,2,4,5-tetrazines 7 dissolved in deuteriomethanol with those observed upon dissolving 7 in a 1:1 mixture of hydrazine hydrate and deuteriomethanol at 233 K (Table II) shows that H_6 undergoes a large upfield shift ($\Delta\delta$ between 8.25 and 8.92 ppm). This considerable upfield shift, of the same magnitude as that observed in liquid ammonia ($\Delta\delta$ = ~8.7 ppm),[1] can only be explained if we assume the formation of the homoaromatic σ adducts 11 (Scheme IV). No ^1H NMR signals of the starting material 7 could be detected.

The formation of σ adducts 11 was further proven by comparison of the ^{13}C chemical shifts of C_6 in 7 dissolved in deuteriomethanol and in a 1:1 mixture of hydrazine hydrate and deuteriomethanol. The upfield shift of $\Delta\delta$ = 59–62 ppm observed for C_6 in the mixed solvent system confirms the formation of 11; this upfield shift is due to the change in hybridization of C_6 ($sp^2 \rightarrow sp^3$). Also the decrease of the coupling constant J_{C_6H}, from 213–215 Hz in 7 to 159–160 Hz in 11, is in agreement with the adduct formation; the value of 159 Hz is of the same magnitude as that in the ammonia adduct 2 (156 Hz).[1]

The question whether the σ adducts 11 are present as neutral species 11A or as anionic species 11B was answered by applying the method discussed in a previous paper.[1]

For 3-(*p*-Y-phenyl)-1,2,4,5-tetrazine derivatives (Y = Br, OCH_3, CH_3) there exists a linear relationship between the ^{13}C substituent chemical shift at C_4 of the aryl ring (SCS-4)[17] and $\delta(C_4)$ (Y = H), which is a measure of the electron demand of the substituted 1,2,4,5-tetrazinyl groups.[1] Therefore, we determined the $\delta(C_4)$ values of the σ adducts 11 (R = C_6H_5, *p*-$OCH_3C_6H_4$). The SCS-4 value and the $\delta(C_4)$ (Y = H) value for the 6-hydrazino-1,6-dihydro-1,2,4,5-tetrazinyl group fit nicely in this plot (r = 0.923,

(13) An asterix is used to indicate that the compound is (possibly) labeled.

(14) Ershov, V. A.; Postovskii, I. Y. *Khim. Geterotsikl. Soedin.* **1971**, *4*, 571.

(15) The mass spectrometric measurements were carried out at high resolving power in order to separate the (M + 2) peaks due to the double ^{15}N label from the (M + 2) peaks due to reduction of the 1,2,4,5-tetrazine ring to a "2H" compound in the mass spectrometer.[11,16]

(16) Yates, P.; Meresz, O.; Weiler, L. S. *Tetrahedron Lett.* **1968**, 3929.

(17) Hügel, H. M.; Kelly, D. P.; Spear, R. J.; Bromilow, J.; Brownlee, R. T. C.; Craik, D. J. *Aust. J. Chem.* **1979**, *32*, 1511.

Table II. ^1H and ^{13}C Chemical Shifts and the Coupling Constants J_{C_6H} (Hz) of 7 and 16 in Deuteriomethanol and in a Mixture of Hydrazine Hydrate and Deuteriomethanol at Various Temperatures

compd	R	solvent	temp, K	$\delta(H_6)$	$\Delta\delta$	$\delta(C_6)$	$\Delta\delta$	J_{C_6H}	$\delta(C_3)$	others, δ
7	CH_3	CD_3OD	308	10.26		159.3		213	171.8	CH_3, 3.03; CH_3, 21.7
11		*a*	233	1.71	8.55	98.9	60.4	159	153.6	CH_3, 2.42; CH_3, 18.2
13		*a*	253	6.92		143		200	152	CH_3, 1.88; CH_3, 16.9
7	C_2H_5	CD_3OD	308	10.32		159.5		213	175.1	CH_2, 3.26; CH_3, 1.44; CH_2, 29.7; CH_3, 12.3
11		*a*	233	1.65	8.67	97.5	62.0	159	158.4	CH_2, 2.76; CH_3, 1.19; CH_2, 24.8; CH_3[b]
13		*a*	253	6.98		141.7		200	153.8	CH_2, 2.22; CH_3;[c] CH_2, 23.7; CH_3[b]
7	t-C_4H_9	CD_3OD	308	10.45		158.9		213	179.5	CH_3, 1.58; CH_3,[d] 29.4
11		*a*	233	1.53	8.92	97.3	61.6	160	160.1	CH_3, 1.31; CH_3,[d] 27.1
13		*a*	273	6.95		141.6		200	163.6	CH_3, 1.20; CH_3,[d] 27.3
7	C_6H_5	CD_3OD	308	10.35		159.5		215	168.0	Ph: C_1, 133.6; C_2, 129.3; C_3, 130.6; C_4, 134.1
11		$N_2H_4 \cdot H_2O$	253	2.10	8.25	100.1	59.4	159	156.5	Ph: C_1, 136.8; C_2, 122.7; C_3, 129.5; C_4, 126.6
13		$N_2H_4 \cdot H_2O$	308	7.15		142.5		201	150	Ph: C_1,[e] C_2, 127.0; C_3, 129.6; C_4, 131.4
13		*f*	308	6.84		142.2		201	150.4	Ph: C_1,[e] C_2, 127.5; C_3, 129.7; C_4, 131.6
11		*a*	233	2.05	8.30	99.7	59.8		156.8	Ph: C_1, 137.2; C_2, 123.3; C_3, 129.7; C_4, 127.1
7	p-$OCH_3C_6H_4$	$CDCl_3$	308	10.11		157.5		213	166.1	Ph: C_1, 124.2; C_2, 130.3; C_3, 115.0; C_4, 164.0
		a	233			99.7	57.8		156.6	Ph: C_1, 130.1; C_2, 124.7; C_3, 114.8; C_4, 159.0
16		CD_3OD	308						166.3[g]	CH_3, 2.98; CH_3, 20.5;[g] CH_3, 3.02 (br)
17[i]		*a*	233							
		a	273[h]						150.6	CH_3, 1.87; CH_3, 16.1

[a] $N_2H_4 \cdot H_2O/CD_3OD$ (1:1). [b] CH_3 was not determined. [c] Due to contamination with ether it is difficult to assign the CH_3 shift with certainty. [d] The quaternary C could not be observed because of aliphatic impurities. [e] C_1 could not be observed. [f] 2 equiv of $N_2H_4 \cdot H_2O$ in CD_3OD. [g] In $CDCl_3$; see ref 23. [h] At intermediate temperatures δ 3.02 disappears, while δ 1.87 is formed. [i] In this solution starting material **16** was also present, as indicated by minor peaks of 166.9 and 20.8 ppm.

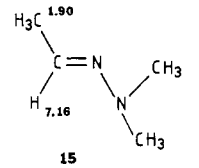
Table III. $\delta(C_4)$ and SCS_4[a,b] for 3-(*p*-Y-phenyl)-1,2,4,5-tetrazine Derivatives (Y = H, OCH_3)[c]

substituted 1,2,4,5-tetrazinyl group	Y = OCH_3 $\delta(C_4)$	Y = OCH_3 SCS-4	Y = H, $\delta(C_4)$	solvent
tetrazinyl	164.01	30.77	133.24	$CDCl_3$
6-aminotetrazinyl	161.28	30.86	130.42	Me_2SO-d_6
1,6-dihydrotetrazinyl	161.22	31.50	129.72	CD_3OD/D_2O
1,6-dihydrotetrazinyl anion	159.44	32.27	127.17	CD_3OD/D_2O[d]
6-hydrazino-1,6-dihydrotetrazinyl anion	159.03	31.98	127.05	$N_2H_4 \cdot H_2O/CD_3OD$ (1:1)

[a] SCS-4 = $[\delta(C_4)(Y \neq H) - \delta(C_4)(Y = H)]$ ppm; a positive value corresponds to a downfield shift. [b] $r = 0.923$; slope 0.24 ± 0.06; intercept 62 ± 7; $t_\alpha = 4.16$. [c] Values are from ref 1. [d] 1.5 equiv of NaOH.

$t_\alpha = 4.16$; Table III). From this plot it is evident that the electron demand of the 6-hydrazino-1,6-dihydro-1,2,4,5-tetrazinyl group resembles mostly that of the 1,6-dihydro-1,2,4,5-tetrazinyl anion. As the σ_I values of the hydrazino group[18] and hydrogen are not very different, we conclude that the σ adducts **11** are present as *anionic* homoaromatic species in hydrazine hydrate/methanol.

When the solutions of **11** are warmed in hydrazine hydrate/methanol [from 233 to 253 K (R = CH_3, C_2H_5), to 273 K (R = t-C_4H_9), or to 308 K (R = C_6H_5)], both the ^1H and ^{13}C NMR adduct signals slowly disappear, and new signals with completely different chemical shifts appear. These could be attributed to open-chain intermediates **13**. Evidence for the formation of **13** is based on two facts: (a) in all these open-chain intermediates **13**, with different groups R, both H_6 and C_6 are found in a narrow chemical shift range (H_6 between 6.92 and 7.15 ppm; C_6 between 141 and 143 ppm); (b) the chemical shifts of H_6 are of the same magnitude as that found for the HC=N group in *N,N*-dimethylacetaldehyde hydrazone (**15**).[19] The ^1H chemical shift of the methyl group in **13** (R = CH_3) at 1.88 ppm is also in suprisingly good agreement with that found for the *C*-methyl group in **15** (1.90 ppm).



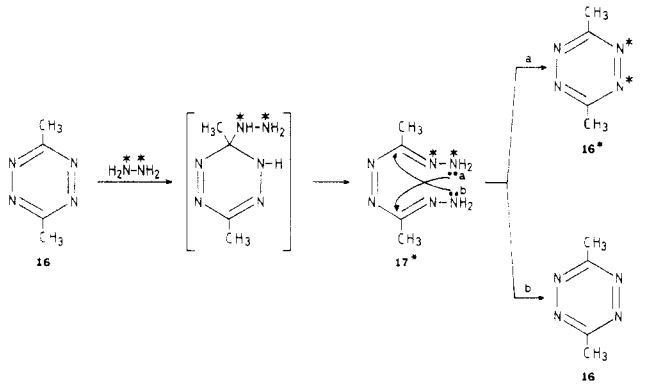
15

Moreover, when 3,6-dimethyl-1,2,4,5-tetrazine (**16**) was dissolved in a 1:1 mixture of hydrazine hydrate and deuteriomethanol at 273 K and the ^1H and ^{13}C NMR spectra of these solutions were measured, chemical shifts were found which could only be attributed to the dihydrazone **17**. Species **17** showed only *one* methyl group, indicating that in **17** both methyl groups are identical. The ^1H chemical shift for the hydrogens of the methyl group (1.87 ppm) is about the same as that found for **13** (R = CH_3, 1.88

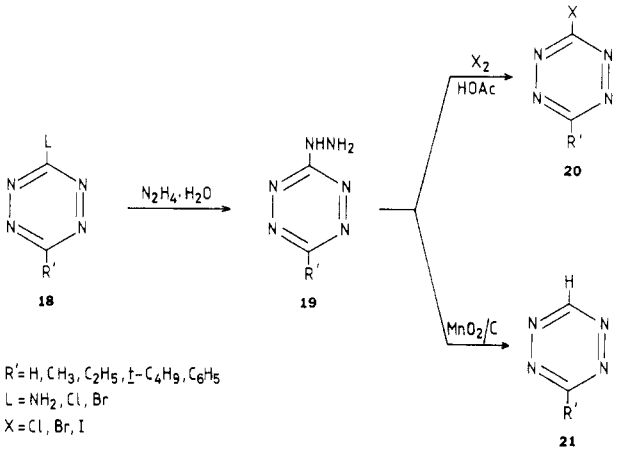
(18) Alder, R. W.; Baker, R.; Brown, J. M. In "Mechanism in Organic Chemistry"; Wiley: New York, 1971; p 30.

(19) Skorianetz, W.; Kovats, E. *Helv. Chim. Acta* **1970**, *53*, 251.

Scheme V



Scheme VI



ppm). Also, nearly identical ^{13}C chemical shifts were observed for C_3 (150.6 ppm) and CH_3 (16.1 ppm) as compared with those in **13** (R = CH_3; Table II). If **16** is treated with ^{15}N-doubly-labeled hydrazine (7% ^{15}N), part of the label is found in the 1,2,4,5-tetrazine ring of the recovered **16** (0.6% ^{15}N). This can be explained by ring closure of the symmetrical open-chain intermediate **17*** (Scheme V).

No NMR evidence has been obtained for the intermediacy of **12***. Its occurrence is necessary, however, to explain the formation of **8*II** from **7** (R = CH_3 or R = C_2H_5) having both labeled nitrogens in the 1,2,4,5-tetrazine ring. All NMR data and the results of ^{15}N labeling are in agreement with the mechanism proposed in Scheme IV. Attack at C_6 (route I) yields the initial homoaromatic σ adduct anion **11*B**, which ring opens to give **13*I**. Attack at C_3, in route II, gives an unstable adduct **12***, which is not observed by NMR. Ring opening yields open-chain intermediate **13*II**, being identical with **13*I** except that the ^{15}N label is present in a different position. The ring closure takes place by attack on C_6, leading to the most stable adduct **14***, which is oxidized by hydrazine[20] present in the reaction mixture.

That ring closure in **13** occurs by attack of the hydrazino nitrogen on C_6 and not on C_3, to which R is attached, is probably due to the homoaromatic stabilization of intermediate **14**. Homoaromaticity is less likely when two large groups (R and hydrazino as in **12***) are present at the methylene bridge.[21] This mechanism is in agreement with the fact that **7** (R = C_6H_5, t-C_4H_9 does not, or only to a very small extent, react with formation of ring-labeled **8*II** (R = C_6H_5, t-C_4H_9). Both groups are blocking groups and probably retard or prevent addition at C_3, to which these substituents are attached.

The fact that in all reactions the recovered starting material **7** is unlabeled indicates that **14*I** or **14*II** does not decompose into **7** or **7***. The recovered starting material **7** is probably *unreacted* starting material. The possibility of a hydrazine-induced rearrangement of **8*I** into **8*II** can be excluded. After reaction of unlabeled 6-hydrazino-3-ethyl-1,2,4,5-tetrazine (**8**, R = C_2H_5) with labeled hydrazine (8% ^{15}N) for 45 min at 25 °C and conversion of the labeled (3%) hydrazino product obtained into the 6-bromo compound **10** (R = C_2H_5), it was found that **10** (R = C_2H_5) did *not* contain ^{15}N. Thus, under these conditions a rearrangement of exocyclic hydrazino nitrogen into ring nitrogen does not take place.

From all the data presented we concluded that *both* routes (I and II) of Scheme IV, leading to the ring-labeled hydrazino compound (**8*II**) as well as to the ring-unlabeled hydrazino compound (**8*I**), occur with an *opening* of the 1,2,4,5-tetrazine ring. Therefore, we have to conclude that both reaction sequences fulfill the definition of the S_N(ANRORC) mechanism (addition of a nucleophile followed by ring opening and ring closure). The only difference between the two routes is the place of initial attack (C_3 or C_6). If a blocking group is present on C_3, attack only takes place at C_6, and no label is found to be built into the ring. To our knowledge this is the first example of a reaction in which both the ring-labeled and the exocyclic-labeled compound follow the S_N(ANRORC) pathway. Thus in these reactions no evidence for an S_N(AE) mechanism has been obtained.

(B) Hydrazino Deamination and Hydrazino Dehalogenation of 1,2,4,5-Tetrazines. When **18** (L = NH_2) is refluxed in ethanol containing 2 equiv of hydrazine hydrate, 6-hydrazino-3-R′-1,2,4,5-tetrazines (**19**) are obtained in yields between 40% and 70% (depending on substituent R′), together with recovered starting material **18**. The yields and reaction conditions are given in Table VI. When the leaving group L is Br or Cl, compounds **18** (L = Br, Cl) react more quickly in ethanol containing 3 equiv of hydrazine hydrate; even at 293 K they are quantitatively converted into **19** (Table VI).

To investigate whether the S_N(ANRORC) mechanism is also operative in the formation of these hydrazino compounds **19** we carried out the reactions with ^{15}N-doubly-labeled hydrazine. After extraction with benzene, the crude reaction product, without further purification, was inserted directly into the mass spectrometer. To establish the percentages of ^{15}N present in the 1,2,4,5-tetrazine ring and on the exocyclic nitrogens of the labeled hydrazino compounds **19***, we converted these compounds into the corresponding 6-halogeno-3-R′-1,2,4,5-tetrazines (**20***; X = Cl, Br, I) by oxidation with halogen[14] in acetic acid or in some cases into the corresponding 3-R′-1,2,4,5-tetrazines **21*** by oxidation with manganese dioxide on carbon[22] (Scheme VI). The excess of ^{15}N in compounds **19*–21*** as found by mass spectrometric measurement at high resolving power[15] is given in Table IV. No label was found in the recovered 6-amino-3-R′-1,2,4,5-tetrazines (**18**, L = NH_2).

From these data it is evident that part of the hydrazino compounds **19*** is formed from **18** by the S_N(ANRORC)

(20) Audrieth, L. F.; Ogg, B. A. In "The Chemistry of Hydrazine"; Wiley: New York, 1951.
(21) 8,8-Dimethylhomotropylium cation is established by ^1H NMR. However, above 223 K it isomerized irreversibly to give an isopropyltropylium cation. Childs, R. F.; Rogerson, C. V. *J. Am. Chem. Soc.* **1978**, *100*, 649.
(22) Carpino, L. A. *J. Org. Chem.* **1970**, *35*, 3971.
(23) Lauterbur, P. C. *J. Chem. Phys.* **1965**, *43*, 360.

Scheme VII

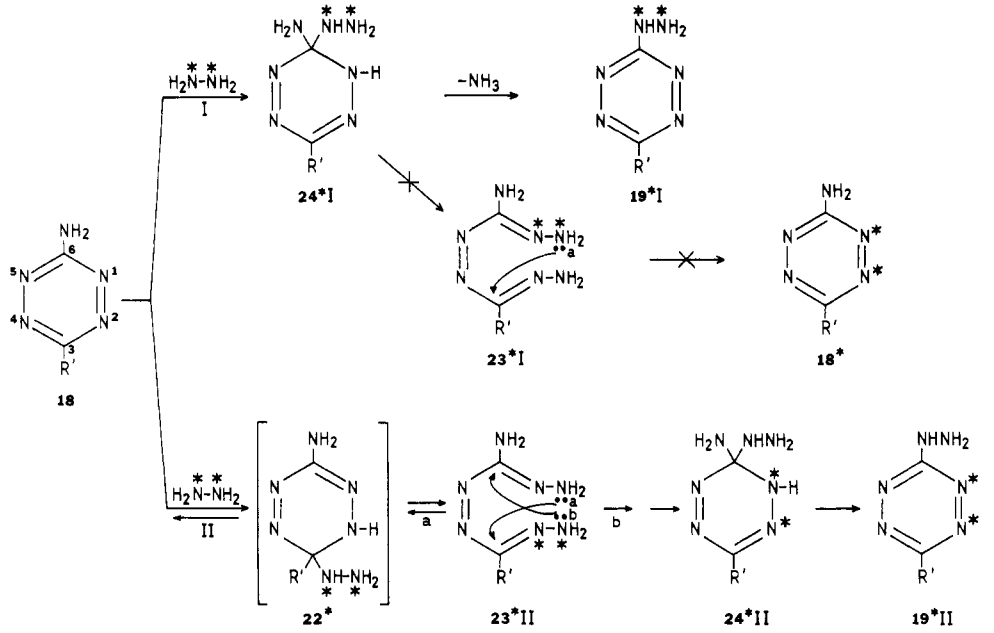


Table IV. ^{15}N Excess in Compounds 19* and 20* or 21*

starting 18		% ^{15}N			
R′	L	19*	20* or 21*	% ANRORC	av of ANRORC
H	NH_2[a]	6.4, 6.1	1.27, 1.42 (X = I)	20.0, 23.2	21.6
CH_3	NH_2[a]	7.1, 6.6	1.77 (X = Br), 1.70 (21*)	24.9, 25.8	25.3
C_2H_5	NH_2[a]	6.1, 6.3	0.99, 1.22 (X = Br)	16.3, 19.5	17.9
t-C_4H_9	NH_2[a]	6.4, 6.4	0, 0 (X = Br)	0, 0	0
C_6H_5	NH_2[a]	5.0, 5.5	0 (21*), 0 (21*)	0, 0	0
CH_3	Cl	5.3, 19.4	0.22, 1.71 (X = Br)	4.1, 8.8	6.5
CH_3	Br	5.8	1.18 (X = Br)	20.5, 18[b]	19.3
C_2H_5	Br	5.2, 5.2	0.19, 0.05 (X = Br)	3.6, 1.0	2.3
SD_{av}		0.4	0.15	2.6	2.6

[a] No label was found in recovered starting material. [b] See ref 12.

mechanism in a decreasing order: L = NH_2 > L = Br > L = Cl. In order to gain more insight into the reaction course of the hydrazinolysis, we investigated the reaction intermediates by ^1H and ^{13}C NMR spectroscopy. The reactions of 18 (L = Br, Cl) could not be followed by NMR spectroscopy, since these compounds react very fast with hydrazine.

On dissolving 6-amino-1,2,4,5-tetrazine (18; R′ = H, L = NH_2) in hydrazine hydrate/deuteriomethanol (1:3) at 273 K, the formation of the σ adduct 22 (R′ = H) was not observed (see Table V). The ^1H NMR signal δ 6.98 was attributed to the open-chain intermediate 23 (R′ = H). This conclusion was based on comparison with the chemical shift of H_6 in 13 (6.92–7.15 ppm, Table II). A similar shift for 23 was also found in a mixture containing one equiv of 18 (R′ = H, L = NH_2) and 2 equiv of hydrazine hydrate in deuteriomethanol. The values of the ^{13}C chemical shifts of C_3 of 23 (δ 144.9) and J_{C_3H} of 23 (199 Hz, Table V) also correspond nicely with those of C_6 (δ 141–143) and J_{C_6H} (200 Hz) of the open-chain compounds 13 (see Table II).

The ^1H NMR spectra of 6-amino-3-methyl-1,2,4,5-tetrazine (18; R′ = CH_3, L = NH_2) with 2 equiv of hydrazine hydrate measured at 323 K during 8 h were analyzed carefully. Four different stages could be discerned, showing the appearance and disappearance of signals. The chemical shifts observed for the methyl group in these four stages indicated by i–iv are (i) 2.73 and 1.85, (ii) 2.73, 1.85, and 2.32, (iii) 1.85 and 2.32, and (iv) 2.32 and 2.68 ppm. The peaks at 2.73 and 2.68 ppm were assigned to starting material 18 (R′ = CH_3, L = NH_2) and hydrazino product

Table V. ^1H and ^{13}C Spectroscopic Data of 6-Amino-3-R′-1,2,4,5-tetrazines (18: R′ = H, CH_3, C_2H_5; L = NH_2) in Deuteriomethanol and in a Mixture of Hydrazine Hydrate and Deuteriomethanol

compd	R′	solvent	temp, K	$\delta(H_3)$	$\delta(C_3)$	J_{C_3H}, Hz	$\delta(C_6)$	others, δ
18	H	CD_3OD	308	9.70	154.2	213	166.7	
23		a	b	6.91	144.9	199	154.3	
		c	233	9.70				
		c	273	6.98[d]				
18	CH_3	CD_3OD	308		162.7		165.0	CH_3, 2.73; CH_3, 19.9
23		a	e		153.3[f]		155.0[f]	CH_3, 1.85; CH_3, 15.9
		a	g					CH_3, 1.85, 2.32, 2.68
18	C_2H_5	CD_3OD	308		166.4		165.0	CH_2, 3.12; CH_3, 1.45; CH_2, 28.1; CH_3, 12.9
23		a	h		157.7		155.2	CH_2, 2.22; CH_3, 1.18; CH_2, 24.4; CH_3, 11.3
		a	g					CH_2, 2.22, 2.77, 3.14; CH_3, 1.18, 1.33, 1.40

[a] 2 equiv of $N_2H_4 \cdot H_2O$ in CD_3OD. [b] 45 min at 308 K, measured at 263 K. [c] $N_2H_4 \cdot H_2O/CD_3OD$ (1:3). [d] At intermediate temperatures δ 9.70 is broadened and disappears, while δ 6.98 is formed. [e] 3 h at 323 K, measured at 303 K. [f] Signals may be interchanged. [g] Measured at 323 K during 8 h. [h] 3 h at 323 K, measured at 258 K.

Table VI. Reaction Conditions and Yields of the Hydrazinolysis of 1,2,4,5-Tetrazines 7 and 18[a]

starting matl	$N_2H_4 \cdot H_2O$, equiv	temp, K	time, min	% hydrazino compd[b,c]	% recovd starting matl[b]
7, R = CH_3	3	298	45[d]	12	10
7, R = C_2H_5	3	298	45[d]	15	14
7, R = t-C_4H_9	3	298	45[d]	12	12
7, R = C_6H_5	3	298	45[d]	9	15
18, R′ = H, L = NH_2	2	351	90	62	2
18, R′ = CH_3, L = NH_2	2	351	90	47	35
18, R′ = C_2H_5, L = NH_2	2	351	90	50	27
18, R′ = t-C_4H_9, L = NH_2	2	351	90	34	33
18, R′ = C_6H_5, L = NH_2	2	351	90	70	2
18, R′ = CH_3, L = Cl	3	293	20	>90	0
18, R′ = CH_3, L = Br	3	293	20	>90	0
18, R′ = C_2H_5, L = Br	3	293	20	>90	0

[a] Reactions were carried out on a 1-mmol scale in 4 mL of ethanol. [b] Yields were determined by UV measurement. [c] The hydrazino compounds were converted to the acetone hydrazones. [d] Under nitrogen.

Table VII. Physical Data of the New 1,2,4,5-Tetrazines Prepared in This Study

compd	mp, °C	MS, m/e (M^+)	^1H NMR, δ	anal., % calcd C (H)	anal., % found C (H)
7, R = C_2H_5 ($C_4H_6N_4$)	oil	110	Table II	43.63 (5.49)	44.41[a] (5.71)
8, R = C_2H_5		140			
8,[b] R = C_2H_5 ($C_{11}H_{12}N_6$)	161-162.5	228	1.47 (t, CH_3), 3.15 (q, CH_2), 7.31-7.90 (m, Ph), 8.33 (s, CH), 12.33 (NH) [Me_2SO-d_6]	57.88 (5.30)	57.84 (5.19)
8, R = t-C_4H_9		168	1.41 (s, CH_3), 5.0 (NH) [Me_2SO-d_6]		
8, R = C_6H_5		188	4.69 (s, NH_2), 9.70 (s, NH), 7.50-7.64 (m, m/p-Ph), 8.20-8.35 (m, o-Ph) [Me_2SO-d_6]		
9, R = CH_3 ($C_6H_{10}N_6$)	112-115	166	2.02 (s, $(CH_3)_2$), 2.74 (s, CH_3), 10.71 (NH) [Me_2SO-d_6]	43.36 (6.07)	43.65 (6.25)
9, R = C_2H_5 ($C_7H_{12}N_6$)	106-109	180	1.33 (t, CH_3), 2.00 (s, $(CH_3)_2$), 3.07 (q, CH_2), 10.76 (NH) [Me_2SO-d_6]	46.65 (6.71)	46.85 (6.86)
9, R = t-C_4H_9 ($C_9H_{16}N_4$)	72.5-77.5	208	1.44 (s, CH_3), 2.03 (s, $(CH_3)_2$), 10.86 (NH) [Me_2SO-d_6]	51.90 (7.74)	51.60 (7.86)
9, R = C_6H_5 ($C_{11}H_{12}N_6$)	180-182	228	2.07 (s, $(CH_3)_2$), 7.52-7.61 (m, m/p-Ph), 8.22-8.36 (m, o-Ph), 11.06 (NH) [Me_2SO-d_6]	57.88 (5.30)	57.68 (5.31)
10, R = C_2H_5 ($C_4H_5BrN_4$)	34.5-35.5	190/188	1.46 (t, CH_3), 3.25 (q, CH_2) [$CDCl_3$]	25.41 (2.67)	25.62 (2.52)
10, R = t-C_4H_9 ($C_6H_9BrN_4$)	oil	218/216	1.57 (s, CH_3) [$CDCl_3$]	33.20 (4.18)	33.34 (4.02)
18, R′ = H, L = NH_2[c] ($C_2H_3N_5$)	170-170.5	97	7.20 (NH), 9.66 (s, H) [CD_3COCD_3]	24.74[e] (3.11)	24.99[e] (3.11)
18, R′ = C_2H_5, L = NH_2[c] ($C_4H_7N_5$)	126.5-127	125	1.49 (t, CH_3), 3.09 (q, CH_2), 7.08 (NH) [CD_3COCD_3]	38.39 (5.64)	38.58 (5.33)
18, R′ = CH_3, L = Cl ($C_3H_3ClN_4$)	83.5-84.5	132/130	3.00 (s, CH_3) [CD_3OD]	27.60 (2.32)	27.94 (2.27)
19, R′ = H		112			
19,[b] R′ = H ($C_9H_8N_6$)	187-187.5	200	7.31-7.82 (m, Ph), 8.30 (s, CH), 9.92 (s, H), 12.35 (NH) [Me_2SO-d_6]	53.99 (4.03)	54.11 (3.81)
10, R′ = H, X = I (C_2HIN_4)	oil	208	10.25 (s, H) [$CDCl_3$]	11.55 (0.48)	*d*

[a] Exact mass measurement gave for $C_4H_6N_4$ (M^+) 110.0596 (theor. 110.0592). [b] Benzaldehyde hydrazone. [c] Compound is mentioned in ref 25, but no physical data are given. [d] Exact mass measurements gave for C_2HIN_4 (M^+) 207.92478 (theor. 207.92478); this compound is unstable but can be stored for short time at −20 °C. [e] Calcd for N, 72.14; found, 72.04.

19 (R′ = CH_3), respectively. The peak at 1.85 ppm is attributed to R′ = CH_3 in open-chain intermediate **23**, because it is in agreement with 1.88 ppm found for the open-chain intermediate **13** (R = CH_3) (Table II). The signal at 2.32 ppm can probably be attributed to compound **24I,II** (R′ = CH_3). Compound **24II** is obtained by ring closure of **23II** according to route b and **24I** by attack of hydrazine on C_6 of **18** (R′ = CH_3, L = NH_2) (route I, Scheme VII). This shift resembles the one at 2.42 ppm found for the CH_3 group of σ-adduct **11** (R = CH_3).

From stage i the corresponding ^{13}C NMR spectra were measured; the ^{13}C chemical shifts of **23** resemble those of the open-chain intermediates **13** in Table II. Similar results were obtained on measuring the ^1H and ^{13}C NMR spectra of 6-amino-3-ethyl-1,2,4,5-tetrazine (**18**; R′ = C_2H_5, L = NH_2) (see Table V). All the NMR data and the results of ^{15}N labeling support the mechanism proposed in Scheme VII.

In contrast to the reaction course presented for the Chichibabin amination of **7** (Scheme IV), we conclude that in the hydrazino deamination a somewhat different reaction sequence takes place (Scheme VII). The ring-labeled hydrazino compound **19*II** is obtained by an S_N(ANRORC) mechanism (route II), and the hydrazino compound with the ^{15}N label in the side chain, i.e., **19*I**, is formed by the S_N(AE) mechanism (route I). Compound **19*II** is formed via the open-chain intermediate **23*II**. The possible occurrence of **23*I** as an intermediate can be excluded, since ring-labeled **18*** would then have been formed; this is, however, not the case. That no S_N(AN-

RORC) mechanism is involved in the formation of the hydrazino compounds **19** (R′ = C_6H_5, t-C_4H_9) from **18** (R′ = C_6H_5, t-C_4H_9) is in agreement with the proposed mechanism since addition to position 3, leading to **22***, is prevented due to the blocking effects of these groups.

Experimental Section

Melting points are uncorrected. Mass spectra were determined on an AEI MS-902 mass spectrometer. Exact mass measurements and intensity ratio measurements on the M and (M + 2) peaks were carried out at a resolving power of 10000. ^{1}H NMR spectra were recorded on a JEOL NM C-60H, a Varian EM 390, or a Varian XL-100-15 spectrometer. Me_4Si was used as an internal standard (δ 0). ^{13}C NMR spectra were recorded on a Varian XL-100-15 spectrometer. Me_4Si was used as an internal standard. Typical spectral parameters for ^{13}C NMR were as follows: spectral width, 5120 Hz (1.25 Hz/point); acquisition time, 0.8 s; pulse delay, 0–1.2 s; pulse width, 10–20 μs (about 30°). UV spectra were measured on a Perkin-Elmer 550 spectrophotometer. Column chromatography was carried out over Merck silica gel 60 (70–230 mesh). ^{15}N-Hydrazine hydrate from Prochem was used. It contained 95 atom % of $^{15}N_2$ and was a 24.6% solution of ^{15}N-hydrazine hydrate in water. This was mixed with unlabeled hydrazine hydrate (100%, from Merck). The enrichment was determined from the labeling of the hydrazone compounds **9*** or the hydrazino compounds **19***. For some of the experiments of Table IV ^{15}N-labeled hydrazine hydrate was prepared from ^{15}N-hydrazine sulfate, as described before.[12]

The melting points, the ^{1}H NMR data, the mass spectrometric measurements, and the microanalyses of the new compounds are summarized in Table VII.

Preparation of Starting Materials. 3-R-1,2,4,5-tetrazines (7; R = CH_3,[12] t-C_4H_9,[6] C_6H_5,[24] p-$OCH_3C_6H_4$[24]) and 6-amino-1,2,4,5-tetrazines (18; R′ = H,[25] CH_3,[25] C_2H_5,[25] C_6H_5;[6] L = NH_2) were prepared according to known synthetic procedures. Compounds **18** (R′ = H, C_2H_5; L = NH_2) were only mentioned in ref 25, but no physical data were given.

3-Ethyl-1,2,4,5-tetrazine (7, R = C_2H_5) was prepared by hydrazinolysis of 6-amino-3-ethyl-1,2,4,5-tetrazine (**18**; R′ = C_2H_5, L = NH_2) and subsequent oxidation of the hydrazino compound with manganese dioxide on carbon,[22] analogously as described before.[12] This oxidation reaction is almost quantitative.

6-Bromo-1,2,4,5-tetrazines (10; R = C_2H_5, t-C_4H_9) were prepared by hydrazinolysis of 6-amino-1,2,4,5-tetrazines (**18**; R′ = C_2H_5, t-C_4H_9; L = NH_2) and subsequent oxidation of the hydrazino compounds with 2 equiv of bromine in acetic acid according to the procedure described before for 6-bromo-3-methyl(phenyl)-1,2,4,5-tetrazine (**10**; R = CH_3,[12] C_6H_5[6]). These reactions give almost quantitative yields.

6-Halogeno-1,2,4,5-tetrazines (20; X = Cl, Br, I; R′ = H, CH_3, C_2H_5, t-C_4H_9, C_6H_5) were prepared from the corresponding 6-amino compounds **18** (R′ = H, CH_3, C_2H_5, t-C_4H_9, C_6H_5; L = NH_2) analogously to the preparation of the 6-bromo compounds **10**. With the other halogens the oxidation reaction is also almost quantitative.

Hydrazinolysis Reactions. These reactions were carried out under the conditions and with the results given in Table VI. The hydrazino compounds **8** and **19** were identified as their benzaldehyde[6,12] or as their acetone hydrazones **9**. The separations were carried out as follows: **7** from **9** (R = CH_3, C_2H_5, t-C_4H_9), column chromatography with 3:1 CH_2Cl_2/petroleum ether (bp 60–80 °C) as eluant; **7** from **9** (R = C_6H_5), thin-layer chromatography over silica gel PF 254 (0.5 mm) with 40:3 CH_2Cl_2/ethylacetate as eluant; **7** from **10**, column chromatography with 1:2 CH_2Cl_2/petroleum ether (bp 60–80 °C) as eluant; **18** (L = NH_2) and the acetone hydrazone of **19**, column chromatography with 1:1 ether/petroleum ether (bp 40–60 °C) as eluant; **18** (L = NH_2) and **20** (L = Cl, Br, I), column chromatography with 1:2 ether/petroleum ether (bp 40–60 °C) or ether/pentane as eluant. The solvents were evaporated on a rotatory evaporator at moderate temperature (<33 °C) because of the instability and volatility of the compounds.

Acetone hydrazones 9 (R = CH_3, C_2H_5, t-C_4H_9, C_6H_5) were prepared by refluxing 1 mmol of pure hydrazino compound **8** or of a mixture containing hydrazino compound **8** with 2 mL of acetone during 5 min. This reaction is quantitative.

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Registry No. **7** (R = CH_3), 67131-36-6; **7** (R = t-C_4H_9), 78114-01-9; **7** (R = C_6H_5), 36022-11-4; **7** (R = p-$OCH_3C_6H_4$), 56107-91-6; **7** (R = C_2H_5), 79357-27-0; **9** (R = CH_3), 79357-28-1; **9** (R = C_2H_5), 79357-29-2; **9** (R = t-C_4H_9), 79357-30-5; **9** (R = C_6H_5), 79357-31-6; **10** (R = C_2H_5), 79329-77-4; **10** (R = t-C_4H_9), 79329-82-1; **10** (R = CH_3), 67131-33-3; **10** (R = C_6H_5), 35011-53-1; **11** (R = CH_3), 79357-32-7; **11** (R = C_2H_5), 79357-33-8; **11** (R = t-C_4H_9), 79357-34-9; **11** (R = C_6H_5), 79357-35-0; **13** (R = CH_3), 79357-36-1; **13** (R = C_2H_5), 79357-37-2; **13** (R = t-C_4H_9), 79357-38-3; **13** (R = C_6H_5), 79329-72-9; **16**, 1558-23-2; **17**, 79329-73-0; **18** (R′ = H, L = NH_2), 79329-74-1; **18** (R′ = CH_3, L = NH_2), 14418-27-0; **18** (R′ = C_2H_5, L = NH_2), 79329-75-2; **18** (R′ = t-C_4H_9, L = NH_2), 78113-95-8; **18** (R′ = C_6H_5, L = NH_2), 14418-30-5; **18** (R′ = CH_3, L = Cl), 79329-76-3; **18** (R′ = CH_3, L = Br), 67131-33-3; **19** (R′ = H), 79329-78-5; **19** (R′ = CH_3), 67131-34-4; **19** (R′ = C_2H_5), 79329-79-6; **19** (R′ = t-C_4H_9), 79329-80-9; **19** (R′ = C_6H_5), 21801-14-9; **20** (R′ = H, X = I), 79329-81-0; **23** (R′ = H), 79329-83-2; **23** (R′ = CH_3), 79329-84-3; **23** (R′ = C_2H_5), 79357-39-4.

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