2.2 (s, 10, CH_3 and NH); IR (KBr) ν(C=O) 1665 cm^{-1}. Anal. Calcd for $C_{13}H_{19}N_3O$: C, 66.93; H, 8.21; N, 18.00. Found: C, 66.16; H, 8.17; N, 17.37.

Product Study of 8. Substrate 8 (1 g, 4.3 mmol) was dissolved in 50 mL of trifluoroacetic acid. The resulting orange solution was refluxed for 1 h. Water (2 mL) was added and the solvents were removed by rotary evaporation. Treatment of the resulting solid with $CHCl_3$ resulted in the precipitation of one solid. A second solid was obtained by removal of the solvent, and both solids were recrystallized from CH_3OH. Solid I (*N,N'*-dimethyl-*N,N'*-bis(trifluoroacetyl)ethylenediamine): 1.2 g, mp 59-65 °C; ^1H NMR (CD_3OD) δ 3.4 (s, 4), 2.8 (s, 6); IR (KBr) ν(C=O) 1665 cm^{-1}; ^{13}C NMR (CD_3OD) δ 163.5 (C=O, q from splitting by CF_3, J = 60 Hz), 137.6, 132.7, 128.0, 123.2 (q, J = 315 Hz, CF_3), 45.7 (s, CH_2), 34.0 (s, CH_3). Solid II (*p*-acetamidobenzaldehyde): 0.55 g, mp 145-147 °C; ^1H NMR ($CDCl_3$) δ 9.9 (s, 1), 7.5-7.9 (m, 5, Ar, NH), 2.2 (s, 3, CH_3); IR (KBr) ν(C=O) 1690, ν(NC=O) 1678 cm^{-1}.

Supplementary Material Available: Figures S-1 through S-7 (8 pages). Ordering information is given on any current masthead page.

A Potassium Amide Induced Ring Transformation of 1,2,4-Triazines into 1,2,4-Triazoles and 1,3,5-Triazines[1]

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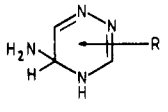
5-Phenyl- and 3,5-diphenyl-1,2,4-triazine, when treated with potassium amide in liquid ammonia, are converted into a mixture of phenyl derivatives of 1,2,4-triazole and amino-1,3,5-triazines. The ring contraction of the 1,2,4-triazine ring into the 1,2,4-triazole ring has been explained by an initial addition of the amide ion to C-6, ring opening by fission of the N1-C6 bond and ring closure (ANRORC-mechanism). The transformation of the 1,2,4-triazine ring into the 1,3,5-triazine ring has been studied by means of ^{15}N-labeled potassium amide. It was found that the nitrogen of the amide ion becomes one of the ring nitrogen atoms in the 1,3,5-triazine ring and that the exocyclic amino group is *un*labeled. Based on these ^{15}N-labeling studies, it is proposed that this ring transformation starts with an initial addition of the amide ion to C-5, ring opening between C-5 and C-6, a dehydrogenative rearrangement of the open-chain intermediate 1-amino-2,4,5-triazahexatriene into 1-amino-4-cyano-2,4-diaza-1,3-butadiene, and ring closure.

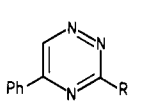
Recently we reported[2] on a new procedure for the introduction of an amino group into the 1,2,4-triazine ring via a nucleophilic displacement of hydrogen. The method is based on the potassium permanganate oxidation of 5-amino-4,5-dihydro-1,2,4-triazines (1), being formed in situ by covalent addition of liquid ammonia to 1,2,4-triazines, having an unoccupied C-5 position. Sound evidence for the intermediary existence of these C-5 adducts **I** was provided by ^1H and ^{13}C NMR spectroscopy.[3]



1

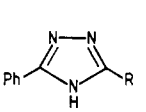
By NMR spectroscopy it was further shown that covalent addition of liquid ammonia to 1,2,4-triazines does not take place when position 5 is blocked by the presence of a substituent. This result was confirmed by the fact that all attempts to convert 5-phenyl-1,2,4-triazine (**2a**) or 3,5-diphenyl-1,2,4-triazine (**2b**) into amino derivatives by oxidation of solutions of **2a** or **2b** in liquid ammonia with potassium permanganate failed.

In view of earlier observations that increase of the nucleophilicity of the aminating agent may change the reaction course,[4,5] we studied the behavior of 1,2,4-triazines **2a** and **2b** toward potassium amide, being a stronger nucleophile than liquid ammonia. We found indeed that **2a** as well as **2b** does react with potassium amide in liquid ammonia, although slowly, however, not leading to the formation of amino derivatives of **2a** or **2b**: but to ring transformation products, i.e., 1,2,4-triazoles and 1,3,5-triazines.



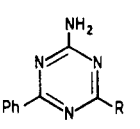
2

a) R = H
b) R = Ph



3

a) R = H
b) R = Ph



4

a) R = H
b) R = Ph
c) R = NH_2

Thus, treatment of **2a** with 4 equiv of potassium amide in dry liquid ammonia at -33 °C for 24 h results in the formation of 3-phenyl-1,2,4-triazole (**3a**, 21%) and 2,4-diamino-6-phenyl-1,3,5-triazine (**4c**, 23%), along with a trace of 2-amino-4-phenyl-1,3,5-triazine (**4a**). 3,5-Diphenyl-1,2,4-triazine (**2b**) reacts similarly, yielding 3,5-

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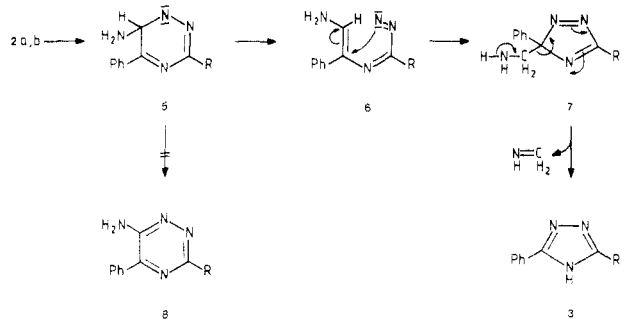
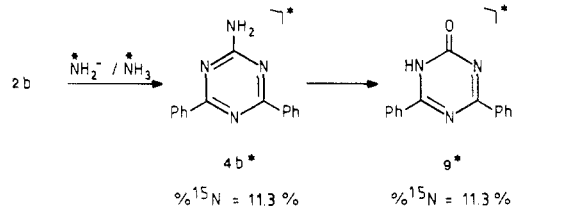
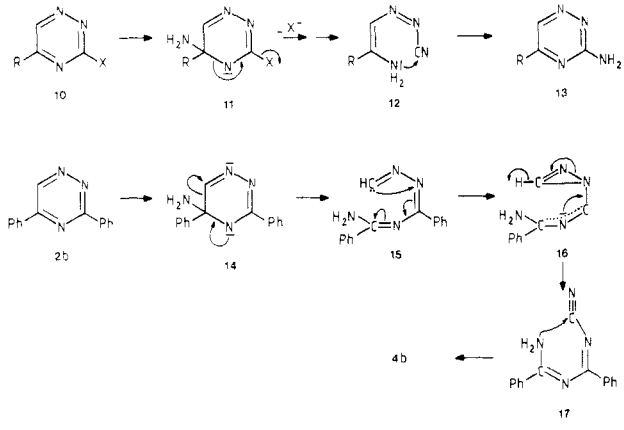
Scheme I



Scheme II



Scheme III



diphenyl-1,2,4-triazole (**3b**, 42%) and 2-amino-4,6-diphenyl-1,3,5-triazine (**4b**, 22%) respectively. All products were easily separated by column chromatography on silica gel and identified by comparison with an authentic specimen.[6-8] Compound **4a** is the precursor of **4c**, as treatment of **4a**, with potassium amide in liquid ammonia under the same conditions as mentioned above for the amination of **2a**, gave **4c** in good yield.

From the structure of the products the transformation of the 1,2,4-triazine ring into the 1,2,4-triazole seems to involve fission of the N1–C6 bond. Amide-induced ring contraction of 1,2,4-triazines into 1,2,4-triazoles were occasionally observed[9,10] in reactions of 3-X-5-phenyl-1,2,4-triazines (X = halogen, methylthio); the yields are, however, very poor, due to the highly competitive amination at C3, to which the leaving group is attached.

The results obtained in this study seem to justify the conclusion that 1,2,4-triazines, that do not contain a leaving group at C3 prefer ring contraction into 1,2,4-triazoles rather than a Chichibabin-type displacement of hydrogen by an amino group. We propose that the formation of **3** proceeds via (i) an initial amide addition at C6,[9] leading to the 1,2,4-triazinide **5**, (ii) ring opening of **5** between N1–C6 into **6**, (iii) ring closure of **6** into 3*H*-1,2,4-triazole **7** and (iv) a base-induced fragmentation of the aminomethyl side chain leading to loss of methanimine. Spectroscopic evidence for the intermediacy of σ-adduct **5** was not obtained, leading to the conclusion that its formation will be slow. The formation of **5** will certainly not take place in a kinetically controlled step, since position 5, having the lowest electron density and not position 6, is favored for this addition.

Additional evidence for the proposed mechanism is obtained from a study of the reaction of **2b** with ^{15}N-labeled potassium amide. It was found that the 1,2,4-triazole obtained was unlabeled!

Attempts to trap **5** (R = Ph) by reacting **2b** with potassium amide in liquid ammonia in the presence of potassium permanganate were not successful: no trace of 6-amino-3,5-diphenyl-1,2,4-triazine **8** (R = Ph)[11] was obtained. It shows that when **5** is formed the ring opening into **6** is more favored than its dehydrogenation into **8** (Scheme I).

In order to obtain some more detailed insight into the mechanism of the ring transformation of the 1,2,4-triazines **2** into the 1,3,5-triazines **4** we investigated the reaction of 3,5-diphenyl-1,2,4-triazine (**2b**) with potassium amide/liquid ammonia, being ^{15}N-labeled (% of excess of ^{15}N = 11.5%). We found that the 2-amino-4,6-diphenyl-1,3,5-triazine obtained contained an excess of 11.3% of ^{15}N (i.e. **4b***) and that after conversion of **4b*** into 2,4-diphenyl-1,3,5-triazin-6-one (**9***) (Scheme II) by treatment with sodium nitrite in acetic acid[12] the triazinone contained the same percentage of ^{15}N excess as **4b*** , i.e., 11.3%. This result proves that in **4b*** only one of the ring nitrogens is ^{15}N-labeled and that the exocyclic amino group in **4b*** is unlabeled.

This labeling experiment allows us to conclude that one of the ring nitrogens of the 1,3,5-triazine ring in **4b*** originated from the amide ion and that the nitrogen present in the exocyclic amino group of **4b*** was originally present in the 1,2,4-triazine ring of **2b**. On the basis of these results we propose the following reaction scheme for the conversion of **2b** in **4b** (Scheme III).

The amide ion adds to position 5 of **2b** (i.e. **14**), although that position is somewhat hindered due to the presence of the phenyl group. Addition of an amide ion to C5 of 5-alkyl(aryl)-1,2,4-triazines **10** containing a leaving group X at C3 has been encountered before.[9] It is well documented that the adduct **11** can undergo ring fission between N4–C5 with expulsion of the leaving group, leading to an open-chain intermediate **12**, which on cyclization leads to 3-amino-5-alkyl(aryl)-1,2,4-triazine (**10** → **11** → **12** → **13**). Since in this study we deal with compounds that do not contain a leaving group at C3, the driving force for ring opening is absent; apparently ring fission in the σ-adduct **14** between C5–C6 is now favored. It yields the anionic 1-amino-2,4,5-triazahexatriene **15**. Since there is overwhelming evidence in the literature that δ-amino nitriles can easily undergo cyclization[12] we suppose that the formation of **4b** requires the intermediacy of 4-amino-1-cyano-2,4-diazabutadiene (**17**). It leads to the conclusion that **15** has to undergo an oxidative rearrangement reaction leading to **17**. We suggest the intermediacy of the diazirine

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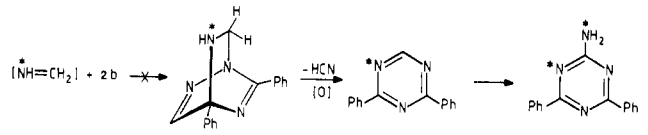
Scheme IV



16, which rearranges with expulsion of the hydride ion. The fate of this hydride ion is unknown, but due to the presence of many reducible double bonds, e.g., in **14** or **15**, reduction may occur. In any case the proposed mechanism explains the presence of the ring-labeled nitrogen atom derived from the amide ion and of the unlabeled exocyclic nitrogen derived from the nitrogen of the 1,2,4-triazine ring.

An alternative pathway to explain the formation of **4b**, involving as first step the nucleophilic addition of the anion of formamidine or aminocyan (both compounds previously found to be formed by amide-induced ring degradation of 1,2,4-triazines),[9] was considered, but this mechanism was excluded: reaction of **2b** with 1 equiv of potassium salt of formamidine, dissolved in liquid ammonia (free of amide ion) or with 1 equiv of potassium cyanamide (formed from aminocyan and 1 equiv of potassium amide) gave no detectable amounts of **4b**.

The possibility that **4b** is formed from **2b** by a Diels–Alder cycloaddition with inverse electron demand involving addition of methanimine, obtained as byproduct in the formation of 3,5-diphenyl-1,2,4-triazole (**3b**, see Scheme I) from **2b**, followed by loss of hydrogen cyanide, oxidation (by air) and subsequent amination (see above) was also taken into consideration (Scheme IV). Although this mechanism nicely explains the presence of the ^{15}N-label in the 1,3,5-triazine ring, it must be rejected, as this mechanism must lead to an amino compound, in which *both* amino group and ring nitrogen are ^{15}N-labeled; this has not been found.

Experimental Section

^1H NMR spectra were obtained with a Varian EM 390 with Me_4Si as internal standard. When measurements were made in liquid ammonia NH_3 was used as standard (adding 0.95 ppm converts the spectra to the Me_4Si scale). Mass spectra and ^{15}N-contents were determined on an AEI MS-902 mass spectrometer.

Amination Procedure for the Reaction of 1,2,4-Triazines 2a,b with Potassium Amide. To 20 mL of dry liquid ammonia in a 50-mL three-neck round-bottom flask equipped with a dry ice/acetone condenser were added a few crystals of ferric nitrate and 160 mg of potassium. After the mixture was stirred for 15 min at −33 °C the 1,2,4-triazine derivative (1 mmol) was added. The reaction was terminated after 24 h by the addition of 220 mg (4 mmol) of ammonium sulfate. After the ammonia was evaporated, the residue was thoroughly extracted with boiling chloroform. Separation of products was achieved by column chromatography on SiO_2 with chloroform for compounds **3b** and **4b** or chloroform–acetone (1:1) for compounds **3a** and **4a,c** as eluents.

The amination in ^{15}N-labeled liquid ammonia with ^{15}N-labeled potassium amide was carried out in the same manner.

Conversion of 2-Amino-4,6-diphenyl(^{15}N)-1,3,5-triazine (4b*) into 4,6-Diphenyl-1,3,5-triazin-6-one (9*). This conversion was performed by the same procedure as that described for the unlabeled compound.[12]

Conversion of 2-Amino-4-phenyl-1,3,5-triazine (4a) into 2,4-Diamino-6-phenyl-1,3,5-triazine (4c). 2-Amino-4-phenyl-1,3,5-triazine (1 mmol) was treated with 5 mmol of potassium amide in 20 mL of dry liquid ammonia. After 24 h the reaction was quenched with ammonium sulfate. The dry residue was extracted with boiling chloroform. Compound **4c** was purified by column chromatography (SiO_2, 1:1 chloroform–acetone). Yield of **4c**, 60%.

Preparation of 3,2′-Annelated 2-Phenylpyridines and Their Cyclopalladation Chemistry

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A series of 3,2′-polymethylene-bridged derivatives of 2-phenylpyridine has been prepared by thermolysis of *O*-allyloximes of 2,3-benzocycloalkanones. The electronic absorption and NMR spectra of these molecules may be related to the degree of nonplanarity of the system resulting from polymethylene bridging. These molecules react with palladium bis(acetylacetonate) and its hexafluoro derivative to give soluble, monomeric cyclopalladated products. Rates of cyclopalladation were measured for these systems as well as for 2-(phenyl-d_5)pyridine, and the results indicate the liklihood that for the less planar substrates the deprotonation step may show increasing importance over the electrophilic attack of palladium on the phenyl ring. The possible oxidative addition of palladium to a phenyl C–H bond cannot be ruled out.

The technique of bridging a biaryl system allows one to conveniently control the orientation of two covalently bonded aromatic rings with respect to one another. We have recently reported on the preparation and study of 3,3′-polymethylene-bridged derivatives of 2,2′-bipyridine,[1] 2,2′-biquinoline,[2] and 2,2′-bi-1,8-naphthyridine[3] as well as analogous bis-annelated derivatives of 2,2′;6′,2″-terpyridine.[4] An intriguing aspect of these molecules stems from our ability to control the orientation of the 1,4-bidentate chelating site by variation of the annelating bridge length. We have examined the effect of ligand conformation in coordination with copper(II),[5] ruthenium(II),[6]

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