isopropylamine, 75-31-0; *tert*-butylamine, 75-64-9; cyclohexylamine, 108-91-8; phenylamine, 62-53-3; dimethyl 8-phenyl-8-azabicyclo-[4.3.0]nona-1(16),3-diene-3,4-dicarboxylate, 50940-17-5; 1,1-dimethyl-3,4-dimethylenepyrrolidinium iodide, 50586-35-1; diethyl azodicarboxylate, 1972-28-7; diiron nonacarbonyl, 15321-51-4; sulfur dioxide, 7446-09-5; 1,4-diisopropenylbenzene, 1605-18-1; 1,4-diisopropenyl-1,4-cyclohexadiene, 56892-50-3; 11-methyl-4,6-dioxo-5-phenyl-5,11-diazatricyclo[7.3.0.0^{3,7}]dodeca-1(9)-ene, 50521-58-9.

Ring Transformations and Amination in Reactions of 3-Halogeno-5-phenyl-1,2,4-triazines with Potassium Amide in Liquid Ammonia[1-3]

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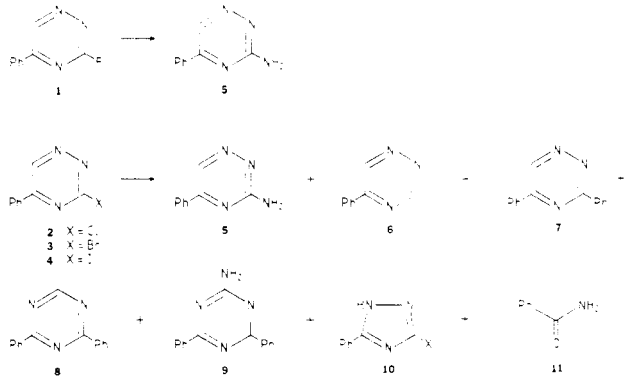
The reactions of 3-X-5-phenyl-1,2,4-triazines (X = fluoro, chloro, bromo, iodo) toward potassium amide/liquid ammonia were studied. Whereas the 3-fluoro compound gives only the 3-amino derivative, the 3-chloro, 3-bromo, and 3-iodo compounds yield a complex mixture containing, besides 3-amino-5-phenyl-1,2,4-triazine and 5-phenyl-1,2,4-triazine, ring-transformation products, i.e., 3,5-diphenyl-1,2,4-triazine, 2,4-diphenyl-1,3,5-triazine, 6-amino-2,4-diphenyl-1,3,5-triazine, and 3-X-5-phenyl-1,2,4-triazole. Evidence is found that in the ring transformation of 3-X-5-phenyl-1,2,4-triazines into 2,4-diphenyl-1,3,5-triazines, benzamidine must be an intermediate. The mechanisms of the amination and ring transformation are extensively discussed.

1. Introduction

Recent investigations of the amination of 3-(methylthio)-1,2,4-triazine with potassium amide in liquid ammonia have shown[4] that this conversion occurs to a great extent according to a mechanism involving ring opening [S_N(ANRORC) mechanism[5]]. This mechanism involves a primary addition of the amide ion to the π-deficient C-5 position of the 1,2,4-triazine ring and ring opening into an open-chain intermediate, which undergoes recyclization into the corresponding 3-amino compound. ^{1}H and ^{13}C NMR spectroscopic studies[1] of solutions of 1,2,4-triazine and some of its derivatives in liquid ammonia confirm that the 1,2,4-triazine ring forms exclusively a σ adduct at C-5. These studies induced us to investigate in more detail the behavior of 5- and/or 6-substituted 1,2,4-triazines with a C-3 group having considerable leaving character with respect to anionic nucleophiles.

In the present paper we report the results of an investigation of the reactions of 3-halogeno-5-phenyl-1,2,4-triazines with potassium amide in liquid ammonia. These compounds are of particular interest since the presence of the phenyl group at C-5 can retard or at least prevent addition of the amide ion to C-5, facilitating the attack of a nucleophile at C-3 of the 1,2,4-triazine ring.

Scheme I



2. Results

The hitherto unknown compounds 3-fluoro- (**1**), 3-chloro- (**2**), 3-bromo- (**3**), and 3-iodo-5-phenyl-1,2,4-triazine (**4**) were synthesized according to standard procedures. The preparations are extensively described in the Experimental Section. It was found that treatment of **1** with potassium amide/liquid ammonia at −75 °C for 5 min gave nearly exclusively 3-amino-5-phenyl-1,2,4-triazine (**5**) (Scheme I). Only a trace of an unidentifiable tar is obtained. In contrast, treatment of the compounds **2**–**4** with potassium amide at −33 °C for 15 min gave complex reaction mixtures. We were able to identify in these mixtures the presence of the 3-amino compound **5**, the dehalogenated product 5-phenyl-1,2,4-triazine (**6**), and the ring transformation products 3,5-diphenyl-1,2,4-triazine (**7**), 2,4-diphenyl-1,3,5-triazine (**8**), 6-amino-2,4-diphenyl-1,3,5-triazine (**9**), 3-X-5-phenyl-1,2,4-triazole (**10**; X =

(1) Part 24 on NMR investigations of σ adducts of heterocyclic systems with nucleophiles. For part 23, see: J. Breuker and H. C. van der Plas, *J. Org. Chem.*, **44**, 4677 (1979).

(2) Part 42 on ring transformations of heterocyclic halogeno compounds with nucleophiles. For previous paper, see: A. Nagel, H. C. van der Plas, G. Geurtsen, and A. van der Kuilen, *J. Heterocycl. Chem.*, **16**, 309 (1979).

(3) Part 26 on the S_N(ANRORC) mechanism. For part 25, see: J. Breuker and H. C. van der Plas, *J. Org. Chem.*, **44**, 4677 (1979). For part 24 see: H. C. van der Plas, *Acc. Chem. Res.*, **11**, 462 (1978).

(4) A. Rykowski and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, **94**, 204 (1975).

(5) For a recent review on the occurrence of the S_N(ANRORC) mechanism in nucleophilic substitution, see: H. C. van der Plas, *Acc. Chem. Res.*, **11**, 462 (1978).

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Scheme II

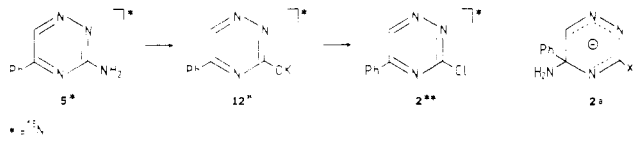


Table I. Percentage of S_N(ANRORC) Mechanism Operative in the Reactions of the Labeled 3-Halogeno-5-phenyl-1,2,4-triazines 2* and 3* with Potassium Amide in Liquid Ammonia and the 3-Halogeno-5-phenyl-1,2,4-triazines 1 and 4 with ^{15}N-Labeled Potassium Amide

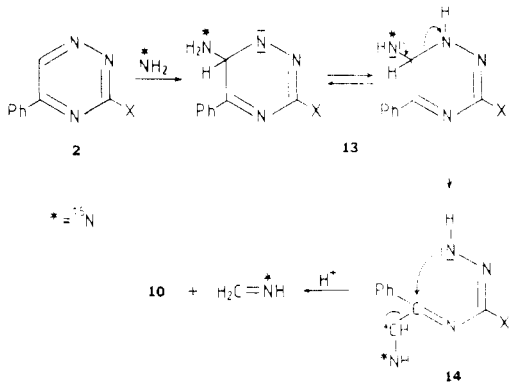
reactant (% excess ^{15}N)	% excess ^{15}N in products		% S_N(ANRORC)
	5*	2**	
1	6.7	1.2	18
2* (4.8)	5.1	0.2	96
3* (11.0)	11.1	0.8	93
4	5.9	3.7	63

chloro, bromo, iodo), and benzamide (11). The yields of products in all four reaction mixtures are summarized in Table II (see Experimental Section). The products 5–9, 10 (X = Br, I), and 11 were identified by comparison of their physicochemical data with those of authentic specimens.[6-10] Compound 10 (X = Cl) was unknown, and its structure was proven by elemental analysis and mass, IR and ^{1}H NMR spectra. From a survey of the results presented above it is evident that the 3-halogeno-5-phenyl-1,2,4-triazines 1–4 are multireactive toward potassium amide. In the next section we will discuss several processes (amination, dehalogenation, and ring transformation) which these compounds undergo.

3. Discussion

3.1. Mechanism of the Amination–Dehalogenation Reaction. There is strong evidence[5,11] that halogeno azaaromatics can react with potassium amide according to an S_N(AE), S_N(EA), and/or S_N(ANRORC) mechanism. In order to establish to which percentage the 1,2,4-triazines react via an S_N(ANRORC) process, we investigated the amination with ^{15}N-labeled compounds. Therefore, we prepared the labeled compounds 2 and 3, being enriched with ^{15}N at position 4; we refer to these compounds as 2* and 3*. The preparation of these compounds is described in the Experimental Section. Amination of compounds 1 and 4 was studied in a different manner, namely, by reacting these compounds with ^{15}N-labeled potassium amide in ^{15}N-labeled ammonia, a technique recently developed.[12] The excess of ^{15}N present in the 3-amino-5-phenyl-[x-^{15}N]-1,2,4-triazine (5*) formed in the amination of 1, 2*, 3* and 4 was determined by mass spectrometry.[4] In order to determine the percentage of excess of ^{15}N present in the ring and in the amino group of 5*, we converted 5* potassium hydroxide into the potassium salt of

Scheme III



5-phenyl-[x-^{15}N]-1,2,4-triazin-3-one (12*), which on treatment with phosphoryl chloride gave the corresponding 3-chloro-5-phenyl-[x-^{15}N]-1,2,4-triazine (2**) (Scheme II). By measuring the excess of ^{15}N present in 5* and 2**, we calculated to what percentage the S_N(ANRORC) mechanism in the amination–dehalogenation reaction has occurred. The values are shown in Table I. From the results listed in Table I the conclusion can be drawn that despite the presence of the phenyl group at C-5 the compounds 2–4 react with potassium amide to a major extent (63–96%) by an S_N(ANRORC) mechanism involving 5-amino-3-X-5-phenyl-2(4),5-dihydro-1,2,4-triazinides (2a) (X = chloro, bromo, iodo) as intermediates (Scheme II). The 3-fluoro compound 1, on the other hand, shows a high percentage (83%) of an S_N(AE) process initiated by attack at C-3 of the 1,2,4-triazine ring.[13] This result is consistent with the recent observation that amination of 4,6-diphenyl-2-fluoropyrimidine occurs according to an S_N(AE) process[14] but that in the amination of 2-fluoro-4-phenylpyrimidine (position 6 is now unsubstituted), the S_N(ANRORC) mechanism is the main process.[15]

3.2. Formation of 5-Phenyl-1,2,4-triazine (6). In the previous section it was unequivocally shown that the 1,2,4-triazine ring can be attacked by the amide ion at positions 3 and 5. The strong nucleophilic amide ion is also able to attack the halogen in compounds 2–4, yielding after protonation the dehalogenated compound 6. Positive halogen transfer in heterocycles has been intensively studied[16,17] but was usually observed only with bromo and iodo compounds. Very recently, amide-induced dehalogenation has also been found with 2-chloro-4,6,7-triphenylpteridine and 6-chloropyrido[2,3-b]pyrazine.[18]

3.3. Ring Contraction of Compounds 2–4 into the Triazoles 10 (X = Halogen). The ring contraction of 1,2,4-triazines into 1,2,4-triazoles by nucleophiles has been described in the literature.[19,20] However, the ring contraction reported in this paper is the first example of a potassium amide induced ring contraction. It raises the interesting question of whether one of the nitrogens

(6) J. A. Elvige, G. T. Newbold, I. R. Senciall, and T. G. Symes, *J. Chem. Soc.*, 4157 (1964).
(7) C. Grundmann, U. Ulrick, and A. Kreutzberger, *Ber. Dtsch. Chem. Ges.*, **86**, 181 (1953).
(8) W. W. Paudler and T. K. Chen, *J. Heterocycl. Chem.*, **7**, 767 (1970).
(9) H. Neunhoeffer, H. Henning, H. W. Frauhauf, and M. Mutterer, *Tetrahedron Lett.*, 3147 (1969).
(10) Gy Simig, H. C. van der Plas, and C. A. Landheer, *Recl. Trav. Chim. Pays-Bas*, **95**, 113 (1976).
(11) H. J. den Hertog and H. C. van der Plas, *Adv. Heterocycl. Chem.*, **4**, 121–42 (1965).
(12) A. Nagel and H. C. van der Plas, *Heterocycles*, **7**, 205 (1977).
(13) The fluorine atom, being highly electron attracting, strongly polarizes the carbon to which it is attached, making the nucleophilic attack of the amide ion to that carbon more favorable than in the case of compounds 6–8.
(14) A. P. Kroon and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, **93**, 227 (1974).
(15) A. P. Kroon and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, **93**, 111 (1974).
(16) G. M. Sanders, M. van Dijk, and H. J. den Hertog, *Recl. Trav. Chim. Pays-Bas*, **93**, 273 (1974).
(17) D. A. de Bie, H. C. van der Plas, G. Geurtsen, and K. Nijdam, *Recl. Trav. Chim. Pays-Bas*, **92**, 245 (1973).
(18) A. Nagel, Thesis, Agricultural University, Wageningen, The Netherlands, 1978.
(19) T. Sasaki and K. Minamoto, *J. Org. Chem.*, **31**, 3917 (1966).
(20) J. Lee and W. W. Paudler, *Chem. Commun.*, 1635 (1971).

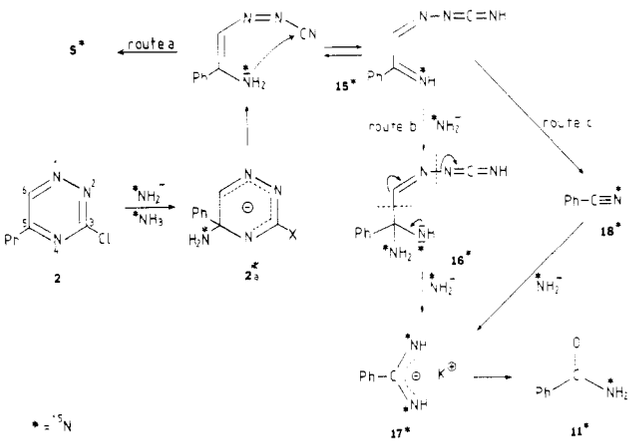
present in the 1,2,4-triazole ring originates from the amide ion. Therefore, we studied the ring contraction of **2** with potassium [^{15}N]amide (5.1% of excess of ^{15}N). Measurement of the excess of ^{15}N in the 1,2,4-triazole isolated from the reaction mixture showed that ^{15}N has *not* been incorporated into the triazole ring; thus the nitrogens of the triazole ring originate from the nitrogens of the 1,2,4-triazine ring. We propose that the initial step in the ring contraction is addition of the amide ion to C-6, involving as the σ adduct the 6-amino-3-X-5-phenyl-1,6-dihydro-1,2,4-triazinide (**13**). Fission between C-6 and N-1 yields the intermediate **14**, which undergoes an intramolecular ring closure to **10** with elimination of iminomethylene (Scheme III). Attempts to measure by ^{1}H NMR spectroscopy the presence of adduct **13**, by the method previously described,[1] failed. However, that addition at C-6 is important is apparent from the fact that 3-chloro-6-phenyl-1,2,4-triazine was recently found[21] to give no ring contraction with potassium amide.

3.4. Ring Transformation of the 1,2,4-Triazines 2–4 into the 1,3,5-Triazines 8 and 9. The occurrence of the ring transformation of 1,2,4-triazines into 1,3,5-triazines under the influence of potassium amide has never been reported. With phenylmagnesium bromide, the ring transformation of triphenyl-1,2,4-triazine into triphenyl-1,3,5-triazine has been found.[22] However, a more detailed study has never been made. In order to gain some insight into the mechanism of the potassium amide induced ring transformation, we were particularly interested to learn from which compound (1,2,4-triazine or potassium amide) the nitrogens of the 1,3,5-triazine ring originate and which carbon (C-3 or C-6) of **2–4** is built into the new heterocyclic ring.[23]

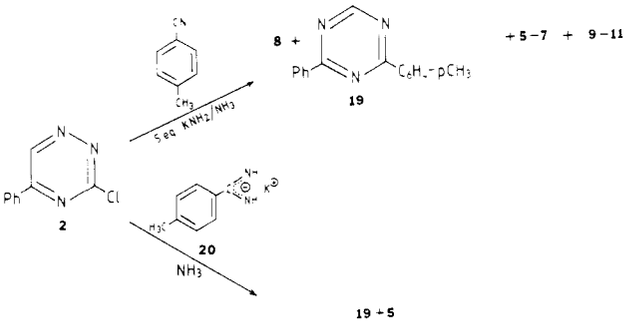
It was found that in 2,4-diphenyl-1,3,5-triazine (**8**) formed from **2*** and **3*** with potassium amide, the ring nitrogens are not enriched with ^{15}N. The conclusion is evident: nitrogen N-4 of the 1,2,4-triazine ring has been replaced during the formation of the 1,3,5-triazine ring by the nitrogen of the potassium amide. When we studied the ring transformation of the *unlabeled* compound **2** with ^{15}N-labeled potassium amide (5.1% of excess of ^{15}N), we found that the excess of ^{15}N in **8** is nearly *twice* the enrichment of the ^{15}N in potassium amide! Both results allowed us to conclude that *two* nitrogens of the 1,3,5-triazine ring must originate from potassium amide, and thus only *one* nitrogen of the 1,2,4-triazine ring (N-1 or N-2) is built into the 1,3,5-triazine ring.

The problem of which carbon atom (C-3 or C-6) of the 1,2,4-triazine ring is built into position C-6 of 2,4-diphenyl-1,3,5-triazine was solved by a study of the reaction with 3-bromo-5-phenyl-[3-^{13}C]-1,2,4-triazine. The synthesis of this ^{13}C-labeled compound was performed as described before for the unlabeled compound with potassium [^{13}C]cyanide as the starting substance (see Experimental Section). When we allowed this bromo compound, containing a 3.8% of excess of ^{13}C (determined by mass spectrometry and ^{13}C NMR spectrometry), to react with potassium amide in liquid ammonia and established the ^{13}C content in **8**, we found that *no* excess of ^{13}C was present. This result proves that not C-3 but C-6 is incorporated in the 1,3,5-triazine ring, and it suggests that N-1 and not N-2 of the 1,2,4-triazine ring has been built into **8**. A fission of the N-1 to N-2 bond is apparently one

Scheme IV



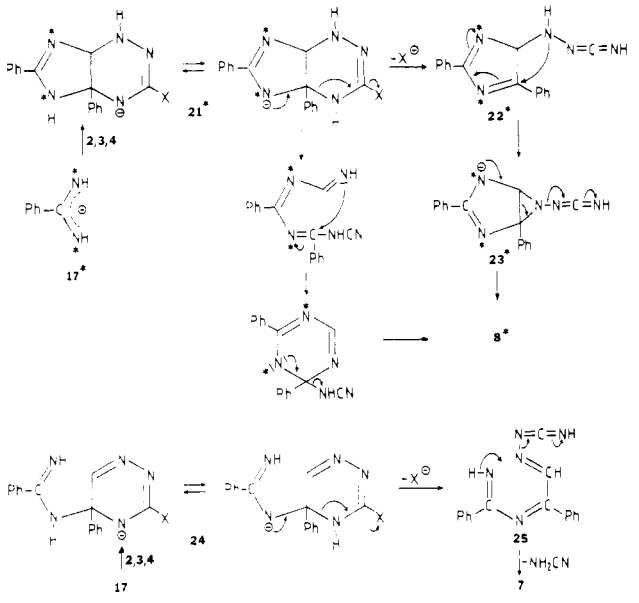
Scheme V



of the processes which takes place during the ring transformation. Another important piece of information was obtained by measuring the enrichment of ^{15}N in the by-product benzamide (**11**). It was found that **11** obtained after the reaction of compound **2** with ^{15}N-labeled potassium amide (5.1% of excess of ^{15}N) has the same (within experimental limits) ^{15}N content as that present in the labeled potassium amide. These results seem to justify the conclusion that the potassium salt of benzamidine (**17***) is an intermediate during the reaction, which after workup gives labeled benzamide (**11***). The formation of the potassium salt of **17*** is pictured in Scheme IV. It involves the open-chain tautomeric intermediates **15*** which either can be converted into **5*** according to an S_N(ANRORC) mechanism (route a) or may alternatively undergo addition with an amide ion (route b) to form anionic intermediate **16***. Base-induced loss of hydrogen cyanide and cyanamide in **16*** leads to fission of the carbon–carbon and nitrogen–nitrogen bonds with formation of the potassium salt of **17***. Another possible route to **17*** is from labeled benzonitrile (**18***) which could be formed by fission of the C–C bond in the open-chain intermediate **15*** (Scheme IV, route c). The mechanism also accounts for the fact that benzamide (**11**) is not formed in the reaction of the 3-fluoro compound **1** with potassium amide, since compound **1** does not react via an initial addition at position 5 but for the greater part by addition of the amide ion at position 3. To ascertain that benzamidine (**17**) plays an important role in the ring transformation of compounds **2–4** into **8**, we carried out an experiment in which 1 equiv of compound **2** and 1 equiv of *p*-cyanotoluene were reacted with a solution of 5 equiv of potassium amide in liquid ammonia. Under these conditions benzonitrile is known to form the potassium salt of benzamidine[24,25] immediately. In the

(21) A. Rykowski, P. Nantka-Namirski, and H. C. van der Plas, *Heterocycles*, **9**, 1490 (1978).
(22) A. Mustafa, A. Kader Mansour, and H. A. A. Azim Zaher, *J. Prakt. Chem.*, **313**, 699 (1971).
(23) It is evident that C-5, which is carrying the phenyl substituent, is incorporated twice into the 1,3,5-triazine ring.
(24) G. Newberry and W. Webster, *J. Chem. Soc.*, 738 (1947).
(25) E. F. Cornell, *J. Am. Chem. Soc.*, **50**, 3311 (1928).

Scheme VI



reaction product obtained we could identify, besides 2,4-diphenyl-1,3,5-triazine (8) and the previously obtained compounds 5–7 and 9–11, 2-phenyl-4-(*p*-methylphenyl)-1,3,5-triazine (19) (Scheme V). On reaction of 2 with the potassium salt of *p*-amidinotoluene (20) dissolved in liquid ammonia (thus free of amide ions), the only products obtained were 19 and 5. No traces of compound 8 were detected in the reaction mixture.[26] This ring transformation reaction provides us with a new method for preparing disubstituted 1,3,5-triazines, with different substituents at positions 2 and 4, from 1,2,4-triazines.

The results obtained with the potassium salt of benzamidine (17) and *p*-amidinotoluene (20), combined with those of ^{15}N- and ^{13}C-labeling experiments, led us to propose tentatively the following reaction pathway for the formation of 8*. Benzamidine (17*) adds to compounds 2, 3, or 4 across the 5,6-bond, yielding the anion 21*. This undergoes rearrangement via open-chain intermediate 22* into the bicyclic compound 23*, which by a base-induced elimination of cyanamide is converted into 8* (see Scheme VI).

The formation of the 6-amino-2,4-diphenyl-1,3,5-triazine (9) is assumed to take place by amination of 2,4-diphenyl-1,3,5-triazine (8) with potassium amide. Previously it was well established by using ^{15}N-labeled potassium amide that compound 8 undergoes amination into 9 via a low-temperature Chichibabin reaction; *no trace* of the ^{15}N label was observed in the 1,3,5-triazine ring.

3.5. Ring Transformation of the Compounds 2–4 into 3,5-Diphenyl-1,2,4-triazine (7). The formation of the intermediary potassium salt of benzamidine (see section 3.4) can also explain the formation of 7 from compounds 2–4. The essential step in this reaction is addition of the amidine at C-5 in 2–4, giving the adduct 24. Ring opening with elimination of X^-, followed by rearrangement of open-chain intermediate 25 as indicated, yields 7. Since in starting materials 2–4 and in the end product 7 a 1,2,4-triazine ring is present, we refer to this ring transformation as a *degenerate* ring transformation. Numerous examples of degenerate ring transformations are known.[28,29] Recently a review on degenerate ring transformations has appeared.[30]

4. Experimental Section

4.1. Synthesis of Starting Materials. 3-Chloro-5-phenyl-1,2,4-triazine (2). A 1.73-g (10 mmol) sample of 5-phenyl-1,2,4-triazin-3-one and 10 mL of phosphoryl chloride were heated at 120 °C for 0.5 h. Then the reaction mixture was concentrated in vacuo, and the resulting brown oil was poured onto ice. The precipitate was filtered off, washed with ammonia and water, and subsequently dried in desiccator over anhydrous $CaCl_2$. The residual product was separated by column chromatography (silica gel, chloroform) to yield 0.86 g (45%) of 6: mp 120–121 °C (from hexane) (lit.[32] mp 122 °C); ^1H NMR ($CDCl_3$) δ 9.05 (s, 1 H), 7.5–7.75 (m, 3 H), 8.05–8.3 (m, 2 H). Anal. Calcd for $C_9H_6N_3Cl$: C, 56.41; H, 3.15; N, 21.91. Found: C, 56.48; H, 3.34; N, 21.85.

3-Fluoro-5-phenyl-1,2,4-triazine (1). A solution of 0.57 g (3 mmol) of 3-chloro-5-phenyl-1,2,4-triazine (2) in benzene was treated with an excess of trimethylamine. The mixture was kept at room temperature for 3 h. The white precipitate of (5-phenyl-1,2,4-triazin-3-yl)trimethylammonium chloride was filtered off and washed with dry hexane; yield 91%, mp 141–142 °C. To a solution of 0.55 g (2.2 mmol) of this ammonium salt in 7 mL of dry Me_2SO was added 0.5 g of anhydrous potassium fluoride. The mixture was then heated at 60 °C for 1.5 h under a weak vacuum. After the mixture cooled, 15 mL of water was added, and the mixture was extracted with ether. After having been dried over anhydrous $MgSO_4$, the solvent was removed. The reaction mixture was separated by column chromatography (silica gel, 15:1 benzene–acetone) to yield 0.1 g (25%) of 5 and 0.12 g (26%) of 3-(dimethylamino)-5-phenyl-1,2,4-triazine. For 5: mp 93–94 °C (hexane); ^1H NMR ($CDCl_3$) δ 9.6–9.7 (d, 1 H, J = 3 Hz), 7.3–7.7 (m, 3 H), 8.0–8.3 (m, 2 H). Anal. Calcd for $C_9H_6N_3F$: N, 24.02; F, 10.86. Found: N, 24.18; F, 10.78. 3-(Dimethylamino)-5-phenyl-1,2,4-triazine was shown by melting point and ^1H NMR and mass spectroscopy to be identical with an authentic specimen.[31]

3-Bromo-5-phenyl-1,2,4-triazine (3). A 1-g (5.7 mmol) sample of 5-phenyl-1,2,4-triazin-3-one and 3 g of phosphoryl bromide were heated at 120–130 °C for 1 h. Then ice was added to the reaction mixture, and the resulting precipitate was filtered off and washed with concentrated ammonia and water. The crude product was purified by column chromatography (silica gel, chloroform) to yield 0.7 g (53%) of 3: mp 124–125 °C (chloroform–hexane); ^1H NMR ($CDCl_3$) δ 9.75 (s, 1 H), 7.5–7.9 (m, 3 H), 8.2–8.5 (m, 2 H). Anal. Calcd for $C_9H_6N_3Br$: C, 45.80; H, 2.54; N, 17.81. Found: C, 45.57; H, 2.61; N, 17.56.

3-Iodo-5-phenyl-1,2,4-triazine (4). A 0.57-g (3 mmol) sample of 2 and 15 mL of aqueous 57% hydriodic acid were mixed and kept at room temperature for 24 h. The precipitate was filtered off and washed with concentrated ammonia and water. The crude product was purified by column chromatography (silica gel, chloroform), and the purified product was crystallized twice from ethanol to yield 0.12 g (14%) of 4: mp 126–128 °C; ^1H NMR ($CDCl_3$) δ 9.7 (s, 1 H), 7.55–7.85 (m, 3 H), 8.1–8.5 (m, 2 H). Anal. Calcd for $C_9H_6N_3I$: C, 38.19; H, 2.12; N, 14.85. Found: C, 38.46; H, 2.15; N, 14.84.

3-Bromo-5-phenyl-[3-^{13}C)]-1,2,4-triazine. This compound was obtained from 5-phenyl-[3-^{13}C]-1,2,4-triazin-3-one by treatment with phosphoryl bromide according to the same procedure as that used for the unlabeled compound 3. 5-Phenyl-[3-^{13}C]-1,2,4-triazin-3-one was prepared in a five-step synthesis from ^{13}C-labeled potassium cyanide via ^{13}C-labeled potassium thio-

(26) It was recently found that compound 2 reacts with liquid ammonia to form compound 5 not according to the S_N(ANRORC) mechanism but via the S_N(AE) process. It probably means that in the reaction of the potassium salt of *p*-amidinotoluene (20) with compound 2 in liquid ammonia free of amide ion (see Scheme IV), the open-chain intermediate 15 is not present.

(27) Gy Simig and H. C. van der Plas, *Recl. Trav. Chim. Pays-Bas*, **95**, 125 (1976).

(28) E. A. Oostveen, H. C. van der Plas, and H. Jongejan, *Recl. Trav. Chim. Pay-Bays*, **95**, 18 (1976).

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Table II. Reaction Conditions, Products, and Yields Obtained on Treatment of the 1,2,4-Triazines 1-4 with Potassium Amide in Liquid Ammonia

starting compd	reactn temp, °C	reactn time, min	product yields, %						
			5	6	7[a,b]	8	9[b]	10[c]	11
1	−75	5	54						
2	−33	15	40	2	3-4	20	<1	4	*d*
3	−33	15	29	1.5	2	11	<1	1-2	*d*
4	−33	15	31	2.3	1-2	8.6	<1	1-2	*d*

[a] The yields were determined by GLC.[33] [b] The compound was identified by an independent synthesis. [c] Identified by mass spectrometry. [d] Yields were not determined; **11** was isolated by preparative GLC.

cyanate, ^{13}C-labeled thiosemicarbazide, ^{13}C-labeled, *S*-methylthiosemicarbazide, and 3-(methylthio)-5-phenyl-[3-^{13}C]-1,2,4-triazine according to procedures as outlined before for the unlabeled compound.[4]

3-Chloro-5-phenyl-[4-^{15}N]-1,2,4-triazine (2*) and 3-Bromo-5-phenyl-[4-^{15}N]-1,2,4-triazine (3*). These compounds were prepared by the same procedure as described for the unlabeled compounds **2** and **3**. The required 5-phenyl-[4-^{15}N]-1,2,4-triazin-3-one was synthesized by the route as outlined above, starting from ^{15}N-labeled potassium cyanide.

4.2. Amination Procedure. General Procedure for the Reactions of the 1,2,4-Triazines with Potassium Amide in Liquid Ammonia. To 25 mL of dry liquid ammonia in a 50-mL three-necked round-bottomed flask, equipped with a dry ice/acetone condenser, were added a few crystals of ferric nitrate and 160 mg (4 mmol) of potassium. After the mixture was stirred for 30 min at −33 °C, the 1,2,4-triazine derivative (1 mmol) was added with the exclusion of moisture. The reaction was terminated by the addition of 220 mg (4 mmol) of ammonium chloride. After the ammonia was evaporated, the residue was thoroughly extracted with warm chloroform and then with absolute ethanol. The combined extracts were concentrated in vacuo, and the residual mixture was separated by column chromatography or preparative thin-layer chromatography to obtain the compounds **5**, **6**, **8** and **10** (Table II). The eluents used were chloroform and chloroform/acetone in the ratio 10:1. Compounds **10** (X = Br), **10** (X = I), **7**, **9**, and **11** were separated by GLC.[33] The structure for **10** (X = Cl; mp 184 °C) was based on evidence from the mass spectrum which showed a parent peak at *m/e* 179 and a fragmentation peak at *m/e* 151 ($M^+ - N - 2$), the IR spectrum (absorption at 3200 cm^{-1} (NH)), and ^1H NMR data ($CDCl_3$): δ 7.3–7.6 (m, 3 H), 7.75–8.0 (m, 2 H). Anal. Calcd for $C_8H_6N_3Cl$: C, 53.49; H, 3.37. Found: C, 53.25; H, 3.25.

The amination in ^{15}N-labeled liquid ammonia with ^{15}N-labeled potassium amide was carried out in the same manner. ^{15}N-labeled ammonia was prepared by treatment of ^{15}N-labeled ammonium nitrate containing an ^{15}N excess in the ammonium group with a concentrated solution of potassium hydroxide in water at 100 °C for 2 h. After the experiment, it was reconverted into ^{15}N-labeled ammonium nitrate.

4.3. Conversion of 3-Amino-5-phenyl-[*x*-^{15}N]-1,2,4-triazine (5*) into the Potassium Salt of 5-Phenyl-[*x*-^{15}N]-1,2,4-triazin-3-one (12*). This conversion was performed by the same procedure as that described for the unlabeled compounds.[34]

4.4. Conversion of 12* into 3-Chloro-5-phenyl-[*x*-^{15}N]-1,2,4-triazines (2).** 3-Chloro-5-phenyl-[*x*-^{15}N]-1,2,4-triazine (**2****) was obtained from **12*** by the same procedure as that used for the unlabeled compounds (see section 4.1).

4.5. Reaction of Compound 2 with Potassium Amide and *p*-Cyanotoluene in Liquid Ammonia. A solution of 0.117 g (1 mmol) of *p*-cyanotoluene in 2 mL of absolute ether was added to a well-stirred solution of potassium amide (5 mmol) in 25 mL of liquid ammonia at −33 °C. After the mixture was stirred for 1 h, compound **2** (1 mmol) was added. The reaction was terminated after 30 min by the addition of ammonium chloride. The resulting mixture was separated as described in section 4.2 to yield compounds **5**–**7**, **8**–**11**, and 2-phenyl-4-(*p*-methylphenyl)-1,3,5-triazine (**19**), mp 77–78 °C. The structure assignment for this compound was made on the basis of the molecular weight (*m/e* 247): ^1H NMR (CCl_4) δ 2.42 (s, 3 H), 7.27 (d, 2 H, *J* = 7.5 Hz), 7.42–7.6 (m, 3 H), 8.5 (d, 2 H, *J* = 7.5 Hz), 8.6–8.8 (m, 2 H), 9.07 (s, 1 H). Anal. Calcd for $C_{16}H_{13}N_3$: C, 77.71; H, 5.3; N, 16.99. Found: C, 77.80; H, 5.26; N, 16.79.

4.6. Reaction of 2 with the Potassium Salt of *p*-Amidinotoluene in Liquid Ammonia. A solution of 0.128 g (1.1 mmol) of *p*-cyanotoluene in 2 mL of absolute ether was added to a well-stirred solution of potassium amide (1 mmol) in 15 mL of liquid ammonia at −33 °C. The mixture was stirred for 1 h. Then compound **2** (1 mmol) was added. The reaction was terminated after 30 min by the addition of 55 mg (1 mmol) of ammonium chloride. The resulting mixture was separated by column chromatography (silica gel, 15:1 chloroform–acetone) to yield compounds **5** (64%) and **19** (18%).

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Registry No. **1**, 72428-35-4; **2**, 72428-36-5; **3**, 72428-37-6; **4**, 72428-38-7; **5**, 942-60-9; **6**, 18162-28-2; **7**, 24108-43-8; **8**, 1898-74-4; **9**, 5418-07-5; **10** (X = Br), 56617-00-6; **10** (X = I), 72428-39-8; **10** (X = Cl), 31803-05-1; **11**, 55-21-0; **19**, 72428-40-1; 5-phenyl-1,2,4-triazin-3-one, 31952-61-1; phosphoryl chloride, 10025-87-3; trimethylamine, 75-50-3; (5-phenyl-1,2,4-triazin-3-yl)trimethylammonium chloride, 72428-41-2; potassium fluoride, 7789-23-3; 3-(dimethylamino)-5-phenyl-1,2,4-triazine, 34103-49-6; phosphoryl fluoride, 13478-20-1; potassium amide, 17242-52-3; ammonia, 7664-41-7; *p*-cyanotoluene, 104-85-8.

(33) A stainless-steel column was used, length 200 cm, internal diameter $^1/_8$ in., filled with 2 g of Chromosorb W-HP, 100–200 mesh, plus 10% DC-430 at 150 °C.

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