Naphthyridine Chemistry. IX. The Bromination and Amination of the 1,X-Naphthyridines

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The bromination and amination of the 1,X-naphthyridines are reported. The bromination of 1,5-naphthyridine gave the 3-bromo- and the 3,7-dibromo-1,5-naphthyridine. The 3-bromo-, 8-bromo-, and 3,8-dibromo-1,6-naphthyridines were obtained from 1,6-naphthyridine. The 1,7-naphthyridine afforded the 5-bromo and the 3,5-dibromo derivatives. The 3-bromo- and the 3,6-dibromo-1,8-naphthyridines were obtained from 1,8-naphthyridine. The Chichibabin amination of the 1,5-, 1,6-, and 1,8-naphthyridines yielded the 2-amino derivative in each case. The 1,7-naphthyridine gave the 8-amino compound.

The development of facile syntheses[1-3] of 1,5-, 1,6-, 1,7- and of 1,8-naphthyridine has made it possible to study their electrophilic and nucleophilic substitutions in some detail.

We now wish to report the results of bromination and of amination experiments of the 1,X-naphthyridines.

Bromination Studies.—Some time ago, Eisch[4] described a novel method for the introduction of bromine into nitrogen heterocyclic compounds. This method involves the formation of a bromine–heterocyclic compound complex, which, by treatment with pyridine, is "decomposed" to afford a halogenated derivative of the heterocyclic compound. In this fashion, 3-bromoquinoline, 3,8-dibromoquinoline, 3,6-dibromoquinoline, and 3,6,8-tribromoquinoline were obtained, the monobromoquinoline being by far the major product. The bromination of isoquinoline by this procedure afforded the 4-bromoisoquinoline in satisfactory yield.

1,5-Naphthyridine.—The bromination of 1,5-naphthyridine (**1**) by the Eisch procedure afforded a three-component mixture which was separated by column chromatography into unreacted starting material and a monobromo- and a dibromo-1,5-naphthyridine. The pmr spectrum of the monobromo compound (27% yield) showed the presence of an ABX proton system similar to that of the starting material. In addition to this pattern, an AB system (*cf.* Table I) was also present. The size of the coupling constant and the chemical shifts of H_A and of H_B clearly identified the compound as the 3-bromo-1,5-naphthyridine (**5**).

The dibromo compound obtained in 10% yield exhibited a pmr spectrum (*cf.* Table I), which was consistent only with 3,7-dibromo-1,5-naphthyridine (**6**).

Czuba[5] brominated 1,5-naphthyridine in a sealed tube at 135° in H_2SO_4–SO_3, and obtained 7–10% of 3-bromo- and 30–35% of 3,7-dibromo-1,5-naphthyridine. The physical properties of our compounds are identical with those prepared by the Czuba method.

1,6-Naphthyridine.—The bromination of 1,6-naphthyridine (**2**) *via* its bromine complex gave, in addition to unreacted starting material, two monobromo- and one dibromo-1,6-naphthyridine. The pmr spectra were analyzed in a manner similar to that described for the 1,5-naphthyridine products and are recorded in Table I. These data clearly identified the compounds as the 3-bromo- (**7**, 18%), 8-bromo- (**8**, 23% yield), and 3,8-dibromo-1,6-naphthyridine (**9**, 11%).

1,7-Naphthyridine.—The "decomposition" of the bromine complex of 1,7-naphthyridine (**3**) afforded only two bromine-containing products. Elemental analyses identified these compounds as a monobromo and a dibromo derivative of 1,7-naphthyridine. Examination of the pmr spectral data of these two compounds (*cf.* Table I) permitted the identification of the compounds as the 5-bromo-1,7-naphthyridine (**10**) and the 3,5-dibromo-1,7-naphthyridine (**11**), respectively. Whereas the monobromo compound was formed in 25% yield, the dibromo compound was obtained in only 2% yield.

1,8-Naphthyridine.—The bromination of this naphthyridine (**4**) afforded by far the lowest yield of bromo products of any of the 1,X-naphthyridines. Thus, only 5% of the monobromo and 0.5% of the dibromo compound was obtained. The pmr spectra of the substances (*cf.* Table I) identified them as the 3-bromo (**12**) and the 3,6-dibromo compounds (**13**), respectively.

Amination Studies.—The Chichibabin amination of quinoline and of isoquinoline is reported to afford the 2- (and some 4-) amino and the 1-amino compounds, respectively.[6] The application of this amination reaction to the 1,X-naphthyridines became of some special interest for the 1,6- and the 1,7-naphthyridines since these compounds present, *a priori*, two different sites for nucleophilic attack.

1,5-Naphthyridine.—The amination with sodium amide of 1,5-naphthyridine (**1**) has been described by Hart,[7] and the structure of the product, formed in 78% yield, has been shown to be the 2-amino-1,5-naphthyridine (**14**). We were, however, unable to duplicate this amination under the conditions described by Hart. We have now repeated this reaction under conditions which we employed for all of the other 1,X-naphthyridines (potassium amide in liquid ammonia at room temperature) and have obtained the 2-amino-1,5-naphthyridine (**14**) in 33% yield. The pmr spectral data of this compound are reported in Table II and agree with the assigned structure.

1,6-Naphthyridine.—When the reaction conditions used for the amination of 1,5-naphthyridine (**1**) were employed on the 1,6-naphthyridine, there was obtained a monoamino compound whose pmr spectrum is void of the deshielded H_2 proton present in the starting material. The H_5 "singlet" was still present in the amination product. Table II describes the remaining features of the pmr spectrum of this compound which are in agreement with the assigned structure, 2-amino-1,6-naphthyridine (**15**).

(1) W. W. Paudler and T. J. Kress, *J. Org. Chem.*, **32**, 832 (1967).
(2) T. J. Kress and W. W. Paudler, *Chem. Commun.*, **3** (1967).
(3) W. W. Paudler and T. J. Kress, *J. Org. Chem.*, **31**, 3055 (1966).
(4) J. J. Eisch, *ibid.*, **27**, 1318 (1962).
(5) W. Czuba, *Rocz. Chem.*, **37**, 1589 (1963).
(6) F. W. Bergstrom, *J. Org. Chem.*, **3**, 411 (1937).
(7) E. P. Hart, *J. Chem. Soc.*, 1879 (1954).

TABLE I

NMR SPECTRAL DATA OF SOME BROMONAPHTHYRIDINES

Compd[a]	Chemical shifts (τ)							Coupling constants, cps									
	H_2	H_3	H_4	H_5	H_6	H_7	H_8	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,8}$	$J_{5,6}$	$J_{5,7}$	$J_{5,8}$	$J_{6,7}$	$J_{6,8}$	$J_{7,8}$
3-Bromo-1,5-naphthyridine (5)	1.04	...	1.44	...	1.04	2.37	1.63	...	2.0	...	0.9	...	...	...	4.3	2.0	8.6
3,7-Dibromo-1,5-naphthyridine (6)	1.03	...	1.45	...	1.03	...	1.45	...	2.0	...	...	...	...	...	...	2.0	...
8-Bromo-1,6-naphthyridine (8)	0.83	2.40	1.70	0.83	...	1.02	...	4.0	1.5	8.3	...	...	...	...	...	...	...
3-Bromo-1,6-naphthyridine (7)	0.97	...	1.70	0.80	...	1.22	2.12	...	1.5	...	0.8	...	...	0.8	...	...	6.0
3,8-Dibromo-1,6-naphthyridine (9)	0.84	...	1.54	0.89	...	1.00	...	...	2.0	...	...	...	...	...	...	...	...
5-Bromo-1,7-naphthyridine (10)	0.95	2.31	1.57	...	1.20	...	0.57	4.0	1.5	8.5	1.0	...	...	...	...	...	...
3,5-Dibromo-1,7-naphthyridine (11)[b]	0.91	...	1.66	...	1.33	...	0.57	...	2.0	...	*b*	...	...	...	...	...	...
3-Bromo-1,8-naphthyridine (12)	0.90	...	1.67	1.89	2.50	0.90	...	...	2.0	...	...	8.0	2.0	...	4.0	...	...
3,6-Dibromo-1,8-naphthyridine (13)	0.91	...	1.73	1.73	...	0.91	...	...	2.0	...	...	...	2.0	...	...	...	...

[a] $CDCl_3$ solutions. [b] This spectrum was obtained with the aid of the C-1024 time averaging computer (Technical Measurements Grp.) and the $J_{2,4}$ coupling constant could only be estimated, while the $J_{4,8}$ coupling constant was only indicated as present by the peak widths.

TABLE II

NMR SPECTRAL DATA OF SOME AMINONAPHTHYRIDINES

Compd[a]	Chemical shifts (τ)							Coupling constants, cps									
	H_2	H_3	H_4	H_5	H_6	H_7	H_8	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,8}$	$J_{5,6}$	$J_{5,7}$	$J_{5,8}$	$J_{6,7}$	$J_{6,8}$	$J_{7,8}$
2-Amino-1,5-naphthyridine (14)	...	2.83	1.54	...	1.02	2.04	1.58	...	...	7.0	0.5	...	...	...	4.0	1.5	9.0
2-Amino-1,6-naphthyridine (15)	...	2.40	1.42	0.52	...	1.08	1.74	...	...	9.6	0.5	...	0.8	0.5	...	...	6.9
8-Amino-1,7-naphthyridine (16)	1.02	2.10	1.75	2.82	2.30	...	...	4.0	1.9	8.2	...	7.0	...	...	...	...	...
2-Amino-1,8-naphthyridine (17)	...	2.67	1.70	1.49	2.31	1.17	...	...	...	9.5	...	8.0	1.7	...	5.3	...	...

[a] DTFAA solutions.

TABLE III

TOTAL π-ELECTRON DENSITIES OF THE NAPHTHYRIDINES

Compd	Position							
	1	2	3	4	5	6	7	8
1,5-Naphthyridine (1)	1.42	0.79	0.99	0.89	1.42	0.79	0.99	0.89
1,6-Naphthyridine (2)	1.44	0.77	1.02	0.83	0.77	1.41	0.86	1.04
1,7-Naphthyridine (3)	1.41	0.78	0.98	0.86	0.99	0.89	1.38	0.81
1,8-Naphthyridine (4)	1.45	0.78	1.02	0.85	0.85	1.02	0.78	1.45
2,6-Naphthyridine	0.79	1.38	0.89	0.99	0.79	1.38	0.89	0.99
2,7-Naphthyridine	0.75	1.41	0.86	1.02	1.02	0.86	1.41	0.75

1,7-Naphthyridine.—The sole amination product of 1,7-naphthyridine was a monoamino derivative whose pmr spectrum is void of the H_8 singlet of the starting material. The pmr spectrum (Table II) showed the typical ABX system expected for H_2, H_3, and H_4. In addition to this, an AB system ascribed to H_5 and H_6 was also present. We consequently conclude that this compound is 8-amino-1,7-naphthyridine (**16**). The structure of this compound was also proven by its unequivocal synthesis from 2,3-diaminopyridine *via* the Skraup reaction. This reaction afforded a compound whose physical properties were identical with those of the amination product of 1,7-naphthyridine. This reaction sequence is outlined in Scheme I,[8] p 1386.

1,8-Naphthyridine.—The amination of 1,8-naphthyridine (**4**) again afforded only one monoamino compound. The pmr spectrum (Table II) of this crystalline material was in agreement with that reported by Wibberly and Hawes[9] for the oily product which they obtained from the decarboxylation of 2-amino-1,8-naphthyridine-3-carboxylic acid. The analysis of the pmr spectrum of the amino compound identified it as the 2-amino-1,8-naphthyridine (**17**).

Discussion of the Substitution Reactions.—We have recently described[10] the development of a HMO nitrogen parameter ($\alpha_N = \alpha°_C + 1.1\beta°$) for a series of nitrogen heterocyclic compounds. This parameter was based on the polarographic half-wave reduction potentials of a large number of heterocyclic compounds. The total π electron densities, calculated with the aid of this parameter, for the various naphthyridines are tabulated in Table III.[11]

These ground-state data suggest that electrophilic substitution should occur at position 3 in all of the 1,X-naphthyridines. Since the total π-electron densities at the 8 position in the 1,6- and the 5 position in the 1,7-naphthyridine are slightly higher than the corresponding 3 positions, these positions are also expected to be subject to electrophilic attack.

Except for the lack of detection of any 3-bromo-1,7-naphthyridine all of the expected monobromo(compounds **5**, **7**, **8**, **10**, **12**) and dibromo-1,X-naphthyridines (compounds **6**, **9**, **11**, **13**) were identified.

The total π-electron densities recorded in Table III predict nucleophilic substitution to occur at position 2 of the 1,X-naphthyridines. In addition to this position, the 5 position in the 1,6- and the 8 position in the 1,7-naphthyridine appear to be possible sites for nucleophilic substitution.

With the exception of 1,7-naphthyridine which formed the 8-amino compound exclusively, all of the other 1,X-naphthyridines were aminated at C_2.

The use of total π-electron densities to predict the sites of substitution in aromatic compounds are gen-

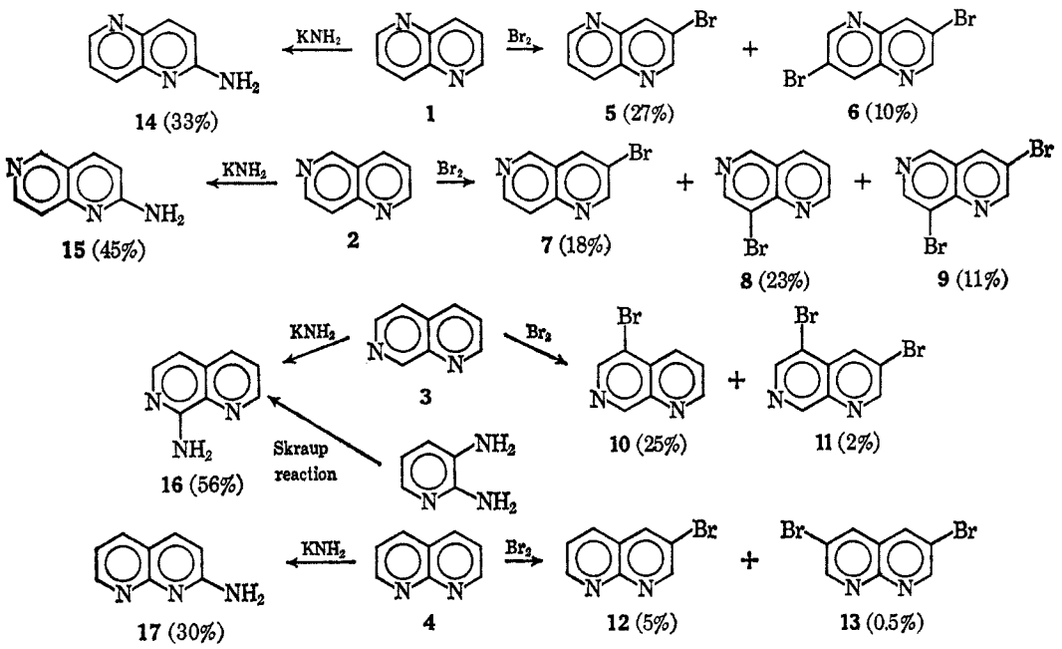
(8) It is of interest to point out that W. Czuba [*Rocz. Chem.*, **41**, 289 (1967)] has shown that one of the products of the Skraup reaction on 3,5-diaminopyridine is the 3-amino-1,5-naphthyridine.

(9) E. M. Hawes and D. G. Wibberly, *J. Chem. Soc., Sect. C*, 1564 (1967).

(10) W. W. Paudler and T. J. Kress, "Some Aspects of the Chemistry of Mono- and Diazanaphthalenes," 1st International Congress of Heterocyclic Chemistry, Albuquerque, N. M., 1967, in press.

(11) See R. G. Shepherd and J. L. Fedrick, *Advan. Heterocycl. Chem.*, **4**, 146 (1965), for an excellent review concerning the reactivity of azines with nucleophiles.

SCHEME I



erally only suitable if there are fairly large numerical differences between the positions under consideration. If the differences are small, these ground-state considerations become less applicable and one must utilize nonground state calculations.

More sophisticated MO calculations might account for the absence of any 3-bromo-1,7-naphthyridine in the electrophilic substitution reactions and the 5-amino-1,6- as well as 2-amino-1,7-naphthyridine in the nucleophilic substitution reactions. The semiempirical rules based on resonance theory described by Shepherd and Fedrick[11] which deal with the Chichibabin amination and related reactions unfortunately do not permit one to account for the facile formation of the 2-amino-1,6-naphthyridine and the lack of formation of any 5-amino derivative other than a possible stability difference between an *ortho,ortho*-quinoidal and a *para,para*-quinoidal transition state. Moreover, the preferred formation of 8-amino-1,7-naphthyridine over the 2-amino-1,7 compound cannot be predicted by these rules.

Experimental Section[12]

General Amination Procedure.—To a dry Carius tube (2 × 60 cm) was added 25 ml of liquid ammonia, followed by a crystal of ferric chloride, and 1.05 g (53 mg-atoms) of freshly cut potassium metal. After the evolution of hydrogen had ceased (about 30 min), 1.09 g (8.45 mmol) of naphthyridine and 1.14 g (11.3 mmol) of potassium nitrate were added simultaneously. The tube was sealed and allowed to stand at room temperature with occasional shaking for 8 days. The cooled tube was opened and a benzene–ethanol (1:1) solution (25 ml) was added in small portions. When the ammonia had evaporated (about 1 hr), water (25 ml) was added, and the organic solvents were removed *in vacuo*. The aminonaphthyridines were then treated as described below.

2-Amino-1,5-naphthyridine (1).—Removal of the organic solvents gave a dark brown gummy solid which was sublimed at 160° (0.1 mm) yielding 365 mg (33%) of white cubes, mp 196–198 (lit.[13] 204–205°).

2-Amino-1,6-naphthyridine (14).—Removal of the organic solvents gave a brown solid which was filtered, dried, and sublimed at 200° (0.1 mm) affording 402 mg, mp 238–240°, of colorless cubes. One additional sublimation did not alter the melting point.

Anal. Calcd for $C_8H_7N_3$: C, 66.19; H, 4.86; N, 29.95. Found: C, 66.26; H, 4.81; N, 29.29.

8-Amino-1,7-naphthyridine (16).—Evaporation *in vacuo* of the mixture afforded a brown solid which was collected, dried, and sublimed at 180° (0.1 mm) to give 446 mg (56%) of pale yellow prisms, mp 165–166°.

Anal. Calcd for $C_8H_7N_3$: C, 66.19; H, 4.86; N, 28.95. Found: C, 65.98; H, 4.80; N, 29.05.

2-Amino-1,8-naphthyridine (17).—The organic solvents were removed leaving a brown gum and water. Continuous extraction with chloroform (24 hr) gave, after removal of the organic layer, a yellow oil which could be converted into a semisolid gum after trituration with ether. Heating of the gum at 200° (0.1 mm) gave 350 mg (30%) of pale yellow cubes, mp 141–142°, on the wall of the test tube.

Anal. Calcd for $C_8H_7N_3$: C, 66.19; H, 4.86; N, 28.95. Found: C, 66.25; H, 4.92; N, 28.75.

General Bromination Procedure.—To an efficiently stirred solution of 1.30 g (10 mmol) of naphthyridine in 60 ml of carbon tetrachloride was added 2.16 g (12 mmol) of bromine in 6 ml of carbon tetrachloride, and the mixture was refluxed for 1 hr. Pyridine (0.79 g, 10 mmol) in 10 ml of carbon tetrachloride was added over a period of 1 hr to the refluxing solution, and the mixture was heated for an additional 12 hr, cooled, and filtered. The collected solid was digested with 10% sodium hydroxide (100 ml) for 1 hr, and the resulting solution was extracted with chloroform. The chloroform solution and the carbon tetrachloride reaction solution were combined and evaporated *in vacuo*, affording, in each case, a tan solid which was chromatographed on alumina (Brockman grade III) and eluted with 5% ethyl acetate in carbon tetrachloride. The various bromonaphthyridines were then treated in the following manner and are reported in the order in which they were eluted from the chromatography column.

Bromo-1,5-naphthyridines. 3,7-Dibromo-1,5-naphthyridine (6) was obtained as needles (306 mg, 10%) from ethanol, mp 239–240° (lit.[5] 240–241°). **3-Bromo-1,5-naphthyridine** (5), a white solid (574 mg, 27%), was recrystallized as needles from cyclohexane, mp 106–107° (lit.[5] 107–107.5°). A total of 576 mg (43%) of starting material, **1,5-naphthyridine** (1), was recovered.

Bromo-1,6-naphthyridines. 3,8-Dibromo-1,6-naphthyridine (9).—The white solid (318 mg, 11%) was recrystallized twice from ethanol affording needles, mp 187–189°.

(12) The nmr spectra were obtained with a Varian A-60 spectrometer The purity of the compounds were ascertained by thin layer chromatography (silica gel G, ether). The mass spectra were determined with a Hitachi Perkin-Elmer RMU-6E mass spectrometer with the liquid sample injection unit at 200° and the ionization voltage at 80 eV. Elemental analyses were performed by Mrs. K. Decker of this department.

(13) W. Czuba, *Rec. Trav. Chim. Pays-Bas*, **82**, 988 (1963).

Anal. Calcd for $C_8H_4N_2Br_2$: C, 33.36; H, 1.40; N, 9.73. Found: C, 33.39; H, 1.37; N, 9.63.

3-Bromo-1,6-naphthyridine (**7**) (372 mg, 18%) was recrystallized twice from cyclohexane giving white crystals, mp 125–126°.

Anal. Calcd for $C_8H_5N_2Br$: C, 45.96; H, 2.41; N, 13.40. Found: C, 45.95; H, 2.45; N, 13.23.

8-Bromo-1,6-naphthyridine (**8**).—Evaporation of the solvent gave 473 mg (22.6%) of fine cottony needles from cyclohexane, mp 84–86°.

Anal. Calcd for $C_8H_5N_2Br$: C, 45.96; H, 2.41; N, 13.40. Found: C, 45.96; H, 2.51; N, 13.12.

1,6-Naphthyridine (**2**).—A total of 160 mg (12%) of starting material was recovered.

Bromo-1,7-naphthyridines.—The same conditions were used as in the general procedure but the amounts were as follows: 1,7-naphthyridine (**3**), 343 mg (2.6 mmol); bromine, 700 mg (3.90 mmol); and pyridine, 240 mg (3.0 mmol).

3,5-Dibromo-1,7-naphthyridine (**11**).—White crystals [mp 149–151°, mass spectral molecular weight, 288, with the characteristic 1:2:1 ratio (two mass units apart) indicating the presence of two bromine atoms; P, *m/e* 288 (100%)], were obtained in a 27% (16 mg) yield.

Anal. Calcd for $C_8H_4N_2Br_2$: C, 33.36; H, 1.40; N, 9.73. Found: C, 33.06; H, 1.26; N, 9.48.

5-Bromo-1,7-naphthyridine (**10**).—The white solid was sublimed at 40° (0.1 mm) affording 140 mg (25%) of small fine needles, mp 69–70°.

Anal. Calcd for C_8H_5N Br: C, 45.96; H, 2.41; N, 13.40. Found: C, 45.90; H, 2.57; N, 13.15.

1,7-Naphthyridine (**3**).—A total of 61 mg (18%) of starting material was recovered.

Bromo-1,8-naphthyridines. 3-Bromo-1,8-naphthyridine (**12**).—The white solid was sublimed at 100° (0.1 mm) giving 50 mg (4.8%), mp 155–156°, of the monobromo derivative.

Anal. Calcd for $C_8H_5N_2Br$: C, 45.96; H, 2.41; N, 13.40. Found: C, 45.90; H, 2.35; N, 13.30.

3,6-Dibromo-1,8-naphthyridine (**13**).—The material obtained from the chromatographic column was sublimed at 150° (0.1 mm) affording 6 mg (0.5%) of a white solid, mp 300°.

Anal. Calcd for $C_8H_4N_2Br_2$: C, 33.36; H, 1.40; N, 9.73. Found: C, 33.16; H, 1.30; N, 9.48.

8-Amino-1,7-Naphthyridine (**16**) **by the Skraup Reaction.**—The previously described procedure[1] for the preparation of 1,8-naphthyridines was employed except that 2,3-diamino- instead of 2-aminopyridine was used. The residue obtained on evaporation of the chloroform extract of the basic reaction mixture, on recrystallization from ethanol, gave 400 mg of a white solid (mp 168–169°). A mixture melting point of this solid with the amination product of 1,7-naphthyridine was not depressed.

Fluorination of Nitroaromatic Amines in Liquid Hydrogen Fluoride and Acetonitrile[1]

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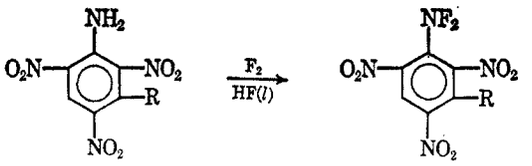
A general synthetic procedure has been found for the preparation of previously unreported nitroaromatic difluoramines. Nitroaromatic monoamines, such as picramide and its analogs, have been converted in high yield into the corresponding difluoramines in liquid hydrogen fluoride and in some cases in organic solvent, such as acetonitrile. Nitroaromatic diamines and triamines undergo similar fluorination reactions. Dinitro-substituted anilines fluorinate in good yield but the amine fluorination is accompanied by ring fluorination *ortho* to the difluoramino group. This reaction and general considerations of aromatic radical stabilization provide evidence for a radical mechanism operating in the fluorination reaction. In addition an unexpected product was obtained in the fluorination of 1,3-dinitro-2,4,6-triaminobenzene, which gave only a small amount of the corresponding trisdifluoramine and a major yield of 1,3-dinitro-2,4,6-tris(difluoramino)-1,2,3,4,5,6-hexafluorocyclohexane. Coupling rather than direct fluorination was obtained with pentafluoroaniline, which yielded bis(pentafluorophenyl)difluorohydrazine by a radical mechanism. The nitroaromatic difluoramino group between adjacent nitro groups was subject to attack by nucleophiles, such as ammonia and water. The synthesis, reaction, and properties of this novel class of compounds are discussed.

There have been relatively few reports of attempts to fluorinate amines by direct elemental fluorination.[2] Among the problems encountered in the direct fluorination of amines are the lack of a suitable solvent medium and decomposition of the reactants owing to the activity of the fluorine. At the least, formation of amine hydrogen fluoride salts can occur as fluorination proceeds, which has on several occasions effectively blocked further reaction. It was felt that, to circumvent these problems, weakly basic amines would be less susceptible to salt formation and, if already substituted with negative groups, they would be less susceptible to oxidation. It also appeared that fluorination in solution would work best, provided reasonable solvation of the starting material and product could be obtained. Since picramide did not form a salt with hydrogen fluoride, it was chosen as an example of a weak base and was fluorinated in liquid hydrogen fluoride, which is an excellent solvent for many nitroaromatic amines. 1-Difluoramino-2,4,6-trinitrobenzene was obtained in good yield, leading us to study the direct fluorination of a variety of nitroaromatic amines to the corresponding nitroaromatic difluoramines, a class of compounds not previously reported. Subsequent research revealed that some organic solvents, particularly acetonitrile, were useful in many cases and provided media for selective fluorinations in solution, a technique not often possible to use.



R = –H, $-CH_3$, $-OCH_3$, $-NO_2$

Results and Discussion

The use of HF as a solvent for direct elemental fluorination of amines is unique and offers several advantages. Anhydrous HF is an excellent solvent for most amines

(1) Presented at the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967.

(2) For reviews on fluorination of organic compounds, see R. Stephens and J. C. Tatlow, *Quart. Rev.* (London), **16**, 57 (1962); J. M. Tedder, *Advan. Fluorine Chem.*, 104 (1960).