with aqueous 10% ferrous ammonium sulfate, and then extracted with aqueous 10% sodium hydroxide. The alkaline extract was acidified to litmus with aqueous 10% hydrochloric acid and extracted with ether. The ether extract was treated with charcoal, dried ($MgSO_4$), and evaporated, leaving a very small amount of green oil, which partially solidified upon being kept and cooled. The mixture was taken up in petroleum ether (bp 60–68°), and a white solid settled out (0.04 g, 1%), mp 98–100°. The infrared spectrum in Nujol was essentially identical with that of the sample prepared by oxidation with oxygen.

Registry No.—**3**, 10075-48-6; **8**, 10075-49-7; **1**, 10075-50-0; **2**, 877-03-2; **4**, 10086-59-6; 1-benzyl-5-bromoindole, 10075-51-1; **5**, 10075-52-2; **6**, 10102-94-0; **7**, 10075-53-3; **10a**, 10075-54-4; **10b**, 10075-55-5; **11**, 10102-95-1.

A One-Step Synthesis of 1,8-Naphthyridines[1]

WILLIAM W. PAUDLER AND THOMAS J. KRESS

Department of Chemistry, Ohio University, Athens, Ohio

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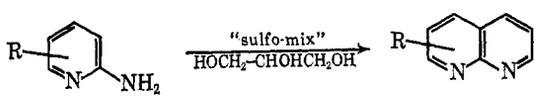
The scarcity of published papers dealing with the chemistry of the various isomeric naphthyridines can be ascribed to the difficulties encountered in attempts to prepare these compounds readily, and in good yields. Our interest in naphthyridines[2-4] has prompted us to investigate synthetic sequences for the preparation of larger amounts of the different naphthyridines. This note describes a facile synthesis of 1,8-naphthyridine and some of its methyl derivatives.

1,8-Naphthyridine has been prepared by Koller[5] and by Albert[6] by a five-step sequence starting with methyl 2-aminonicotinate, but this compound requires a multistep synthesis, and conversion to 1,8-naphthyridine proceeds in only 28% yield. Previous attempts to obtain 1,8-naphthyridines by the Skraup reaction on 2-aminopyridine have failed,[7] but in view of our recent success[2b,4] in applying the Skraup reaction to 4-aminopyridine, it became of interest to attempt this reaction with 2-aminopyridine.



1
R = H
R = 6-CH_3
R = 4-CH_3
R = 4,6-di-CH_3

2, R = H
3, R = 2-CH_3
4, R = 4-CH_3
5, R = 2,4-di-CH_3

The condensation of 2-aminopyridine employing Utermohlen's "sulfo-mix"[8a] and glycerol afforded 1,8-naphthyridine in 30% yield. It is of some interest to note that 1,5-naphthyridines[8b] as well as 1,6-naphthyridine[2b,4] are isolated from the reaction mixtures by steam distillation while 1,8-naphthyridine is not steam volatile under these conditions. It is conceivable that earlier reported failures[7] in attempts to apply the Skraup reaction to 2-aminopyridines might be accounted for by the traditional steam distillation procedures in isolating Skraup reaction products.

The structure proof of the 1,8-naphthyridine rests upon the identity of the reported melting points of the base itself, and of its picrate, as well as the analysis of the nmr spectrum, which clearly establishes the structure assignment.

The condensation of 6-methyl-, 4-methyl-, and of 4,6-dimethyl-2-aminopyridines with glycerol under similar reaction conditions as those employed for the preparation of the parent 1,8-naphthyridine yielded the 2-methyl-, 4-methyl-, and the 2,4-dimethyl-1,8-naphthyridines (compounds **3**, **4**, and **5**), respectively. The yields of these substituted 1,8-naphthyridines are between 10 and 20%.

The 2-methyl-1,8-naphthyridine obtained in this fashion was compared with an authentic sample of 2-methyl-1,8-naphthyridine prepared by the reaction sequence described by Brown[9] and the two compounds were shown to be identical. The physical constants of the other 1,8-naphthryidines, as well as the nmr spectra (Table I) are in agreement with the assigned structures.

Experimental Section[10]

1,8-Naphthyridine (**2**).—To a chilled, homogeneous mixture of 117 g of "sulfo-mix"[8a] and 25 g of anhydrous glycerol was added 7.5 g (0.08 mole) of 2-aminopyridine and 45 ml of water. The mixture was vigorously stirred in an oil bath at 130° for 5 hr, cooled in an ice bath, and made alkaline with concentrated aqueous sodium hydroxide. This solution was extracted with four 100-ml portions of chloroform. The combined chloroform extracts were then extracted with four 100-ml portions of aqueous hydrochloric acid (pH 3). The pH of the aqueous acid solution was adjusted to 5 and was reextracted with four 100-ml portions of chloroform. After several of these extractions the combined chloroform solutions were dried over anhydrous magnesium sulfate and evaporated to dryness. The solid residue of "crude" 1,8-naphthyridine (3.0 g, 30%), melted at 96–97° (lit.[6] 98°), picrate mp 207–208° (lit.[5] 207–208°), mol wt 130 (mass spectral value). Sublimation at 80° (0.3 mm) gave colorless, glassy needles (mp 98–99°, 2.95 g) of pure 1,8-naphthyridine.

2-Methyl-1,8-naphthyridine (**3**).—The same procedure was used as for the preparation of 1,8-naphthyridine except that 8.7 g (0.08 mole) of 2-amino-6-picoline was substituted for 2-aminopyridine. Three crystallizations from cyclohexane afforded white, cottony needles (1.2 g, 10%, mp 99–100°) of **8**. A mixture melting point with an authentic sample purified by sublimation (mp 99–100°) was not depressed. This melting point differs from that reported by Brown[9] (114–115°).

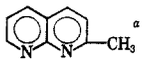
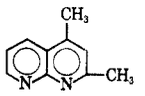
4-Methyl-1,8-naphthyridine (**4**).—The same general procedure was used except for the substitution of 8.6 g (0.08 mole) of 2-amino-4-picoline in place of 2-aminopyridine. 4-Methyl-1,8-naphthyridine [picrate mp 204–205° (lit.[11] 204–205°)] was obtained in 17% yield (2.0 g).

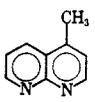
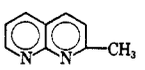
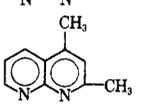
2,4-Dimethyl-1,8-naphthyridine (**5**).—The same procedure was followed except for the substitution of 2-amino-4,6-dimethylpyridine in place of 2-aminopyridine. The yield was 1.3 g

(1) This is paper V in the series "Naphthyridine Chemistry."
(2) (a) W. W. Paudler and T. J. Kress, *J. Heterocyclic Chem.*, **2**, 393 (1965); (b) W. W. Paudler and T. J. Kress, *J. Org. Chem.*, **31**, 3055 (1966).
(3) W. W. Paudler and T. J. Kress, *Chem. Ind.* (London), 1557 (1966).
(4) T. J. Kress and W. W. Paudler, *Chem. Commun.*, 3 (1967).
(5) G. Koller, *Ber.*, **60**, 1918 (1927).
(6) A. Albert, *J. Chem. Soc.*, 1790 (1960).
(7) R. C. Elderfield, "Heterocyclic Compounds," Vol. 7, John Wiley and Sons, Inc., New York, N. Y., 1961, pp 198–236.
(8) (a) W. P. Utermohlen, Jr., *J. Org. Chem.*, **8**, 544 (1943); (b) H. Rapoport and A. Batcho, *ibid.*, **28**, 1753 (1963).
(9) E. Brown, *ibid.*, **30**, 1607 (1965).
(10) The nmr spectra were obtained with a Varian A-60 spectrometer. The purity of the compounds was ascertained by tlc [silica gel G, ethyl acetate–ether (20:80)]. The molecular weight was determined with a Hitachi Perkin-Elmer RMU-6E mass spectrometer (the mass spectral cleavage patterns of various naphthyridines will be described in a forthcoming paper).
(11) E. Ockiai and M. Miyaki, *Ber.*, **74**, 1115 (1941).

TABLE I

NUCLEAR MAGNETIC RESONANCE SPECTRAL DATA OF SOME 1,8-NAPHTHYRIDINES

Compd	Chemical shifts, CH3-2	CH3-4	H-2	H-3	H-4	H-5	H-6	H-7
	...	...	0.87	2.52	1.78	1.78	2.52	0.87
	...	7.35	1.02	2.68	...	1.62	2.47	0.88
 [a]	7.24	...	...	2.69	1.92	1.99	2.65	0.97
	7.28	7.40	...	2.85	...	1.74	2.60	0.84

Compd	Coupling constants, cps J_{H-3,CH_3}	$J_{2,3}$	$J_{3,4}$	$J_{2,4}$	$J_{5,6}$	$J_{5,7}$	$J_{6,7}$
	...	4.2	8.0	2.0	8.0	2.0	4.2
	0.90	4.2	...	...	8.2	2.0	4.2
	...	...	8.4	...	8.4	2.0	4.4
	0.90	...	...	...	8.2	2.0	4.2

[a] Because of a typographic error, the chemical shift of H-5 was not listed in a previous paper[2b] of this series.

(10%). One crystallization from cyclohexane gave straw-like needles, mp 84–85° (lit.[10] 85–86°), picrate mp 204–205° (lit.[11] 204–206°).

Registry No.—2, 254-60-4; 3, 1569-16-0; 4, 1569-17-1; 5, 7544-64-1.

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Simplified Method for the Preparation of Fluoroalkyl Iodides

DONALD PASKOVICH, PETER GASPAR,[1] AND GEORGE S. HAMMOND

University of Ottawa, Ottawa, Ontario, Canada, Washington University, St. Louis, Missouri, and California Institute of Technology, Pasadena, California

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Several methods are presently available for the synthesis of fluoroalkyl iodides. The reactions are carried out in sealed tubes and consist of treatment of fluoroolefins with iodine fluoride (IF) formed *in situ* from various halogen compounds,[2] chain lengthening of fluoroalkyl iodides with tetrafluoroethylene and an antimony halide catalyst,[3] decomposition of fluoroacyl chlorides in the presence of potassium iodide at 200°,[4] decomposition of fluoro acid anhydrides in the presence of iodine at 350–400°,[5] and decomposition of metal salts of fluoro acids in the presence of excess iodine at high temperatures.[6]

Silver salts are most commonly used in the latter method, and yields of 80 to 100% have been reported. Other metal salts such as sodium, potassium, barium, mercury and lead give lower yields of fluoroalkyl iodides.[6a,c,e] For example Haszeldine[6c] reports heating a mixture of 27.2 g of sodium trifluoroacetate and 100 g of iodine with a free flame to give 10% trifluoromethyl iodide, while a 40% yield was obtained when 13.6 g of potassium trifluoroacetate was heated with 500 g of iodine. When the reactions were carried out at 280° in a stainless steel autoclave, 61 and 55% yields of trifluoromethyl iodide were obtained from the sodium and potassium salts of trifluoroacetic acid, respectively. Heating sodium heptafluorobutyrate and a 300% excess of iodine with a free flame gave 9% heptafluoroiodopropane and 41% hexafluoropropene. The same

(1) To whom inquiries should be addressed at the Department of Chemistry, Washington University, St. Louis, Mo. 63130

(2) (a) J. H. Simons and T. J. Brice, U. S. Patent 2,614,131 (1953); *Chem. Abstr.*, **47**, 8770c (1953); (b) R. D. Chambers, W. K. R. Musgrave, and J. Savory, *J. Chem. Soc.*, 3779 (1961); (c) W. K. R. Musgrave, J. Perret, and J. Savory, British Patent 885,007 (1962); *Chem. Abstr.*, **57**, 11018*i* (1962); (d) C. G. Krespan, U. S. Patent 3,052,732 (1963); *Chem. Abstr.*, **58**, 7828*d* (1963).

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(5) R. N. Haszeldine, British Patent 757,893 (1957); *Chem. Abstr.*, **51**, 12129*h* (1957).

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