[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

# The Preparation of Heterocyclic Fluorine Compounds by the Schiemann Reaction.
## II. The Monofluoroquinolines[1]

BY ARTHUR ROE AND G. F. HAWKINS

An earlier paper[2] described the application of the Schiemann reaction to the synthesis of the monofluoropyridines. This paper reports the preparation by this same method of all the monofluoroquinolines, 4-fluoroquinoline possibly excepted.

Aromatic diazonium fluoborates, the intermediates in the Schiemann reaction, are usually quite stable. In contrast to this the three pyridinediazonium fluoborates were found[2] to be quite unstable, decomposing at room temperature or below. It is interesting to note, however, that 3-quinolinediazonium fluoborate, unlike its pyridine analog, is stable enough to be isolated and dried; it decomposes at 95°. Of further interest is the fact that 5-, 6-, 7- and 8-quinolinediazonium fluoborates—all of which have the diazonium group on the benzene ring—are stable compounds which may be dried and decomposed in the usual manner, behaving like the aromatic diazonium fluoborates in this way.

The fluoroquinolines are colorless liquids whose properties are shown in the accompanying table. All the compounds are soluble in dilute hydrochloric acid except 2-fluoroquinoline. Both 3- and 6-fluoroquinoline form solid hydrates.

TABLE I

FLUOROQUINOLINES

| Compound | Overall % yield | B. p. |  | $n^{25}\text{D}$ | $d^{25}$ | Fluorine, % |  | Picrate M. p., °C. | Nitrogen, % |  |
|---|---|---|---|---|---|---|---|---|---|---|
|  |  | °C. | Mm. |  |  | Calcd. | Obs. |  | Calcd. | Obs. |
| 2-Fluoro- | 28 | 133 | 30 | 1.5827 | ... | 12.91 | 12.92 | ..... | ... | ... |
| 3-Fluoro- | 74 | 102 | 15 | 1.5902 | 1.194 | 12.91 | 12.90 | 183–185 | 14.89 | 14.67 |
| 4-Fluoro- | .. | 119 (?) | 30 | .... | ... | ... | ... | ..... | 14.89 | ... |
| 5-Fluoro- | 59 | 123 | 30 | 1.5916 | 1.197 | 12.91 | 12.74 | 199–200 | 14.89 | 14.96 |
| 6-Fluoro- | 57 | 124 | 30 | 1.5908 | 1.200 | 12.91 | 13.19 | 218–219 | 14.89 | 14.68 |
| 7-Fluoro- | 27 | 129 | 30 | 1.5845 | ... | 12.91 | 12.95 | 227–229 | 14.89 | 14.78 |
| 8-Fluoro- | 25 | 148 | 30 | 1.6028 | 1.215 | 12.91 | 12.95 | 170–172 | 14.89 | 15.06 |

A liquid that may have been 4-fluoroquinoline was isolated. Decomposition of 4-quinolinediazonium fluoborate suspended in ether was carried out at 15–20°; after neutralizing with sodium hydroxide the ether layer was dried and distilled. A large amount of tarry material and a small amount of colorless liquid boiling at 119° at 30 mm. was obtained; the liquid rapidly changed into a light brown solid. The structure of this brown decomposition product was not definitely determined. It might be pointed out that 4-fluoropyridine changes rapidly into N-(4′-pyridyl)-4-fluoropyridinium fluoride, which hydrolyzes easily to form N-(4′-pyridyl)-4-pyridone.[2] The decomposition of 4-fluoroquinoline may follow a similar course; the analytical data does not answer this question satisfactorily.

Work on the preparation of heterocyclic fluorine compounds is continuing in this Laboratory.

### Experimental[3]

**Starting Materials.**—2-Aminoquinoline,[4] 4-aminoquinoline,[5] 5-aminoquinoline,[6] 6-aminoquinoline,[7] 7-aminoquinoline,[6] and 8-aminoquinoline[8] were prepared by methods reported in the literature; 3-aminoquinoline was purchased from Eastman.

**2-Fluoroquinoline.**—A solution of 3.5 g. of 2-aminoquinoline in 50 ml. of 40% fluoboric acid was prepared; a voluminous precipitate formed. A solution of 1.75 g. of sodium nitrite dissolved in 3 ml. of water was added a little at a time to the fluoborate solution at room temperature; the resulting diazonium fluoborate decomposed as it was formed. When decomposition was complete the solution was transferred to a separatory funnel and covered with ether; 5% sodium hydroxide was added slowly with shaking after each addition until the solution was alkaline. The ether extract was dried over sodium sulfate and distilled; 0.9 g. (28%) of 2-fluoroquinoline was obtained. This compound did not react with picric acid to form a picrate.

**3-Fluoroquinoline.**—A solution of 30 g. of 3-aminoquinoline in 100 ml. of 40% fluoboric acid was diazotized at 5° or lower with 15 g. of sodium nitrite dissolved in 20 ml. of water. The resulting diazonium fluoborate was filtered, washed once with cold fluoboric acid, once with 75 ml. of cold ethanol, and four times with 100 ml. of dry ether. The yield of 3-quinolinediazonium fluoborate was 55 g. (80%), m. p. 95° (dec.).

A suspension of 42 g. of 3-quinolinediazonium fluoborate in 150 ml. of dry toluene in a 500-ml. flask was heated slowly; decomposition, once started, was rapid. The toluene was decanted from the solid residue and extracted with two 50-ml. portions of 10% hydrochloric acid; the acid extracts were added to the solid residue in the decomposition flask and the contents of the flask subjected to steam distillation to remove the toluene. The mixture in the flask was then made alkaline and the steam distillation continued; a solid, evidently a hydrate of 3-fluoro-

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(1) Presented before the American Chemical Society, Organic Division, New York Meeting, September 16, 1947.

(2) Roe and Hawkins, THIS JOURNAL, **69**, 2443 (1947).

(3) All melting points uncorrected.

(4) Shreve, Riechers, Rubenkoenig and Goodman, *Ind. Eng. Chem.*, **32**, 173 (1940).

(5) Wenzel, *Monatsh.*, **15**, 453 (1894).

(6) Prepared by the reduction of 5-nitroquinoline using the method described for 7-nitroquinoline by Winterbottom, THIS JOURNAL, **62**, 160 (1940).

(7) Knueppel, *Ann.*, **310**, 75 (1900).

(8) Dikshoorn, *Rec. trav. chim.*, **48**, 147 (1929).

quinoline, collected in the condenser and receiving flask. Thirty grams of the moist white solid was obtained. The liquid distillate was saturated with sodium sulfate and extracted with two 50-ml. portions of ether; these extracts were added to the white solid which dissolved. The solution was dried over sodium sulfate for two days. Distillation produced 17 g. of 3-fluoroquinoline (91.5% from the diazonium salt; 73.5% from the amine). Addition of water to the fluoroquinoline resulted in the formation of the solid hydrate.

**Attempted Preparation of 4-Fluoroquinoline.**—A solution of 3 g. of 4-aminoquinoline in 45 ml. of 40% fluoboric acid was cooled to 0° and diazotized with 1.5 g. of sodium nitrite in 2 ml. of water. The mixture was then cooled to −10° to ensure complete precipitation and filtered rapidly through a cold filter, washed thrice with cold dry ether, and transferred to a beaker of cold ether. The ether suspension was allowed to warm slowly; decomposition of the diazonium salt started at 10°, was moderate at 15°, and quite rapid at 22°. After decomposition was complete the solution was made alkaline with sodium hydroxide; the mixture was vigorously shaken and the ether layer separated and dried over sodium sulfate for twelve hours. Distillation produced a small amount of colorless liquid boiling at 119° (30 mm.), which was presumably 4-fluoroquinoline, with a considerable quantity of tarry material remaining in the distillation flask. The distillate solidified quite rapidly to a tan solid which shrivelled at 149°, softened at 165°, and melted at 180–195°. Analytical data suggest that this may be impure N-(4′-quinolyl)-4-fluoroquinolinium fluoride.

*Anal.* Calcd. for $C_{18}H_{12}N_2F_2$: N, 9.53; F, 12.91. Found: N, 7.54, 7.49; F, 11.58.

A picrate of this material was prepared; it contained no fluorine, but no other analysis was attempted because it could not be obtained pure; m. p. 180–195°. This may be the picrate of N-(4′-quinolyl)-4-quinolone if 4-fluoroquinoline is analogous to 4-fluoropyridine in its decomposition.[2]

**5-Fluoroquinoline.**—The treatment of 4.2 g. of 5-aminoquinoline by the method used for 3-aminoquinoline produced 9.5 g. (94%) of a brick-red diazonium fluoborate, m. p. 95° (dec.). Decomposition of this salt in toluene produced 2.6 g. of 5-fluoroquinoline (59% from the amine).

**6-Fluoroquinoline.**—A yield of 10.4 g. (95.5%) of 6-quinolinediazonium fluoborate was obtained from 5 g. of 6-aminoquinoline; the salt was precipitated from the fluoboric acid solution by addition of 50% ethanol–ether to the diazotized solution. Decomposition was carried out without solvent producing 3 g. of 6-fluoroquinoline (60% from the diazonium fluoborate).

**7-Fluoroquinoline.**—A 100% yield of 7-quinolinediazonium fluoborate, m. p. 123° (dec.), was prepared from 5.5 g. of the corresponding amine using the method described for 3-aminoquinoline. Decomposition of the salt in xylene gave 1.5 g. (26.7%) of 7-fluoroquinoline.

**8-Fluoroquinoline.**—A 74% yield of 8-quinolinediazonium fluoborate was obtained from 15 g. of the corresponding amine using the method described for 3-aminoquinoline. The salt was decomposed without solvent in 6-g. portions; the resulting tar was dissolved in dilute hydrochloric acid, the solution neutralized with sodium carbonate, extracted with ether, dried over sodium sulfate, and distilled. A yield of 4.9 g. (33.1% from the diazonium salt) was obtained.

## Summary

The Schiemann reaction has been employed to prepare all the monofluoroquinolines with the possible exception of 4-fluoroquinoline; the latter compound is quite unstable, changing from a colorless liquid to a tan solid quite rapidly after distillation.

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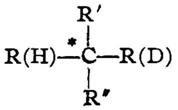
# Optical Activity in Compounds Containing Deuterium. I. 2,3-Dideutero-*trans*-Menthane

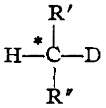
BY ELLIOT R. ALEXANDER AND A. G. PINKUS

An interesting aspect of stereochemistry is the question of whether or not a molecule can be optically active when the sole cause of asymmetry is the replacement of a hydrogen by a deuterium atom. Such molecules can be divided into the two general types, I and II



$$R(H)-\overset{\overset{R'}{|}}{\underset{\underset{R''}{|}}{\overset{*}{C}}}-R(D)$$

I



$$H-\overset{\overset{R'}{|}}{\underset{\underset{R''}{|}}{\overset{*}{C}}}-D$$

II

With the first of these, asymmetry results from a difference between two groups which are the same except that one contains hydrogen and the other contains deuterium. In the other (II), deuterium and hydrogen are compared directly at an asymmetric center. Many attempts have been made to demonstrate optical activity in compounds of type I[1–7] and type II,[8–14] but none of these investigations has shown conclusively that activity is present.

It is interesting, however, that when hydrogen is replaced by deuterium in an optically active molecule other than a hydrocarbon, there is often

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(1) Clemo, Raper and Robson, *J. Chem. Soc.*, 431 (1939).
(2) Clemo and McQuillan, *ibid.*, 808 (1936).
(3) Clemo and Swan, *ibid.*, 1960 (1939); 370 (1942).
(4) Adams and Tarbell, THIS JOURNAL, **60**, 1260 (1938).
(5) McGrew and Adams, *ibid.*, **59**, 1497 (1937).
(6) Burwell, Hummel and Wallis, *J. Org. Chem.*, **1**, 332 (1936).
(7) Erlenmeyer and Schenkel, *Helv. Chim. Acta*, **19**, 1169 (1936).
(8) Erlenmeyer and Gärtner, *ibid.*, **19**, 145, 331 (1936).
(9) Erlenmeyer, Fischer and Baer, *ibid.*, **20**, 1012 (1937).
(10) Biilman, Jensen and Knuth, *Ber.*, **69**, 1031 (1936).
(11) Biilman, Jensen and Bak, *ibid.*, **69**, 1947 (1936).
(12) Leffler and Adams, THIS JOURNAL, **58**, 1551 (1936).
(13) Leffler and Adams, *ibid.*, **58**, 1555 (1936).
(14) Porter, *ibid.*, **57**, 1436 (1935).