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# Studies on the Organic Fluorine Compounds. XXIV.[1] Photochemical Trifluoromethylation of Aromatic Compounds[2]

Yoshiro Kobayashi, Itsumaro Kumadaki, Akio Ohsawa, Shin-ichi Murakami, and Takaharu Nakano

*Tokyo College of Pharmacy*[3]

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Photochemical trifluoromethylation of pyridine gave a mixture of three (trifluoromethyl)pyridines. Pyrrole and N-methylpyrrole were trifluoromethylated in α-position. Benzene gave very low yield of benzotrifluoride.

**Keywords**——trifluoromethylation; photochemistry; benzotrifluoride; (trifluoromethyl)pyridine; (trifluoromethyl)pyrrole; benzene; pyridine; pyrrole

Several methods for the synthesis of trifluoromethylated aromatic compounds have been reported. For example, one of the modern methods developed by Tullock *et al.* is transformation of carboxyl group to trifluoromethyl group by means of sulfur tetrafluoride.[4] This method has wide applicability, but high toxicity of sulfur tetrafluoride is disadvantageous. Present authors and others[5] reported the trifluoromethylation of aryl halide with trifluoromethyl iodide and copper powder. This method is a very simple and safe method, but it needs prior halogenation of aromatic compounds. Here, we should like to report a one-step photochemical trifluoromethylation, which we found in the study of nucleic acid.

We had tried photochemical trifluoromethylation of adenosine by irradiation of trifluoromethyl iodide in pyridine. While none of the trifluoromethylated adenosine was obtained, formation of (trifluoromethyl)pyridines was observed. Therefore, we planned to study the applicability of this trifluoromethylation.

Pyridine (I) and trifluoromethyl iodide were sealed in a quartz tube under vacuum and irradiated with a low pressure mercury lamp for three days. Gas-chromatographic analysis of the products showed that α-II, β-III and γ-(trifluoromethyl)pyridine (IV) were formed in 38%, 27% and 16% yield, respectively, with a trace of bis(trifluoromethyl)pyridines (Chart 1).

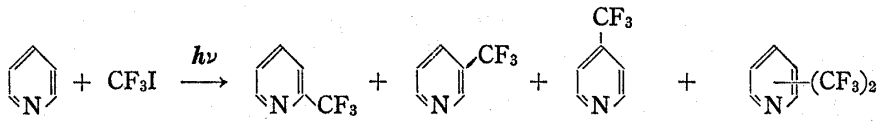


Chart 1

Next, we applied this reaction to π-electron-excessive pyrrole (V) and N-methylpyrrole (VI). Pyrrole (V) gave α-(trifluoromethyl)pyrrole (VII) in 33%. Its structure was deter-

1) Part XXIII: Y. Kobayashi, I. Kumadaki, A. Ohsawa, Y. Sekine, and A. Ando, *J. Chem. Soc., Perkin Trans. I*, **1977**, 2355.
2) A part of this work was presented at the 96th Annual meeting of the Pharmaceutical Society of Japan, Nagoya, April, 1976.
3) Location: *Horinouchi, Hachioji, Tokyo 192-03, Japan.*
4) C.W. Tullock, F.S. Fawatt, W.C. Smith, and D.D. Cattman, *J. Am. Chem. Soc.*, **82**, 539 (1960).
5) Y. Kobayashi and I. Kumadaki, *Tetrahedron Lett.*, **1969**, 4095; Y. Kobayashi, I. Kumadaki, S. Sato, N. Hara, and E. Chikame, *Chem. Pharm. Bull.* (Tokyo), **18**, 2334 (1970).

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mined by derivation of VII to methyl pyrrole-2-carboxylate (VIII) by treatment with potassium hydroxide in methanol. Similarly, VI gave N-methyl-α-(trifluoromethyl)pyrrole (IX) in 35% yield. The structure of IX was determined by the comparison of its NMR spectrum with that of VII. (Chart 2)

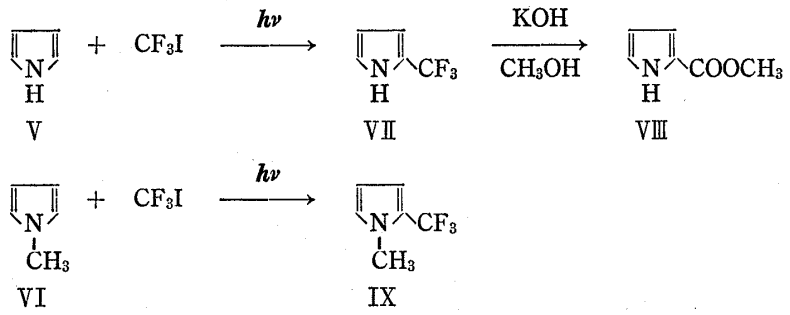

Chart 2

Quite recently, Cantacuzène *et al.*[6] reported thermal perfluoroalkylation of N-alkylpyrrole with perfluoroalkyl iodide ($C_nF_{2n+1}I$: $n=2$, and 6) at 165°, while pyrrole itself did not give perfluoroalkyl compound under their condition. Usually, the introduction of trifluoromethyl group is more difficult than that of other perfluoroalkyl groups. Therefore, our method is superior to their method.

Finally, this method was applied to benzene. Benzotrifluoride was obtained in 14% yield;

$$C_6H_6 + CF_3I \longrightarrow C_6H_5CF_3$$

Application of this method to substituted benzenes was attempted, but no appreciable amount of trifluoromethyl compounds was formed. Birchall *et al.*[7] reported that the reaction of a trifluoromethyl radical with benzene in the presence of mercury using an excess of benzene gave a little better yield of benzotrifluoride (38%).

In summary, trifluoromethylation occurred in both π-electrondeficient and π-excessive nitrogen compounds, while that of the benzene series did not give a satisfactory result. This may be ascribed to the formation of charge transfer complex of trifluoromethyl iodide with lone-pair electrons on a nitrogen atom.

## Experimental

**General Procedure**——A mixture of an aromatic compound and $CF_3I$ was sealed in a silica tube (300 ml) under vacuum and irradiated with a low pressure mercury lamp. After irradiation, gaseous products were degassed at room temperature and the residue was distilled with a vacuum line and analyzed by gas liquid chromatography (GLC).

**Reaction of Pyridine**——$CF_3I$ (2 ml) and pyridine (2.7 g, 1.5 mol, eq.) were irradiated for 3 days. Products were analyzed qualitatively and quantitatively by GLC. Column: DEGS, column temp. 50°. Yields are estimated on the basis of $CF_3I$. A trace of bis(trifluoromethyl)pyridines was confirmed by GLC-mass spectroscopy.

**α-(Trifluoromethyl)pyrrole (VII)**——$CF_3I$ (1.5 ml) and pyrrole (1.7 g, 1.5 mol, eq.) were irradiated for 2 days. The product was analyzed by GLC. Column: DEGS, column temp., 100° Yield 33% (based on $CF_3I$).

α-(Trifluoromethyl)pyrrole (VII) was separated from V by preparative GLC. Column: DEGS, $\phi=10$ mm, L=7 m, temp., 100°. bp 100°; MS *m/e*: 135 ($M^+$); high resolution mass spectrum Calcd. for $C_5H_4F_3N$ 135.0296, Found: 135.0326; $^1$H-NMR ($CDCl_3$) δ: 6.06 (d-d, $J_{3,4}=3.5$ Hz, $J_{4,5}=2.5$ Hz, 4-H), 6.40 (d-d, $J_{3,4}=3.5$ Hz, $J_{3,5}=2.3$ Hz, 3-H) 6.60 (d-d, $J_{3,5}=2.3$ Hz, $J_{4,5}=2.5$ Hz, 5-H), 8.20 (broad, N-H); $^{19}$F-NMR ($CDCl_3$; BTF as an internal standard) −3.6 ppm.

**N-Methyl-α-(trifluoromethyl)pyrrole (IX)**——$CF_3I$ (1.4 ml) and N-methylpyrrole (VI) (2 g) were irradiated for 2 days. The product was analyzed by GLC. Column: DEGS, column temp., 80°. Yield 35% (based on

6) I. Cantacuzène, C. Wakselman, and R. Korme, *J. Chem. Soc., Perkin Trans I*, **1977**, 1365.
7) J.M. Birchall, G.P. Irvin, and R.A. Boyson, *J. Chem. Soc., Perkin Trans. II*, **1975**, 435.

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$CF_3I$). IX was separated from VI by prep. GLC. under the same condition as VII. bp 80°; MS *m/e*: 149 ($M^+$); $^1$H-NMR ($CDCl_3$) $\delta$: 3.60 (s, N-$CH_3$), 5.90 (d-d, $J_{3,4}$=3.0 Hz, $J_{4,5}$=2.5 Hz, 4-H), 6.36 (d-d, $J_{3,4}$=3.0 Hz, $J_{3,5}$=2.4 Hz, 3-H), 6.48 (d-d, $J_{3,5}$=2.4 Hz, $J_{4,5}$=2.5 Hz, 5-H); $^{19}$F-NMR ($CDCl_3$) −4.0 ppm.

**Benzotrifluoride**——$C_6H_6$ (1 g) and $CF_3I$ (2 ml) was irradiated for 2 weeks. The reaction mixture was analyzed by GLC. Column: Ucon 50 HB, $\phi$=4 mm, L=2 m; temp. 40°. Yield 14% (based on benzene).

**Alcoholysis of 2-(Trifluoromethyl)pyrrole**——KOH (550 mg) was added into the solution of 2-(trifluoromethyl)pyrrole (380 mg) in methanol (10 ml) with stirring, and the mixture was refluxed for 10 hr. The cooled reaction mixture was poured into ice-water, and neutralized with concentrated hydrochloric acid. The mixture was extracted with ether, and the extract was dried over $Na_2SO_4$. Removal of ether afforded 170 mg (52%) of colorless crystals, mp 68—71° which were identified with the authentic sample.[8]

8) P. Hodge and R.W. Rickards, *J. Chem. Soc.*, **1963**, 2543.

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