# Chemical oxidation of fluoroanilines to fluoroazobenzenes and fluorophenazines with potassium ferricyanide and potassium hydroxide

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**Abstract:** The oxidation of several fluoroanilines with potassium ferricyanide and potassium hydroxide is described. In this oxidation, the major products are fluoroazobenzenes. In the case of 2-fluoro-substituted anilines, heterocyclic fluorophenazines were obtained in low to moderate yields. The optimal conditions for the reaction and the mechanism are presented.

Key words: oxidation, fluoroanilines, fluoroazobenzenes, fluorophenazines.

**Résumé :** On décrit l'oxydation de plusieurs fluoroanilines avec du ferricyanure de potassium et de l'hydroxyde de potassium. Dans cette oxydation, les produits principaux sont des fluoroazobenzènes. Dans le cas des 2-fluoroanilines, des fluorophénazines hétérocycliques ont été obtenues avec des rendements allant de faibles à moyens. On présente les conditions optimales et le mécanisme de cette réaction.

Mots clés : oxydation, fluoroanilines, fluoroazobenzènes, fluorophénazines.

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# Introduction

Fluoroazobenzenes are extensively used as dyes and analytical reagents (1). They are also useful as materials with nonlinear optical properties (2–5). These fluorocarbon compounds exhibit the properties of water and oil repellency, high lubricity, and thermal and chemical stability (6). They are useful synthetic intermediates. Decafluoroazobenzene has been used as a precursor of several hydroxyfluoroazobenzenes that have been evaluated as inhibitors of steroid biosynthesis (7).

The oxidation of substituted anilines to azobenzenes with a variety of oxidizing agents, such as barium manganate (8), lead tetraacetate (9), sodium hypochlorite (10) and manganese dioxide (11), has been reported. However, the oxidation of fluoroanilines with inorganic oxidants in aqueous solution is complicated by the poor solubility of anilines under these conditions. The addition of an organic solvent inmiscible with the aqueous phase slows the reaction further, since the solubility of the fluoroanilines is inhibited. The oxidation of pentafluoroaniline under phase-transfer conditions (12) gave decafluoroazobenzene in only 28% yield. Tatlow and coworkers (13) reported the formation of decafluoroazobenzene (18%) and octafluorophenazine (6%) during the electrochemical oxidation of pentafluoroaniline.

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The oxidation of aromatic anilines with potassium ferricyanide and KOH was first reported by Goldstein and McNelis (14). Mesidine was oxidized by this reagent in a methanol-water mixture at 45 °C for 10 days to give the corresponding azobenzene. In a short communication, we reported the oxidation of fluoroanilines with this oxidant (15). In the present paper, we report the oxidation of several fluoroanilines 1 to azobenzenes 2 and phenazines 3 by means of potassium ferricyanide and KOH. The optimal conditions for this reaction and the mechanism are presented.

# **Results and discussion**

In general, the oxidation of fluoroanilines with inorganic oxidants in aqueous media gives very low yields due to the poor solubility of anilines under these conditions. The addition of an inmiscible organic solvent does not improve the yields. In our hands, several fluoroanilines **1a–1h** (Scheme 1) reacted with potassium ferricyanide to give the corresponding fluoroazobenzenes **2a–2h** in good to moderate yields when a mixture of ethanol and water was used as the solvent. All the fluoroanilines had good solubility in the solvent mixture used, although some are not very soluble in other solvents such as dichloromethane.

For each aniline **1a–1h**, the main product was the corresponding fluoroazobenzene **2a–2h** (Table 1). A particularly high yield (94%) was obtained with 4-fluoroaniline (**1c**). Even the oxidation of pentafluoroaniline (**1h**) gave decafluoroazobenzene (**2h**) in higher yield than that previously reported (12). With 2-fluoro-substituted anilines **1a**, **1d**, **1e**, **1f**, and **1h**, in addition to the fluoroazobenzenes **2**, the corresponding phenazines **3** were also obtained in variable amounts as yellow crystalline compounds. With 2,4-

#### Scheme 1.



Table 1. Products formed in the oxidation of fluoroanilines.

Aniline 1	Yield (%)	
	Azobenzene 2	Phenazine 3
1a: 2-Fluoroaniline	52	Trace
<b>1b</b> : 3-Fluoroaniline	50	None
<b>1c</b> : 4-Fluoroaniline	94	None
1d: 2,4-Difluoroaniline	52	20
<b>1e</b> : 2,5-Difluoroaniline	62	Trace
1f: 2,6-Difluoroaniline	65	25
<b>1g</b> : 3,4-Difluoroaniline	60	None
1h: Pentafluoroaniline	60	25

difluoroaniline (1d), phenazine 3d was obtained in moderate yield. In the case of anilines with two *o*-fluoro substituents, the yields of phenazines were slightly higher.

The formation of the products observed in the oxidation of fluoroanilines can be explained by a mechanism involving a singlet fluorophenylnitrene as an intermediate (Scheme 2). Under these conditions, the fluorophenylnitrene would form from the fluoroaniline by reaction with potassium ferricyanide and KOH. Singlet fluorophenylnitrene is anticipated to be an ambident electrophile because the electron deficiency of the nitrogen could be neutralized by attack of a nucleophile not only on nitrogen but also on the ortho position of the aromatic ring. Nucleophilic attack by remaining fluoroaniline on nitrogen would give the fluorohydrazobenzene, which would oxidize to form the fluoroazobenzene. On the other hand, the electron-deficient singlet fluorophenylnitrene could be attacked at the ortho position of the aromatic ring by the nucleophilic aniline. Elimination of HF, heterocyclic ring closure, and further elimination of HF would give the phenazine 3. In agreement with this mechanism is the observation that several equivalents of oxidant are required for the reaction to occur. A similar mechanism has been proposed for the oxidation of pentafluoroaniline to decafluoroazobenzene with sodium hypochlorite (12). Consistent with the proposed intermediacy of fluorophenylnitrene in this oxidation is the reported formation of both decafluoroazobenzene and octafluorophenazine in the thermal decomposition of azidopentafluorobenzene in the presence of pentafluoroaniline, where singlet nitrene is considered to be an intermediate (16).

# Conclusions

The oxidation of fluoroanilines with potassium ferricyanide and KOH in an ethanol-water mixture gives the cor-

#### Scheme 2.



responding fluoroazobenzene in good to moderate yields. With 2-fluoro-substituted anilines, the corresponding fluorophenazines are also obtained in variable amounts. With 2,4difluoroaniline, the phenazine is obtained in moderate yield. In the case of anilines with two *o*-fluoro substituents, the yields of phenazines are slightly higher.

#### Experimental section

### **General methods**

All melting points were measured with a Fisher-Johns apparatus. IR spectra were recorded on a Nicolet 205 FT-IR spectrometer. UV–vis spectra were determined on a Shimadzu UV-2401PC spectrophotometer. <sup>1</sup>H NMR spectra were obtained on a Varian EM-200 using deuterated chloroform as solvent and were recorded in ppm from tetramethylsilane. <sup>19</sup>F NMR spectra were obtained on a Bruker AC 250 with a QNP probe and were recorded in ppm from trifluoroacetic acid or hexafluorobenzene. Mass spectra were obtained with a Hewlett Packard Model 5971 gas chromatograph equipped with a Hewlett Packard 5972 quadrupole mass detector. The chromatographic separation was performed on a capillary column (crosslinked 5% phenyl methyl silicone, 0.2 mm i.d. 0.33  $\mu$ m × 25 m) using helium as carrier gas.

#### General procedure for oxidation

A given fluoroaniline (0.01 mol) was dissolved in an ethanol-water (1:1) mixture. Then, potassium hydroxide (0.018 mol) in a 1:1 ethanol-water mixture was added. Finally, potassium ferricyanide (0.04 mol) was added slowly. The resulting mixture was kept under reflux for 6 h. After this time, the mixture was filtered to remove the remaining

oxidant and extracted with dichloromethane. The organic phase was washed several times with water and dried with anhydrous sodium sulfate. The solvent was removed in a rotary evaporator, and the resulting mixture was passed through a silica gel column using hexane as the solvent to obtain the corresponding fluoroazobenzene as a crystalline orange solid. In the case of 2-fluoro-substituted anilines, fluorophenazines were obtained in low to moderate yields as yellow crystalline solids.

#### 2,2'-Difluoroazobenzene (2a)

Orange crystals; yield 52%; mp 94–96 °C. IR (neat, cm<sup>-1</sup>) 1219 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 7.5 (m, 4H, aromatic CH), 7.73 (m, 2H, aromatic), 8.05 (td, 2H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>),  $\delta$  (ppm): –121.3 (s, 2F). EI-MS (70 eV) *m*/*z*: 218 (45%) [M<sup>+</sup>], 123 (48%) [M<sup>+</sup> – C<sub>6</sub>H<sub>4</sub>F], 95 (100%) [M<sup>+</sup> – C<sub>6</sub>H<sub>4</sub>FN<sub>2</sub>], 75 (25%) [M<sup>+</sup> – C<sub>6</sub>H<sub>5</sub>F<sub>2</sub>N<sub>2</sub>]; exact mass for C<sub>12</sub>H<sub>8</sub>F<sub>2</sub>N<sub>2</sub>: 218.0653; observed: 218.0663.

#### 3,3'-Difluoroazobenzene (2b)

Orange crystals; yield 50%; mp 70–72 °C. IR (neat, cm<sup>-1</sup>) 1247 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 7.24 (m, 2H, aromatic), 7.52 (q, 2H, aromatic), 7.62 (dd, 2H, aromatic), 7.78 (d, 2H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –108 (s, 2F). EI-MS (70 eV) *m*/*z*: 218 (32%) [M<sup>+</sup>], 123 (22%) [M<sup>+</sup> – C<sub>6</sub>H<sub>4</sub>F], 95 (100%) [M<sup>+</sup> – C<sub>6</sub>H<sub>4</sub>FN<sub>2</sub>], 75 (24%) [M<sup>+</sup> – C<sub>6</sub>H<sub>5</sub>F<sub>2</sub>N<sub>2</sub>]; exact mass for C<sub>12</sub>H<sub>8</sub>F<sub>2</sub>N<sub>2</sub>: 218.0653; observed: 218.0655.

#### 4,4'-Difluoroazobenzene (2c)

Orange crystals; yield 94%; mp 99–100 °C. IR (neat, cm<sup>-1</sup>) 1231 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 7.3 (dd, 4H, aromatic), 8.04 (dd, 4H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –106 (s, 2F). EI-MS (70 eV) *m/z*: 218 (29%) [M<sup>+</sup>], 123 (20%) [M<sup>+</sup> – C<sub>6</sub>H<sub>4</sub>F], 95 (100%) [M<sup>+</sup> – C<sub>6</sub>H<sub>4</sub>FN<sub>2</sub>], 75 (18%) [M<sup>+</sup> – C<sub>6</sub>H<sub>5</sub>F<sub>2</sub>N<sub>2</sub>]; exact mass for C<sub>12</sub>H<sub>8</sub>F<sub>2</sub>N<sub>2</sub>: 218.0653; observed: 218.0650.

#### 2,2',4,4'-Tetrafluoroazobenzene (2d)

Orange crystals; yield 52%; mp 150–152 °C. IR (neat, cm<sup>-1</sup>) 1270 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 7.01 (m, 4H, aromatic), 7.85 (m, 2H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –101.2 (s, 2F) –116.3 (s, 2F). EI-MS (70 eV) *m*/*z*: 254 (40%) [M<sup>+</sup>], 141 (45%) [M<sup>+</sup> – C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>], 113 (100%) [M<sup>+</sup> – C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>N<sub>2</sub>]; exact mass for C<sub>12</sub>H<sub>6</sub>F<sub>4</sub>N<sub>2</sub>: 254.0466; observed: 254.0407.

#### 2,2',5,5'-Tetrafluoroazobenzene (2e)

Orange crystals; yield 62%; mp 128–130 °C. IR (neat, cm<sup>-1</sup>) 1253 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 7.25 (m, 4H, aromatic), 7.54 (m, 2H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –116.3 (s, 2F), –127.8 (s, 2F). EI-MS (70 eV) *m*/*z*:254 (45%) [M<sup>+</sup>], 141 (50%) [M<sup>+</sup> – C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>], 113 (100%) [M<sup>+</sup> – C<sub>6</sub>H<sub>4</sub>FN<sub>2</sub>]; exact mass for C<sub>12</sub>H<sub>6</sub>F<sub>4</sub>N<sub>2</sub>: 254.0466; observed: 254.0477.

#### 2,2',6,6'-Tetrafluoroazobenzene (2f)

Orange crystals; yield 65%; mp 121–123 °C. IR (neat, cm<sup>-1</sup>) 1017 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 6.85 (m, 4H, aromatic), 7.20 (m, 2H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –125.3 (s, 4F). EI-MS (70 eV) *m*/*z*: 254 (47%) [M<sup>+</sup>], 141 (72%) [M<sup>+</sup> – C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>], 113 (100%) [M<sup>+</sup> –

 $C_6H_3F_2N_2$ ]; exact mass for  $C_{12}H_6F_4N_2$ : 254.0466; observed: 254.0476.

# 3,3',4,4'-Tetrafluoroazobenzene (2g)

Orange crystals; yield 60%; mp 70–72 °C. IR (neat, cm<sup>-1</sup>) 1275 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 7.36 (m, 2H, aromatic), 7.78 (m, 4H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –129.3 (s, 2F), –132.4 (s, 2F). EI-MS (70 eV) *m/z*: 254 (41%) [M<sup>+</sup>], 141 (45%) [M<sup>+</sup> – C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>], 113 (100%) [M<sup>+</sup> – C<sub>6</sub>H<sub>3</sub>F<sub>2</sub>N<sub>2</sub>]; exact mass for C<sub>12</sub>H<sub>6</sub>F<sub>4</sub>N<sub>2</sub>: 254.0466; observed: 254.0471.

#### 2,2',3,3',4,4',5,5',6,6'-Decafluoroazobenzene (2h)

Red–orange crystals; yield 60%; mp 142–143 °C. IR (neat, cm<sup>-1</sup>) 1258 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 7.36 (m, 2H, aromatic), 7.78 (m, 4H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –151.9 (m, 6F), –164.7 (m, 4F). EI-MS (70 eV) exact mass for C<sub>12</sub>F<sub>10</sub>N<sub>2</sub>: 361.9901; observed 361.9890.

#### 3,8-Difluorophenazine (3d)

Yellow crystals; yield 20%; mp 169–171 °C. IR (neat, cm<sup>-1</sup>) 1535 (C=C), 1478 (C=C), 1638 (C=N), 1201 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): 8.35 (m, 1H, aromatic), 8.42 (m, 1H, aromatic), 8.54 (m, 1H, aromatic), <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –125 (s, 2F). EI-MS (70 eV) exact mass for C<sub>12</sub>H<sub>6</sub>F<sub>2</sub>N<sub>2</sub>: 216.0499; observed 216.0480.

#### 2,7-Difluorophenazine (3e)

Yellow crystals; yield 25%; mp 205–206 °C. IR (neat, cm<sup>-1</sup>) 1533 (C=C), 1487 (C=C), 1639 (C=N), 1104 (C–F). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ (ppm): 8.25 (m, 1H, aromatic), 8.55 (m, 1H, aromatic), 8.65 (m, H, aromatic). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$ (ppm): –123.5 (s, 2F). EI-MS (70 eV) exact mass for C<sub>12</sub>H<sub>6</sub>F<sub>2</sub>N<sub>2</sub>: 216.0499; observed 216.0489.

#### 2,3,4,5,7,8,9,10-Octafluorophenazine (3h)

Yellow crystals; yield 25%; mp 233–234 °C. IR (neat, cm<sup>-1</sup>) 1638 (C=C), 1478 (C=C), 1201 (C–F). <sup>19</sup>F NMR (CDCl<sub>3</sub>)  $\delta$  (ppm): –155.5 (s, 2F), –157 (s, 2F), –162.4 (s, 2F), 166 (s, 2F). EI-MS (70 eV) exact mass for C<sub>12</sub>F<sub>8</sub>N<sub>2</sub>: 323.9934; observed 323.9920.

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