Pergamon

Tetrahedron Letters, Vol. 38, No. 45, pp. 7847-7848, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10131-9

Oxidation of Fluoroanilines to Fluoroazobenzenes with Potassium Ferricyanide and KOH

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Abstract: The oxidation of several fluoroanilines to fluoroazobenzenes with potassium ferricyanide and KOH in a solvent mixture of ethanol/water is described.
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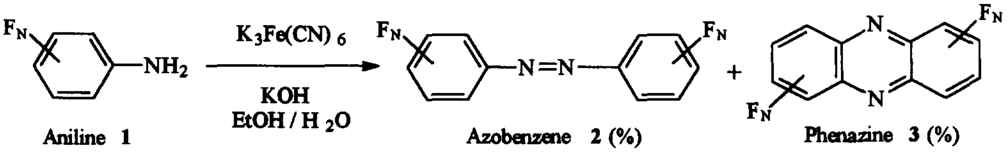
The oxidation of aromatic amines to azobenzenes with several reagents such as barium manganate,[1] lead tetraacetate,[2] sodium hypochlorite[3] and manganese dioxide[4] has been reported. However, the oxidation of fluoroanilines with inorganic oxidants in aqueous solution is complicated by the poor solubility of the fluoroanilines. The addition of an organic solvent immiscible with the aqueous phase slows the reaction further, since the solubility of the fluoroanilines is inhibited. The oxidation of pentafluoroaniline under phase transfer conditions[5] gave the decafluoroazobenzene in only 28%.

Fluoroazobenzenes are useful synthetic intermediates. In a recent report, decafluoroazobenzene was used as a precursor of several hydroxyfluoroazobenzenes which were evaluated as inhibitors of steroid biosynthesis.[6]

There is only a previous report on the oxidation of an aromatic amine with potassium ferricyanide.[7] The oxidation of mesidine with this oxidant and KOH in a methanol/water mixture gave the corresponding azobenzene. In our hands, the oxidation of several fluoroanilines **1a-h** (Scheme 1) with potassium ferricyanide and KOH in an ethanol/water mixture (50/50) gave fluoroazobenzenes **2a-h** as the main products. These products were characterized by melting point,[8] IR, ^{1}H NMR, ^{19}F NMR and GC/MS.



Aniline **1**	Azobenzene **2** (%)	Phenazine **3** (%)
1a: 2-fluoro	50	trace
1b: 3-fluoro	50	----
1c: 4-fluoro	92	----
1d: 2,4-difluoro	52	10
1e: 2,5-difluoro	62	trace
1f: 2,6-difluoro	62	10
1g: 3,4-difluoro	65	-----
1h: pentafluoro	60	10

Scheme 1

For all the amines **1a-h** the main product was the corresponding azobenzene **2a-h**. A particularly high yield (90%) was obtained with 4-fluoroaniline **1c**. Even the oxidation of pentafluoroaniline **1h** gave the decafluoroazobenzene **2h** in higher yield that the previously reported.[5] With the 2-fluoroanilines **1a**, **1d**, **1e**, **1f** and **1h**, in addition to the fluoroazobenzenes **2a**, **2d**, **2e**, **2f** and **2h**, the corresponding fluorophenazines **3a**, **3d**, **3e**, **3f** and **3h** were also obtained in variable amounts as yellow crystalline compounds.

The formation of the products observed in the oxidation of fluoroanilines **1a-h** can be explained by a mechanism involving a singlet fluorophenylnitrene as an intermediate. This nitrene would form from the aniline **1**. The electron deficient singlet fluorophenylnitrene could be attacked by the nucleophilic aniline on the ortho and para positions of the aromatic ring. Attack on the ortho position, elimination of HF, heterocyclic ring closure, and further elimination of HF, would give the phenazine **2**. Nucleophilic attack on the nitrogen of the nitrene, by the remaining fluoroaniline **1**, would give hydrazobenzene that can be easily oxidized to azobenzene. Consistent with this mechanism is the observation that several equivalents of the oxidant are required for the reaction. This mechanism has been proposed for the oxidation of pentafluoroaniline to decafluoroazobenzene with sodium hypochlorite.[5]

Acknowledgement

Financial support by CONACyT (Grant 0762-M9109) is gratefully acknowledged.

References and Notes

1. Firouzabadi, H.; Mostafavipoor, Z. *Bull. Chem. Soc. Jpn.* **1983**, 56, 914-917.
2. Birchall, J. M.; Haszeldine, R. N.; Kemp, J. E. G. *J. Chem. Soc.* C. **1970**, 449-455.
3. Burdon, J.; Morton, C. J.; Thomas, D. F. *J. Chem. Soc.* **1965**, 2621-2627.
4. Wheeler, O. H.; Gonzalez, D. *Tetrahedron*, **1964**, 20, 189-193.
5. Deadman, J. J.; Jarman, M.; McCague, R. *J. Chem. Soc.* Perkin Trans. II, **1989**, 971-975.
6. Jarman, M.; Barrie, S. E.; Deadman, J. J.; Houghton, J.; McCague, R.; Rowlands, M. G. *J. Med. Chem.* **1990**, 33, 2452-2455.
7. Goldstein, S. L.; McNelis, E. *J. Org. Chem.* **1973**, 38, 183-185.
8. Leyva, E.; Munoz, D.; Platz, M. S. *J. Org. Chem.* **1989**, 54, 5938-5945.
9. General procedure for the oxidation. The respective fluoroaniline **1a-h** (0.01 mols) was added to a stirred ethanol/water (50/50) mixture. Then, potassium hydroxide (0.018 mols) and potassium ferricyanide (0.08 mols) were added. The resulting mixture was kept under reflux for six to eight hours. After this time, the mixture was filtered to remove the remaining oxidant and extracted with CH_2Cl_2. The organic solution 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 get the corresponding fluoroazobenzene **2a-h** as a crystalline orange solid.
10. All the fluoroazobenzenes **2a-h** were characterized by melting point,[8] IR, ^{1}H NMR, ^{19}F NMR and GC/MS. The fluorophenazines **3d**, **3f** and **3h** were characterized by melting point,[2] UV, IR, ^{1}H NMR and ^{19}F NMR.
11. The melting points were recorded on a Melt Temp Sybron/Thermoline apparatus. The IR spectra were recorded on a Nicolet 205 FTIR. The UV spectra were recorded on a Shimadzu UV-160. All ^{1}H NMR and ^{19}F NMR spectra were recorded on a Bruker AC 200 (200 MHz) spectrometer. The GC/MS analyses were done a Hewlett Packard 5971 with a quadrupole MS detector Hewlett Packard 5972.

(*Received in USA* 13 *August* 1997; *revised* 9 *September* 1997; *accepted* 10 *September* 1997)