

Iodination of Aniline Using Thallium(III)-trifluoroacetate and Potassium Iodide

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A new procedure for a specific micro-synthesis of *p*-iodo-aniline has been developed. It consists of the reaction of aniline with thallium(III)-trifluoroacetate followed by the iodination with aqueous potassium iodide.

Electrophilic aromatic thallation followed by addition of aqueous potassium iodide is a simple and effective way to synthesize aromatic iodo compounds [1, 2]. Although this procedure is applicable to a wide range of aromatic compounds, the reaction of aromatic amines with thallium(III)-trifluoroacetate has not been described. With unprotected amino groups *a priori* one would consider this reaction unlikely because of a possible oxidation by the thallium(III)salt or a complex formation leading to full inertness [3]. Nevertheless, we succeeded in preparing *p*-iodo-aniline from aniline *via* the direct thallation reaction without any protection of the amino group. The method presented here will be used further for a highly specific micro-synthesis of radioactively labelled p - ^{125}I -aniline, where we will work only with minute amounts of tracer.

Under the conditions described we obtained nearly exclusively *p*-iodo-aniline (see Fig. 1). *o*-Iodo-aniline and higher iodinated anilines like di-iodo-aniline were formed only in trace amounts (<1%). *m*-Iodo-aniline could not be detected. Only 5% of the aniline remained unreacted, the yield of *p*-iodo-aniline was 92–94%.

The simple procedure of thallation as described with 2 to 10 min incubation at room temperature gave the best results. A prolonged incubation time up to 24 h did not improve the thallation process. However, the reaction is highly influenced by temperature. Thallation between 0 °C and 10 °C reduces the yield of *p*-iodo-aniline drastically, most of the aniline remaining unreacted. At a thallation temperature of 50 °C oxidation reactions are strongly

enhanced, resulting in the formation of azobenzene and a variety of unidentified compounds.

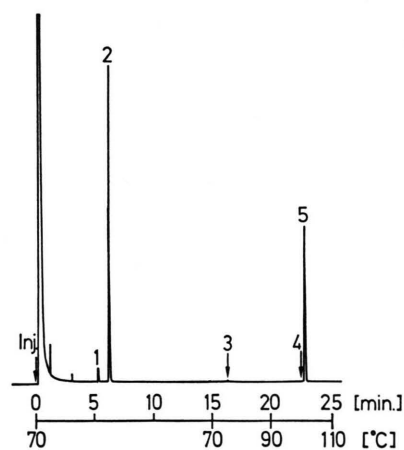


Fig. 1. Gas chromatographic analysis of a typical preparation of *p*-iodo-aniline.

Peaks: 1 aniline, 2 *o*-toluidine (internal standard), 3 *o*-iodo-aniline, 4 *m*-iodo-aniline, 5 *p*-iodo-aniline. Gas chromatographic conditions: 25 m SP-1000 glass capillary column, carrier gas N_2 (3 ml/min).

Thus we conclude that the direct thallation of aromatic amines can be specifically performed without side-reactions, provided that appropriate reaction conditions are applied.

Experimental

All thallation experiments were carried out in an atmosphere of dried argon. Gas chromatographic analyses were obtained with a model 1445 gas chromatograph (Varian) equipped with a 25 m SP-1000 glass capillary column. Injector 110 °C; column oven isothermal at 70 °C for 15 min, temperature program 70–140 °C with a heating rate of 4 °C/min; carrier gas N_2 3 ml/min; split ratio 1:10;

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detector 240 °C (flame ionization detector). Combined gas chromatography – mass spectrometry was performed with a model MAT 311-A double focusing mass spectrometer (Finnigan-MAT) coupled with a model 1445 gas chromatograph, which was fitted to the ion source of the mass spectrometer with an all-glas open split-type connection. Gas chromatographic conditions were as described above with the exception of He as the carrier gas.

p-Iodo-aniline

17 mg (0.18 mmol) aniline in 0.4 ml purified and anhydrous acetonitrile were mixed with 97.8 mg (0.18 mmol) thallium(III)-trifluoroacetate, dissolved in 0.4 ml acetonitrile, and 0.05 ml trifluoroacetic acid. The reaction mixture was stirred for 2 to 10 min at room temperature (20 to 25 °C).

According to the procedure of McKillop *et al.* [1] thallation was followed by the stepwise addition of 29.9 mg (0.18 mmol) potassium iodide in 1 ml water and 17.1 mg (0.09 mmol) sodium metabisulfite. The solution was brought to pH 11 with 0.2 ml 5 mol/l sodium hydroxide. *p*-Iodo-aniline (yield 92 to 94%) was extracted with three 1 ml portions of diethylether. Positive identification of the reaction product was by combined gas chromatography – mass spectrometry comparing both the retention time and the mass spectrum with those of an authentic sample. The yield was determined by gas chromatography using *o*-toluidine as the internal standard, which was added prior to the extraction step.

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[3] A. McKillop, personal communication.