



Iodination of Benzylanilines with Potassium Dichloroiodate

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INTRODUCTION

Iodinated organic compounds are widely used in organic synthesis as electrophilic agents for cross-coupling reactions that result in carbon-carbon and carbon-heteroatom bond formation.¹ In this context we are interested in the preparation of *ortho*-iodoaniline derivatives and we have previously made use of an aqueous solution of potassium dichloroiodate (KICl_2) for the iodination of some (hetero-) aromatic systems.²

The iodination of activated aromatic compounds (such as anilines) readily leads to a mixture of mono-, di- or even tri- iodo products. For example the reaction of *p*-toluidine with 1.1 equivalents of KICl_2 resulted in the obtention of 20% substrate, 60% mono-iodo- and 20% diiodo- *p*-toluidine. The poor selectivity and a literature precedent for mono-iodination of *N*-alkylanilines³ prompted us to investigate the iodination of *N*-benzylanilines.

RESULTS AND DISCUSSION

N-Benzylanilines (**4**) were prepared by reductive amination of *p*-substituted anilines (**1**) using NaBH_4 , Figure 1. Initially, the reaction of 2N aqueous KICl_2 with *N*-benzyl-*p*-toluidine was studied under various conditions and the respective reactions analyzed by GCMS. Some results are detailed in Table 1.

Table 1. GCMS results (relative % uncorrected peak areas) for reaction of *N*-benzyl-*p*-toluidine with KICl_2 .

†	1 Sub (%)	3 [O]Sub (%)	5 Prod (%)	6 [O]Prod (%)
a	17	2	70	11
b	22	12	63	3
c	<1	<1	93	6
d	<1	<1	98	2
e	<1	<1	97	3
f	<1	<1	96	4

† Conditions [Table entry – solvent, equiv.s NaOAc , equiv.s KICl_2 , time (mins)]: a – MeOH, 0, 1.5, 140; b – MeOH, AcOH (4:1 V/V), 2.5, 1.2, 100; c – MeOH, AcOH, EtOAc (5:1:4 V/V/V), 3.7, 1.5, 100; d(e,f) = c, time = 5 min; e 15 min; f 25 min.

The experiments identified a tri-solvent system in the presence of NaOAc as a potentially effective combination for the rapid mono-iodination of **4**

with partial success (Table 2). Oxidative debenzilation of the substrate, or product, was identified as the principle side reaction resulting in some low yields of **5** (Table 2).

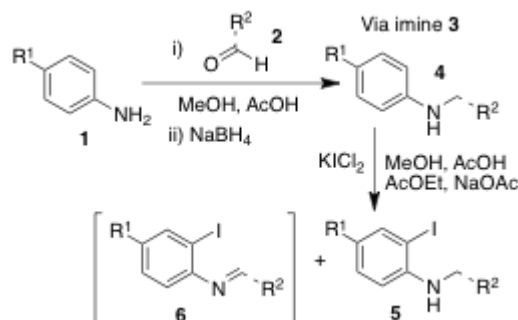


Figure 1. General reaction scheme: reductive amination followed by iodination with aqueous KICl_2 .

Table 2. Purified product yields for the iodination of *N*-benzylanilines.

R ¹	R ²	Yield (%)	R ¹	R ²	Yield (%)
Br		36	Br		47
Cl		48	Cl		30
F		28	Me		43
Me		75	Cl		35

CONCLUSION

The chemoselective iodination of *N*-benzylanilines is potentially an interesting reaction for the obtention of substrates for application in cross-coupling reactions. The use of aqueous KICl_2 in a tri-solvent system has allowed the synthesis of a number of mono-iodinated *N*-benzylaniline derivatives in moderate to good yields.

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