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Ag^+ mediated deaminations of *N*-Boc aryl hydrazines for the efficient synthesis of *N*-Boc aryl amines

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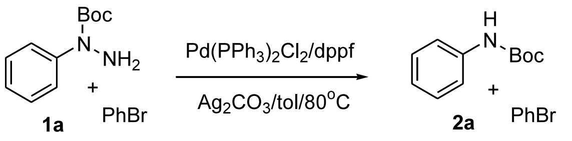
Abstract—N-Boc-aryl hydrazines were converted into *N*-Boc-aryl amines under the action of Ag^+. Its mild reaction conditions tolerate the presence of a variety of functional groups. © 2002 Elsevier Science Ltd. All rights reserved.

During the study involving Pd-catalyzed coupling reactions of hydrazides with aryl halides, we have found that the attempted coupling reaction of *N*-Boc phenyl hydrazine (**1a**) with PhBr provided *N*-Boc-aniline (**2a**) and recovered PhBr under the catalytic conditions comprised of $Pd(PPh_3)_2Cl_2$/dppf and Ag_2CO_3 in toluene (Scheme 1).



Scheme 1.

Also found was that the deamination reaction proceeded without Pd catalyst, but not without Ag_2CO_3.

There are few methods available in the literature for the deamination of hydrazides, which includes Leblanc's condition[1] using Zn metal with acetic acid. In most cases, the hydrazides were converted into hydrazines, prior to the metal catalyzed hydrogenolytic N–N bond cleavage to the corresponding amines.[2] A thorough literature search revealed no examples related to our Ag^+ mediated deamination reactions of aryl hydrazides.

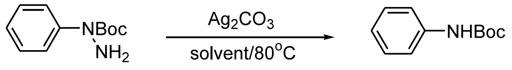
Prompted by the novelty and mild reaction conditions of our deamination method, we studied its scope and limitation in detail. Herein, we wish to present our new deamination reaction of Boc-aryl hydrazides mediated by Ag^{+1}.[3]

A set of experiments using different salts (Na_2CO_3, K_2CO_3, Cs_2CO_3) confirmed that the reaction was indeed mediated by Ag^{+1} (data not shown). The reaction did not go to completion even after 24 h, when the reaction was run with less than 1.0 equiv. of Ag_2CO_3 (2.0 equiv. for Ag^+). Thus, 1.1 equiv. of Ag_2CO_3 was used for the next deamination experiments.

The deamination reaction proceeded quite smoothly in most organic solvents under anhydrous conditions. Both reaction rates and chemical yields dropped rather significantly when the reactions were carried out in wet solvent. DME is slightly better than any other solvents in terms of isolated product yields (Table 1). The reaction rate appeared to be roughly proportional to the solvent polarity.

With DME as an optimal solvent, we investigated the effect of counter ions by using different silver salts. We

Table 1. Deamination with Ag_2CO_3 in various solvents



Entry	Solvent	Time (h)	Yield (%)
1	Benzene	3	83
2	Toluene	3	92
3	THF	3.5	83
4	CH_2Cl_2	1	82
5	DME	1	95
6	EtOAc	6.5	67
7	MeCN	2.5	78
8	DMF	0.5	72
9	MeOH	1	64
10	DMSO	0.5	68

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Table 2. Deamination with other silver salts

Entry[a]	Salt[b]	Time (h)	Yield (%)
1	Ag_2CO_3	1	95
2	Ag_2O	1.5	78
3	AgOAc	1.5	87
4	$AgIO_3$	48	0
5	$AgNO_3$	5	73
6	Ag_2SO_4	5	Trace
7	AgOTf	5	Trace
8	$AgClO_4$	16	26
9	Ag_3PO_4	5	Trace

[a] The reaction was conducted with *N*-Boc phenyl hydrazine in DME at 80°C.

[b] 1.1 equiv. of the salt was used in all reactions.

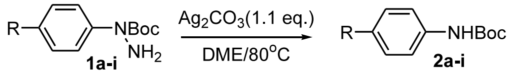
used 1.1 equiv. of silver salts, which is based on the reagent, not on Ag^+. Thus, the actual equivalency of Ag^+ varies with the type of silver salts (Table 2).

As seen, the reaction is highly dependent on the nature of the counter ion; while Ag_2CO_3 is better than any other salts in terms of isolated yields, virtually no reaction was observed with $AgIO_3$, Ag_2SO_4, AgOTf and $AgClO_4$. Basicity (or nucleophilicity) of the counter ion may be an important factor in the reaction. In fact, we observed smooth deamination reactions with the silver salts exhibited little activity (entries 4, 6, 7, 8 and 9), when the reactions were carried out in the presence of added NaOH. However, successful deamination with $AgNO_3$ carrying weak base (entry 5) does not fall into our basicity hypothesis. Also notable is that 1.1 equiv. of AgOAc gave a similar result to 1.1 equiv. of Ag_2CO_3 (2.2 equiv. for Ag^+).

For experimental consistency, we continued to use Ag_2CO_3 for the deaminations of aryl hydrazides bearing various functional groups to furnish the products **2b–i** (Table 3).

As a general trend, aryl hydrazides with electron donating groups underwent faster deamination reactions than those with electron withdrawing groups.

Table 3. Deaminations with other hydrazides

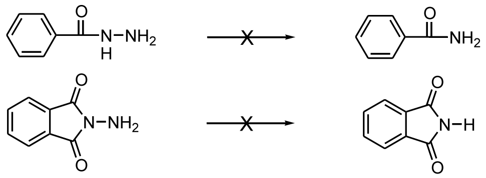


Entry	R	Time (h)	Yield (%)
1	H	1	95
2	Me	1	88
3	NO_2	48	64
4	MeO	1.5	88
5	CN	3	76
6	CO_2Me	72	70
7	COMe	2.5	74
8	Ph	1	87
9	^{t}Bu	1	83

The starting *N*-Boc aryl hydrazines were prepared from the coupling reactions of the corresponding aryl halides with Boc hydrazine (Boc-$NHNH_2$) according to the literature method.[4]

N-Boc hydrazines with aryl substituents at N′ position did not undergo deamination reactions. No deaminated products were obtained from the compounds bearing usual N–N single bond, for example, phenyl hydrazine.

Neither *N*-aminophthalimide nor benzoic hydrazide gave the desired deamination products (Scheme 2).



Scheme 2. Attempted deaminations of other systems.

In summary, we have found that *N*-Boc aryl hydrazines undergo facile deamination reactions in the presence of Ag_2CO_3 or other silver salts to give rise to the corresponding *N*-Boc aryl amines in good to excellent isolated yields. Its mild reaction conditions tolerate the presence of a variety of functional groups. Further work is needed to elucidate its reaction mechanism.

Acknowledgements

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3. Representative procedure: A mixture of *N*-Boc phenyl hydrazine (**1a**, 50 mg, 0.24 mmol), 1.1 equiv. of Ag_2CO_3 (73 mg, 0.26 mmol) in 2 mL of anhydrous DME was heated at 80°C for 1 h. Upon cooling to rt, the reaction mixture was partitioned into CH_2Cl_2 and H_2O. The separated organic layer was dried over $MgSO_4$, concentrated in vacuo and column chromatographed (hexanes/EtOAc: 15/1) to give 44 mg of *N*-Boc phenylamine **2a** as a white solid in 95% yield.
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