Tetrahedron Letters 52 (2011) 4324–4326

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A novel method for tosyloxylation of anilides using phenyliodine bistrifluoroacetate (PIFA)

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ARTICLE INFO

Article history:
Received 16 March 2011
Revised 5 June 2011
Accepted 10 June 2011
Available online 17 June 2011

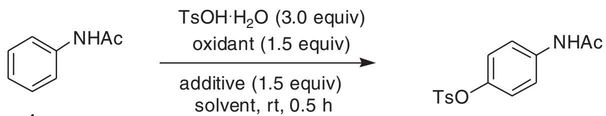
ABSTRACT

The direct tosyloxylation of anilides was described in this Letter. In the presence of phenyliodine bis(trifluoroacetate) (PIFA) and $BF_3 \cdot Et_2O$, the reaction of anilides with TsOH provided *para*-tosyloxylated products with high regioselectivity under mild conditions.

Over the past two decades, hypervalent iodine compounds have been the focus of great attention in organic synthesis due to their unique features as mild, environmentally friendly and selective oxidizing properties.[1] Many new applications of hypervalent iodine compounds in the formation of C–O[2], C–N[3] and C–C[4] bonds have been developed. Among them [hydroxyl(tosyloxy)iodo]benzene (PhI(OH)(OTs), Koser's reagent) mediated tosyloxylation is one of the attractive processes.[5] Tosyloxylation of ketone with PhI(OH)(OTs) provided α-tosyloxyketones, which are valuable intermediates to synthesize heterocyclic compounds.[6] Despite numerous studies of oxidation of ketone with PhI(OH)(OTs), comparably, little has been known about the tosyloxylation of aromatics with hypervalent iodine compounds. In 2006, Koser et al. found that oxidative substitution of polycyclic aromatic hydrocarbons with PhI(OH)(OTs) provided the corresponding sulfonates in moderate yields.[7] Recently Parakash and coworkers reported a tosyloxylation of substituted phenols with PhI(OH)(OTs).[8] It was founded that *ortho*-substituted phenol could be tosyloxylated at *para*-position of phenol using PhI(OH)(OTs) as an oxidant. However, for this reaction is required an electron withdrawing substituent at the *ortho* position of phenol. In our recent studies, we found that oxidation of anilides with phenyliodine(III) bis(trifluoroacetate) (PIFA) in the presence of AcOH or alcohols provided the *para*-oxygenated products.[9] In continuation of our interest in hypervalent iodine chemistry, we herein report a novel tosyloxylation of anilide using phenyliodine(III) bis(trifluoroacetate) (PIFA) with toluenesulfonic acid (TsOH) to provide aryl tosylate, an important structure motif in coupling reactions[10] and medicinal chemistry.[11]

Acetanilide (**1a**) was employed as the substrate for optimizing reaction conditions and the results are outlined in Table 1. Initially PhI(OH)(OTs) was chosen as a tosyloxylating reagent, treatment of **1a** with 1.5 equiv of PhI(OH)(OTs) in CH_3CN afforded only 12% of *para*-tosyloxylated product **2a** (entry 1). Interestingly, adding 3.0 equiv of $TsOH \cdot H_2O$ in the reaction improved the yield of **2a** to 35% (entry 2). Thus, we investigated the use of other hypervalent iodine compounds as the oxidant and TsOH as a nucleophile. When the combination of phenyliodine(III) diacetate (PIDA) and $TsOH \cdot H_2O$ was employed, the reaction gave product **2a** in 36% yield (entry 4). When more reactive PIFA was used, the reaction proceeded efficiently to give **2a** in 61% yield (entry 6). Using $BF_3 \cdot OEt_2$ as a Lewis acid accelerated the reaction and dramatically improved the yield of **2a** (entry 7). After careful optimization of reaction conditions (solvent and temperature), the best result was achieved when the reaction was carried out in the presence of 1.5 equiv of PIFA and 1.5 equiv of $BF_3 \cdot OEt_2$ with 3.0 equiv of $TsOH \cdot H_2O$ in CH_3CN at room temperature for 0.5 h.

Table 1
Optimization of reaction conditions[a]



1a **2a**

Entry	Oxidant	Additive	Solvent	Yield[b] (%)
1	PhI(OH)OTs	None	CH_3CN	12[c]
2	$PhI(OH)OT_s$	None	CH_3CN	35
3	$PhI(OH)OT_s$	$BF_3 \cdot OEt_2$	CH_3CN	51
4	PIDA	None	CH_3CN	36
5	PIDA	$BF_3 \cdot OEt_2$	CH_3CN	45
6	PIFA	None	CH_3CN	61
7	PIFA	$BF_3 \cdot OEt_2$	CH_3CN	93
8	PIFA	$BF_3 \cdot OEt_2$	CF_3CH_2OH	<5
9	PIFA	$BF_3 \cdot OEt_2$	CH_2Cl_2	<5

[a] Unless otherwise specified, all the reactions were carried out in the presence of 0.2 mmol of **1a**, 0.6 mmol of $TsOH \cdot H_2O$, 0.3 mmol of oxidant and 0.3 mmol of additive in 1 mL of solvent at room temperature for 0.5 h.
[b] Isolated yield after column chromatography.
[c] 0.3 mmol of PhI(OH)OTs was used, no $TsOH \cdot H_2O$ was employed.

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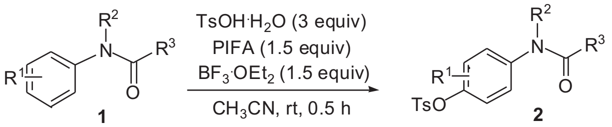
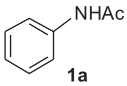
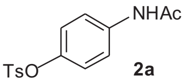
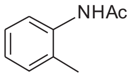
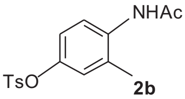
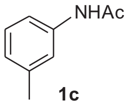
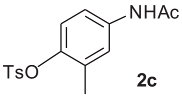
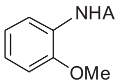
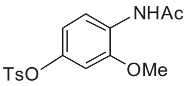
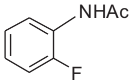
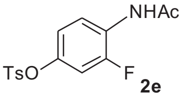
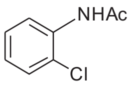
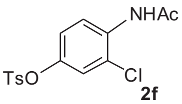
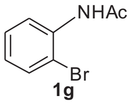
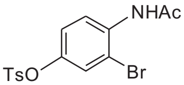
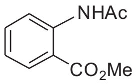
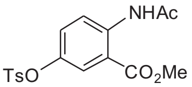
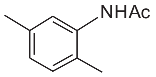
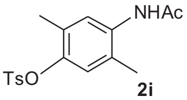
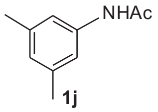
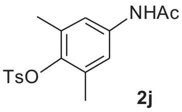
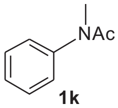
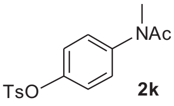
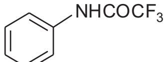
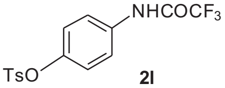
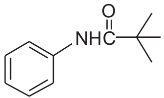
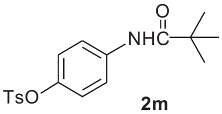
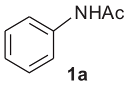
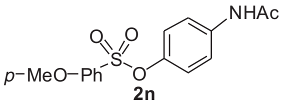
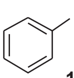
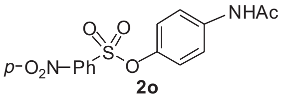
doi:10.1016/j.tetlet.2011.06.041

Table 2
Direct sulfonyloxylation of anilides with PIFA[a]



Entry	Substrate	Product	Yield[b]
1	 **1a**	 **2a**	93
2	 **1b**	 **2b**	97
3	 **1c**	 **2c**	85
4	 **1d**	 **2d**	92
5	 **1e**	 **2e**	56[c]
6	 **1f**	 **2f**	36(68)[d]
7	 **1g**	 **2g**	27(56)[d]
8	 **1h**	 **2h**	16
9	 **1i**	 **2i**	92
10	 **1j**	 **2j**	88
11	 **1k**	 **2k**	65[c]
12	 **1l**	 **2l**	44[e]
13	 **1m**	 **2m**	39
14	 **1a**	 **2n**	66[f]
15	 **1a**	 **2o**	62[g]

[a] Unless otherwise specified, all the reactions were carried out in the presence of 0.2 mmol of **1**, 0.6 mmol of $TsOH{\cdot}H_2O$, 0.3 mmol of PIFA and 0.3 mmol of $BF_3{\cdot}OEt_2$ in 1 mL of CH_3CN at room temperature for 0.5 h.

[b] Isolated yield after column chromatography.

[c] The reaction was carried out at 50 °C.

[d] The yield in parenthesis based on the recovered starting materials.

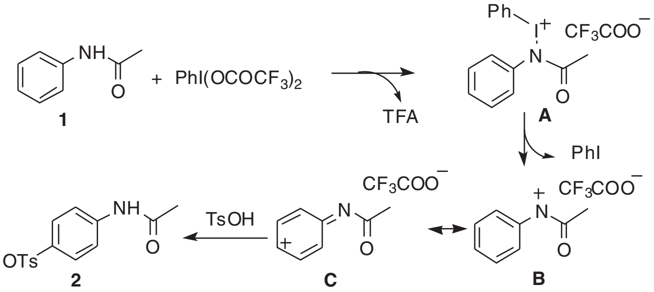
[e] 0.3 mmol of PhI(OH)(OTs) was used instead of PIFA.

[f] *p*-methoxybenzenesulfonic acid was used instead of TsOH.

[g] *p*-nitrobenzenesulfonic acid was used instead of TsOH.

With an optimized reaction condition in hand, we started an investigation of substrate scope and results are summarized in Table 2. In the presence of 1.5 equiv of PIFA and 1.5 equiv of $BF_3{\cdot}OEt_2$, the reactions of anilides with $TsOH{\cdot}H_2O$ provided the corresponding *para*-tosyloxylated products in 16–97% yields. These reactions are tolerant to a variety of functional groups, such as alkyl, methoxyl, fluoride, chloride, bromide, ester groups (entries 2–10). Generally the electron donating substitute at the anilide facilitates the reaction. For example, tosyloxylation of 2-methoxyanilide (**1d**) with TsOH and PIFA provided the corresponding product **2d** in excellent yield (entry 4). In contrast, when an electron withdrawing group, such as an ester group, was introduced at the *ortho* position of anilide, the reaction gave only 16% *para*-tosyloxylated product **2h** with most of starting materials recovered (entry 8). Prolonged reaction time and higher temperature were not effective in this transformation. Next we examined the substitution effect on the acetamino group. Tosyloxylation of *N*-methylacetanilide (**1k**) proceeded well to give **2k** in 65% yield at 50 °C for 0.5 h (entry 11). Notably, the reaction of the electron-deficient trifluoroacetanilide (**1l**) with PIFA and TsOH provided only the trace amount of tosyloxylated product **2l**. When PhI(OH)(OTs) was used as the oxidant instead of PIFA, the reaction gave **2l** in 44% yield (entry 12). When R^3 of anilide is substituted with the bulky *t*-butyl group, the reaction provided the *para*-tosyloxylated product **2m** in 39% yield probably due to steric effect (entry 13). Finally, other sulfonyloxylations were also explored. Both electron-rich and electron-deficient sulfonic acids are good substrates in this transformation. The reaction of **1a** with *p*-methoxybenzenesulfonic acid or *p*-nitrobenzenesulfonic acid afforded the desired product **2n** or **2o** in 66% and 62% yield, respectively (entries 14 and 15).

A possible mechanism of PIFA-induced tosyloxylation of anilides is proposed in Scheme 1. The mechanism of this reaction proceeds through the electrophilic substitution pathway, similar to the previously postulated for the acetoxylation of anilides by PIFA.



Scheme 1. Proposed mechanism for the tosyloxylation of anilides.

First, a nucleophilic attack of PIFA with anilide **1** forms the iodonium intermediate **A**, followed by cleavage of N–I bond to furnish iodobenzene and a nitrenium ion **B**, which is stabilized by the charge delocalization on the phenyl ring. The charge extensively delocalized intermediate **C** is highly preferred and trapped with TsOH to give the *para*-substituted products **2**.

In summary, we have developed a novel method for the direct tosyloxylation of anilides. Using PIFA as an oxidant, the reactions of anilides with TsOH provided *para*-tosyloxylated anilides with high regioselectivity in good yields. Further work on hypervalent iodine compound-mediated oxidation of other aromatic compounds is underway in our laboratory.

Acknowledgments

We gratefully acknowledge the National Natural Science Foundation of China (No. 21072180) and National Basic Research Program of China (2006CB922001) for financial support.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.06.041.

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