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**Authors:** Andreas Boelke and Boris Johannes Nachtsheim

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# Evolution of *N*-Heterocycle-substituted Iodoarenes (NHIA) to efficient Organocatalysts in Iodine(I/III)-mediated Oxidative Transformations

Andreas Boelke<sup>a</sup> and Boris J. Nachtsheim<sup>a,\*</sup><sup>a</sup>Address: Institute for Organic and Analytical Chemistry, University of Bremen, 28359 Bremen, Germany

Prof. Dr. Boris J. Nachtsheim, Phone: +49 421 218-63113; E-mail: nachtsheim@uni-bremen.de

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**Abstract.** The reactivity of *ortho*-functionalized *N*-heterocycle-substituted iodoarenes (NHIA) as organocatalysts in iodine(I/III)-mediated oxidations was systematically investigated in the  $\alpha$ -tosyloxylation of ketones as the model reaction. During a systematic catalyst evolution, it was found that NH-triazoles and benzoxazoles have the most significant positive influence on the reactivity of the central iodine atom. A further catalyst improvement which focused on the substitution pattern of the arene revealed a remarkable *ortho*-effect. By introduction of an *o*-OMe group we were able to generate a novel NHIA with a so far unseen

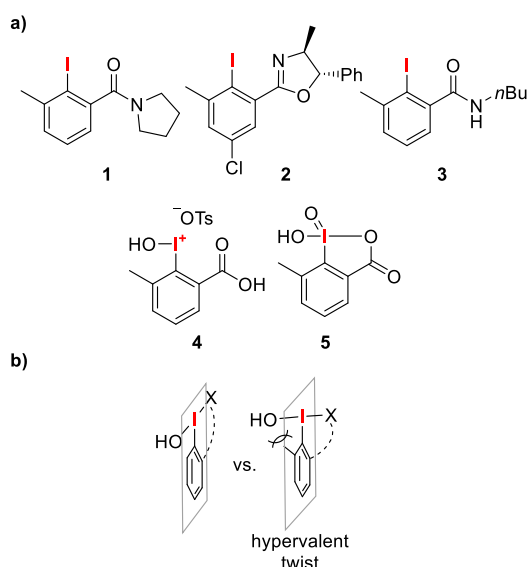
catalytic efficiency. This new catalyst is not only easy to synthesize but also enabled the  $\alpha$ -tosyloxylation of carbonyl compounds at the lowest reported catalyst loading of only 1 mol%. Finally, the performance of this iodine(I) catalyst was successfully demonstrated in intramolecular oxidative couplings of biphenyls and oxidative rearrangements.

**Keywords:** homogeneous catalysis; hypervalent iodine; *N*-heterocycles; organocatalysis; oxidative transformations

## Introduction

Over recent decades, hypervalent iodine compounds gained widespread attention as versatile and environmental benign reagents in organic synthesis. In particular aryl- $\lambda^3$ -iodanes were utilized in a plethora of oxidative transformations, including group transfer reactions, dearomatizations, cyclizations and rearrangements. They can either be applied as stoichiometric oxidants or in catalytic amounts when combined with a terminal co-oxidant.<sup>[1-17]</sup> The latter approach, in which only catalytic amounts of a iodine(I) pre-catalyst are needed, is in general more desirable in terms of sustainability and atom economy.<sup>[18-20]</sup> Therefore, recent years witnessed a fast growing field of aryl iodides exclusively designed for these catalytic applications. Many of which obtain one or two tethered Lewis basic units. Through direct dative interactions with the oxidized iodine(III) center these units are able to enhance the reactivity of the *in situ* generated hypervalent iodine species. When embedded into a chiral scaffold, they are also crucial to induce chirality in enantioselective oxidative couplings.<sup>[21-23]</sup>

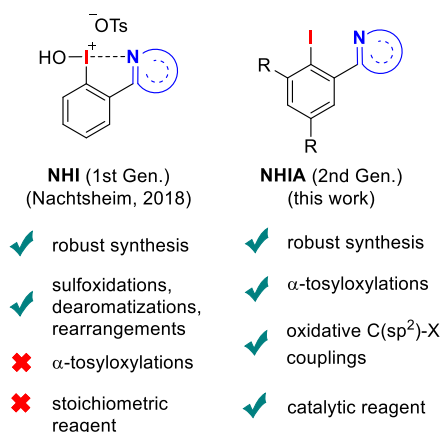
In 2012, Legault and co-workers observed that catalysts which exhibit a strong dative bond between the Lewis basic moiety and the hypervalent iodine center were inefficient in the  $\alpha$ -tosyloxylation of carbonyl compounds.<sup>[24]</sup> However, their reactivity could be greatly enhanced by the introduction of steric demand *ortho* to the iodine center, as proved for amide **1** (Figure 1 - a). In the oxidized state this methyl group leads to an out-of-plane distortion of both the amide unit and the I-OH bond which subsequently decreases the overall stability of the iodine(III) intermediate (Figure 1 - b). This dramatically enhances reactivity by accelerating further ligand exchange processes and favoring the final reductive collapse of the iodine(III) into its monovalent iodine(I) state within the final oxidative coupling step. Based on this so-called “hypervalent twist”, chiral iodoarene pre-catalysts were designed employing an *ortho*-oxazoline moiety, with the *p*-chloro derivative **2** being the most efficient.<sup>[25,26]</sup> A similar reactivity enhancing effect was observed for the *o*-Me-substituted iodoarene catalyst **3** by Whitehead and co-workers.<sup>[27]</sup> Furthermore, this was also observed for aryl- $\lambda^3$ -iodanes such as for pseudocyclic benziodoxole tosylates **4** introduced by Zhdankin and co-workers.<sup>[28]</sup>



**Figure 1.** a) *o*-Methyl substituted iodoarenes and aryl- $\lambda^3$ -iodanes based on amides, carboxylic acids and *N*-heterocycles. b) “hypervalent twist”.

However, originally, the “hypervalent twist” was proposed in an early work by Goddard and co-workers for  $\lambda^5$ -iodanes, as being the structural rationale for the enhanced reactivity of 2-iodoxybenzoic acid **5** in alcohol oxidations.<sup>[29]</sup> This was experimentally further confirmed by Moorthy and co-workers.<sup>[30,31]</sup>

Very recently, Muñiz, Postnikov as well as our group systematically investigated *N*-heterocycle-stabilized  $\lambda^3$ -iodanes (NHIs, Figure 2).<sup>[32–35]</sup> These (pseudo)cyclic aryl- $\lambda^3$ -iodanes can be readily synthesized on a gram scale through robust heterocycle chemistry allowing a fast variation of the *N*-heterocyclic ligand. We could show that the *N*-heterocycle has a significant effect on the



**Figure 2.** Chemical structures of “first generation” *N*-heterocyclic stabilized  $\lambda^3$ -iodanes (NHIs) and *N*-heterocyclic substituted iodoarenes (NHIA) as improved “second generation” catalysts employing the concept of the hypervalent twist.

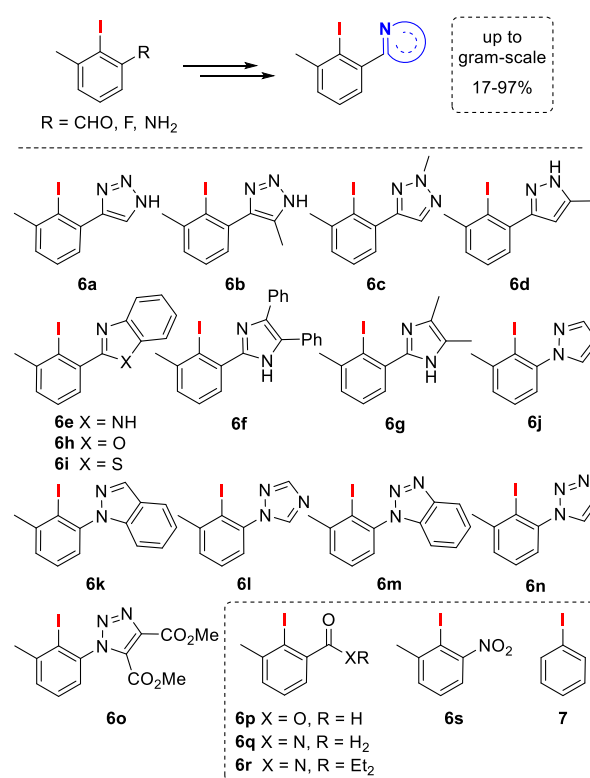
reactivity of the hypervalent iodine center in the oxygenation of thioanisole. In particular, triazole-

substituted iodoarenes exhibited a high efficiency, not only in sulfoxidations, but also in oxidative dearomatization and rearrangements. However, in initial studies we found that these “first-generation” reagents proved to be inefficient in  $\alpha$ -oxygenations of enolizable ketones both under stoichiometric as well as under catalytic conditions.

Herein, we want to report the systematic improvement of these initially reported “first-generation” heterocycle-stabilized iodoarenes based on the concept of the “hypervalent twist”. Through rational variation of the stabilizing *N*-heterocycle and the substituent of the iodoarene in *ortho*-position *N*-heterocycle-substituted iodoarenes (NHIA) were generated that can be applied as efficient organocatalysts in combination with terminal co-oxidants in a variety of oxidative transformations.

## Results and Discussion

Starting from the corresponding aryl aldehyde, fluoro or aniline derivative a variety of different *o*-Me-substituted iodoarenes **6a–o** were synthesized (Figure 3, for further synthetic details see ESI).



**Figure 3.** Investigated *o*-Me-*N*-heterocyclic-, acid-, amide- or nitro-stabilized iodoarenes **6a–s** and iodobenzene (**7**).

Throughout the studies NHIA will be compared with *O*-stabilized iodoarenes **6p–s** as well as with iodobenzene (**7**) as reference catalysts (Table 1). Reactivity of all shown iodoarenes was systematically investigated in the catalytic  $\alpha$ -tosyloxylation of propiophenone (**8a**) as the model reaction. This reaction was chosen since previously prepared *ortho*-

unsubstituted NHIs could not be applied in this reaction giving the desired products only in trace amounts.

**Table 1.** *α*-Tosyloxylation of propiophenone (**8a**) with *o*-Me substituted catalysts **6a-s** in comparison with iodobenzene (**7**).

entry <sup>a</sup>	iodine(I)	yield [%] <sup>b</sup>	
		rt	50 °C
1	<b>7</b>	66	78
2	<b>6a</b>	64	71
3	<b>6b</b>	57	79
4	<b>6c</b>	73	81
5	<b>6d</b>	2	3
6	<b>6e</b>	58	80
7	<b>6f</b>	53	78
8	<b>6g</b>	48	80
9	<b>6h</b>	55	75
10	<b>6i</b>	5	27
11	<b>6j</b>	41	50
12	<b>6k</b>	29	26
13	<b>6l</b>	10	41
14	<b>6m</b>	6	23
15	<b>6n</b>	2	8
16	<b>6o</b>	6	23
17	<b>6p</b>	42	60
18	<b>6q</b>	35	72
19	<b>6r</b>	43	50
20	<b>6s</b>	8	28

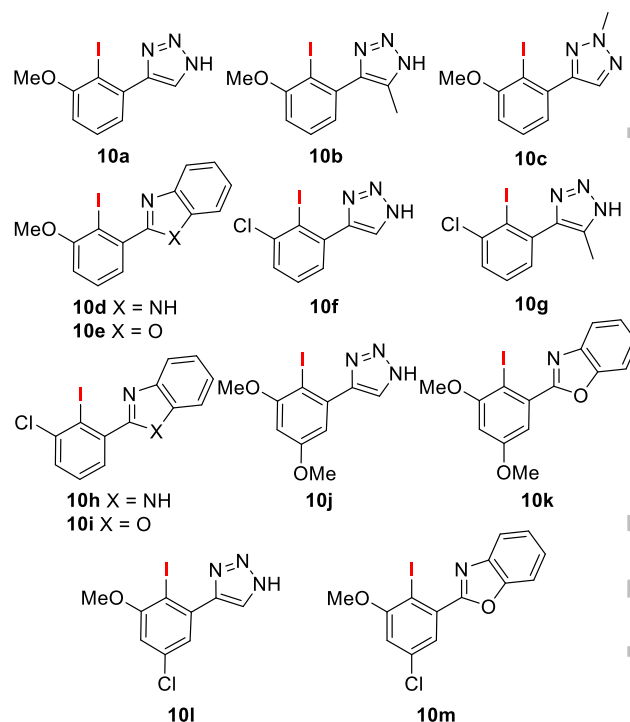
<sup>a</sup>Reaction conditions: To a stirred solution of *m*CPBA (2 equiv) and TsOH·H<sub>2</sub>O (2 equiv) in MeCN (0.1 M) was added the catalyst (10 mol%) followed by propiophenone (**8a**, 0.1 mmol) and the mixture was stirred at rt or 50 °C for 24 h. <sup>b</sup>Yields were determined by <sup>1</sup>H-NMR with anisole as the internal standard.

As expected, iodobenzene (**7**) showed a high reactivity giving 66% yield of the desired product **9a** at room temperature and 78% yield at 50 °C (entry 1). The triazoles **6a** and **6b** showed similar final yields (entries 2-3). Higher reactivity was observed for the 2*H*-Me-triazole catalyst **6c**, which gave the highest yield both at room temperature (73%) and at 50 °C (81%, entry 4). The pyrazole **6d** was completely unreactive (entry 5). Imidazoles **6e-g** as well as the benzoxazole **6h** showed a reactivity comparable to the triazoles **6a** and **6b** (entries 6-9), whereas the benzothiazole **6i** proved to be inefficient (entry 10). As an initial finding we can conclude that all *N*-aryl bound heterocycles **6j-o** (entries 11-16) gave only low yields in the tosyloxylation, even though the corresponding (hydroxy)iodoarenes showed a high

reactivity in the previously investigated oxidation of thioanisole.<sup>[33]</sup>

In comparison with the most efficient *o*-Me-NHIAs **6a-c** and **6e-h** all *O*-stabilized iodoarenes **6p-s** showed lower yields and a slower conversion, with amide **6q** as the only catalyst to give the desired product **9a** in more than 70% yield after 24 h at 50 °C (entries 17-20).

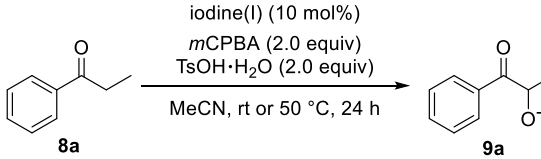
After determining triazoles, benzimidazoles and benzoxazoles as the most beneficial stabilizing heterocycles, the influence of the “twisting” *ortho*-functionality was further investigated. For this purpose, different methoxy- and chloro-substituted iodoarenes **10a-10m** were synthesized (Figure 4).



**Figure 4.** Investigated *o*-OMe and *o*-Cl-substituted iodoarenes **10a-m**.

With the introduction of a more electron-donating methoxy group in *ortho*-position to the iodine center an increasing reactivity was observed for all NHIs **10a-e**, except for the 2*H*-methyl triazole **10c** (Table 2, entries 1-5). In particular, triazole **10a** showed promising results, as this catalyst gave the highest yields for all tested iodoarenes with 75% at room temperature and 88% at 50 °C (entry 1).

Substituting the methoxy group to an electron withdrawing chloro substituent resulted in a diminished performance for all tested derivatives **10f-i** (entries 6-9), clearly demonstrating the superiority of the electron donating OMe-functionality. The introduction of another methoxy group *para* to the iodine, however, drastically lowered yields to ≤50% for both triazole- (**10j**) and the benzoxazole-substituted NHIs (**10k**) (entries 10-11). Another *p*-Cl substituent (**10l-m**) had a minor negative influence on catalyst performance (entries 12-13).

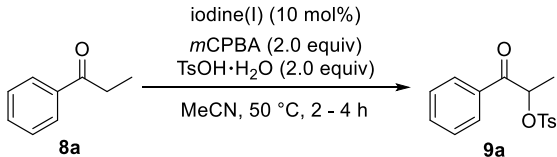
**Table 2.**  $\alpha$ -Tosyloxylation of propiophenone (**8a**) with *o*-OMe- and *o*-Cl-substituted catalysts **10a-m**.


entry <sup>a</sup>	iodine(I)	yield [%] <sup>b</sup>	
		rt	50 °C
1	<b>10a</b>	75	88
2	<b>10b</b>	69	83
3	<b>10c</b>	73	79
4	<b>10d</b>	70	83
5	<b>10e</b>	71	82
6	<b>10f</b>	49	75
7	<b>10g</b>	46	77
8	<b>10h</b>	38	75
9	<b>10i</b>	17	45
10	<b>10j</b>	22	41
11	<b>10k</b>	44	50
12	<b>10l</b>	73	77
13	<b>10m</b>	69	81

<sup>a</sup>Reaction conditions: To a stirred solution of *m*CPBA (2 equiv) and TsOH·H<sub>2</sub>O (2 equiv) in MeCN (0.1 M) was added the catalyst (10 mol%) followed by propiophenone (**8a**, 0.1 mmol) and the mixture was stirred at rt or 50 °C for 24 h. <sup>b</sup>Yields were determined by <sup>1</sup>H-NMR with anisole as the internal standard.

To further distinguish differences in catalyst reactivity, additional measurements after 2 h and 4 h at 50 °C were conducted (Table 3). Following the initial performance tests with yields determined after 24 h, triazole **10a** showed a high reactivity outperforming iodobenzene (**7**) after both 2 h and 4 h (entries 1-2), while triazoles **10b-c** and benzimidazole **10d** gave slightly diminished results (entries 3-5). In contrast, benzoxazole **10e** proved to be highly efficient as the only catalyst to give >70% yield after only 2 h reaction time (entry 6). Finally, the reactivity of the *p*-Cl-derivatives **10l-m** was slightly reduced compared to the *p*-unsubstituted NHIA **10a** and **10e** (entries 7-8).

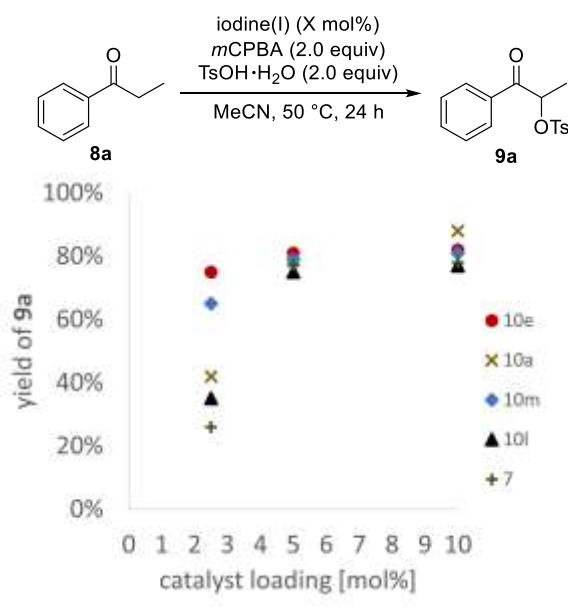
One of the major disadvantages of aryl iodide-catalyzed oxidative couplings, in particular compared to transition metal-mediated reactions, is the general necessity of high catalyst loadings (usually 10-20 mol%). Intrigued by the excellent reactivity of the *ortho*-substituted NHIA **10a** and **10e** in the  $\alpha$ -tosyloxylation we wanted to further investigate their performance under significantly lower catalyst loadings. During these investigations, the *p*-chloro-substituted derivatives **10l-m** were also further

**Table 3.**  $\alpha$ -Tosyloxylation of propiophenone (**8a**) with yields determined after 2 h and 4 h at 50 °C.


entry <sup>a</sup>	Iodine(I)	yield [%] <sup>b</sup>	
		2 h	4 h
1	<b>7</b>	64	78
2	<b>10a</b>	69	81
3	<b>10b</b>	65	77
4	<b>10c</b>	62	76
5	<b>10d</b>	63	78
6	<b>10e</b>	72	79
7	<b>10l</b>	66	75
8	<b>10m</b>	64	77

<sup>a</sup>Reaction conditions: To a stirred solution of *m*CPBA (2 equiv) and TsOH·H<sub>2</sub>O (2 equiv) in MeCN (0.1 M) was added the catalyst (10 mol%) followed by propiophenone (**8a**, 0.1 mmol) and the mixture was stirred at 50 °C for 2 h or 4 h. <sup>b</sup>Yields were determined by <sup>1</sup>H-NMR with anisole as the internal standard.

investigated due to their potentially higher stability towards undesired catalysts oxidations (Figure 5). Reduction of the catalyst loading from 10 to 5 mol% resulted in only slightly lowered yields for all catalysts, even iodobenzene, to give product **9a** in 75-81% yield.

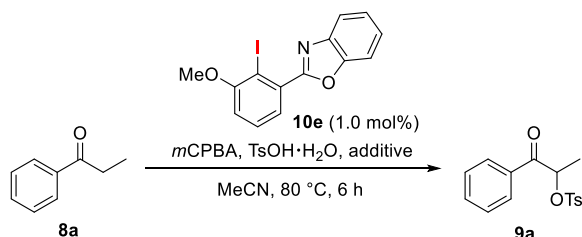
**Figure 5.** Correlation between catalyst loading and yield of **9a** in the  $\alpha$ -tosyloxylation of propiophenone (**8a**) with NHIA catalysts **10a**, **10e**, **10l-m** and iodobenzene (**7**) as reference. Yields were determined by <sup>1</sup>H-NMR spectroscopy with anisole as the internal standard.

However, further lowering the catalyst loading to 2.5 mol% proved to have a dramatic impact on catalyst reactivities. The yield using iodobenzene (**7**) dropped

from 77% to 26% and using triazole **10a** to 42%. Contrary to this finding, benzoxazole **10e** still showed a robust performance yielding **9a** in 75% yield. In comparison, both *p*-chloro derivatives **10l-m** rendered a significantly diminished reactivity.

Following these promising results, we wanted to investigate if **10e** can show turnover numbers comparable to typical transition metal catalyzed reactions. With only 1 mol% of **10e** as catalyst the yield of **9a** dropped to 32% (Table 4, entry 1). As the major side reaction Baeyer-Villiger oxidation of **8a** was observed. An overall increase of the reaction rate by increasing reaction temperature and a general adjustment of the pH by using less TsOH or mixtures of free TsOH and the corresponding alkali metal tosylates should prevent this undesired oxidative insertion. Indeed, keeping the catalyst loading constant at 1 mol%, but increasing the reaction temperature to 80 °C followed by subsequent reduction of the amount of TsOH to 1 equivalent raised the yield of **9a** to 57% (Table 4, entries 2-4).

**Table 4.** Optimization of the  $\alpha$ -tosyloxylation of propiophenone (**8a**) with 1 mol% NHIA **10e**.



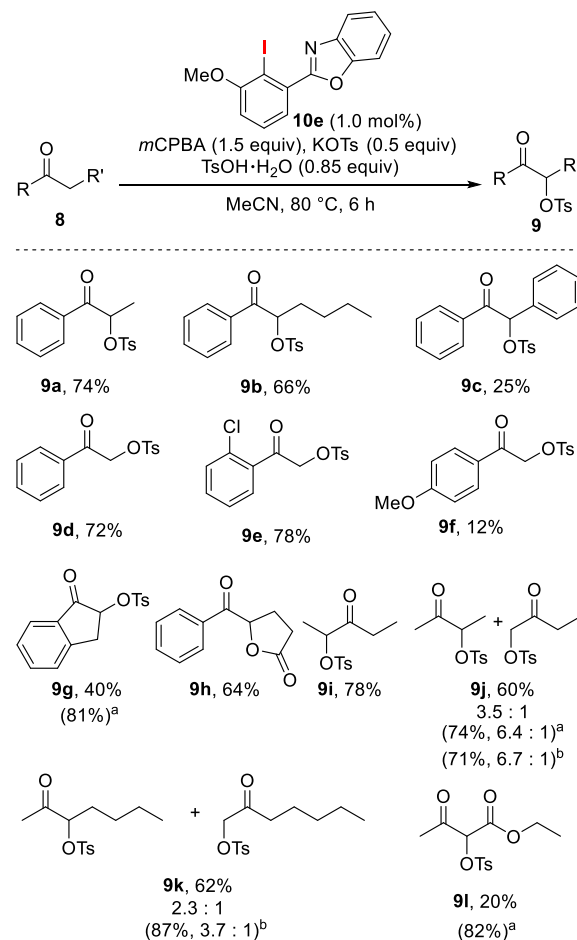
entry <sup>a</sup>	<i>m</i> CPBA [equiv]	TsOH [equiv]	Additive [equiv]	yield [%] <sup>b</sup>
1 <sup>c,d</sup>	2.0	2.0	---	32
2 <sup>d</sup>	2.0	2.0	---	43
3	2.0	<b>1.2</b>	---	53
4	2.0	<b>1.0</b>	---	57
5	2.0	1.0	<b>NaOTs (1.0)</b>	65
6	2.0	1.0	<b>NaOTs (1.5)</b>	64
7	2.0	<b>0.75</b>	NaOTs (1.0)	64
8	2.0	0.75	<b>NaOTs (0.75)</b>	65
9	2.0	0.75	<b>KOTs (0.75)</b>	70
10 <sup>e</sup>	<b>1.5</b>	0.75	KOTs (0.75)	70
11 <sup>e</sup>	1.5	0.75	<b>KOTs (0.5)</b>	68
12 <sup>e</sup>	1.5	<b>0.85</b>	KOTs (0.5)	<b>73</b>
13 <sup>e,f</sup>	1.5	0.85	KOTs (0.5)	21

<sup>a</sup>Reaction conditions: To a stirred solution of *m*CPBA, TsOH·H<sub>2</sub>O and additive in MeCN (0.1 M) was added the catalyst **10e** (1 mol%) followed by propiophenone (**8a**, 0.1 mmol) and the mixture was stirred at 80 °C for 6 h. <sup>b</sup>Determined by <sup>1</sup>H-NMR with anisole as the internal standard. <sup>c</sup>At 50 °C. <sup>d</sup>For 24 h. <sup>e</sup>0.2 M. <sup>f</sup>Iodobenzene as catalyst.

Addition of NaOTs further increased the yield to 65% (entry 5). Varying the ratios between free TsOH and NaOTs did not improve the overall yield (entries 6-8), however the overall TsO-equivalents could be finally

decreased to 1.5 equivalents in a 1:1 mixture. Switching to potassium tosylate (entry 9) together with a reduction of the amount of *m*CPBA and further fine adjustment of the TsOH/KOTs ratio finally gave the desired product in 73% yield (entry 12).

Under these optimized conditions, catalytic amounts of iodobenzene (**7**) gave the desired product **9a** in only 21% yield (entry 13). Therefore, we can claim that NHIA **10e** is – to the best of our knowledge – the most efficient aryl iodide catalyst that has ever been described for this benchmark reaction. With the optimized conditions in hand, the reaction was scaled up to 1 mmol and tested with different types of ketones (Scheme 1).

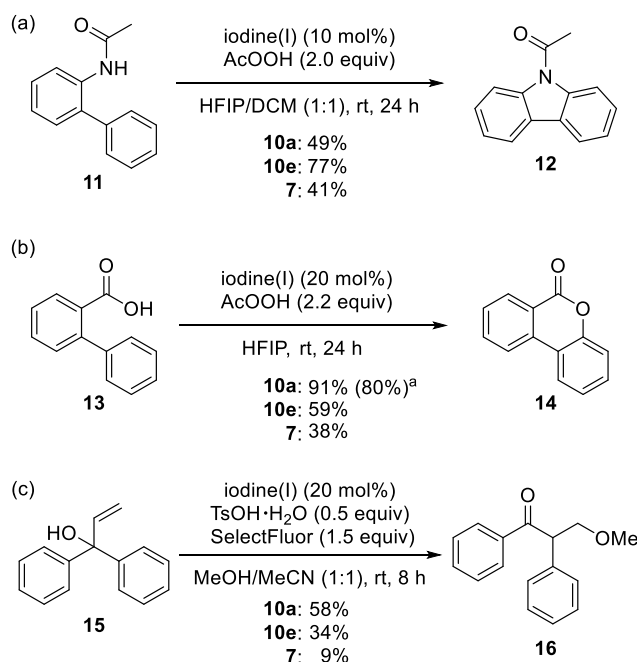


**Scheme 1.**  $\alpha$ -Tosyloxylation of carbonyl compounds **8** with NHIA catalyst **10e**. Reaction conditions: To a stirred solution of *m*CPBA (1.5 equiv), TsOH·H<sub>2</sub>O (0.85 equiv) and KOTs (0.5 equiv) in MeCN (0.2 M) was added catalyst **10e** (1.0 mol%) followed by the ketone **8** (1.0 mmol) and the mixture was stirred at 80 °C for 6 h. Yields refer to isolated product. <sup>a</sup>**10e** (10 mol%), *m*CPBA (1.5 equiv), TsOH·H<sub>2</sub>O (1.5 equiv), rt, 24 h. <sup>b</sup>**10e** (5.0 mol%), *m*CPBA (1.5 equiv), TsOH·H<sub>2</sub>O (1.5 equiv), 50 °C, 6 h.

On this larger scale, the tosyloxyated model substrate **9a** was isolated in 74% yield. The  $\alpha$ -tosyloxylation of hexanophenone (**8b**) yielded **9b** in 66%, while the reaction with deoxybenzoin (**8c**) proved to be troublesome yielding only 25% of **9c**. Tosyloxyated acetophenones **9d** and **9e** were obtained in 72% and 78% yield, while the yield of the

*p*-methoxy derivative **9f** was considerably lower (12%). The reaction with 1-indanone (**8g**) under these conditions gave the desired product **9g** in 40% yield. With 10 mol% of **10e** at room temperature the yield increased to 81%. The intramolecular cyclization of 5-oxo-phenylpentanoic acid (**8h**) gave the lactone **9h** in 64%. Furthermore, aliphatic ketones were efficiently tosyloxylated, such as diethyl ketone (**8i**) to give **9i** in 78% yield. In the reaction with 2-butanone (**8j**) a high C3 vs. C1 selectivity was observed, yielding the product **9j** in 60% with 3.5:1-C3/C1-ratio. With 10 mol% catalyst at room temperature this ratio was significantly increased to 6.4:1 and with 5 mol% at 50 °C even to 6.7:1 (71% yield). This is again the highest reported selectivity for this substrate, in particular under catalytic conditions.<sup>[36,37]</sup> The reaction with 2-heptanone (**8k**) gave **9k** in 62% yield with a 2.3:1-ratio using 1 mol% and a 3.7:1-ratio (87% yield) using 5 mol% catalyst. Finally, dicarbonyl compounds seemed to be less suitable substrates under the optimized conditions, as the reaction with ethyl acetoacetate (**8l**) gave the desired product **9l** in only 20% yield. With 10 mol% catalyst at room temperature, the yield was again increased to 82%.

As the triazole **10a** and the benzoxazole **10e** showed high reactivity in the  $\alpha$ -tosyloxylation even at low catalyst loadings, both catalysts were further tested in more sophisticated oxidative cyclizations of biphenyl derivatives (Scheme 2). These transformations give typically low product yields with catalytic amounts of



**Scheme 2.** Further reactions with the best *N*-heterocyclic catalysts **10a** and **10e** in comparison with iodobenzene (**7**). a) Oxidative cyclization of biphenyl **11** to *N*-acyl carbazole **12**; b) Oxidative cyclization of biphenyl **13** to lactone **14**; c) Oxidative rearrangement of allylic alcohol **15** to propanone **16**. <sup>a</sup>10 mol% catalyst loading.

iodobenzene (**7**).<sup>[38,39]</sup> In the intramolecular C-H-amination<sup>[38]</sup> of aminobiphenyl **11** (Scheme 2 - a) catalyst **10e** showed a high reactivity yielding carbazole **12** in 77% yield, while triazole **10a** gave a lowered yield of 49%. With catalytic amounts of iodobenzene (**7**) only 41% of **12** were obtained.

In the oxidative cyclization of 2-biphenylcarboxylic acid (**13**)<sup>[39]</sup> (Scheme 2 - b) NHIA **10e** gave the product **14** in moderate yield of 59%, whereas iodobenzene (**7**) gave only 38%. In contrast, NHIA **10a** showed a high reactivity yielding the desired lactone **14** in 91% and still in good yield of 80% with only 10 mol% catalyst loading. Finally, the oxidative rearrangement of allylic alcohol **15**<sup>[40]</sup> (Scheme 2 - c) was investigated. Compared to the low yield (9%) with iodobenzene (**7**) as the catalyst, NHIAs **10e** and **10a** gave the rearrangement product **16** in moderate to good yield (34 and 58%).<sup>[41]</sup>

## Conclusion

In conclusion, 28 novel *N*-heterocyclic substituted iodoarenes (NHIAs) **6a-o** and **10a-m** with different *ortho*-substituents were synthesized and their reactivity systematically evaluated in the  $\alpha$ -tosyloxylation of propiophenone (**8a**). Triazole and benzoxazole-substituted aryl iodides further bearing an *ortho*-methoxy group as the superior “twisting” unit were found as the most efficient catalysts. Benzoxazole **10e** showed outstanding reactivity even at catalyst loadings of 1 mol% which is the most efficient aryl iodide catalyst ever described so far for this reaction. This high reactivity was also accompanied by unprecedented high regioselectivities in the tosyloxylation of aliphatic ketones bearing two distinct enolic carbon atoms. Finally, the synthetic potential of the catalysts **10a** and **10e** were investigated in two oxidative cyclizations and in an oxidative rearrangement reaction. A further catalyst evolution together with theoretical investigations to better rationalize the high reactivity of NHIAs for each investigated reaction should in the near future lead to the rational development of the next generation NHIAs and improved catalyst turnovers in these and other oxidative transformations.

## Experimental Section

### General Procedure for the determination of <sup>1</sup>H-NMR Yields in the $\alpha$ -Tosyloxylation of Propiophenone (**8a**).

To a stirred solution of *m*CPBA (85%, 40.8 mg, 0.200 mmol, 2.0 equiv) and TsOH·H<sub>2</sub>O (38.0 mg, 0.200 mmol, 2.0 equiv) in MeCN (1 mL, 0.1 M) was added the catalyst (10 mol%) followed by propiophenone (**8a**, 13.4 mg, 0.100 mmol) and the mixture was stirred at rt or 50 °C for 2-24 h. The reaction was quenched with dimethylsulfide (14.6  $\mu$ L, 0.200 mmol, 2.0 equiv) and the solvent was removed under reduced pressure. The yield of the crude

mixture was determined by <sup>1</sup>H-NMR with anisole as the internal standard.

### General Procedure for the $\alpha$ -Tosyloxylation of Carbonyl Compounds **8** with 1 mol% Catalyst **10e**.

To a stirred mixture of *m*CPBA (85%, 306 mg, 1.50 mmol, 1.5 equiv), KOTs (105 mg, 0.500 mmol, 0.5 equiv) and TsOH•H<sub>2</sub>O (162 mg, 0.850 mmol, 0.85 equiv) in MeCN (5 mL, 0.2 M) is added the catalyst **10e** (3.5 mg, 0.010 mmol, 1 mol%) followed by the corresponding carbonyl compound **8** (1.00 mmol) and the mixture was stirred at 80 °C for 6 h. Then water (10 mL) and sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>-solution (2 mL) was added and the mixture was extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with sat. NaHCO<sub>3</sub>-solution (2 x 20 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. The residue was purified via column chromatography on silica gel (cyclohexane/EtOAc) to give the corresponding product **9**.

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Andreas Boelke and Boris J. Nachtsheim\*

