Oxidative Coupling of N-Methoxyamides and Related Compounds toward Aromatic Hydrocarbons by Designer μ-Oxo Hypervalent Iodine Catalyst

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Abstract Oxidative coupling strategies that can directly convert the C–H group for chemical transformations are, in theory, ideal synthetic methods to reduce the number of synthetic steps and byproduct generation. Hypervalent iodine reagents have now become one of the most promising tools in developing oxidative couplings due to their unique reactivities that are replacing metal oxidents. As part of our continuous development of oxidative coupling reactions, we describe in this report highly efficient μ-oxo hypervalent iodine catalysts for the direct oxidative coupling of N-methoxyamides and related compounds with aromatic hydrocarbons. The excellent TONs, up to over 100 times, with a best catalyst loading of 0.5 mol% were determined for the oxidative C–H/N–H coupling method, which can provide the most straightforward route to obtaining these unique arenyl amide compounds.

Key words hypervalent compound, iodine, oxidative coupling, amidation, electrophilic substitution

The transition-metal-catalyzed cross-coupling strategies established in the 20th century for the reactions of unreactive organic halides with nucleophilic organic molecules, such as organometallic compounds (e.g., metal = [Zn] Negishi, [B] Suzuki, etc.)1 and amines (Buchwald–Hartwig),2 as the coupling partner are powerful tools in organic synthesis due to the high reliability of the reactions to construct the target structures found in pharmaceuticals and other fine chemicals. Due to their high importance in scientific fields as well as in industrial production processes,3 much effort has been devoted to some improvement of the original coupling strategies; considering the recent demand for green and sustainable chemistry, a more step-economical C–H coupling route avoiding the preparation of organic halides and/or organometallic compounds has emerged in the past few decades.4 In theory, the coupling reaction between two X–H bonds (X = carbon or heteroatom) present in organic molecules is ideal,5 which is an important goal of the modern coupling challenge that requires the nonproduction of metal waste and byproducts during the reaction and preparation of the substrates. In this regard, the oxidative coupling between nucleophile–H bonds would principally match with the concept (Scheme 1), but early studies usually suffered from over-oxidation of the products and low reaction selectivities, such as uncontrolled homodimer formations.6

Recently, the catalysis of oxidative C–H couplings without a prefunctionalized substrate has been quite progressive for transformations of aromatics, particularly by using transition-metal chemistry,7 while the catalyst loadings in these reported cases are somewhat unsatisfactory when compared to first-generation cross-coupling methodology. Therefore, developing a new metal-catalyst-free method should be indispensable, especially in this oxidative coupling area, for further advancement of the green strategy.7 Hypervalent iodine reagents have received significant attention in modern synthesis as a safe tool for oxidation reactions8 and they have become promising in realizing met-
Biographical Sketches

**Toshifumi Dohi** received his Ph.D. in 2005 (Y. Kita), subsequently became Assistant Professor at Osaka University and Ritsumeikan University, and was promoted to Associate Professor and Professor in 2014 and 2019, respectively. He received the IUPAC-ICOS 15 Poster Award for most excellent presentation, the PSJ Award for Young Scientists (2009), Banyu Chemist Award (2013), Thieme Chemistry Journal Award (2014), and GSC Encouragement Award (2015). His current research interest is focused on reagent/catalyst design and asymmetric oxidation in hypervalent iodine chemistry.

**Hirotaka Sasa** was born and grew up in Shiga, Japan. He obtained his B.Sc. degree under the supervision of Prof. Toshifumi Dohi in 2018. Now he receives the support of the Nagai Memorial Research Encouragement from The Pharmaceutical Society of Japan (PSJ) and works as a Ph.D. course student in the same group at the Graduate School of Pharmaceutical Sciences, Ritsumeikan University. His current interest is synthetic studies using hypervalent iodine catalysts.

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**Yasuyuki Kita** was born in 1945 in Osaka, Japan. He received his Ph.D. (1972) from Osaka University and subsequently was a member of the faculty of Pharmaceutical Sciences of the university. After two years (1975–1977) of postdoctoral work with Professor George Büchi at MIT, he moved back to Osaka University. He was promoted to Associate Professor in 1983 and to Full Professor of Osaka University in 1992. In 2008, he retired from Osaka University and joined Ritsumeikan University as the Dean of the Faculty of Pharmaceutical Sciences. From 2011 to 2015, he held Vice-President of the Research Organization of Science and Technology, Ritsumeikan University. Since April 2015, he has been Invited Research Professor and Director of Research Center for Drug Discovery and Pharmaceutical Development Science of the same University. He has a wide range of research interest in synthetic chemistry including the development of new asymmetric synthesis, new reagents, and the total synthesis of biologically active natural products. His current research interest is in hypervalent iodine chemistry. He has published more than 500 original papers. His awards include the Pharmaceutical Society of Japan (PSJ) Award for Young Scientists (1986), the PSJ Award for Divisional Scientific Contribution (1997), the PSJ Award (2002), the Japanese Society for Process Chemistry (JSPC) Award for Excellence (2005), the Society of Iodine Science (SIS) Award (2007), and the E.C. Taylor Senior Award (2017).
al-free oxidative coupling reactions based on our pioneering studies. As a part of our continuous development, we now report the efficient oxidative C–H couplings of aromatic hydrocarbons toward N–H amides to easily produce functionalized arylamides using our unique μ-oxo hypervalent iodine catalyst even at less than 1 mol% catalyst loadings at room temperature in the presence of dilute peracetic acid (Scheme 2).

![Scheme 2](image)

The oxidative coupling chemistry of the hypervalent iodine reagent for the conversion of aromatics has a long history since the appearances of the reactive reagents, activators, and solvents that can increase the oxidation abilities of the iodonyl groups. We first proposed the use of phenyliodine(III) bis(trifluoroacetate) (PIFA) in fluoroalcohols, i.e., hexafluorisopropanol (HFIP) and trifluoroethanol (TFE), as an efficient oxidative coupling system for the deaeromatization of phenolic substrates introducing nucleophiles (Nu–H) in the mid 1980s. With this significant improvement as a turning point, the hypervalent iodine reagent now plays a crucial role in reproducing the biosynthetic oxidative phenolic coupling processes and syntheses of natural products. A further important contribution in the metal-free oxidative C–H coupling area is the direct activation of aromatic rings triggered by single-electron-transfer (SET) processes discovered in the early 1990s. Phenyl ether (and alkyarene) rings, not causing oxidation unlike phenols, are smoothly SET activated by treatment with PIFA, and the introduction of an azide by ligand transfer from in situ formed electrophilic amido-μ-oxo hypervalent iodine organocatalyst.

Complimentary to the Buchwald–Hartwig aryl amination procedures, substantial advances in the oxidative C–H aminations aiming at a greener goal, which can directly install amines into non-preactivated aromatic substrates to give valuable N-arylated molecules, have been extensively found in recent years under transition-metal catalysis and even other metal-free conditions. The amide alternative of the hypervalent iodine induced C–H azidation involving in situ formed electrophilic amido-μ-oxo hypervalent iodine species bearing a methoxy or phthalimide-substituted nitrogen group was reported in 1990 by the Kikugawa group for a few nucleophilic arenes (Scheme 4). Later, this C–H amiation was successfully improved by using PIFA and/or by the aid of fluoroalcohols (see Scheme 3) in order to use many different substrates in an intramolecular manner. For example, the optimized C–H amiation protocols have been applied to the construction of interesting compounds in the field of medicinal chemistry as well as the deaeromatizing spirocyclizations to provide facile access to the unique spirolactam structures known as useful precursors for some biologically active alkaloids and natural products. On the other hand, the intermolecular coupling for unreactive aromatic hydrocarbons remains relatively difficult, particularly with the catalytic use of a conventional hypervalent iodine reagent.

Indeed, the catalytic generation of PIFA (see Figure 1) under the re-oxidizing conditions for the oxidative C–N coupling of arenes is not as effective as other hypervalent iodine mediated reactions, and their typical turnover number (TON) for intermolecular C–H amiations is estimated to be less than only 10 times. Therefore, based on the structures of μ-oxo PIDA and PIFA, we have previously introduced the μ-oxo catalysts as more efficient tools to realize practical and greener oxidative C–N couplings. These catalysts are rationally designed to steadily keep their activated forms and thus reproduce the high electrophilicity of the iodine(III) atoms caused by the strong trans-influence of the μ-oxo oxygen during the catalytic cycle.
However, the suggested conditions for the intermolecular direct C–H coupling of toluene (2a) toward the N-methoxyamide N–H bond using peracetic acid as a stoichiometric oxidant in an ordinary solvent failed and produced very low TONs for our μ-oxo catalysts (see Table 1). Thus, the reaction of N-methoxyamide 1a with toluene (2a; 15 equiv) performed using 4 mol% of the pre-catalysts Ia’ (R’ = H) with 1.5 equiv of peracetic acid (9% solution in acetic acid) and trifluoroacetic acid (5 equiv) in 1,2-dichloroethane (DCE, 0.3 M of amide 1a) resulted in the formation of the corresponding C–N coupling product 3aa in only 13% yield as a mixture of regioisomers, with a TON of ca. 3 after 2 hours at room temperature; and a large amount of amide 1a remained unreacted in this case (Table 1, entry 1).

On the other hand, our reported catalytic conditions of a mixed fluoroalcohol solvent system (HFIP/DCE 10:1) were found to dramatically improve the TON of the catalyst Ia as well as its turnover frequency (TOF) (Table 1, entry 2); this is probably because the fluoroalcohol not only accelerates the generation of the active μ-oxo species I by enhancing the re-oxidation ability of peracetic acid by powerful hydrogen bondings, but also facilitates the smooth generation of the cationic nitrenium (or pseudo-nitrenium) species. In a short reaction time, the target products 3aa were thus obtained in 76% yield by simply changing the solvent in which the addition of trifluoroacetic acid takes place to produce active μ-oxo species 1a (R = CF3 in Figure 1) and this was essential for this catalytic coupling (entry 3). Regarding the catalyst, the derivative Ib’ (R’ = Me) showed similar catalytic efficiencies for the coupling of amide 1a (entry 4). It also appears that the slight modification of the concentration affects the TON value (entry 5). In this reaction, the molar balance of the substrates is rather important, and the yield of the products 3aa decreased by using 5 equiv of toluene (2a) relative to the amide 1a (entry 6). Subsequently, we then examined the reaction to further lower the catalyst loading. To our delight, a comparable result was obtained in regard to the yield of the product when using a 2 mol% catalyst loading after a 12 h reaction (entry 9). To the best of our knowledge, this observed TON score for the catalyst Ib’ is the highest among all the intermolecular C–H/N–H aromatic amidations. Of course, the coupling product 3aa was

<table>
<thead>
<tr>
<th>Entry</th>
<th>μ-Oxo catalyst</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield of 3aa [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ia’ (4 mol%)</td>
<td>DCE</td>
<td>2</td>
<td>13% (2.6:1:2.8)</td>
</tr>
<tr>
<td>2</td>
<td>Ia’ (4 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>2</td>
<td>76% (2.6:1:2.6)</td>
</tr>
<tr>
<td>3</td>
<td>Ia’ (4 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>2</td>
<td>66% (3.7:1:3.4)</td>
</tr>
<tr>
<td>4</td>
<td>Ib’ (4 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>2</td>
<td>78% (2.1:1:2.2)</td>
</tr>
<tr>
<td>5</td>
<td>Ib’ (4 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>2</td>
<td>67% (2.2:1:2.3)</td>
</tr>
<tr>
<td>6</td>
<td>Ib’ (4 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>2</td>
<td>61% (2.7:1:1.8)</td>
</tr>
<tr>
<td>7</td>
<td>Ib’ (2 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>2</td>
<td>81% (2.3:1:2.4)</td>
</tr>
<tr>
<td>8</td>
<td>Ib’ (1 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>1</td>
<td>80% (2.1:1:2.4)</td>
</tr>
<tr>
<td>9</td>
<td>Ib’ (0.5 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>12</td>
<td>68% (2.3:1:2.7)</td>
</tr>
<tr>
<td>10</td>
<td>none</td>
<td>HFIP/DCE (10:1)</td>
<td>16</td>
<td>-b</td>
</tr>
</tbody>
</table>

a Reaction conditions: amide 1a, toluene (2a; 15 equiv), catalyst, peracetic acid (9% solution in AcOH, 1.5 equiv), TFA (5 equiv), solvent (0.3 M of amide 1a), rt; unless otherwise stated.
b The product yields after purification were calculated basis on the amide 1a used.

The regioisomeric ratio (ortho/meta/para) is indicated in parentheses (calculated value by 1H NMR measurement).

c Large amount of amide 1a was recovered.
d Using TFA (1 equiv).
e Higher concentration (0.6 M of amide 1a).
f Using toluene (2a; 5 equiv).

Figure 1: Hypervalent iodine reagents, PIDA, PIFA, and their μ-oxo dimers and designer μ-oxo reagent I.

Table 1 Optimization: Hypervalent Iodine Induced C–H Amidation of Toluene by μ-oxo Catalysts Ia’ and Ib’

Scheme 4: Intermolecular oxidative coupling of N-functionalized amides with aromatic hydrocarbons by using hypervalent iodine reagent (NPhth = phthalimido)
not produced in the absence of the μ-oxo catalysts (entry 10). In 2016, Muñiz and co-workers also reported a new iodine catalyst, 1,2-diodobenzene, for this type of coupling reaction.\textsuperscript{31}

We then evaluated the optimized catalytic system for the μ-oxo catalyst 1b′ using the same-type couplings of a further series of simple non-activated aromatics 2b–f (Scheme 5). The reactions of ethylbenzene (2b) and p-xylene (2c) both smoothly produced the corresponding C–N coupling products 3ab and 3ac within 2 hours using 2 mol% of the catalyst. Although bromobenzene (2d) is less reactive during the coupling (see product 3ad), the method can provide an aryl-deuterated amine with an aromatic halogen functionality in a single step from the isotopic aromatic substrate (i.e., bromobenzene-d\textsubscript{3}), which is beneficial for further elaboration of the structure and scalable synthesis. Other aliphatic and aromatic amides 1b and 1c and sulfonamide 1d were applicable for the couplings with benzene 2e and other aromatic hydrocarbons. The N-methoxy groups found in anilides are known to show unique reactivities, and new reactions utilizing cleavage between the heteroatom bond as a driving force have been reported by several research groups.\textsuperscript{32}

The reaction of anisole (2h) with N-methoxybenzamide (1c) unexpectedly did not occur using either of the μ-oxo iodine catalysts 1a′ and 1b′ under the conditions in a fluoro alcohol (see the note for Scheme 7). Obviously, a competitive diarylidonium salt forming path for condensation with anisole 2h to prevent the catalytic cycle was dominant in this electron-rich aromatic case in a fluoroalcohol\textsuperscript{33,34} compared to the rate of the generation of the amide-λ\textsubscript{3}-iodane intermediate for the C–N coupling. Therefore, the use of DCE only as a solvent was plausible for this coupling combination. Interestingly, the formation of an ortho-coupling product of anisole 2h over the para isomer was preferred by specific control of the methoxy group.\textsuperscript{35}

As a complement to the transition-metal-catalyzed amidation of halogenated aryls, Hartwig and co-workers proposed in 2013 the intermolecular direct coupling of simple

\begin{figure}
\centering
\includegraphics[width=\textwidth]{scheme6.png}
\caption{Catalytic C–H amidation of arenes 2a–f using μ-oxo catalyst 1b′. Reagents and conditions: amide 1a–d, ane 2a–f (15 equiv), peracetic acid (9% solution in AcOH, 1.5 equiv), TFA (5 equiv), catalyst (2 mol%), HFIP/DCE (10:1), rt, 2 h, unless otherwise stated. The ortho/meta ratio calculated by \textsuperscript{1}H NMR is indicated in parentheses. \textsuperscript{a}Catalyst: 3 mol%. \textsuperscript{b}Overnight. \textsuperscript{c}ortho/meta ratio.}
\end{figure}

\begin{table}
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
Catalyst & Time & Product & \textsuperscript{1}H NMR & \textsuperscript{1}H NMR \\
\hline
\hline
μ-oxo 1b′ (2 mol%) & 2 h & 50% & 55% & 70% \\
\hline
& 12 h & quant & 91% & 99% \textsuperscript{b} & 92% \textsuperscript{b} \\
\hline
\hline
μ-oxo 1a′ (3 mol%) & 2 h & 88% & 94% & 96% \\
\hline
& (1/2.4) & (1/4.5) & (1/3.1) \textsuperscript{d} \\
\hline
\end{tabular}
\caption{Steric influence of μ-oxo catalysts 1a′ (R′ = H) and 1b′ (R′ = Me) in the coupling of N-phthalimide 1e. Reagents and conditions: amide 1e, ane 2a.e.d.g (15 equiv), peracetic acid (9% solution in AcOH, 1.5 equiv), TFA (5 equiv), catalyst (2–3 mol%), HFIP/DCE (10:1), rt, unless otherwise stated. \textsuperscript{a}The ortho and para products are separable. \textsuperscript{b}Exclusively para. \textsuperscript{c}ortho/meta ratio of the mixture, calculated by \textsuperscript{1}H NMR. \textsuperscript{d}The regioisomeric ratio is calculated by \textsuperscript{1}H NMR.}
\end{table}
arenes with phthalimide by employing the hypervalent iodine reagent as the oxidant for the palladium catalyst.\textsuperscript{36a} Similarly, the metal-catalyzed intermolecular amidations by converting the C–H group of aromatic hydrocarbons not having a directing group typically required the hypervalent iodine reagent as a stoichiometric activator.\textsuperscript{36b–d} In addition, enhancing the TON was difficult in these catalyses.\textsuperscript{36e,f} Thus, the fact that the direct couplings between the amide N–H group and aromatic C–H bond can proceed by using such a small amount of hypervalent iodine catalyst without adding any transition-metal element in our case is particularly noteworthy. The differences in the chemoselectivity during the C–H amidations were also found during the couplings of the anilides 4a and 4b (see Scheme 8). It was reported by the Buchwald group that ortho C–C bond-forming alylations leading to the formation of biaryl compounds 6ai and 6bi would exclusively occur for these anilide substrates under their conditions using a palladium catalyst,\textsuperscript{37} rather than the coupling at the nitrogen group. In clear contrast, our organocatalytic conditions based on the use of the μ-oxo catalyst \textsuperscript{I}' instead afforded the C–N coupling products 5ai and 5bi in moderate to good yields (see experimental section).\textsuperscript{38}

In general, melting points were measured using a Büchi B 545 apparatus and are uncorrected. 1H and 13C NMR spectra were recorded with a Jeol JMN-300 spectrometer operating at 400 MHz and 100 MHz in CDCl\textsubscript{3} at 25 °C with TMS (δ = 0) as the internal standard. Infrared spectra were recorded by using a Hitachi 270-50 spectrometer. Flash column chromatography and analytical TLC were carried out on Merck silica gel 60 (230–400 mesh) and Merck silica gel F\textsubscript{254} plates (0.25 mm), respectively. The spots and bands were detected by UV irradiation (254, 365 nm) or by staining with 5% phosphomolybdic acid followed by heating.

All arenes 2 employed for the coupling reactions are commercially available and used without further purification. The amides 1a–d,\textsuperscript{31,44a–c} 4a, and 4b were prepared from 0-methylhydroxylamine, acetohydrazide, and corresponding anilines according to the literature. Solvents were purchased from commercial suppliers and used as received for the reactions, extraction, and eluent for column chromatography and TLC.

Regarding the μ-oxo hypervalent iodine catalysts \textsuperscript{I}' and \textsuperscript{Ib}', 2,2-diiodobiphenyl (\textsuperscript{Ib}') is commercially available, while 2,2’-diiodo-4,4’,6,6’-tetramethylbiphenyl (\textsuperscript{Ib}) was prepared from 1-iodo-3,5-di-methylbenzene in one step by our method.\textsuperscript{45}

2,2’-Diiodo-4,4’,6,6’-tetramethylbiphenyl (\textsuperscript{Ib})

Under N\textsubscript{2} atmosphere at –78 °C, to a stirred solution of 1-iodo-3,5-di-methylbenzene (1.62 g, 7.0 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (8.75 mL) was added dropwise a mixture of PIFA (1.51 g, 3.5 mmol) and BF\textsubscript{3}·OEt\textsubscript{2} (0.88 mL, 7.7 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (8.75 mL) over a few minutes. The mixture was stirred at this temperature for 5 h. When the reaction was complete, the mixture was quenched with sat. aq NaHCO\textsubscript{3} and the aqueous layer was extracted with CH\textsubscript{2}Cl\textsubscript{2}. The combined organic layers were washed with brine and dried (anhyd Na\textsubscript{2}SO\textsubscript{4}). After removal of the solvent, the residue was purified by column chromatography (silica gel, hexane/EtOAc) to give \textsuperscript{Ib} (1.02 g, 2.21 mmol, 63%) as a white powder; mp 111–113 °C.

IR (KBr): 3014, 1599, 1541, 1035 cm\textsuperscript{-1}.
1H NMR (400 MHz, CDCl\textsubscript{3}); δ = 1.95 (s, 6 H), 2.31 (s, 6 H), 7.06 (s, 2 H), 7.62 (s, 2 H).
13C NMR (100 MHz, CDCl\textsubscript{3}); δ = 20.4, 21.2, 100.7, 130.7, 136.9, 137.0, 139.0, 144.3.

2,2,2-Trichloroethyl Methoxy(toly)carbamate 3aa; Typical Procedure for Oxidative Coupling Using a Combination of Diodobiphenyl Catalyst \textsuperscript{Ib} with Stoichiometric Peracetic Acid (Schemes 5 and 6)

2,2,2-Trichloroethyl carbamate (1a; 111.2 mg, 0.50 mmol, 1 equiv), toluene (691 mg, 7.5 mmol, 15 equiv), and catalyst \textsuperscript{Ib} (4.6 mg, 0.010 mmol, 0.02 equiv) were dissolved in HFP/DCE (10:1, 1.6 mL) in a round-bottomed flask at rt. Peracetic acid (9% solution in AcOH, 0.6 mL, 0.75 mmol, 1.5 equiv), and TFA (285 mg, 2.5 mmol, 5 equiv) were added sequentially. The mixture was then stirred at rt for 2 h. When the reaction was complete, the resulting solution was washed with water and extracted with CH\textsubscript{2}Cl\textsubscript{2}, and the combined organic extracts were dried (anhyd Na\textsubscript{2}SO\textsubscript{4}). After removal of the solvents by a rotary evaporation method, the residue was purified by column chromatography (silica gel, hexane/EtOAc) to give \textsuperscript{Ib} (1.02 g, 2.21 mmol, 63%) as a white powder; mp 111–113 °C.

IR (KBr): 3014, 1599, 1541, 1035 cm\textsuperscript{-1}.
1H NMR (400 MHz, CDCl\textsubscript{3}); δ = 1.95 (s, 6 H), 2.31 (s, 6 H), 7.06 (s, 2 H), 7.62 (s, 2 H).
13C NMR (100 MHz, CDCl\textsubscript{3}); δ = 20.4, 21.2, 100.7, 130.7, 136.9, 137.0, 139.0, 144.3.
Following the typical procedure for 3aa using Ib’ (3 mol%), reaction time: overnight; pale yellow oil: yield: 81.0 mg (40%); ratio ortho/para 1:7.1 (1H NMR).

1H NMR (400 MHz, CDCl3): δ = 3.81 (s, 3 H, para), 3.83 (s, 3 H, ortho), 4.82–4.88 (m, 4 H), 7.22–7.29 (m, 1 H), 7.36–7.43 (m, 4 H, ortho and para), 7.46–7.53 (m, 2 H, para), 7.68 (dd, J = 8.1, 1.4 Hz, 1 H).

13C NMR (100 MHz, CDCl3): δ = 123.4, 123.6, 128.4, 129.2, 130.1, 133.7, 138.0, 138.1, 152.3, 153.2.

13C NMR (100 MHz, CDCl3): δ = 17.7, 61.9, 67.7, 126.4, 127.9, 128.1, 128.5, 128.9, 131.0, 136.0, 136.5, 138.0, 155.2.

Benzyl Methoxy(3-toly)carbamate (meta-3ba) and Benzyl Methoxy(4-toly)carbamate (para-3ba)

Yellowish oil: yield: 61.5 mg (41%).

1H NMR (400 MHz, CDCl3): δ = 2.32 (s, 3 H, para), 2.34 (s, 3 H, meta), 3.72 (s, 3 H, para), 3.73 (s, 3 H, meta), 5.24 (s, 2 H, para), 5.25 (s, 2 H, meta), 6.95–7.07 (m, 1 H, meta), 7.12–7.42 (m, 17 H).

13C NMR (100 MHz, CDCl3): δ = 21.8, 64.4, 123.7, 127.6, 128.4, 129.1, 129.8, 130.2, 141.0, 144.8.

N-(2,5-Dimethylphenyl)-N-methoxybenzamide (3cc)

Colorless oil; yield: 103.7 mg (81%).

1H NMR (400 MHz, CDCl3): δ = 2.22 (s, 6 H), 3.50–3.85 (br s, 3 H), 6.93–7.71 (m, 8 H).

13C NMR (100 MHz, CDCl3): δ = 17.7, 20.9, 61.0, 128.0, 128.4, 128.5, 130.2 (2 ×), 130.8, 131.2, 133.5, 133.6, 136.5.

N-Methoxy-N-phenylbenzamide (3ce)

Light yellow oil: yield: 69.5 mg (60%).

1H NMR (400 MHz, CDCl3): δ = 3.69 (s, 3 H), 7.20–7.52 (m, 8 H), 7.56–7.64 (m, 2 H).

13C NMR (100 MHz, CDCl3): δ = 61.8, 124.5, 127.2, 128.1, 128.6, 129.1, 130.8, 134.7, 139.4, 168.3.

N-Methoxy-N-tolylbenzamide (3ca)

Light yellow oil: yield: 91.1 mg (76%); ratio ortho/para 1:1.3 (1H NMR).

1H NMR (400 MHz, CDCl3): δ = 2.25 (s, 3 H, para), 2.28 (s, 3 H, ortho), 3.62 (s, 6 H), 7.03–7.62 (m, 18 H).

13C NMR (100 MHz, CDCl3): δ = 18.2, 21.2, 61.0, 61.5, 125.1, 126.6, 128.1 (2 ×), 128.5, 128.6, 129.3, 130.0, 130.7, 130.8, 131.4, 134.5, 134.8, 136.8, 136.9, 137.5, 168.1.

N-(3,4-Dimethylphenyl)-N-methoxybenzamide (3cf)

Light yellow oil; yield: 107.6 mg (75%); ratio ortho/para 1:2.8 (1H NMR).

1H NMR (400 MHz, CDCl3): δ = 2.39 (s, 3 H), 3.86 (s, 3 H), 7.05–7.13 (m, 2 H), 7.15–7.45 (m, 7 H).

13C NMR (100 MHz, CDCl3): δ = 21.8, 64.4, 123.7, 127.6, 128.4, 129.1, 129.8, 130.2, 141.0, 144.8.

N-(1,3-Dioxoisindolin-2-yl)-N-phenylacetamide (3ee)

Following the typical procedure for 3aa using catalyst Ib’ for 12 h gave 3ee; yellowish solid: yield: 56.8 mg (quant.); mixture of rotamers.
N-(1,3-Dioxoisodolin-2-yl)-N-(tolyl)acetamide (3ea)

Following the typical procedure for 3aa using catalyst Ib for 12 h gave a mixture of para/ortho isomers 2.5:1 that were separated by column chromatography.

N-(1,3-Dioxoisodolin-2-yl)-N-(4-tolyl)acetamide (para-3ea)

White amorphous; yield: 85.9 mg (65%).

N-(1,3-Dioxoisodolin-2-yl)-N-(2-tolyl)acetamide (ortho-3ea)

White amorphous; yield: 34.4 mg (26%).

N-(4-Bromophenyl)-N-(1,3-dioxoisodolin-2-yl)acetamide (para-3eg)

Following the typical procedure for 3aa using catalyst Ib for 12 h gave para-3ed; brownish solid; yield: 169.0 mg (99%); mp 169–171 °C.

N-(4-Chlorophenyl)-N-(1,3-dioxoisodolin-2-yl)acetamide (para-3eg)

Yellowish solid; yield: 57.9 mg (92%); mp 138–140 °C.

N-Methoxy-N-(methoxyphenyl)benzamide (3ch)

Following the typical procedure for 3aa, but using DCE instead of the mixed fluoroalcohol solvent (Scheme 7) and µ-oxo catalyst Ib (5 mol%) gave 3ch; light yellow oil; yield: 91.3 mg (70%); ratio ortho/para 1.7:1.

N-(4-tert-Butylphenyl)-N-(3,4-dimethylphenyl)acetamide (5ai)

Following to the typical procedure for 3aa, but using the µ-oxo catalyst Ia (10 mol%) in TFE/CH2Cl2 (2:1, 0.067 M) and wet MCPBA (69% purity, 1.5 equiv) instead of 9% peracetic acid solution for 3 h gave 5ai; yellowish oil; yield: 44.4 mg (75%).

IR (KBr): 2966, 2869, 1675, 1608, 1509, 1369, 1308, 1024 cm⁻¹.

N-(4-Ethylphenyl)-N-(3,4-dimethylphenyl)acetamide (5bi)

Following to the typical procedure for 3aa, but using the µ-oxo catalyst Ia (10 mol%) in TFE/CH2Cl2 (2:1, 0.067 M) (Scheme 8) and wet MCPBA (69% purity, 1.5 equiv) instead of 9% peracetic acid solution for 3 h gave 5bi; yellowish oil; yield: 27.6 mg (52%).

IR (KBr): 3025, 2964, 2928, 2873, 1671, 1618, 1509, 1454, 1369, 1305, 1121, 1024 cm⁻¹.

(1H NMR (400 MHz, CDCl3, 50 °C): δ = 2.02 (s, 3 H), 2.61 (s, 3 H), 2.22 (s, 6 H), 2.97 (d, J = 8.8 Hz, 2 H), 6.37 (dd, J = 8.3, 2.0 Hz, 1 H), 7.03 (d, J = 2.0 Hz, 1 H), 7.10–7.28 (m, 5 H).


5,7-Diacetoxy-5,7-dihydro-1,3,9,11-tetramethylbiphenyl (4a)

To a stirred solution of peracetic acid (9% solution in AcOH, 6.1 mL, 7.6 mmol) in MeCN (47.5 mL) was successively added AcOH (17.1 mL) and 2,2′-diido-4,4′-tetramethylthiobiphenyl (Ib; 0.88 g, 1.9 mmol), and the mixture was stirred overnight at rt. After removal of MeCN under reduced pressure, the resulting residue was extracted with CH2Cl2, and then the organic solution was dried (anhyd Na2SO4). After evaporation of the solvent, the crude solid, that is, Ib, was dissolved in minimal amount of CH2Cl2, which was then added dropwise to stirred hexane. The resulting suspension was filtered and dried to give pure 4a; 3.32 g, 61% yield.

IR (KBr): 3035, 2959, 2925, 2877, 1662, 1509, 1454, 1305, 1121, 1024 cm⁻¹.


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References


(10) Dilute peracetic acid is known as a safe and environmentally friendly oxidant that releases nontoxic acetic acid as the co-product. It is commercially available and frequently employed in industrial-scale oxidations, such as epoxidation. Furthermore, its aqueous 0.2–0.3% solution is widely used as a disinfectant in medical situations.


(15) See ref. 9b and selected examples for introducing heteroatoms:

(16) Recent reviews on dehydrogenative aromatic C–H aminations:


Utilizing our spirobindane catalysts (see refs 42a and 42b), Cai and co-workers recently developed intramolecular oxidative C–N cyclizations accompanying asymmetric desymmetrization of the substrates, see: Ding, Q.; He, H.; Cai, Q. Org. Lett. 2018, 20, 4554.
