Oxidative Coupling of N-Methoxyamides and Related Compounds toward Aromatic Hydrocarbons by Designer \( \mu \)-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 oxidants. As part of our continuous development of oxidative coupling reactions, we describe in this report highly efficient \( \mu \)-oxo hypervalent iodine catalysts for the direct oxidative coupling of \( \text{N-methoxyamides and related compounds with aromatic hydrocarbons.} \) The excellent TONs, up to over 100 times, with a best catalyst loading of 0.5 mol% were determined for the oxidative \( \text{C–H/N–H coupling method, which can provide the most straightforward route to obtaining these unique arylamide compounds.} \)

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.⁸ Hypervalent iodine reagents have received significant attention in modern synthesis as a safe tool for oxidation reactions⁹ 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.

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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 post-doctoral 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 biological-ly 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).

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 iodonium salts. We first proposed the use of phenyliodine(III) bis(trifluoroacetate) (PIFA) in fluoroalcohols, i.e., hexafluoroisopropanol (HFIP) and trifluoroethanol (TFE), as an efficient oxidative coupling system for the dearomatization 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 alkylarene) 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 generated Phi(N3)X (X = N3 or OCOCF3) leads to the formation of aromatic C–H azidation products. Again, the highly polar, non-nucleophilic fluoroalcohol was determined to dramatically affect the aromatic azidation process and the product yield reached 85% when employing this specific activator as a solvent (Scheme 3). Based on this strategy, a series of metal-free oxidative couplings of aromatic rings with nucleophiles (Nu–H) and that having a TMS group (Nu–TMS) has become possible; we believe that these early discoveries by us were the beginning of hypervalent iodine coupling chemistry, leading to the recent breakthrough and elucidations of the metal-free aromatic C–H functionalization strategy.

Complimentary to the Buchwald–Hartwig arylamination 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-iodane 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 amidation 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 amidative cyclization protocols have been applied to the construction of interesting compounds in the field of medicinal chemistry as well as the deearomatizing spirocyclizations to provide facile access to the unique spirolactam structures known as useful precursors of 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 amidations 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 catalyst I 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 I (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 with 1.5 equiv of peracetic acid (9% solution in acetic acid) corresponding C–N coupling product 2a was recovered.

The product yields after purification were calculated basis on the amide used.

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

Large amount of amide 1a was recovered.

Using TFA (1 equiv).

Higher concentration (0.6 M of amide 1a).

Using toluene (2a; 5 equiv).

Not determined.

Table 1 Optimization: Hypervalent Iodine Induced C–H Amidation of Toluene by μ-Oxo Catalysts 1a and Ib

<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>Ib’ (4 mol%)</td>
<td>DCE</td>
<td>2</td>
<td>13% (2.6:1:2.8)</td>
</tr>
<tr>
<td>2</td>
<td>Ib’ (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>Ib’ (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% (2:2:1:3)</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)</td>
</tr>
<tr>
<td>8</td>
<td>Ib’ (1 mol%)</td>
<td>HFIP/DCE (10:1)</td>
<td>6</td>
<td>80% (2:3:1:2)</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>~</td>
</tr>
</tbody>
</table>

* 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.

The observed TON score for the catalyst Ia’ was 136 times for the 0.5 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

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 Ib’ 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 Ib 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 Ib (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% amount of the catalyst Ib’ with a higher catalyst TON (entry 7). The coupling reactions proceeded at room temperature, and the robustness of our catalyst Ib’ under the reaction conditions maintained the original activity for prolonged times (entry 8). Thus, the TON giving the product 3aa in an acceptable yield reached 136 times for the 0.5 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.
not produced in the absence of the \( \mu \)-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.\(^{31}\)

We then evaluated the optimized catalytic system for the \( \mu \)-oxo catalyst Ib 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-\( d_5 \)), 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.\(^{32}\)

For \( N \)-(acetylamino)phthalimide (1e), the catalyst Ib’ (\( R = Me \)) and the steric nitrogen group are quite mismatched;\(^{26c}\) the rates of the product formation were quite slow in comparison to that for the \( N \)-methoxyamides 1a-d, and the amide 1e was not completely consumed within 2 hours (Scheme 6). As a result, the longer reaction time of 12 hours was required in order to achieve the full conversion of the substrate. Interestingly, the more flexible \( \mu \)-oxo catalyst 1a’ (\( R = H \)) was somewhat preferred in terms of the TOFs for the reactions. The bulky \( N \)-phthalimidogroup (NPth) of the amide 1e strongly directed the regioselectivities at the aromatic rings to para over the ortho positions.

The reaction of anisole (2h) with \( N \)-methoxybenzamide (1c) unexpectedly did not occur using either of the \( \mu \)-oxo iodine catalysts 1a’ and Ib’ under the conditions in a fluoro alcohol (see the note for Scheme 7). Obviously, a competitive diaryliodonium salt forming path for condensation with anisole 2h to prevent the catalytic cycle was dominant in this electron-rich aromatic case in a fluoroalcohol\(^{33,34}\) compared to the rate of the generation of the amide-\( \lambda^3 \)-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.\(^{35}\)

As a complement to the transition-metal-catalyzed amination of halogenated aryls, Hartwig and co-workers proposed in 2013 the intermolecular direct coupling of simple...
arenes with phthalimide by employing the hypervalent iodine reagent as the oxidant for the palladium catalyst.\textsuperscript{36a} Similarly, the metal-catalyzed intermolecular aminations 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 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 \texttextsuperscript{4a} and \texttextsuperscript{4b} (see Scheme 8). It was reported by the Buchwald group that \textit{ortho} C–C bond-forming alylations leading to the formation of biaryl compounds \texttextsuperscript{6ai} and \texttextsuperscript{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 \textit{I′} instead afforded the C–N coupling products \texttextsuperscript{5ai} and \texttextsuperscript{5bi} in moderate to good yields (see experimental section).\textsuperscript{38}

In this study, we have clarified the extremely high catalytic efficiencies of our designer μ-oxo hypervalent iodine catalysts \textit{I} for the intermolecular direct oxidative coupling of suitable amides with aromatic hydrocarbons. The C–H and N–H coupling methods can provide the most straightforward route to these arylamide compounds with excellent TONs of over 100 times with a 0.5 mol% catalyst loading. This allows many new direct amination strategies to extend the scopes recently developed on the basis of the stoichiometric hypervalent iodine chemistry\textsuperscript{39–41} and our idea for the catalyst design might contribute to the developments of practical catalysts for these transformations. In addition, the use of related chiral hypervalent iodine catalysts based on the μ-oxo structures\textsuperscript{42} has a significant potential for the asymmetric oxidative C–N coupling reactions under metal-free conditions.\textsuperscript{43}

In general, melting points were measured using a Büchi B 545 apparatus and are uncorrected. \textsuperscript{1} H and \textsuperscript{13} C 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 \textit{2} employed for the coupling reactions are commercially available and used without further purification. The amides \textit{1a–d, 5ai} and \textit{Ib′} were prepared from 0-methylhydroxyamine, 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 \textit{Ia′} and \textit{Ib′}, 2,2′-diiodobiphenyl (\textit{Ia′}) is commercially available, while 2,2′-diiodo-4,4′,6,6′-tetramethylbiphenyl (\textit{Ib′}) was prepared from 1-iodo-3,5-di-methylbenzene in one step by our method.\textsuperscript{45}

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 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (8.75 mL) over a few minutes. The mixture was stirred 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 by rotary evaporation, \textit{1a} (1.02 g, 2.21 mmol, 63%) as a white powder; mp 111–113 °C.

IR (KBr): 3014, 1599, 1541, 1035 cm\textsuperscript{-1}.

\textsuperscript{1} H 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).

\textsuperscript{13} C NMR (100 MHz, CDCl\textsubscript{3}): δ = 20.4, 21.2, 100.7, 130.7, 136.9, 137.0, 139.0, 144.3.

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

Under N\textsubscript{2} atmosphere at ~78 °C, to a 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 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (8.75 mL) over a few minutes. The mixture was stirred 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 by rotary evaporation, \textit{1a} (1.02 g, 2.21 mmol, 63%) as a white powder; mp 111–113 °C.

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\textsuperscript{2,2,2-Trichloroethyl Methoxy(toly)carbamate 3aa; Typical Procedure for Oxidative Coupling Using a Combination of Diiodobiphenyl Catalyst Ib′ with Stoichiometric Peracetic Acid (Schemes 5 and 6)}
3,3,3-Trichloro-N-(ethylphenyl)-N-methoxypropanamide 3ab
Yellow oil; yield: 164.5 mg (99%); ratio ortho/meta/para 2.1:1.2:5 (1H NMR).

1H NMR (400 MHz, CDCl3): δ = 2.30 (s, 3 H, ortho), 2.31 (s, 3 H, para), 2.33 (s, 3 H, meta), 2.74 (s, 3 H, ortho), 2.76 (s, 3 H, para), 2.77 (s, 3 H, meta), 4.78 (2 H, ortho), 4.81 (s, 2 H, para), 4.83 (s, 2 H, meta), 6.99–7.03 (m, 1 H, meta), 7.12–7.35 (m, 11 H, ortho, meta, para).

13C NMR (100 MHz, CDCl3): δ = 18.0, 21.1, 21.6, 62.1, 62.4, 62.6, 75.2, 75.3, 75.4, 95.2, 95.3 (2 x), 119.7, 123.1, 123.3, 126.6, 127.5, 128.2, 128.9, 129.4, 129.6, 131.2, 136.2, 136.7, 136.9, 139.7, 138.6, 139.0, 152.6, 152.7, 153.5.

The analytical data of all the products 3 are listed below. The physical and spectral data of all these compounds well matched those previously reported.

3,3,3-Trichloro-N-(2,5-dimethylphenyl)-N-methoxypropanamide 3ac
Pale yellow oil; yield: 119.2 mg (73%); mixture of rotamers.

1H NMR (400 MHz, CDCl3): δ = 2.29 (s, 3 H), 2.30 (s, 3 H), 2.33 (s, 3 H), 2.34 (s, 3 H), 3.77 (s, 3 H), 3.79 (s, 3 H), 4.83 (m, 2 H), 7.03–7.05 (m, 1 H), 7.09–7.13 (m, 3 H), 7.15–7.19 (m, 2 H).

13C NMR (100 MHz, CDCl3): δ = 17.4, 17.7, 20.8, 21.2, 61.8, 62.0, 75.1, 95.3, 127.2, 128.0, 128.5, 130.1, 130.8, 131.8, 133.3, 134.5, 136.3, 136.8, 139.4, 153.4, 153.5.

N-(Bromophenyl)-3,3,3-trichloro-nitropropanamide 3ad
Following the typical procedure for 3aa using 1b’ (3 mol%), reaction time: overnight; pale yellow oil; yield: 81.0 mg (40%); ratio ortho/meta/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 = 62.8, 63.0, 75.5 (2 x), 95.0 (2 x), 119.6, 123.4, 123.6, 128.4, 129.2, 130.1, 133.7, 138.0, 138.1, 152.3, 153.2.

Benzy1 Methoxy(tolyl)carbamate 3ba
Following the typical procedure for 3aa using 1b (3 mol%) gave 3ba which was separated by column chromatography to give ortho-3ba and a mixture of meta-3ba and para-3ba; ratio ortho/meta/para 2.6:1:2.2 (1H NMR).

Benzy1 Methoxy(2-tolyl)carbamate (ortho-3ba)
Colorless oil; yield: 38.3 mg (33%).

1H NMR (400 MHz, CDCl3): δ = 2.23 (s, 3 H), 3.71 (s, 3 H), 5.20 (s, 2 H), 7.16–7.38 (m, 9 H).
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-Dioxoisooxindolin-2-yl)-N-(4-toly)acetamide (para-3ea)**

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

**N-(1,3-Dioxoisooxindolin-2-yl)-N-(4-toly)acetamide (ortho-3ea)**

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

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

Following the typical procedure for 3aa using catalyst Ib gave 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-tert-Butylphenyl-N-(3,4-dimethylphenyl)acetamide (5ai)**

Following to the typical procedure for 3aa, but using the μ-oxo catalyst la’ (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 5ai; yellowish oil; yield: 44.4 mg (75%).

IR (KBr): 2966, 2869, 1675, 1608, 1509, 1369, 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 la’ (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.

**7,5-Diacetoxy-5,7-dihydroxy-1,3,9,11-tetramethylidibenzo[d,f][1,3,2]dioxadipin (Ib) (Figure 1)**

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'-diodo-4,4',6,6'-tetramethylidibenzophenil (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 Ib, which was then recrystallized from MeCN/hexane solution. For cry- stallographic data of Ib, see CCDC 779814.

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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:

(17) X-ray crystal structure data of PIFA: (a) Stergioudis, G. A.; Kokkou, S. C.; Bozopoulos, A. P.; Rentzepis, P. J. Acta Crystallogr., Sect. C 1994, 40, 877. PIDA: (b) Lee, C.-K.; Mak, T. C. W.; Li, W.-K. Acta Crystallogr., Sect. B 1977, 33, 1620. (c) The reported bond lengths of iodine(III) ligands in the hypervalent iodine reagents, PIDA and PIFA as well as μ-oxo-bridged PIFA dimer and our biaryl alternative Ib (see Figure 1 for the structures), are summarized in Table 2 below.

### Table 2 Bond Lengths

<table>
<thead>
<tr>
<th>Reagent</th>
<th>I–X [Å]</th>
<th>I–O* [Å]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph(OCOAc)$_2$</td>
<td>2.16 (X = OAc)</td>
<td>-</td>
</tr>
<tr>
<td>Ph(OCOCF$_3$)$_2$</td>
<td>2.16 (X = OCOCF$_3$)</td>
<td>-</td>
</tr>
<tr>
<td>μ-oxo-bridged PIFA dimer</td>
<td>2.27 (R = CF$_3$)</td>
<td>2.02</td>
</tr>
<tr>
<td>our μ-oxo catalyst Ib</td>
<td>2.23 (R = R' = Me)</td>
<td>2.06 (X = OAc)</td>
</tr>
</tbody>
</table>

* a Averaged bond length for the reagents; O*: bridged oxygen.

* For the crystallographic data in CIF, see CCDC 779814.

(28) The existence of strong secondary bondings between the iodine atoms and the ligand’s carbonyl oxygens appears in the structure, which was confirmed by the lower shift of carbonyl frequencies for the μ-oxo PIFA in the infrared resonance spectra compared to that of PIFA. These observations clearly account for the enhanced cationic character of the iodine center, see: (a) Alcock, N. W.; Countryman, R. M.; Esperas, S.; Sawyer, J. F. J. Chem. Soc., Dalton Trans. 1979, 854. (b) Alcock, N. W.; Harrison, W. D. J. Chem. Soc., Dalton Trans. 1984, 1709. (c) Bell, R.; Morgan, K. J. Chem. Soc. 1960, 1209.


(34) For the reactivities of diaryliodonium(III) salt, see: (a) Merritt, E. A.; Olofsson, B. Angew. Chem. Int. Ed. 2009, 48, 9052.
(b) Yusubov, M. S.; Maskaev, A. V.; Zhdkankin, V. V. ARKIVOC 2011, (j), 370. (c) Olofsson, B. Top. Curr. Chem. 2016, 373, 135.


(43) Utilizing our spirorbindane 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.
