ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2025, **61**, 756

Received 28th September 2024,
Accepted 6th December 2024

DOI: 10.1039/d4cc05058d

rsc.li/chemcomm

N-Heterocycle-coordinated λ^5-iodanes as IBX alternatives for alcohol oxidations†

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We report the synthesis of novel N-coordinated λ^5-iodanes as a unique class of hypervalent iodine compounds. X-ray diffraction analysis revealed their intriguing (pseudo)cyclic structure, showcasing distinctive N···I-secondary bonding interactions. We demonstrate the *in situ* generation of reactive diacetoxy derivatives, which exhibits remarkable efficacy in alcohol oxidation reactions. Thermal stability assessments using TGA/DSC analysis provide crucial insights into the handling and potential applications of these compounds. This work expands the frontier of hypervalent iodine chemistry, offering new tools for selective oxidation reactions.

λ^5-Iodanes are widely applied in selective oxidations of alcohols,[1,2] amines[3] and phenols.[4] The pentavalent iodine derivatives can be considered as the close-to-perfect metal-free oxidants possessing a high potential for selective dehydrogenations of carbonyl compounds[5] or N-heterocycles,[6] the oxidative cleavage of unsaturated bonds,[7] and many more.[8,9]

The majority of λ^5-iodanes are O-tethered species.[8] 2-Iodoxybenzoic acid (IBX) and Dess–Martin periodinane (DMP) are the most widespread derivatives among them due to their established preparation methods and predictable selectivity. Despite its widespread use, IBX's limited solubility and low ambient reactivity remain challenging. The development of new λ^5-iodanes remains crucial, as even DMP, a more soluble and active IBX analogue, suffers from moisture sensitivity.[10] Different approaches were proposed to overcome these downsides. The functionalization of both C-ligands[10–15] and O-ligands[16–18] was used to improve reactivity and solubility of the iodanes. Another route to advanced hypervalent iodine reagents is the (pseudo)cyclic derivatives exhibiting secondary bonding interactions (*e.g.*, halogen bonding) which partially break problematic polymeric structures and hence increase solubility.[19] Many examples of (pseudo)cyclic λ^5-iodanes have been introduced over the past years and their majority utilizes an oxygen atom as an electron donor for these secondary interactions (Fig. 1A).[20–35]

To the best of our knowledge there are few examples of N-tethered (pseudo)cyclic λ^5-iodanes in the literature (Fig. 1B).[36–40] Derivatives introduced by Birman[37] and Powers[38] showed poor

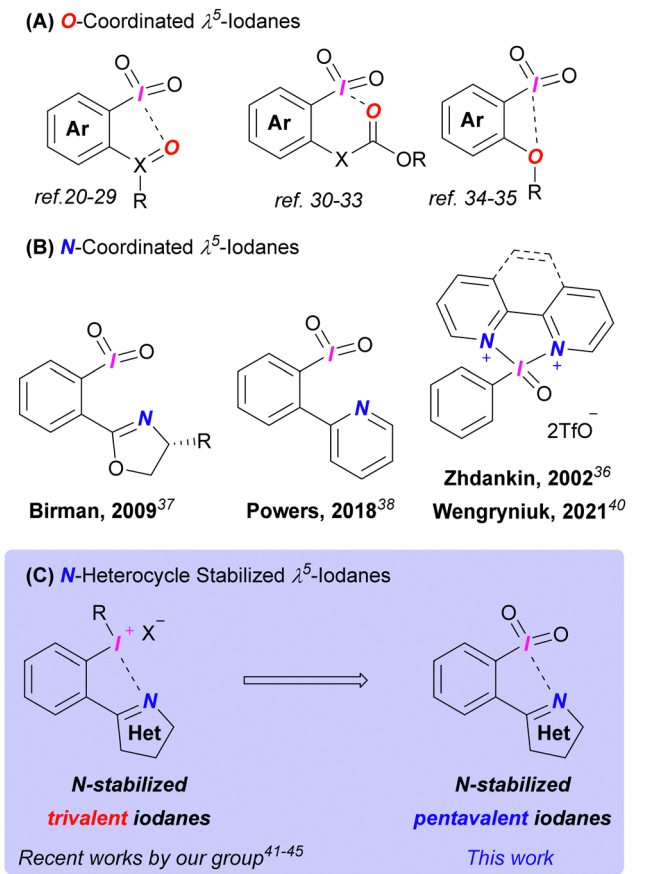

Fig. 1 Background and the concept of this work.

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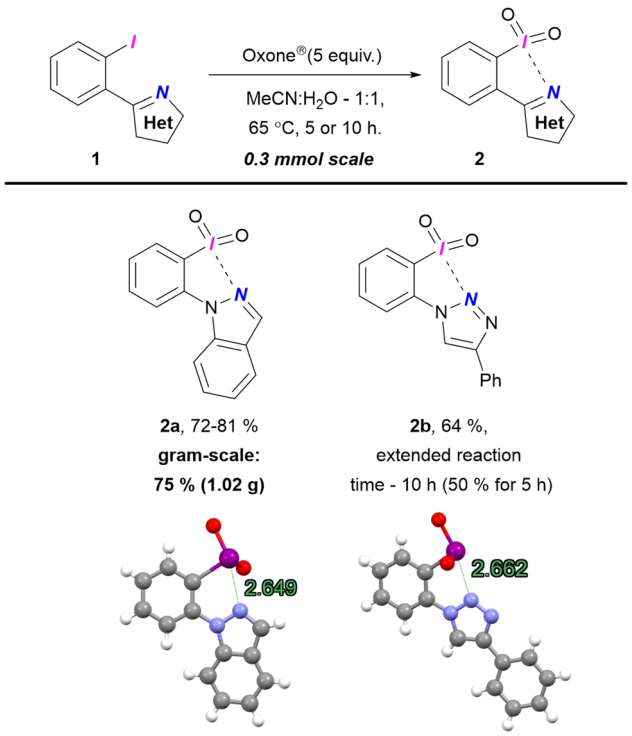
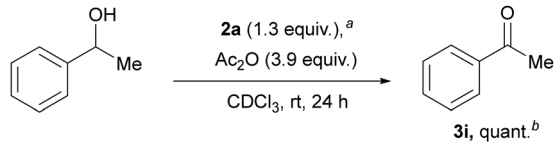
† Electronic supplementary information (ESI) available. CCDC 2364396–2364398. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d4cc05058d

reactivity. A bipyridyl derivative established by Zhdankin in 2002 was not applied so far in synthetic applications,[36] until a series of similar pentavalent iodanes were presented by Wengryniuk's lab.[39,40] These derivatives possessed unique reactivity compared to O-ligated iodanes (*e.g.*, oxidation of electron-deficient phenols)[39] alongside with common oxidative properties toward alcohols and sulfides.[40] However, these compounds are not "bench-stable" and there is no experimental evidence of **N···I** coordination in any of the abovementioned iodanes. Based on our previous work[41–45] and Wengryniuk's recent findings,[39,40] we herein developed novel N-heterocycle-coordinated (pseudo)-cyclic λ^5-iodanes and report their structure, reactivity in alcohol oxidations, and thermal stability.

Initially, we synthesized λ^5-iodanes **2a** and **2b** using Oxone® in MeCN : H_2O (Scheme 1). Iodane **2a** was obtained in 5 h with full conversion, with a yield of 72–81% across multiple preparations. A gram-scale synthesis of **2a** yielded 75% (1.02 g). For iodide **1b**, incomplete conversion resulted in 50% yield of **2b**. Extending the reaction to 10 h improved the yield to 64% but further extension to 15 h reduced it to 48% due to decomposition. X-Ray analysis confirmed the structures of iodanes **2a–b**, revealing **N···I** secondary interactions with contact lengths of 2.649 Å and 2.662 Å, respectively (ESI,† Section S7). These distances are comparable to those in five-membered (pseudo)-cyclic O-tethered iodanes (2.40–3.04 Å), confirming (pseudo)-cyclic nature of **2a–b**.[19] This work presents the first confirmed (pseudo)cyclic λ^5-iodanes with intramolecular **N···I** interaction. Unlike the previously reported intermolecular example that forms less soluble polymeric structures,[35] our (pseudo)cyclic iodanes **2a–b** show improved solubility in water, organic solvents, and weak acids, likely due to the basic tertiary nitrogen in the heterocycles.



Scheme 1 Preparation of λ^5-iodanes **2a–b**.

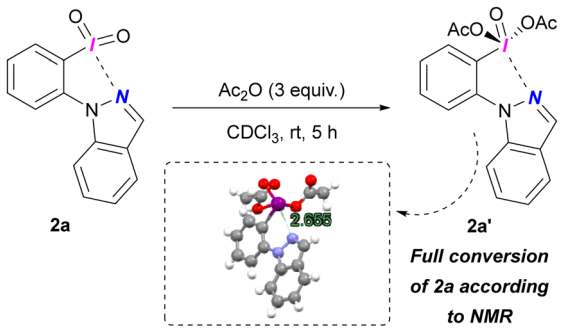


Scheme 2 Optimized conditions of the alcohol oxidation with iodane **2a**.[a] Reaction conditions: 0.1 mmol of 1-phenylethanol (0.1 mmol, 12 mg), **2a** (0.13 mmol, 46 mg), Ac_2O (0.39 mmol, 36.6 μL), $CDCl_3$ (2 mL). [b] Yield was determined by NMR with 1,2-dibromoethane as an internal standard.

TGA/DSC analysis revealed the thermal stability of iodanes **2a–b** compared to IBX (ESI,† Section S6). Triazole derivative **2b** showed a decomposition energy of 823.2 J g^{-1} at 218.5 °C, exploding violently. Derivative **2a** decomposed at 202.6 °C with 396.3 J g^{-1}, lower than IBX (506.8 J g^{-1} at 220.1 °C), suggesting **2a** is safer regarding explosive properties. Both new derivatives meet the "100 K rule" for thermal stability, indicating safe use under ambient conditions.[46] It is also worth mentioning, that no explosions of both **2a** and **2b** were experienced under severe impact with a metal hammer. However, for **2a–b** as well as for IBX we observed explosion under rapid heating (*e.g.*, with a heat gun). Therefore, these compounds should be operated with precautions.

We investigated the oxidation of 1-phenylethanol as a model reaction to evaluate iodanes **2a–b** (ESI,† Section S4 and Table S1 and Note S1 for details on optimization and preparation of carbonyl compounds **3**). Iodane **2a** demonstrated superior reactivity compared to **2b**. Then various additives were explored, particularly anhydrides, which could potentially form more reactive carboxy-ligated iodane species.[10] Using a three-fold excess of Ac_2O relative to **2a** in $CDCl_3$ provided **3i** in quantitative yield (Scheme 2), while lower anhydride ratios reduced yields. Although TFAA proved to be highly active for the oxidation, rapid alcohol acylation diminished the yield of ketone **3i**. A control experiment using twice the amount of AcOH compared to Ac_2O yielded only traces of **3i**, indicating the *in situ* formation of (diacetoxy)iodylbenzene **2a′** from **2a** and Ac_2O rather than acid-catalyzed activation.

We successfully generated diacetate **2a′** from treating iodane **2a** with Ac_2O (Scheme 3). ^1H NMR confirmed full conversion of **2a**. Despite high moisture sensitivity preventing isolation, we



Scheme 3 Preparation of diacetate **2a′**.

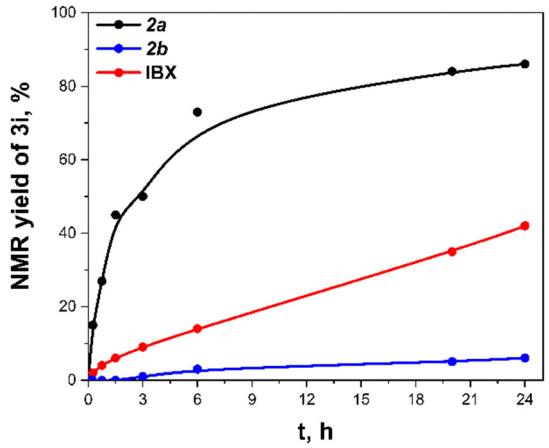


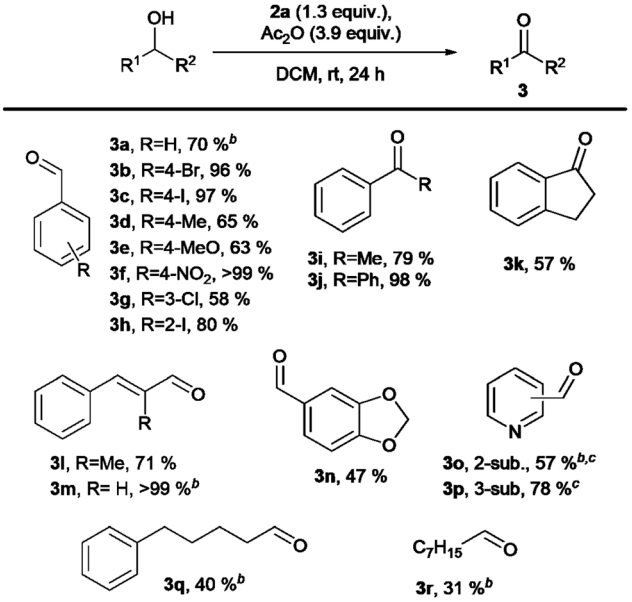
Fig. 2 Reactivity comparison between **2a–b** and IBX.

confirmed the structure of **2a′** by X-Ray diffraction, revealing a (pseudo)cyclic structure with an **N···I** contact distance of 2.655 Å (ESI,† Section S7).

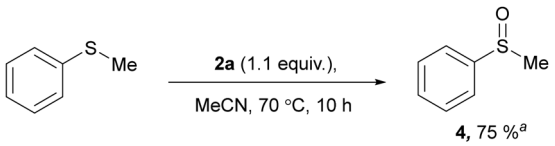
A reactivity comparison of iodanes **2a–b** with IBX under optimal conditions (Fig. 2) (conditions from Scheme 2) revealed that **2a** is superior to IBX in oxidizing 1-phenylethanol to acetophenone **3i**. This enhanced performance is likely due to the easier formation of acetoxy derivative **2a′** compared to acetoxylated IBX derivatives, which require substantial heating, *p*-TsOH catalysis, and Ac_2O as a solvent.[47] When conducted open to atmosphere, the reaction yielded 96% of **3i**, compared to quantitative yield in a closed vessel (ESI,† Section S5, Note S2). This suggests the discrepancy between quantitative yield during optimization and 86% yield in comparison experiments stems from unreacted iodane **2a** present in samples during the initial hours. It is also noteworthy that the iodane **2a′** is more active than acyclic (diacetoxy)iodylbenzene since the latter one gave no oxidation product after 24 hours.[40] We linked that fact with the increased solubility of (pseudo)cyclic derivative **2a′**. Furthermore, the iodane **2a′** in contrast to diacetate of IBX ester introduced by Zhdankin do not require activation by TFA.[26]

Finally, under our optimal conditions, we investigated the oxidation of a variety of alcohols using **2a** (Scheme 4). The oxidation generally yielded carbonyl compounds **3** in good to excellent yields. The observed moderate yields for **3k** and **3n** were due to isolation challenges, while lower yields of aldehydes **3d**, **3e**, and **3g** were primarily attributed to product volatility rather than incomplete conversion or overoxidation. For alcohols containing basic nitrogen atoms (aldehydes **3o–p**), we used TFA instead of Ac_2O to avoid acylation side products. This approach gave 57% yield for **3o** and 78% for **3p**. Primary alcohols were oxidized to aldehydes **3q** and **3r** in 40% and 31% yields, respectively, though complete conversion required more than 24 h. Beyond alcohol oxidation, iodane **2a** effectively converted thioanisole to sulfoxide **4** in 75% yield (Scheme 5). Attempts to synthesize α,β-unsaturated ketones from 4-methylcyclohexanone were unsuccessful under various conditions (ESI,† Section S5).

In conclusion, we developed novel N-heterocycle coordinated (pseudo)cyclic λ^5-iodanes, providing the first experimental evidence



Scheme 4 Reaction scope. [a] Isolated yields unless otherwise stated. Reaction conditions: 0,1 mmol of an alcohol, 0.13 mmol of λ^5-iodane, λ^5-iodane was premixed with Ac_2O (0.39 mmol, 37 μL) in 1 mL of the solvent for 30 minutes and alcohol was added afterwards as the solution (1 mL, 2 mL for a reaction in total). [b] Yields were determined by NMR with 1,2-dibromoethane as an internal standard. [c] TFA (0.39 mmol, 30 μL) instead of Ac_2O.



Scheme 5 Oxidation of thioanisole. [a] Isolated yield.

of intramolecular N-coordination in pentavalent iodine derivatives *via* X-Ray data. Iodanes **2a–b** show unique solubility and form reactive species like diacetate **2a′**. The *in situ* generated **2a′** oxidizes alcohols to carbonyl compounds **3** in 47% to quantitative yields, outperforming IBX under similar conditions. Thermal stability analysis suggests **2a** as a potentially safer, less explosive alternative to IBX.

This work was supported by the Russian Science Foundation (No. 23-73-10091). NSA is personally thankful to the DAAD Research Grants – Short-Term Grants program.

Data availability

The data supporting this article have been included as part of the ESI† (NMR spectra). Crystallographic data for **2a**, **2a′** and **2b** compounds has been deposited at the CCDC under 2364396, 2364397, 2364398 correspondingly.

Conflicts of interest

There are no conflicts to declare.

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