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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} amines³ 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 compounds⁵ 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

^b Institut für Organische und Analytische Chemie, Universität Bremen, Leobener Straße NW2C, 28359 Bremen, Germany. E-mail: nachtsheim@uni-bremen.de 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 Birman³⁷ and Powers³⁸ showed poor



Fig. 1 Background and the concept of this work.

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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: H₂O (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 $N \cdots I$ 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** \cdots **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



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), Ac₂O (0.39 mmol, 36.6 μ L), CDCl₃ (2 mL). ^{*b*} Yield was determined by NMR with 1,2-dibromoethane as an internal standard.

solvents, and weak acids, likely due to the basic tertiary nitrogen in the heterocycles.

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 Ac₂O relative to 2a in CDCl₃ 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 Ac₂O yielded only traces of 3i, indicating the *in situ* formation of (diacetoxy)iodylbenzene 2a' from 2a and Ac₂O rather than acid-catalyzed activation.

We successfully generated diacetate 2a' from treating iodane 2a with Ac₂O (Scheme 3). ¹H NMR confirmed full conversion of 2a. Despite high moisture sensitivity preventing isolation, we



Scheme 3 Preparation of diacetate 2a'.

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confirmed the structure of 2a' by X-Ray diffraction, revealing a (pseudo)cyclic structure with an $N \cdots I$ 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 Ac₂O 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 30-p), we used TFA instead of Ac₂O to avoid acylation side products. This approach gave 57% yield for 30 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 Ac₂O (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 Ac₂O.



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.

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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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