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Organic Synthesis

Saccharin-Based μ-Oxo Imidoiodane: A Readily Available and Highly Reactive Reagent for Electrophilic Amination

Akira Yoshimura,*[a] Steven R. Koski,[a] Jonathan M. Fuchs,[a] Akio Saito,[b] Victor N. Nemykin,[a] and Viktor V. Zhdankin*[a]

Abstract: Three new saccharin-based hypervalent iodine compounds were prepared by the reaction of saccharine with (diacetoxyiodo)arenes or acetoxybenziodoxole. Structures of these new imidoiodanes were established by X-ray crystallography. The saccharin-based μ-oxo-bridged imidoiodane readily reacts with silyl enol ethers under mild conditions to give the corresponding α-aminated carbonyl compounds in moderate yields.

In recent years, hypervalent iodine reagents have emerged as environmentally friendly and efficient oxidizing reagents for various synthetically useful oxidative transformations.[1] Particularly important are hypervalent iodine(III) compounds with iodine–nitrogen bonds,[2] such as azidoiodanes,[2a–e] benziodazoles,[2f,g] amidobenziodoxoles,[2j] and iminoiodanes,[2j–o] all of which are efficient reagents for C–N bond forming reactions. Representative recent examples of synthetic applications of these reagents include direct azidation, amination, imidation, aziridination, metal-catalyzed imidation, and C–H insertion reactions.[2] Most of these studies[2] were performed by using cyclic or pseudocyclic hypervalent iodine reagents; in contrast, non-cyclic imidoiodanes of the types $ArI(NR_2)_2$ or $ArI(NR_2)OR$ are uncommon compounds and, with a few exceptions, their reactivity has not been investigated. In particular, Varvoglis and co-workers first reported the synthesis and reactions with ketones of several hypervalent iodine(III) bisimidiates, such as bis(saccharin)iodobenzene, bis(succinimide)iodobenzene, and bis(phthalimido)iodobenzene.[3] More recently, Muniz and co-workers have reported the preparation of new bis(imido)iodobenzenes, acetoxy(imido)iodobenzenes, and μ-oxo-bridged bis(imido)iodobenzenes, and these compounds were characterized by X-ray crystallography. The same group has also demonstrated that these new imidoiodanes are useful nitrogen transfer reagents in reactions with alkenes, alkynes, and allenes.[4] Togo and co-workers have reported the nitrogen-containing hypervalent iodine(III) compound, bis(phthalimido)iodobenzene, as an active intermediate species in the Hofmann rearrangement reaction.[5] Minakata and co-workers have also described the oxidative decarboxylative nitrogenation reaction of β,γ-unsaturated carboxylic acids by using bis(ditosylimido)iodobenzene or bis(phthalimido)iodobenzene as the nitrogen source.[6]

In a search for readily available electrophilic aminating reagents with enhanced reactivity, we decided to investigate saccharin-based μ-oxo-bridged imidoiodanes. The μ-oxo-bridged hypervalent iodine derivatives are known compounds and several examples of their crystal structures have been previously reported.[7] Enhanced reactivity of μ-oxo-bridged hypervalent iodine(III) compounds has been reported by Kita[8a–g] and other groups.[8h,i] However, to the best of our knowledge, μ-oxo-bridged imidoiodanes derived from cyclic imides have not been previously reported.

Herein, we report the design, preparation, structural investigation, and reactivity of new μ-oxo-bridged bis(saccharin)iodobenzene and several other saccharin-based hypervalent iodine compounds.

The μ-oxo-bridged bis(saccharin)iodobenzene **1a** was synthesized in moderate yield by a one-pot procedure from (diacetoxyiodo)benzene (1.0 equiv) and saccharin (1.1 equiv) in methylene chloride in the presence of water by stirring for 24 h at room temperature (Scheme 1). For comparison, two additional saccharin derivatives, bis(saccharinyl)iodobenzene **1b** and saccharinylbenziodoxole **1c**, were also prepared from saccharin and the corresponding iodine(III) acetates (Scheme 1). Two of these saccharin derivatives, **1a** and **1c**, were characterized by single-crystal X-ray crystallography.

X-ray crystal data for products **1a** and **1c** demonstrate the presence of both iodine–nitrogen and iodine–oxygen bonds in the molecule (Figure 1). The lengths of these bonds are similar to the previously reported structures of imidoiodanes and μ-oxo-bridged iodine(III) compounds.[2b,4f,g,7]

In the initial reactivity study of compounds **1**, we investigated the α-saccharinization reaction by using the silyl enol ether of acetophenone **2a** (1 equiv) with μ-oxo-bridged bis(saccharinyl)iodobenzene **1a** as the nitrogen source (0–2 equiv) under various reaction conditions in the presence of trifluoromethanesulfonic acid as additive (1 equiv). In the absence of iodine(III) reagent **1a**, the reaction of silyl enol ether **2a** and sac-

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[a] Dr. A. Yoshimura, S. R. Koski, J. M. Fuchs, Prof. Dr. V. N. Nemykin, Prof. Dr. V. V. Zhdankin
Department of Chemistry and Biochemistry
University of Minnesota Duluth, Duluth, MN 55812 (USA)
E-mail: ayoshimu@d.umn.edu
vzhdanki@d.umn.edu
Homepage: http://www.d.umn.edu/~vzhdanki/

[b] Prof. Dr. A. Saito
Division of Applied Chemistry, Institute of Engineering
Tokyo University of Agriculture and Technology
2-24-16 Naka-cho, Koganei, Tokyo 184-8588 (Japan)

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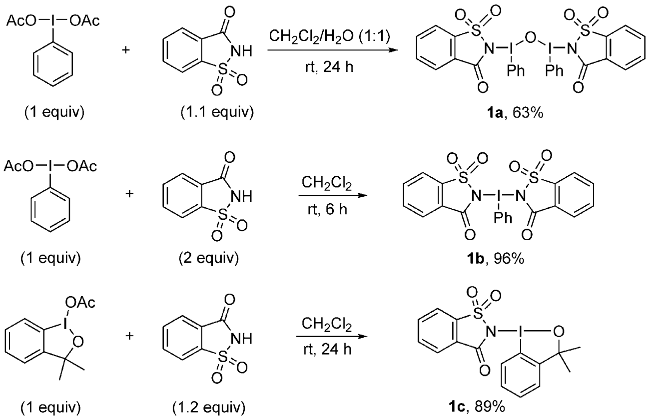


Scheme 1. Preparation of saccharin-based hypervalent iodine(III) compounds **1a–1c**.

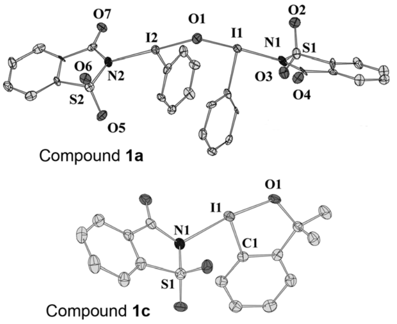
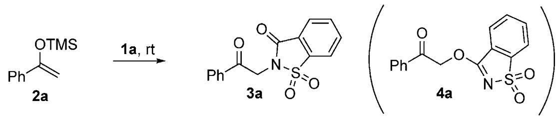


Figure 1. X-ray crystal structures of compounds **1a** and **1c**.

charine failed to produce the desired product **3a** (Table 1, entry 1), whereas in the presence of reagent **1a** the reaction resulted in the formation of product **3a** (entry 2). Comparison of different solvents demonstrated that acetonitrile is most suited for this reaction (Table 1, entries 2–7). Further studies revealed that reactions in acetonitrile in the absence of trifluoromethanesulfonic acid afforded product **3a** in improved yield (69% yield, entry 8), and decreasing the amount of iodine(III) reagent **1a** from 1 to 0.6 equivalents did not reduce the yield of product **3a** (entry 9). An isomeric product of O-alkylation, compound **4a**, was also isolated in this reaction as a minor product (29% yield, entry 9). Structures of isomeric products **3a** and **4a** were established by single-crystal X-ray analysis (see the Supporting Information for details). The similar reactions of silyl enol ether **2a** with reagents **1b** and **1c** afforded products **3a** and **4a** in lower yields, which demonstrates that μ-oxo-bridged reagent **1a** has higher reactivity compared with **1b** and **1c**.

Table 1. Optimization of α- saccharinization of silyl enol ether **2a**.[a]



Entry	1a [equiv]	Solvent	t [h]	3a [%][b]
1[c]	0	MeCN	24	0
2[c]	1	MeCN	24	56
3[c]	1	Et_2O	24	<1
4[c]	1	$CHCl_3$	24	<1
5[c]	1	acetone	24	23
6[c]	1	MeOH	24	17
7[c]	1	EtOAc	24	0
8	1	MeCN	12	69
9	0.6	MeCN	2	70 (68)[d]
10[e]	0.6	MeCN	2	37 (33)
11[f]	1.2	MeCN	2	35 (32)
12[g]	0.6	MeCN	24	1

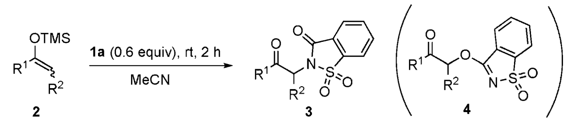
[a] Reactions were performed in the specified solvent at room temperature for several hours using iodine(III) reagent **1a** (0–1 equiv), and silyl enol ether **2a** (1 equiv). [b] Yields of product **3a** were determined from ^1H NMR spectra of reaction mixtures (numbers in parentheses show yields of isolated product **3a**). [c] Trifluoromethanesulfonic acid (1 equiv) was used as additive in this reaction. [d] Isomeric byproduct **4a** was isolated in 29%. [e] Iodine(III) reagent **1b** was used instead of **1a**. [f] Iodine(III) reagent **1c** was used instead of **1a**. [g] Acetophenone was used instead of **2a**.

Using the optimized reaction conditions, we investigated the conversion of various substituted silyl enol ethers, **2**, to the respective α-saccharinated derivatives, **3**, and isomeric byproducts, **4** (see the Supporting Information). In general, all aryl-substituted silyl enol ethers with electron-donating or electron-withdrawing substituents in the aromatic ring afforded the corresponding α-saccharinated products **3** in moderate to good yields (Table 2, entries 1–9). In the reactions of heteroaromatic (2-furanyl and 3-pyridine) silyl enol ethers, both isomeric products **3** and **4** were obtained in comparable yields (entries 10 and 11 and the Supporting Information). It is noteworthy that the reactions of silyl enol ethers of secondary ketones under optimized conditions gave the C–N bonded products **3** in lower yields (entries 12–15), whereas the C–O bonded structural isomers **4** were the major products isolated in 52–74% yield (see the Supporting Information). Similar selectivity trends in the oxidative imidation reactions of ketones were previously reported by other groups, and our results are in agreement with these reports.[9] The structures of **3j** and **4l** were established by single-crystal X-ray analysis (see the Supporting Information for details).

Recently, Kita and co-workers have reported that heterocyclic dinuclear hypervalent iodine(III) reagents (e.g., compound **5** in Scheme 2) demonstrate especially high reactivity in oxidative spirolactamization reactions.[8a–g] Thus, we have prepared the similar dinuclear heterocyclic disaccharin derivative **6** (Scheme 2). The structure of product **6** was established by single-crystal X-ray analysis (Scheme 2, see the Supporting Information for details). We tested compound **6** in the α-saccharinization reaction with **2a** under our optimized conditions. No products **3a** and **4a** were formed in these reactions, which may be explained by the steric bulkiness and rigidity of the structure of compound **6**.[8a]

In conclusion, we have reported the preparation, X-ray structure, and reactivity of new μ-oxo-bridged saccharin-derived hypervalent iodine(III) reagent **1a**. This new reagent reacts with silyl enol ethers under mild conditions, affording products of α-saccharinization in moderate yields.

Table 2. Reactions of silyl enol ether **2** with μ-oxo reagent **1 a** under optimized conditions.[a]



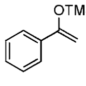
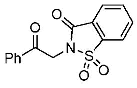
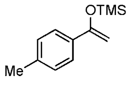
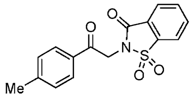
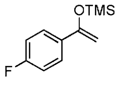
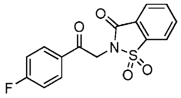
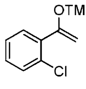
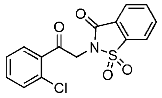
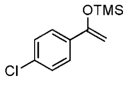
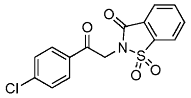
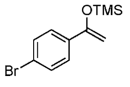
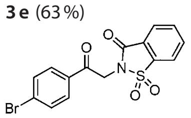
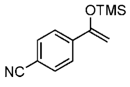
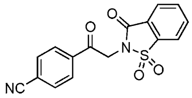
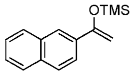
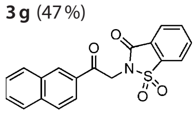
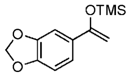
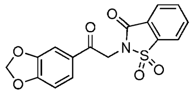
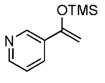
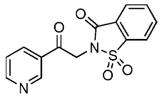
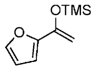
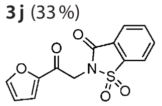
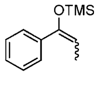
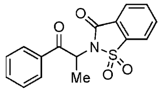
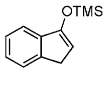
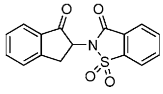
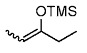
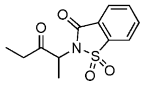
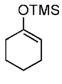
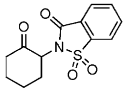
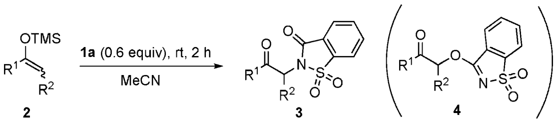
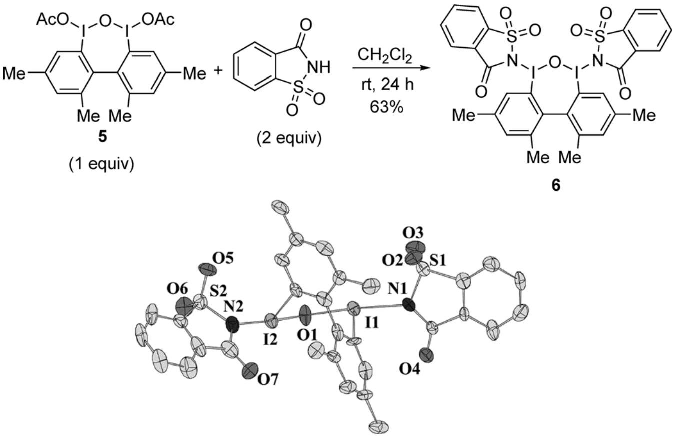
Entry	2	Product 3 [yield][b,c]
1	 **2 a**	 **3 a** (68 %)
2	 **2 b**	 **3 b** (60 %)
3	 **2 c**	 **3 c** (62 %)
4	 **2 d**	 **3 d** (62 %)
5	 **2 e**	 **3 e** (63 %)
6	 **2 f**	 **3 f** (61 %)
7	 **2 g**	 **3 g** (47 %)
8	 **2 h**	 **3 h** (54 %)
9	 **2 i**	 **3 i** (46 %)
10	 **2 j**	 **3 j** (33 %)
11	 **2 k**	 **3 k** (43 %)
12	 **2 l**	 **3 l** (24 %)
13	 **2 m**	 **3 m** (22 %)
14	 **2 n**	 **3 n** (40 %)
15	 **2 o**	 **3 o** (23 %)

Table 2. (Continued)



[a] All reactions of **1 a** (0.6 equiv) with silyl enol ethers **2** were performed in MeCN at room temperature for 2 h. [b] Yields of isolated products. [c] Isomeric products **4** were also isolated from the reaction mixture (see the Supporting Information).



Scheme 2. Preparation and X-ray crystal structure of heterocyclic dinuclear hypervalent iodine reagent **6**.

Experimental Section

Synthesis of 1 a

Water (2 mL) was added to a stirring mixture of (diacetoxyiodo)-benzene (322 mg, 1.0 mmol) and saccharin (202 mg, 1.1 mmol) in CH_2Cl_2 (2 mL). The reaction was stirred at 25 °C for 24 h. After completion of the reaction, the precipitate was filtered and washed with dichloromethane, then washed several times with diethyl ether and dried in vacuum to give compound **1 a** (481 mg, 61 %) as a white solid.

Typical reaction of 1 a with 2

Freshly prepared silyl enol ether **2** (0.25 mmol) was added to a solution of μ-oxo imidoiodane **1 a** (118 mg, 0.15 mmol) in acetonitrile (1.5 mL). The reaction mixture was stirred at room temperature for 2 h (monitored by TLC for full conversion of silyl enol ether **2**). The resulting solution was concentrated under reduced pressure. Purification by column chromatography on silica gel (hexane/ethyl acetate, 1:1) afforded analytically pure α-imide compounds **3** and α-oxy compounds **4**.

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Keywords: amination · hypervalent · iodine · oxidation · saccharin

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