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2-Iodoxybenzenesulfamides: new pseudobenziodoxole-based hypervalent iodine reagents

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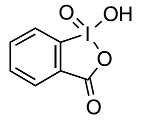
Abstract—Amides of 2-iodoxybenzenesulfonic acid were prepared by the dioxirane oxidation of the corresponding 2-iodobenzenesulfamides and isolated as stable, microcrystalline products. These new representatives of the pseudocyclic hypervalent iodine compounds can selectively oxidize benzylic alcohols to aldehydes.

Hypervalent iodine reagents based on the heterocyclic system of benziodoxole have recently emerged as reagents of choice for various synthetically useful oxidative transformations.[1] In particular, the heterocyclic λ^5-iodane-1-hydroxy-1,2-benziodoxol-3(1*H*)-one-1-oxide (IBX, **1**), has received a widespread application in organic synthesis as a highly efficient and mild oxidant that can be used for a selective oxidation of primary and secondary alcohols, and for a variety of other important oxidations.[1,2] However, despite its useful oxidizing properties, practical application of IBX is restricted due to the potentially explosive nature and the extremely low solubility of this reagent. Several research groups have tried to improve IBX by structurally modifying it,[3,4] or by developing the polymer supported analogs.[5] Recently, we reported the synthesis of IBX-amides (**2**)[4a] and IBX-esters (**3**),[4b] which are stable and soluble reagents having oxidizing properties similar to IBX. According to X-ray data, these new reagents (**2** and **3**) have the pseudobenziodoxole structure due to the intramolecular nonbonding iodine–oxygen interaction. In comparison with IBX and other benziodoxoles, pseudobenziodoxoles have much better solubility, which is explained by a partial disruption of their polymeric nature due to the redirection of I···O secondary bonding.[4] Very recently, Lee and co-workers reported the preparation of the polymer supported IBX-esters and IBX-amides, which showed excellent oxidative activity toward benzylic alcohols.[6]



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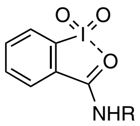

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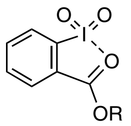

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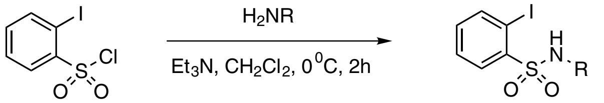
We now report the preparation of new pseudocyclic hypervalent iodine reagents by the oxidation of the readily available 2-iodobenzenesulfamides. The starting materials, amides **4** were obtained from 2-iodobenzenesulfonyl chloride[7] and the appropriate amino compounds, such as esters of natural amino acids (**4a**–**d**) or (*R*)-1-phenylethylamine (**4e**) (Scheme 1).[8]

Oxidation of iodoarenes **4** with dioxirane afforded 2-iodoxybenzenesulfamides **5** in good yield (Scheme 2).[9] All products were isolated by filtration of the reaction mixture in the form of stable, white, microcrystalline solids.



4a-e (43-71%)

a: R = (S)-$CH(CH_3)CO_2CH_3$
b: R = (S)-$CH(CH_2Ph)CO_2CH_3$
c: R = (S)-CH(i-Pr)CO_2CH_3
d: R = (S)-CH(i-Bu)CO_2CH_3
e: R = (R)-CH(Ph)CH_3

Scheme 1.

Keywords: Hypervalent iodine; Oxidation; Benziodoxole; IBX.

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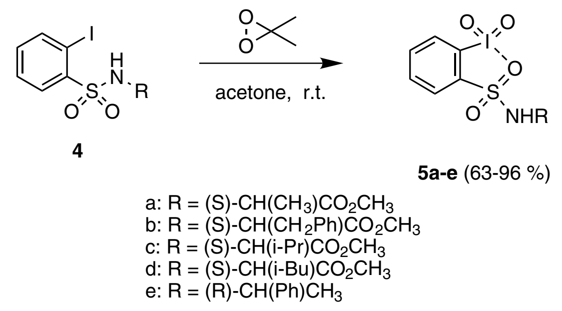

Scheme 2.

Products **5** were identified on the basis of spectroscopy data and elemental analysis. In particular, IR spectra of all compounds showed sulfonyl absorption at 1330–1340 cm^{-1}, the I=O absorption at 740–780 cm^{-1}, as well as the carbonyl stretch at 1720–1740 cm^{-1} for the amino acid derivatives **4a–d**. In ^{1}H NMR spectra, N–H protons were observed as doublets at 8.40–8.60 ppm in addition to the signals corresponding to the aromatic fragment and group R. In ^{13}C NMR of iodoxyarenes **5**, the most characteristic was the signal of C–IO_2 at 146 ppm. The ESI-HRMS spectra of compounds **5** demonstrated strong $[M+Na]^+$ peaks as well as weaker peaks corresponding to the dimers $[2M+Na]^+$, and the trimers $[3M+Na]^+$.

Based on the literature data on pseudobenziodoxoles,[4,10] we assume that compounds **5** have a planar cyclic structure due to a strong intramolecular secondary bonding between the hypervalent iodine center and the oxygen atom in the *ortho*-substituent. Several X-ray structures of pseudobenziodoxoles were reported in the literature,[4,10] including the 2-sulfonyl substituted iodylarene.[10a] However, in contrast to the previously reported pseudobenziodoxoles **2** and **3**,[4] compounds **5** have a relatively low solubility in nonpolar organic solvents such as chloroform and methylene chloride. Moreover, the presence of $2M^+$ and $3M^+$ peaks in the ESI-MS data indicates the oligomeric or polymeric structure of these compounds. A similar oligomeric assembly directed by a relatively weak intermolecular I···O secondary bonding and by hydrogen bonding between the amide proton of one molecules and an oxygen atom of the neighboring molecule was previously reported for IBX-amides **2**.[4a]

Preliminary experiments demonstrate that 2-iodoxybenzenesulfamides show aspects of reactivity similar to previously reported IBX-amides **2**. In particular, reagents **5a–e** can cleanly oxidize benzyl alcohol to benzaldehyde in chloroform at 50 °C (Table 1). Reagent **5e** shows the highest reactivity in this reaction and **5a** the lowest reactivity, which is probably explained by the lowest solubility of **5a** in chloroform.

Table 1. Oxidation of $PhCH_2OH$ with reagents **5** in $CHCl_3$ at 50 °C[a]

Entry	Reagent[b]	Reaction time (h)	Conversion[c] (%)
1	**5a**	22.5	20
2	**5b**	22.5	77
3	**5c**	22.5	43
4	**5d**	22.5	65
5	**5e**	17	100

[a] Benzaldehyde and the respective iodoarene **4** were the only reaction products detected by GC and NMR.
[b] The ratio of $PhCH_2OH$ to reagent **5** was 1:1.
[c] Determined by NMR.

The oxidation of benzyl alcohol by reagents **5** in DMSO under similar conditions afforded benzaldehyde with a very low conversion (0–7%). The low reactivity toward alcohols in DMSO can be explained by the formation of a stable complex of iodoxyarene **5** with a molecule of DMSO, which leads to a lower electrophilicity of the iodine reagent.[11]

In conclusion, we have reported the preparation of new pseudobenziodoxole-based pentavalent iodine compounds, amides of 2-iodoxybenzenesulfonic acid. Our preliminary experiments have demonstrated that these compounds are potentially useful reagents for mild oxidation of alcohols.

Acknowledgements

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8. *Representative experimental procedure for the preparation of 2-iodobenzenesulfamides* **4**: To a stirred, ice-bath cooled mixture of L-alanine ester hydrochloride (4.0 mmol) in

CH_2Cl_2 (40 mL), triethylamine (8.0 mmol, 1.11 mL), and 2-iodobenzenesulfonyl chloride (1.51 g, 5.0 mmol) were slowly added. After 2 h of additional stirring, water (40 mL) was added, and organic layer was separated. The organic layer was washed with 10% HC1 (1 × 20 mL). The solution was dried with $MgSO_4$ and the solvent evaporated to give a yellow solid. Recrystallization from ethyl acetate/hexane and drying in vacuum afforded 1.05 g (71%) of product **4a**, isolated as oil. IR (KBr): 3294, 2952, 1736, 1341, 1169 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.12 (dd, $J_1 = 7.8$ Hz, $J_2 = 1.7$ Hz, 1H), 8.08 (dd, $J_1 = 7.8$ Hz, $J_2 = 1.2$ Hz, 1H), 7.49 (td, $J_1 = 7.7$ Hz, $J_2 = 1.2$ Hz, 1H), 7.21 (td, $J_1 = 7.6$ Hz, $J_2 = 1.7$ Hz, 1H), 5.92 (d, $J = 7.8$ Hz, 1H), 4.01 (m, 1H), 3.56 (s, 3H), 1.41 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 171.9, 142.3, 142.1, 133.5, 130.8, 128.4, 92.7, 52.6, 51.8, 19.6. Anal. Calcd for $C_{10}H_{12}INO_4S$: C, 32.53; H, 3.28; N, 3.79; I, 34.37; S, 8.69. Found: C, 32.47; H, 3.30; N, 3.80; I, 34.20; S, 8.49.

9. *Representative experimental procedure for the preparation of 2-iodoxybenzenesulfamides* **5**: Freshly prepared 0.1 M solution of dimethyldioxirane in acetone (30 mL, 3 mmol) was added to a stirred mixture of compound **4d** (0.411 g, 1 mmol) in 5 mL of dry CH_2Cl_2 at 0 °C. The color of the solution immediately changed from colorless to light yellow. The reaction mixture was stirred at room temperature for an additional 8 h, the resulting white microcrystalline precipitate was collected by filtration, then hexane was added to the filtered solution, and precipitate was filtered, both solids were washed with ether, and dried in vacuum to afford 0.281 g (63 %) of product **5d**, mp 154–155 °C. IR (KBr): 3017, 2958, 1747, 1334, 1146, 805, 768 cm^{-1}; ^1H NMR (DMSO-d_6): δ 8.64 (d, $J = 8.6$ Hz, 1H, NH), 8.25 (d, $J = 7.8$ Hz, 1H), 7.99 (t, $J = 6.9$ Hz, 1H), 7.86 (m, 2H), 4.27 (m, 1H), 3.42 (s, 3H), 1.45 (m, 3H), 0.78 (d, $J = 6.3$ Hz, 3H), 0.61 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (DMSO-d_6): 172.0, 146.5, 137.4, 133.5, 132.1, 128.3, 123.6, 53.2, 51.9, 40.9, 23.9, 22.8, 20.9. Anal. Calcd for $C_{13}H_{18}INO_6S$: C, 35.23; H, 4.09; N, 3.16; I, 28.63; S, 7.23. Found: C, 34.97; H, 4.08; N, 3.17; I, 28.87; S, 7.20. ESI MS: m/z (%) 465.98 (100), $[M+Na]^+$, 908.9 (55), $[2M+Na]^+$, 1351.9 (6), $[3M+Na]^+$.

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