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Preparation, X-ray Structure, and Oxidative Reactivity of *N*-(2-Iodylphenyl)tosylamides and 2-Iodylphenyl Tosylate: Iodylarenes Stabilized by Ortho-Substitution with a Sulfonyl Group

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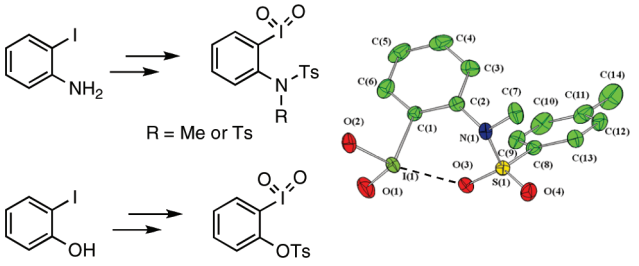
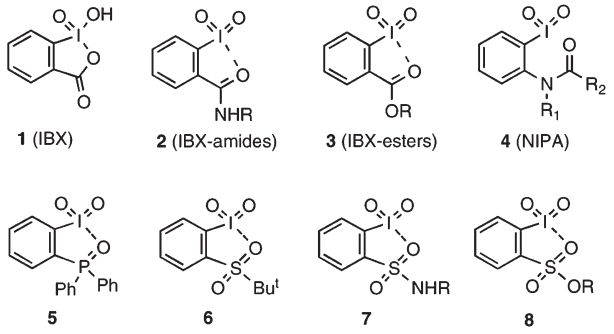


New tosyl derivatives of 2-iodylaniline and 2-iodylphenol were prepared by the dimethyldioxirane oxidation of the corresponding 2-iodophenyltosylamides or 2-iodophenyl tosylate and isolated as stable, microcrystalline products. Single-crystal X-ray diffraction analysis of *N*-(2-iodylphenyl)-*N*,4-dimethylbenzenesulfonamide revealed pseudocyclic structure formed by intramolecular I···O interactions between the hypervalent iodine center and the sulfonyl oxygens in the tosyl group. This tosylamide has an excellent solubility in organic solvents and is a potentially useful hypervalent iodine oxidant.

During the past decade the chemistry of pentavalent iodine oxidizing reagents has attracted a significant research interest.[1] Various types of hypervalent iodine(V) compounds (λ^5-iodanes) have been reported and some of them have emerged as reagents of choice for synthetically useful oxidative transformations due to their high chemoselectivity, mild reaction conditions, and environmentally benign nature. Cyclic and pseudocyclic hypervalent iodine reagents based on the benziodoxole system represent an especially important class of iodanes with rich and synthetically useful chemistry. In particular, the heterocyclic λ^5-iodane, 1-hydroxy-1-oxo-1*H*-1λ^5-benzo[*d*][1,2]iodoxol-3-one (**1**), known under the name of its tautomeric form of 2-iodoxybenzoic acid (IBX), has received widespread application in organic synthesis as a highly efficient and mild oxidant that can be used for selective oxidation of primary and secondary alcohols and for a variety of other important oxidations.[1,2] However, the explosive character and low solubility of IBX in common organic solvents except DMSO restrict practical application of this reagent.



The low solubility of IBX **1** arises from strong intermolecular secondary I···O contacts, hydrogen bonding, and π-stacking observed for IBX in the solid state.[3] Several research groups have tried to overcome this preparative limitation by performing oxidation at elevated temperatures,[4a] using an ionic liquid and water as a reaction medium,[4b] or functionalizing IBX aromatic core.[4c,d] Also, several solid-supported reagents in which IBX scaffold is linked to a polymer have been reported.[5] Another fruitful approach initially proposed by Protasiewicz[6] consists of incorporation of an ortho-substituent into

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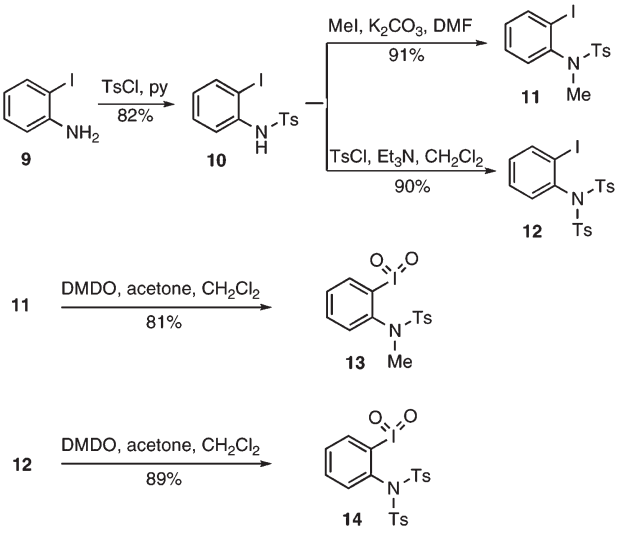
iodylarene (e.g., phosphine oxide **5**[6b] or sulfone **6**[6a]) thus resulting in intramolecular secondary bonding. This ortho-stabilization leads to a partial disruption of the polymeric network, and consequently enhances solubility. More recently, investigations from our group have resulted in a series of stable and soluble IBX analogues: IBX-amides **2**,[7a] IBX-esters **3**,[7b] as well as 2-iodylbenzenesulfonamides **7**[7c,d] and 2-iodylbenzenesulfonate esters **8**.[7e] According to X-ray data, a planar pseudo-benziodoxole moiety due to the intramolecular nonbonding iodine−oxygen interaction is a key structural feature present in this series of compounds.[6,7] Readily available hypervalent iodine reagents **2** and **3** possess reactivity similar to that of IBX and Dess−Martin periodinane, and proved to be useful oxidizing reagents toward alcohols[7] and sulfides.[8] The synthesis of polymer-supported IBX esters and amides has been reported as well.[9] Recently, we have described the preparation and oxidative reactivity of *N*-(2-iodylphenyl)acylamides (NIPA, **4**), which are soluble and stable IBX analogues having pseudo-benziodoxazine structure.[10]

To further explore the effects of ortho-substituents in the analogous to *N*-(2-iodylphenyl)acylamides **4** pseudo-six-membered heterocycles, we considered the preparation of iodylarenes derived from the readily available tosyl derivatives of 2-iodoaniline and 2-iodophenol. Herein we report the preparation and study of two new *N*-(2-iodylphenyl)tosylamides and the 2-iodylphenyl tosylate.

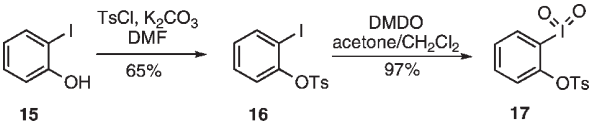
Synthesis of *N*-(2-iodylphenyl)tosylamides **13** and **14** was performed by the tosylation of commercially available 2-iodoaniline **9** with tosyl chloride in pyridine, followed by the alkylation of tosylamide **10** with iodomethane or additional tosylation with TsCl. Oxidation of the iodides **11** and **12** with 3,3-dimethyldioxirane according to the previously reported procedure[7e] afforded *N*-(2-iodylphenyl)tosylamides **13** and **14** in good yields (Scheme 1). Products **13** and **14** were isolated as white microcrystalline compounds and were analyzed by NMR spectroscopy. In particular, ^{13}C NMR spectra of both products **13** and **14** showed characteristic signals of the *ipso*-carbon, C-IO_2, at about 151 ppm, which is typical of iodylarenes.[7] Both iodylarene derivatives are stable at room temperature and do not possess any explosive properties upon heating or impact. A slow decomposition is observed during heating of compound **13** or **14** in a capillary tube above the melting point. Compound **13** has excellent solubility in chloroform and acetonitrile, while the bis-tosylate **14** has a relatively low solubility in organic solvents.

Synthesis of the *o*-tosyloxy-substituted iodylarene **17** was performed by tosylation of commercially available

SCHEME 1. Preparation of 2-Iodophenyltosylamides 13 and 14



SCHEME 2. Preparation of 2-Iodophenyl Tosylate 17



2-iodophenol **15**, using 4-toluenesulfonyl chloride in DMF, followed by the oxidation of the tosylate **16** with 3,3-dimethyldioxirane (Scheme 2). Product **17** was isolated as a white, stable microcrystalline compound in excellent yield and was identified by NMR spectroscopy and elemental analysis. Specifically, the NMR spectra of this product showed the appropriate pattern of protons and carbons and a signal of the *ipso*-carbon, C-IO_2, at about 147 ppm, which is comparable with the tosylamides **13** and **14**. The same as the tosylamides, the tosylate **17** is indefinitely stable at room temperature and does not have any explosive properties. It has a low solubility in nonpolar solvents, but is soluble in DMSO.

The structure of 2-iodophenyl tosylamide **13** was confirmed by single-crystal X-ray crystallography. The CAMERON diagrams of **13** are presented in Figures 1 and 2. The X-ray data reveal eight molecules of **13** located in the unit cell. The iodine atom forms two short I−O double bonds with O(1) and O(2) atoms and a single bond with C(1). In addition to these three covalent bonds, the molecular structure of **13** exhibits three short contacts between iodine center and oxygen atoms forming overall pseudo-octahedral configuration around iodine (Figure 2). These short contacts consist of one relatively weak intramolecular I···O interaction (I(1)−O(3), 3.035(3) Å) and two intermolecular interactions between I(1) and O(1A) as well as I(1) and O(4B) with the former being short (2.727(3) Å) and the later being relatively long (3.167(2) Å).

The intramolecular secondary bonding between the hypervalent iodine center and the oxygen atom in the ortho-substituent [I(1)···O(3) 3.035(3) Å] in **13** is noticeably weaker compared to the I···O secondary bonding of 2.647 Å previously reported for the pseudo-benziodoxazine structure **4** and close to the sum of van der Waals radii of iodine

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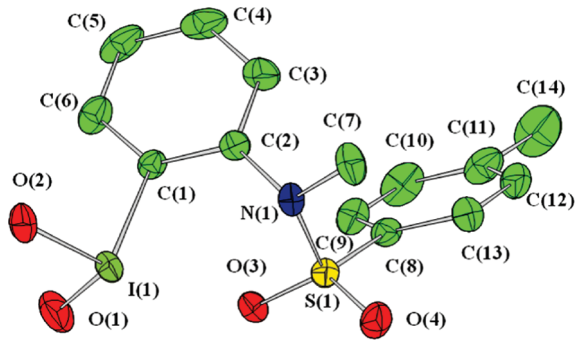

FIGURE 1. Perspective view of *N*-(2-iodylphenyl)tosylamide **13** with 50% ellipsoid probability. Selected distances [Å] and angles [deg]: I(1)−C(1) 2.104(3), I(1)−O(1) 1.807(2), I(1)−O(2) 1.786(3), C(1)−I(1)−O(1) 97.89(11), C(1)−I(1)−O(2) 99.39(13), O(1)−I(1)−O(2) 100.13(11).

and oxygen (3.55 Å).[7d,10a,11] This difference can be explained by the longer N−S bond distance in **13** as compared to the N−C bond distance in **4**. Nevertheless, this additional interaction in the molecule of **13** partially replaces intermolecular secondary bonding between the iodine atom I(1) and the oxygen atom (O1A) of the iodyl group in the neighboring molecule (Figure 2) and thus weakens the polymeric network typical of iodylarenes in the solid state. It is particularly important that this structural feature leads to the excellent solubility of compound **13** in nonpolar solvents such as chloroform.

We were not able to grow single crystals of ditosylamide **14** and tosylate **17** because of the low solubility of these compounds. It can be hypothesized that the polymeric character of these compounds is explained by a significant intermolecular secondary interaction between the hypervalent iodine center and the sulfonyl oxygens in tosyl groups of neighboring molecules, similar to the I(1)···O(4B) secondary bonding in structure **13** (Figure 2). Indeed, the previously reported 2-iodylphenol ethers, in which the Ts moiety of structure **17** is replaced with an alkyl group, have excellent solubility in organic solvents.[12] Such a striking difference in the solubility of structurally similar 2-iodylphenol alkyl ethers and the 2-iodylphenol tosylate **17** is indicative of the importance of intermolecular secondary interactions involving the tosyl group.

Due to its excellent solubility in organic solvents, *N*-(2-iodylphenyl)tosylamide **13** is a potentially useful hypervalent iodine oxidant. We have found that the oxidizing reactivity of compound **13** is generally similar to the previously reported *N*-(2-iodylphenyl)acylamides (NIPA, **4**). In particular, the tosylamide **13** reacts with various benzylic alcohols (e.g., benzyl alcohol, 4-nitro- and 4-methoxy-substituted benzyl alcohols, pyridin-3-ylmethanol, thiophen-2-ylmethanol, and 1-phenylethanol) in acetonitrile under mild conditions to afford the respective aldehydes or ketones in quantitative yield in 4−6 h. The oxidation of aliphatic and allylic alcohols proceeds much slower, even at elevated temperatures. For example, geraniol is oxidized by compound **13** to the respective aldehyde with only 4% conversion

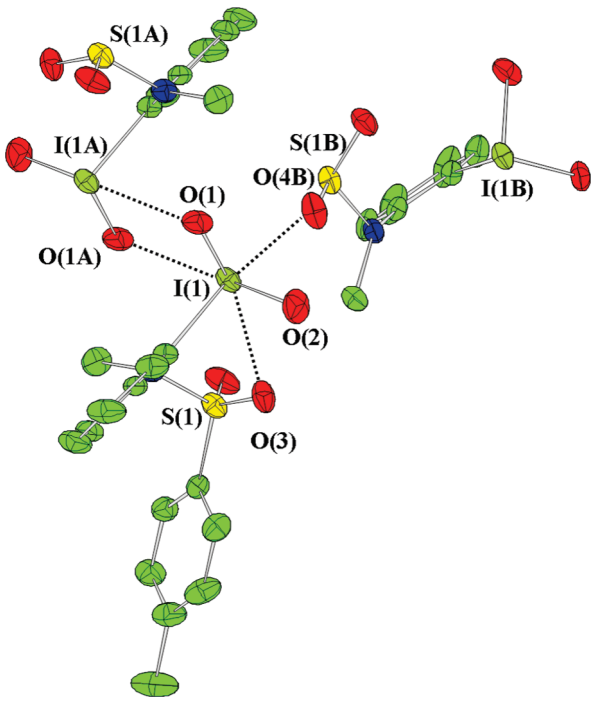

FIGURE 2. Intra- and intermolecular secondary bonding in **13**. Selected distances [Å]: I(1)···O(1A) 2.727(3), I(1)···O(4B) 3.167(2), I(1)−O(3) 3.035(3). Tolyl groups of molecules A (located at $^3/_2 - x$, $^1/_2 - y$, $1 - z$ position) and B (located at $^3/_2 - x$, $^1/_2 + y$, $^3/_2 - z$ position) are omitted for clarity.

after 6 h under reflux conditions in acetonitrile. The details of these oxidations are provided in the Supporting Information. In comparison with tosylamide **13**, the previously reported IBX esters **3** showed even lower reactivity toward alcohols (the oxidation with **3** required acid catalysis),[7b] while IBX amides **2**[7a] demonstrated higher reactivity and were capable of oxidizing aliphatic alcohols.

In conclusion, we have reported the preparation of new tosyl derivatives of 2-iodylaniline and 2-iodylphenol. Single-crystal X-ray diffraction analysis of *N*-(2-iodylphenyl)-*N*,4-dimethylbenzenesulfonamide, **13**, revealed the presence of intramolecular secondary bonding between the hypervalent iodine center and the oxygen atom in the ortho-substituent. This additional interaction in the molecule of **13** partially replaces intermolecular secondary bonding between the iodine atom and the oxygen atom of the iodyl group of the neighboring molecule and thus weakens the polymeric network typical of iodylarenes in the solid state. Due to this structural feature compound **13** has excellent solubility in nonpolar solvents such as chloroform. Compound **13** is an efficient oxidant toward organic substrates and can oxidize benzylic alcohols to the respective aldehydes or ketones.

Experimental Section

Additional experimental details can be found in the Supporting Information.

***N*-(2-Iodylphenyl)-*N*,4-dimethylbenzenesulfonamide (13).** A freshly prepared 0.1 M solution of dimethyldioxirane in dichloromethane[13] (120 mL, approximately 12 mmol) was added to a

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stirred mixture of *N*-(2-iodophenyl)-*N*,4-dimethylbenzenesulfonamide (**11**) (0.19 g, 0.50 mmol) in 5 mL of dry CH_2Cl_2 at 0 °C. The reaction mixture was stirred at room temperature overnight, then the solvent was removed under vacuum. Crude product was recrystallized from the mixture of ethyl ether/dichloromethane (1:1). The resulting precipitate was filtered and dried to afford 0.17 g (81%) of product **13** in the form of a white microcrystalline solid, mp 159−160 °C dec. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, 1H), 7.66 (t, 1H), 7.43 (t, 1H), 7.42 (d, 2H), 7.3 (d, 2H), 6.59 (d, 1H), 3.27 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 151.2, 145.5, 140.3, 133.6, 131.5, 130.7, 130.0, 128.8, 126.9, 126.3, 39.4, 21.9.

Single crystals of product **13** suitable for X-ray crystallographic analysis were obtained by slow crystallization from the ethyl ether/dichloromethane solution. X-ray diffraction data were collected on a Bruker APEX CCD diffractometer, using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) at −100 °C. Absorption corrections were applied to the data by using the DIFABS method. The structure was solved by the Patterson method and refined by full-matrix least-squares refinement on F^2, using the Crystals for Windows program. Crystal data for **13**: $C_{14}H_{14}INO_4S$, M = 419.24, monoclinic, space group $C2/c$, a = 25.253(3) Å, b = 8.3071(11) Å, c = 16.289(2) Å, β = 117.351(2)°, V = 3035.1(7) Å^3, Z = 8, $\mu(\lambda$ = 0.80000 Å) = 3.154 mm^{-1}, d_{calc} = 2.183 g/cm^3, 10346 reflections measured, 10346 unique, R_1 = 0.0205, wR_2 = 0.0376 ($I > 3\sigma(I)$), R_1 = 0.0433, wR_2 = 0.0492 (all data), GOF = 0.898. For further details on crystal structures see the Crystallographic Information File (deposited as Supporting Information).

***N*-(2-Iodylphenyl)-4-methyl-*N*-tosylbenzenesulfonamide (14).** The oxidation of *N*-(2-iodophenyl)-4-methyl-*N*-tosylbenzenesulfonamide (**12**) (0.40 g, 0.76 mmol) with 0.1 M solution of dimethyldioxirane in dichloromethane (120 mL, approximately 12 mmol), using the same procedure as for compound **13**, afforded 0.38 g (89%) of product **14** in the form of a white powder, mp 191−192 °C dec. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (d, 1H), 7.81 (t, 1H), 7.79 (d, 4H), 7.51 (t, 1H), 7.45 (d, 4H), 6.73 (d, 1H), 2.45 (s, 6H); ^{13}C NMR (500 MHz, DMSO-d_6) δ 151.1, 147.0, 134.2, 133.6, 132.5, 132.3, 132.1, 130.4, 129.8, 128.4, 21.5. Anal. Calcd for $C_{20}H_{18}INO_6S_2$: C, 42.94; H, 3.24; N, 2.50; S, 11.46; I, 22.69. Found: C, 42.74; H, 3.20; N, 2.39; S, 11.48; I, 22.54.

2-Iodylphenyl 4-Methylbenzenesulfonate (17). The oxidation of 2-iodophenyl 4-methylbenzenesulfonate (**16**) (0.35 g, 0.94 mmol) with a 0.1 M solution of dimethyldioxirane in dichloromethane (100 mL, approximately 10 mmol), using the same procedure as for compound **13**, afforded 0.37 g (97%) of product **17** as a white powder, mp 194−195 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.91 (two overlapping d, 3H), 7.60 (t, 1H), 7.58 (t, 1H), 7.50 (d, 2H), 7.21 (d, 1H), 2.42 (s, 6H); ^{13}C NMR (500 MHz, DMSO-d_6) δ 147.4, 147.3, 142.4, 134.3, 131.4, 131.1, 129.2, 128.6, 127.4, 122.1, 21.9. Anal. Calcd for $C_{13}H_{11}IO_5S$: C, 38.44; H, 2.73; S, 7.89; I, 31.24. Found: C, 38.37; H, 2.68; S, 7.79; I, 31.17.

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Supporting Information Available: Details of the experimental procedures, spectroscopic data of the reaction products, and X-ray data for compound **13** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.