

Synthesis and characterization of novel polyvalent organoiodine compounds

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Dedicated to Professor Anastasios Varvoglis

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Abstract

Synthesis and characterization of soluble analogues of iodosylbenzene PhIO and (tosyliminoiodo)benzene PhINTs are reported. The syntheses of 4-trifluoromethyl-2-(*tert*-butylsulfonyl)iodosylbenzene (**3**) and 4-trifluoromethyl-2-(*tert*-butylsulfonyl)-(tosylimino)iodobenzene (**4**) increase the repertoire of available soluble organoiodine(III) based oxo- and nitrene precursors. We also report the synthesis of a new organoiodine(V) compound, 4-trifluoromethyl-2-(*tert*-butylsulfonyl)iodylbenzene.

Keywords: Polyvalent organoiodine compounds, PhINTs, PhIO, secondary bonding

Introduction

Polyvalent organoiodine compounds have found wide synthetic applications in many organic transformations.¹ In particular, tosyliminoiodobenzene (PhINTs) and iodosylbenzene (PhIO) have found favor as primary oxidants in metal-catalyzed aziridinations and epoxidations of various olefins.² However, the insoluble nature of these reagents, and hence the heterogeneous conditions involving them, hinder efforts to ascertain the reaction mechanism and improve efficiency. The insoluble nature of organoiodine(III) compounds of type ArIX₂ (where X = NTs, O or Cl₂) stems in large part from polymeric networks of I-X secondary bonding in the solid state.³ Recent efforts in our group have been focussed on the solubilization of these important compounds by the modification of secondary bonding interactions.⁴

The characteristic I-O secondary bonding in polyvalent iodine compounds have been utilized to direct self-assembly of organoiodine(III) molecules into chiral and optically pure hypervalent iodine macromolecules and to promote asymmetric oxytosylation reactions.⁵ During the course of our study of secondary bonding interactions in organoiodine(III) compounds, soluble

analogues of PhIO and PhINTs were realized in the synthesis of iodosylarene **1** and (tosyliminoiido)arene **2**, by placing an appropriate substituent in the *ortho* position of the phenyl ring.⁶

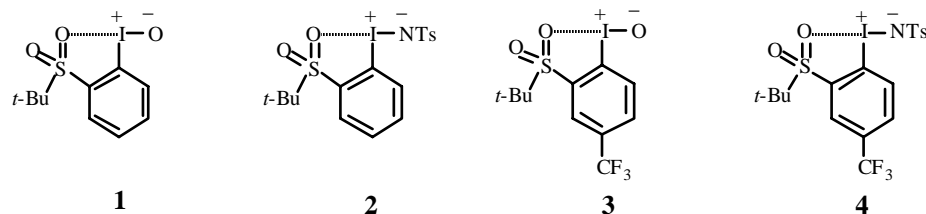
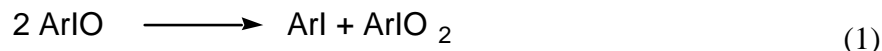


Figure 1

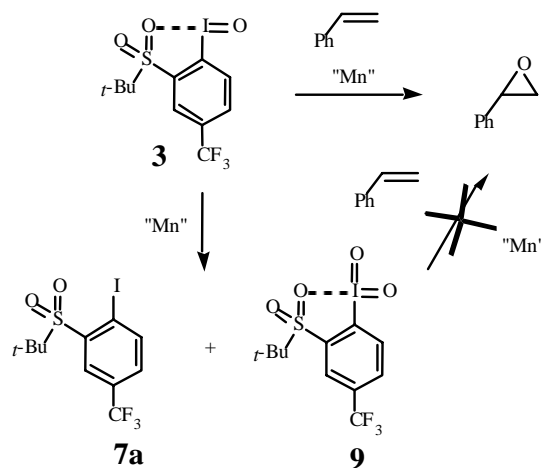
Isolation of primary nitrene sources such as **2** and other ArINSO₂Ar' typically require the electron withdrawing and stabilizing effects of a sulfonyl group. Compound **2** is thus closely related to the well known related carbene source phenyliodonium bis(phenylsulfonyl)methylide PhI=C(SO₂Ph)₂ first reported by Varvoglis and coworkers.⁷ Compounds **1** and **2** were found to be effective in metal catalyzed oxidations; however, the epoxidation reactions involving iodosylarene **1** were plagued by the competing disproportionation of **1** to the corresponding iodoarene (I(I)) and iodylarene (I(V)) (equation 1). Iodosylbenzene has been reported to undergo ready disproportionation catalyzed by metal porphyrin or upon heating.⁸ The outcome of metal catalyzed epoxidation reactions might be improved by stabilizing soluble iodosylarene **1** toward disproportionation.



Electron-withdrawing substituents on the ring have been reported to enhance the stability of organoiodine(III) compounds such as ArICl₂, in solution. For instance, a solution of PhICl₂ in CCl₄ loses its oxidizing power at the rate of 0.5% per day at 20 °C. Under similar conditions, *p*-FC₆H₄ICl₂ is reduced only at the rate of 0.04% per day.⁹ Derivatives of polyvalent iodine compounds with an alkyl substituent at iodine, such as perfluoroalkyliodosyl derivatives, have shown significant stabilization upon introduction of an electron-withdrawing substituent in the alkyl moiety.¹⁰ It can be reasoned that reducing the electron density around the iodine atom can stabilize iodosylarene **1** and reduce its tendency towards disproportionation. With the aim of further stabilization of soluble organoiodine(III) species, iodosylarene **3** and (tosyliminoiido)arene **4**, possessing the electron withdrawing trifluoromethyl group were prepared and characterized.

Results and Discussion

However, iodylarene **9** does quantitatively oxidize methyl phenyl sulfide to methyl phenyl sulfoxide.



Scheme 2

Conclusions

In summary, the synthesis and characterization of further soluble analogues of PhINTs and PhIO are reported. The new iodylans contain an electron-withdrawing substitute in iodoarene residue and were assessed to be moderately effective oxidants, but the iodyl derivative still underwent rather facile disproportionation. Introduction of even stronger electron-withdrawing moiety in the design of these organoiodine(III) compounds might have a greater impact upon the stability of iodylans for use as primary oxo- and nitrene precursors in catalytic atom and group transfer.

Experimental Section

General Procedures. Alkylolithium reagents were purchased from Aldrich and titrated with diphenylacetic acid prior to use. Reactions involving the manipulation of air and water sensitive reagents were performed under a nitrogen atmosphere using Schlenk techniques. THF was distilled from sodium benzophenone ketyl. CH₂Cl₂ and CH₃CN were distilled from calcium hydride. ¹H and ¹³C {¹H} NMR spectra were recorded on Varian XL200 or Varian XL 300 spectrometers. ¹⁹F{¹H} NMR spectra were recorded on Varian XL 300 spectrometer. Chemical shifts were referenced internally to residual solvent signals (¹H) or externally by using TFA (¹⁹F). HR-MS spectra were recorded on a Carlo-Erba Mass Spectrometer. GC-MS spectra were recorded on a HP5890 Series II Gas Chromatograph equipped with a HP 5972 Mass Selective Detector. Elemental analyses were performed by Qualitative Technologies Inc.(QTI), Whitehouse, NJ.

3-(Trifluoromethylphenyl) *tert*-butyl thioether (5). To a magnetically stirred solution of 3-(trifluoromethyl)bromobenzene (11.3 g, 50.0 mmol) in THF (200 mL), cooled to -42 °C, was added *t*-BuLi (46 mL of 1.2M soln in pentane, 55 mmol) dropwise over a period of 40 minutes. The resulting reddish brown solution was stirred for 40 minutes and *tert*-butyl disulfide (8.9 g, 50 mmol) added into the reaction flask dropwise *via* syringe with constant stirring. The reaction mixture was slowly allowed to reach room temperature and water (50 mL) added to the flask to yield two homogeneous phases. The organic phase was separated and the aqueous phase extracted with diethyl ether (3 x 25 mL). The combined organic extracts were washed with brine and dried over MgSO₄. The solvents were removed *in vacuo* to obtain a brown viscous liquid. The crude liquid was distilled to obtain a colorless liquid and identified by GC-MS analysis to be **5**. Yield: 5.26 g (45%). ¹H NMR (CDCl₃, 200 MHz): δ 7.80 (s, 1 H), 7.72 (d, 1 H, ²J_{HH} = 7.7 Hz), 7.62 (d, 1 H, ²J_{HH} = 7.7 Hz), 7.46 (t, 1 H, ²J_{HH} = 7.7 Hz), 1.30 (s, 9 H).

3-(Trifluoromethylphenyl) *tert*-butyl sulfone (6). To thioether 6.5 g of **5** (28 mmol) was added 30% H₂O₂ (20 mL) and glacial acetic acid (20 mL), and the mixture stirred at 85 °C for 4 h to obtain a white precipitate. This solid was isolated by filtration and washed with water until the washings showed no trace of acid by pH paper. The solid was recrystallised from MeOH, and dried *in vacuo* to obtain **6** as a colorless crystalline solid. Yield: 6.10 g (82%). Mp = 63 °C. ¹H NMR (CDCl₃, 200 MHz): δ 8.15 (s, 1 H), 8.09 (d, 1 H, J = 7.8 Hz), 7.72 (t, 1 H, J = 7.8 Hz), 7.92 (d, 1 H, J = 7.78 Hz), 1.36 (s, 9 H). ¹⁹F NMR (CDCl₃, 282.2 MHz) δ: 32.4. Anal. Calcd for C₁₁H₁₃O₂SF₃: C, 49.62; H, 4.92. Found: C, 49.46; H, 4.76.

4-Trifluoromethyl-2-(*tert*-butylsulfonyl)iodobenzene (7a). To a magnetically stirred solution of **6** (0.50 g, 2.3 mmol) in THF (20 mL) cooled to -78 °C was added 0.98 mL of *n*-BuLi (2.56M solution in hexanes, 2.5 mmol) dropwise, to obtain a dark red solution. The reaction mixture was stirred for 20 minutes, and a solution of iodine (0.70 g, 2.7 mmol) in THF (20 mL) added *via* cannula. After allowing the reaction mixture to warm to room temperature, aqueous Na₂SO₃ was added to quench excess elemental iodine. The organic layer was separated and the aqueous layer

extracted with diethyl ether (3 x 25 mL). The combined organic extracts were washed with brine and dried over MgSO_4 . The solvents were removed *in vacuo* to obtain a viscous oil. This material was recrystallized from diethyl ether to obtain **7a**. Yield: 0.52 g (58%). ^1H NMR (CDCl_3 , 300 MHz): δ 8.32 (a doublet and singlet are superimposed, 2 H, $^2\text{J} = 8.5$ Hz), 7.46 (dd, 1 H, $^2\text{J} = 8.2$ Hz, $^4\text{J} = 1.6$ Hz), 1.43 (s, 9 H). ^{19}F NMR (CDCl_3 , 282.2 MHz): δ 32.1 (s). $^{13}\text{C}\{\text{H}\}$ NMR (CDCl_3 , 75.5 MHz): δ 24.2, 63.0, 99.3 (q, $^3\text{J}_{\text{HF}} = 19.8$ Hz), 130.9 (q, $^1\text{J}_{\text{HF}} = 22.8$ Hz), 139.2, 144.8. HR-MS (EI, $\text{C}_{11}\text{H}_{12}\text{O}_2\text{F}_3\text{IS}$) Calcd: 391.9554. Found: 391.9552. Pertinent NMR signals assigned to **7b** (as deduced from spectra of mixtures of **7a** and **7b**. No attempt was made to isolate or purify **7b**): ^1H NMR (CDCl_3 , 300 MHz) δ 7.87 (d, 1 H, $^2\text{J} = 6.6$ Hz), 7.46 (multiplet, 1 H), 1.44 (s, 9 H). (signal due to the third proton on the ring in **7b** could not be distinguished due to overlap with signals from aromatic protons of **7a**). ^{19}F NMR (CDCl_3 , 282.2 MHz): δ 34.4 (s).

4-Trifluoromethyl-2-(tert-butylsulfonyl)iodosylbenzene (3). Acetic anhydride (2.4 mL) and 30% H_2O_2 (0.6 mL) was stirred at 42 °C for 5 h. Iodoarene **7a** (0.78 g, 2.0 mmol) was added to the resulting solution and the reaction mixture stirred at 30 °C for 24 h to result in a pale yellow solution. The progress of the reaction was monitored by TLC (benzene/silica gel plate) to ensure complete oxidation of **7a**. The solvents were removed *in vacuo*, and the white solid obtained was treated with aqueous 3N NaOH (10 mL) at 0 °C, to obtain a yellow precipitate. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 1 h. The yellow solid was isolated by filtration, washed with water and diethyl ether to obtain **3**. Yield: 0.52 g (64%). ^1H NMR (CDCl_3 , 300 MHz): δ 8.32 (d, 1 H, $^2\text{J} = 8.4$ Hz), 8.05 (a singlet and a doublet superimposed, $^2\text{J} = 5.7$ Hz), 1.43 (s, 9 H). ^{19}F NMR (CDCl_3 , 282.2 MHz): δ 32.6 (s). Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}_3\text{SF}_3\text{I}$: C, 32.37; H, 2.96. Found: C, 32.31; H, 2.80.

Solubility: 0.67 mL of CDCl_3 was required to completely dissolve 83.3 mg of **3** (ca 0.3M)

4-Trifluoromethyl-2-(tert-butylsulfonyl)-(tosylimino)iodobenzene (4). Acetic anhydride (1.2 mL) and 30% H_2O_2 (0.3 mL) were stirred at 42 °C for 5 h. Iodoarene **7a** (0.40 g, 1.0 mmol) was added to the resulting solution and the reaction mixture stirred at 30 °C for 24 h to afford a pale yellow solution. The progress of the reaction was monitored by TLC (benzene/silica gel plate) to ensure complete oxidation of **7a**. The solvents were removed *in vacuo*, and the white solid obtained was treated with an ice-chilled solution of KOH (0.20 g, 3.5 mmol) and *para*-toluenesulfonamide (0.17 g, 1.0 mmol) in methanol (5 mL). The resulting pale yellow solution was stirred for 1 h at 0 °C and for 1 h at room temperature. Crushed ice was added to the reaction mixture to obtain a yellow precipitate. This solid was isolated by filtration, washed with water and diethyl ether and dried *in vacuo* to obtain **4**. Yield: 0.30 g (55%). ^1H NMR (CDCl_3 , 300 MHz): δ 8.49 (d, 1 H, $^2\text{J} = 8.5$ Hz), 8.10 (s, 1 H), 8.03 (dd, 1 H, $^2\text{J} = 8.3$ Hz, $^4\text{J} = 1.7$ Hz), 7.81 (d, 2 H, $^2\text{J} = 8.3$ Hz), 7.24 (d, 2 H, $^2\text{J} = 7.9$ Hz). ^{19}F NMR (CDCl_3 , 282.2 MHz): δ 32.4 (s). Anal. Calcd for $\text{C}_{18}\text{H}_{19}\text{O}_4\text{S}_2\text{F}_3\text{IN} \cdot 0.5\text{H}_2\text{O}$: C, 37.90; H, 3.52; N, 2.45. Found: C, 37.77; H, 3.29; N 2.25. Solubility: 0.75 mL of CDCl_3 was required to completely dissolve 21.2 mg of **4**. (ca 0.05M)

4-Trifluoromethyl-2-(tert-butylsulfonyl)iodylbenzene (9). A mixture containing 6:4 ratio of **7a** and **7b** (~1g) was dissolved in glacial acetic acid (4 mL) and mixed with commercial bleach (5.25% aqueous NaOCl, 20 mL). A white precipitate was observed immediately along with a sticky yellow paste. The mixture was stirred at room temperature for 16 h followed by the addition of water (50 mL). The white solid was isolated by filtration, washed with diethyl ether and dried to obtain the target iodylarene. Yield: 0.43 g (66%) based on a 6:4 ratio of **7a**:**7b**. M.p = 162 °C (detonates). ¹H NMR (DMSO-*d*₆, 300 MHz): δ 8.67 (d, 1 H, ²J = 8.0 Hz), 8.53 (d, 1 H, ²J = 8.0 Hz), 8.10 (s, 1 H), 1.35 (s, 9 H). Anal. Calcd for C₁₁H₁₂O₄SF₃I · 0.5H₂O: C, 30.50; H, 3.02. Found: C, 30.59; H, 2.76.

Epoxidation using 4-trifluoromethyl-2-(tert-butylsulfonyl)iodosylbenzene (3). To a suspension of styrene (0.32 mL, 2.8 mmol) and (1R, 2R)-(-)-[1, 2-cyclohexanediamino-N, N'-bis(3, 5-di-*t*-butylsalicylidene)]manganese(III) chloride (8.9 mg, 14 μmol) in CH₂Cl₂ (5 mL) was added **3** (0.10 g, 0.25 mmol), and the resulting dark brown solution stirred at room temperature for 1 h until all of **3** was consumed. Hexane (10 mL) was added and the resulting mixture passed through a short column of silica gel to remove the catalyst. The column was eluted with 1:1 mixture of diethyl ether: hexanes (10 mL). The solvents were removed *in vacuo* to obtain a white solid. The yield was determined by ¹H NMR integration, using 1,4-dimethoxybenzene as an internal standard, to be 15%.

Attempt at epoxidation using 4-trifluoromethyl-2-(tert-butylsulfonyl)iodylbenzene. To a suspension of styrene (0.32 mL, 2.8 mmol) and (1R, 2R)-(-)-[1, 2-Cyclohexanediamino-N, N'-bis(3, 5-di-*t*-butylsalicylidene)]manganese(III) chloride (8.9 mg, 14 μmol) in CH₂Cl₂ (5 mL) was added the iodylarene **9** (0.11 g, 0.25 mmol), and the resulting dark brown suspension stirred at room temperature for 3 h. Unreacted iodylarene was isolated from the reaction mixture along with a small amount of iodoarene **7a** (10%). No evidence was obtained for styrene epoxide.

Acknowledgements

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References

- (a) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: London, 1997.
(b) Varvoglis, A. *The Organic Chemistry of Polycoordinated Iodine*; VCH Publishers, Inc.: New York, 1992. (c) Varvoglis, A.; Spyroudis, S. *Synlett* **1998**, 221. (d) Varvoglis, A. *Tetrahedron* **1997**, 53, 1179. (e) Varvoglis, A. *Chim. Chron.* **1995**, 24, 3. (f) Wirth, T.; Hirt,

- U. H. *Synthesis* **1999**, 8, 1271. (g) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **1996**, 96, 1123.
- (a) Johnson, R. A.; Sharpless, K. B. *Catalytic Asymmetric Synthesis*, 2nd Edn; Ojima, I., Ed.; Wiley-VCH: New York, 2000. (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, 102, 2523.
 - (a) Carmalt, C. J.; Crossley, J. G.; Knight, J. G.; Lightfoot, P.; Martin, A.; Muldowney, M. P.; Norman, N. C.; Orpen, A. G. *J. Chem. Soc. Chem. Commun.* **1994**, 2367. (b) Boucher, M.; Macikenas, D.; Ren, T.; Protasiewicz, J. D. *J. Am. Chem. Soc.* **1997**, 9366. (c) Protasiewicz, J. D. *Acta. Cryst. C.* **1996**, 1570.
 - Macikenas, D.; Meprathu, B. V.; Protasiewicz, J. D. *Tet. Lett.* **1998**, 39, 191.
 - (a) Zhdankin, V. V.; Kuposov, A. E.; Smart, J. T.; Tykwinski, R. R.; McDonald, R.; Morales-Izquierdo, A. *J. Am. Chem. Soc.* **2001**, 123, 4065. (b) Hirt, U. H.; Springler, B.; Wirth, T. *J. Org. Chem.* **1998**, 63, 7674. (c) Wirth, T.; Hirt, U. H. *Tetrahedron Asymmetry* **1997**, 8, 32.
 - (a) Macikenas, D.; Skrzypczak-Jankun, E.; Protasiewicz, J. D. *J. Am. Chem. Soc.* **1999**, 121, 7164. (b) Macikenas, D.; Skrzypczak-Jankun, E.; Protasiewicz, J. D. *Angew. Chem. Int. Ed.* **2000**, 39, 2007.
 - Hadjarapoglou, L.; Spyroudis, S.; Varvoglis, A. *J. Am. Chem. Soc.* **1985**, 107, 7178.
 - (a) Nappa, M. J.; Tolman, C. A. *Inorg. Chem.* **1985**, 24, 4711. (b) Bressan, M.; Morvillo, A. *Inorg. Chem.* **1989**, 28, 950.
 - Zorn, H.; Reisinger, K. *Allg. Prakt. Chem.* **1966**, 17, 160.
 - Zhdankin, V. V.; Kuehl, C. J.; Simonsen, A. J. *Main Group Chemistry* **1996**, 1(3), 349.
 - Ipatieff, V. N.; Pines, H.; Friedman, B. S. *J. Am. Chem. Soc.* **1938**, 60, 2732.
 - Iwao, M.; Iihama, T.; Mahanablis, K. K.; Perrier, H.; Snieckus, V. *J. Org. Chem.* **1989**, 54, 26.