Oxidations

Preparation and Reactivity of 1,3,5,7-Tetrakis[4-(diacetoxyiodo)phenyl]adamantane, a Recyclable Hypervalent Iodine(III) Reagent**

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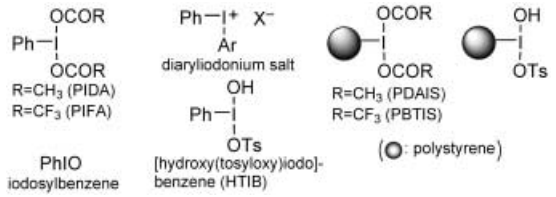
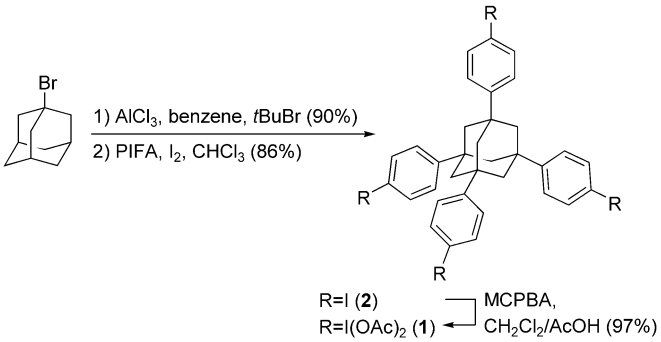
Over the past decade, the use of hypervalent iodine reagents[1] has gained importance as a safe alternative to heavy-metal reagents for performing a variety of organic transformations. In view of recent demands for ecologically friendly chemical processes in the agrochemical and pharmaceutical industries, polymer-supported hypervalent iodine reagents should be a new and useful tool as a result of their versatility, low toxicity, high yields, simple work-up procedures, and recyclability. Accordingly, Togo and co-workers,[1h,2] Ley and co-workers,[3] and we[4] demonstrated that both poly(diacetoxyiodo)styrene (PDAIS)[5] and polybis(trifluoroacetoxyiodo)styrene (PBTIS) exhibit reactivities similar to those of phenyliodine diacetate (PIDA) and phenyliodine bis(trifluoroacetate) (PIFA), respectively, and utilized them as environmentally benign replacements for I^{III} reagents such as PIDA, PIFA, and iodosyl benzene (PhIO) (Scheme 1).

Despite the utility and versatility of these polymer-supported reagents, they still have several drawbacks: 1) the loading efficiency of I^{III} sites is difficult to control, which has made the marketing of polymer-supported iodine reagents difficult; 2) the degradative loss of resin is accompanied by benzylic oxidation of the polystyrene chain after repeated use; and 3) they are much less reactive than the corresponding monomeric forms owing to steric hindrance of the reactive sites as well as their low solubility in various solvents. Therefore, slightly vigorous conditions and/or an excess amount of reagents are generally needed. Herein we report the preparation and characterization of a novel, recyclable, and nonpolymeric hypervalent iodine(III) reagent, 1,3,5,7-tetrakis[4-(diacetoxyiodo)phenyl] adamantane (**1**), and its derivatives.



Scheme 1. Hypervalent iodine(III) reagents.

As a part of our continuing research into the development of new hypervalent iodine compounds, we planned to synthesize an unprecedented tetrahedral I^{III} compound **1**, which should be a precursor to build a unique hypervalent iodine-based supramolecular structure as well as a new oxidizing agent. We prepared 1,3,5,7-tetrakis(4-iodophenyl)-adamantane (**2**) in good yield in two steps from commercially available 1-bromoadamantane according to a literature procedure.[6] Oxidation of **2** by conventional methods[7] with peracetic acid (30% H_2O_2 and acetic anhydride), sodium perborate ($NaBO_3$) in acetic acid, or sodium periodate ($NaIO_4$) unexpectedly gave **1** in low yield, accompanied by poorly soluble and unidentifiable polymeric products. After further investigations, we finally succeeded in synthesizing **1** in 97% yield by using *m*-chloroperbenzoic acid (MCPBA) in CH_2Cl_2/AcOH (1:1) under dilute conditions (Scheme 2).



Scheme 2. Preparation of 1,3,5,7-tetrakis[4-(diacetoxyiodo)phenyl]adamantane (**1**). Ts = tosyl = *p*-toluenesulfonyl.

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Adamantane **1** was fully characterized by single-crystal X-ray analysis[8] as well as elemental and spectroscopic analysis. A single crystal of **1** suitable for X-ray crystallographic analysis was obtained through slow growth by the vapor diffusion from CH_2Cl_2/AcOH/hexanes. Figure 1 reveals the geometry around the iodine in **1** to be a pentagonal-planar arrangement of three strong (e.g. I1-C14, I1-O1, and I1-O3) and two weak secondary (e.g. I1-O2 and I1-O4) bonds similar to the well-known geometry of PIDA, and the unit cell consists of a tetrahedral structure.

Several I^{III} derivatives[9] such as 1,3,5,7-tetrakis[4-bis(trifluoroacetoxyiodo)phenyl]adamantane (**3**), 1,3,5,7-tetrakis[4-{hydroxy(tosyloxy)iodo}phenyl]adamantane (**4**), and 1,3,5,7-

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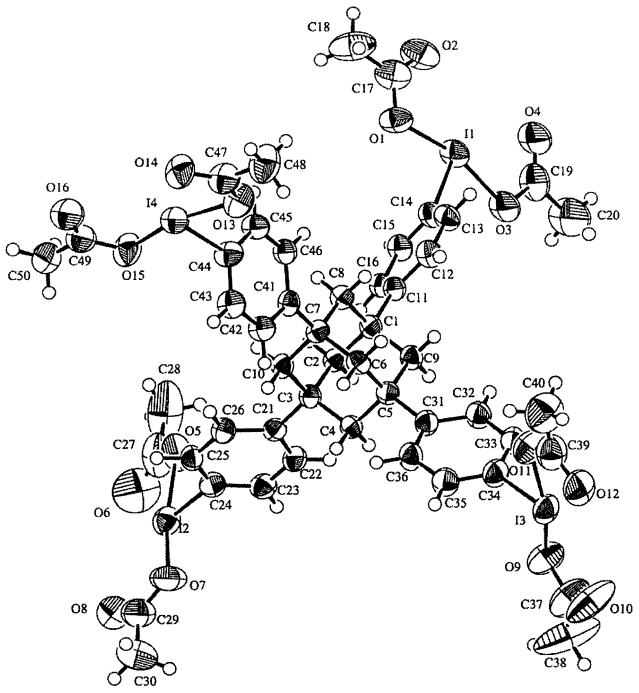
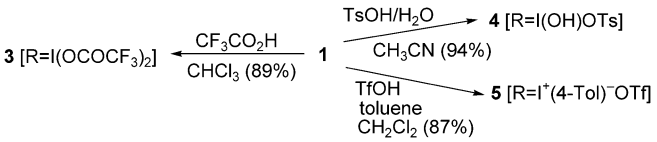


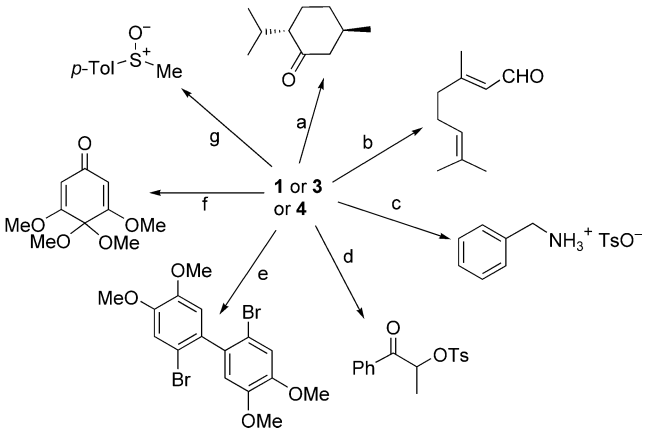
Figure 1. ORTEP drawing of **1**. Selected bond lengths [Å] and angles [°]: I1-C14 2.097(6), I1-O1 2.170(5), I1-O2 2.863(6), I1-O3 2.174(6), I1-O4 2.875(5), O1-I1-C1 80.6(2), C14-I1-O3 81.9(2), O1-I1-O3 162.4(2).

tetrakis[4-(4-tolyliodonium)phenyl]adamantane (**5**) were also prepared from **1** by conventional procedures[10] (Scheme 3).



Scheme 3. Transformation of **1** into other iodanes. Tf = trifluoromethanesulfonyl.

During the above study, we found that **2** is poorly soluble in polar protic solvents, especially in MeOH. This prompted us to develop **1** and its derivatives as new and recyclable reagents, because **2** is generated as the reduced form after oxidation reactions with **1**. Thus, we tested several oxidative transformations with **1**, **3**, and **4** to confirm the reactivity and recyclability. Consequently, all the reactions, such as phenolic oxidation,[4b,11] oxidation of alcohols,[4a,d,12] oxidation of sulfides,[2b] α-tosyloxylation of ketones,[13] and Hofmann-type rearrangement,[14] proceeded smoothly under homogeneous conditions (except for reaction a) to afford oxidation products in excellent yields (Scheme 4).



Scheme 4. Reactivity of **1**, **3**, and **4**. Conditions: a) L-menthol, **1** (0.28 equiv), KBr, H_2O, room temperature, 4 h, quant. (95% recovery of **2**); b) geraniol, **1** (0.25 equiv), TEMPO (0.2 equiv), CH_2Cl_2, room temperature, 1 h, 91% (95% recovery of **2**); c) phenylacetamide, **4** (0.25 equiv), CH_3CN, reflux, 1 h, 82% (quant. recovery of **2**); d) propiophenone, **4** (0.25 equiv), CH_3CN, reflux, 3 h, 76% (98% recovery of **2**); e) 4-bromoveratrole, **3** (0.14 equiv), $BF_3{\cdot}Et_2O$, CH_2Cl_2, −40°C, 3 h, 98% (quantitative recovery of **2**); f) 3,4,5-trimethoxyphenol, **1** (0.25 equiv), MeOH, room temperature, 10 min, quant. (quant. recovery of **2**); g) methyl p-tolylsulfide, **1** (0.25 equiv), CH_2Cl_2 (1% H_2O), reflux, 2 h, 97% (quant. recovery of **2**).

In all cases, tetraiodide **2** was recovered nearly quantitatively in pure form after a simple work-up (i.e. quenching the reaction with MeOH followed by filtration or centrifugation), and reoxidation of **2** to **1** with MCPBA also proceeded quantitatively without loss of activity. Next, we compared the reactivity of **1** or **3** with other I^{III} reagents. As a result, reagents **1** and **3** showed high reactivities equal to those of PIDA, PIFA, and PhIO, as well as excellent recyclability (95–100%) similar to that of PDAIS (Scheme 4 and Table 1).

The high reactivity of **1** is probably caused by the tetrahedral structure, whose reactive sites do not interfere with each other. Furthermore, no degradation loss was observed in the reoxidation step to **1**, even after repeated use, because **2** has no benzylic proton. The key features of these unique I^{III} reagents are highlighted as follows: 1) high reactivity in a variety of solvents owing to their tetrahedral structure and to their improved solubility over those of conventional polymer-supported I^{III} reagents; 2) high recyclability without degradation loss; and 3) well-defined structure and convenient preparation, suitable for commercialization.

Table 1: Comparison of reactivities of **1** and **3** with PIDA, PIFA, PhIO, and PDAIS.[a]

Reaction a[b]	Reaction e[b]	Reaction g[b]
quant. (**1** (0.28 equiv), 4 h, RT)	98% (**3** (0.14 equiv), 3 h, −40°C)	97% (**1** (0.25 equiv), 2 h, reflux)
quant. (PhIO (1.1 equiv), 7 h, RT)	97% (PIFA (0.55 equiv), 1.5 h, −40°C)	97% (PIDA (1.0 equiv), 2 h, reflux)
86% (PDAIS (1.1 equiv), 20 h, RT)	58% (PDAIS (0.55 equiv), 24 h, RT)[c]	83% (PDAIS (1.0 equiv), 24 h, reflux)

[a] See Scheme 4: reaction a: oxidation of L-menthol, reaction e: biaryl coupling of 4-bromoveratrole, reaction g: oxidation of methyl *p*-tolyl sulfide. [b] Yield (reagent (equiv), time, temperature). [c] No reaction at −40°C.

In conclusion, we have developed novel, nonpolymeric, and recyclable hypervalent iodine(III) reagents. These reagents show promise as useful and safe tools for a wide range of pharmaceutical and agrochemical research, as they are highly reactivity *and* recyclable. Application of **1** and related compounds to the construction of supramolecular structures as well as in oxidation reactions is now underway.

Experimental Section

MCPBA (3.12 g, 18 mmol) was added to a stirred solution of **2** (1.416 g, 1.5 mmol) in CH_2Cl_2 (150 mL) and AcOH (150 mL) at room temperature. The mixture was stirred for 12 h under the same reaction conditions. The resultant mixture was filtered, and CH_2Cl_2 was removed from the filtrate by using a rotary evaporator. Hexanes were added to the residue to precipitate **1**. After filtration, crude **1** was washed with hexanes several times, and was dried in vacuo to give **1** (2.07 g, 97%), colorless crystal; m.p. (decomp.) 195–196°C (from AcOH-CH_2Cl_2-hexanes by vapor diffusion method); ^{1}H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta = 8.09$ (d, $^3J(H,H) = 8.7$ Hz, 8H; ArH), 7.56 (d, $^3J(H,H) = 8.7$ Hz, 8H; ArH), 2.20 (s, 12H; AdH), 2.01 ppm (s, 24H; $OCOCH_3$); ^{13}C NMR (75 Hz, $CDCl_3$, 25°C, TMS): $\delta = 176.5$, 151.9, 135.2, 127.7, 119.5, 46.4, 39.6, 20.4 ppm; elemental analysis: calcd for $C_{50}H_{52}I_4O_{16}\cdot 2H_2O$: C 41.34, H 3.89, I 34.95; found: C 41.30, H 3.70, I 35.03.

Typical Oxidation Procedure: Adamantane **1** (354.2 mg, 0.25 mmol) was added to a stirred solution of 3,4,5-trimethoxyphenol (184.2 mg, 1.0 mmol) in MeOH (5 mL) at room temperature. The mixture was stirred for 10 min. MeOH (10 mL) was then added to the reaction mixture, and the mixture was filtered. The residue was washed with MeOH several times, and the residue was recovered as pure **2** quantitatively. The filtrate was then centrifuged. The supernatant liquid was evaporated in vacuo to give 3,4,4,5-tetramethoxycyclohexa-2,5-dienone[15] quantitatively.

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[8] Crystal data for **1** ($C_{50}H_{56}I_4O_{18}$): $M_w = 1452.60$, monoclinic, *C*2/*c* (no. 15), $a = 24.11(1)$, $b = 17.011(9)$, $c = 33.45(2)$ Å, $\beta = 91.57(4)$, $V = 13711(11)$ Å^3, $Z = 8$, $T = 90$ K, $\rho_{calcd} = 1.407$ g cm^{-3}, $Mo_{K\alpha}$ radiation, $m = 18.74$ cm^{-1}, colorless block $0.30 \times 0.15 \times 0.05$ mm^3; 78690 measured reflections, F^2 refinement, $R_1 = 0.067$, $wR_2 = 0.183$, 19969 independent observed absorption-corrected reflections [$(I > 3.00\sigma(I))$, $2\theta = 60.1$], 700 parameters. CCDC 232058 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

[9] **3**: m.p. (decomp.) 196–203°C (from CH_2Cl_2/hexanes); ^{1}H NMR (300 MHz, $CDCl_3/CF_3CO_2H$ (10:1), 25°C, TMS): $\delta = 8.24$ (d, $^3J(H,H) = 8.7$ Hz, 8H; ArH), 7.73 (d, $^3J(H,H) = 8.7$ Hz, 8H; ArH), 2.30 ppm (s, 12H; AdH); ^{19}F NMR (200 MHz, $CDCl_3/CF_3CO_2H$ (10:1), 25°C, hexafluorobenzene (−162.9 ppm)): $\delta = -74.51$ ppm (s, 24F; $OCOCF_3$); elemental analysis: calcd for $C_{50}H_{28}F_{24}I_4O_{16}$: C 32.49, H 1.53; found: C 32.82, H 1.86. **4**: m.p. (decomp.) 183–190°C; ^{1}H NMR (300 MHz, $CDCl_3/CF_3CO_2H$ (10:1), 25°C, TMS): $\delta = 8.25$ (d, $^3J(H,H) = 8.9$ Hz, 8H; ArH), 7.70 (d, $^3J(H,H) = 8.9$ Hz, 8H; ArH), 7.65 (d, $^3J(H,H) = 8.4$ Hz, 8H; ArH), 7.26 (d, $^3J(H,H) = 8.1$ Hz, 8H; ArH), 2.38 (s, 12H; $ArCH_3$), 2.26 ppm (s, 12H; AdH); ^{13}C NMR (75 Hz, $CDCl_3/CF_3CO_2H$ (10:1), 25°C, TMS): $\delta = 154.2$, 144.5, 135.9, 135.1, 129.8, 129.0, 126.3, 121.1, 45.8, 39.9, 21.4 ppm; elemental analysis: calcd for $C_{62}H_{60}I_4O_{16}S_4\cdot 4H_2O$: C 42.09, H 3.87, I 28.69, S 7.25; found: C 42.03, H 3.64, I 28.32, S 7.25. **5**: m.p. (decomp.) 186–190°C; ^{1}H NMR (270 MHz, CD_3CN, 25°C, TMS): $\delta = 8.00$ (d, $^3J(H,H) = 8.6$ Hz, 8H; ArH), 7.94 (d, $^3J(H,H) = 8.4$ Hz, 8H; ArH), 7.62 (d, $^3J(H,H) = 8.6$ Hz, 8H; ArH), 7.32 (d, $^3J(H,H) = 8.1$ Hz, 8H; ArH), 2.37 (s, 12H; $ArCH_3$), 2.04 ppm (s, 12H; AdH); ^{13}C NMR (67.8 Hz, CD_3CN, 25°C, TMS): $\delta = 154.6$, 145.1, 136.2, 136.1, 133.8, 130.3, 124.0, 112.0, 110.9, 45.8, 40.6, 21.4 ppm; High-resolution cold-spray ionization (CSI-MS; CH_3CN): $m/z = 1755.88990$ ($C_{65}H_{56}F_9I_4O_9S_3^+$) [$(M-OTf)^+$].

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[15] M.p. 122–123 °C (from AcOH/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.59$ (s, 2H; 2-H, 6-H), 3.78 (s, 6H; 3-, 5-C-OMe), 3.25 ppm (s, 6H; 4-C-$(OMe)_2$); elemental analysis: calcd for $C_{10}H_{14}O_5$: C 56.07, H 6.59; Found: C 55.74, H 6.58.

