Alternative, Easy and Efficient Preparation of Poly[4-(diacetoxyiodo)styrene] from Poly(4-iodostyrene) Using Sodium Perborate as the Oxidant

Md. Delwar Hossain, Tsugio Kitamura*

Department of Chemistry and Applied Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi, Saga 840-8502, Japan
Fax +81(952)288548; E-mail: kitamura@cc.saga-u.ac.jp

Received 8 November 2005; revised 8 December 2005

Abstract: An operationally simple, efficient, and considerably improved preparative procedure of poly[4-(diacetoxyiodo)styrene] (PSDIB) is reported. This procedure is performed with acetic acid, 1,2-dichloroethane, commercially available sodium perborate tetrahydrate as an oxidant, and triflic acid as an additive, and gives PSDIB after a short reaction time. PSDIB is employed as an oxidizing agent in organic synthesis and can be regenerated and reused in the same reaction.

Key words: poly[4-(diacetoxyiodo)styrene], sodium perborate, triflic acid, oxidation, hypervalent iodine

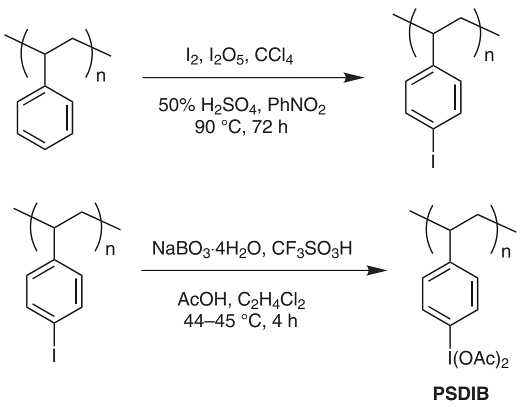
In the last 20 years, hypervalent iodine reagents have enjoyed an increase in popularity in organic synthesis.[1] They were used for a wide range of chemical transformations, especially as reagents for oxidations.[2] The advantages of hypervalent iodine reagents are the simple experimental operation and low toxicity of the reagents. Several polymer-bound oxidants have been reported,[3] and polymer-supported hypervalent iodine reagents should be a welcome addition due to their versatility, low toxicity, and high reactivity. Among hypervalent iodine compounds, (diacetoxyiodo)benzene has attracted significant interest, while poly[4-(diacetoxyiodo)styrene] (PSDIB) is expected to have the same reactivity as (diacetoxyiodo)benzene.[4] Hitherto, PSDIB has found application in many reactions, such as the preparation of phenylpolystyryl iodonium bisulfate, 3,4-dihydro-2,1-benzothiazine 2,2-dioxides, 2,5-disubstituted oxazoles, 5–7 membered cyclic ethers, and methyl carbamates. It has also been applied to the oxidation of amines and alcohols, iodination of aromatic compounds, and the oxidative 1,2-aryl migration of alkyl aryl ketones.[5] The major advantage of polymer-bound reagents is that the polymeric reagents can be regenerated and reused as an environmentally benign reagent. Preparation of the polymeric version of the iodine(III) reagent as a form of polymer-supported (diacetoxyiodo)benzene was reported by several research groups. For example, Okawara et al.[6] showed that PSDIB could be prepared by iodination of polystyrene followed by peracetic acid oxidation; Giannis et al.[7] reported the preparation of aminomethylpolystyrene-supported (diacetoxyiodo)benzene; Ko et al.[8] synthesized Merrifield's peptide-supported (diacetoxyiodo)benzene from Merrifield's peptide resin.

The standard and most general method for the synthesis of PSDIB is the oxidative diacetoxylation of poly(4-iodostyrene) by peracetic acid at room temperature or 48 °C,[4a,5s,6] however, it requires prolonged reaction times (15–24 h). Aminomethylated polystyrene is an inexpensive and commercially available prefunctionalized polymer for the preparation of aminomethylpolystyrene-supported (diacetoxyiodo)benzene,[7] which should be protected from direct sunlight and can be stored in a refrigerator although no appreciable decomposition was observed at room temperature. The activity of Merrifield's peptide-supported (diacetoxyiodo)benzene was found to be 1.4 mmol/g.[8] The oxidation of Hantzsch 1,4-dihydropyridines with Merrifield's peptide-supported (diacetoxyiodo)benzene afforded good yields but the presence of electron-withdrawing groups such as a nitro group retarded the oxidation. In order to circumvent these problems we envisaged an alternative method for the preparation of PSDIB from poly(4-iodostyrene) using sodium perborate.[9]

In our laboratory, we found a quick (4 h) and efficient method for preparing PSDIB from the corresponding poly(4-iodostyrene) in acetic acid and 1,2-dichloroethane using commercial sodium perborate as an oxidant and triflic acid as an additive at 44–45 °C (Scheme 1). After filtration, PSDIB was washed with diethyl ether and dried. Poly(4-iodostyrene) was prepared by the reaction of polystyrene with iodine, iodine pentoxide, carbon tetrachloride, and sulfuric acid (50%) in nitrobenzene at 90 °C for 72 hours.[5d] The oxidizing ability of sodium perborate is much improved by addition of triflic acid. Triflic acid is 30 times stronger than concentrated sulfuric acid,[10] while the thermal stability of triflic acid is far superior to that of other acids.[11] Sodium perborate, a stable, colorless, and crystalline solid, is used as a strong oxidizing agent in many applications and has the advantages of being very cheap, safe, non-toxic, and easy to handle.[12] The polymer loading of PSDIB in terms of the (diacetoxyiodo)phenyl group was determined by iodometric titration[13] to be 1.86 mmol/g. When triflic acid was replaced with concentrated sulfuric acid, the activity of PSDIB was not improved.

In order to test their activity, benzyl alcohol was converted to benzaldehyde, after a short reaction time, with a defined quantity of PSDIB. The yield of benzaldehyde (Table 1) was about the same as that reported in the liter-

SYNTHESIS 2006, No. 8, pp 1253–1256
Advanced online publication: 27.03.2006
DOI: 10.1055/s-2006-926402; Art ID: F19205SS



Scheme 1 Synthesis of PSDIB from polystyrene

ature.[5f] Subsequently, several other substrates, 1-phenylethanol, benzamide, cyclohexanecarboxamide, and propiophenone, were converted to acetophenone, methyl *N*-phenylcarbamate, methyl *N*-cyclohexylcarbamate, and methyl 2-phenylpropionate, respectively, with short reaction times in excellent yields (Table 1).[5f–h]

We also studied the regeneration and recycling of used PSDIB. After the first run, the polymer was recovered by filtration, washed with methanol, and the recovered polymer was then reoxidized with sodium perborate in the usual manner. The activity of the regenerated PSDIB was found to be 1.63 mmol/g by iodometric titration. Oxidation of 1-phenylethanol with the regenerated PSDIB under the same conditions gave acetophenone in 90% yield.

In conclusion, we successfully improved the procedure for the preparation of PSDIB by using poly(4-iodostyrene), acetic acid, dichloroethane, and triflic acid in the presence of sodium perborate at 44–45 °C within short reaction times. The product, PSDIB, is highly reactive and can serve as an improved and recyclable oxidant for modern organic synthesis, particularly in combinatorial chemistry.

Melting points were determined on a Yanaco micro-melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-AL300 spectrometer and the chemical shifts are expressed in ppm downfield from TMS. IR spectra were recorded on a Perkin Elmer FT-IR spectrometer Spectrum 2000. Polystyrene was purchased from Aldrich (33165-1).

Poly(4-iodostyrene)[5d]

A mixture of polystyrene (5 g, 47.81 mmol), I_2 (5.62 g, 22.19 mmol), I_2O_5 (2.19 g, 6.56 mmol), CCl_4 (12.5 mL), H_2SO_4 (50%, 10.9 mL), and nitrobenzene (62.5 mL) was kept at 90 °C for 72 h. After the reaction was complete, the reaction mixture was diluted with $CHCl_3$ (32 mL), then MeOH (469 mL) was added, and a precipitate formed. The precipitate was collected by filtration; yield: 5.80 g.

IR (KBr): 3050, 3023, 2919, 2749, 1524, 1482, 1003, 818, 757, 699, 538 cm^{-1}.

PSDIB

A solution of poly(4-iodostyrene) (0.231 g), AcOH (5 mL), DCE (7 mL), and TfOH (6 mmol) was heated with stirring at 44–45 °C. Then, $NaBO_3·4H_2O$ (6 mmol) was added slowly portionwise over 10 min and stirring was continued for 4 h. The solution was then concentrated by evaporation of DCE and AcOH under reduced pressure. H_2O (10 mL) was added, the precipitate was collected by filtration, washed with H_2O (10 mL), Et_2O (20 mL), and dried; yield: 0.275 g.

A large-scale synthesis of PSDIB was conducted in a similar manner. A solution of poly(4-iodostyrene) (1.38 g) in a mixture of AcOH (30 mL), DCE (50 mL), and TfOH (36 mmol) was heated at 44–45 °C with stirring. Then, $NaBO_3·4H_2O$ (36 mmol) was added portionwise over 20 min and stirring was continued for 4 h. Workup as above gave PSDIB; yield: 1.62 g.

IR (KBr): 3055, 3018, 2923, 2848, 1628 (br), 1581 (br), 1483, 1450, 1406, 1274, 1172, 1029, 1005, 819, 762, 702, 640, 540 cm^{-1}.

Iodometric Titration[13]

Deionized H_2O (12.5 mL), H_2SO_4 (6 N, 1.25 mL), KI (0.250 g), $CHCl_3$ (1.25 mL), and finally the prepared PSDIB (0.0310 g) were placed in a 100-mL round-bottom flask, the mixture was stirred for 4 h, and then titrated against $Na_2S_2O_3$ (0.1 N). The polymer loading of the (diacetoxyiodo)phenyl group was calculated to be 1.86 mmol/g.

Oxidation of Alcohols with PSDIB; General Procedure

PSDIB (0.64 g, 1.2 mmol) was added to a solution of alcohol (1 mmol) and TEMPO (31 mg, 0.2 mmol) in acetone (3 mL) and the mixture was stirred at r.t. for the time given in Table 1. At the end of the reaction, Et_2O (10 mL) was added and the mixture was filtered to remove the polymer. After removal of the solvent, the filtrate was poured into H_2O (10 mL), and extracted with Et_2O (3 × 10

Table 1 Oxidation of Alcohols, Carboxamides, and Propiophenone Using PSDIB

Entry	Reagent	Product	Time (h)	Yield (%)
1	Benzyl alcohol	Benzaldehyde[a]	2	85
2	1-Phenylethanol	Acetophenone[a]	8	95
3	Benzamide	Methy *N*-phenylcarbamate[b]	4	90
4	Cyclohexanecarboxamide	Methyl *N*-cyclohexylcarbamate[b]	4	82
5	Propiophenone	Methyl 2-phenylpropionate[c]	10 min	80

[a] Alcohol (1 mmol), TEMPO (31 mg, 0.2 mmol), Me_2CO (3 mL), PSDIB (0.64 g, 1.2 mmol), r.t.

[b] KOH (2.5 equiv), MeOH (10 mL), carboxamide (1 equiv), PSDIB (0.54 g, 1 equiv), 5–10 °C to r.t.

[c] H_2SO_4 (2 mmol), propiophenone (1 mmol), $HC(OMe)_3$ (3 mL), PSDIB (0.64 g,1.2 mmol), 60 °C.

mL). The combined organic layer was dried (Na_2SO_4), filtered, and the solvent was removed in vacuo. The residue was chromatographed (silica gel) to give the pure carbonyl product. The products, benzaldehyde and acetophenone, are commercially available compounds, and the spectral data were in agreement with those from a commercial source.

Substituted Methyl Carbamates; General Procedure

To a stirred solution of KOH (2.5 equiv) in MeOH (10 mL) was added carboxamide (1 equiv). The mixture was stirred at r.t. until a homogeneous solution was obtained and then the solution was cooled to –10 °C in an ice–water bath. PSDIB (0.54 g, 1 equiv) was added in one portion and dissolved within 5 min to give a clear yellow solution. The reaction was stirred at ice-bath temperature for 15 min and then warmed to r.t. with stirring for an additional 4 h. Upon completion of the reaction (TLC), MeOH was removed in vacuo, the yellow residue was poured into H_2O (10 mL), and extracted with CH_2Cl_2 (3×10 mL). The CH_2Cl_2 extracts were combined, washed with H_2O (10 mL) and brine (10 mL), dried over anhyd Na_2SO_4, and filtered. The CH_2Cl_2 was removed in vacuo to give the crude carbamate, which was purified by flash column chromatography (silica gel) to afford the pure final product.

Methyl *N*-Phenylcarbamate

Yield: 0.142 g (90%); mp 46–47 °C (Lit.[14] mp 48–49 °C).

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.76$ (s, 3 H, OCH_3), 6.80 (br s, 1 H, NH), 7.05 (t, $J = 8$ Hz, 1 H, Ph) 7.29 (t, $J = 8$ Hz, 2 H, Ph), 7.37 (d, $J = 8$ Hz, 2 H, Ph).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 52.25$, 118.74, 123.40, 128.96, 137.82, 154.09.

Methyl *N*-Cyclohexylcarbamate

Yield: 0.130 g (82%); mp 72–73 °C (Lit.[15] mp 76–78 °C).

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.01$–1.86 (m, 10 H, C_6H_{11}), 3.38 (br s, 1 H, C_6H_{11}), 3.57 (s, 3 H, OCH_3), 4.81 (br s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 24.63$, 25.30, 33.20, 49.66, 51.52, 156.13.

Methyl 2-Phenylpropionate[5h]

H_2SO_4 (2 mmol) was added dropwise to a stirred solution of PSDIB (0.64 g, 1.2 mmol) and propiophenone (1 mmol) in trimethylorthoformate (3 mL) at r.t. The reaction mixture was stirred at 60 °C for 10 min, quenched with H_2O (10 mL), and extracted with Et_2O (3×10 mL). The combined organic layer was dried (Na_2SO_4), filtered, and the solvent was removed in vacuo. The residue was chromatographed (silica gel) to give the pure methyl 2-phenylpropionate.

Yield: 0.142 g (80%).

^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.49$ (d, $J = 7$ Hz, 3 H, Me), 3.64 (s, 3 H, OMe), 3.72 (q, $J = 7$ Hz, 1 H, C*H*Me), 7.29 (s, 5 H, Ph).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 18.53$, 45.37, 51.92, 127.07, 127.41, 128.56, 140.52, 174.92,

Acknowledgment

The authors are grateful to the Central Glass Co. for a generous gift of triflic acid. This work was partly supported by a President's Grant (research project expenditure) from Saga University.

References

(1) (a) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: San Diego, California, **1997**.
(b) Varvoglis, A. *Tetrahedron* **1997**, *53*, 1179.
(c) Varvoglis, A.; Spyroudis, S. *Synlett* **1998**, 221.
(d) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123.
(e) Kirschning, A. *Eur. J. Org. Chem.* **1998**, 2267.
(f) Pohnert, G. *J. Prakt. Chem.* **2000**, *342*, 731.

(2) (a) Frigerio, M.; Santagostino, M.; Sputore, S.; Palmisano, G. *J. Org. Chem.* **1995**, *60*, 7272. (b) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1996**, *61*, 9272. (c) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1995**, *35*, 8019. (d) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156. (e) Corey, E. J.; Palani, A. *Tetrahedron Lett.* **1995**, *36*, 7945.

(3) (a) Goudarzian, N.; Ghahramani, P.; Hossini, S. *Polym. Int.* **1996**, *39*, 61. (b) Lee, R. A.; Donald, D. S. *Tetrahedron Lett.* **1997**, *38*, 3857. (c) Hinzen, B.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1907. (d) Harris, J. M.; Liu, Y.; Chai, S.; Andrews, M. D.; Vederas, J. C. *J. Org. Chem.* **1998**, *63*, 2407. (e) Abraham, S.; Rajan, P. K.; Sreekumar, K. *Polym. Int.* **1998**, *45*, 271. (f) Habermann, J.; Ley, S. V.; Scott, J. S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1253.

(4) (a) Togo, H.; Nogami, G.; Yokoyama, M. *Synlett* **1998**, 534. (b) Ley, S. V.; Thomas, A. W.; Finch, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 669. (c) Ley, S. V.; Schucht, O.; Thomas, A. W.; Murray, P. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1251.

(5) (a) Yamada, Y.; Okawara, M. *Makromol. Chem.* **1972**, *152*, 153. (b) Hallensleben, M. L. *Angew. Makromol. Chem.* **1972**, *27*, 223. (c) Zupan, M.; Pollak, A. *J. Chem. Soc., Chem. Commun.* **1975**, 715. (d) Sakuratani, K.; Togo, H. *ARKIVOC* **2003**, *(vi)*, 11. (e) Xian, H.; Jiang-Min, C. *Chin. J. Chem.* **2004**, *22*, 222. (f) Sakuratani, K.; Togo, H. *Synthesis* **2003**, 21. (g) Moriarty, R. M.; Chany, C. J. II; Vaid, R. K.; Prakash, O.; Tuladhar, S. M. *J. Org. Chem.* **1993**, *58*, 2478. (h) Tamura, Y.; Yakura, T.; Shirouchi, Y.; Haruta, J. *Chem. Pharm. Bull.* **1985**, *33*, 1097.
(i) Kawamura, Y.; Maruyama, M.; Tokuoka, T.; Tsukayama, M. *Synthesis* **2002**, 2490. (j) Cheng, D.; Chen, Z. *Synth. Commun.* **2002**, *32*, 2155. (k) Chen, D.; Chen, Z. *Synth. Commun.* **2001**, *31*, 421. (l) Huang, X.; Zhu, Q. *Synth. Commun.* **2001**, *31*, 111. (m) Jonathan, H. J.; Rath, N. P.; Spilling, C. D. *J. Org. Chem.* **2005**, *70*, 6398. (n) Sheng, S.; Zhong, M.; Liu, X.; Luo, Q.; Chen, H. *J. Chem. Res., Synop.* **2004**, 392. (o) Cheng, D.; Chen, Z.; Zheng, Q. *Synth. Commun.* **2003**, *33*, 2671. (p) Tohma, H.; Maegawa, T.; Kita, Y. *Synlett* **2003**, 723. (q) Tohma, H.; Maegawa, T.; Takizawa, S.; Kita, Y. *Adv. Synth. Catal.* **2002**, *344*, 328.
(r) Tohma, H.; Takizawa, S.; Maegawa, T.; Kita, Y. *Angew. Chem. Int. Ed.* **2000**, *39*, 1306. (s) Wang, G.; Chen, Z. *Synth. Commun.* **1999**, *29*, 2859. (t) Yamada, K.; Urakawa, H.; Oku, H.; Katakai, R. *J. Peptide Res.* **2004**, *64*, 43.
(u) Liu, S.; Zhang, J.; Tian, G.; Liu, P. *Synth. Commun.* **2005**, *35*, 1753. (v) Teduka, T.; Togo, H. *Synlett* **2005**, 923. (w) Abo, T.; Sawaguchi, M.; Senboku, H.; Hara, S. *Molecules* **2005**, *10*, 183. (x) Okawara, M.; Kurusu, Y.; Imoto, E. *Kogyo Kagaku Zasshi* **1962**, *65*, 816; *Chem. Abstr.* **1962**, *58*, 3477. (y) Boehlow, T. R.; Harburn, J. J.; Spilling, C. D. *J. Org. Chem.* **2001**, *66*, 3111.

(6) Okawara, M.; Mizuta, K. *Kogyo Kagaku Zasshi* **1961**, *64*, 232; *Chem. Abstr.* **1962**, *57*, 23901.

(7) Ficht, S.; Mulbaier, M.; Giannis, A. *Tetrahedron* **2001**, *57*, 4863.

(8) Lee, J.; Ko, K. *Bull. Korean Chem. Soc.* **2004**, *25*, 19.

(9) Very recently we have found an efficient method for the synthesis of(diacetoxyiodo)arenes using sodium perborate: Hossain, M. D.; Kitamura, T. *J. Org. Chem.* **2005**, *70*, 6984.
(10) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper & Row: New York, **1987**, 280–297.
(11) A general description of triflic acid and its derivatives is available from Klaus F. Meyer GmbH, see: http://www.klausfmeyer.de/triflic_description.htm.
(12) Firouzabadi, H.; Iranpoor, N.; Amani, K. *Green Chem.* **2001**, *3*, 131.
(13) Lucas, H. J.; Kennedy, E. R.; Formo, M. W. *Org. Synth.* **1942**, *22*, 70.
(14) George, D. K.; Moore, D. H.; Brian, W. P.; Garman, J. A. *J. Agric. Food Chem.* **1954**, *2*, 356.
(15) Curini, M.; Epifano, F.; Maltese, F.; Rosati, O. *Tetrahedron Lett.* **2002**, *43*, 4895.