

Environmentally-Friendly TEMPO-Mediated Oxidation of Alcohols with Poly[4-(diacetoxyiodo)styrene]

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Abstract: Primary and secondary alcohols were successfully oxidized to the corresponding aldehydes and ketones in good yields, respectively, with poly[4-(diacetoxyiodo)styrene] (PSDIB) in the presence of TEMPO (cat.) in acetone, as an environment-friendly method.

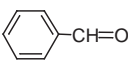
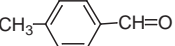
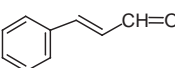
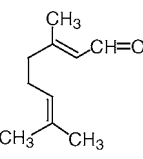
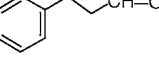
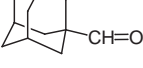
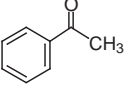
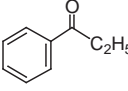


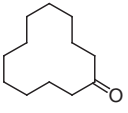
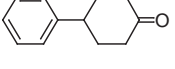
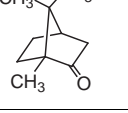
Key words: poly[4-(diacetoxyiodo)styrene] (PSDIB), oxidation, aldehyde, ketone, environment

Selective, less toxic (especially, non-metallic), and secure oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones, respectively, under mild conditions is very important in organic synthesis.¹ Therefore, the oxidation of alcohols has been intensively studied, and numerous reagents and methods have been developed to carry out important oxidation reactions. Among them, Moffatt and Swern oxidations and related reactions with DMSO/(COCl)₂ or DMSO/DCC,² and Dess–Martin oxidation with 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one and related reagents such as *o*-iodoxybenzoic acid (IBX)³ are the most effective and chemoselective methods, and have been popularly used for the oxidation of complex natural products and biologically active compounds. However, it is well known that the former reactions require toxic dichloromethane as a solvent and the reaction mixtures are extremely malodorous because of the formation of dimethyl sulfide. The latter reagents are potentially explosive due to the organopentavalent iodine structure and can not be stocked. Therefore, effective, operationally safe, and environmentally benign reagents for the oxidation of alcohols have long been desired. Generally, oxidation of alcohols with organotrivalent iodine compounds, which are potentially much more stable than organopentavalent iodine compounds, is less effective and limited.⁴ On the other hand, it is well known that *N*-oxoammonium salts formed from the oxidation of nitroxyl radicals such as 2,2,6,6-tetramethyl-1-piperidinyloxy free radical (TEMPO) promote oxidation of various alcohols to the corresponding carbonyl compounds effectively under mild reaction conditions.⁵ Recently, mild and highly selective oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones, respectively, with (di-

acetoxyiodo)benzene in the presence of a catalytic amount (0.1 equiv) of TEMPO was reported.⁶ The reactions were completed within a few hours at room temperature in dichloromethane to give carbonyl compounds in good yields. This oxidation system is much superior to the previous methods mentioned above in view of its non-explosive and the lack of malodor. We have recently reported the synthetic use of novel (diacetoxyiodo)arenes⁷ and poly[4-(diacetoxyiodo)styrene] (PSDIB)⁸ for the iodination of aromatics, the oxidative 1,2-aryl migration of alkyl aryl ketones, and the oxidation of hydroquinones and sulfides. Here, we would like to report the environment-friendly TEMPO-mediated oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones, respectively, without any overoxidation, with PSDIB in acetone as a green solvent. The results are shown in Table 1. Here, 2 mL of acetone was required for effective stirring of the heterogeneous reaction mixture, and addition of 0.2 equivalent of TEMPO is effective for the complete conversion of alcohols to the carbonyl compounds with PSDIB. As shown in Table 1, the corresponding aldehydes (entries 1–7) and ketones (entries 8–14) were obtained in good yields from saturated primary and secondary alcohols, and benzylic, allylic, and olefinic alcohols at room temperature in acetone. In the present TEMPO-mediated oxidation of alcohols with PSDIB, the polymer species, i.e. poly(4-iodostyrene), was quantitatively recovered by simple filtration from the reaction mixture, and PSDIB was regenerated by treatment with peracetic acid and reused successfully (entry 8).

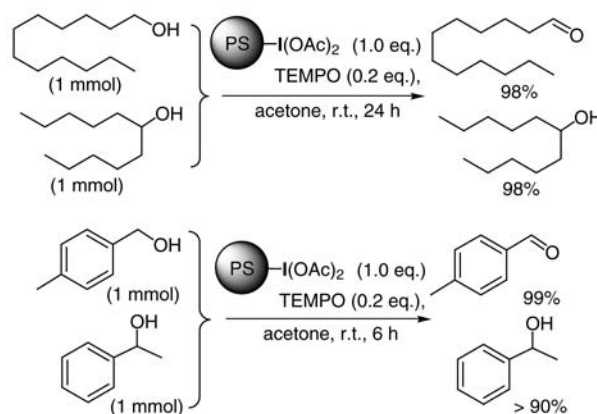
Selective oxidation of alcohols with a mixture of primary and secondary alcohols is shown in Scheme 1. In both mixtures of dodecan-1-ol and undecan-6-ol, and *p*-methylbenzyl alcohol and 1-phenylethan-1-ol, selective oxidation of primary alcohols predominantly proceeded to generate *n*-dodecanal and *p*-methylbenzaldehyde, respectively. Thus, regioselective oxidation of alcohols with PSDIB in the presence of TEMPO can be carried out. Recently, oxidation of alcohols with KBr-mediated PSDIB in water under sonicated conditions was reported.^{4g} There, ketones were obtained from the secondary alcohols in good yields; however, primary alcohols were converted to carboxylic acids, not aldehydes. More recently, polystyrene-supported⁹ and silica gel¹⁰ supported 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide (IBX) reagents were reported for the oxidation of benzylic, allylic, and secondary alcohols to the corresponding aldehydes and ketones

Table 1 Oxidation of Alcohols with Poly[4-(diacetoxyiodo)styrene] Catalysed by TEMPO

| $ \begin{array}{c} \text{R}^1\text{-CH}_2\text{OH} \\ \text{or} \\ \begin{array}{c} \text{R}^2 \\ \\ \text{R}^3\text{-CH-OH} \end{array} \end{array} \xrightarrow[\text{acetone, r.t.}]{\text{PS-I(OAc)}_2 \text{ (1.2 eq.)}, \text{TEMPO (0.2 eq.)}} \begin{array}{c} \text{R}^1\text{-CHO} \\ \text{or} \\ \begin{array}{c} \text{R}^2 \\ \\ \text{R}^3\text{-C=O} \end{array} \end{array} $ | | | |
|--|---|------|--|
| Entry | Product | Time | Yield (%) ^a |
| 1 |  | 2 | 90 |
| 2 |  | 2 | 93 |
| 3 |  | 2 | 96 |
| 4 |  | 2 | 98 |
| 5 |  | 16 | 93 |
| 6 |  | 24 | 91 |
| 7 | $\text{CH}_3(\text{CH}_2)_{10}\text{-CH=O}$ | 16 | 97 |
| 8 |  | 6 | 93 (92) ^b (93) ^c |
| 9 |  | 6 | 94 |
| 10 |  | 6 | 94 |
| 11 |  | 8 | 92 |
| 12 |  | 30 | 84 |
| 13 |  | 30 | 80 |
| 14 |  | 24 | 92 |

^a Isolated yield.^b Yield with the first regenerated PSDIB.^c Yield with the second regenerated PSDIB.

in good yields in THF or dichloromethane at room temperature. However, we believe PSDIB would be a much more effective reagent than polymer-supported 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide, because (diacetoxyiodo)benzene has wide synthetic utility to carry out reactions, such as 1,2-aryl migration of alkyl aryl ketones, α -hydroxylation of ketones, alkylation of heteroaromatic bases, radical reaction, etc.,¹¹ and PSDIB can be reused for the same reaction.^{4g,8}

**Scheme 1** Competitive Oxidation of Primary and Secondary Alcohols

The previous methods such as Swern oxidation and Dess–Martin oxidation may be substituted by the present method, since the present oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones, respectively, is effective and secure as an operationally simple and environmentally benign method, and can be used for the synthesis of pharmaceutical and agrochemical substances.

¹H NMR spectra were recorded on Jeol-JNM-GSX400 (400 MHz) and Jeol-JNM-GSX500 (500 MHz) spectrometers. Melting points were determined on Yamato Model MP-21 electrothermal apparatus in open capillary tubes and are uncorrected. IR spectra were obtained by using Jasco FT/IR-200 IR spectrometer. Microanalysis of C, H, and I were performed with a Perkin-Elmer 2400 elemental analyzer at Chemical Analysis Center of Tsukuba University. Silica Gel 60 (Merck) was used for column chromatography, Kieselgel 60 F254 (Merck) was used for TLC, and Wakogel B-5F was used for preparative TLC.

Poly[4-(diacetoxyiodo)styrene]⁸

A mixture of polystyrene (Aldrich Co. No. 33165-1, average M.W. ca. 200 000 and 4 000, 16 g, 153 mmol), I₂ (18 g, 71 mmol), I₂O₅ (7 g, 21 mmol), CCl₄ (40 mL), and 50% H₂SO₄ (35 mL) in nitrobenzene (200 mL) was kept at 90 °C for 72 h. The reaction mixture was then diluted with CHCl₃ (100 mL) and precipitated by the addition of MeOH (1500 mL). The precipitates were collected by filtration to give poly(4-iodostyrene). IR peaks of 700 and 760 cm⁻¹ in polystyrene disappeared and a new peak at 820 cm⁻¹ appeared in poly(4-iodostyrene). (Anal. Found: C, 40.40; H, 3.20; I, 51.12). (loading rate of iodophenyl group is 4.2 mmol/g). 30% H₂O₂ (40 mL) was added dropwise to Ac₂O (145 mL) at 0 °C. The solution was slowly warmed to r.t., and stirred overnight. To this solution, was added poly(4-iodostyrene) (8 g) and the solution was kept at 50 °C over-

night. Et₂O was then added to the solution for precipitation and the product (ca. 9 g) was collected by filtration.

IR (KBr): 1630 (br), 1560 (br), 1480, 1450, 1410, 1260, 1180, 1000, 770 (br) cm⁻¹.

Anal. Found: C, 38.86; H, 3.51; I, 37.17.

Loading rate of (diacetoxyiodo)phenyl group was estimated by elemental analysis and iodometry analysis; loading rate was 2.0–2.6 mmol/g.

Oxidation of Alcohols with Poly[4-(diacetoxyiodo)styrene] (PSDIB); General Procedure

PSDIB (600 mg, 1.2 mmol) was added to a solution of the appropriate alcohol (1 mmol) and TEMPO (31 mg, 0.2 mmol) in acetone (2 mL) and the mixture was stirred at r.t. for the time given in Table 1. At end of the reaction, Et₂O (10 mL) was added and the mixture was filtered to remove the polymer. After removal of the solvent from the filtrate, the corresponding carbonyl compound was obtained in over 95% purity. If necessary, the filtrate was poured into H₂O and extracted with Et₂O (3 × 10 mL). The combined organic layers were dried (Na₂SO₄), filtered, and the solvent was removed in vacuo. The residue was chromatographed on silica gel to give the pure carbonyl product (Table 1). The polymer reagent can be regenerated by treating poly(4-iodostyrene) with peracetic acid to give PSDIB and re-used for the same reaction.

All aldehydes and ketones mentioned in this work are commercially available. Thus, all compounds were identified by comparison with the authentic samples.

Regeneration of Poly[4-(diacetoxyiodo)styrene]

Recovered polymer species [poly(4-iodostyrene)] was treated with peracetic acid under the same conditions as mentioned above, to form poly[4-(diacetoxyiodo)styrene].

Acknowledgement

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