Communication

Oxidative Methyl Esterification of Primary Alcohols with Iodine-Mediated Poly[4-(diacetoxyiodo)styrene]

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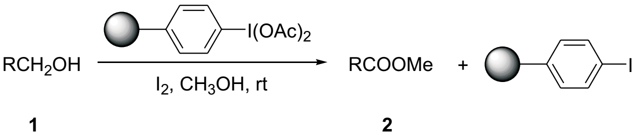
An operationally simple oxidative methyl esterification of primary alcohols in good yields using an iodine-mediated poly[4-(diacetoxyiodo)styrene] in methanol at room temperature is described. The polymeric reagent can be regenerated and reused as an environmentally benign reagent.

Keywords: Oxidation; Alcohol; Carboxylic acid methyl ester; Poly[4-(diacetoxyiodo)styrene]; Iodine.

It is well known that the transformation of a carboxylic acid into an ester is one of the most important reactions in organic synthesis.[1] The oxidation of alcohols to carbonyl compounds is a fundamental organic transformation, and numerous methods utilizing various reagents have been reported.[2] One of the most useful and efficient approaches is the direct oxidative transformation of alcohols to the corresponding esters in one step. Many methods have been developed for this direct transformation, among which the oxidation of primary alcohols to esters using hypervalent iodine(III) reagents such as $PhI(OAc)_2$ (DIB),[3] etc. is an important procedure. Hypervalent iodine(III) reagents have now been widely used in organic synthesis due to their mild reaction conditions, high selectivity and low toxicity.[4,5] Despite the simple experimental operation and low toxicity with DIB, it has a major shortcoming: the iodobenzene formed is difficult to separate from the product and is hard to reuse. Polymer supported trivalent iodine reagents could solve the problem. After the reaction, the poly(4-iodostyrene) formed could be easily removed from the reaction mixture just by filtration and reused. Recently, Kita et al[6] reported the oxidation of primary alcohols to the corresponding carboxylic acid esters with poly[4-(diacetoxyiodo)styrene](PSDIB)/KBr in methanol. As a part of our study on environmentally friendly organic synthesis with polymeric hypervalent iodine,[7] we here would like to report another operationally simple and environmentally benign oxidation of primary alcohols to the corresponding carboxylic acid esters in methanol, using an iodine-mediated PSDIB system at room temperature as shown in Scheme I.

Scheme I



PSDIB was prepared from commercial polystyrene (MW = 45,000) according to a literature method.[8] With the PSDIB in hand, we have selected the model oxidation reaction of benzyl alcohol (1.0 mmol) and PSDIB (2.0 mmol) with molecular iodine in methanol (10 mL) with stirring in an open vessel for a given time in Table 1 at room temperature to examine this process. Seen from Table 1, the oxidative conversion did not proceed at all without iodine (Entry 1). The reaction with 0.1 equiv of iodine was rather slow (entry 2), and the reaction with 0.5 equiv of iodine was the most effective for conversion of benzyl alcohol (**1a**) to the corresponding methyl ester (**2a**) in 92% yield (entry 3). Additionally, we found that other alcohols such as ethanol, 1-propanol, and 2-propanol also provide their corresponding esters in moderate to good yields, although oxidation in *t*-butyl alcohol furnished benzoic acid as the sole product (entries 5-8). Having succeeded with methyl benzoate (**2a**) formation, we then further investigated the direct oxidative

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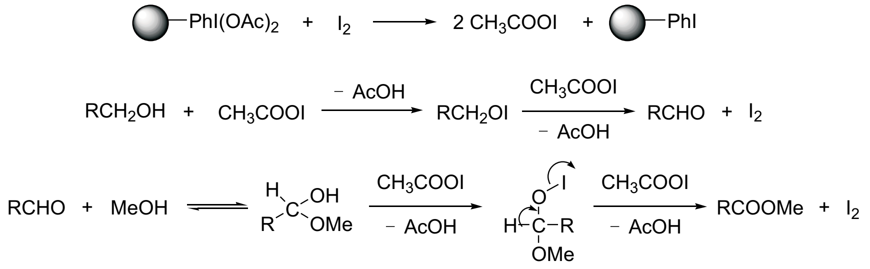
Table 1. Oxidation of primary alcohols to the corresponding esters in methanol using PSDIB/I_2

Entry	Substrate (**1**)	Time (h)	Product (**2**)	Yield (%) [a]
1	$C_6H_5CH_2OH$ (**1a**)	4	(**2a**) [b]	0
2	$C_6H_5CH_2OH$ (**1a**)	4	(**2a**) [c]	55
3	$C_6H_5CH_2OH$ (**1a**)	4	(**2a**) [d]	92
4	$C_6H_5CH_2OH$ (**1a**)	4	(**2a**) [e]	89
5	$C_6H_5CH_2OH$ (**1a**)	4	PhCOOEt [f]	82
6	$C_6H_5CH_2OH$ (**1a**)	4	*n*-PrOCOPh [g]	75
7	$C_6H_5CH_2OH$ (**1a**)	5	*i*-PrOCOPh [h]	70
8	$C_6H_5CH_2OH$ (**1a**)	5	PhCOOH [i]	88
9	4-$CH_3C_6H_4CH_2OH$ (**1b**)	5	(**2b**)	84
10	4-$CH_3OC_6H_4CH_2OH$ (**1c**)	5	(**2c**)	86
11	4-$ClC_6H_4CH_2OH$ (**1d**)	5	(**2d**)	85
12	3,4-$(MeO)_2C_6H_3CH_2OH$ (**1e**)	5	(**2e**)	84
13	4-$NO_2C_6H_4CH_2OH$ (**1f**)	5	(**2f**)	88
14	(*E*)-$C_6H_5CH{=}CHCH_2OH$ (**1g**)	5	(**2g**)	90
15	Phenylpropiolic alcohol (**1h**)	5	(**2h**)	86
16	$C_6H_5CH_2CH_2OH$ (**1i**)	4	(**2i**)	88
17	Cyclohexylcarbinol (**1j**)	4	(**2j**)	90
18	$CH_3(CH_2)_5CH_2OH$ (**1k**)	4	(**2k**)	91

[a] Isolated yield; [b] Without iodine; [c] I_2 (0.1 equiv); [d] I_2 (0.5 equiv); [e] By applying PSDIB recycled 4 times; [f] EtOH was used in place of methanol; [g] *n*-PrOH was used in place of methanol; [h] *i*-PrOH was used in place of methanol; [i] *t*-BuOH was used in place of methanol.

methyl esterification of other primary alcohols. As anticipated, various primary alcohols (**1a-1k**) were converted smoothly to their corresponding carboxylic acid methyl esters (**2a-2k**) with good yields and in short reaction times (4-5 h) under similar experimental conditions. It should be noted that both substituted benzylic alcohols either with electron releasing or withdrawing substituents (entries 9-13) and primary aliphatic alcohol (entries 16-18) afforded their corresponding methyl esters in equally good yields. Interestingly, olefinic and alkynyl alcohols such as cinnamyl alcohol (entry 14) and phenylpropiolic alcohol (entry 15) were also oxidized efficiently without any observable reaction at the carbon-carbon double and triple bond functionality. After the reaction with PSDIB, the formed poly(4-iodostyrene) was nearly quantitatively recovered by simple filtration with an addition of water. The recovered poly(4-iodostyrene) was again oxidized with peracetic acid, prepared from the reaction of hydrogen peroxide and acetic anhydride to afford PSDIB. To show the reactivity of the regenerated polymeric reagent, the conversion of benzyl alcohol (**1a**) to methyl benzoate (**2a**) was repeated four times using the same batch of regenerated PSDIB after each reaction. As seen from Table 1 (entry 4), the yield of **2a** remained almost the same as when the first prepared PSDIB was used, which showed that the PSDIB has good recyclable reactivity for this conversion. The possible mechanism of the formation of carboxylic acid methyl esters **2** is shown in Scheme II.

Scheme II



In summary, we have developed a simple and efficient procedure for the direct oxidation of primary alcohols into methyl esters using poly[4-(diacetoxy)iodo]styrene in combination with molecular iodine. This one-step reaction is facile, high yielding and uses only readily available starting materials; moreover, the polymeric reagent can be regenerated and reused as an environmentally benign reagent.

EXPERIMENTAL SECTION

Polystyrene (average MW = 45,000), all primary alcohols except MeOH, EtOH, *n*-PrOH, *i*-PrOH and *t*-BuOH were purchased from Aldrich and used directly without further purification. Melting points were uncorrected; ^{1}H NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using $CDCl_3$ as the solvent and with TMS as internal standard; IR spectra were determined on a Perkin-Elmer SP One FT-IR spectrophotometer. Poly[4-(diacetoxy)iodo]styrene containing 1.85 mmol/g of functional group by elemental analysis was prepared according to the reported method.[8]

General procedure for the synthesis of carboxylic acid methyl esters 2

To a stirred solution of primary alcohol **1a** (1.0 mmol), iodine (0.5 mmol) in methanol (10 mL) was added PSDIB (2.0 mmol, 1.08 g), and the mixture was stirred at room temperature in an open vessel for the times mentioned in Table 1. After the reaction, the mixture was quenched with water (30 mL) and filtered to remove the polymer species, which was then washed with ether (3 × 5 mL). The filtrate was extracted with ether (2 × 15 mL), washed with water and dried with magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel using ethyl acetate/hexane (10/1) as eluent to give pure products **2a-2k**. All these esters were characterized by ^{1}H NMR and IR spectral analysis and by comparison with authentic compounds.

Methyl benzoate (2a)[9]: Oil; ^{1}H NMR δ 8.01-7.93 (m, 2H), 7.51-7.40 (m, 3H), 3.90 (s, 3H); IR (neat) ν_{max} 1725 cm^{-1}.

Methyl *p*-methylbenzoate (2b)[9]: Colorless solid; mp 35-36 °C (lit. mp 33-36 °C); ^{1}H NMR δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 2H), 3.84 (s, 3H), 2.34 (s, 3H); IR (neat) ν_{max} 1727 cm^{-1}.

Methyl *p*-methoxybenzoate (2c)[9]: Colorless solid; mp 48-49 °C (lit. mp 49-51 °C); ^{1}H NMR δ 7.87 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H); IR (neat) ν_{max} 1725 cm^{-1}.

Methyl *p*-chlorobenzoate (2d)[9]: Colorless solid; mp 43-44 °C (lit. mp 42-44 °C); ^{1}H NMR δ 7.95 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H); IR (neat) ν_{max} 1718 cm^{-1}.

Methyl 3,4-dimethoxybenzoate (2e)[9]: Colorless solid; mp 60-61 °C (lit. mp 59-62 °C); ^{1}H NMR δ 7.83 (d, *J* = 8.7 Hz, 1H), 7.32 (s, 1H), 7.14 (d, *J* = 8.7 Hz, 1H), 3.83 (s, 3H), 3.75 (s, 3H), 3.73 (s, 3H); IR (neat) ν_{max} 1726 cm^{-1}.

Methyl *p*-nitrobenzoate (2f)[9]: Pale yellow solid; mp 91-92 °C (lit. mp 90-92 °C); ^{1}H NMR δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 8.8 Hz, 2H), 3.90 (s, 3H); IR (neat) ν_{max} 1735, 1528 cm^{-1}.

Methyl *trans*-cinnamate (2g)[9]: Colorless solid; mp 36-37 °C (lit. mp 36-38 °C); ^{1}H NMR δ 7.57 (d, *J* = 15.8 Hz, 1H), 7.11-6.90 (m, 3H), 7.10 (d, *J* = 15.8 Hz, 1H), 6.82-6.71 (m, 2H), 3.80 (s, 3H); IR (neat) ν_{max} 1720, 1635 cm^{-1}.

Methyl 3-phenylpropynoate (2h)[10]: Oil, ^{1}H NMR δ 7.60-7.45 (m, 2H), 7.31-7.22 (m, 3H), 3.81 (s, 3H); IR (neat) ν_{max} 2110, 1721 cm^{-1}.

Methyl 2-phenylethanoate (2i)[11]: Oil, ^{1}H NMR δ 7.35-7.27 (m, 5H), 3.71 (s, 3H), 3.62 (s, 2H); IR (neat) ν_{max} 1730 cm^{-1}.

Methyl cyclohexylmethanoate (2j)[11]: Oil, ^{1}H NMR δ 3.61 (s, 3H), 2.26-2.23 (m, 1H), 1.86-1.82 (m, 2H), 1.71-1.64 (m, 2H), 1.60-1.57 (m, 1H), 1.41-1.30 (m, 2H), 1.26-1.17 (m, 3H); IR (neat) ν_{max} 1741 cm^{-1}.

Methyl *n*-heptylate (2k)[9]: Oil, ^{1}H NMR δ 3.62 (s, 3H), 2.26 (t, *J* = 7.5 Hz, 2H), 1.60-1.53 (m, 2H), 1.26-1.22 (m, 6H), 0.85 (t, *J* = 7.1 Hz, 3H); IR (neat) ν_{max} 1743 cm^{-1}.

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