Supplementary Information

An excellent dual recycling strategy for the hypervalent iodine/nitroxyl radical mediated selective oxidation of alcohols to aldehydes and ketones

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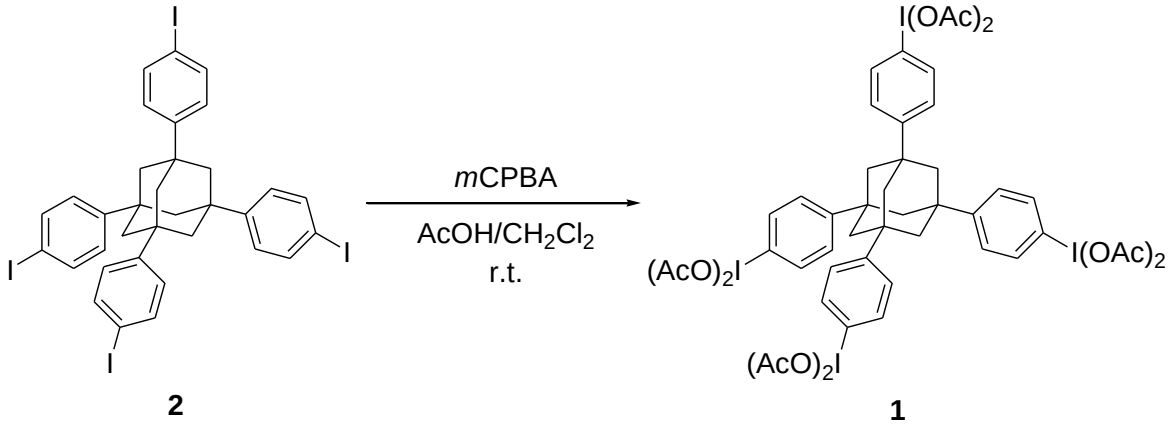
General Melting points were measured using a Büchi B 545 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL JMN-300 spectrometer operating at 400 MHz and 100 MHz in $CDCl_3$ at 25 ^{o}C with tetramethylsilane (δ = 0 ppm) as the internal standard. The data are reported as follows: chemical shifts (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br s = broad singlet, m = multiplet), coupling constant (J) in Hz, and integration. Infrared spectra (IR) were recorded by using a Hitachi 270-50 spectrometer; intensities of absorptions are reported in reciprocal centimeters (cm^{-1}) for strong and structurally important peaks. Flash column chromatography and analytical TLC were carried out on Merck silica gel 60 (230–400 mesh) and Merck silica gel F_{254} plates (0.25 mm), respectively. The spots and bands were detected by UV irradiation (254, 365 nm) or by staining with 5% phosphomolybdic acid followed by heating. Elemental analysis was performed by the Elemental Analysis Section of Osaka University. Dichloromethane, methanol, and other solvents and eluents for the column chromatography and TLC were obtained from commercially suppliers. The alcohols except for **3c** and catalysts, 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO), 2-azaadamantane-N-oxyl (AZADO), and the silica-supported TEMPO [Aldrich Co. Ltd. (catalog

No. 576344, 120-230 mesh, extent of labeling: 0.7 mmol/g loading)] are commercially available and used without further purification.

1. Preparation of the recyclable hypervalent iodine reagent 1 from the tetraiodide 2

*(Regeneration step for the reagent **1**)*



2 **1**

To a stirred solution of the (recovered) tetraiodide **2**[1)] (1.42 g, 1.5 mmol) in dichloromethane (150 mL) and acetic acid (150 mL) was added *m*-chloroperbenzoic acid (*m*CPBA) (*ca.* 69% purity, 3.12 g, 18 mmol) at room temperature. The mixture was stirred for 12 hours under the same reaction conditions until the cloudy solution became clear. The resultant mixture was filtered, and dichloromethane was removed from the filtrate using a rotary evaporator. Hexanes were added to the residue to precipitate 1,3,5,7-tetrakis[4-(diacetoxyiodo)phenyl]adamantane **1**. After filtration, the crude **1** was washed se-veral times with the hexanes, and then dried *in vacuo* to give **1** (2.09 g, 97%) as a white solid.

1,3,5,7-Tetrakis[4-(diacetoxyiodo)phenyl]adamantane (1) [2)]

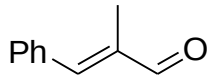
Colorless crystal; mp (decomp.) 195-196 ^{o}C (from AcOH-dichloromethane-hexanes by vapor diffusion method); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.01 (s, 24H), 2.20 (s, 12H), 7.56 (d, *J* = 8.7 Hz, 8H), 8.09 (d, *J* = 8.7 Hz, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.4, 39.6, 46.4, 119.5, 127.7, 135.2, 151.9, 176.5 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.

2. Typical procedure for TEMPO catalyzed oxidations of alcohols 3 to aldehydes 4 using the recyclable hypervalent iodine reagent 1 (Table 1)

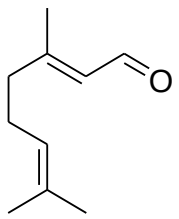
The recyclable reagent **1** (77.9 mg, 0.22 x 1/4 mmol) was added to a dichloromethane solution (1 mL) including the alcohol **3** (0.20 mmol) and catalytic amount of TEMPO (3.1 mg, 0.02 mmol). The reaction mixture was stirred until the alcohol **3** was no longer detectable by TLC. After removal of the solvent using a rotary evaporator, methanol (5 mL) was added to the residue to precipitate the tetraiodide **2**. After filtration, the crude **2** on the filter was washed several times with small amounts of methanol, and the residue was nearly quantitatively recovered as the pure tetraiodide **2**. From the filtrate, the crude product **4** was obtained after evaporation, which was purified by short column chromatography on silica gel to give the pure aldehyde. Physical and spectral data matched those authentic samples.

(*E*)-α-Methylcinnamaldehyde (4a)



Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08 (s, 3 H), 7.25 (s, 1 H), 7.53-7.83 (m, 5 H), 9.57 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.1, 128.9, 129.7, 130.2, 135.3, 138.5, 149.5, 195.6 ppm; IR (KBr): 1711 cm^{-1}.

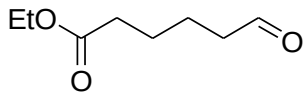
Geranaldehyde (4b)



Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60 (s, 3H), 1.70 (s, 3H), 1.90 (s, 3H),

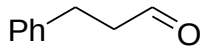
2.13-2.21 (m, 4H), 4.93 (t, *J* = 8.1 Hz, 1H), 5.81 (s, 1H), 9.94 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.4, 17.5, 25.5, 25.6, 40.4, 122.4, 127.2, 132.7, 163.6, 191.1 ppm; IR (KBr): 1716 cm^{-1}.

Ethyl 6-oxohexanoate (4c)



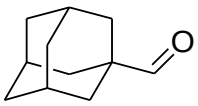
Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, *J* = 7.8 Hz, 3H), 1.61-1.65 (m, 4H), 2.29 (t, *J* = 6.8 Hz, 2H), 2.43 (t, *J* = 6.6 Hz, 2H), 4.09 (q, *J* = 7.8 Hz, 2H), 9.73 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 21.5, 24.4, 34.0, 43.5, 60.4, 173.1, 202.2 ppm; IR (KBr): 2981, 2941, 2874, 1732, 1713, 1374, 1184 cm^{-1}.

Hydrocinnamaldehyde (4d)



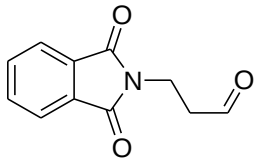
Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.83 (t, *J* = 7.4 Hz, 2H), 3.01 (t, *J* = 7.4 Hz, 2H), 7.25-7.38 (m, 5H), 9.83 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.2, 125.8, 126.0, 128.4, 129.2, 201.7 ppm; IR (KBr): 1718 cm^{-1}.

1-(Adamantyl) carbaldehyde (4e)



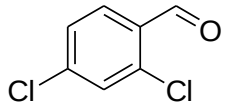
White crystals; mp 134-136 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.69-1.81 (m, 12H), 2.02-2.15 (m, 3H), 9.32 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.3, 35.8, 36.5, 44.8, 206.0 ppm; IR (KBr): 2905, 2850, 1723 cm^{-1}.

3-(*N*-Phthalimido)propionaldehyde (4f)



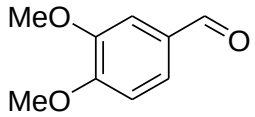
White crystals; mp 126-127 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.86 (t, *J* = 7.3 Hz, 2H), 4.02 (t, *J* = 7.3 Hz, 2H), 7.70-7.72 (m, 2H), 7.82-7.84 (m, 2H), 9.80 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.7, 42.3, 123.3, 131.9, 134.1, 168.0, 199.4 ppm; IR (KBr): 1771, 1709, 1469, 1441, 913, 743, 718 cm^{-1}.

2,4-Dichlorobenzaldehyde (4g)



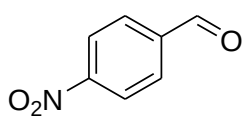
Colorless crystals; mp 65-66 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 10.40 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 127.9, 130.3, 130.4, 130.9, 138.5, 141.1, 188.5 ppm; IR (KBr): 1697 cm^{-1}.

Veratraldehyde (4h)



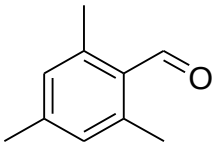
Colorless crystals; mp 40-41 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 3H), 3.91 (s, 3H), 6.93 (d, *J* = 8.4 Hz, 1H), 7.35 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 9.79 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.8, 56.0, 108.7, 110.2, 126.7, 130.0, 149.4, 154.3, 190.7 ppm; IR (KBr): 1682 cm^{-1}.

***p*-Nitrobenzaldehyde (4i)**



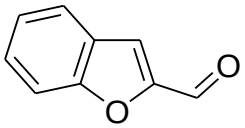
Yellow crystals; mp 103-104 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.0 Hz, 2H), 8.41 (d, *J* = 8.0 Hz, 2H), 10.18 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 124.2, 130.4, 139.9, 151.0, 190.2 ppm; IR (KBr): 1708, 1539 cm^{-1}.

2,4,6-Trimethylbenzaldehyde (4j)



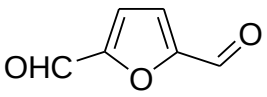
Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3H), 2.57 (s, 6H), 6.88 (s, 2H), 10.55 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.5, 21.5, 130.1, 130.5, 141.5, 143.8, 192.9 ppm; IR (KBr): 2992, 2863, 2766, 1682 cm^{-1}.

2-Benzofurancarboxaldehyde (4k)



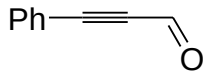
Slightly yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, *J* = 7.2 Hz, 1H), 7.46-7.57 (m, 3H), 7.72 (d, *J* = 7.8 Hz, 1H), 9.84 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 112.4, 117.7, 123.5, 124.0, 126.4, 129.0, 152.4, 156.0, 179.5 ppm; IR (KBr): 1687, 1258 cm^{-1}.

2,5-Diformylfuran (4l)



Colorless crystals; mp 108-109 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (s, 2H), 9.80 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 120.4, 154.8, 179.7 ppm; IR (KBr): 1682, 1266, 810 cm^{-1}.

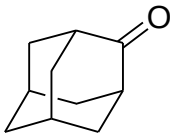
Phenylpropiolaldehyde (4m)



Slightly yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (t, *J* = 8.0 Hz, 2H), 7.48 (t, *J* = 8.1 Hz, 1H), 7.59 (d, *J* = 8.3 Hz, 2H), 9.41 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 88.2, 94.9, 119.2, 128.5, 131.1, 133.1, 176.6 ppm; IR (KBr): 2190, 1660, 1489, 758 cm^{-1}.

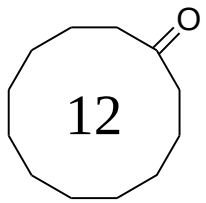
The corresponding ketones **4n-r** were obtained from alcohols **3n-r** by the same procedure.

2-Adamantanone (4n)



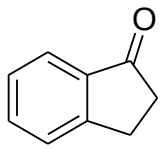
Colorless crystals; mp 256-258 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.93-2.10 (m, 12H), 2.55 (br s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.4, 36.2, 39.2, 46.9, 218.2 ppm; IR (KBr): 2914, 2854, 1719, 1452 cm^{-1}.

Cyclododecanone (4o)



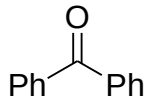
Colorless crystals; mp 59-61 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24-1.28 (m, 14H), 1.66-1.72 (m, 4H), 2.42-2.46 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3, 22.5, 24.2, 24.6, 24.7, 40.4, 212.9 ppm; IR (KBr): 1710 cm^{-1}.

1-Indanone (4p)



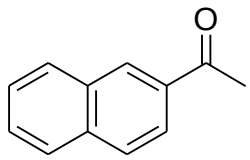
Colorless crystals; mp 38-40 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.68-2.71 (m, 2H), 3.15 (t, *J* = 5.9 Hz, 2H), 7.35-7.77 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9, 35.2, 122.5, 125.9, 126.3, 133.6, 136.1, 154.2, 205.6 ppm; IR (KBr): 2925, 1713, 758 cm^{-1}.

Benzophenone (4q)



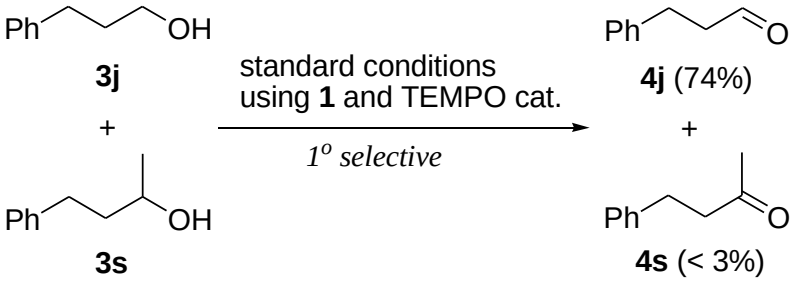
Colorless crystals; mp 47-51 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (t, *J* = 7.2 Hz, 4H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.81 (d, *J* = 7.2 Hz, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 128.3, 130.1, 132.4, 137.6, 196.7 ppm; IR (KBr): 1662 cm^{-1}.

2'-Acetonaphthone (4r)



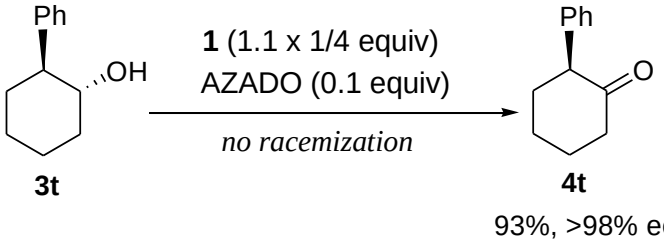
Colorless crystals; mp 52-56 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.73 (s, 3H), 7.53-7.62 (m, 2H), 7.88 (t, *J* = 8.0 Hz, 2H), 7.96 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 8.46 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.7, 123.8, 126.7, 127.7, 128.4, 128.4, 129.5, 130.2, 132.4, 134.4, 135.5, 198.1 ppm; IR (KBr): 1680 cm^{-1}.

3. Cross-over experiment: selective synthesis of aldehyde 4j from primary alcohol 3j in the presence of a secondary alcohol 3s (Scheme 4)



The recyclable reagent **1** (88.5 mg, 0.25 x 1/4 mmol) was added to a dichloromethane solution (1.2 mL) containing the alcohol **3j** (34.0 mg, 0.25 mmol), 4-phenyl-2-butanol **3s** (37.5 mg, 0.25 mmol), and a catalytic amount of TEMPO (3.9 mg, 0.025 mmol) at 0 ^{o}C. The reaction mixture was stirred until the alcohol **3j** was no longer detectable by TLC. Workup of the reaction mixture and recovery of the tetraiodide **2** were conducted according to the typical procedure already described. From the filtrate, the crude product **4j** and remaining 4-phenyl-2-butanol **3s** were obtained as a mixture after evaporation, which was separated by short column chromatography on silica gel to give the pure aldehyde or ketone **4j** in 73% yield with a 97% recovery of the 4-phenyl-2-butanol **3s**.

4. Non-racemic synthesis of enolizable ketone 4t (Scheme 5)



The enalizable ketone **4t** was obtained in the optically pure form from the corresponding alcohol **3t** by a procedure similar to that described for the alcohols in Table 1 using AZADO instead of TEMPO. The optical purity of the obtained ketone **4t** was measured by HPLC (Daicel OD

column, hexane:*i*-PrOH = 95:5, flow rate 0.8 mL/min, t_R = 10.0 min. [(*S*)-(–)-enantiomer].

(*S*)-(-)-2-Phenylcyclohexanone (4t) [3)]

Colorless crystals; mp 56-59 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 1.78-1.84 (m, 2H), 1.97-2.07 (m, 2H), 2.12-2.16 (m, 1H), 2.23-2.29 (m, 1H), 2.40-2.54 (m, 2H), 3.60 (dd, *J* = 12.2, 5.4 Hz, 1H), 7.11-7.34 (m, 5H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 25.2, 27.7, 35.0, 42.1, 57.3, 126.8, 128.3, 128.5, 138.7, 210.2 ppm; IR (KBr): 1698 cm^{-1}.

5. General experimental procedure for a green oxidation of alcohols using a combination of the recyclable hypervalent iodine reagent 1 and supported TEMPO catalyst: The dual recycling strategy (Tables 2 and 3)

The adamantane reagent **1** (77.9 mg, 0.22 x 1/4 mmol) was added to a stirred mixture of the alcohol **3** (0.20 mmol) and catalytic amount of silica-supported TEMPO **5**[4)] (65.6 mg, 0.04 mmol) in dichloromethane (1 mL) at room temperature. After consumption of the alcohol **3**, the insoluble TEMPO **5** was recovered in a quantitative amount by filtration after washing several times with dichloromethane. After removal of the solvent from the filtrate, methanol (5 mL) was added to the residue to precipitate the tetraiodide **2**. After filtration, the crude **2** was washed several times with small amounts of methanol, and the residue on the filter was nearly quantitatively collected as the pure **2**. From the filtrate, the crude product **4** was obtained after evaporation, which was purified by short column chromatography on silica gel to give the pure aldehyde or ketone if required.

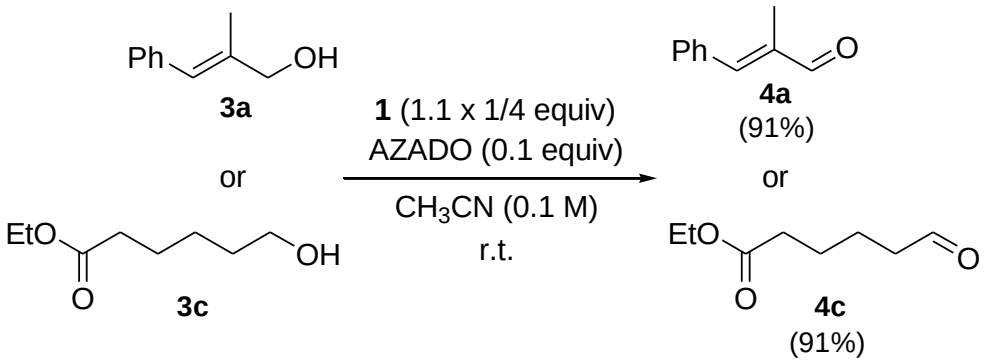
The results of alcohol oxidation using the adamantane **1** and silica-supported TEMPO **5** are summarized in Table 2.

Reusability of the recovered adamantane reagent **1** and silica-supported TEMPO catalyst **5** for the alcohol oxidation was evaluated at least four times using the alcohol **3g** as a model substrate

in the dual recycling strategy (see Table 3).

6. Use of acetonitrile instead of dichloromethane as solvent

The reactions were generally carried out in dichloromethane since the chlorinated solvent is the most popularly employed for the conventional PIDA/TEMPO-mediated oxidations of alcohols in previous studies. We already confirmed possible use of other solvents, such as acetonitrile, and representative results are described herein.



The recyclable reagent **1** (0.11 x 1/4 mmol) was added to an acetonitrile solution (2 mL) including the alcohol **3a** (0.20 mmol) or **3c** (0.20 mmol) and catalytic amount of AZADO (0.02 mmol). The reaction mixture was stirred for 4 hours at room temperature. After removal of the solvent, methanol (5 mL) was added to the residue to precipitate the tetraiodide **2**. After filtration, the crude **2** on the filter was washed several times with small amounts of methanol, and the residue was nearly quantitatively recovered as the pure tetraiodide **2**. From the filtrate, the crude product **4** was obtained after evaporation, which was purified by short column chromatography on silica gel to give the pure aldehyde **4a** or **4c** in 91% yield in both cases.

References

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