A simple and efficient oxidation of alcohols with ruthenium on carbon

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General experimental. 10% Ru/C (dry K-type, Lot No. 41A-070069) was supplied by the N.E. Chemcat Corporation (Tokyo, Japan). Dehydrated DMSO and MeCN were purchased from Wako Pure Chemical Industries, Ltd., *t*-BuOH was purchased from Tokyo Chemical Industry Co. Ltd. These solvents were used without purification. The HPLC grade toluene (purchased from Wako Pure Chemical Industries, Ltd.) was desulfurized by washing con. H_2SO_4, and then distilled from Sodium metal. All other reagents were purchased from commercially sources and used without further purification. Flash column chromatography was performed using Silica Gel 60 N (Kanto Chemical Co., Inc., 63-210 μm spherical, neutral). ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL AL 400 spectrometer or JEOL EX 400 spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). Chemical shifts (δ) are expressed in ppm and are internally referenced (0.00 ppm for TMS for $CDCl_3$ for ^{1}H NMR and 77.0 ppm for $CDCl_3$ for ^{13}C NMR). EI and FAB mass spectra were taken on a JEOL JMS-SX102A instrument.

Optimization of reaction conditions (Table 1): A 15 mL-test tube containing a stir bar was charged with 1-phenyl-1-pentanol (**1**) (164 mg, 1.00 mmol), 10% Ru/C (50.5 mg, 0.0500 mmol), and solvent (2 mL) given in Table 1 (2 mL). The system was sealed with a septum and the air inside was replaced with O_2 by three vacuum/O_2 (balloon) cycles. The mixture was placed on the Chemistation personal organic synthesizer (EYELA, Tokyo), and heated at 70 °C. After 24 h, the reaction mixture was diluted with ether (10 mL) and then passed through a membrane filter (Millipore, Millex–LH, 0.45 μm). The filtrate was concentrated in vacuo, and the product ratio of **1** and varelophenone (**2**) was determined by ^{1}H NMR analysis of the residue based on the signal intensity of 7.90 ppm for **1** (the *o*-position of the benzene ring) and 4.56 ppm for **2** (the benzylic position).

Entry 1 Toluene was used as the solvent. **1** : **2** = 7 : 93.

Entry 2 Toluene was used as the solvent. Norit (45.4 mg) was used instead of 10% Ru/C. **1** : **2** = 98 : 2.

Entry 3 Toluene was used as the solvent. The reaction was carried out under an Ar atmosphere. **1** : **2** = 82 : 18.

Entry 4 DMSO was used as the solvent. **1** : **2** = 96 : 4.

Entry 5 *t*-BuOH was used as the solvent. **1** : **2** = 87 : 13.

Entry 6 MeCN was used as the solvent. **1** : **2** = 43: 57.

Entry 7 The reaction was carried out in toluene at rt. **1** : **2** = 84: 16.

Entry 8 The reaction was carried out in toluene at 70 °C. Only **2** was obtained.

Synthesis of substrate (3b and 3e–3g)

1-*o*-Tolylethanol (3b)[1]

To a solution of 2-methylacetophenone (403 mg, 3.00 mmol) in EtOH (3 mL) was added $NaBH_4$ (170 mg, 4.5 mmol) at rt. After 1 h, the reaction mixture was diluted with H_2O (10 mL) and then partitioned between EtOAc (30 mL) and H_2O (30 mL). The water layer was washed with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (40 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica-gel column chromatography with *n*-hexane /EtOAc (5/1) as the eluent to give 1-*o*-tolylethanol (**3f**, 354 mg, 97%) as a colorless oil. The ^{1}H NMR data was identical with that of the literature.

1-(4-Nitrophenyl)ethanol (3e)[2]

To a solution of 4-nitroacetophenone (495 mg, 3.00 mmol) in EtOH (3 mL) was added $NaBH_4$ (170 mg, 4.5 mmol) at rt. After 40 minutes, the reaction mixture was diluted with H_2O (10 mL) and then partitioned between EtOAc (30 mL) and H_2O (30 mL). The water layer was washed with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (40 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica-gel column chromatography with *n*-hexane /EtOAc (10/1) as the eluent to give 1-(4-nitrophenyl)ethanol (**3d**, 477 mg, 95%) as a pale yellow oil. The ^{1}H NMR data was identical with that of the literature.

1-(4-Methoxyphenyl)ethanol (3f)[3]

To a solution of 4-methoxyacetophenone (451 mg, 3.00 mmol) in THF (2.7 mL) and H_2O (0.3 mL) was added $NaBH_4$ (283 mg, 7.5 mmol) at rt. After 48 h, the reaction mixture was diluted with H_2O (10 mL) and then partitioned between EtOAc (30 mL) and H_2O (30 mL). The water layer was washed with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (40 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica-gel column chromatography with *n*-hexane /EtOAc (1/1) as the eluent to give 1-(4-methoxyphenyl)ethanol (**3e**, 245 mg, 54%) as a colorless oil. The ^{1}H NMR data was identical with that of the literature.

1-(Thiophen-1-yl)ethanol (3g)[4]

To a solution of 2′-acetylthiophene (379 mg, 3.00 mmol) in EtOH (3 mL) was added $NaBH_4$ (170 mg, 4.5 mmol) at rt. After 1 h, the reaction mixture was diluted with H_2O (10 mL) and then

partitioned between EtOAc (30 mL) and H_2O (30 mL). The water layer was washed with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (40 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica-gel column chromatography with *n*-hexane /EtOAc (4/1) as the eluent to give 1-(thiophen-1-yl)ethanol (**3g**, 391 mg, quantitative) as a colorless oil. The ^{1}H NMR data was identical with that of the literature.

General procedure for oxidation of secondary benzylic alcohols (Table 2): A 15 mL–test tube containing a stir bar was charged with substrate (**3a**–**3g**) (0.500 mmol), 10% Ru/C (25.3 mg, 0.0250 mmol), and toluene (1 mL). The system was sealed with a septum and the air inside was replaced with O_2 by three vacuum/O_2 (balloon) cycles. The mixture was placed on the Chemistation personal organic synthesizer (EYELA, Tokyo), and heated at 70 °C. After the reaction time given in Table 2, the reaction mixture was diluted with ether (10 mL) and then passed through a membrane filter (Millipore, Millex–LH, 0.45 μm). The filtrate was concentrated in vacuo, and the residue was purified by silica-gel column chromatography with *n*-hexane or *n*-pentane/ether as the eluent.

Acetophenone (4a, Entry 1) 59.7 mg (99%)
Obtained from 1-phenylethanol (**3a**) (61.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

2-Methylacetophenone (4b, Entry 6) 57.8 mg (86%)
Obtained from 1-*o*-tolylethanol (**3f**) (68.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

2,2-Dimethyl-1-phenylpropan-1-one (4c, Entry 2) 72.4 mg (89%)
Obtained from 2,2-dimethyl-1-phenyl-1-propanol (**3b**) (82.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

(4-Chlorophenyl)(phenyl)methanone (4d, Entry 3) 209 mg (96%)
Obtained from 4-chlorobenzhydrol (**3c**) (219 mg, 1.00 mmol) in toluene (2 mL) using 10% Ru/C (50.5 mg, 0.0500 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.
4-Nitroacetophenone (4e, Entry 4) 78.3 mg (95%)
Obtained from 1-(4-nitrophenyl)ethanol (**3d**) (83.6 mg, 0.500 mmol) using 10% Ru/C (25.3 mg,

0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

4-Methoxyacetophenone (4f, Entry 5) 43.4 mg (58%)
Obtained from 1-(4-methoxyphenyl)ethanol (**3e**) (76.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

2´-Acetylthiophene (4g, Entry 7) 54.4 mg (86%)
Obtained from 1-(thiophen-2-yl)ethanol (**3g**) (64.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

General procedure for oxidation of primary benzylic alcohols (Table 3): A 15 mL–test tube containing a stir bar was charged with substrate (**5a**–**5g**) (0.500 mmol), 10% Ru/C (25.3 mg, 0.0250 mmol), and toluene (1 mL). The system was sealed with a septum and the air inside was replaced with O_2 by three vacuum/O_2 (balloon) cycles. The mixture was placed on the Chemistation personal organic synthesizer (EYELA, Tokyo), and heated at 50 or 90 °C. After the reaction time given in Table 3, the reaction mixture was diluted with ether (10 mL) and then passed through a membrane filter (Millipore, Millex–LH, 0.45 μm). The filtrate was concentrated in vacuo, and the residue was purified by silica-gel column chromatography with *n*-hexane or *n*-pentane/ether as the eluent.

4-Chlorobenzaldehyde (6a, Entry 1) 116 mg (82%)
Obtained from 4-chlorobenzylalcohol (**5a**) (143 mg, 1.00 mmol) using 10% Ru/C (50.5 mg, 0.0500 mmol), and toluene (2 mL) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

4-Nitrobenzaldehyde (6b, Entry 2) 130 mg (86%)
Obtained from 4-nitrobenzylalcohol (**5b**) (153 mg, 1.00 mmol) using 10% Ru/C (50.5 mg, 0.0500 mmol), and toluene (2 mL) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

4-Benzyloxybenzaldehyde (6c, Entry 3) 191 mg (89%)
Obtained from 4-benzyloxybenzylalcohol (**5c**) (214 mg, 1.00 mmol) using 10% Ru/C (50.5 mg, 0.0500 mmol), and toluene (2 mL) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

Salicylaldehyde (6d, Entry 4) 48.3 mg (79%)

Obtained from salicyl alcohol (**5d**) (62.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

1-Naphthylaldehyde (6e, Entry 5) 155 mg (91%)

Obtained from 1-naphthalene methanol (**5e**) (158 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

2-Thiophenaldehyde (6f, Entry 6) 48.7 mg (87%)

Obtained from 2-thiophene methanol (**5f**) (57.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

3-Pyridine carboxyaldehyde (6g, Entry 7) 60.0 mg (quantitative)

Obtained from pyridine 3-methanol (**5g**) (54.6 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) at 90 °C according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

General procedure for oxidation of cinnamyl and aliphatic alcohols (Table 4): A 15 mL–test tube containing a stir bar was charged with substrate (**7a**–**7e**) (0.500 mmol), 10% Ru/C (25.3 mg, 0.0250 mmol), and toluene (1 mL). The system was sealed with a septum and the air inside was replaced with O_2 by three vacuum/O_2 (balloon) cycles. The mixture was placed on the Chemistation personal organic synthesizer (EYELA, Tokyo), and heated at 50–90 °C. After 24 h, the reaction mixture was diluted with ether (10 mL) and then passed through a membrane filter (Millipore, Millex–LH, 0.45 μm). The filtrate was concentrated in vacuo, and the residue was purified by silica-gel column chromatography with *n*-hexane or *n*-pentane/ether as the eluent.

4-Nitrocinnamaldehyde (8a, Entry 1) 74.9 mg (85%)

Obtained from 4-nitrocinnamyl alcohol (**7a**) (89.6 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) at 50 °C according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Tokyo Chemical Industry Co. Ltd..

***Trans*-cinnamaldehyde (Entry 2, 8b)** 52.0 mg (79%)

Obtained from cinnamyl alcohol (**7b**) (67.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) at 70 °C according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

4-Phenyl-2-butanone (Entry 3, 8c) 48.9 mg (66%)

Obtained from 4-phenyl-2-butanol (**7c**) (75.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) at 90 °C according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

2-Decanone (Entry 4, 8d) 48.0 mg (61%)

Obtained from 2-decanol (**7d**) (79.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) at 90 °C according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

Decanal (Entry 6, 8e) 11.1 mg (14%)

Obtained from 1-decanol (**7e**) (79.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) in toluene (0.8 mL)–H_2O (0.2 mL) at 90 °C according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

Decanoic acid (Entry 6, 8f) 50.8 mg (59%)

Obtained from 1-decanol (**7e**) (79.1 mg, 0.500 mmol) using 10% Ru/C (25.3 mg, 0.0250 mmol) in toluene (0.8 mL)–H_2O (0.2 mL) at 90 °C according to the general procedure. The ^{1}H NMR data was identical with that of the commercial product from Aldrich.

Assay of Residual Ruthenium in the Reaction Mixture

The reaction of 1-phenyl-1-pentanol (1.31 g, 8.00 mmol) using 10% Ru/C (404 mg, 400 μmol) and in toluene (16 mL) under O_2 was carried out at 70 °C for 26 h. The mixture was passed through a Celite pad and membrane filters (Millipore, Millex®–LH, 0.45 μm and 0.2 μm). The filtrate was diluted with toluene to 50 mL of total volume and the residual ruthenium was assayed using Shimadzu ICP8000 (Shimadzu, Kyoto, Japan).

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