

# A mild oxidative transformation of nitro compounds into ketones by tetrapropylammonium perruthenate

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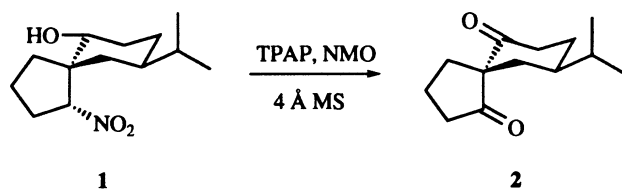
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Oxidation of secondary nitro compounds with a catalytic amount of tetrapropylammonium perruthenate in the presence of *N*-methylmorpholine *N*-oxide, silver(I) acetate, potassium carbonate and 4 Å molecular sieves provides the corresponding ketones in moderate to good yields.

The nitro group is a versatile functionality for carbon-carbon bond formation in organic synthesis and can be converted into other functionalities. One of the most useful of such conversions is the formation of a carbonyl group, and a variety of conditions have been employed: acidic,<sup>1</sup> reductive,<sup>2</sup> oxidative<sup>3</sup> and basic.<sup>4</sup> Some of these conditions are not, however, compatible with the presence of other sensitive functionalities.

Ley and Griffith have demonstrated various types of oxidations using tetrapropylammonium perruthenate and *N*-methylmorpholine *N*-oxide, including, in particular, the transformation of alcohols into carbonyl compounds.<sup>5</sup> In recent communications, Guertin and Kende<sup>6</sup> showed that tetrapropylammonium perruthenate was a good catalyst for the oxidation of sulfides to sulfones, and Goti and co-workers recorded its use for conversions of secondary amines into imines<sup>7</sup> and of hydroxylamines into nitrones.<sup>8</sup> We now describe that tetrapropylammonium perruthenate is an efficient catalyst for the oxidative conversion of nitro derivatives into ketones.<sup>9</sup>

We have recently reported the transformation of the nitro compound **1** into the ketone **2** by using a stoichiometric amount of tetrapropylammonium perruthenate in the presence of *N*-methylmorpholine *N*-oxide and 4 Å molecular sieves (Scheme 1).<sup>10</sup> The conversion of **3**<sup>11</sup> into **4** has been further investigated



TPAP = tetrapropylammonium perruthenate  
NMO = *N*-methylmorpholine *N*-oxide  
MS = molecular sieves

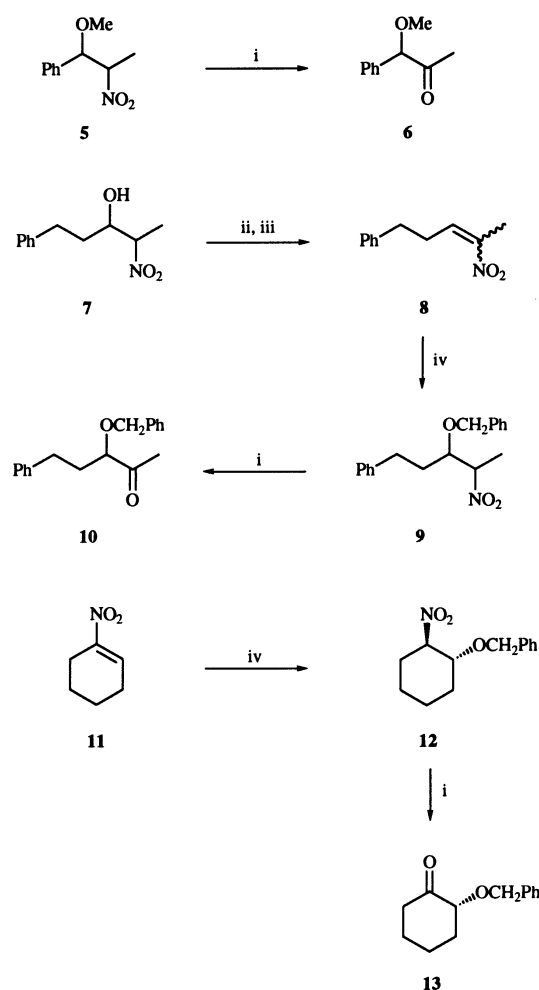
Scheme 1

utilizing a catalytic amount of the reagent (Table 1). Although the oxidation using 5 mol% of tetrapropylammonium perruthenate and *N*-methylmorpholine *N*-oxide as a co-oxidant with  $\text{K}_2\text{CO}_3$  gave a poor result (entry 1), addition of various silver(I) salts improved the yield. The oxidations using 5 mol% of tetrapropylammonium perruthenate and a small excess of *N*-methylmorpholine *N*-oxide in the presence of silver(I) cyanide (entry 2), silver(I) perchlorate (entry 3), silver(I) carbonate (entry 4), silver(I) acetate (entry 5) and silver(I) sulfate (entries 6–8) were examined. It has been suggested from the results that silver(I) carbonate, silver(I) acetate and silver(I) sulfate are effective, and the addition of potassium carbonate and the use of acetonitrile as a solvent are favourable.

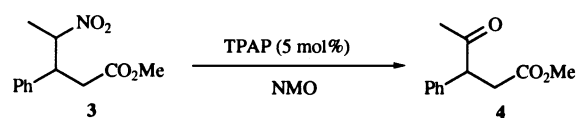
Next, the oxidation of **3** with 10 mol% of tetrapropylammonium perruthenate and 1.5 mol equiv. of *N*-methylmorpholine *N*-oxide in the presence of potassium carbonate and 4 Å

molecular sieves was examined using silver(I) sulfate, silver(I) carbonate or silver(I) acetate (Table 2). Although the use of a stoichiometric amount of tetrapropylammonium perruthenate gave the best result (entry 4), the treatment of **3** with 10 mol% of tetrapropylammonium perruthenate in the presence of *N*-methylmorpholine *N*-oxide, silver(I) acetate and potassium carbonate in acetonitrile provided **4** in 89% yield (entry 3).

The treatment of **5**<sup>11</sup> under the conditions of entry 3 in Table 2 afforded **6** in 52% yield (75% yield based on the recovered starting material). The benzyl ethers **9** and **12** were prepared from known nitro compounds **7**<sup>12</sup> and **11**, respectively. Treatment of **9** and **12** under the same conditions as above provided **10** and **13** in 76 and 62% yields, respectively (Scheme 2). How-



Scheme 2 Reagents and conditions: i, TPAP, NMO, AgOAc, 4 Å molecular sieves,  $\text{K}_2\text{CO}_3$ , acetonitrile; ii,  $\text{Ac}_2\text{O}$ , DMAP; iii, DMAP, basic alumina; iv,  $\text{PhCH}_2\text{ONa}$

**Table 1** Oxidation of **3** with TPAP–NMO<sup>a</sup>

Entry	Silver salt (equiv.)	K <sub>2</sub> CO <sub>3</sub> (equiv.)	Solvent	Conversion yield (%) <sup>b</sup>
1	None	5	CH <sub>2</sub> Cl <sub>2</sub>	Trace
2	AgCN (0.5)	5	CH <sub>2</sub> Cl <sub>2</sub>	22
3	AgClO <sub>4</sub> (0.5)	5	CH <sub>2</sub> Cl <sub>2</sub>	25
4	Ag <sub>2</sub> CO <sub>3</sub> (0.25)	5	CH <sub>2</sub> Cl <sub>2</sub>	40
5	AgOAc (0.5)	5	CH <sub>2</sub> Cl <sub>2</sub>	38
6	Ag <sub>2</sub> SO <sub>4</sub> (0.25)	5	CH <sub>2</sub> Cl <sub>2</sub>	40
7	Ag <sub>2</sub> SO <sub>4</sub> (0.25)	None	CH <sub>2</sub> Cl <sub>2</sub>	26
8	Ag <sub>2</sub> SO <sub>4</sub> (0.25)	None	MeCN	36

<sup>a</sup> All reactions were performed at room temperature unless otherwise stated. <sup>b</sup> The conversion yields were determined by <sup>1</sup>H NMR spectroscopy of crude products.

**Table 2** Conversion of **3** into **4** using TPAP–NMO in acetonitrile

Entry	TPAP (equiv.)	NMO (equiv.)	Additive (equiv.)	Yield (%) <sup>a</sup>
1	0.1	1.5	Ag <sub>2</sub> SO <sub>4</sub> (1), K <sub>2</sub> CO <sub>3</sub> (5) 4 Å molecular sieves	64
2	0.1	1.5	Ag <sub>2</sub> CO <sub>3</sub> (1), K <sub>2</sub> CO <sub>3</sub> (5) 4 Å molecular sieves	55
3	0.1	1.5	AgOAc (2), K <sub>2</sub> CO <sub>3</sub> (5) 4 Å molecular sieves	89
4 <sup>b</sup>	1.1	None	None	97

<sup>a</sup> Isolated yield. <sup>b</sup> Solvent is CH<sub>2</sub>Cl<sub>2</sub>.

ever, the treatment of a primary nitro compound under the same conditions yielded an intractable mixture.

In conclusion, we have developed a mild procedure for the conversion of secondary nitro compounds into the corresponding ketones.

## Experimental

### General details

IR Spectra were recorded on a JASCO IR-Report 100 spectrophotometer. NMR Spectra were measured for CDCl<sub>3</sub> solutions with JNM-GX-500 and Hitachi R-3000 spectrometers. Chemical shifts are recorded relative to internal tetramethylsilane; *J* values are in Hz. Mass spectra were taken on JEOL-DX-300 and JEOL-JMS-DX-303 spectrometers.

All reactions were carried out under a positive atmosphere of dry argon. Solvents were distilled prior to use: diethyl ether was distilled from sodium–benzophenone, while 1,2-dimethoxyethane, dichloromethane, 1,2-dichloroethane and acetonitrile were distilled from calcium hydride and stored over 4 Å molecular sieves. The organic extracts were dried over magnesium sulfate and the solvent was removed by rotary evaporation under reduced pressure. All new compounds described in the Experimental section were homogeneous on TLC and HPLC.

### (±)-(5*R*\*,9*R*\*)-9-Isopropylspiro[4.5]decane-1,6-dione **2**

To a suspension of **1**<sup>10</sup> (8.0 mg, 0.031 mmol), 4 Å molecular sieves (10 mg) and *N*-methylmorpholine *N*-oxide (11.7 mg, 0.010 mmol) in dry dichloromethane (1 cm<sup>3</sup>) was added tetrapropylammonium perruthenate (14.2 mg, 0.031 mmol), and the mixture was stirred for 22 h at the ambient temperature. After evaporation of the solvent, the residue was subjected to chromatography on silica gel with hexane–diethyl ether (3:1, v/v) as eluent to give **2** (5.4 mg, 81%) as an oil (Found: C, 74.75; H,

9.75. C<sub>13</sub>H<sub>20</sub>O<sub>2</sub> requires C, 74.95; H, 9.7%);  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1740 (C=O) and 1690 (C=O);  $\delta_{\text{H}}(500 \text{ MHz})$  0.88 (3 H, d, *J* 7.1, Me), 0.90 (3 H, d, *J* 6.4, Me), 1.29–1.57 (4 H, m), 1.82–2.16 (5 H, m), 2.21–2.29 (1 H, m), 2.34–2.45 (2 H, m) and 2.76–2.88 (2 H, m);  $\delta_{\text{C}}(75 \text{ MHz})$  19.2, 19.6, 20.0, 29.6, 32.1, 33.6, 37.6, 38.7, 39.8, 40.6, 64.2, 207.0 and 214.9; *m/z* (EI) 208 (M<sup>+</sup>).

### 2-Nitro-5-phenylpent-2-ene **8**

To a solution of **7**<sup>12</sup> (303.5 mg, 1.452 mmol) and acetic anhydride (1.48 g, 14.4 mmol) in dry diethyl ether (10 cm<sup>3</sup>) was added 4-dimethylaminopyridine (8.9 mg, 0.073 mmol) and the mixture was stirred for 24 h at ambient temperature. The reaction mixture was partitioned between saturated aqueous sodium hydrogen carbonate and diethyl ether. The organic layer was washed with brine, dried and evaporated. To the residue were added 1,2-dichloroethane (10 cm<sup>3</sup>), 4-dimethylaminopyridine (443 mg, 3.63 mmol) and basic alumina (grade I, 440 mg) and the mixture was stirred for 3 h at 40 °C. After filtration, followed by evaporation of the filtrate, the residue was chromatographed on silica gel. Elution with hexane–diethyl ether (10:1, v/v) gave **8** (185.1 mg, 67%) as an oil;  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1675 (C=C) and 1670 (C=C) and 1520 and 1335 (NO<sub>2</sub>);  $\delta_{\text{H}}(300 \text{ MHz})$  2.04 (3 H, br s, Me), 2.54 (2 H, q, *J* 7.5, 4-H<sub>2</sub>), 2.82 (2 H, br t, *J* 7.5, 5-H<sub>2</sub>), 7.10–7.35 (6 H, m, 3-H and Ph) (HRMS: found M<sup>+</sup> – NO<sub>2</sub>, 145.1008. C<sub>11</sub>H<sub>13</sub> requires 145.1017).

### 3-Benzyloxy-2-nitro-5-phenylpentane **9**

To a suspension of sodium hydride (60% in oil; 23.5 mg, 0.0587 mmol) in dry 1,2-dimethoxyethane (1.0 cm<sup>3</sup>) at 0 °C was added benzyl alcohol (680 mg, 0.627 mmol). After being stirred for 30 min at the same temperature, the mixture was treated with a solution of **8** (74.8 mg, 0.392 mmol) in dry 1,2-dimethoxyethane (1.0 cm<sup>3</sup>). The mixture was stirred for 70 min at 0 °C and then partitioned between saturated aqueous ammonium chloride and diethyl ether. The organic layer was washed with brine, dried and evaporated. Column chromatography of the residue on silica gel with hexane–diethyl ether (10:1, v/v) as eluent provided a 4:1 diastereoisomeric mixture of **9** (73.3 mg, 66%) as an oil;  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1540 and 1360 (NO<sub>2</sub>);  $\delta_{\text{H}}(300 \text{ MHz})$  1.49 (3/5 H, d, *J* 7.0, Me), 1.55 (12/5 H, d, *J* 7.0, Me), 1.75–1.99 (2 H, m, 4-H<sub>2</sub>), 2.54–2.82 (2 H, m, 5-H<sub>2</sub>), 3.96 (1/5 H, dt, *J* 7.3 and 4.0, 3-H), 4.03 (4/5 H, ddd, *J* 8.4, 4.6 and 4.0, 3-H), 4.49 (4/5 H, d, *J* 11.1, PhCH<sub>2</sub>O), 4.56 (1 H, d, *J* 11.1, PhCH<sub>2</sub>O), 4.51 (1/5 H, d, *J* 11.1, PhCH<sub>2</sub>O), 4.62 (4/5 H, td, *J* 7.0 and 4.0, 2-H), 4.72 (1/5 H, td, *J* 7.3 and 7.0, 2-H) and 7.07–7.34 (10 H, m, Ph) (HRMS: found M<sup>+</sup> – CH<sub>3</sub>CHNO<sub>2</sub>, 225.1293. C<sub>16</sub>H<sub>17</sub>O requires 225.1279).

### 1-Benzyloxy-2-nitrocyclohexane **12**

In a procedure similar to that described above using sodium hydride (60% in oil; 167 mg, 4.18 mmol) and benzyl alcohol (482 mg, 4.46 mmol), **11** (354.2 mg, 2.78 mmol) was converted into **12** (578 mg, 88%) as an oil;  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1545 and 1360 (NO<sub>2</sub>);  $\delta_{\text{H}}(300 \text{ MHz})$  1.20–1.70 (4 H, m), 1.76–2.36 (4 H, m), 4.28–4.63 (4 H, m, PhCH<sub>2</sub>O, 1-H and 2-H) and 7.23–7.36 (5 H, m, Ph) (HRMS: found M<sup>+</sup> + H, 236.1325. C<sub>13</sub>H<sub>18</sub>NO<sub>2</sub> requires 236.1287).

### Methyl 4-oxo-3-phenylpentanoate **4**

**Method A.** A mixture of **3** (58.2 mg, 0.246 mmol) and tetrapropylammonium perruthenate (95.0 mg, 0.270 mmol) in dichloromethane (1.0 cm<sup>3</sup>) was stirred at ambient temperature for 20 min after which it was diluted with diethyl ether and filtered through Celite. Evaporation of the filtrate gave a residue, which was purified by chromatography on silica gel. Elution with hexane–diethyl ether (5:2, v/v) afforded **4** (49.2 mg, 97%) as an oil;  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1710 (C=O) and 1700 (C=O);  $\delta_{\text{H}}(300 \text{ MHz})$  2.11 (3 H, s, Me), 2.53 (1 H, dd, *J* 17.2 and 5.1, 2-H), 3.21 (1 H, dd, *J* 17.2 and 9.9, 2-H), 3.67 (3 H, s, OMe), 4.19 (1 H, dd, *J* 9.9 and 5.1, 3-H) and 7.17–7.38 (5 H, m, Ph); *m/z* 206 (M<sup>+</sup>).

**Method (B).** To a suspension of **3** (30.6 mg, 0.129 mmol), *N*-methylmorpholine *N*-oxide (22.7 mg, 0.194 mmol), silver(i) acetate (43.0 mg, 0.258 mmol), potassium carbonate (90.0 mg, 0.646 mmol) and 4 Å molecular sieves (30 mg) in dry acetonitrile (2.0 cm<sup>3</sup>) was added tetrapropylammonium perruthenate (4.5 mg, 0.013 mmol). The mixture was stirred at 40 °C for 10 h after which work-up followed by purification above gave **4** (23.6 g, 89%) as an oil, which was identical with the above compound in all respects.

### 1-Methoxy-1-phenylpropan-2-one **6**

By a procedure (method B) similar to that for the preparation of **4**, compound **5**<sup>11</sup> (54.0 mg, 2.77 mmol) was converted into **6** (23.6 mg, 52%) as an oil;  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1720 (C=O);  $\delta_{\text{H}}(300 \text{ MHz})$  2.11 (3 H, s, Me), 3.38 (3 H, s, OMe), 4.65 (1 H, s, 1-H) and 7.30–7.42 (5 H, m, Ph);  $m/z$  164 (M<sup>+</sup>). Starting material **5** (16.8 mg, 31%) was also recovered.

### 3-Benzyloxy-5-phenylpentan-2-one **10**

By a similar method to that described above, **9** (30.5 mg, 0.102 mmol) was transformed into **10** (20.9 mg, 76%) as an oil;  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1708 (C=O);  $\delta_{\text{H}}(300 \text{ MHz})$  1.88–2.08 (2 H, m, 4-H<sub>2</sub>), 2.17 (3 H, s, Me), 2.67 (1 H, ddd, *J* 14.0, 8.8 and 7.3, 5-H), 2.78 (1 H, ddd, *J* 14.0, 9.2 and 5.3, 5-H), 3.77 (1 H, dd, *J* 8.1 and 4.8, 3-H), 4.16 (1 H, d, *J* 11.4, PhCHHO), 4.58 (1 H, d, *J* 11.4, PhCHHO) and 7.11–7.38 (10 H, m, Ph) (HRMS: found M<sup>+</sup> – OCH<sub>2</sub>Ph, 161.0972. C<sub>11</sub>H<sub>13</sub>O requires 161.0966).

### 2-Benzyloxycyclohexanone **13**

The nitro compound **12** (47.4 mg, 0.202 mmol) was similarly converted into **13** (25.6 mg, 62%) as a powder;  $\nu_{\max}(\text{CHCl}_3)/\text{cm}^{-1}$  1722 (C=O);  $\delta_{\text{H}}(300 \text{ MHz})$  1.55–2.00 (5 H, m), 2.14–2.42 (2 H, m), 2.45–2.60 (1 H, m), 3.89 (1 H, ddd, *J* 9.9, 5.5 and 1.1, 2-H), 4.48 (1 H, d, *J* 12.1, PhCHHO), 4.76 (1 H, d, *J* 12.1, PhCHHO) and 7.26–7.42 (5 H, m, Ph) (HRMS: found M<sup>+</sup> – H, 203.1037. C<sub>13</sub>H<sub>15</sub>O<sub>2</sub> requires 203.1072).

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Paper 6/06332B

Received 13th September 1996

Accepted 14th October 1996