# Efficient and Facile Glycol Cleavage Oxidation Using Improved Silica Gel-Supported Sodium Metaperiodate

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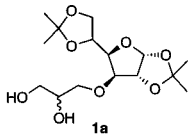
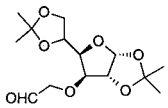
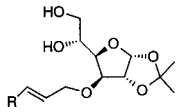
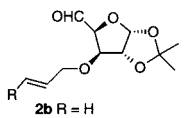
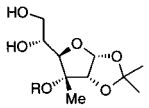
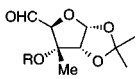
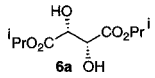
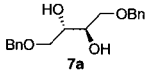
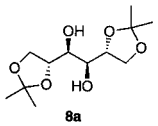
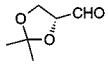
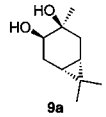
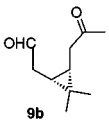
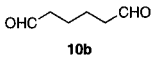
Sodium metaperiodate has been an attractive and popular reagent for the oxidative cleavage of vicinal diols (α- or 1,2-glycols) and related functional groups into dicarbonyls.[1] The popularity stems from its specificity, its reactivity under neutral and mild conditions which is compatible with a wide range of functionalities, its stability, and its low cost.[2] This reagent is particularly valuable in organic synthesis entailing carbohydrates because the generation of aldehydes from 1,2-diols is generally more efficient than those from oxidation of the corresponding primary alcohols.[1a]

Glycol scission oxidations using sodium metaperiodate are generally performed in aqueous alcohols or THF, but the effectiveness of the oxidant in nonpolar solvents is limited by its insolubility.[3,4] To solve the solubility problem, Hodge and co-workers employed silica gel-supported sodium metaperiodate to oxidize α-glycols and hydroquinones smoothly in dichloromethane, benzene, or ether.[5] However, this early anhydrous silica gel-supported sodium metaperiodate reagent is of little synthetic value because its preparation is tedious and the oxidative cleavage reactions require relatively long reaction times. Recently, an alternative method using sodium metaperiodate supported on wet silica gel has appeared.[6] This alternative protocol involves the addition of a freshly prepared aqueous solution of sodium metaperiodate to a stirring suspension of silica gel in dichloromethane followed by the introduction of a solution of the diol in dichloromethane. However, this method requires vigorous stirring during reaction, and the resultant silica gel readily forms a colloid that impedes efficient stirring. Column chromatography is occasionally required to fractionate the products in order to obtain pure aldehydes.[6]

**Table 1. Oxidative Cleavage of 1,2-Diols into Aldehydes by Silica Gel-Supported $NaIO_4$**

| entry | substrate | temp, °C | time, min | product | isolated yield, % |
|---|---|---|---|---|---|
| 1 |  **1a** | rt | 15 |  **1b** | 99 |
| 2 |  **2a** R = H | rt | 15 |  **2b** R = H | 96 |
| 3 | **3a** R = $CO_2Me$ | rt | 20 | **3b** R = $CO_2Me$ | 98 |
| 4 |  **4a** R = H | rt | 15 |  **4b** R = H | 100 |
| 5 | **5a** R = $CH_2CH{=}CH_2$ | rt | 20 | **5b** R = $CH_2CH{=}CH_2$ | 98 |
| 6 |  **6a** | rt | 90 | $(HO)_2HCCO_2Pr^i$ **6b** | 90 |
| 7 |  **7a** | rt | 30 | $BnOCH_2CHO$ **7b** | 98 |
| 8 |  **8a** | 0 | 30 |  **8b** | 95 |
| 9 |  **9a** | rt | 20 |  **9b** | 95 |
| 10 |  **10a** | rt | 15 |  **10b** | 98 |

Now, we report an improved silica gel-supported metaperiodate reagent in powder form for the efficient and facile preparation of aldehydes from vicinal glycols. The oxidative cleavage reagent, a free-flowing powder, is easily and conveniently prepared by adding silica gel to aqueous sodium metaperiodate and can be stored in a bottle for 1 month with negligible loss of activity. The scission products obtained from this improved protocol are pure enough for further synthetic operations without the need for chromatography.

Glycol oxidative fission reactions are easily carried out by stirring a suspension of the reagent and the vicinal diol in dichloromethane at room temperature or below. The results of a variety of diols (compounds **1**−**10**) are shown in Table 1. In all cases, we have not encountered stirring problems due to colloid formation of the silica gel. The glycol scission reactions generally proceed smoothly and quickly and, after a simple workup procedure of filtration, afford essentially pure aldehydes in excellent yields.

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(5) Gupta, D. N.; Hodge, P.; Davies, J. E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2970.

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The present protocol is attractive particularly for vicinal diols that are not readily soluble in aqueous alcohols or THF and for aldehydes that are water soluble (product recovery from an aqueous solvent is difficult).

## Experimental Section

Melting points are measured in degrees Celsius and are uncorrected. IR spectra were recorded on a FT-IR spectrophotometer as neat films on KBr plates. Optical rotations were obtained at 589 nm. $^1$H and $^{13}$C NMR spectra were measured in $CDCl_3$ solutions at 250 and 62.9 MHz, respectively. High-resolution mass spectra were obtained using the FAB technique. All reactions were monitored by analytical TLC on Merck aluminum-precoated plates of silica gel 60 F254 with detection by spraying with 5% (w/v) dodecamolybdophosphoric acid in ethanol and subsequent heating. All reagents and solvents were of general reagent grade and were used without further purification. E. Merck silica gel 60 (230−400 mesh) was used for column chromatography and as the support for $NaIO_4$.

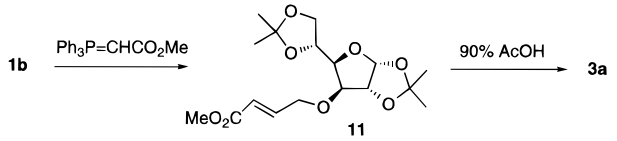
**Preparation of Silica Gel-Supported $NaIO_4$ Reagent.** $NaIO_4$ (2.57 g, 12.0 mmol) was dissolved in 5 mL of hot water (∼70 °C) in a 25 mL round-bottomed flask. To the hot solution was added silica gel (230−400 mesh, 10 g) with vigorous swirling and shaking. The resultant silica gel coated with $NaIO_4$ was in a powder form and was free-flowing. The reagent can be kept in a bottle for 1 month with negligible loss of activity.

**General Procedure for Glycol Cleavage Oxidations.** To a vigorously stirred suspension of silica gel-supported $NaIO_4$ reagent (2.0 g) in $CH_2Cl_2$ (5 mL) in a 25 mL round-bottomed flask was added a solution of the vicinal diol (1.0 mmol) in $CH_2Cl_2$ (5 mL). The reaction was monitored by TLC until disappearance of the starting material (generally 10−30 min). The mixture was filtered through a sintered glass funnel, and the silica gel was thoroughly washed with $CHCl_3$ (3 × 10 mL). Removal of solvents from the filtrate afforded the aldehyde that was pure enough for most purposes.

**Aldehyde 1b.** Diol **1a**[7] was oxidatively cleaved to give **1b** as a colorless syrup in 99% yield: $R_f$ 0.45 (EtOAc:$CH_2Cl_2$ = 2:1); $[\alpha]^{20}_D$ −46.1 (*c* 1.0, $CHCl_3$); IR (KBr) 1737, 1633 cm$^{-1}$; $^1$H NMR $\delta$ 1.32 (3H, s), 1.34 (3H, s), 1.42 (3H, s), 1.49 (3H, s), 3.93 (1H, d, *J* = 2.8 Hz), 4.01 (1H, dd, *J* = 8.7, 5.2 Hz), 4.06−4.16 (2H, m), 4.28 (2H, s), 4.32 (1H, dd, *J* = 5.8, 2.8 Hz), 4.65 (1H, d, *J* = 3.6 Hz), 5.91 (1H, d, *J* = 3.6 Hz), 9.72 (1H, s); $^{13}$C NMR $\delta$ 25.3, 26.2, 26.8 (2C), 67.5, 72.3, 76.3, 81.2, 83.0, 83.7, 105.2, 109.2, 112.0, 199.8; HRMS *m*/*z* calcd for $C_{14}H_{23}O_7$ (M + H)$^+$ 303.1438, found 303.1417.

**Aldehyde 2b.** Diol **2a**[8] was oxidatively cleaved to give **2b** as a colorless syrup in 96% yield: $R_f$ 0.29 ($Et_2O$:hexane = 1:1); $[\alpha]^{20}_D$ −56.1 (*c* 1.4, $CHCl_3$); IR (KBr) 1740, 1643 cm$^{-1}$; $^1$H NMR $\delta$ 1.33 (3H, s), 1.48 (3H, s), 3.94 (1H, ddt, *J* =12.9, 5.8, 1.4 Hz), 4.07 (1H, ddt, *J* = 12.9, 5.4, 2.1 Hz), 4.29 (1H, d, *J* = 3.7 Hz), 4.56 (1H, dd, *J* = 3.7, 1.6 Hz), 4.61 (1H, d, *J* = 3.5 Hz), 5.18−5.29 (2H, m), 5.79 (1H, m), 6.11 (1H, d, *J* = 3.5 Hz), 9.67 (1H, d, *J* = 1.6 Hz); $^{13}$C NMR $\delta$ 26.2, 26.9, 71.2, 82.3, 83.6, 84.5, 106.1, 112.4, 118.0, 133.2, 199.8; HRMS *m*/*z* calcd for $C_{11}H_{17}O_5$ (M + H)$^+$ 229.1071, found 229.1082.

**Enoate 11.** To a solution of aldehyde **1b** (1.21 g, 4.0 mmol) in $CH_2Cl_2$ (10 mL) was added $Ph_3P{=}CHCO_2Me$ (1.47 g, 4.4 mmol), and the resultant solution was stirred at rt for 12 h. The reaction mixture was then filtered through a silica gel pad and the filtrate concentrated. The residue was chromatographed ($Et_2O$:hexane = 2:3) to give enoate (*E*)-**11** (773 mg, 54%) as a colorless syrup: $R_f$ 0.40 ($Et_2O$:hexane = 1:1); $[\alpha]^{20}_D$ −37.8 (*c* 1.0, $CHCl_3$); IR (KBr) 1724, 1661 cm$^{-1}$; $^1$H NMR $\delta$ 1.31 (3H, s), 1.35 (3H, s), 1.42 (3H, s), 1.49 (3H, s), 3.74 (3H, s), 3.95 (1H, d, *J* = 3.2 Hz), 3.98−4.14 (3H, m), 4.26−4.33 (3H, m), 4.54 (1H, d, *J* = 3.8 Hz), 5.88 (1H, d, *J* = 3.8 Hz), 6.17 (1H, dt, *J* = 15.7, 1.6 Hz), 6.93 (1H, dt, *J* = 15.7, 4.0 Hz); $^{13}$C NMR $\delta$ 25.2, 26.2, 26.7 (2C), 51.4, 67.5, 68.8, 72.2, 81.2, 82.2, 82.7, 105.2, 109.1, 111.8, 121.1, 143.6, 166.5; MS *m*/*z* (rel int) 359 [(M + H)$^+$, 71], 315 (73), 301 (55), 243 (79). Anal. Calcd for $C_{17}H_{26}O_8$: C, 56.97; H, 7.31. Found: C, 56.72; H, 7.10.




**Diol 3a.** A solution of the enoate **11** (716 mg, 2.0 mmol) in 90% aqueous AcOH (5 mL) was stirred at rt for 24 h. The AcOH was removed *in vacuo*, and the residue was chromatographed on silica gel ($Et_2O$:hexane = 2:1) to give diol **3a** (572 mg, 90%) as a colorless syrup: $R_f$ 0.10 ($Et_2O$:hexane = 3:1); $[\alpha]^{20}_D$ −32.8 (*c* 1.0, $CHCl_3$); IR (KBr) 3433, 1722, 1645 cm$^{-1}$; $^1$H NMR $\delta$ 1.31 (3H, s), 1.48 (3H, s), 2.17 (2H, brs, $D_2O$ exchangeable), 3.74 (3H, s), 3.70−3.78 (1H, m), 3.86 (1H, dd, *J* = 11.3, 3.0 Hz), 4.00 (1H, m), 4.05 (1H, d, *J* = 3.6 Hz), 4.13 (1H, dd, *J* = 8.4, 3.0 Hz), 4.23−4.41 (2H, m), 4.56 (1H, d, *J* = 3.6 Hz), 5.90 (1H, d, *J* = 4.8 Hz), 6.10 (1H, dt, *J* = 15.8, 2.1 Hz), 6.94 (1H, dt, *J* = 15.8, 4.2 Hz); $^{13}$C NMR $\delta$ 26.1, 26.6, 51.6, 64.3, 68.7 (2C), 80.8, 82.1, 82.6, 105.1, 111.8, 121.2, 143.6, 166.6; MS *m*/*z* (rel int) 319 [(M + H)$^+$, 38], 301 (8), 261 (100), 243 (21). Anal. Calcd for $C_{14}H_{22}O_8$: C, 52.82; H, 6.97. Found: C, 52.50; H, 6.87.

**Aldehyde 3b.** Glycol cleavage oxidation of **3a** afforded aldehyde **3b** as a colorless syrup in 98% yield: $R_f$ 0.25 ($Et_2O$:hexane = 2:1); $[\alpha]^{20}_D$ −77.6 (*c* 1.0, $CHCl_3$); IR (KBr) 1746, 1683, 1634 cm$^{-1}$; $^1$H NMR $\delta$ 1.34 (3H, s), 1.48 (3H, s), 3.74 (3H, s), 4.13 (1H, ddd, *J* = 15.9, 4.3, 2.0 Hz), 4.25 (1H, ddd, *J* = 15.9, 4.3, 2.0 Hz), 4.28 (1H, d, *J* = 3.7 Hz), 4.58 (1H, dd, *J* = 3.7, 1.2 Hz), 4.61 (1H, d, *J* = 3.5 Hz), 5.97 (1H, dt, *J* = 15.7, 2.0 Hz), 6.12 (1H, d, *J* = 3.5 Hz), 6.84 (1H, dt, *J* = 15.7, 4.3 Hz), 9.69 (1H, d, *J* = 1.2 Hz); $^{13}$C NMR $\delta$ 26.1, 26.7, 51.5, 68.7, 81.9, 84.3, 84.5, 105.9, 112.5, 121.3, 142.5, 166.1, 199.6; HRMS *m*/*z* calcd for $C_{13}H_{19}O_7$ (M + H)$^+$ 287.1125, found 287.1116.

**Aldehyde 4b.** Diol **4a**[2b] was oxidatively cleaved to give aldehyde **4b** as colorless needles in quantitative yield: mp 75−76 °C; $R_f$ 0.21 (EtOAc:$CH_2Cl_2$ = 1:1); $[\alpha]^{20}_D$ +14.7 (*c* 1.0, $CHCl_3$); IR (KBr) 1731, 1644 cm$^{-1}$; $^1$H NMR $\delta$ 1.24 (3H, s), 1.38 (3H, s), 1.58 (3H, s), 3.04 (1H, s, $D_2O$ exchangeable), 4.19 (1H, d, *J* = 3.6 Hz), 4.25 (1H, d, *J* = 0.8 Hz), 5.90 (1H, d, *J* = 3.6 Hz), 9.70 (1H, d, *J* = 0.8 Hz); $^{13}$C NMR $\delta$ 19.0, 26.4, 26.5, 79.0, 84.2, 85.4, 103.8, 113.2, 198.9; HRMS *m*/*z* calcd for $C_9H_{15}O_5$ (M + H)$^+$ 203.0914, found 203.0925.

**Aldehyde 5b.** Glycol cleavage oxidation of **5a**[2b] afforded aldehyde **5b** as a colorless syrup in 98% yield: $R_f$ 0.47 ($Et_2O$:hexane = 1:1); $[\alpha]^{20}_D$ +70.8 (*c* 0.4, $CHCl_3$); IR (KBr) 1739, 1648 cm$^{-1}$; $^1$H NMR $\delta$ 1.22 (3H, s), 1.34 (3H, s), 1.34 (3H, s), 4.12 (2H, dt, *J* = 5.5, 1.4 Hz), 4.32 (1H, d, *J* = 3.5 Hz), 4.59 (1H, s), 5.18 (1H, dd, *J* = 10.3, 1.4 Hz), 5.32 (1H, dq, *J* = 19.2, 1.4 Hz), 5.82 (1H, d, *J* = 3.5 Hz), 5.96 (1H, m), 9.67 (1H, s); $^{13}$C NMR $\delta$ 17.0, 26.6, 27.0, 66.0, 83.4, 83.5, 85.1, 104.5, 113.6, 116.8, 134.7, 198.7; HRMS *m*/*z* calcd for $C_{12}H_{19}O_5$ (M + H)$^+$ 243.1227, found 243.1236.

**Aldehyde 6b.** Glycol cleavage oxidation of diisopropyl L-tartrate (**6a**) afforded aldehyde **6b**[9] as a colorless oil in 90% yield: $R_f$ 0.27 (EtOAc:hexane = 2:1); IR (KBr) 3567−3211 (br), 1733, 1633 cm$^{-1}$; $^1$H NMR $\delta$ 1.27 (3H, s), 1.29 (3H, s), 3.78−4.48 (2H, brs, $D_2O$ exchangeable), 5.08−5.12 (1H, m), 5.20−5.28 (1H, m); $^{13}$C NMR $\delta$ 21.3 (2C), 69.8, 87.0, 170.1.

**Aldehyde 7b.** Diol **7a**[7a] was oxidatively cleaved to give aldehyde **7b**,[6,10,11] obtained as a colorless oil in 98% yield: $R_f$ 0.45 (EtOAc:hexane = 1:2); IR (KBr) 3062, 1732, 1636 cm$^{-1}$; $^1$H NMR $\delta$ 4.10 (2H, s), 4.63 (2H, s), 7.34 (5H, m), 9.71 (1H, s); $^{13}$C NMR $\delta$ 72.3, 73.6, 128.1 (2C), 128.4, 128.5 (2C), 136.8, 200.4.

**Aldehyde 8b.** Diol **8a**[12] was oxidatively cleaved to give aldehyde **8b**[12,13] as a colorless oil in 95% yield: $R_f$ 0.27 ($Et_2O$:hexane = 2:1); $[\alpha]^{20}_D$ +61.6 (*c* 2.3, $CH_2Cl_2$); $^1$H NMR $\delta$ 1.41 (3H, s), 1.48 (3H, s), 4.06 (1H, dd, *J* = 13.6, 4.8 Hz), 4.14 (1H, dd, *J*

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= 13.6, 7.1 Hz), 4.36 (1H, ddd, $J$ = 7.1, 4.8, 1.8 Hz), 9.68 (1H, d, $J$ = 1.8 Hz); $^{13}$C NMR $\delta$ 25.1, 26.2, 65.5, 79.8, 111.3, 201.7.

**Aldehyde 9b.** Glycol cleavage oxidation of **9a**[7] provided keto aldehyde **9b**[14] as a colorless oil in 95% yield: $R_f$ 0.57 (EtOAc:hexane = 1:1); $[\alpha]^{20}_D$ +33.3 ($c$ 1.0, CHCl3); $^1$H NMR $\delta$ 1.13 (3H, s), 1.28 (3H, s), 1.37 (1H, dd, $J$ = 14.6, 8.4 Hz), 1.57 (1H, dd, $J$ = 8.4, 5.6 Hz), 1.80−2.05 (2H, m), 2.09 (3H, s), 2.43 (2H, t, $J$ = 7.2 Hz), 9.48 (1H, d, $J$ = 5.6 Hz); $^{13}$C NMR $\delta$ 14.8, 18.4, 28.9, 29.8, 30.0, 36.8, 38.3, 43.3, 199.6, 201.6.

(14) Kula, J. *Synth. Commun.* **1986**, *16*, 833.

**Aldehyde 10b.** Glycol cleavage oxidation of **10a**[7] provided aldehyde **10b**[6] as a colorless oil in 98% yield: $R_f$ 0.49 (EtOAc:hexane = 2:1); IR (KBr) 1717 cm$^{-1}$; $^1$H NMR $\delta$ 1.59−1.65 (4H, m), 2.42−2.47 (4H, m), 9.73 (2H, t, $J$ = 1.5 Hz); $^{13}$C NMR $\delta$ 21.3 (2C), 43.4 (2C), 201.9 (2C).

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