Oxidation of Terminal Diols Using an Oxoammonium Salt:  
A Systematic Study

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Key to Abbreviated Terms:

CDCl$_3$: deuterated chloroform
CH$_2$Cl$_2$: dichloromethane
TLC: Thin layer chromatography
General Considerations:

General:
NMR Spectra ($^1$H, $^{13}$C) were performed at 298 K on a Brüker DRX-400 400 MHz NMR. $^1$H-NMR Spectra obtained in CDCl$_3$ were referenced to residual non-deuterated chloroform (7.26 ppm) in the deuterated solvent. $^{13}$C-NMR Spectra obtained in CDCl$_3$ were referenced to chloroform (77.3 ppm). $^{19}$F-NMR spectra were referenced to hexafluorobenzene (−164.9 ppm). Reactions in CH$_2$Cl$_2$ could be monitored with $^1$H NMR by irradiating the solvent peak at 5.30 ppm. Flash chromatography and silica plugs utilized Dynamic Adsorbents Inc. Flash Silica Gel (60Å porosity, 32-63 µm). TLC analysis was performed using hexanes/ethyl acetate as the eluent and visualized using iodine. IR spectra were obtained on a Brüker ALPHA FT-IR spectrometer. High-resolution mass spectra were performed on either a JEOL AccuTOF-DART SVP 100 in positive direct analysis in real time (DART) ionization method, using PEG as the internal standard.

Chemicals:
Deuterated chloroform was purchased from Cambridge Isotope Laboratories and stored over 4Å molecular sieves. All chemicals were purchased from commercial suppliers with exception of the oxoammonium salt 4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate, 1, which was prepared according to an established protocol.\(^1\)

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Oxidation of Diols

GENERAL PROCEDURE

1,10-Decanedial (3a) (1.294 g, 76%) was prepared from 1,10-decanediol (1.743 g, 10 mmol, 1 equiv). To a 250-mL round bottom flask equipped with a stir bar was added 1,10-decanediol and dichloromethane (100 mL, 0.1 M in diol). After stirring for 5 min, the oxoammonium salt (6.302 g, 21 mmol, 2.1 equiv) was added, followed by silica gel (2.644 g, 2 mass equiv to substrate). The flask was sealed with a rubber septa and the mixture was allowed to stir until the slurry became white. Once white, the slurry was filtered through a thin pad of silica gel. The solid was washed using CH₂Cl₂. The CH₂Cl₂ was removed in vacuo by rotary evaporation to afford the pure dialdehyde product, 1,10-decanedial, as a pale yellow oil.²

¹H NMR (CDCl₃, 400 MHz) δ ppm 1.30 (s, 8 H) 1.56 - 1.65 (m, 4 H) 2.40 (td, J=1.77, 7.30 Hz, 4 H) 9.74 (t, J=1.82 Hz, 2 H)
¹³C NMR (CDCl₃, 100 MHz) δ ppm 22.25 (CH₂) 29.29 (CH₂) 29.36 (CH₂) 44.10 (CH₂) 203.04 (CHO)

1,9-Nonanedial (3b) (0.690 g, 83%) was prepared from 1,9-nonanediol (0.801 g, 5 mmol, 1 equiv) using the general procedure to afford the product as a colorless oil.³

¹H NMR (CDCl₃, 400 MHz) δ ppm 1.19 (bs, 6H) 1.48 (m, 4H) 2.29 (t, J = 7.0 Hz, 4H) 9.61 (bs, 2H)
¹³C NMR (CDCl₃, 100 MHz) δ ppm 21.15 (CH₂) 28.10 (CH₂) 28.28 (CH₂) 43.00 (CH₂) 201.89 (CO)

1,8-Octanediol (3c) (1.201 g, 84%) was prepared from 1,8-octanediol (1.462 g, 10 mmol, 1 equiv) using the general procedure to afford the product as a colorless oil.  

$^1$H NMR (CDCl$_3$, 400 MHz) δ ppm 1.27 - 1.35 (m, 4 H) 1.54 - 1.64 (m, 4 H) 2.39 (td, J=1.70, 7.25 Hz, 4 H) 9.72 (t, J=1.75 Hz, 2 H)  

$^{13}$C NMR (CDCl$_3$, 100 MHz) δ ppm 21.96 (CH$_2$) 29.01 (CH$_2$) 43.90 (CH$_2$) 202.78 (CHO)

Heptanediol (3d) (0.826 g, 64%) was prepared from 1,7-heptanediol (1.322 g, 10 mmol, 1 equiv) using the general procedure to afford the product as a pale yellow oil.  

$^1$H NMR (CDCl$_3$, 400 MHz) δ ppm 1.28 - 1.39 (m, 2 H) 1.62 (quin, J=7.52 Hz, 4 H) 2.41 (td, J=1.61, 7.27 Hz, 4 H) 9.73 (t, J=1.63 Hz, 2 H)  

$^{13}$C NMR (CDCl$_3$, 100 MHz) δ ppm 21.94 (CH$_2$) 28.79 (CH$_2$) 43.79 (CH$_2$) 202.49 (CHO)

Adipaldehyde (3e) (26%) was prepared from 1,6-hexanediol (1.182 g, 10 mmol, 1 equiv) using the general procedure to afford the products adipaldehyde and caprolactone (4e) as an inseparable mixture of a colorless oil (0.874 g, 87%).  

$^1$H NMR (CDCl$_3$, 400 MHz) δ ppm 1.62 (m, 4H) 2.44 (m, 4H) 9.73 (t, J = 1.5 Hz, 2H)  

$^{13}$C NMR (CDCl$_3$, 100 MHz) δ ppm 21.63 (CH$_2$) 43.71 (CH$_2$) 202.12 (CHO)  

Caprolactone (4e) (74%)  

$^1$H NMR (CDCl$_3$, 400 MHz) δ ppm 2.24 (quin, J=7.58 Hz, 2 H) 2.47 (t, J=8.26 Hz, 2 H) 4.32 (t, J=7.06 Hz, 2 H)  

$^{13}$C NMR (CDCl$_3$, 100 MHz) δ ppm 29.12 (CH$_2$) 29.47 (CH$_2$) 23.11 (CH$_2$) 34.73 (CH$_2$) 69.48 (CH$_2$) 176.42 (CHO)  

δ-Valerolactone (4f) (0.817 g, 82%) was prepared from 1,5-pentanediol (0.994 g, 10 mmol, 1 equiv) using the general procedure to afford the product as a white solid.  

$^1$H NMR (CDCl$_3$, 400 MHz) δ ppm 1.86 (m, 1H) 2.53 (t, J=6.97 Hz, 1H) 4.32 (t, J=5.62 Hz, 1H)  

$^{13}$C NMR (CDCl$_3$, 100 MHz) δ ppm 19.03 (CH$_2$) 22.26 (CH$_2$) 29.79 (CH$_2$) 69.44 (OCH$_2$) 171.46 (CO)  

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Butyro lactone (4g) (0.523 g, 61%) was prepared from 1,4-butanediol (0.901 g, 10 mmol, 1 equiv) using the general procedure to afford the product as a colorless oil.\(^6\)

\(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) ppm 2.24 (quin, \(J=7.58\) Hz, 2 H) 2.47 (t, \(J=8.26\) Hz, 2 H) 4.32 (t, \(J=7.06\) Hz, 2 H)

\(^13\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) ppm 22.38 (CH\(_2\)) 27.98 (CH\(_2\)) 68.72 (CH\(_2\)) 177.92 (CO)

2-Hydroxymethyl-1,3-dioxolane (6) (1.363 g, 65%) was prepared from freshly distilled ethylene glycol (2.483 g, 40 mmol, 1 equiv), using the following modification the general procedure: Ethylene glycol was stirred in CH\(_2\)Cl\(_2\) (200 mL, 0.2 M in diol), then 0.55 equiv (6.602 g, 22 mmol) oxoammonium salt was added, followed by 1.98 g silica gel (0.8 mass equiv to the substrate). The mixture was refluxed for 20 h, at which point the white slurry was filtered through a pad of silica gel. Due to volatility, the solvent was removed via evaporation through a 30 cm Vigreux column to afford the product as a pale yellow oil.\(^7\)

\(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) ppm 3.64 (br. d, \(J=2.40\) Hz, 2 H) 3.67 (br. s, 1 H) 3.85 - 4.04 (m, 4 H) 4.96 (t, \(J=3.24\) Hz, 1 H)

\(^13\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) ppm 62.68 (CH\(_2\)O) 65.09 (CH\(_2\)O) 103.21 (OCHO)

2-Hydroxyethyl-1,3-dioxane (7) (0.485 g, 73%) was prepared from 1,3-propanediol (0.761 g, 10 mmol, 1 equiv) using the following modifications to the general procedure: 0.5 equiv (1.501 g, 5 mmol) oxoammonium salt was added, followed by 1.501 g silica gel (1 mass equiv to the oxoammonium salt). The product was afforded as a yellow oil.\(^8\)

\(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) ppm 1.30 - 1.37 (dm, \(J=1.28, 13.42\) Hz, 1 H) 1.84 (q, \(J=5.28\) Hz, 2 H) 2.01 - 2.14 (qt, \(J=1.28, 13.42\) Hz, 1 H) 2.62 (br. s, 1 H) 3.69 - 3.80 (m, 4 H) 4.09 (dd, \(J=5.06, 10.56\) Hz, 2 H) 4.73 (t, \(J=4.84\) Hz, 1 H)

\(^13\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) ppm 25.91 (CH\(_2\)) 37.35 (CH\(_2\)) 58.87 (CH\(_2\)O) 67.10 (CH\(_2\)O) 102.01 (OCHO)

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Aldol Reaction

1-Cycloheptene-1-carboxaldehyde (9) (1.06 g, 50%) was prepared from the oxidation of 1,8-octanediol (2.5 g, 17.1 mmol, 1 equiv) using the procedure outlined above for oxidation, followed by a subsequent Aldol reaction. To the resulting solution of 1,8-octanediol, filtered off from the silica gel and o xo ammonium salt, was added L-proline (1.5 g, 13 mmol, 0.76 eq) and 1.5 g of activated 4Å molecular sieves. The mixture was refluxed for 2 days, then filtered through a pad of silica gel. Due to volatility, the solvent was removed via evaporation through a 30 mm Vigreux column to afford the product as an orange oil.9

\[ ^1H \text{ NMR (CDCl}_3, 400 \text{ MHz)} \delta \text{ ppm 1.45 (m, 1H) 1.56 (m, 1H) 1.75 (m, 1H) 2.37 (t, } J = 5.6 \text{ Hz, 1H) 2.42 (q, } J = 5.9 \text{ Hz, 1H) 6.83 (t, } J = 6.3 \text{ Hz, 1H) } \]

13C NMR (CDCl3, 100 MHz) \( \delta \) ppm 24.01 (CH2) 26.17 (CH2) 26.23 (CH2) 30.08 (CH2) 31.89 (CH2) 147.64 (C) 157.22 (CH) 194.54 (CHO)

Wittig Reaction

1,10-Undecadiene (10) (0.655 g, 86%) was prepared from the oxidation of 1,9-nonanediol (0.801 g, 5 mmol, 1 equiv) using the procedure outlined above for oxidation, followed by a subsequent Wittig reaction. The Wittig reagent, methylenetriphenylphosphorane, was prepared by stirring methyltriphenylphosphonium bromide (5.355 g, 15 mmol, 3 equiv to diol) and potassium t-butoxide (1.68 g, 15 mmol, 3 equiv to diol) in dry diethyl ether (75 mL, 0.2 M) for 7 hours. The filtered solution of 1,9-nonanediol was added directly to this solution and the mixture was filtered overnight. The solution was filtered and the solvent was removed in vacuo, resulting in a thick oil. Pentane (50 mL) was added to precipitate excess triphenylphosphine and the oxide byproduct. The resulting slurry was filtered through silica and the solvent was removed in vacuo to afford the product as a colorless oil.10

\[ ^1H \text{ NMR (CDCl}_3, 400 \text{ MHz)} \delta \text{ ppm 1.34 (m, 10H). 2.05 (q, } J = 7.1 \text{ Hz, 4H), 4.94 (dd, } J = 1.4, 8.00 \text{ Hz, 2H) 5.00 (dd, } J = 1.9, 17.1 \text{ Hz, 2H) 5.84 (tq, } J = 6.8, 14.8 \text{ Hz, 2H) } \]

13C NMR (CDCl3, 100 MHz) \( \delta \) ppm 29.25 (CH2) 29.41 (CH2) 29.66 (CH2) 34.12 (CH2) 114.41 (CH2) 139.46 (CH)

Grignard Reaction

\[
\begin{align*}
\text{O} & \quad \text{CH}_3\text{MgCl} \\
\text{CH}_2\text{OH} & \quad \text{Et}_2\text{O}
\end{align*}
\]

2,11-Dodecanediol (11) (0.900 g, 89%) was prepared from 1,10-decanediol (0.870 g, 5 mmol, 1 equiv) using the procedure outlined above for oxidation, followed by a subsequent Grignard reaction. A solution of 1,10-decanedial, filtered off of the silica gel and o xo ammonium salt, was added to a solution of commercially available 3 M methyl magnesium chloride in anhydrous diethyl ether (7 mL, 21 mmol, 4.2 equiv). The solution was stirred overnight, then aliquots (~25 drops) of aqueous saturated potassium carbonate were added dropwise about 10 min apart. After 5 aliquots a white precipitate formed. The solution was filtered, and the solvent removed \textit{in vacuo} to afford the product as white solid.\(^{10}\)

\( ^1\text{H NMR} \) (CDCl\(_3\), 400 MHz) Δ ppm 1.13 (d, J=8.00 Hz, 6H) 1.33 (m, 16H) 1.98 (br. s, 2 H) 3.72 (m, 2H)

\( ^{13}\text{C NMR} \) (CDCl\(_3\), 100 MHz) Δ ppm 23.62 (CH\(_2\)) 25.95 (CH\(_2\)) 29.73 (CH\(_2\)) 29.83 (CH\(_2\)) 29.53 (CH\(_3\)) 68.21 (CHOH)

Oxidative Functionalization

\[
\begin{align*}
\text{NHAc} & \quad \text{BF}_4^{-} \\
\text{F}_3\text{C} & \quad \text{OH}
\end{align*}
\]

Bis(1,1,3,3,3-hexafluoropropan-2-yl) heptanedioate (12) (0.768 g, 77%) was prepared from 1,7-heptanediol (0.676 g, 5 mmol, 1 equiv) using the procedure outlined above for oxidation, followed by subsequent oxidative functionalization using previously published method.\(^{11}\) To the resulting solution of 1,7-heptan dialdehyde (5 mmol), filtered off the silica gel and o xo ammonium salt slurry, was added pyridine (10.085 g, 127.5 mmol, 25.5 equiv) and hexafluoroisopropanol (5.041 g, 30 mmol, 6 equiv). After stirring for 5 min, the oxo ammonium salt (7.502 g, 25 mmol, 5 equiv) was added all at once. The flask was sealed with a rubber septum and stirred until the solution turned red. Once the reaction was determined complete by TLC, the hexafluoroisopropanol and CH\(_2\)Cl\(_2\) was removed \textit{in vacuo}. Pentane or diethyl ether was

added to the resulting slurry to precipitate the nitroxide. After stirring for 5 min, the solution was filtered through a fritted funnel with medium porosity and transferred to a separatory funnel. The organic layer was washed with 1 M HCl (2×150 mL), deionized water (150 mL), and brine (150 mL). The organic layer was dried over sodium sulfate, and the solvent was removed in vacuo, affording the ester as a pale yellow oil. (Note: The CH₂Cl₂ may be removed in vacuo before the oxidative functionalization, however the reaction is slightly exothermic. With this particular substrate, the formation of the nitroxide, and subsequent red color, occurs within 5 min when concentrated and within 30 min when dilute).

**¹H NMR** (CDCl₃, 400 MHz) δ ppm 1.42 (m, 2H) 1.74 (m, J = 7.6 Hz, 2H), 2.53 (t, J = 7.3 Hz, 4H), 5.77 (m, J = 6.1 Hz, 2H),

**¹³C NMR** (CDCl₃, 100 MHz) δ ppm 24.29 (CH₂) 28.17 (CH₂) 33.23 (CH₂) 66.69 (m, JOB-CH-(CF₃)₂=34.74 Hz) 120.71 (q, JC=CF₂ = 282.77 Hz) 170.25 (CO)

**¹⁹F NMR** (CDCl₃, 377 MHz) δ ppm -76.56 (s, 6 F), -76.57 (s, 6 F)

**HRMS** (ESI+), calc for C₁₃H₁₂F₁₂O₄ [MH]+, calc. 461.0622, obs. 461.0635; [MNH₄]+, calc. 478.0888, obs. 478.0888

**FT-IR** (neat, ATR, cm⁻¹) 2996-2852 (w, b) 1774 (s) 1381 (m) 1357 (m) 1287 (s) 1267 (m) 1229 (s) 1193 (vs) 1103 (vs) 901 (s) 730 (w) 689 (s) 529 (w) 488 (w)
1,10-Decanedial
400 MHz, CDCl3

ppm

9.8
2.45
2.40
1.8
1.7
1.6
1.4
1.3

ppm

3
1,9-Nonanedial
100 MHz, CDCl₃

2.6 2.4 2.2 ppm
1.6 1.5 1.4 ppm
1,8-Octanedial
400 MHz, CDCl3
Adipaldehyde
400 MHz, CDCl3
Caprolactone
400 MHz, CDCl3
δ-Valerolactone
400 MHz, CDCl3
Butyrolactone
400 MHz, CDCl3
2-Hydroxy-1,3-dioxane
400 MHz, CDCl3

[Diagram of 2-Hydroxy-1,3-dioxane NMR spectrum with peaks at 4.9, 4.8, 4.7 ppm; 4.2, 4.0, 3.8 ppm; 2.2, 2.1 ppm; 2.0, 1.9, 1.8 ppm; 1.4, 1.3 ppm]
2-Hydroxymethyl-1,3-dioxolane
400 MHz, CDCl₃
1-Cycloheptene-1-carboxaldehyde
400 MHz, CDCl3
1,10-Undecadiene
400 MHz, CDCl₃

S20
2,11-Dodecanediol
400 MHz, CDCl3
Bis(1,1,1,3,3,3-hexafluoropropan-2-yl) heptanedioate
400 MHz, CDCl3
1,10-Decanedial
100 MHz, CDCl3
1,9-Nonanedial
100 MHz, CDCl3
1.8-Octanodial
100 MHz, CDC13
Heptanodialdehyde
100 MHz, CDCl3
Adipaldehyde
100 MHz, CDCl3
Caprolactone
100 MHz, CDCl₃
δ-Valerolactone
100 MHz, CDCl₃
2-Hydroxy-1,3-dioxane
100 MHz, CDCl₃
2-Hydroxymethyl-1,3-dioxolane
100 MHz, CDCl3
1-Cycloheptene-1-carboxaldehyde
100 MHz, CDCl3
1,10-Undecadiene
100 MHz, CDCl3
2,11-Dodecanediol
100 MHz, CDCl3
Bis(1,1,3,3,3-hexafluoropropan-2-yl) heptanedioate
100 MHz, CDCl3
Bis(1,1,1,3,3,3-hexafluoropropan-2-yl) heptanedioate
377 MHz, CDCl3