Supporting Information

Metal-Free Oxidative Cleavage of C-C bond in $\alpha$-Hydroxy-$\beta$-oxophosphonates

Satyanarayana Battula, Atul Kumar, Qazi Naveed Ahmed*

Medicinal Chemistry Division, IIIM, Jammu, Jammu and Kashmir, 180001, India.
Academy of Scientific and Innovative Research (AcSIR), CRRI P.O., New Delhi-110025, India.
## Contents with page no.:

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Contents</th>
<th>Page no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>General information</td>
<td>3</td>
</tr>
<tr>
<td>2.</td>
<td>Experimental procedures</td>
<td>3</td>
</tr>
<tr>
<td>3.</td>
<td>Spectral data of acid compounds</td>
<td>4</td>
</tr>
<tr>
<td>4.</td>
<td>References</td>
<td>7</td>
</tr>
<tr>
<td>5.</td>
<td>$^1$H, $^{13}$C-NMR spectra</td>
<td>8</td>
</tr>
</tbody>
</table>
1. General Information.

All chemicals were obtained from Sigma-Aldrich Company and used as received. $^1$H and $^{13}$C NMR spectra were recorded on Brucker-Avance DPX FT-NMR 500 and 400 MHz instruments. Chemical shifts of protons reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual proton in the NMR solvents (CDCl$_3$: 7.26 ppm). $^{13}$C-NMR spectra were recorded at 125 MHz or 100 MHz: chemical data for carbons are reported in parts per million (ppm, δ scale) down field from tetra methyl silane and are referenced to the carbon resonance of the solvent (CDCl$_3$:77.0 ppm). Mass spectra of compounds were recorded with ESI-MS.

2. Experimental procedures

Synthesis of $\alpha$-Hydroxy-$\beta$-oxo phosphonates (HOP).$^1$

$\alpha$-Hydroxy-$\beta$-oxo phosphonates were synthesized by the standard reported protocol.

Synthesis of Diethyl (2-oxo-2-phenylethyl)phosphonate (4).$^2$

Diethyl (2-oxo-2-phenylethyl)phosphonate (4) was synthesized by the reported protocol

**Procedure for oxidative C-C bond cleavage in HOP to acids.** Reaction vessel charged with 1 mmol of $\alpha$-hydroxy-$\beta$-oxo phosphonate 1 and was added 2 mL of toluene, 2 mmol of TBHP. The reaction mixture allowed stirring for 4 days at room temperature. After completion of the reaction, crude mass was extracted with ethyl acetate. Then it was purified by column chromatography using silica gel (# 100-200 mesh size) and eluted with ethyl acetate and hexane (1:4) to produced desire product 2 in good yields (68-95 %).
3. Spectral data of acid compounds.

*Benzoic acid (2a).*

\[
\text{COOH} \\
\text{C}_6\text{H}_5
\]

$^1$H NMR (400 MHz, MeOD) $\delta$ 8.03 (d, $J = 7.6$ Hz, 2H), 7.54 (t, $J = 7.3$ Hz, 1H), 7.43 (t, $J = 7.6$ Hz, 2H); $^{13}$C NMR (101 MHz, MeOD) $\delta$ 170.06, 134.11, 131.86, 130.80, 129.50; ESI-MS: 145.1 (M$^+$ + Na).

*4-Fluorobenzoic acid (2b).*

\[
\text{COOH} \\
\text{C}_6\text{H}_5 \text{F}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.14 (dd, $J = 8.2$, 5.8 Hz, 2H), 7.15 (t, $J = 8.5$ Hz, 2H); $^{13}$C NMR (101 MHz, MeOD) $\delta$ 168.77, 168.45, 165.94, 133.53, 133.43, 128.42, 116.51, 116.29; ESI-MS: 139.0 (M$^+$ -1).

*4-Chlorobenzoic acid (2c).*

\[
\text{COOH} \\
\text{C}_6\text{H}_5 \text{Cl}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (d, $J = 8.6$ Hz, 2H), 7.46 (d, $J = 8.6$ Hz, 2H); $^{13}$C NMR (101 MHz, MeOD) $\delta$ 168.76, 140.29, 132.35, 130.73, 129.76; ESI-MS: 155.2 (M$^+$ -1).

*4-Bromobenzoic acid (2d).*

\[
\text{COOH} \\
\text{C}_6\text{H}_5 \text{Br}
\]

$^1$H NMR (400 MHz, MeOD) $\delta$ 7.82 (d, $J = 8.5$ Hz, 2H), 7.55 (d, $J = 8.5$ Hz, 2H); $^{13}$C NMR (126 MHz, MeOD) $\delta$ 168.89, 132.84, 132.50, 131.15, 128.81; ESI-MS: 199.2 (M$^+$ -1).

*3-Nitrobenzoic acid (2e).*

\[
\text{COOH} \\
\text{C}_6\text{H}_5 \text{NO}_2
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.97 (s, 1H), 8.53 – 8.43 (m, 2H), 7.73 (t, $J = 8.0$ Hz, 1H); $^{13}$C NMR (126 MHz, MeOD) $\delta$ 165.95, 148.25, 135.02, 132.47, 129.67, 126.89, 123.89; ESI-MS: 166.1 (M$^+$ -1).
4-Nitrobenzoic acid (2f).\(^3\)

\[
\begin{align*}
\text{COOH} \\
\text{NO}_2
\end{align*}
\]

\(^1\)H NMR (400 MHz, MeOD) \(\delta\) 8.23 (d, \(J = 8.8\) Hz, 2H), 8.13 (d, \(J = 8.8\) Hz, 2H); \(^{13}\)C NMR (126 MHz, MeOD) \(\delta\) 167.63, 151.96, 137.63, 131.97, 124.57; ESI-MS: 166.2 (M\(^+\) -1).

4-Methylbenzoic acid (2g).\(^3\)

\[
\begin{align*}
\text{COOH} \\
\text{O}
\end{align*}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.01 (d, \(J = 8.2\) Hz, 2H), 7.28 (d, \(J = 8.0\) Hz, 2H), 2.43 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 172.22, 144.64, 130.27, 129.22, 126.60, 21.76; ESI-MS: 137.4 (M\(^+\) + 1).

3,4-Dimethylbenzoic acid (2h).\(^5\)

\[
\begin{align*}
\text{COOH} \\
\text{O}
\end{align*}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.88 (s, 1H), 7.85 (d, \(J = 7.8\) Hz, 1H), 7.23 (d, \(J = 7.8\) Hz, 1H), 2.33 (s, 3H), 2.32 (s, 3H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 172.57, 143.41, 136.92, 131.22, 129.81, 127.87, 126.85, 20.18, 19.74; ESI-MS: 148.8 (M\(^+\) -1).

4-Methoxybenzoic acid (2i).\(^3\)

\[
\begin{align*}
\text{COOH} \\
\text{O}
\end{align*}
\]

\(^1\)H NMR (500 MHz, MeOD) \(\delta\) 7.87 (d, \(J = 8.9\) Hz, 2H), 6.87 (d, \(J = 8.9\) Hz, 2H), 3.75 (s, 3H); \(^{13}\)C NMR (126 MHz, MeOD) \(\delta\) 169.83, 165.09, 132.85, 124.01, 114.69, 55.98; ESI-MS: 151.2 (M\(^+\) -1).

4-Methoxy-2-methylbenzoic acid (2j).\(^6\)

\[
\begin{align*}
\text{COOH} \\
\text{O}
\end{align*}
\]
$^1$H NMR (400 MHz, DMSO) $\delta$ 7.84 (d, $J = 8.3$ Hz, 1H), 6.84 (s, 1H), 6.82 (d, $J = 2.4$ Hz, 1H), 3.82 (s, 3H); $^{13}$C NMR (126 MHz, DMSO) $\delta$ 168.00, 161.71, 142.15, 132.78, 122.02, 116.69, 111.11, 55.22, 21.86; ESI-MS: 167.1 (M$^+$+1).

2,4-Dichlorobenzoic acid (2k).$^4$

\[
\begin{array}{c}
\text{COOH} \\
\text{Cl} \\
\text{Cl}
\end{array}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.99 (d, $J = 8.5$ Hz, 1H), 7.53 (d, $J = 1.9$ Hz, 1H), 7.35 (dd, $J = 8.5$, 2.0 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 169.27, 139.56, 136.01, 133.50, 131.46, 127.18, 126.64; ESI-MS: 189.2 (M$^+$ -1).

3-Bromo-4-Fluorobenzoic acid (2l).$^7$

\[
\begin{array}{c}
\text{COOH} \\
\text{Br} \\
\text{F}
\end{array}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.34 (dd, $J = 6.6$, 2.1 Hz, 1H), 8.07 (ddd, $J = 8.6$, 4.7, 2.1 Hz, 1H), 7.23 (dd, $J = 16.5$, 8.1 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.20, 163.97, 161.43, 136.11, 136.09, 131.55, 131.46, 126.77, 126.73, 116.82, 116.59, 109.68, 109.47; ESI-MS: 216.8 (M$^+$-1).

4-Hydroxybenzoic acid (2m).$^8$

\[
\begin{array}{c}
\text{COOH} \\
\text{OH}
\end{array}
\]

$^1$H NMR (400 MHz, DMSO) $\delta$ 10.28 (s, 1H), 7.80 (d, $J = 8.7$ Hz, 2H), 6.83 (d, $J = 8.7$ Hz, 2H); $^{13}$C NMR (101 MHz, DMSO) $\delta$ 167.66, 162.05, 132.01, 121.79, 115.59; ESI-MS: 137.0 (M$^+$-1).

5-Methylthiophene-2-carboxylic acid (2n).$^9$

\[
\begin{array}{c}
\text{S} \\
\text{O} \\
\text{OH}
\end{array}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.71 (d, $J = 3.6$ Hz, 1H), 6.81 (d, $J = 3.1$ Hz, 1H), 2.56 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 165.61, 147.76, 133.41, 128.01, 124.63, 13.78; ESI-MS: 141.0 (M$^+$-1).
Benzofuran-2-carboxylic acid (20)\(^9\)

\[
\begin{align*}
\text{\text{O}} \\
\text{\text{O}} \\
\text{\text{O}} \\
\text{\text{OH}} \\
\end{align*}
\]

1H NMR (500 MHz, MeOD) \(\delta\) 7.72 (d, \(J = 7.9\) Hz, 1H), 7.57 (t, \(J = 4.2\) Hz, 2H), 7.50 – 7.43 (m, 1H), 7.31 (t, \(J = 7.5\) Hz, 1H); \(^{13}\)C NMR (126 MHz, MeOD) \(\delta\) 161.09, 155.74, 146.02, 127.33, 127.10, 123.50, 122.64, 113.45, 111.56; ESI-MS: 163.1 (M\(^+\)+1).

Diethyl (2-oxo-2-phenylethyl)phosphonate (4)\(^2\)

\[
\begin{align*}
\text{\text{O}} \\
\text{\text{O}} \\
\text{\text{O}} \\
\text{\text{P}} \\
\end{align*}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.04 – 7.99 (m, 2H), 7.62 – 7.56 (m, 1H), 7.52 – 7.45 (m, 2H), 4.20 – 4.08 (m, 4H), 3.64 (d, \(J = 22.7\) Hz, 2H), 1.28 (t, \(J = 7.1\) Hz, 6H); ESI-MS: 257.0 (M\(^+\)+1).

4. References:

5. NMR spectra of products (2a-2l)

2a. Benzoic acid
2b. 4-Fluorobenzoic acid
2c. 4-Chlorobenzoic acid
2d. 4-Bromobenzoic acid
2e. 3-Nitrobenzoic acid

![NMR Spectrogram of 3-Nitrobenzoic Acid]
2f. 4-Nitrobenzoic acid

![NMR Spectrogram of 4-Nitrobenzoic Acid]

- δ (ppm) values: 8.24, 8.21, 8.13, 8.12
- COOH and NO₂ groups are indicated on the diagram.

Chemical shifts and spectrums typically correspond to the presence of aromatic protons, carboxylic acid, and nitro groups.
2g. 4-Methylbenzoic acid
2h. 3,4-Dimethylbenzoic acid

COOH

COOH
2i. 4-Methoxybenzoic acid

![NMR spectrum of 4-Methoxybenzoic acid]

**Chemical Structure:**

- COOH
- O
- O
2j. 4-Methoxy-2-methylbenzoic acid

COOH

O

COOH

O
2k. 2,4-Dichlorobenzoic acid
2l. 3-Bromo-4-Fluorobenzoic acid

\[ \text{COOH} \]
\[ \text{F} \]
\[ \text{Br} \]
2m. 4-Hydroxybenzoic acid

![NMR spectrum of 4-Hydroxybenzoic acid](image)

The NMR spectrum shows peaks at various ppm values, indicating the presence of protons and other functional groups. The spectrum is characterized by sharp peaks at 7.98, 7.81, and 6.84 ppm, which correspond to the aromatic protons. Additionally, there are peaks at 2.04 ppm, likely representing the methyl group.

The chemical structure of 4-Hydroxybenzoic acid is shown below:

```
   COOH
  /     |
 /      |
OH      |
```

The IR spectrum and mass spectrum are also shown, with key peaks and masses indicated.

**Additional Information:**
- **Formula:** C₇H₆O₄
- **Molecular Weight:** 152.11 g/mol
- **CAS Number:** 93-98-8

This information is crucial for understanding the chemical structure and properties of 4-Hydroxybenzoic acid.
2n. 5-Methylthiophene-2-carboxylic acid

\[ \begin{align*}
\text{f1 (ppm)}: & \quad 7.72 \quad 7.71 \quad 6.82 \quad 6.81 \quad 3.02 \quad 1.00 \quad 1.00
\end{align*} \]

\[ \begin{align*}
\text{S} & \quad \text{O} \quad \text{OH}
\end{align*} \]
2o. Benzofuran-2-carboxylic acid
Diethyl (2-oxo-2-phenylethyl)phosphonate (4)

\[
\begin{array}{c}
\text{O} \\
\text{P} \\
\text{O} \\
\end{array}
\]

\[
\begin{array}{c}
\text{O} \\
\text{P} \\
\text{O} \\
\end{array}
\]

[Chemical structure image]