Copper and neocuproine catalysed synthesis of cinnamyl ether derivatives directly from secondary and tertiary cinnamyl alcohols

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Supporting Information

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1. General information

Instrumentation

\textsuperscript{1}H NMR spectra were recorded on JEOL JNM-ECZS 400 MHz spectrometers. \textsuperscript{13}C NMR spectra were recorded on JEOL JNM-ECZS 101 MHz spectrometer. Chemical shifts (δ values) were reported in parts per million (ppm), with coupling constants in Hz. Chemical shifts (δ) were reported with respect to the corresponding solvent residual peak at 7.26 ppm for CDCl\textsubscript{3}, 3.31 for CD\textsubscript{3}OD, 1.94 for CD\textsubscript{3}CN and 2.50 DMSO-d\textsubscript{6} for \textsuperscript{1}H-NMR. \textsuperscript{13}C-NMR spectra were reported in ppm using the central peak of CDCl\textsubscript{3} (77.16 ppm), CD\textsubscript{3}OD (49.00), CD\textsubscript{3}CN (118.26) and 39.52 DMSO-d\textsubscript{6}. Spectra were processed with MestReNova 14.0. HPLC-MS Spectra were obtained on Agilent 6120 electron spray ionization-quadrupole mass spectrometer (ESI-MS). HRMS spectra were acquired with Agilent 1100 Series LC/MSD and AB SCIEX TripleTOF 5600+ mass spectrometers. HPLC analyses were recorded on Agilent 1260 liquid chromatography (C18, mobile phase A: water; mobile phase B: acetonitrile).

Solvents

Experiments were performed under air or an atmosphere of nitrogen, using anhydrous solvents. (Petroleum ether (PE), ethyl acetate (EA), dichloromethane (DCM) and methyl alcohol (MeOH)) were used as received for column chromatography.

Others

Bulk chemicals were purchased from Adamas, TCI, or J&K and used as received unless otherwise stated. All glassware is oven-dried before the usage. The reactions were monitored by thin-layer chromatography (TLC) using plates coated with silica gel (HSGF254) form Qingdao Ocean chemical and visualization of the spots was achieved by exposure to 254 nm UV light or iodine fumigation. Column chromatography was performed using 300-400 mesh silica with the corresponding solvent system.
2. Experimental procedures and methods.
2.1 General procedure A for the preparation of tertiary cinnamyl alcohols

\[
\begin{align*}
\text{Ph} & + \text{CH}_2=\text{CH}-\text{C}_6\text{H}_4-\text{CH}_2\text{OH} & \xrightarrow{\text{Pd(OAc)}_2, \text{K}_2\text{CO}_3, \text{TBAB}, \text{DMF}, \text{N}_2, 100^\circ\text{C}} & \text{PhCH}=\text{CH}-\text{C}_6\text{H}_4-\text{CH}_2\text{OH} \\
\end{align*}
\]

According to the modified Heck’s method,\(^1\) a mixture of 1-iodo-4-methylbenzene (10.0 g, 45.9 mmol), 2-methylbut-3-en-2-ol (5.9 g, 68.9 mmol), \(\text{K}_2\text{CO}_3\) (9.5 g, 68.9 mmol), Tetrabutylammonium bromide (TBAB) (4.5 g, 13.8 mmol), palladium(II) acetate (260 mg, 1.2 mmol) and DMF (100 mL) in a three-neck flask under \(\text{N}_2\) atmosphere was stirred at 100°C for 12 hours. Then, the reaction mixture was cooled followed by the addition of \(\text{H}_2\text{O}\) (50 mL) and extraction with EA (50 mL × 3). The organic layers were combined, washed with brine, dried over anhydrous \(\text{Na}_2\text{SO}_4\), filtered and concentrated in vacuo. The crude product was purified by silica gel column chromatography (EA/PE = 1:4, retention factor values (R_{f}) = 0.2) to afford compound 1a.

2.2 General procedure B for the preparation of secondary cinnamyl alcohols

\[
\begin{align*}
\text{Ph} & + \text{CH}_2=\text{CH}-\text{C}_6\text{H}_4-\text{CH}_2\text{OH} & \xrightarrow{\text{Pd(OAc)}_2, \text{K}_2\text{CO}_3, \text{TBAB}, \text{PPh}_3, \text{AgOAC}, \text{DMF}, \text{N}_2, 100^\circ\text{C}} & \text{PhCH}=\text{CH}-\text{C}_6\text{H}_4-\text{CH}_2\text{OH} \\
\end{align*}
\]

According to the modified Jeffery’s method,\(^2\) a mixture of 1-iodo-4-methylbenzene (1.5 g, 6.9 mmol), but-3-en-2-ol (0.75 g, 10.4 mmol), \(\text{K}_2\text{CO}_3\) (1.4 g, 10.4 mmol), Tetrabutyl ammonium bromide (TBAB, 0.68 g, 2.1 mmol), \(\text{PPh}_3\) (0.14g, 0.52 mmol), silver acetate (0.58g, 3.5mmol), palladium(II) acetate (38 mg, 0.17 mmol) and DMF (20 mL) in a three-neck flask under \(\text{N}_2\) atmosphere was stirred at 100°C for 12 hours. Then, the reaction mixture was cooled to room temperature, then \(\text{H}_2\text{O}\) (30mL) was added and the mixture was extracted by EA (20mL × 3). The organic layers were washed with brine, dried over anhydrous \(\text{Na}_2\text{SO}_4\), filtered and concentrated in vacuo. The combined crude product was purified by silica gel column chromatography (EA/PE = 1:9, \(R_{f} = 0.2\)) to afford compound 3a.

2.3 General procedure C for the preparation of secondary and tertiary cinnamyl ether

\[
\begin{align*}
\text{PhCH}=\text{CH}-\text{C}_6\text{H}_4-\text{CH}_2\text{OH} & \xrightarrow{\text{CuSO}_4\cdot5\text{H}_2\text{O}, \text{neocuproine}, \text{EtOH}, 60^\circ\text{C}} & \text{PhCH}=\text{CH}-\text{OCH}_2\text{C}_6\text{H}_4-\text{CH}_2\text{OH} \\
\end{align*}
\]

In a 25 mL round-bottom flask, (\(E\))-2-methyl-4-(p-tolyl)but-3-en-2-ol (1a, 0.35 g, 2.0 mmol) was dissolved in EtOH (5 mL), then \(\text{CuSO}_4\cdot5\text{H}_2\text{O}\) (25 mg, 0.1 mmol) and neocuproine (21 mg, 0.1 mmol) were added subsequently. The reaction was stirred at 60 °C for 1 hour. TLC (EA/PE = 1:9) and LC-MS indicated the completion of the transformation. After cooling to room temperature, the reaction mixture was poured into water (40 mL), extracted with EA (3 × 20 mL), washed with brine (30 mL) and dried over anhydrous \(\text{Na}_2\text{SO}_4\). After evaporation of the solvent, the residue was purified by silica gel chromatography (EA/PE = 1:19, \(R_{f} = 0.2\)) to afford compound 2a.

2.4 Establishment of HPLC standard method

A HPLC method was established to calculate the conversion ratio. The UV absorption characteristics of 1a, 2a, and 2aa are different. If the peak area ratio was used for yield calculation directly, it will bring non-negligible error. A method for calculating the concentration through a standard curve was developed.

HPLC method: EC-C18; water/acetonitrile gradient elute (Table S1); flow rate = 1.0 mL/min; \(\lambda = 254 \text{ nm}\); mobile phase A, \(\text{H}_2\text{O}\); mobile phase B, MeCN. Compounds 1a, 2a and 2aa were well separated by the HPLC method. The results were demonstrated in Figure S1.
Table S1. Time table of the gradient elution conditions of the HPLC method

<table>
<thead>
<tr>
<th>Time</th>
<th>A % (H₂O)</th>
<th>B % (MeCN)</th>
<th>Flow rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 min</td>
<td>40</td>
<td>60</td>
<td>1 mL/min</td>
</tr>
<tr>
<td>9 min</td>
<td>20</td>
<td>80</td>
<td>1 mL/min</td>
</tr>
<tr>
<td>10 min</td>
<td>40</td>
<td>60</td>
<td>1 mL/min</td>
</tr>
<tr>
<td>11 min</td>
<td>60</td>
<td>40</td>
<td>1 mL/min</td>
</tr>
<tr>
<td>12 min</td>
<td>80</td>
<td>20</td>
<td>1 mL/min</td>
</tr>
</tbody>
</table>

Figure S1. HPLC analysis of compound 1a (left), 2a (middle) and 2aa (right). The relative position was determined by the standard sample after structure identification. \( t_R^{1a} = 5.771 \text{ min} \), \( t_R^{2a} = 10.529 \text{ min} \), \( t_R^{2aa} = 11.529 \text{ min} \).

Then, five different concentrations of compounds 1a, 2a, and 2aa were performed by HPLC method. The standard curves of compounds 1a, 2a, and 2aa were achieved and shown in Figure S2, Figure S3, and Figure S4, respectively. A mixture of EtOH solution of these three compounds (1a, 2a, and 2aa; 0.54 mmol/L) was subjected to HPLC by this method, and the result was shown in Figure S5. Calculated concentrations and actual concentrations were stated in Table S2. The concentrations calculated by the standard curve are matching the actual concentrations. These results show that it is reliable to calculate the concentration through their respective standard curves.

Figure S2. Standard curve of compound 1a.

Figure S3. Standard curve of compound 2a.

Figure S4. Standard curve of compound 2aa.
Figure S5. HPLC analysis report of compound 1a (left) (0.54 mmol/L), 2a (middle) (0.54 mmol/L) and 2aa (right) (0.54 mmol/L). The relative position was determined by the standard sample after structure identification. \(t_R^{1a} = 5.771\) min, \(t_R^{2a} = 10.529\) min, \(t_R^{2aa} = 11.529\) min.

Table S2. Calculated concentration by standard curve compared with the actual concentration of 1a (0.54 mmol/L), 2a (0.54 mmol/L), and 2aa (0.54 mmol/L)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Area (mAu)</th>
<th>calculated concentration</th>
<th>Accuracy rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>5558.6</td>
<td>0.54</td>
<td>100%</td>
</tr>
<tr>
<td>2a</td>
<td>6017.5</td>
<td>0.53</td>
<td>98.1%</td>
</tr>
<tr>
<td>2aa</td>
<td>1759</td>
<td>0.53</td>
<td>98.1%</td>
</tr>
</tbody>
</table>

2.5 Yield calculation example

Here we choose entry 2 in Table 1 as an example to illustrate how to calculate yield. After the reaction was continued for 1 h, reaction solution (15 \(\mu\)L) was diluted by MeOH (985 \(\mu\)L) and then subjected to HPLC by method. The peak areas (mAu·s) of compounds 1a, 2a, and 2aa were shown in Figure S6. The molar concentration of these three compounds could be easily calculated by the formula of the standard curve. Thus, the HPLC yields of compounds 2a and 2aa were 64 and 36%, respectively (Table S3).

Figure S6. HPLC reports of entry 2 in Table 1. HPLC method, \(t_R^{1a} = 5.678\) min, \(t_R^{2a} = 10.181\) min, \(t_R^{2aa} = 11.251\) min.

Table S3. Calculated Yield of 2a and 2aa about Entry 2 in Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>Area (mAu)</th>
<th>Calculated concentration</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>157.83096</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2a</td>
<td>12204</td>
<td>1.1</td>
<td>64%</td>
</tr>
<tr>
<td>2aa</td>
<td>1985.5</td>
<td>0.6</td>
<td>36%</td>
</tr>
</tbody>
</table>
3 Characterization data for the substrates and products

3.1 Characterization data for the substrates

\((E)\)-2-methyl-4-(p-tolyl)but-3-en-2-ol (1a)

\[
\begin{align*}
\text{Synthesis procedure was depicted in 2.1 general procedure A.} \\
\text{Brown solid (5.76 g, 71%). m.p.} & = 67.4-68.9 \degree C. \\
\text{\(^1H NMR (400 MHz, Chloroform-d) \delta \)} & = 7.27 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 7.9 Hz, 2H), 6.54 (d, J = 16.1 Hz, 1H), 6.29 (d, J = 16.1 Hz, 1H), 2.32 (s, 3H), 1.57 (s, 1H), 1.41 (s, 6H). \\
\text{\(^{13}C\{^1H\) NMR (101 MHz, Chloroform-d) \delta} & = 137.34, 136.57, 134.18, 129.36, 126.39, 126.32, 71.16, 29.98, 21.26. \\
\text{HRMS (Q-TOF): m/z [M+Na]^+} & \text{calcd for } C_{12}H_{16}ONa 199.1093, \text{found: 199.1091.}
\end{align*}
\]

\((E)\)-2-methyl-4-phenylbut-3-en-2-ol (1b)

\[
\begin{align*}
\text{Following general procedure A, iodobenzene (5 g, 25 mmol), 2-methylbut-3-en-2-ol (3.23 g, 37.5 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 1b.} \\
\text{Brown oil (3.45 g, 84.1%). \(^1H NMR (400 MHz, Chloroform-d) \delta \)} & = 7.40 – 7.35 (m, 2H), 7.31 (td, J = 7.5, 1.3 Hz, 2H), 7.25 – 7.19 (m, 1H), 6.58 (d, J = 16.1 Hz, 1H), 6.35 (d, J = 16.1 Hz, 1H), 1.78 (s, 1H), 1.42 (s, 6H). \\
\text{\(^{13}C\{^1H\) NMR (101 MHz, Chloroform-d) \delta} & = 137.64, 137.03, 128.68, 127.53, 126.52, 126.46, 71.17, 29.97. \\
\text{HRMS (Q-TOF): m/z [M+Na]^+} & \text{calcd for } C_{11}H_{14}ONa 185.0937, \text{found: 185.0938.}
\end{align*}
\]

\((E)\)-4-(4-(tert-butyl)phenyl)-2-methylbut-3-en-2-ol (1c)

\[
\begin{align*}
\text{Following general procedure A, 1-(tert-butyl)-4-iodobenzene (2 g, 25 mmol) and 2-methylbut-3-en-2-ol (3.23 g, 37.5 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 1c.} \\
\text{Brown oil (1.04 g, 67.9%). \(^1H NMR (400 MHz, Chloroform-d) \delta \)} & = 7.35 (m, 4H), 6.58 (d, J = 16.1 Hz, 1H), 6.34 (d, J = 16.1 Hz, 1H), 1.98 (s, 1H), 1.43 (s, 6H), 1.33 (s, 9H). \\
\text{\(^{13}C\{^1H\) NMR (101 MHz, Chloroform-d) \delta} & = 150.61, 136.99, 134.27, 126.26, 126.18, 125.61, 71.18, 34.65, 31.43, 30.01. \\
\text{HRMS (Q-TOF): m/z [M+Na]^+} & \text{calcd for } C_{15}H_{22}ONa 241.1563, \text{found: 241.1561.}
\end{align*}
\]

\((E)\)-4-(2-aminophenyl)-2-methylbut-3-en-2-ol (1d)

\[
\begin{align*}
\text{According to a reported literature, a mixture of 2-iodoaniline (1.0 g, 4.57 mmol), 2-methylbut-3-en-2-ol (1.97 g, 22.85 mmol), palladium acetate (0.1 g, 0.457 mmol) and DPPF (0.67 g, 0.91 mmol) [with } K_2CO_3 \text{ (0.95 g, 6.86 mmol) in the case of basic conditions] in } H_2O \text{ (25 mL) at 100 } \degree C \text{ under } N_2 \text{ atmosphere for 3 h. Then the reaction}
\end{align*}
\]
mixture was cooled to room temperature, extracted with DCM (20 mL × 3), and the organic layer was washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. The combined crude product was purified by silica gel column chromatography (EA/PE = 3:7) to afford 1d.
Brown oil (0.52 g, Yield: 64%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.25 – 7.21 (m, 1H), 7.05 (td, $J = 7.6, 1.6$ Hz, 1H), 6.75 (td, $J = 7.5, 1.2$ Hz, 1H), 6.69 – 6.61 (m, 2H), 6.20 (d, $J = 15.8$ Hz, 1H), 3.18 (s, 3H), 1.40 (s, 6H).

$^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) $\delta$ 143.63, 139.57, 128.47, 127.39, 123.50, 121.75, 119.20, 116.32, 71.35, 30.14. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{11}$H$_{15}$NONa 200.1046, found: 200.1045.

(E)-3-(3-hydroxy-3-methylbut-1-en-1-yl)phenol (1e)

Following general procedure A, 3-iodophenol (2 g, 9.1 mmol) and 2-methylbut-3-en-2-ol (1.17 g, 13.64 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:4) to afford 1e.
Brown oil (1.25 g, 77.2%). $^1$H NMR (400 MHz, Methanol-d$_4$) $\delta$ 7.07 (t, $J = 7.8$ Hz, 1H), 6.84 – 6.78 (m, 2H), 6.61 (ddd, $J = 8.1, 2.5, 1.0$ Hz, 1H), 6.46 (d, $J = 16.1$ Hz, 1H), 6.28 (d, $J = 16.1$ Hz, 1H), 1.34 (s, 6H).

$^{13}$C($^1$H) NMR (101 MHz, Methanol-d$_4$) $\delta$ 157.32, 138.77, 137.20, 129.16, 126.13, 117.68, 113.99, 112.50, 70.06, 28.58. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{11}$H$_{14}$O$_2$Na 201.0886, found: 201.0888.

(E)-1-(4-(3-hydroxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (1f)

Following general procedure A, 1-(4-iodophenyl)ethan-1-one (1.0 g, 4.06 mmol) and 2-methylbut-3-en-2-ol (0.52 g, 6.09 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 3:17) to afford 1f.
Yellow oil (0.43 g, 51.8%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.88 – 7.82 (m, 2H), 7.43 – 7.37 (m, 2H), 6.60 (d, $J = 16.1$ Hz, 1H), 6.44 (d, $J = 16.1$ Hz, 1H), 2.54 (s, 3H), 1.40 (s, 6H).

$^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) $\delta$ 197.87, 141.95, 140.71, 135.87, 128.84, 126.54, 125.49, 71.09, 29.89, 26.63. LC-MS (ESI): m/z [M + Na]$^+$ calcd for C$_{13}$H$_{16}$O$_2$Na 227.1; found 227.1.

Methyl (E)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzoate (1g)

Following general procedure A, methyl 4-iodobenzoate (0.86 g, 3.28 mmol) and 2-methylbut-3-en-2-ol (0.42 g, 4.92 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19 to 1:9) to afford 1g.
Brown oil (0.58 g, 80.6%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.96 (d, $J = 8.4$ Hz, 1H), 7.94 (d, $J = 8.6$ Hz, 1H), 7.42 – 7.40 (m, 1H), 7.40 – 7.37 (m, 1H), 6.60 (d, $J = 16.1$ Hz, 1H), 6.44 (d, $J = 16.1$ Hz, 1H), 3.88 (s, 3H), 1.80 (s, 1H), 1.41 (s, 6H).

$^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) $\delta$ 167.06, 141.66, 140.31, 130.01, 128.88, 126.39, 125.65, 71.17, 52.17, 29.91. HRMS (Q-TOF): m/z calcd for [M+Na]$^+$ C$_{13}$H$_{16}$O$_3$Na 243.0992, found: 243.1001.
(E)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzonitrile (1h)

Following general procedure A, 4-iodobenzonitrile (2 g, 7.7 mmol) and 2-methylbut-3-en-2-ol (0.99 g, 11.6 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 1h.

Brown oil (0.73 g, 44.8%). ¹H NMR (400 MHz, Chloroform-d) δ 7.56 (d, J = 8.5 Hz, 2H), 7.45 – 7.40 (m, 2H), 6.60 (d, J = 16.1 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 1.71 (s, 1H), 1.41 (s, 6H). ¹³C{¹H} NMR (101 MHz, Chloroform-d) δ 141.73, 141.55, 132.48, 127.00, 125.07, 119.07, 110.64, 71.17, 29.93. HRMS (Q-TOF): m/z calcd for [M+Na]⁺ C₁₂H₁₃NONa 210.0889, found: 210.0886.

(E)-4-(3,4-dichlorophenyl)-2-methylbut-3-en-2-ol (1i)

Following general procedure A, 1,2-dichloro-4-iodobenzene (1.0 g, 3.66 mmol) and 2-methylbut-3-en-2-ol (0.47 g, 5.49 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford 1i.

Brown oil (0.48 g, 56.5%). ¹H NMR (400 MHz, Chloroform-d) δ 7.39 (d, J = 2.1 Hz, 1H), 7.30 (d, J = 8.3 Hz, 1H), 7.12 (dd, J = 8.3, 2.1 Hz, 1H), 6.45 (d, J = 16.1 Hz, 1H), 6.29 (d, J = 16.0 Hz, 1H), 2.23 (s, 1H), 1.38 (s, 6H). ¹³C{¹H} NMR (101 MHz, Chloroform-d) δ 139.65, 137.27, 132.65, 130.97, 130.48, 128.15, 125.73, 124.32, 71.11, 29.90. HRMS (Q-TOF): m/z calcd for [M+Na]⁺ C₁₁H₁₂Cl₂ONa 253.0157, found: 253.0164.

(E)-4-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-methylbut-3-en-2-ol (1j)

Following general procedure A, 4-bromo-4'-iodo-1,1'-biphenyl (0.3 g, 0.83 mmol) and 2-methylbut-3-en-2-ol (0.1 g, 1.24 mmol) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 1j.

Brown solid (0.21 g, 79.8%). m.p. = 157.5-159.1 °C. ¹H NMR (400 MHz, Acetonitrile-d₃) δ 7.61 – 7.52 (m, 6H), 7.49 – 7.44 (m, 2H), 6.58 (d, J = 16.1 Hz, 1H), 6.44 (d, J = 16.1 Hz, 1H), 1.31 (d, J = 1.1 Hz, 6H). ¹³C{¹H} NMR (101 MHz, Acetonitrile-d₃) δ 139.17, 138.23, 137.19, 131.91, 128.62, 127.02, 126.89, 124.90, 121.04, 117.37, 70.11, 29.28. HRMS (Q-TOF): m/z calcd for [M+Na]⁺ C₁₇H₁₇BrONa 339.0355, found: 339.0362.

3-(2-hydroxy-2-methylpropylidene)isobenzofuran-1(3H)-one (1k)

A suspension of 2-iodobenzoic acid (5 g, 0.02 mol), 2-methylbut-3-en-2-ol (1.85 g, 0.022 mol), Pd(PPh₃)₂Cl₂, (0.28 g, 0.4 mmol), Cul(0.19 g, 10 mmol) and TEA (60 mL) in a round-bottom flask under N₂ atmosphere was stirred at room temperature for 12 h. Then, H₂O (50 mL) was added, and the mixture was extracted with EA (50
The organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo, and the combined crude product was purified by silica gel column chromatography (EA/PE= 1:9 to 1:4) to afford compound 1k.

Brown oil (3.6 g, 90%). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 8.06 (d, $J = 8.0$ Hz, 1H), 7.76 (t, $J = 7.5$ Hz, 1H), 7.60 (d, $J = 7.8$ Hz, 1H), 7.49 (t, $J = 8.2$ Hz, 1H), 6.74 (s, 1H), 5.49 (s, 1H), 1.38 (s, 6H). $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 163.61, 162.25, 137.70, 135.77, 129.21, 128.65, 126.76, 119.74, 99.94, 69.98, 28.76. LC-MS (ESI): m/z [M + H]$^+$ calcd for C$_{12}$H$_{13}$O$_2$ 205.2; found 205.2.

$^9$(E)-4-(4-(dimethylamino)phenyl)but-3-en-2-ol (3a)

To a 100 mL three-necked flask was added a solution of (E)-3-(4-(dimethylamino)phenyl)acrylaldehyde (0.5 g, 2.85 mmol) in dry THF (15 mL) followed by dropwise addition of CH$_3$MgBr (8.5 mL, 1 mol/L) at 0 ºC under N$_2$ atmosphere for 3 hours. The mixture was quenched with saturated aqueous NH$_4$Cl (20 mL), extracted with EA (15 mL × 3), the combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. The combined crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford 3a.

Orange solid (0.48 g, 89%). m.p.= 83.6-84.9 ºC. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.26 (dd, $J = 8.2$, 1.4 Hz, 2H), 6.69 – 6.64 (m, 2H), 6.45 (d, $J = 15.8$ Hz, 1H), 6.05 (dd, $J = 15.8$, 6.8 Hz, 1H), 4.43 (t, $J = 6.4$ Hz, 1H), 2.94 (s, 6H), 1.74 (s, 1H), 1.34 (d, $J = 6.4$ Hz, 3H). $^{13}$C {$^1$H} NMR (101 MHz, Chloroform-$d$) $\delta$ 150.27, 129.74, 129.44, 127.53, 125.25, 112.59, 69.44, 40.61, 23.59. LC-MS (ESI): m/z [M + H]$^+$ calcd for C$_{12}$H$_{18}$NO 192.2; found 192.2.

$^{10}$$(E)$-4-(p-tolyl)but-3-en-2-ol (3b)

Yellow oil (320 mg, 88%). m.p.= 83.6-84.9 ºC. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.32 – 7.20 (m, 2H), 7.11 (d, $J = 7.9$ Hz, 2H), 6.52 (d, $J = 15.9$ Hz, 1H), 6.20 (dd, $J = 15.9$, 6.5 Hz, 1H), 4.46 (p, $J = 6.4$ Hz, 1H), 2.33 (s, 3H), 1.36 (d, $J = 6.4$ Hz, 3H). $^{13}$C {$^1$H} NMR (101 MHz, Chloroform-$d$) $\delta$ 137.56, 133.99, 132.65, 129.44, 129.38, 126.47, 69.11, 23.50, 21.27. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{11}$H$_{14}$NO 185.0937, found: 185.0937.

$^{11}$(E)-4-(4-(tert-butyl)phenyl)but-3-en-2-ol (3c)

Following general procedure B, 1-(tert-butyl)-4-iodobenzene (0.5 g, 1.9 mmol) and but-3-en-2-ol (0.21 g, 2.9 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 3c.

Light yellow oil (0.3 g, 76%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.37 – 7.29 (m, 4H), 6.54 (dd, $J = 15.9$, 1.2 Hz, 1H), 6.22 (dd, $J = 15.9$, 6.5 Hz, 1H), 4.47 (pd, $J = 6.4$, 1.2 Hz, 1H), 1.82 (s, 1H), 1.36 (d, $J = 6.4$ Hz, 3H), 1.31
(s, 9H). $^{13}$C$\{^1$H$\}$ NMR (101 MHz, Chloroform-$d$) $\delta$ 150.87, 134.00, 132.94, 129.28, 126.28, 125.61, 69.12, 34.66, 31.38, 23.52. HRMS (Q-TOF): m/z calcd for [M+Na]$^+$ C$_{14}$H$_{20}$ONa 227.1406, found: 227.1420.

$(E)$-3-(3-hydroxybut-1-en-1-yl)phenol (3d)

Following general procedure B, 3-iodophenol (0.5 g, 2.3 mmol), but-3-en-2-ol (0.25 g, 3.5 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:4) to afford 3d.

Colorless oil (0.25 g, 67.1%). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.29 (d, $J$ = 3.3 Hz, 1H), 7.05 (t, $J$ = 7.8 Hz, 1H), 6.83 – 6.69 (m, 2H), 6.58 (dd, $J$ = 7.9, 2.6 Hz, 1H), 6.41 – 6.31 (m, 1H), 6.14 (dd, $J$ = 15.9, 5.5 Hz, 1H), 4.79 (d, $J$ = 4.3 Hz, 1H), 4.23 (q, $J$ = 5.8 Hz, 1H), 1.15 (d, $J$ = 6.3 Hz, 3H).

$^{13}$C$\{^1$H$\}$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 158.06, 138.75, 135.75, 130.04, 127.83, 117.68, 114.86, 113.22, 67.10, 24.32. HRMS (Q-TOF): m/z calcd for [M+Na]$^+$ C$_{10}$H$_{12}$O$_2$Na 187.0730, found: 187.0734.

$(E)$-4-(4-aminophenyl)but-3-en-2-ol (3e)$^{11}$

Following general procedure B, 4-iodoaniline (1.0 g, 4.6 mmol), but-3-en-2-ol (0.5 g, 6.9 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE= 1:4) to afford 3e.

Yellow oil (0.45 g, 60%). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 7.20 – 7.15 (m, 2H), 6.65 – 6.59 (m, 2H), 6.44 (d, $J$ = 14.8 Hz, 1H), 6.04 (dd, $J$ = 15.8, 6.8 Hz, 1H), 4.43 (pd, $J$ = 6.4, 1.1 Hz, 1H), 1.33 (d, $J$ = 6.3 Hz, 3H). $^{13}$C$\{^1$H$\}$ NMR (101 MHz, DMSO-$d_6$) $\delta$ 146.18, 129.99, 129.63, 127.72, 115.22, 113.52, 69.37, 23.55. HRMS (Q-TOF): m/z calcd for [M+H]$^+$ C$_{10}$H$_{14}$NO 164.1070, found: 164.1067.

Methyl $(E)$-4-(3-hydroxybut-1-en-1-yl)benzoate (3f)$^{12}$

Following general procedure B, methyl 4-iodobenzoate (0.5 g, 1.9 mmol), but-3-en-2-ol (0.21 g, 2.9 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 3f.

White solid (0.2 g, 51%). m.p.=71.1-73.0 °C. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.02 – 7.90 (m, 2H), 7.40 (dd, $J$ = 8.4, 1.8 Hz, 2H), 6.58 (d, $J$ = 16.0 Hz, 1H), 6.36 (ddd, $J$ = 15.9, 6.0, 1.7 Hz, 1H), 4.57 – 4.43 (m, 1H), 3.89 (d, $J$ = 1.7 Hz, 3H), 1.83 (s, 1H), 1.36 (d, $J$ = 6.5 Hz, 3H). $^{13}$C$\{^1$H$\}$ NMR (101 MHz, Chloroform-$d$) $\delta$ 167.01, 141.38, 136.37, 130.02, 129.10, 128.35, 126.41, 68.73, 52.16, 23.45. LC-MS (ESI): m/z [M + H]$^-$ calcd for C$_{12}$H$_{13}$O$_3$ 207.1; found 207.1.

$(E)$-4-(3-hydroxybut-1-en-1-yl)benzonitrile (3g)$^{13}$

Following general procedure B, 4-iodobenzonitrile (1.5 g, 6.5 mmol) and but-3-en-2-ol (0.7 g, 9.8 mmol) were added. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 3g.
Yellow oil (0.48 g, 44%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.61 – 7.55 (m, 2H), 7.47 – 7.40 (m, 2H), 6.63 – 6.54 (m, 1H), 6.37 (dd, $J = 16.0$, 5.8 Hz, 1H), 4.51 (p, $J = 5.8$ Hz, 1H), 1.65 (s, 1H), 1.37 (d, $J = 6.5$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) $\delta$ 141.44, 137.60, 132.51, 127.55, 127.01, 119.03, 110.85, 68.50, 23.47. LC-MS (ESI): m/z [M + H]$^+$ calcd for C$_{11}$H$_{12}$NO 174.1; found 174.1.

3.2 Characterization data for the products

(E)-1-(3-ethoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (2a)

Synthesis procedure was depicted in 2.3 general procedure C.

Colorless oil (0.34 g, 90.0%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.29 (d, $J = 8.1$ Hz, 2H), 7.13 (d, $J = 7.9$ Hz, 2H), 6.44 (d, $J = 16.3$ Hz, 1H), 6.17 (d, $J = 16.3$ Hz, 1H), 3.40 (q, $J = 7.0$ Hz, 2H), 2.34 (s, 3H), 1.38 (s, 6H), 1.18 (t, $J = 7.0$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) $\delta$ 137.34, 134.98, 134.28, 129.37, 128.54, 126.37, 75.00, 58.06, 26.62, 21.26, 16.27. HRMS (Q-TOF): m/z calcd for [M+Na]$^+$ C$_{14}$H$_{20}$ONa 227.1406, found: 227.1412.

(E)-1-methyl-4-(3-methylbuta-1,3-dien-1-yl)benzene (2aa)$^{14}$

To a 25 mL round bottom flask, (E)-2-methyl-4-(p-tolyl)but-3-en-2-ol (1a, 0.35 g, 2.0 mmol) dissolving in EtOH (10 mL) was added followed by the addition of H$_2$SO$_4$ (9.8 mg, 0.1 mmol). The reaction was stirred at 60°C for 1 hour. After cooling, the reaction mixture was poured into water (40 mL), extracted with EA (3 × 20 mL), washed with brine (30 mL) and dried over anhydrous Na$_2$SO$_4$. After evaporation of the solvent, the residue was purified by silica gel chromatography and eluted with PE ($R_f$ = 0.8) to afford compound 2aa.

Colourless oil (0.25 g, 80%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.41 – 7.34 (m, 2H), 7.22 – 7.15 (m, 2H), 6.90 (d, $J = 16.1$ Hz, 1H), 6.56 (d, $J = 16.1$ Hz, 1H), 5.19 – 5.07 (m, 2H), 2.38 (s, 3H), 2.05 – 2.00 (m, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) $\delta$ 142.30, 137.41, 134.73, 130.86, 129.49, 128.77, 126.54, 117.00, 21.38, 18.78. LC-MS (ESI): m/z [M + H]$^+$ calcd for C$_{12}$H$_{15}$ 159.1; found 159.1.

(E)-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2b)

Following general procedure C, 1b (0.32 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 3:97) to afford 2b.

Yellow oil (0.31 g, 82%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.44 – 7.39 (m, 2H), 7.37 – 7.30 (m, 2H), 7.27 – 7.22 (m, 1H), 6.50 (d, $J = 16.4$ Hz, 1H), 6.25 (d, $J = 16.3$ Hz, 1H), 3.42 (q, $J = 7.0$ Hz, 2H), 1.41 (s, 6H), 1.21 (t, $J = 7.0$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) $\delta$ 137.14, 136.08, 128.74, 128.70, 127.58, 126.52, 74.97, 58.11, 26.65, 16.32. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{12}$H$_{15}$ONa 213.1250, found: 213.1264.

(E)-1-(tert-butyl)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2c)
Following general procedure C, 1c (0.44 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford 2c.

Light yellow oil (0.37 g, 75.4%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.41 (s, 4H), 6.53 (d, $J = 16.3$ Hz, 1H), 6.26 (d, $J = 16.4$ Hz, 1H), 3.46 (q, $J = 7.0$ Hz, 2H), 1.44 (s, 6H), 1.38 (s, 9H), 1.24 (t, $J = 7.0$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-$d$) $\delta$ 150.67, 135.28, 134.36, 128.53, 126.28, 125.63, 75.01, 58.10, 34.67, 31.47, 26.73, 16.35. HRMS (Q-TOF): m/z [M+Na]$^+$ calcld for C$_{17}$H$_{26}$ONa 269.1876, found: 269.1892.

(E)-2-(3-ethoxy-3-methylbut-1-en-1-yl)aniline (2d)

Following general procedure C, 1d (0.35 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford 2d.

Brown oil (0.22 g, 56%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.29 – 7.23 (m, 1H), 7.07 (td, $J = 7.6$, 1.6 Hz, 1H), 6.76 (td, $J = 7.5$, 1.2 Hz, 1H), 6.67 (dd, $J = 7.9$, 1.2 Hz, 1H), 6.53 (d, $J = 16.2$ Hz, 1H), 6.10 (d, $J = 16.2$ Hz, 1H), 3.78 (s, 2H), 3.43 (q, $J = 7.0$ Hz, 2H), 1.39 (s, 6H), 1.19 (t, $J = 7.0$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-$d$) $\delta$ 143.70, 137.90, 128.54, 127.49, 124.06, 123.50, 119.12, 116.20, 75.16, 58.12, 26.75, 16.28. HRMS (Q-TOF): m/z [M+Na]$^+$ calcld for C$_{13}$H$_{19}$NONa 228.1359, found: 228.1363.

(E)-3-(3-ethoxy-3-methylbut-1-en-1-yl)phenol (2e)

Following general procedure C, 1e (0.36 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 2e.

Colorless oil (0.26 g, 55%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.22 – 7.15 (m, 2H), 6.98 (t, $J = 2.1$ Hz, 1H), 6.90 (dt, $J = 7.7$, 1.3 Hz, 1H), 6.77 (ddd, $J = 8.1$, 2.5, 0.9 Hz, 1H), 6.44 (d, $J = 16.3$ Hz, 1H), 6.22 (d, $J = 16.2$ Hz, 1H), 3.47 (q, $J = 7.0$ Hz, 2H), 1.39 (s, 6H), 1.19 (t, $J = 7.1$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-$d$) $\delta$ 156.57, 138.32, 135.39, 129.95, 129.09, 119.26, 115.19, 112.63, 75.94, 58.54, 26.44, 16.06. HRMS (Q-TOF): m/z [M+Na]$^+$ calcld for C$_{13}$H$_{18}$O$_2$Na 229.1199, found: 229.1208.

(E)-1-(4-(3-ethoxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (2f)

Following general procedure C, 1f (0.41 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:49 to 1:19) to afford 2f.

Colorless oil (0.28 g, 60%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.91 – 7.86 (m, 2H), 7.43 (d, $J = 8.2$ Hz, 2H), 6.50 (d, $J = 16.3$ Hz, 1H), 3.38 (q, $J = 7.0$ Hz, 2H), 2.56 (s, 3H), 1.37 (d, $J = 1.2$ Hz, 6H), 1.16 (t, $J = 7.0$ Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-$d$) $\delta$ 197.63, 141.82, 139.22, 136.03, 128.84, 127.62, 126.52, 74.96, 58.19, 26.64, 26.45, 16.19. HRMS (Q-TOF): m/z [M+Na]$^+$ calcld for C$_{15}$H$_{20}$O$_2$Na 255.1356, found: 255.1375.
Methyl (E)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzoate (2g)

Following general procedure C, 1g (0.44 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:49) to afford 2g.

White oil (0.23 g, 46%).

\[ \text{1H NMR (400 MHz, Chloroform-}d\text{)} \delta 8.01 – 7.91 (m, 2H), 7.43 – 7.38 (m, 2H), 6.49 (d, \text{J} = 16.3 \text{ Hz, 1H}), 6.32 (d, \text{J} = 16.3 \text{ Hz, 1H}), 3.88 (s, 3H), 3.38 (q, \text{J} = 7.0 \text{ Hz, 2H}), 1.36 (s, 6H), 1.16 (t, \text{J} = 7.0 \text{ Hz, 3H}). \]

\[ \text{13C\{1H} \text{ NMR (101 MHz, Chloroform-}d\text{)} \delta 166.95, 141.62, 138.93, 129.99, 128.95, 127.72, 126.33, 74.93, 58.17, 52.09, 26.46, 16.19. \]

HRMS (Q-TOF): m/z [M+Na]+ calcd for C_{15}H_{20}O_{3}Na 271.1305, found: 271.1324.

(E)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzonitrile (2h)

Following general procedure C, 1h (0.37 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 2h.

Colorless oil (0.28 g, 66%).

\[ \text{1H NMR (400 MHz, Chloroform-}d\text{)} \delta 7.57 – 7.53 (m, 2H), 7.46 – 7.38 (m, 2H), 6.46 (d, \text{J} = 16.3 \text{ Hz, 1H}), 6.32 (dd, \text{J} = 16.4, 0.7 \text{ Hz, 1H}), 3.36 (q, \text{J} = 7.0 \text{ Hz, 2H}), 1.35 (s, 6H), 1.15 (t, \text{J} = 7.0 \text{ Hz, 3H}). \]

\[ \text{13C\{1H} \text{ NMR (101 MHz, Chloroform-}d\text{)} \delta 141.66, 140.31, 132.45, 127.01, 126.96, 119.04, 110.67, 74.89, 58.22, 26.39, 16.19. \]

HRMS (Q-TOF): m/z [M+Na]+ calcd for C_{14}H_{17}NONa 238.1202, found: 238.1217.

(E)-1,2-dichloro-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2i)

Following general procedure C, 1i (0.48 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford 2i.

Light yellow oil (0.31 g, 60%).

\[ \text{1H NMR (400 MHz, Chloroform-}d\text{)} \delta 7.43 (d, \text{J} = 2.1 \text{ Hz, 1H}), 7.33 (d, \text{J} = 8.3 \text{ Hz, 1H}), 7.18 (d, \text{J} = 2.1 \text{ Hz, 1H}), 6.36 (d, \text{J} = 16.3 \text{ Hz, 1H}), 6.20 (d, \text{J} = 16.3 \text{ Hz, 1H}), 3.37 (q, \text{J} = 7.0 \text{ Hz, 2H}), 1.35 (s, 6H), 1.16 (t, \text{J} = 7.0 \text{ Hz, 3H}). \]

\[ \text{13C\{1H} \text{ NMR (101 MHz, Chloroform-}d\text{)} \delta 138.29, 137.28, 132.71, 131.05, 130.48, 128.15, 126.33, 125.67, 74.83, 58.15, 26.45, 16.19. \]

HRMS (Q-TOF): m/z [M+H]+ calcd for C_{13}H_{17}Cl_{2}O 259.0651, found: 259.0612.

(E)-4-bromo-4’-(3-ethoxy-3-methylbut-1-en-1-yl)-1,1’-biphenyl (2j)

Following general procedure C, 1j (0.63 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford 2j.

White oil (0.36 mg, 52%).

\[ \text{1H NMR (400 MHz, Chloroform-}d\text{)} \delta 7.59 – 7.48 (m, 4H), 7.45 (dd, \text{J} = 8.5, 3.5 \text{ Hz, 4H}), 6.50 (d, \text{J} = 16.3 \text{ Hz, 1H}), 6.28 (d, \text{J} = 16.3 \text{ Hz, 1H}), 3.41 (q, \text{J} = 7.0 \text{ Hz, 2H}), 1.40 (s, 6H), 1.19 (t, \text{J} = 7.0 \text{ Hz, 3H}). \]

\[ \text{13C\{1H} \text{ NMR (101 MHz, Chloroform-}d\text{)} \delta 139.71, 139.03, 136.58, 136.55, 131.98, 128.57, 128.04, 127.14, \]

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3-(2-ethoxy-2-methylpropylidene)isobenzofuran-1(3H)-one (2k)

Following general procedure C, 1k (0.63 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford 2k.

White solid. (0.36 mg, 52%).

\[ \begin{align*}
\text{HRMS (Q-TOF): m/z [M+Na]⁺ } & \text{ calcd for } C_{19}H_{21}BrONa 367.0668, \text{ found: 367.0712.} \\
\end{align*} \]

\( \text{(E)} \)-4-(3-ethoxybut-1-en-1-yl)-N,N-dimethylaniline (4a)

Following general procedure C, 3a (0.38 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford 4a.

Yellow oil (0.44 g, 62%).

\[ \begin{align*}
\text{HRMS (Q-TOF): m/z [M+H]⁺ } & \text{ calcd for } C_{14}H_{22}NO 220.1696, \text{ found: 220.1710.} \\
\end{align*} \]

\( \text{(E)} \)-1-(3-ethoxybut-1-en-1-yl)-4-methylbenzene (4b)

Following general procedure C, 3b (0.32 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:99) to afford 4b.

Colorless oil (0.22 g, 58.3%).

\[ \begin{align*}
\text{HRMS (Q-TOF): m/z [M+Na]⁺ } & \text{ calcd for } C_{13}H_{18}ONa 213.1250, \text{ found: 213.1246.} \\
\end{align*} \]

\( \text{(E)} \)-1-(tert-butyl)-4-(3-ethoxybut-1-en-1-yl)benzene (4c)

Following general procedure C, 3c (0.32 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:99) to afford 4c.

Colorless oil (0.22 g, 58.3%).

\[ \begin{align*}
\text{HRMS (Q-TOF): m/z [M+Na]⁺ } & \text{ calcd for } C_{13}H_{18}ONa 213.1250, \text{ found: 213.1246.} \\
\end{align*} \]
Following general procedure C, 3c (0.41 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford 4c.

Colorless oil (0.37 g, 77%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.34 (d, $J = 8.0$ Hz, 4H), 6.48 (d, $J = 15.9$ Hz, 1H), 6.07 (dd, $J = 16.1$, 7.8 Hz, 1H), 3.99 (q, $J = 7.3$, 6.8 Hz, 1H), 3.60 - 3.51 (m, 1H), 3.44 - 3.35 (m, 1H), 1.32 (s, 3H), 1.30 (s, 9H), 1.19 (t, $J = 6.9$ Hz, 3H). $^{13}$C{$^1$H} NMR (101 MHz, Chloroform-d) $\delta$ 150.82, 134.02, 131.44, 130.72, 126.24, 125.58, 76.53, 63.59, 31.37, 30.28, 21.93, 15.51. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{16}$H$_{24}$ONa 255.1719, found: 255.1734.

(E)-3-(3-ethoxybut-1-en-1-yl)phenol (4d)

Following general procedure C, 3d (0.33 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:4) to afford 4d.

Colorless oil (0.18 g, 48%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.17 (t, $J = 7.8$ Hz, 1H), 6.94 - 6.91 (m, 1H), 6.89 (dt, $J = 7.6$, 1.3 Hz, 1H), 6.74 (dd, $J = 8.1$, 2.5, 1.0 Hz, 1H), 6.46 (d, $J = 15.9$ Hz, 1H), 6.09 (dd, $J = 15.9$, 7.8 Hz, 1H), 4.04 (tt, $J = 7.2$, 6.3 Hz, 1H), 3.62 (dq, $J = 9.4$, 7.0 Hz, 1H), 3.45 (dq, $J = 9.4$, 7.0 Hz, 1H), 2.04 (s, 1H), 1.34 (d, $J = 6.4$ Hz, 3H), 1.22 (t, $J = 7.0$ Hz, 3H). $^{13}$C{$^1$H} NMR (101 MHz, Chloroform-d) $\delta$ 156.41, 138.15, 131.79, 131.25, 129.93, 119.46, 119.41, 115.21, 112.59, 63.89, 21.73, 15.34. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{12}$H$_{16}$O$_2$Na 215.1043, found: 215.1054.

(E)-4-(3-ethoxybut-1-en-1-yl)aniline (4e)

Following general procedure C, 3e (0.33 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 4e.

Yellow oil (0.17 g, 46%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.22 - 7.15 (m, 2H), 6.67 - 6.59 (m, 2H), 6.38 (d, $J = 15.9$ Hz, 1H), 5.89 (dq, $J = 9.4$, 7.1 Hz, 1H), 4.01 - 3.90 (m, 1H), 3.55 (dq, $J = 9.4$, 7.0 Hz, 1H), 3.37 (dq, $J = 9.4$, 7.0 Hz, 1H), 1.30 (d, $J = 6.4$ Hz, 3H), 1.18 (t, $J = 7.0$ Hz, 3H). $^{13}$C{$^1$H} NMR (101 MHz, Chloroform-d) $\delta$ 146.11, 130.94, 128.45, 127.68, 127.48, 115.19, 76.71, 63.45, 22.00, 15.50. HRMS (Q-TOF): m/z [M+H]$^+$ calcd for C$_{12}$H$_{18}$NO 192.1383, found: 192.1395.

Methyl (E)-4-(3-ethoxybut-1-en-1-yl)benzoate (4f)

Following general procedure C, 3f (0.41 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford 4f.

Yellow oil (0.2 g, 43%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.99 - 7.93 (m, 2H), 7.45 - 7.38 (m, 2H), 6.54 (d, $J = 16.0$ Hz, 1H), 6.24 (ddd, $J = 16.0$, 7.3 Hz, 1H), 4.02 (ddd, $J = 7.4$, 6.4, 1.1 Hz, 1H), 3.89 (s, 3H), 3.55 (dq, $J = 9.2$, 7.0 Hz, 1H), 3.42 (dq, $J = 9.2$, 7.0 Hz, 1H), 1.32 (d, $J = 6.4$ Hz, 4H), 1.20 (t, $J = 7.0$ Hz, 3H). $^{13}$C{$^1$H} NMR (101 MHz, Chloroform-d) $\delta$ 166.99, 141.36, 135.07, 130.01, 129.74, 129.07, 126.39, 76.15, 63.93, 52.15, 21.63, 15.51. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{14}$H$_{16}$O$_3$Na 257.1148, found: 257.1171.
(E)-4-(3-ethoxybut-1-en-1-yl)benzonitrile (4g)

Following general procedure C, 3g (0.35 g, 2.0 mmol) and EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:48) to afford 4g.

Yellow oil (0.16 g, 41%). \(^1\)H NMR (400 MHz, Chloroform-\(d_2\)) \(\delta\) 7.58 (d, \(J = 7.8\) Hz, 2H), 7.44 (d, \(J = 7.8\) Hz, 2H), 6.52 (d, \(J = 15.8\) Hz, 1H), 6.25 (dd, \(J = 16.0, 6.9\) Hz, 1H), 4.10 – 3.97 (m, 1H), 3.60 – 3.49 (m, 1H), 3.43 (t, \(J = 7.8\) Hz, 1H), 1.32 (d, \(J = 5.9\) Hz, 3H), 1.24 (t, \(J = 8.7\) Hz, 3H). \(^1\)C\{\(^1\)H\} NMR (101 MHz, Chloroform-\(d_2\)) \(\delta\) 141.39, 136.41, 132.49, 128.87, 127.00, 119.04, 110.84, 75.90, 64.06, 21.49, 15.50. HRMS (Q-TOF): m/z [M+Na]\(^+\) calcd for C\(_{13}\)H\(_{15}\)NONa 224.1046, found: 224.1063.

(E)-1-(3-(2-methoxyethoxy)-3-methylbut-1-en-1-yl)-4-methylbenzene (5a)

Following general procedure C, 1a (0.35 g, 2 mmol) and 2-methoxyethan-1-ol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford 5a.

Colorless oil (0.45 g, 96%). \(^1\)H NMR (400 MHz, Chloroform-\(d_2\)) \(\delta\) 7.29 (d, \(J = 8.2\) Hz, 2H), 7.15 – 7.08 (m, 2H), 6.47 (d, \(J = 16.4\) Hz, 1H), 6.18 (d, \(J = 16.3\) Hz, 1H), 3.51 (d, \(J = 0.7\) Hz, 4H), 3.38 (s, 3H), 2.33 (s, 3H), 1.40 (s, 6H). \(^1\)C\{\(^1\)H\} NMR (101 MHz, Chloroform-\(d_2\)) \(\delta\) 137.39, 134.55, 134.20, 129.36, 129.00, 126.41, 75.34, 72.14, 59.12, 26.50, 21.25. HRMS (Q-TOF): m/z [M+Na]\(^+\) calcd for C\(_{16}\)H\(_{24}\)ONa 257.1512, found: 257.1544.

(E)-1-(3-(benzyloxy)-3-methylbut-1-en-1-yl)-4-methylbenzene (5b)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and benzyl alcohol (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford 5b.

Colorless oil (0.45 g, 85%). \(^1\)H NMR (400 MHz, Chloroform-\(d_2\)) \(\delta\) 7.40 – 7.26 (m, 7H), 7.14 (d, \(J = 8.0\) Hz, 2H), 6.53 (d, \(J = 16.3\) Hz, 1H), 6.26 (d, \(J = 16.4\) Hz, 1H), 4.43 (s, 2H), 2.34 (s, 3H), 1.47 (s, 6H). \(^1\)C\{\(^1\)H\} NMR (101 MHz, Chloroform-\(d_2\)) \(\delta\) 139.84, 137.52, 134.66, 134.14, 129.41, 129.15, 128.69, 128.41, 127.56, 127.26, 127.10, 126.44, 75.76, 65.24, 26.70, 21.30. LC-MS (ESI): m/z [M + Na]\(^+\) calcd for C\(_{19}\)H\(_{22}\)ONa 289.2, found 289.2. HRMS (Q-TOF): m/z [M+Na]\(^+\) calcd for C\(_{19}\)H\(_{22}\)ONa 289.1563, found: 289.1566.

(E)-1-(3-methoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (5c)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and MeOH (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to give the product 5c.

Light yellow oil (0.25 g, 65%). \(^1\)H NMR (400 MHz, Chloroform-\(d_2\)) \(\delta\) 7.29 (d, \(J = 8.1\) Hz, 2H), 7.15 – 7.10 (m, 2H), 6.46 (d, \(J = 16.4\) Hz, 1H), 6.14 (d, \(J = 16.3\) Hz, 1H), 3.20 (s, 3H), 2.33 (s, 3H), 1.37 (s, 6H). \(^1\)C\{\(^1\)H\} NMR
(E)-1-((3-butoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (5d)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and butan-1-ol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford 5d.

Colorless oil (0.34 g, 74%). 1H NMR (400 MHz, Chloroform-d) δ 7.28 (d, J = 7.9 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 6.43 (d, J = 16.3 Hz, 1H), 6.16 (d, J = 16.3 Hz, 1H), 3.32 (t, J = 6.7 Hz, 2H), 2.33 (s, 3H), 1.55 - 1.48 (m, 2H), 1.36 (s, 9H), 0.90 (t, J = 7.3 Hz, 3H). 13C{1H} NMR (101 MHz, Chloroform-d) δ 137.30, 135.17, 134.34, 129.35, 128.49, 126.35, 74.78, 62.51, 32.83, 26.55, 21.24, 19.50, 14.06. HRMS (Q-TOF): m/z [M+Na]^+ calcld for C_{16}H_{24}ONa 255.1719, found: 255.1719.

(E)-2-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)ethan-1-ol (5e)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and ethane-1,2-diol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford 5e.

Colorless oil (0.25 g, 57%). 1H NMR (400 MHz, Chloroform-d) δ 7.28 (d, J = 8.2 Hz, 2H), 7.16 – 7.08 (m, 2H), 6.45 (d, J = 16.4 Hz, 1H), 6.15 (d, J = 16.3 Hz, 1H), 3.72 – 3.65 (m, 2H), 3.48 – 3.41 (m, 2H), 2.33 (s, 3H), 2.26 (s, 1H), 1.39 (s, 6H). 13C{1H} NMR (101 MHz, Chloroform-d) δ 137.54, 134.26, 134.03, 129.38, 129.13, 126.42, 75.37, 63.86, 62.44, 26.48, 21.25. HRMS (Q-TOF): m/z [M+Na]^+ calcld for C_{14}H_{20}O_{2}Na 243.1356, found: 243.1385.

(E)-6-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)hexan-1-ol (5f)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and hexanediol (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 3:17) to afford 5f.

Light yellow oil (0.3 g, 54.5%). 1H NMR (400 MHz, Chloroform-d) δ 7.32 – 7.25 (m, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.42 (d, J = 16.4 Hz, 1H), 6.15 (d, J = 16.3 Hz, 1H), 3.59 (t, J = 6.6 Hz, 2H), 3.31 (t, J = 6.7 Hz, 2H), 2.32 (s, 3H), 1.89 (s, 1H), 1.58 – 1.50 (m, 4H), 1.35 (d, J = 4.9 Hz, 10H). 13C{1H} NMR (101 MHz, Chloroform-d) δ 137.36, 134.97, 134.25, 129.37, 128.61, 126.36, 74.92, 62.91, 62.71, 32.79, 30.62, 26.53, 26.12, 25.71, 21.26. HRMS (Q-TOF): m/z [M+Na]^+ calcld for C_{18}H_{28}O_{2}Na 299.1982, found: 299.2018.

(E)-2-(2-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)ethoxy)ethanol (5g)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and 2,2’-(ethane-1,2-diylbis(oxy))bis(ethan-1-ol) (5 mL)
were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:3) to afford 5g.

Light yellow oil (0.38 g, 62%). 1H NMR (400 MHz, Chloroform-d) δ 7.24 (dd, J = 8.1, 2.0 Hz, 2H), 7.13 – 7.02 (m, 2H), 6.42 (dd, J = 16.5, 1.9 Hz, 1H), 6.13 (dd, J = 16.4, 2.0 Hz, 1H), 3.69 – 3.46 (m, 12H), 3.38 (s, 1H), 2.28 (d, J = 2.1 Hz, 3H), 1.34 (d, J = 2.2 Hz, 6H). 13C{1H} NMR (101 MHz, Chloroform-d) δ 137.36, 134.32, 134.10, 129.34, 129.06, 126.40, 75.47, 72.76, 71.14, 70.62, 70.36, 61.64, 26.42, 21.24.

(E)-1-methyl-4-(3-methyl-3-(octadecyloxy)but-1-en-1-yl)benzene (5h)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and 1-Octadecanol (5 mL) were used. The crude product was purified by silica gel column chromatography and eluted with PE to afford 5h.

Brown solid (0.5 g, 60%). m.p. = 38.0-39.2 °C. 1H NMR (400 MHz, Chloroform-d) δ 7.28 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 6.43 (d, J = 16.4 Hz, 1H), 6.16 (d, J = 16.3 Hz, 1H), 3.31 (t, J = 6.8 Hz, 2H), 2.33 (s, 3H), 1.36 (s, 6H), 1.25 (d, J = 4.2 Hz, 32H), 0.88 (t, J = 6.8 Hz, 3H). 13C{1H} NMR (101 MHz, Chloroform-d) δ 137.30, 135.14, 134.32, 129.34, 128.50, 126.35, 74.81, 62.86, 32.02, 30.72, 29.80, 29.63, 29.46, 26.55, 26.32, 22.79, 21.24, 14.21. HRMS (Q-TOF): m/z [M+Na]+ calcld for C30H52ONa 451.3910, found: 451.3840.

(E)-19,19-dimethyl-21-(p-tolyl)-3,6,9,12,15,18-hexaoxahenicos-20-en-1-ol (5i)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and hexaethylene glycol (5 mL) were used. The crude product was purified by silica gel column chromatography (MeOH/DCM= 1:49) to afford 5i.

Yellow oil (0.51 g, 58%). 1H NMR (400 MHz, Chloroform-d) δ 7.25 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 7.9 Hz, 2H), 6.43 (d, J = 16.3 Hz, 1H), 6.13 (d, J = 16.3 Hz, 1H), 3.70 – 3.55 (m, 24H), 2.31 (s, 3H), 1.35 (s, 6H). 13C{1H} NMR (101 MHz, Chloroform-d) δ 137.39, 134.51, 134.15, 129.34, 128.91, 126.38, 75.38, 72.67, 71.19, 70.65, 70.62, 70.58, 70.36, 62.21, 61.78, 26.49, 21.27. HRMS (Q-TOF): m/z [M+Na]+ calcld for C30H52ONa 451.3910, found: 451.3910.

8-Iodo-7-methoxy-2H-chromen-2-one

According to a reported literature, umbelliferone (5.00 g, 31 mmol) was dissolved in 20% ammonium hydroxide solution (125 mL). A solution of potassium iodide (12.28 g, 74 mmol) and iodine (7.87 g, 31 mmol) in water (240 mL) was added over 60 min. The mixture was stirred for 24 h at room temperature before sulfuric acid (300 mL, 2.5M) was carefully added. The crude product was collected by filtration and was purified by recrystallisation (acetone) to afford a pale brown powder. After that, the pale brown powder was dissolved in acetone (50 mL), then anhydrous potassium carbonate (4.7 g, 34.1 mmol) and the corresponding MeI (2.1 mL, 34.1 mmol) were added. The solution was heated to reflux for 5 h. Water (50 mL) was added and the mixture was extracted with DCM. The combined organic extracts were washed with brine, dried over anhydrous Na2SO4, filtered and concentrated in vacuum. The crude product was purified by silica gel column (EA/PE = 1:4) to afford
the title product.

White solid (1.87g, 20%). m.p.=147.4-148.2°C. $^1$H NMR (400 MHz, Chloroform-d) δ 7.56 (d, J = 9.5 Hz, 1H), 7.42 (d, J = 8.6 Hz, 1H), 6.79 (d, J = 8.6 Hz, 1H), 6.24 (d, J = 9.4 Hz, 1H), 3.97 (s, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) δ 161.75, 160.62, 155.09, 143.21, 129.20, 113.97, 113.80, 107.51, 76.09, 57.10.

HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{10}$H$_7$IO$_3$Na 324.9332, found: 324.9335.

(E)-8-(3-hydroxy-3-methylbut-1-en-1-yl)-7-methoxy-2$H$-chromen-2-one (6)$^7$

Following general procedure A, 8-Iodo-7-methoxy-2$H$-chromen-2-one (0.3 g, 1.0 mmol) and 2-methylbut-3-en-2-ol (0.13g, 1.5mmol) were used. The product was purified by silica gel column chromatography (EA/PE = 1:3 to 2:3) to afford 6.

Brown oil (0.33 g, 56.9%). $^1$H NMR (400 MHz, Chloroform-d) δ 7.62 (d, J = 9.5 Hz, 1H), 7.29 (d, J = 8.7 Hz, 1H), 7.02 (d, J = 16.5 Hz, 1H), 6.92 (d, J = 16.5 Hz, 1H), 6.86 (d, J = 8.7 Hz, 1H), 6.25 (d, J = 9.5 Hz, 1H), 3.95 (s, 3H), 1.47 (s, 6H).

$^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) δ 161.13, 160.30, 152.66, 144.59, 144.05, 127.12, 114.38, 113.73, 113.08, 113.02, 107.64, 71.72, 56.21. LC-MS (ESI): m/z [M + Na]$^+$ calcd for C$_{15}$H$_{16}$O$_4$Na 283.1; found 283.1.

(E)-8-(3-ethoxy-3-methylbut-1-en-1-yl)-7-methoxy-2$H$-chromen-2-one (6a)$^7$

Following general procedure C, 6 (0.52 g, 2.0 mmol), EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:9) to afford 6a.

White solid (0.33 g, 57%). $^1$H NMR (400 MHz, Chloroform-d) δ 7.54 (d, J = 9.5 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H), 6.81 – 6.72 (m, 3H), 6.16 (d, J = 9.3 Hz, 1H), 3.88 (s, 3H), 3.42 (q, J = 7.0 Hz, 2H), 1.36 (s, 6H), 1.16 (t, J = 7.1 Hz, 3H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) δ 160.93, 160.28, 152.56, 143.97, 142.89, 127.16, 116.62, 113.73, 113.03, 112.95, 107.64, 75.76, 58.26, 56.18, 26.58, 16.25. LC-MS (ESI): m/z [M + Na]$^+$ calcd for C$_{17}$H$_{20}$O$_4$Na 311.1; found 311.1254, found: 311.1256.

(E)-8-(3-((6-hydroxyhexyl)oxy)-3-methylbut-1-en-1-yl)-7-methoxy-2$H$-chromen-2-one (6b)$^7$

Following general procedure C, 6 (0.52 g, 2.0 mmol), Hexanediol (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 2:3) to afford 6b.

Yellow oil (0.45 g, 62%). $^1$H NMR (400 MHz, Chloroform-d) δ 7.57 (d, J = 9.5 Hz, 1H), 7.25 (d, J = 8.6 Hz, 1H), 6.82 (d, J = 8.7 Hz, 1H), 6.74 (d, J = 1.1 Hz, 2H), 6.19 (d, J = 9.5 Hz, 1H), 3.89 (s, 3H), 3.56 (t, J = 6.6 Hz, 2H), 3.36 (t, J = 6.8 Hz, 2H), 2.08 (s, 1H), 1.59 – 1.48 (m, 4H), 1.40 – 1.31 (m, 10H). $^{13}$C($^1$H) NMR (101 MHz, Chloroform-d) δ 161.10, 160.32, 152.56, 143.97, 142.89, 127.16, 116.62, 113.73, 113.03, 112.95, 107.64, 75.76, 58.26, 56.18, 26.53, 26.09, 25.71. LC-MS (ESI): m/z [M + Na]$^+$ calcd for C$_{21}$H$_{28}$O$_5$Na 383.2; found 383.2. HRMS (Q-TOF): m/z [M+Na]$^+$ calcd for C$_{21}$H$_{28}$O$_5$Na 383.1829, found: 383.1832.

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(E)-8-(1-hydroxy-19,19-dimethyl-3,6,9,12,15,18-hexaoxhenicos-20-en-21-yl)-7-methoxy-2H-chromen-2-one (6c)

Following general procedure C, 6 (0.52 g, 2.0 mmol), Hexaethylene glycol (5 mL) were used. The crude product was purified by silica gel column chromatography (CH$_2$OH/DCM = 1:19) to afford 6c.

Yellow oil (0.52 g, 50%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.61 (d, $J$ = 9.5 Hz, 1H), 7.29 (d, $J$ = 8.6 Hz, 1H), 6.85 (d, $J$ = 8.7 Hz, 1H), 6.77 (s, 2H), 6.24 (d, $J$ = 9.5 Hz, 1H), 3.93 (s, 3H), 3.74 – 3.53 (m, 24H), 1.41 (s, 6H).

$^{13}$C{^1}H NMR (101 MHz, Chloroform-d) $\delta$ 160.96, 160.35, 152.67, 143.93, 142.64, 127.17, 117.06, 113.82, 113.21, 113.02, 107.64, 76.23, 72.67, 71.19, 70.61, 70.28, 62.35, 61.73, 56.23, 26.39. LC-MS (ESI): m/z [M + Na]$^+$ calcld for C$_{27}$H$_{40}$O$_{10}$Na 547.2; found 547.2. HRMS (Q-TOF): m/z [M+Na]$^+$ calcld for C$_{27}$H$_{40}$O$_{10}$Na 547.2514, found: 547.2515.

3(3R,E)-5-ethoxy-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)-3-hydroxyhept-6-enoic acid (7a)

Following general procedure C, 7 (0.96 g, 2.0 mmol), EtOH (5 mL) were used. The crude product was purified by silica gel column chromatography (EA/PE = 2:3) to afford 7a.

Yellow oil (0.64 g, 62%). $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.68 – 7.61 (m, 2H), 7.13 – 7.05 (m, 2H), 6.64 (dd, $J$ = 16.1, 1.6 Hz, 1H), 5.45 (dd, $J$ = 16.1, 5.2 Hz, 1H), 4.49 – 4.43 (m, 1H), 4.19 (q, $J$ = 7.2 Hz, 3H), 3.57 (s, 3H), 3.52 (s, 3H), 3.37 (p, $J$ = 6.6 Hz, 1H), 2.48 – 2.44 (m, 2H), 1.56 (dt, $J$ = 14.3, 9.8 Hz, 1H), 1.45 (dt, $J$ = 14.3, 3.0 Hz, 1H), 1.27 (dd, $J$ = 6.9, 5.6 Hz, 9H). $^{13}$C{^1}H NMR (101 MHz, Chloroform-d) $\delta$ 175.01, 172.77, 163.58, 157.36, 139.46, 134.66, 132.28, 132.19, 122.74, 121.51, 115.21, 114.99, 72.06, 68.57, 61.10, 42.51, 41.94, 41.36, 33.20, 32.21, 21.71, 21.68, 14.23. LC-MS (ESI): m/z [M + H]$^+$ calcld for C$_{24}$H$_{33}$FN$_3$O$_6$S 510.2; found 510.2. HRMS (Q-TOF): m/z [M+Na]$^+$ calcld for C$_{24}$H$_{32}$FN$_3$O$_6$SNa 532.1888, found: 532.1892. [α]$_{25}^D$: +7.6 (c = 1.0 g / mL, methanol: water =1:1).


(21R)-19-((E)-2-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)vinyl)-1,21-dihydroxy-3,6,9,12,15,18-hexaoxatricosan-23-oic acid (7b)

Following general procedure C, 7 (0.96 g, 2.0 mmol), Hexaethylene glycol (5 mL) were used. The crude product
was purified by silica gel column chromatography (EA/PE = 2:3) to afford 7b.

Yellow oil (1.0 g, 45%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.67 – 7.60 (m, 2H), 7.11 – 7.03 (m, 2H), 6.59 (dd, $J$ = 16.1, 1.6 Hz, 1H), 5.44 (dd, $J$ = 16.1, 5.2 Hz, 1H), 4.42 (ddd, $J$ = 7.8, 4.4, 1.7 Hz, 1H), 4.29 – 4.20 (m, 3H), 3.71 – 3.56 (m, 2H), 3.49 (s, 3H), 3.40 – 3.31 (m, 1H), 2.52 – 2.44 (m, 2H), 1.61 – 1.40 (m, 2H), 1.24 (d, $J$ = 6.7 Hz, 6H). $^{13}$C {$^1$H} NMR (101 MHz, Chloroform-$d$) $\delta$ 175.02, 172.02, 163.53, 157.31, 139.70, 132.30, 132.22, 122.47, 121.64, 115.20, 114.99, 72.87, 71.85, 70.60, 70.55, 70.53, 70.48, 70.43, 70.09, 69.02, 68.47, 63.78, 61.60, 42.49, 42.44, 42.21, 33.20, 32.13, 21.74, 21.71. LC-MS (ESI): $m/z$ [M + Na]$^+$ calcld for C$_{34}$H$_{52}$FN$_3$O$_{12}$SNa 768.2; found 768.2. HRMS (Q-TOF): $m/z$ [M+Na]$^+$ calcld for C$_{34}$H$_{52}$FN$_3$O$_{12}$SNa 768.3148, found: 768.3164. [α]$_{25}^D$: +8.2 (c = 1.0 g / mL, methanol: water = 1:1).

Following a reported literature, benzylbromide (2.00 mL, 16.7 mmol) was heated to 75°C in a sealed flask. Diisopropylethylamine (2.16 g, 16.7 mmol) and heavy water (300 µL, 16.7 mmol) were added and the mixture was stirred for 24 hours. Water (10 mL) and dichloromethane (50 mL) were added and the organic layer was washed twice with brine. The organic layer was dried (Na$_2$SO$_4$) and evaporated to dryness. The product was purified by column chromatography (EA/PE = 1:19 to 1:9) to afford Bn $^{18}$OH.

Colorless liquid (0.83 g, 45%). Repeat this procedure, 2.0 g product was prepared. $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.36 (d, $J$ = 4.4 Hz, 4H), 7.32 – 7.26 (m, 1H), 4.67 (s, 2H). $^{13}$C {$^1$H} NMR (101 MHz, Chloroform-$d$) $\delta$ 140.96, 128.67, 127.77, 127.10, 65.43. HRMS (Q-TOF): $m/z$ [M+H]$^+$ calcld for C$_7$H$_9$O 111.0804, found: 111.0817.

(E)-1-(3-(Benzyl oxygen 18)-3-methylbut-1-en-1-yl)-4-methylbenzene (8)

Following general procedure C, 1a (0.35 g, 2.0 mmol) and Bn $^{18}$OH (2g) were used. The crude product was purified by silica gel column chromatography (EA/PE = 1:19) to afford 8.

Yellow oil (0.43 g, 80%). $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.39 – 7.26 (m, 7H), 7.14 (d, $J$ = 8.0 Hz, 2H), 6.53 (d, $J$ = 16.3 Hz, 1H), 6.26 (d, $J$ = 16.4 Hz, 1H), 4.43 (s, 2H), 2.34 (s, 3H), 1.47 (s, 6H). $^{13}$C {$^1$H} NMR (101 MHz, Chloroform-$d$) $\delta$ 139.84, 137.52, 134.66, 134.14, 129.41, 129.15, 128.41, 127.56, 127.26, 75.76, 65.24, 26.70, 21.34, 21.30. LC-MS (ESI): $m/z$ [M + Na]$^+$ calcld for C$_{19}$H$_{23}$O$_{18}$Na 291.1; found 291.1. HRMS (Q-TOF): $m/z$ [M+H]$^+$ calcld for C$_{19}$H$_{23}$O$_{18}$ 269.1752, found: 269.2070.
4 Copy of NMR

4.1 $^1$H-NMR and $^{13}$C($^1$H) NMR Spectra of the Substrates

$^1$H-NMR and $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$) Spectra of (E)-2-methyl-4-(p-tolyl)but-3-en-2-ol (1a)

1a $^1$H NMR (400 MHz, CDCl$_3$)

1a $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C($^1$H)NMR Spectra of (E)-2-methyl-4-phenylbut-3-en-2-ol (1b)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C $[^1$H$]$ NMR Spectra of (E)-4-(4-(tert-butyl)phenyl)-2-methylbut-3-en-2-ol (1c)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-4-(2-aminophenyl)-2-methylbut-3-en-2-ol (1d)

1d $^1$H NMR (400 MHz, CDCl$_3$)

1d $^{13}$C/{$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C [$^1$H] NMR Spectra of (E)-3-(3-hydroxy-3-methylbut-1-en-1-yl)phenol (1e)

1e $^1$H NMR (400 MHz, CD$_3$OD)

1e $^{13}$C [$^1$H] NMR (101 MHz, CD$_3$OD)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-1-(4-(3-hydroxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (1f)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of methyl (E)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzoate (1g)

**$^1$H NMR (400 MHz, CDCl$_3$)**

**$^{13}$C {$^1$H} NMR (101 MHz, CDCl$_3$)**
$^{1}H$-NMR and $^{13}C\{^1H\}$ NMR Spectra of ($E$)-4-(3-hydroxy-3-methylbut-1-en-1-yl)benzonitrile (1h)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (E)-4-(3,4-dichlorophenyl)-2-methylbut-3-en-2-ol (1i)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (101 MHz, CDCl$_3$)

$^1$H $^1$H NMR (400 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-4-(4'-bromo-[1,1'-biphenyl]-4-yl)-2-methylbut-3-en-2-ol (1j)

$^1$H NMR (400 MHz, CD$_3$CN)

$^{13}$C NMR (101 MHz, CD$_3$CN)

1j $^1$H NMR (400 MHz, CD$_3$CN)

1j $^{13}$C{$^1$H} NMR (101 MHz, CD$_3$CN)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of 3-(2-hydroxy-2-methylpropylidene)isobenzofuran-1(3$H$)-one (1k)

1k $^1$H NMR (400 MHz, DMSO)

1k $^{13}$C{$^1$H} NMR (101 MHz, DMSO)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-4-(4-(dimethylamino)phenyl)but-3-en-2-ol (3a)
$^1$H-NMR and $^{13}$C-$^1$H NMR Spectra of (E)-4-(p-tolyl)but-3-en-2-ol (3b)

3b $^1$H NMR (400 MHz, CDCl$_3$)

3b $^{13}$C-$^1$H NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C [$^1$H] NMR Spectra of (E)-4-(4-(tert-butyl)phenyl)but-3-en-2-ol (3c)

3c $^1$H NMR (400 MHz, CDCl$_3$)

3c $^{13}$C [$^1$H] NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C $[^1$H$]$ NMR Spectra of (E)-3-(3-hydroxybut-1-en-1-yl)phenol (3d)

3d $^1$H NMR (400 MHz, DMSO)

3d $^{13}$C $[^1$H$]$ NMR (101 MHz, DMSO)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (E)-4-(4-aminophenyl)but-3-en-2-ol (3e)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of methyl (E)-4-(3-hydroxybut-1-en-1-yl)benzoate (3f)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$)

$M^1$H NMR (400 MHz, CDCl$_3$)

$M^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C [$^1$H] NMR Spectra of (E)-4-(3-hydroxybut-1-en-1-yl)benzonitrile (3g)
4.2 $^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of the products

$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-1-(3-ethoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (2a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$)

2a $^1$H NMR (400 MHz, CDCl$_3$)

2a $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-1-methyl-4-(3-methylbuta-1,3-dien-1-yl)benzene (2aa)

2aa $^1$H NMR (400 MHz, CDCl$_3$)

2aa $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2b)

2b $^1$H NMR (400 MHz, CDCl$_3$)

2b $^{13}$C {$^1$H} NMR (101 MHz, CDCl$_3$)
"$^{1}$H-NMR and $^{13}$C [$^{1}$H] NMR Spectra of (E)-1-(tert-butyl)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzene (2c)"

$^{1}$H NMR (400 MHz, CDCl$_3$)

$^{13}$C [$^{1}$H] NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-2-(3-ethoxy-3-methylbut-1-en-1-yl)aniline (2d)

2d $^1$H NMR (400 MHz, CDCl$_3$)

2d $^{13}$C {$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C{$^1$H} NMR Spectra of (E)-3-(3-ethoxy-3-methylbut-1-en-1-yl)phenol (2e)

2e $^1$H NMR (400 MHz, CDCl$_3$)

2e $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-1-(4-(3-ethoxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one (2f)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C{$^1$H} NMR Spectra of methyl (E)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzoate (2g)

2g $^1$H NMR (400 MHz, CDCl$_3$)

2g $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (E)-4-(3-ethoxy-3-methylbut-1-en-1-yl)benzonitrile (2h)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (101 MHz, CDCl$_3$)
'$^1$H-NMR and $^{13}$C $[^1$H] NMR Spectra of (E)-1,2-dichloro-4-(3-ethoxy-3-methylbut-1-yn-1-yl)benzene (2i)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-4-bromo-4'-[(3-ethoxy-3-methylbut-1-en-1-yl)-1,1'-biphenyl (2j)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C {$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR, $^{13}$C $^1$H NMR, DEPT, HMQC and HMBC Spectra of 3-(2-ethoxy-2-methylpropylidene)isobenzofuran-1(3H)-one (2k)

2k $^1$H NMR (400 MHz, DMSO)

2k $^{13}$C $^1$H NMR (101 MHz, DMSO)
2k DEPT (101 MHz, DMSO)

2k HMQC (400 MHz, DMSO)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (E)-4-(3-ethoxybut-1-en-1-yl)-N,N-dimethylaniline (4a)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-1-(3-ethoxybut-1-en-1-yl)-4-methylbenzene (4b)

4b $^1$H NMR (400 MHz, CDCl$_3$)

4b $^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-1-(tert-butyl)-4-(3-ethoxybut-1-en-1-yl)benzene (4c)

**$^1$H NMR (400 MHz, CDCl$_3$)**

![NMR spectrum image]

**$^{13}$C {$^1$H} NMR (101 MHz, CDCl$_3$)**

![NMR spectrum image]
$^1$H-NMR and $^{13}$C [$^1$H] NMR Spectra of (E)-3-(3-ethoxybut-1-en-1-yl)phenol (4d)

4d $^1$H NMR (400 MHz, CDCl$_3$)

4d $^{13}$C [$^1$H] NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C [$^1$H] NMR Spectra of (E)-4-(3-ethoxybut-1-en-1-yl)aniline (4e)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C [$^1$H] NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of methyl (E)-4-(3-ethoxybut-1-en-1-yl)benzoate (4f)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-4-(3-ethoxybut-1-en-1-yl)benzonitrile (4g)

4g $^1$H NMR (400 MHz, CDCl$_3$)

4g $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (E)-1-(3-(2-methoxyethoxy)-3-methylbut-1-en-1-yl)-4-methylbenzene (5a)

5a $^1$H NMR (400 MHz, CDCl$_3$)

5a $^{13}$C $^1$H NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-1-(3-(benzyloxy)-3-methylbut-1-en-1-yl)-4-methylbenzene (5b)

5b $^1$H NMR (400 MHz, CDCl$_3$)

5b $^{13}$C{$^1$H} NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-1-(3-methoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (5c)

5c $^1$H NMR (400 MHz, CDCl$_3$)

5c $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C [$^1$H] NMR Spectra of (E)-1-(3-butoxy-3-methylbut-1-en-1-yl)-4-methylbenzene (5d)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-2-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)ethan-1-ol (5e)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-6-((2-methyl-4-(p-tolyl)but-3-en-2-yl)oxy)hexan-1-ol (5f)

5f $^1$H NMR (400 MHz, CDCl$_3$)

5f $^{13}$C/($^1$H) NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (E)-2-(2-(2-((2-methyl-4-(p-tolyl)but-3-en-2-yloxy)ethoxy)ethoxy)ethoxy)ethan-1-ol (5g)

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C $^1$H NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-1-methyl-4-(3-methyl-3-(octadecyloxy)but-1-en-1-yl)benzene (5h)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-19,19-dimethyl-21-(p-tolyl)-3,6,9,12,15,18-hexaoxahenicos-20-en-1-ol (5i)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of 8-Iodo-7-methoxy-2H-chromen-2-one$^a$

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$)

$^a$ H NMR (400 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C {$^1$H} NMR Spectra of (E)-8-(3-hydroxy-3-methylbut-1-en-1-yl)-7-methoxy-2H-chromen-2-one (6)\(^7\)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-8-(3-ethoxy-3-methylbut-1-en-1-yl)-7-methoxy-2H-chromen-2-one (6a)

6a $^1$H NMR (400 MHz, CDCl$_3$)

6a $^{13}$C($^1$H) NMR (101 MHz, CDCl$_3$)
$^{1}H$-NMR and $^{13}C\{^{1}H\}$ NMR Spectra of (E)-8-(3-((6-hydroxyhexyl)oxy)-3-methylbut-1-en-1-yl)-7-methoxy-2$H$-chromen-2-one (6b)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (E)-8-(1-hydroxy-19,19-dimethyl-3,6,9,12,15,18-hexaoxahenicos-20-en-21-yl)-7-methoxy-2H-chromen-2-one (6c)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (3R,E)-5-ethoxy-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)-3-hydroxyhept-6-enoic acid (7a)
19F NMR of (3R, E)-5-ethoxy-7-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)-3-hydroxyhept-6-enoic acid (7a)
$^1$H-NMR and $^{13}$C $^1$H NMR Spectra of (21R)-19-((E)-2-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-yl)vinyl)-1,21-dihydroxy-3,6,9,12,15,18-hexaoxatricosan-23-oic acid (7b)

7b $^1$H NMR (400 MHz, CDCl$_3$)

7b $^{13}$C $^1$H NMR (101 MHz, CDCl$_3$)
$^{19}$F NMR of (21R)-19-((E)-2-(4-(4-fluorophenyl)-6-isopropyl-2-(N-methylmethylsulfonamido)pyrimidin-5-y1)vinyl)-1,21-dihydroxy-3,6,9,12,15,18-hexaoxatricosan-23-oic acid (7b)
$^1$H-NMR and $^{13}$C [$^1$H] NMR Spectra of Bn $^{18}$OH

Bn $^{18}$OH $^1$H NMR (400 MHz, CDCl$_3$)

Bn $^{18}$OH $^{13}$C/$^1$H NMR (101 MHz, CDCl$_3$)
$^1$H-NMR and $^{13}$C ($^1$H) NMR Spectra of (E)-1-(3-(Benzyl oxygen 18)-3-methylbut-1-en-1-yl)-4-methylbenzene (8)
5 Copy of HRMS (Q-TOF) spectra

5.1 Copy of HRMS (Q-TOF) spectra (positive) of Bn $^{18}$OH

5.2 Copy of HRMS (Q-TOF) spectra (positive) of (E)-1-(3-(Benzyl oxygen 18)-3-methylbut-1-en-1-yl)-4-methylbenzene (8)

5.3 Copy of HRMS (Q-TOF) spectra of Cu(neocuproine)$_2$. 
6 References