Remote meta C–H Bond functionalization of 2-phenethylsulphonic acid and 3-phenylpropanoic acid derivatives

Atanu Modak, Anirban Mondal, Rahul Watile, Semanti Mukherjee, Debabrata Maiti*

Department of Chemistry, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India
Email: dmaiti@chem.iitb.ac.in

Supporting Information
Reagent information. Unless otherwise stated, all reactions were carried out under air in screw cap reaction tubes. All the solvents were bought from Aldrich in sure-seal bottle and were used as received. Palladium catalysts were got from Johnson Matthey and ligands were purchased from Aldrich and Alfa aesar. For column chromatography, silica gel (60–120 mesh or 100–200 mesh) from SRL Co. was used. A gradient elution-using pet–ether and ethyl acetate was performed, based on Merck aluminium TLC sheets (silica gel 60F254).

Analytical Information. All isolated compounds were characterized by $^1$H, $^{13}$C, IR spectroscopy, HR-MS. Copies of the $^1$H-NMR, $^{13}$C-NMR can be found in the supporting information. Nuclear Magnetic Resonance spectra were recorded on a Bruker 400 and 500 MHz instrument. The references used for the NMR are tetramethylsilane (TMS) or residual solvent for $^1$H and $^{13}$C-NMR. All $^1$H-NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All $^{13}$C-NMR spectra were reported in ppm relative to deuterochloroform (77.2 ppm), unless otherwise stated, and all were obtained with $^1$H decoupling. Neat infrared spectra were recorded on a Perkin-Elmer spectrum one FT-IR spectrometer. The data was recorded in transmittance mode (%T, cm$^{-1}$). GCMS analysis was done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). High-resolution mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.

Description of Reaction Tube:

Fig.1. Pictorial description of reaction tube: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E) [right]; Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A) [right].

Optimization details for Activation of Remote Meta C-H Bonds of 2 phenylethanesulfonic acid:

1. Optimization by varying temperature

$$\begin{align*}
\text{Pd(OAc)}_2 (10 \text{ mol\%}) & + \text{Ac-Gly-OH (20 mol\%)} \\
\text{Ag}_2\text{CO}_3 (2 \text{ equiv.}), & \text{HFIP (0.5 mL),} \\
\text{temperature, 24 h} & \text{OEt} (2 \text{ equiv.})
\end{align*}$$
<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Temperature (°C)</th>
<th>Yield on mono olefinated Product (meta:other)</th>
<th>Yield on di olefinated Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>41% (6:1)</td>
<td>21%</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>56% (6:1)</td>
<td>25%</td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>48% (6:1)</td>
<td>35%</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>40% (6:1)</td>
<td>39%</td>
</tr>
<tr>
<td>4</td>
<td>90</td>
<td>42% (5:1)</td>
<td>55%</td>
</tr>
</tbody>
</table>

2. Optimization by varying Oxidant

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Oxidant</th>
<th>Yield on mono olefinated Product (meta:other)</th>
<th>Yield on di olefinated Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AgOAc</td>
<td>64% (6:1)</td>
<td>10%</td>
</tr>
<tr>
<td>2</td>
<td>Ag₂CO₃</td>
<td>67% (6:1)</td>
<td>25%</td>
</tr>
<tr>
<td>3</td>
<td>Ag₂SO₄</td>
<td>12% (2:1)</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>Cu(OAc)₂</td>
<td>30% (3:1)</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>K₂S₂O₈</td>
<td>22% (1:1)</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>O₂ atmosphere</td>
<td>18% (2:1)</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>Benzoquinone</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

3. Optimization by varying ligand
<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ligand</th>
<th>Yield on mono olefinated Product (meta:other)</th>
<th>Yield on di olefinated Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>20% (3:1)</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>Ac-For-OH</td>
<td>67% (8:1)</td>
<td>10%</td>
</tr>
<tr>
<td>3</td>
<td>Ac-Gly-OH</td>
<td>64% (6:1)</td>
<td>13%</td>
</tr>
<tr>
<td>4</td>
<td>Ac-Phe-OH</td>
<td>61% (4:1)</td>
<td>7%</td>
</tr>
<tr>
<td>5</td>
<td>Ac-Lys-OH</td>
<td>19% (5:1)</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Ac-Gly-Gly-OH</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>Ac-Ala-OH</td>
<td>58% (4:1)</td>
<td>8%</td>
</tr>
<tr>
<td>8</td>
<td>Benzoyl-Gly-OH</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>Boc-Gly-OH</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>PPh₃</td>
<td>22% (1:1)</td>
<td>-</td>
</tr>
</tbody>
</table>

4. Optimization by varying amount of oxidant

![Chemical structure diagram]

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ligand</th>
<th>Yield on mono olefinated Product (meta:other)</th>
<th>Yield on di olefinated Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 equiv.</td>
<td>55% (6:1)</td>
<td>11%</td>
</tr>
<tr>
<td>2</td>
<td>2 equiv.</td>
<td>64% (7:1)</td>
<td>13%</td>
</tr>
<tr>
<td>3</td>
<td>3 equiv.</td>
<td>63% (6:1)</td>
<td>19%</td>
</tr>
</tbody>
</table>

5. Optimization by varying amount of olefin
Optimization details for Activation of Remote Meta C-H Bonds of 3-phenylpropanoic acid:

1. Optimization by varying catalyst loading

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Olefin amount</th>
<th>Yield on mono olefinated Product (meta:other)</th>
<th>Yield on di olefinated Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1.5 equiv.</td>
<td>55% (7:1)</td>
<td>11%</td>
</tr>
<tr>
<td>3</td>
<td>2 equiv.</td>
<td>66% (7:1)</td>
<td>13%</td>
</tr>
<tr>
<td>4</td>
<td>3 equiv.</td>
<td>56% (7:1)</td>
<td>25%</td>
</tr>
</tbody>
</table>

2. Optimization by varying amount of oxidant

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Pd (OAc)$_2$</th>
<th>Yield (%)</th>
<th>Mono: Di (ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10 mol%</td>
<td>63</td>
<td>8:1</td>
</tr>
<tr>
<td>2</td>
<td>7 mol %</td>
<td>57</td>
<td>9:1</td>
</tr>
<tr>
<td>3</td>
<td>5 mol%</td>
<td>45</td>
<td>8:1</td>
</tr>
<tr>
<td>4</td>
<td>2 mol %</td>
<td>30</td>
<td>10:1</td>
</tr>
<tr>
<td>5</td>
<td>1 mol %</td>
<td>14</td>
<td>10:1</td>
</tr>
</tbody>
</table>
H + O

Pd(OAc)$_2$ (10 mol%) Ac-Gly-OH (20 mol%)

Ag$_2$CO$_3$ (x equiv.),
DCE (0.5mL)
HFIP (3 equiv.), 65 °C, 48 h

metally exclusively

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ag$_2$CO$_3$ (equiv)</th>
<th>Yield (%)</th>
<th>Mono: Di (ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>51</td>
<td>5 : 1</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>66</td>
<td>8 : 1</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>65</td>
<td>10 : 1</td>
</tr>
<tr>
<td>4</td>
<td>3.0</td>
<td>66</td>
<td>7 : 1</td>
</tr>
</tbody>
</table>

3. Optimization by varying temperature

H + O

Pd(OAc)$_2$ (10 mol%)
Ac-gly-OH (20 mol%)

Ag$_2$CO$_3$ (3 equiv.),
DCE (0.5mL)
HFIP (3 equiv.), temp, 48 h

exclusively meta

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Temperature (°C)</th>
<th>Yield (%)</th>
<th>Mono: Di (ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>60</td>
<td>9 : 1</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>66</td>
<td>9 : 1</td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>60</td>
<td>6 : 1</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>67</td>
<td>5 : 1</td>
</tr>
<tr>
<td>5</td>
<td>90</td>
<td>68</td>
<td>5 : 1</td>
</tr>
</tbody>
</table>

4. Optimization by varying ligand amount

H + O

Pd(OAc)$_2$ (7 mol%)
Ac-gly-OH (x mol%)

Ag$_2$CO$_3$ (3 equiv.),
DCE (0.5mL)
HFIP (3 equiv.), 65 °C, 48 h

exclusively meta

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ligand (mol %)</th>
<th>Yield (%)</th>
<th>Mono: Di (ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>66</td>
<td>9 : 1</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>69</td>
<td>10 : 1</td>
</tr>
</tbody>
</table>

5. Optimization by varying oxidant
Pd(OAc)$_2$ (7 mol%), Ac-Gly-OH (21%), oxidant (3 equiv.),
DCE (0.5mL), HFIP (3 equiv.), 65 °C, 48 h

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Oxidant</th>
<th>Yield (%)</th>
<th>Mono: Di (ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AgOAc</td>
<td>66</td>
<td>10:1</td>
</tr>
<tr>
<td>2</td>
<td>AgCO$_3$</td>
<td>69</td>
<td>10:1</td>
</tr>
<tr>
<td>3</td>
<td>AgI</td>
<td>21</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>AgNO$_3$</td>
<td>29</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>Cu(OAc)$_2$</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>K$_2$S$_2$O$_8$</td>
<td>18</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>PhI(OAc)$_2$</td>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>BQ</td>
<td>11</td>
<td>-</td>
</tr>
</tbody>
</table>

6. Optimization by varying ligand

Pd(OAc)$_2$ (7 mol%)
Ac-Gly-OH (21%), Ag$_2$CO$_3$ (3 equiv.),
DCE (0.5mL), HFIP (3 equiv.), 65 °C, 48 h

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ligand</th>
<th>Yield (%)</th>
<th>Mono: Di (ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(R)(+) 2-Amino-1-butanol</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>H$_3$C$_2$OH$_2$NH$_2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Ac-For-OH</td>
<td>63</td>
<td>8:1</td>
</tr>
<tr>
<td></td>
<td>O$_2$N$_2$H$_2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Ac-Gly-OH</td>
<td>71</td>
<td>10:1</td>
</tr>
<tr>
<td></td>
<td>O$_2$N$_2$H$_2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Ac-Ala-OH</td>
<td>52</td>
<td>8:1</td>
</tr>
<tr>
<td></td>
<td>O$_2$N$_2$H$_2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Compound</td>
<td>R</td>
<td>11:1</td>
</tr>
<tr>
<td>---</td>
<td>-------------------</td>
<td>----</td>
<td>------</td>
</tr>
<tr>
<td>5</td>
<td>Ac-DL-Val-OH</td>
<td>39</td>
<td>11:1</td>
</tr>
<tr>
<td>6</td>
<td>Ac-Leu-OH</td>
<td>51</td>
<td>8:1</td>
</tr>
<tr>
<td>7</td>
<td>Ac-Phe-OH</td>
<td>52</td>
<td>8:1</td>
</tr>
<tr>
<td>8</td>
<td>Boc-Phe-OH</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>Ac-Trp-OH</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>D,L-Proline</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>No Ligand</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**General Procedure A for mono olefination through remote meta C-H activation of 2-phenylethanesulfonic acid:**

In a clean, oven–dried screw cap reaction tube, with previously placed magnetic stir–bar substrate (0.2 mmol); Pd(OAc)₂ (0.1 equiv, 0.02 mmol, 4.5 mg); N-Formyl-glycine (0.4 equiv, 0.04 mmol, 4.1 mg), AgOAc (2 equiv, 0.4 mmol, 46 mg) were taken. Then alkene (2 equiv, 0.4 mmol), hexafluoroisopropanol (0.5mL) were added to this mixture by syringe. The tube was tightly closed by screw cap and placed in a preheated oil bath at 60 °C. The reaction mixture was vigorously stirred for 24h. The reaction mixture was cooled to room temperature and filtered through celite. Reaction tube
was washed with 10 mL of ethyl acetate. Total organic portion was concentrated and purified via column chromatography through silica gel using pet ether-ethyl acetate as eluent.

**(E)-ethyl 3-(3-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)acrylate** (Scheme 3, Entry 2a): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether (70:30 v/v) mixture as eluent. Isolated yield: 66% (50 mg) with 7:1 regioisomeric mixture. \(^1\)H NMR (500 MHz, Chloroform-\(d\)) \(\delta\) 7.73 (dd, \(J = 7.7, 1.7\) Hz, 1H), 7.70 – 7.63 (m, 2H), 7.56 (dd, \(J = 8.4, 1.1\) Hz, 1H), 7.47 – 7.41 (m, 3H), 7.37 (t, \(J = 7.5\) Hz, 1H), 7.31 (dt, \(J = 7.6, 1.4\) Hz, 1H), 6.45 (d, \(J = 16.0\) Hz, 1H), 4.27 (q, \(J = 7.2\) Hz, 2H), 3.76 – 3.67 (m, 2H), 3.47 – 3.35 (m, 2H), 1.34 (t, \(J = 7.1\) Hz, 3H). \(^13\)C NMR (126 MHz, Chloroform-\(d\)) \(\delta\) 167.0, 149.9, 144.1, 137.6, 135.4, 134.8, 134.0, 130.5, 129.7, 128.3, 127.7, 127.2, 123.9, 119.1, 115.2, 107.4, 60.8, 53.6, 29.8, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{20}\)H\(_{19}\)NO\(_5\)SNa: 408.0876, found: 408.0876.

**(E)-2-cyanophenyl 2-(3-(3-oxopent-1-en-1-yl)phenyl)ethanesulfonate** (Scheme 3, Entry 2b): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: R = 52% (38 mg) with 7:1 regioisomeric mixture. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.74 – 7.70 (m, 1H), 7.70 – 7.64 (m, 1H), 7.58 – 7.50 (m, 2H), 7.48 (s, 1H), 7.47 – 7.41 (m, 2H), 7.40 – 7.34 (m, 1H), 7.32 (t, \(J = 7.2\) Hz, 1H), 6.76 (d, \(J = 16.0\) Hz, 1H), 3.76 – 3.69 (m, 2H), 3.45 – 3.36 (m, 2H), 2.73 – 2.66 (m, 2H), 1.20 – 1.12 (m, 3H). \(^13\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 200.9, 150.0, 141.7, 137.7, 135.7, 134.8, 134.0, 130.6, 129.8, 128.4, 127.7, 127.5, 126.7, 123.9, 115.2, 107.4, 53.8, 34.4, 29.8, 8.4. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{20}\)H\(_{19}\)NO\(_4\)SNa: 392.0927, found: 392.0925.

**(E)-2-cyanophenyl 2-(3-(2-(diethoxyphosphoryl)vinyl)phenyl)ethanesulfonate** (Scheme 3, Entry 2c): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (40:60 v/v) mixture as eluent. Isolated yield: R = 55% (49 mg) with 11:1 regioisomeric mixture. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.73 – 7.63 (m, 2H), 7.55 – 7.51 (m, 1H), 7.51 – 7.44 (m, 1H), 7.44 – 7.31 (m, 4H), 7.29 (dt, \(J = 7.2, 1.7\) Hz, 1H), 7.04 – 7.34 (m, 1H), 7.32 (t, \(J = 7.2\) Hz, 1H), 6.76 (d, \(J = 16.0\) Hz, 1H), 3.76 – 3.69 (m, 2H), 3.45 – 3.36 (m, 2H), 2.73 – 2.66 (m, 2H), 1.20 – 1.12 (m, 3H). \(^13\)C NMR (126 MHz, Chloroform-\(d\)) \(\delta\) 149.8, 148.2 (d; \(J = 7.6\) Hz), 137.6, 135.6, 134.6, 134.0, 130.6, 129.8, 128.4, 127.7, 127.5, 126.7, 123.9, 115.2, 107.4, 53.8, 34.4, 29.8, 16.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{21}\)H\(_{24}\)NO\(_6\)SPNa: 427.0954, found: 427.0956.

**(E)-2-cyanophenyl 2-(3-(3-(dimethylamino)-3-oxoprop-1-en-1-yl)phenyl)ethanesulfonate** (Scheme 3, Entry 2d): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (35:65 v/v) mixture as eluent. Isolated yield: R = 51% (39 mg) with 11:1 regioisomeric mixture. \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.72 (dd, \(J = 7.8, 1.7\) Hz, 1H), 7.71 – 7.60 (m, 2H), 7.55 (dd, \(J = 8.4, 1.0\) Hz, 1H), 7.49 (s, 1H), 7.47 – 7.37 (m, 2H), 7.35 (t, \(J = 7.6\) Hz, 1H), 7.27 (d, \(J = 1.5\) Hz, 1H), 6.93 (d, \(J = 15.4\) Hz, 1H), 3.79 – 3.63 (m, 2H), 3.48 – 3.34 (m, 2H), 3.20 (s, 3H), 3.08 (s, 3H). \(^13\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 150.0, 141.8, 137.4, 136.4, 134.8, 134.0, 129.8, 129.7, 127.7, 127.5, 123.9, 118.3, 115.2, 109.0, 107.4, 53.8, 37.6, 36.1, 29.8. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{21}\)H\(_{30}\)N\(_2\)O\(_4\)SNa: 407.1036, found: 407.1034.
E)-2-cyanophenyl 2-(3-(2-(methylsulfonyl)vinyl)phenyl)ethanesulfonate (Scheme 3, Entry 2e): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (40:60 v/v) mixture as eluent. Isolated yield: R = 71% (55 mg) with 11:1 regioisomeric mixture. 

1H NMR (500 MHz, Chloroform-d) d 7.72 (dd, J = 7.8, 1.7 Hz, 1H), 7.70 – 7.66 (m, 1H), 7.59 (d, J = 15.5 Hz, 1H), 7.54 (dd, J = 8.4, 1.1 Hz, 1H), 7.49 (d, J = 1.4 Hz, 1H), 7.47 – 7.35 (m, 4H), 6.97 (d, J = 15.5 Hz, 1H), 3.86 – 3.64 (m, 2H), 3.50 – 3.34 (m, 2H), 3.03 (s, 3H).

13C NMR (126 MHz, Chloroform-d) d 149.8, 143.4, 138.0, 134.8, 134.0, 133.0, 131.6, 130.0, 128.6, 128.0, 127.7, 127.0, 123.9, 115.2, 107.2, 53.5, 43.4, 29.7. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C18H17NO5S2Na: 414.0440, found: 414.0442.

(E)-2-Cyanophenyl 2-(3-(2-(phenylsulfonyl)vinyl)phenyl)ethanesulfonate (Scheme 3, Entry 2f): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (40:60 v/v) mixture as eluent. Isolated yield: R = 65% (58 mg) with 12:1 regioisomeric mixture.

1H NMR (500 MHz, Chloroform-d) d 8.00 – 7.93 (m, 2H), 7.72 (dd, J = 7.7, 1.7 Hz, 1H), 7.70 – 7.61 (m, 3H), 7.59 – 7.53 (m, 3H), 7.46 – 7.42 (m, 2H), 7.41 – 7.33 (m, 3H), 6.90 (d, J = 15.4 Hz, 1H), 3.86 – 3.57 (m, 2H), 3.55 – 3.31 (m, 2H).

13C NMR (126 MHz, Chloroform-d) d 149.9, 142.0, 140.8, 137.9, 134.8, 134.0, 133.6, 133.3, 131.5, 130.0, 129.6, 128.7, 128.2, 127.9, 127.7, 123.9, 115.2, 107.3, 53.6, 29.7.


(Dimethyl 2-(3-(2-(cyanoxy)sulfonyl)ethyl)phenyl)fumarate (Scheme 3, Entry 2g): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (50:50 v/v) mixture as eluent. Isolated yield: R = 72% (61 mg) with 20:1 regioisomeric mixture. 

1H NMR (500 MHz, Chloroform-d) d 7.72 (dd, J = 7.7, 1.7 Hz, 1H), 7.70 – 7.65 (m, 1H), 7.54 (dd, J = 8.4, 1.0 Hz, 1H), 7.43 (td, J = 7.7, 1.1 Hz, 1H), 7.41 – 7.34 (m, 4H), 6.33 (s, 1H), 3.95 (s, 3H), 3.79 (s, 3H), 3.73 – 3.67 (m, 2H), 3.45 – 3.37 (m, 2H).

13C NMR (126 MHz, Chloroform-d) d 168.3, 165.5, 149.9, 148.5, 137.9, 134.8, 134.1, 134.0, 130.9, 129.9, 127.7, 127.1, 126.0, 123.9, 117.9, 115.1, 107.3, 53.5, 53.0, 52.3, 29.8.

HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C21H19NO7SNa: 452.0774, found: 452.0785.

Dimethyl 2-(3-(2-(cyanooxy)sulfonyl)ethyl)phenyl)maleate (Scheme 3, Entry 2h): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (50:50 v/v) mixture as eluent. Isolated yield: R = 52% (44 mg) with 7:1 regioisomeric mixture. 

1H NMR (400 MHz, Chloroform-d) d 7.77 – 7.68 (m, 1H), 7.65 (dd, J = 7.8, 6.2 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.49 – 7.39 (m, 1H), 7.36 (dd, J = 13.6, 6.0 Hz, 1H), 7.30 (d, J = 7.8 Hz, 1H), 7.20 – 7.12 (m, 2H), 7.03 (s, 1H), 3.81 (s, 3H), 3.76 – 3.69 (m, 2H), 3.61 (s, 3H), 3.46 – 3.35 (m, 2H).

13C NMR (126 MHz, Chloroform-d) d 166.7, 165.5, 149.9, 143.9, 134.3, 134.7, 134.6, 134.0, 129.2, 129.1, 128.9, 128.6, 128.0, 127.6, 123.8, 115.1, 107.5, 53.6, 53.2, 52.1, 29.8.

HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C21H19NO7SNa: 452.0774, found: 452.0770.

(E)-decyl 3-(3-(2-(cyanoxy)sulfonyl)ethyl)phenyl)acrylate (Scheme 3, Entry 2i): Oily liquid. Isolated through 100-200 mesh silica gel using pet
ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: R = 6% (60 mg) with 6.5:1 regioisomeric mixture. 

1H NMR (400 MHz, Chloroform-d) δ 7.73 (dd, J = 7.8, 1.7 Hz, 1H); 7.47 – 7.41 (m, 3H); 7.40 – 7.34 (m, 1H); 7.31 (dt, J = 7.5, 1.6 Hz, 1H); 6.46 (d, J = 16.0 Hz, 1H); 4.20 (t, J = 6.7, 2.0 Hz, 2H); 3.80 – 3.66 (m, 2H); 3.46 – 3.08 (m, 2H); 1.70 (p, J = 6.6 Hz, 2H); 1.44 – 1.22 (m, 14H); 0.94 – 0.82 (m, 3H).

13C NMR (126 MHz, Chloroform-d) δ 167.1, 149.9, 144.0, 137.6, 135.4, 134.7, 134.0, 130.5, 129.7, 128.3, 127.7, 127.2, 123.9, 119.1, 115.1, 107.4, 65.0, 53.6, 32.0, 29.8, 29.7, 29.5, 29.4, 28.9, 26.1, 22.8, 14.3. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C28H35NO5SNa: 520.2188, found: 520.2188.

Oily liquid. Isolated yield: R = 63% (97 mg) with 6:1 regioisomeric mixture.

1H NMR (400 MHz, CDCl3) δ 7.88 (d, J = 16.0 Hz, 1H); 7.75-7.71 (m, 2H); 7.69 – 7.52 (m, 2H); 7.44 – 7.35 (m, 3H); 7.30 – 7.28 (m, 1H); 6.73 (d, J = 16.1 Hz, 1H); 3.77-3.70 (m, J = 7.3, 2H); 3.46 – 3.38 (m, 2H); 2.62 (t, J = 7.0 Hz, 2H); 2.12 (s, 3H); 2.06 (s, 3H); 2.02 (s, 3H); 1.86 – 1.74 (m, 2H); 1.59-1.50 (m, J = 3H); 1.30 – 1.21 (m, 12H); 1.17-1.06 (m, 7H); 0.84-0.82 (m, 12H).

13C NMR (101 MHz, CDCl3) δ 165.6, 149.9, 149.6, 145.7, 140.6, 137.7, 135.3, 134.8, 134.7, 134.0, 130.8, 129.8, 129.2, 128.7, 128.5, 127.7, 127.6, 127.5, 127.0, 125.2, 123.9, 123.9, 123.2, 118.2, 117.6, 115.2, 107.4, 75.2, 53.8, 53.7, 39.5, 37.6, 37.5, 32.9, 32.9, 29.9, 29.8, 28.2, 25.0, 24.6, 22.9, 22.8, 21.2, 20.8, 19.0, 19.9, 13.2, 12.4, 12.0. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C47H63NO6SNa: 792.4268, found: 792.4264.

Oily liquid. Isolated yield: R = 52% (63 mg) with 6:1 regioisomeric mixture.

1H NMR (500 MHz, CDCl3) δ 7.84 (d, J = 16 Hz, 1H); 7.75 – 7.66 (m, 2H); 7.56 (d, J = 8.4 Hz, 1H); 7.53 – 7.47 (m, 2H); 7.47 – 7.38 (m, 2H); 7.35 (q, J = 7.3 Hz, 1H); 7.31 (t, J = 7.6 Hz, 1H); 6.99 – 6.87 (m, 2H); 6.67 – 6.61 (d, J = 16 Hz, 1H); 3.78 – 3.70 (m, 2H); 3.49 – 3.39 (m, 2H); 2.97 – 2.89 (m, 2H); 2.54 – 2.46 (m, 1H); 2.46 – 2.38 (m, 1H); 2.36 – 2.27 (m, 1H); 2.14 (m, 1H); 2.09 – 1.94 (m, 4H); 1.67 – 1.46 (m, 3H); 1.27 (dd, J = 12.3, 5.9 Hz, 2H); 0.92 (s, 3H).

13C NMR (101 MHz, CDCl3) δ 221.1, 165.7, 149.9, 148.8, 145.9, 138.2, 137.7, 137.6, 135.1, 134.8, 134.0, 130.9, 129.9, 128.6, 127.7, 127.4, 126.6, 123.9, 121.8, 119.0, 118.2, 115.2, 107.4, 53.6, 50.6, 48.1, 44.3, 38.2, 36.0, 31.7, 29.8, 29.6, 26.5, 25.9, 21.8, 14.0. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C36H35NO6SNa: 632.2077, found: 632.2079.
7.27 (m, 1H), 7.08 (dd, J = 10.2, 8.5 Hz, 1H), 6.55 (d, J = 16.2 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 3.80 – 3.65 (m, 2H), 3.49 – 3.26 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H). \( ^{13} \text{C} \) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 166.8, 160.7 (d, \( J = 252 \)), 149.9, 136.8, 136.8, 134.8, 134.0, 133.1, 133.1, 131.9, 131.8, 129.3, 129.3, 127.7, 124.0, 123.2, 123.1, 121.7, 121.6, 117.1, 116.9, 115.2, 107.3, 60.9, 53.7, 29.2, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{20}\)H\(_{18}\)NFO\(_2\)SNa: 426.0782, found: 426.0782.

3-(2,4-dichloro-5-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)acrylate (Scheme 3, Entry 2m): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: R = 50% (45 mg). \( ^{1} \text{H} \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.96 (d, J = 16.1 Hz, 1H), 7.72 (dd, \( J = 7.7, 1.6 \) Hz, 1H), 7.68 – 7.65 (m, 2H), 7.59 – 7.54 (m, 1H), 7.48 (s, 1H), 7.40 – 7.40 (m, 1H), 6.46 (d, \( J = 16.0 \) Hz, 1H), 4.28 (q, \( J = 7.1 \) Hz, 2H), 3.73 (ddd, \( J = 10.3, 7.7, 5.4 \) Hz, 3H), 3.49 (ddd, \( J = 10.5, 8.1, 5.4 \) Hz, 3H), 1.34 (t, \( J = 7.1 \) Hz, 3H). \( ^{13} \text{C} \) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 166.4, 149.8, 138.8, 135.9, 134.8, 134.7, 134.0, 133.8, 132.3, 131.1, 129.9, 127.7, 123.9, 122.2, 115.2, 107.4, 61.0, 51.5, 28.0, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{20}\)H\(_{17}\)NO\(_3\)SClNa: 476.0096, found: 476.0098.

3-(3-bromo-5-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)acrylate (Scheme 3, Entry 2n): Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: R = 56% (51 mg) with 5.5:1 regioisomeric mixture. \( ^{1} \text{H} \) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.73 (dt, \( J = 7.7, 1.8 \) Hz, 1H), 7.71 – 7.66 (m, 1H), 7.59 – 7.54 (m, 3H), 7.46 – 7.44 (m, 2H), 7.38 (s, 1H), 6.44 (d, \( J = 16.0 \) Hz, 1H), 4.27 (q, \( J = 7.1 \) Hz, 2H), 3.95 – 3.49 (m, 2H), 3.46 – 3.29 (m, 2H), 1.34 (t, \( J = 7.1 \) Hz, 3H). \( ^{13} \text{C} \) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 166.6, 149.9, 142.5, 139.6, 137.4, 134.8, 134.0, 133.2, 129.9, 127.8, 127.2, 124.0, 123.6, 120.7, 115.2, 107.4, 61.0, 53.4, 29.5, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{20}\)H\(_{13}\)BrNO\(_2\)SNa: 485.9981, found: 485.9989. In this reaction (E)-ethyl 3-(3-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)acrylate also formed as side product.

3-(2,4′-dichloro-5-(2-((2-cyanophenoxy)sulfonyl)ethyl)-1,1′-biphenyl)-3-yl)acrylate (Scheme 3, Entry 2o): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: R = 58% (61 mg) with 10:1 regioisomeric mixture. \( ^{1} \text{H} \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.75 – 7.70 (m, 2H), 7.69 – 7.65 (m, 1H), 7.58 – 7.54 (m, 1H), 7.51 – 7.47 (m, 2H), 7.46 – 7.43 (m, 1H), 7.40 (d, \( J = 5.9, 3.5, 1.6 \) Hz, 1H), 7.37 – 7.32 (m, 2H), 7.29 (dt, \( J = 8.1, 5.3 \) Hz, 1H), 6.52 – 6.46 (d, \( J = 16.0 \) Hz, 1H), 4.30 – 4.23 (m, 2H), 3.80 – 3.73 (m, 2H), 3.50 – 3.42 (m, 2H), 1.40 – 1.29 (m, 3H). \( ^{13} \text{C} \) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 166.9, 149.9, 143.6, 139.9, 137.9, 137.7, 135.5, 134.8, 134.5, 134.0, 133.3, 132.1, 131.4, 130.1, 128.2, 127.8, 127.7, 127.6, 123.9, 119.8, 115.2, 107.4, 60.8, 53.6, 29.8, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{20}\)H\(_{13}\)Cl\(_2\)O\(_2\)SNa: 552.0410, found: 552.0405.

(R)-2-cyanophenyl 2-(3-(2-acetylcyclohex-2-enyl)phenyl)ethanesulfonate (Scheme 4, Entry 3a): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (65:35 v/v) mixture as eluent. Isolated yield: R = 56% (45 mg) with 7:1 regioisomeric mixture. \( ^{1} \text{H} \) NMR (500 MHz, Chloroform-\( d \)) \( \delta \) 7.71 (d, \( J = 7.1 \) Hz, 1H), 7.68 – 7.65 (m, 1H), 7.59 – 7.54 (m, 1H), 7.49 (s, 1H), 7.40 – 7.36 (m, 1H), 7.34 – 7.29 (m, 1H), 7.29 – 7.23 (m, 1H), 7.22 (d, \( J = 8.1 \) Hz, 1H), 7.18 – 7.12 (m, 1H), 7.04 – 6.97 (m, 1H), 6.44 (d, \( J = 8.1 \) Hz, 1H), 4.28 (q, \( J = 7.1 \) Hz, 2H), 3.73 (ddd, \( J = 7.1, 1.8 \) Hz, 3H). HRMS (ESI-QTOF) m/z: [M+Na]+: calcd. for C\(_{20}\)H\(_{16}\)BrNO\(_2\)SNa: 485.9981, found: 485.9989. In this reaction (E)-ethyl 3-(3-(2-acetylcyclohex-2-enyl)phenyl)ethanesulfonate also formed as side product.
$J = 7.8, 1.7 \text{ Hz, 1H}), 7.66 (\text{ddd, } J = 8.4, 7.6, 1.7 \text{ Hz, 1H}), 7.53 (\text{dd, } J = 8.4, 1.1 \text{ Hz, 1H}), 7.42 (\text{td, } J = 7.6, 1.1 \text{ Hz, 1H}), 7.25 – 7.14 (\text{m, 2H}), 7.07 (\text{dt, } J = 7.6, 1.4 \text{ Hz, 1H}), 2.51 – 2.37 (\text{m, 1H}), 2.35 – 2.27 (\text{m, 1H}), 2.25 (\text{s, 3H}), 1.95 – 1.82 (\text{m, 1H}), 1.80 – 1.69 (\text{m, 1H}).$

$^{13}$C NMR ($126 \text{ MHz, CDCl}_3$) $\delta 198.7, 149.9, 146.1, 142.8, 140.8, 136.5, 134.7, 134.0, 128.9, 128.0, 127.6, 126.9, 126.2, 123.8, 115.1, 107.4, 53.7, 38.3, 31.2, 29.8, 26.2, 25.9, 16.9$. HRMS (ESI-QTOF) m/z: [$\text{M+Na}^+]$: calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_4\text{SNa}$: 432.1240, found: 432.1237.

Mixture of methyl 2-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)benzyl)acrylate and (E)-methyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)-2-methylacrylate (1:0.6) (Scheme 4, Entry 3b): Oily liquid. Isolated through 100-200 mesh silica gel using petrol ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: $R = 50\%$ (38 mg). $^1$H NMR (500 MHz, CDCl$_3$) $\delta 7.75 - 7.70 (\text{m, 1H(A) + .6H (B)}), 7.67 (\text{m, 1H(A) + .6H (B)}), 7.55 (\text{m, 1H(A) + .6H (B)}), 7.47 - 7.34 (\text{m, 2H(A) + 1.2H (B)}), 7.33 - 7.27 (\text{m, 2H(A) + 1.2H (B)}), 7.12 (\text{m1H(A) + .6H (B)+1H (A)}), 6.24 (\text{s, 1H(A)}), 5.49 (\text{s, 1H(A)}), 3.82 (\text{s, 1.6 H(B)}), 3.73 (\text{s, 3H(A)}), 3.72 - 3.67 (\text{m, 2H(A)+ 1.2H(B)}), 3.62 (\text{s, 2H(A)}), 3.44 - 3.38 (\text{m, 1.2H(B)}), 3.37 - 3.33 (\text{m, 2H(A)}), 2.11 (\text{d, J = 1.3 Hz, 1.8H(B)}). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta 169.2, 167.4, 149.9, 139.9, 139.8, 138.5, 137.0, 137.0, 136.8, 134.7, 134.7, 134.0, 129.9, 129.3, 129.1, 128.7, 128.6, 128.2, 127.7, 127.6, 126.8, 126.7, 123.9, 123.8, 115.1, 107.5, 53.8, 53.7, 52.3, 52.1, 38.1, 29.8, 29.8, 14.3$. HRMS (ESI-QTOF) m/z: [$\text{M+Na}^+]$: calcd. for $\text{C}_{20}\text{H}_{19}\text{NO}_5\text{SNa}$: 408.0876, found: 408.08764.

Mixture of 2-(2-methoxyethoxy)ethyl 2-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)benzyl)acrylate and 2-(2-methoxyethoxy)ethyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)but-2-enoate (1:0.4) (Scheme 4, Entry 3c): Oily liquid. Isolated through 100-200 mesh silica gel using petrol ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: $R = 48\%$ (45mg). $^1$H NMR (400 MHz, CDCl$_3$) $\delta 7.74 - 7.63 (\text{m, 2H(A) + .8H (B)}), 7.61 - 7.49 (\text{m, 1H(A) + .4H (B)}), 7.43-7.40 (\text{m, 1H(A) + .4H (B)}), 7.12 (\text{m1H(A) + .6H (B)+1H (A)}), 6.24 (\text{s, 1H(A)}), 5.49 (\text{s, 1H(A)}), 4.42 - 4.34 (\text{m, .8H(B)}), 4.34 - 4.24 (\text{m, 2H(A)}), 3.85 - 3.29 (\text{m, 15H(A)+5.2H(B)}), 2.11 (\text{s, 1.2H(B)}). 13C NMR (101 MHz, CDCl$_3$) $\delta 168.6, 166.9, 149.9, 139.8, 139.8, 138.7, 136.9, 134.8, 134.7, 134.0, 129.9, 129.4, 129.2, 128.7, 128.2, 127.7, 127.6, 127.0, 126.7, 123.8, 115.1, 107.5, 59.2, 53.8, 38.1, 29.8, 14.3$. HRMS (ESI-QTOF) m/z: [$\text{M+Na}^+]$: calcd. for $\text{C}_{24}\text{H}_{27}\text{NO}_7\text{SNa}$: 496.1400, found: 496.1402.

**General Procedure B for sequential di olefination through remote meta C-H activation of 2-phenylethanesulfonic acid:** In a clean, oven–dried screw cap reaction tube, with previously placed magnetic stir–bar substrate (0.2 mmol); Pd(OAc)$_2$ (0.1 equiv, 0.02 mmol, 4.5 mg); N-Formyl-glycine (0.4 equiv, 0.04 mmol, 4.1 mg), AgOAc (3 equiv, 0.4 mmol, 66.4 mg) were taken. Then alkene (3 equiv, 0.6 mmol), hexafluoroisopropanol (1 mL) were added to this mixture by syringe. The tube was tightly closed by screw cap and placed in a preheated oil bath at 80 °C. The reaction mixture was
vigorously stirred for 48h. The reaction mixture was cooled to room temperature and filtered through celite. Reaction tube was washed with 10 mL of ethyl acetate. Total organic portion was concentrated and purified via column chromatography through silica gel using pet ether-ethyl acetate as eluent.

(E)-ethyl 3-(3-((2-cyanophenoxy)sulfonyl)ethyl)-5-((E)-3-oxopent-1-en-1-yl)phenyl)acrylate (Scheme 5, Entry 4a): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether (50:50 v/v) mixture as eluent. Isolated yield: 51% (48 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.75 – 7.71 (m, 1H), 7.71 – 7.68 (m, 1H), 7.68 – 7.62 (m, 1H), 7.59 – 7.56 (m, 1H), 7.55 (s, 1H), 7.50 (s, 1H), 7.50 (s, 1H), 7.48 – 7.41 (m, 2H), 6.79 (d, J = 16.2 Hz, 1H), 6.48 (d, J = 16.0 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 3.78 – 3.70 (m, 2H), 3.47 – 3.39 (m, 2H), 2.75 – 2.64 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 200.75, 166.8, 149.9, 143.2, 140.8, 138.4, 136.3, 136.2, 134.9, 134.0, 129.8, 129.8, 127.8, 127.3, 127.0, 124.0, 120.1, 115.3, 107.3, 60.9, 53.5, 34.7, 29.7, 14.5, 8.3. HRMS (ESI-QTOF) m/z: [M+Na]⁺: calcd. for C₂₅H₂₅NO₆SNa: 490.1294, found: 490.1297.

(E)-ethyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)-5-((E)-3-(dimethylamino)-3-oxoprop-1-en-1-yl)phenyl)acrylate (Scheme 5, Entry 4b): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (40:60 v/v) mixture as eluent. Isolated yield: 50% (48 mg). ¹H NMR (500 MHz, CDCl₃) δ 7.75 (dd, J = 7.7, 1.7 Hz, 1H), 7.73 – 7.70 (m, 1H), 7.67 (dd, J = 15.9, 12.3 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.49 – 7.44 (m, 2H), 6.98 (d, J = 15.5 Hz, 1H), 6.50 (d, J = 16.0 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 3.79 – 3.71 (m, 2H), 3.49 – 3.42 (m, 2H), 3.23 (s, 3H), 3.11 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.8, 166.4, 143.7, 141.1, 138.2, 137.1, 136.0, 134.8, 134.0, 129.2, 129.0, 127.7, 126.9, 124.0, 119.9, 119.3, 115.3, 107.3, 60.9, 53.7, 37.7, 36.2, 29.8, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]⁺: calcd. for C₂₅H₂₆N₂O₆SNa: 505.1403, found: 505.1403.

**General Procedure C for mono olefination through remote meta C-H activation of 3-phenylpropanoic acid:**

In a clean, oven–dried screw cap reaction tube, with previously placed magnetic stir–bar substrate (0.2 mmol); Pd(OAc)$_₂$ (0.07 equiv, 0.014 mmol, 3.2 mg); N-Acetyl-glycine (0.21 equiv, 0.042 mmol, 4.9 mg), Ag$_2$CO$_3$ (2 equiv, 0.4 mmol, 110 mg) were taken. Then alkene (1.5 equiv, 0.3 mmol), dichloroethane (DCE) (1 mL)/ hexafluoroisopropanol (64µL) were added to this mixture by syringe. The tube was tightly closed by screw cap and placed in a preheated oil bath at 65 °C. The reaction mixture was vigorously stirred for 48h. The reaction mixture was cooled to room temperature and filtered through celite. Reaction tube was washed with 10 mL of ethyl acetate. Total organic portion was concentrated and purified via column chromatography through silica gel using pet ether-ethyl acetate as eluent.

(E)-ethyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)-5-((E)-3-(dimethylamino)-3-oxoprop-1-en-1-yl)phenyl)acrylate (Scheme 6, Entry 5a): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether (90:10 v/v) mixture as eluent. Isolated yield: 68% (47 mg). ¹H NMR (500 MHz, CDCl₃) δ 7.70 – 7.65 (m, 2H), 7.63 – 7.59 (m, 1H), 7.43 (s, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.30 (d, J = 7.6 Hz, 1H), 7.20 (dd, J = 8.3, 0.5 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 3.14 (t, J = 7.6 Hz, 2H), 3.00 (t, J = 11.4, 4.2 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H).
IR (thin film) 676, 868, 918, 1118, 1155, 1223, 1449, 1648, 1707, 1773, 2343, 2354 cm$^{-1}$

HRMS (ESI-QTOF) m/z: [M+Na]$^+$: calcd. for $C_{21}H_{19}NO_4Na$: 372.1206, found: 372.1203.

(E)-Tert-butyl 3-(3-(2-cyanophenoxy)-3-oxopropyl)phenyl)acrylate (Scheme 6, Entry 5b): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (90:10 v/v) mixture as eluent. Isolated yield: R = 68% (51 mg). $^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 7.67 (dd, $J$ = 7.7, 1.6 Hz, 1H), 7.64 – 7.54 (m, 2H), 7.44 – 7.37 (m, 2H), 7.37 – 7.27 (m, 3H), 7.19 (dd, $J$ = 8.3, 1.0 Hz, 1H), 6.38 (d, $J$ = 15.9 Hz, 1H), 3.13 (t, $J$ = 8.0 Hz, 2H), 3.00 (ddd, $J$ = 8.3, 7.2, 1.1 Hz, 2H), 1.53 (s, 9H). $^{13}$C NMR (101 MHz, Chloroform-\textit{d}) $\delta$ 170.4, 166.5, 152.4, 143.5, 140.6, 135.2, 134.3, 133.5, 130.2, 129.4, 128.1, 126.6, 126.5, 126.4, 120.6, 115.3, 107.3, 80.7, 35.7, 30.7, 28.4. HRMS (ESI-QTOF) m/z: [M+Na]$^+$: calcd. for $C_{22}H_{22}NO_5Na$: 400.1519, found: 400.1517. IR (thin film) 676, 868, 918, 1118, 1155, 1223, 1449, 1648, 1707, 1773, 2343, 2354 cm$^{-1}$

(E)-2-Cyanophenyl 3-(3-(3-oxobut-1-en-1-yl)phenyl)propanoate (Scheme 6, Entry 5c): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (86:14 v/v) mixture as eluent. Isolated yield: R = 66% (42 mg). $^1$H NMR (500 MHz, Chloroform-\textit{d}) $\delta$ 7.68 (dd, $J$ = 7.8, 1.6 Hz, 1H), 7.61 (td, $J$ = 8.0, 1.6 Hz, 1H), 7.51 (d, $J$ = 16.3 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.39 – 7.30 (m, 3H), 7.20 (d, $J$ = 8.3 Hz, 1H), 6.73 (d, $J$ = 16.3 Hz, 1H), 3.14 (t, $J$ = 7.6 Hz, 2H), 3.01 (t, $J$ = 7.6 Hz, 2H), 2.39 (s, 3H). $^{13}$C NMR (126 MHz, Chloroform-\textit{d}) $\delta$ 198.7, 170.3, 152.4, 143.5, 140.7, 135.0, 134.3, 133.5, 130.8, 129.5, 128.5, 122.7, 126.7, 126.6, 123.3, 115.3, 107.2, 35.6, 30.6, 27.7. HRMS (ESI-QTOF) m/z: [M+Na]$^+$: calcd. for $C_{22}H_{18}NO_3Na$: 342.1100, found: 342.1098. IR (thin film) 682, 774, 1111, 1179, 1216, 1424, 1650, 1776, 1847, 2087, 2345, 2363 cm$^{-1}$.

(E)-2-Cyanophenyl 3-(3-(2-(methylsulfonyl)vinyl)phenyl)propanoate (Scheme 6, Entry 5d): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: R = 66% (42 mg). $^1$H NMR (500 MHz, Chloroform-\textit{d}) $\delta$ 7.67 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.45 (s, 1H), 7.41 – 7.32 (m, 4H), 7.21 (dd, $J$ = 8.3, 1.0 Hz, 1H), 6.94 (d, $J$ = 15.6 Hz, 1H), 3.15 (t, $J$ = 7.6 Hz, 2H), 3.02 (d, $J$ = 9.5 Hz, 5H). $^{13}$C NMR (126 MHz, Chloroform-\textit{d}) $\delta$ 170.2, 152.4, 144.0, 141.0, 134.3, 133.5, 132.7, 131.6, 129.7, 128.6, 127.2, 126.7, 126.6, 123.3, 115.3, 107.2, 43.5, 35.5, 30.5. HRMS (ESI-QTOF) m/z: [M+Na]$^+$: calcd. for $C_{19}H_{17}NO_3SNa$: 378.0770, found: 378.0773.

(E)-2-Cyanophenyl 3-(3-(2-(phenylsulfonyl)vinyl)phenyl)propanoate (Scheme 6, Entry 5e): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (65:35 v/v) mixture as eluent. Isolated yield: R = 76% (77 mg). $^1$H NMR (500 MHz, Chloroform-\textit{d}) $\delta$ 7.99 – 7.92 (m, 2H), 7.70 – 7.52 (m, 6H), 7.43 – 7.31 (m, 5H), 7.22 – 7.16 (m, 1H), 6.89 (d, $J$ = 15.4 Hz, 1H), 3.11 (t, $J$ = 7.6 Hz, 2H), 2.98 (t, $J$ = 7.6 Hz, 2H). $^{13}$C NMR (126 MHz, Chloroform-\textit{d}) $\delta$ 170.2, 152.3, 142.5, 142.4, 140.9, 140.8, 134.3, 133.4, 133.5, 132.9, 131.4, 129.6, 129.5, 128.6, 128.4, 127.8, 127.6, 127.2, 126.6, 123.3, 115.3, 107.1, 35.5, 30.5. HRMS (ESI-QTOF) m/z: [M+Na]$^+$: calcd. for $C_{23}H_{18}NO_4SNa$: 440.0927, found: 440.0919. IR (thin film) 661, 689, 766, 1004, 1050, 1079, 1261, 1313, 1495, 1898, 2012, 2281, 2381, 2380, 2433, 2521 cm$^{-1}$.
(E)-2-Cyanophenyl 3-(3-(2-(phenylsulfonyl)vinyl)phenyl)propanoate (Scheme 6, Entry 5f): oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (65:35 v/v) mixture as eluent. Isolated yield: R = 77% (56 mg). 
1H NMR (500 MHz, Chloroform-δ) δ 7.68 (dd, J = 7.8, 1.7 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.45 – 7.32 (m, 5H), 7.21 (dd, J = 8.3, 1.0 Hz, 1H), 6.80 (d, J = 15.5 Hz, 1H), 6.67 (dd, J = 16.5, 9.8 Hz, 1H), 6.46 (d, J = 16.5 Hz, 1H), 6.10 (d, J = 9.8 Hz, 1H), 3.13 (t, J = 7.6 Hz, 2H), 3.01 (t, J = 7.6 Hz, 2H). 13C NMR (126 MHz, Chloroform-δ) δ 170.2, 152.3, 144.5, 141.0, 137.8, 134.3, 133.5, 132.9, 131.7, 129.7, 129.0, 128.7, 127.2, 126.6, 125.8, 123.3, 115.3, 107.2, 35.5, 30.7, 16.6. HRMS (ESI-QTOF) m/z: [M+Na]^+ : calcd. for C_{24}H_{23}NO_3SNa: 390.0770, found: 390.0774. IR (thin film) 653, 764, 847, 976, 1129, 1216, 1309, 1450, 1488, 1605, 1770, 2233 cm⁻¹.

(R)-2-Cyanophenyl 3-(6’-acetyl-1’,2’,3’,4’-tetrahydro-[1,1’-biphenyl]-3-yl)propanoate (Scheme 6, Entry 5h): oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (85:15 v/v) mixture as eluent. Isolated yield: R = 57% (56 mg). 
1H NMR (500 MHz, Chloroform-δ) δ 8.06 (dd, J = 8.4, 1.1 Hz, 1H), 7.93 – 7.88 (m, 1H), 7.87 (d, J = 1.6 Hz, 1H), 7.83 (d, J = 16.0 Hz, 1H), 7.70 (dd, J = 7.8, 1.6 Hz, 1H), 7.66 – 7.58 (m, 3H), 7.54 (dd, J = 8.0, 6.8, 1.2 Hz, 1H), 7.38 – 7.33 (m, 1H), 7.22 (dd, J = 8.4, 1.1 Hz, 1H), 6.57 (d, J = 15.9 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 3.60 (m, 2H), 3.22 – 2.99 (m, 2H), 1.36 (t, J = 7.1 Hz, 3H). 13C NMR (126 MHz, Chloroform-δ) δ 170.5, 167.2, 152.5, 146.6, 136.9, 134.3, 134.1, 133.5, 132.6, 131.8, 129.9, 129.6, 127.9, 126.8, 126.6, 124.0, 123.6, 123.4, 118.8, 115.3, 107.3, 60.7, 35.1, 28.2, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]^+ : calcd. for C_{25}H_{25}NO_4Na: 422.1362, found: 422.1366.
(E)-ethyl 3-(4-(3-(2-cyanophenoxy)-3-oxopropyl)naphthalen-2-yl)acrylate (Scheme 6, Entry 5j): brown solid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (88:12 v/v) mixture as eluent. Isolated yield: R = 52% (39 mg) \(^1\)H NMR (500 MHz, Chloroform-\(d\)) \(\delta\) 7.96 (d, \(J = 16.2\) Hz, 1H), 7.67 (dd, \(J = 7.7, 1.7\) Hz, 1H), 7.61 (ddd, \(J = 8.3, 7.6, 1.7\) Hz, 1H), 7.40 (d, \(J = 2.4\) Hz, 1H), 7.33 (td, \(J = 7.7, 1.1\) Hz, 1H), 7.26 (dd, \(J = 8.4, 2.3\) Hz, 1H), 7.20 (dd, \(J = 8.3, 1.1\) Hz, 1H), 6.87 (d, \(J = 8.5\) Hz, 1H), 6.54 (d, \(J = 16.1\) Hz, 1H), 4.26 (q, \(J = 7.1\) Hz, 2H), 3.87 (s, 3H), 3.07 (m, 2H), 2.96 (m, 2H), 1.33 (t, \(J = 7.1\) Hz, 3H).

\(^{13}\)C NMR (126 MHz, Chloroform-\(d\)) \(\delta\) 170.4, 167.7, 157.3, 152.4, 140.1, 134.3, 133.5, 132.0, 131.5, 129.0, 126.5, 123.7, 119.2, 115.3, 111.6, 107.2, 60.6, 55.8, 36.0, 30.0, 14.6. HRMS (ESI-QTOF) m/z: [M+Na]\(^+\): calcd. for C\(_{25}\)H\(_{21}\)NO\(_4\)Na: 422.1362, found: 422.1366.

(E)-Ethyl 3-(3-(3-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-3-oxopropyl)-4-(trifluoromethyl)phenyl)acrylate (Scheme 6, Entry 5k): Oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (97:3 v/v) mixture as eluent. Isolated yield: R = 44% (41 mg).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.69 – 7.61 (m, 2H), 7.54 – 7.44 (m, 2H), 6.50 (d, \(J = 16.0\) Hz, 1H), 5.78 (p, \(J = 6.1\) Hz, 1H), 4.28 (q, \(J = 7.1\) Hz, 2H), 3.21 (t, \(J = 7.8\) Hz, 2H), 2.86 (t, \(J = 7.8\) Hz, 2H), 1.35 (t, \(J = 7.1\) Hz, 3H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 169.3, 166.5, 142.4, 138.4, 130.4, 127.3, 126.4, 121.4, 67.5, 67.2, 66.8, 66.5, 66.2, 61.0, 34.6, 14.4.

((E)-Ethyl 3-(3-(3-(2-cyanophenoxy)-4-(trifluoromethyl)phenyl)acrylate (Scheme 6, Entry 5k): Oily liqiud. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (88:12 v/v) mixture as eluent. Isolated yield: R = 24% (20 mg).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.74 – 7.61 (m, 4H), 7.58 (s, 1H), 7.52 – 7.48 (m, 1H), 7.36 (td, \(J = 7.7, 1.1\) Hz, 1H), 7.31 – 7.24 (m, 1H), 6.52 (d, \(J = 16.1\) Hz, 1H), 4.28 (q, \(J = 7.1\) Hz, 2H), 3.31 (t, \(J = 7.7\) Hz, 2H), 3.01 (t, \(J = 7.7\) Hz, 2H), 1.35 (t, \(J = 7.1\) Hz, 3H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 170.0, 166.6, 152.3, 142.6, 138.3, 134.3, 133.5, 130.8, 127.2, 127.1, 126.6, 126.2, 123.3, 121.3, 115.2, 107.3, 61.0, 35.6, 27.7, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]\(^+\): calcd. for C\(_{22}\)H\(_{18}\)F\(_3\)NO\(_4\)Na: 440.1087, found: 440.1087.

General Procedure D for sequential di olefination through remote meta C-H activation of 3-phenylpropanoic acid:

In a clean, oven–dried screw cap reaction tube, with previously placed magnetic stir–bar substrate (0.1 mmol); Pd(OAc)\(_2\) (0.1 equiv, 0.01 mmol, 2.2 mg); N-Acetyl-glycine (0.2 equiv, 0.02 mmol, 2.2 mg), Ag\(_2\)CO\(_3\) (3 equiv, 0.3 mmol, 83 mg) were taken. Then alkene (2 equiv, 0.2 mmol), hexafluoroisopropanol (0.6 mL) were added to this mixture by syringe. The tube was tightly closed by screw cap and placed in a preheated oil bath at 70 °C. The reaction mixture was vigorously stirred for 48h. The reaction mixture was cooled to room temperature and filtered through celite. Reaction tube was washed with 10 mL of ethyl acetate. Total organic portion was concentrated and purified via column chromatography through silica gel using pet ether- ethyl acetate as eluent.

(E)-Ethyl 3-(3-(3-(2-cyanophenoxy)-3-oxopropyl)-5-((E)-3-oxobut-1-en-1-yl)phenyl)acrylate (Scheme 7, Entry 6a): oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (70:30 v/v) mixture as eluent. Isolated yield: R = 71% (30 mg) \(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.71 – 7.65 (m, 2H), 7.62 (ddd, \(J = 8.3, 7.6, 1.7\) Hz, 1H), 7.56 (d, \(J = 1.6\) Hz, 1H), 7.54 – 7.45 (m,
3H), 7.35 (td, J = 7.7, 1.1 Hz, 1H), 7.21 (dd, J = 8.4, 1.0 Hz, 1H), 6.76 (d, J = 16.2 Hz, 1H), 6.48 (d, J = 16.1 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.16 (t, J = 7.5 Hz, 2H), 3.03 (t, J = 7.3 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H). 13C {H NMR (126 MHz, CDCl3) δ 198.4, 170.1, 166.9, 152.3, 143.6, 142.5, 141.5, 135.8, 134.3, 133.5, 130.0, 129.9, 128.1, 126.6, 126.3, 123.3, 119.8, 115.3, 107.2, 100.1, 60.9, 35.4, 30.5, 28.0, 14.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcld. for C25H23NO5Na: 440.1468, found 440.1470. IR (thin film) 765, 981, 1114, 1182, 1450, 1493, 1717, 1771, 2281, 2371, cm⁻¹.

Dimethyl 2-(3-(3-(2-cyanophenoxy)-3-oxopropyl)-5-((E)-2-(phenylsulfonyl)vinyl)phenyl)fumarate (Scheme 7, Entry 6b): oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (55:45 v/v) mixture as eluent. Isolated yield: R = 51% (28 mg) 1H NMR (400 MHz, Chloroform-d) δ 8.01 – 7.92 (m, 2H), 7.71 – 7.60 (m, 4H), 7.60 – 7.53 (m, 2H), 7.47 (s, 1H), 7.43 (m, 2H), 7.34 (td, J = 7.7, 1.1 Hz, 1H), 7.20 (dd, J = 8.3, 1.0 Hz, 1H), 6.92 (d, J = 15.4 Hz, 1H), 6.32 (s, 1H), 3.94 (s, 3H), 3.79 (s, 3H), 3.13 (t, J = 7.5 Hz, 2H), 2.99 (t, J = 7.5, 2H). 13C NMR (126 MHz, CDCl3) δ 170.0, 168.0, 165.3, 152.2, 147.7, 141.20, 141.2, 140.4, 134.9, 134.4, 133.9, 133.8, 133.5, 130.4, 129.6, 129.4, 129.2, 128.0, 126.7, 125.5, 123.3, 119.0, 115.3, 107.2, 53.2, 52.4, 35.3, 30.5. HRMS (ESI-QTOF) m/z: [M+Na]+: calcld. for C30H25NO8SNa: 582.1193, found: 582.1196.

(2E,2’E)-Dimethyl 3,3’-(5-(3-(2-cyanophenoxy)-3-oxopropyl)-1,3-phenylene)bis(but-2-enoate) (Scheme 7, Entry 6c): oily liquid. Isolated through 100-200 mesh silica gel using pet ether: ethyl acetate (50:50 v/v) mixture as eluent. Isolated yield: R = 55% (25 mg) 1H NMR (500 MHz, CDCl3) δ 7.68 (d, J = 7.1 Hz, 1H), 7.64 – 7.59 (m, 1H), 7.40 (s, 1H), 7.36 (s, 2H), 7.34 (d, J = 7.7 Hz, 1H), 7.21 (d, J = 8.3 Hz, 1H), 6.14 (s, 2H), 3.78 (s, 6H), 3.15 (t, J = 7.7 Hz 2H), 3.02 (t, J = 7.7 Hz, 2H), 2.58 (s, 6H). 13C NMR (126 MHz, CDCl3) δ 170.2, 167.2, 165.3, 155.5, 152.4, 143.3, 140.6, 134.3, 133.5, 130.4, 129.6, 129.4, 129.2, 128.0, 126.7, 125.5, 123.3, 107.2, 51.4, 35.8, 30.9, 18.4. HRMS (ESI-QTOF) m/z: [M+Na]+: calcld. for C26H25NO6: 470.1574, found: 470.1570.

General Procedure for sulphonate ester synthesis:
The synthesis was done following the literature procedure with few modifications.

Step 1: In an oven dried 250 mL round bottomed flask the desired benzyl chloride/bromide was added along with thiourea (1.1 eq.). Absolute ethanol was added to it as solvent and refluxed for 12 h. Upon completion the round bottomed flask was cooled and evaporated under reduced pressure yielding white solid compound, which was directly used in the next step.

Step 2: N-chlorosuccinimide (4 eq.) was taken in clean round bottomed flask charged with stir-bar. 2(N) HCl was added to it along with MeCN. The reaction mixture was stirred on an ice cooled water bath. The solid salt obtained from the first step was added slowly to this reaction mixture and stirred vigorously. The addition led to an exothermic reaction. However the temperature was maintained below 25 °C. Upon forming a clear solution the mixture was warmed to the room temperature and stirred for 1.5 h. The reaction was evaporated under reduced pressure to remove the acetonitrile. The remaining solution was diluted with water and extracted with ethyl acetate. The organic portion was dried over
anhydrous Na$_2$SO$_4$. The solution was concentrated under reduced pressure and purified through column chromatography.

**Step 3:** In an oven dried round bottomed flask 2-hydroxybenzonitrile was dissolved in dry DCM. Et$_3$N (3 eq.) was added to the reaction mixture slowly until the clear solution was observed. Benzylsulphonyl chloride was added to the reaction mixture slowly. Upon completion of addition the reaction was stirred at room temperature overnight. Once completed the reaction was quenched with distilled water and extracted with ethyl acetate. The organic portion was dried over anhydrous Na$_2$SO$_4$. The solution was concentrated under reduced pressure and purified through column chromatography.

**2-Cyanophenyl 2-phenylethanesulfonate:** $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.72 (dd, $J = 7.8, 1.4$ Hz, 1H), 7.68 (ddd, $J = 8.4, 7.6, 1.7$ Hz, 1H), 7.56 (dd, $J = 8.4, 0.6$ Hz, 1H), 7.43 (td, $J = 7.7, 1.0$ Hz, 1H), 7.37 – 7.32 (m, 2H), 7.29 (d, $J = 7.6$ Hz, 3H), 3.75 – 3.67 (m, 2H), 3.45 – 3.34 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 150.0, 136.8, 134.7, 134.0, 129.2, 128.7, 127.6, 127.5, 123.9, 115.1, 107.5, 53.8, 29.9.

HRMS (ESI-QTOF) m/z: [M+Na]$^+$: calcd. for C$_{15}$H$_{13}$NNaO$_3$S: 310.0508, found: 310.0501.

**2-Cyanophenyl 2-(4-fluorophenyl)ethanesulfonate:** $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.72 (d, $J = 7.7$ Hz, 1H), 7.68 (td, $J = 8.1, 0.9$ Hz, 1H), 7.55 (d, $J = 8.4$ Hz, 1H), 7.43 (t, $J = 7.7$ Hz, 1H), 7.26 (dd, $J = 8.4, 5.3$ Hz, 2H), 7.03 (t, $J = 8.6$ Hz, 2H), 3.83 – 3.56 (m, 2H), 3.47 – 3.28 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 163.2, 161.2, 149.9, 134.8, 134.0, 132.5, 130.3, 130.3, 127.7, 127.6, 123.9, 115.2, 107.4, 53.8, 29.1.

**2-Cyanophenyl 2-(3-bromophenyl)ethanesulfonate:** $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.72 (dd, $J = 7.7, 1.6$ Hz, 1H), 7.68 (ddd, $J = 8.4, 7.7, 1.7$ Hz, 1H), 7.58 – 7.53 (m, 1H), 7.46 – 7.39 (m, 3H), 7.24 – 7.20 (m, 2H), 3.73 – 3.67 (m, 2H), 3.40 – 3.34 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 149.9, 139.1, 134.7, 134.0, 131.8, 130.7, 127.7, 127.4, 123.9, 123.1, 115.1, 107.4, 53.5, 29.5.

**2-Cyanophenyl 2-(2,3-dichlorophenyl)ethanesulfonate** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.72 (dd, $J = 7.8, 1.6$ Hz, 1H), 7.68 (ddd, $J = 8.4, 7.6, 1.7$ Hz, 1H), 7.56 (dd, $J = 8.4, 0.7$ Hz, 1H), 7.46 – 7.39 (m, 3H), 7.24 – 7.20 (m, 2H), 7.32 (d, $J = 8.2$ Hz, 1H), 7.23 (dd, $J = 8.2, 2.1$ Hz, 1H), 3.75 – 3.68 (m, 2H), 3.51 – 3.44 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 149.8, 134.8, 134.7, 134.3, 134.0, 133.1, 132.0, 129.9, 127.9, 127.7, 123.7, 115.1, 107.4, 51.5, 27.8.

**2-Cyanophenyl 2-(2',4'-dichloro-[1,1'-biphenyl]-3-yl)ethanesulfonate:** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.73 (d, $J = 1.6$ Hz, 1H), 7.71 (d, $J = 1.6$ Hz, 1H), 7.70 – 7.64 (m, 2H), 7.58 – 7.53 (m, 1H), 7.49 (d, $J = 1.9$ Hz, 1H), 7.45 – 7.38 (m, 3H), 7.34 (m, 1H), 7.32 – 7.27 (m, 1H), 3.82 – 3.69 (m, 2H), 3.48 – 3.41 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 149.9, 139.1, 138.6, 136.8, 1347, 134.0, 134.0, 133.3, 132.2, 129.9, 129.6, 129.0, 128.5, 128.2, 127.6, 127.4, 123.8, 115.1, 107.4, 53.6, 29.8.

**General Procedure for hydrocinamic ester synthesis:**

**Form corresponding acid chloride:** In an oven dried round bottom flask charged with a magnetic stir bar, 2-cyanophenol (2 mmol) was taken. Then dry THF (3 mL) was added to it. The reaction solution was put in an ice bath. NaH (2 equiv. 4 mmol) was added to the solution in two portion. When the gas evolution is stopped then acid chloride (1.2 equiv., 2.4 mmol) was dropwise added to the reaction
solution with constant stirring at 0°C temperature. The reaction mixture was stirred at room temperature for overnight. After that, 1 mL water was poured to the reaction mixture. 15 mL ethyl acetate was added and the organic portion was separated by separating funnel. Total organic portion was dried over anhydrous Na₂SO₄ and concentrated in rota vap. The pure ester was isolated trough column chromatography.

2-Cyanophenyl 3-phenylpropanoate: ¹H NMR (400 MHz, CDCl₃) δ 7.68 (dd, J = 7.8, 1.5 Hz, 1H), 7.61 (ddd, J = 8.3, 7.7, 1.7 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.30 – 7.26 (m, 2H), 7.23 (dt, J = 3.0, 1.8 Hz, 1H), 7.19 (dd, J = 8.3, 0.6 Hz, 1H), 3.16 – 3.09 (m, 2H), 3.03 – 2.96 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 170.5, 152.4, 139.9, 134.2, 133.4, 128.8, 128.5, 126.7, 126.5, 123.4, 115.3, 107.2, 35.8, 30.9. HRMS (ESI-QTOF) m/z: [M+Na]⁺: calcd. for C₁₆H₁₃NNaO₂: 274.0838, found: 274.0831.

2-Cyanophenyl 3-(2-(trifluoromethyl)phenyl)propanoate ¹H NMR (500 MHz, CDCl₃) δ 7.74 – 7.62 (m, 3H), 7.55 (t, J = 7.5 Hz, 1H), 7.47 (d, J = 7.5 Hz, 1H), 7.38 (td, J = 7.6, 3.7 Hz, 2H), 7.30 (s, 1H), 3.33 (t, J = 7.9 Hz, 2H), 3.12 – 2.84 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 170.2, 152.4, 138.6, 134.3, 133.5, 132.3, 131.2, 128.7, 127.0, 126.6, 126.5, 126.4, 123.6, 123.4, 115.3, 107.3, 35.7, 27.7. HRMS (ESI-QTOF) m/z: [M+Na]⁺: calcd. for C₁₇H₁₂F₃NaO₂: 342.0712, found: 342.0720.

2-Cyanophenyl 3-(4-methoxyphenyl)propanoate ¹H NMR (400 MHz, CDCl₃) δ 7.67 (dd, J = 7.7, 1.6 Hz, 1H), 7.61 (ddd, J = 8.3, 7.7, 1.7 Hz, 1H), 7.33 (td, J = 7.7, 1.0 Hz, 1H), 7.20 (ddd, J = 9.5, 3.9, 1.8 Hz, 3H), 6.90 – 6.83 (m, 2H), 3.80 (s, 3H), 3.12 – 3.03 (m, 2H), 2.99 – 2.92 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 170.6, 158.5, 152.5, 134.2, 133.5, 132.0, 129.5, 126.4, 123.4, 115.3, 114.2, 107.3, 55.5, 36.2, 30.1.

2-Cyanophenyl 3-(naphthalen-1-yl)propanoate ¹H NMR (400 MHz, CDCl₃) δ 8.13 – 8.05 (m, 1H), 7.89 (dd, J = 8.1, 1.4 Hz, 1H), 7.78 (dd, J = 5.7, 3.8 Hz, 1H), 7.69 (dd, J = 7.7, 1.5 Hz, 1H), 7.67 – 7.59 (m, 1H), 7.58 – 7.55 (m, 1H), 7.51 (ddd, J = 8.0, 6.8, 1.3 Hz, 1H), 7.44 (q, J = 2.6, 2.0 Hz, 2H), 7.35 (tt, J = 7.7, 1.1 Hz, 1H), 7.22 (dd, J = 8.3, 1.0 Hz, 1H), 3.66 – 3.54 (m, 2H), 3.13 (dd, J = 8.7, 7.2 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 170.7, 152.5, 137.5, 135.9, 134.3, 134.1, 133.5, 131.7, 129.2, 127.7, 126.5, 126.3, 125.9, 125.8, 123.5, 123.4, 107.4, 35.2, 28.1. HRMS (ESI-QTOF) m/z: [M+Na]⁺: calcd. for C₂₀H₁₅NNaO₂: 324.0995, found: 324.0996.

De-protection of acid moieties and recovery of the directing template:

(E)-2-(3-(2-(phenylsulfonyl)vinyl)phenyl)ethanesulfonic acid: In a clean, oven–dried reaction tube, with previously placed magnetic stir–bar, (E)-2-cyanophenyl 2-(3-(2-(phenylsulfonyl)vinyl)phenyl)ethanesulfonate (0.2 mmol, 90 mg) was taken. Then the 10% KOH in MeOH was added to dissolve it. The reaction mixture was stirred at room temperature till full conversion of starting material. After that, methanol was evaporated to dryness. Then 5mL ethyl acetate was added to the reaction mixture and the reaction mixture was acidified with 2 (N) HCl solution. White solid (E)-2-(3-(2-(phenylsulfonyl)vinyl)phenyl)ethanesulfonic acid was appeared as insoluble part in both the layer. (E)-2-(3-(2-(phenylsulfonyl)vinyl)phenyl)ethanesulfonic acid was isolated through filtration of the total mixture. Yield 97%. And the organic portion was dried and concentrated to get pure 2-cyano phenol. ¹H NMR (400 MHz, DMSO-d₆) δ 7.96 – 7.89 (m, 2H), 7.76 – 7.70 (m, 1H), 7.69 – 7.60 (m, 5H), 7.53 (dt, J = 7.2, 1.8 Hz, 1H), 7.35 – 7.27 (m, 2H), 3.00 –
2.80 (m, 2H), 2.75 – 2.60 (m, 2H), 2.55 – 2.41 (m, 1H). \(^{13}\)C NMR (126 MHz, DMSO) \(\delta\) 142.1, 142.0, 140.8, 133.5, 132.4, 131.2, 129.6, 129.0, 128.4, 127.9, 127.1, 126.9, 52.6, 31.3.

**(E)-3-(3-(2-Carboxyethyl)phenyl)acrylic acid:** In a clean, oven-dried reaction tube, with previously placed magnetic stir–bar (E)-ethyl 3-(3-(2-cyanophenoxy)-3-oxopropyl)phenyl)acrylate (0.2 mmol, 70 mg) and LiOH.H2O (1.2 mmol) were taken. Then 3 mL MeOH, 2 mL THF, 1 mL H\(_2\)O were added to this. The reaction mixture was stirred at room temperature until the reaction was completed. Then the organic solvent was removed in rotavap. Then the remaining portion was washed with ethyl acetate. After that, 2 M HCl solution was added to the aqueous solution to reach the pH 1. Then ethyl acetate was poured to it organic portion was extracted from the aqueous part three times. Total Organic part was with brine solution, dried over Na2SO4, concentrated in rotavap and performed column chromatography to get the desired product.

\[\text{In a clean, oven-dried reaction tube, with previously placed magnetic stir–bar (E)-ethyl 3-(3-(2-cyanophenoxy)-3-oxopropyl)phenyl)acrylate (0.2 mmol, 70 mg) and LiOH.H2O (1.2 mmol) were taken. Then 3 mL MeOH, 2 mL THF, 1 mL H}\_2\text{O were added to this. The reaction mixture was stirred at room temperature until the reaction was completed. Then the organic solvent was removed in rotavap. Then the remaining portion was washed with ethyl acetate. After that, 2 M HCl solution was added to the aqueous solution to reach the pH 1. Then ethyl acetate was poured to it organic portion was extracted from the aqueous part three times. Total Organic part was with brine solution, dried over Na2SO4, concentrated in rotavap and performed column chromatography to get the desired product.}\]

\[\text{Total NMR (500 MHz, DMSO) } \delta \text{ 12.27 (s, 1H), 7.59 – 7.53 (m, 1H), 7.50 (d, } J = 7.6 \text{ Hz, 1H), 7.32 (t, } J = 7.6 \text{ Hz, 1H), 2.85 (t, } J = 7.6 \text{ Hz, 1H), 2.58 (t, } J = 7.7 \text{ Hz, 1H). } \]

\[\text{Preparation of methyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)propanoate}\]

In a clean, oven-dried round bottom flask, with previously placed magnetic stir–bar (E)-methyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)acrylate (0.5 mmol, 185 mg) and Pd/charcoal (10 mol%, 0.05 mmol, 106 mg (5 wt % Pd on charcoal)) were taken. Then the round bottom flask was evacuated and filled with hydrogen gas. Then methanol (30 mL) was added to this mixture by syringe. Then the reaction mixture was vigorously stirred for 3h with continuous flow of hydrogen. After that reaction mixture was filtered through celite. Total organic portion was concentrated and purified via column chromatography through silica gel using pet ether-ethyl acetate as eluent. Isolated yield 97%.

\[\text{Preparation of methyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)propanoate}\]

\[\text{Preparation of methyl 2,3-dibromo-3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)propanoate}\]

In a clean, oven-dried reaction tube, with previously placed magnetic stir–bar (E)-methyl 3-(3-(2-((2-cyanophenoxy)sulfonyl)ethyl)phenyl)acrylate (0.3 mmol, 114 mg) and NBS (1.2 equiv. 0.36 mmol, 63 mg) and catalytic amount AIBN were taken. Then CCl\(_4\) (5 mL) was added to this mixture by syringe.
Then the reaction mixture was vigorously stirred for 24h at 75°C. After that reaction mixture was cooled to room temperature and washed with water (10 mL). The total organic portion was dried over anhyd. \( \text{Na}_2\text{SO}_4 \) and concentrated in rota vap. The desired product was purified via column chromatography through silica gel using pet ether-ethyl acetate as eluent (70:30 v/v). Isolated yield 90%. \(^{1}H\) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.77 – 7.73 (m, 1H), 7.72 – 7.67 (m, 1H), 7.60 – 7.55 (m, 1H), 7.46 (tdd, \( J = 7.7, 3.0, 1.1 \) Hz, 1H), 7.42 – 7.36 (m, 2H), 7.35 – 7.30 (m, 2H), 5.37 – 5.33 (m, 1H), 4.89 – 4.85 (m, 1H), 3.92 (s, 3H), 3.78 – 3.72 (m, 2H), 3.48 – 3.41 (m, 2H). \(^{13}C\) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 168.4, 149.9, 138.6, 137.7, 134.7, 134.0, 129.7, 129.7, 128.4, 127.6, 127.2, 123.9, 115.1, 107.4, 53.6, 53.5, 50.30, 46.7, 29.7. HRMS (ESI-QTOF) m/z: [M+Na]\(^+\): calcd. for C\(_{19}\)H\(_{17}\)Br\(_2\)NO\(_5\)SNa: 551.9086, found: 551.9073.

Mass spectrometric studies of the reaction mixture

In an oven dried reaction tube, charged with magnetic stir-bar, Pd(OAc)\(_2\) (1 equiv.), N-For-Gly-OH (2 equiv.), substrate (1 equiv.) and HFIP (1 mL) were added. Then the reaction tube was capped and stirred at room temperature for 15 mins and then placed to a preheated oil-bath at 65 °C. After 5 h of the reaction the reaction mixture was analysed in mass spectrometry.

**Fig.2.** Mass spectrometric studies of the reaction mixture

**Determination of order**
The order of the reaction with respect to the substrate and olefin was determined using Initial slope method.

**Order determination with respect to substrate:**

In an oven dried reaction tube, charged with magnetic stir-bar, Pd(OAc)$_2$, N-For-Gly-OH, substrate were added. Olefin (ethyl acrylate) was added to the reaction mixture followed by the HFIP (1 mL). The reaction tube was capped and then placed to a preheated oil-bath at 70 °C. The reaction was stirred vigorously for a definite amount of time and then taken out to cool it to the room temperature. The reaction mixture was diluted with ethyl acetate and equivalent amount of 1,3,5-trimethoxybenzene (external standard) was added to the reaction mixture. 200 μL aliquot was taken out from the mixture, evaporated and dissolved in CDCl$_3$ for NMR study.

<table>
<thead>
<tr>
<th>A</th>
<th>Substrate</th>
<th>olefin</th>
<th>Pd(OAc)$_2$</th>
<th>Ac-For-OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red line</td>
<td>0.4 mmol</td>
<td>0.4 mmol</td>
<td>0.02 mmol</td>
<td>0.04 mmol</td>
</tr>
<tr>
<td>(run 1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blue line</td>
<td>0.2 mmol</td>
<td>0.4 mmol</td>
<td>0.02 mmol</td>
<td>0.04 mmol</td>
</tr>
<tr>
<td>(run 2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Fig.3.** Decay of substrate 1a with respect to time. Reaction was done with 0.2 mmol (red line) and 0.2 mmol (black line) of substrate and 0.4 mmol of ethyl acrylate.

**0.4 mmol substrate (run1)**

X (concentration axis) = 0.0178937072, Y (time axis) = 0.396134535

X = 0.031210534, Y = 0.395024906

At t=0

Dx= -0.0133

Dy= 0.0011

$\{Dx/dy\}_{run1} = -0.0833$

**0.2 mmol substrate (run 2)**
X (concentration axis) = 0.0137080927, Y (time axis) = 0.197826772

X = 0.0703978785, Y = 0.195998307

At t=0

Dx= -0.0566

Dy= 0.0018

\(\{Dx/dy\}_{run2} = -0.0322\)

We know

Rate \(Dx/dy = k[substrate]^x[olefin]^y\)

\(\{Dx/dy\}_{run1}/\{Dx/dy\}_{run2} = \{k[substrate]_{run1}^x[olefin]_{run1}^y\}/\{k[substrate]_{run2}^x[olefin]_{run2}^y\}\)

At t=0; [olefin]_{run1} = [olefin]_{run2}

2.58 = [substrate]_{run1}^y/[ substrate]_{run2}^y

At t=0; [substrate]_{run1}^y/[ substrate]_{run2}^y = 2

So, 2.58 = 2^y

0.41 = y log 2

y = 0.41/log2

\[=0.41/0.30 =1.3 = \sim 1\]

**Order determination with respect to olefin:**

In an oven dried reaction tube, charged with magnetic stir-bar, Pd(OAc)\_2, N-For-Gly-OH, substrate were added. Olefin (phenyl vinyl sulfone) was added to the reaction mixture followed by the HFIP (1 mL). The reaction tube was capped and then placed to a preheated oil-bath at 70 °C. The reaction was stirred vigorously for a definite amount of time and then taken out to cool it to the room temperature. The reaction mixture was diluted with ethyl acetate and equivalent amount of 1,3,5-trimethoxybenzene (external standard) was added to the reaction mixture. 200 µL aliquot was taken out from the mixture, evaporated and dissolved in CDCl\_3 for NMR study.

<table>
<thead>
<tr>
<th>B</th>
<th>Substrate</th>
<th>olefin</th>
<th>Pd(OAc)_2</th>
<th>Ac-For-OH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black line</td>
<td>0.2 mmol</td>
<td>0.4 mmol</td>
<td>0.02 mmol</td>
<td>0.04 mmol</td>
</tr>
<tr>
<td>(run 3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red line</td>
<td>0.2 mmol</td>
<td>0.8 mmol</td>
<td>0.02 mmol</td>
<td>0.04 mmol</td>
</tr>
<tr>
<td>(run 2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fig. 4. Overlap of the product growth plot using 2 eq. (black line) and 4 eq. (red line) of olefin with respect to substrate

The overlapping of the rate of the reaction for run 3 and run 4 implies that the rate of the reaction is not dependent on olefin concentration. So $x=0$

**NMR Spectra**
Entry 2a; Scheme 3

1H NMR (500 MHz, Chloroform-d)

- J (m) 7.44
- G (m) 7.67
- F (d) 7.77
- E (s) 8.0
- D (s) 7.27
- C (m) 3.72
- B (s) 3.41
- A (d) 6.45
- H (d) 7.56
Entry 2b; Scheme 3
Entry 2c; Scheme 3
Entry 2d; Scheme 3
Entry 2e; Scheme 3
Entry 2f; Scheme 3
Entry 2g; Scheme 3
Entry 2h; Scheme 3
Entry 2i; Scheme 3
Entry 2j; Scheme 3
Entry 2k; Scheme 3
Entry 2l; Scheme 3
Entry 2m; Scheme 3
Entry 2n; Scheme 3
Entry 3a; Scheme 4
Entry 3b; Scheme 4
Entry 3b; Scheme 4
Entry 4a; Scheme 5
Entry 5a; Scheme 6
Entry 5b; Scheme 6

**1H NMR (400 MHz, Chloroform-d)**

**13C NMR (101 MHz, CDCl3)**
Entry 5c; Scheme 6
Entry 5d; Scheme 6

1H NMR (500 MHz, CDCl3)

13C NMR (126 MHz, CDCl3)
Entry 5e; Scheme 6

1H NMR (500 MHz, Chloroform-d)

13C NMR (126 MHz, CDCl3)
Entry 5f; Scheme 6

1H NMR (500 MHz, Chloroform-d)

13C NMR (126 MHz, CDCl3)

Entry 5g; Scheme 6
Entry 5j; Scheme 6
Entry 5k; Scheme 6
Entry 6a; Scheme 7
Entry 6c; Scheme 7

$^1$H NMR (300 MHz, CDCl$_3$)

$^1$C NMR (125 MHz, CDCl$_3$)
Starting materials:
$^1$H NMR (400 MHz, CDCl$_3$)

- H (m) 7.61
- D (dd) 7.53
- C (s) 7.61
- A (m) 7.50
- E (dd) 7.22
- G (s) 4.44
- I (m) 7.59

13C NMR (126 MHz, CDCl$_3$)

- 179.30
- 57.04
- 56.98
- 36.22
- 28.13
De-protection of acid moiety; Scheme 8