A novel substrate directed multicomponent reaction for the synthesis of tetrahydro-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidines and tetrahydro-pyrazolo[4,3-f]pyrimido[4,5-b]quinolines via selective multiple C-C bonds formation under metal-free reaction condition

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Crystal X-ray report of compound 5g [CCDC:1990292].

Figure S1. Crystal X-ray structure of compound 5g.

Table S1. Crystal data and structure refinement for 5g.

<table>
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<th>5g</th>
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<tr>
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<tr>
<td>Formula weight</td>
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<tr>
<td>Temperature</td>
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<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
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<tr>
<td>Crystal system</td>
<td>Triclinic</td>
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<td>Space group</td>
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<td></td>
<td>β = 97.256° (4).</td>
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<td></td>
<td>c = 12.8286(16) Å</td>
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<td>γ = 111.253° (3).</td>
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<tr>
<td>Density (calculated)</td>
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Crystal X-ray report of compound 7b [CCDC:1978229].

![Crystal structure of compound 7b](image)

Figure S2. Crystal X-ray structure of compound 7b.

**Table S2.** Crystal data and structure refinement for 7b.

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<th>Property</th>
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<td>Temperature</td>
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<td>Wavelength</td>
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<td>Crystal system</td>
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<td>Space group</td>
<td>P 21/c</td>
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\[ b = 15.1736 (7) \, \text{Å} \quad \beta = 101.750^\circ (2). \]
\[ c = 18.5825 (9) \, \text{Å} \quad \gamma = 90^\circ. \]

Volume  
2677.5(2)Å³

Density (calculated)  
1.326 g/Cm³

F(000)  
1104.0

Data completeness  
0.993

Crystal X-ray report of compound 7h [CCDC: 1968978].

Figure S3. Crystal X-ray structure of compound 7h.

Table S3. Crystal data and structure refinement for 7h.

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<th>7h</th>
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<td>Formula weight</td>
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Temperature 293 K
Wavelength 0.71073 Å
Crystal system Orthorhombic
Space group P 21 21 21
Unit cell dimensions
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\[b = 12.4871(16) \text{Å}, \quad \gamma = 90°.\]
\[c = 16.249(2) \text{Å}, \quad \alpha = 90°.\]
Volume 2492.0(5) Å³
Density (calculated) 1.401 g/Cm³
F(000) 1104.0
Data completeness 1.76/0.99


Spectroscopic and analytical characterization of 11-aryl-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-diones 5(a-k).

11-phenyl-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5a)

Light pink solid, %purity (HPLC) =88.1%, mp. 282-284°C; $^1$H-NMR (400 MHz, DMSO-d$_6$) (δ, ppm): 12.98 (s, 1H, NH), 10.54 (s, 1H, NH), 10.34 (s, 1H, NH), 8.88(s, 1H, ArH), 8.02(s, 1H, ArH), 7.30-7.39 (m, 3H, ArH), 7.13-7.19 (m, 3H, ArH), 7.05 (t, $J$= 7.2 Hz, 1H, ArH), 5.41 (s, 1H, CH); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) (δ, ppm): 162.77, 150.25, 147.13, 145.66, 137.23, 131.76, 128.45, 128.23, 127.92, 127.49, 125.92, 121.48, 117.07, 113.94, 109.43, 85.26, 64.88, 38.08, 15.13; MS(MM-ES+APCI) 329.9 [M+H]$^+$.  

11-(4-chlorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5b)

Off white solid, mp. 280-282°C; $^1$H-NMR (400 MHz, DMSO-d$_6$) (δ, ppm): 13.05 (s, 1H, NH), 10.67 (s, 1H, NH), 10.45 (s, 1H, NH), 7.52(s, 1H, ArH),7.45 (d, $J$= 9.2 Hz, 2H, ArH), 7.30-7.39 (m, 2H, ArH), 7.22 (d, $J$= 7.6 Hz, 2H, ArH), 7.07 (d, $J$= 9.2 Hz, 1H, ArH), 6.91 (s, 1H, CH), 4.91 (s, 1H, CH);$^{13}$C-NMR (100 MHz, DMSO-d$_6$) (δ, ppm):169.98, 165.22, 162.76, 153.25, 146.01, 139.90, 137.25, 137.23, 132.07, 131.24, 130.48, 130.27, 130.20, 129.35, 128.70, 128.66, 128.59, 128.22,
127.87, 127.79, 121.36, 117.13, 116.54, 113.68, 113.29, 109.70, 109.57, 84.89; MS(MM-ES+APCI) 365.8 [M+H]+.

11-(4-nitrophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5c)

Pale yellow solid, mp. 268-270°C; 13C-NMR (100 MHz, DMSO-d_6) (δ, ppm): 169.69, 167.73, 162.74, 154.26, 153.20, 150.12, 145.78, 145.72, 137.24, 131.63, 129.57, 128.80, 128.33, 123.92, 123.30, 121.36, 117.27, 112.31, 110.19, 110.12, 84.35; MS(MM-ES+APCI) 376.8 [M+H]+.

11-(4-methoxyphenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5d)

Off white solid, %purity (HPLC) =98.7%, mp. 278-280°C; 1H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 8.82 (s, 1H, ArH), 7.34(d, J= 8.8 Hz, 1H, ArH), 7.13 (d, J= 8.4 Hz, 2H, ArH), 6.72 (d, J= 8.8 Hz, 2H, ArH), 5.36 (s, 1H, CH), 3.63 (s, 1H, OCH_3); 13C-NMR (100 MHz, DMSO-d_6) (δ, ppm): 162.78, 157.41, 150.19, 145.41, 139.47, 137.24, 131.78, 128.41, 128.10, 121.46, 117.05, 114.26, 113.28, 109.30, 85.46, 54.86, 37.17; MS(MM-ES+APCI) 359.8 [M+H]+.

11-((p-tolyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5e)

Off white solid, %purity (HPLC) =98.5%, mp. >300°C; 1H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 12.97 (s, 1H, NH), 10.54 (s, 1H, NH), 10.29 (s, 1H, NH), 8.82 (s, 1H, ArH), 7.34(d, J= 8.8 Hz, 1H, ArH), 7.19 (d, J= 8.4 Hz, 2H, ArH), 7.13 (d, J= 8.8 Hz, 1H, ArH), 6.96 (d, J= 8.0 Hz, 2H, ArH), 5.36 (s, 1H, CH), 2.15 (s, 1H, CH_3); 13C-NMR (100 MHz, DMSO-d_6) (δ, ppm): 162.75, 150.15, 145.45, 144.25, 134.87, 131.79, 128.46, 128.12, 127.37, 117.07, 114.11, 110.66, 109.37, 109.32, 108.0, 90.66, 85.34, 84.77, 20.49; MS(MM-ES+APCI) 345.0 [M+H]^+.

11-(4-fluorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5f)

Off white solid, %purity (HPLC) =99.5%, mp. >300°C; 1H-NMR (400 MHz, DMSO-d_6) (δ, ppm): 13.0 (s, 1H, NH), 10.57 (s, 1H, NH), 10.33 (s, 1H, NH), 8.88 (s, 1H, ArH), 8.01 (s, 1H, ArH), 7.33-7.38(m, 3H, ArH), 7.15 (d, J= 8.8 Hz, 1H, ArH), 6.99 (t, J= 8.8 Hz, 2H, ArH), 5.45 (s, 1H, CH); 13C-NMR (100 MHz, DMSO-d_6) (δ, ppm): 162.77, 161.69, 159.29, 150.16, 145.53, 143.33, 143.29, 137.25,
11-(4-bromophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5g)

Off white solid, mp. 290-292°C; $^1$H-NMR (400 MHz, DMSO-d$_6$) (δ, ppm): 13.05 (s, 1H, NH), 10.66 (s, 1H, NH), 10.45 (s, 1H, NH), 7.57 (d, J = 8.4 Hz, 2H, ArH), 7.44 (d, J = 8.8 Hz, 1H, ArH) 7.24-7.34(m, 2H, ArH), 7.08 (d, J = 8.8 Hz, 1H, ArH), 6.92 (s, 1H, ArH), 4.90 (s, 1H, CH); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) (δ, ppm): 169.98, 165.21, 162.79, 153.27, 146.42, 140.32, 137.25, 131.64, 131.28, 131.24, 130.80, 130.55, 130.41, 130.29, 129.86, 129.77, 121.36, 120.61, 119.02, 116.59, 113.61, 110.06, 84.85, 54.91, 42.62; MS(MM-ES+APCI) 408.8 [M+H]$^+$. 

11-(3-methoxyphenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5h)

White solid, %purity (HPLC) =99.6%, mp. >300°C; $^1$H-NMR (400 MHz, DMSO-d$_6$) (δ, ppm): 12.98 (s, 1H, NH), 10.54 (s, 1H, NH), 10.32 (s, 1H, NH), 8.85 (s, 1H, ArH), 7.36 (d, J= 8.8 Hz, 1H, ArH), 7.06-7.15(m, 2H, ArH), 6.91 (s, 1H, ArH), 6.85 (d, J= 7.6 Hz, 1H, ArH), 6.64 (dd, J= 6.4 Hz, J=1.6 Hz, 1H, ArH), 5.39 (s, 1H, CH), 3.66 (s, 3H, OCH$_3$); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) (δ, ppm): 162.77, 158.90, 148.59, 138.51, 128.95, 121.49, 119.81, 119.67, 119.53, 117.12, 117.05, 113.90, 113.86, 113.65, 110.66, 109.46, 109.44, 109.41, 109.35, 107.37, 73.14, 54.82; MS(MM-ES+APCI) 360.0 [M+H]$^+$. 

11-[(1,1'-biphenyl]-4-yl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5i)

Off white solid, mp. >300°C; $^1$H-NMR (400 MHz, DMSO-d$_6$) (δ, ppm): 12.97 (s, 1H, NH), 10.54 (s, 1H, NH), 10.32 (s, 1H, NH), 8.85 (s, 1H, ArH), 8.06 (d, J= 16.8 Hz, 1H, ArH), 7.26-7.79(m, 10H, ArH), 5.44 (s, 1H, CH); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) (δ, ppm): 162.81, 162.78, 150.22, 150.20, 146.34, 145.63, 140.06, 138.01, 137.26, 131.81, 129.29, 128.99, 128.92, 128.76, 128.24, 128.04, 127.96, 127.09, 126.69, 126.51, 126.40, 126.08, 121.52, 121.50, 117.13, 117.10, 113.81, 113.78, 109.50, 85.17; MS(MM-ES+APCI) 407.0 [M+H]$^+$. 

11-(3-chlorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5j)
Off white solid, % purity (HPLC) = 99.5%, mp. >300°C; $^1$H-NMR (400 MHz, DMSO-d$_6$) ($\delta$, ppm): 13.02 (s, 1H, NH), 10.59 (s, 1H, NH), 10.36 (s, 1H, NH), 8.91 (s, 1H, ArH), 8.05 (s, 1H, ArH), 7.38 ($d$, $J$ = 8.4 Hz, 2H, ArH), 7.12-7.28 ($m$, 4H, ArH), 5.46 (s, 1H, CH); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) ($\delta$, ppm): 162.75, 157.90, 150.14, 150.13, 149.39, 145.67, 143.05, 137.25, 136.75, 132.60, 131.76, 129.85, 128.30, 128.24, 127.42, 127.23, 126.53, 126.26, 125.98, 117.17, 113.05, 110.22, 109.82, 109.81, 109.61, 107.35, 84.77, 79.21; MS (MM-ES+APCI) 365.8 [M+H]$^+$. 

11-(2-chlorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5k)

Off white solid, % purity (HPLC) = 99.0%, mp. >300°C; $^1$H-NMR (400 MHz, DMSO-d$_6$) ($\delta$, ppm): 13.04 (s, 1H, NH), 10.49 (s, 1H, NH), 10.30 (s, 1H, NH), 8.93 (s, 1H, ArH), 7.88 (s, 1H, ArH), 7.37 ($d$, $J$ = 8.4 Hz, 1H, ArH), 7.30 ($d$, $J$ = 6.8 Hz, 1H, ArH), 7.09-7.19 ($m$, 3H, ArH), 5.82 (s, 1H, CH); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) ($\delta$, ppm): 162.57, 150.16, 145.61, 144.39, 137.15, 131.39, 131.29, 131.24, 128.98, 128.52, 127.68, 127.28, 121.59, 117.30, 112.70, 109.91, 84.77; MS (MM-ES+APCI) 365.8 [M+H]$^+$. 

Spectroscopic and analytical characterization of 7,9-diaryl-3,6,7,9-tetrahydro-1'H-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidine]-2',4',6'(3'H)-triones (7a-i).

1',3'-dimethyl-7,9-diphenyl-3,6,7,9-tetrahydro-2'H-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione. (7a)

White solid, % purity (HPLC) = 98.7%, mp. 252-254°C; $^1$H-NMR (400 MHz, CDCl$_3$) ($\delta$, ppm): 7.46-7.52 (m, 1H, ArH), 7.29-7.40 (m, 7H, ArH), 7.23-7.27 (m, 2H, ArH), 7.05-7.14 (m, 2H, ArH), 6.81 ($d$, $J$ = 7.6 Hz, 1H, ArH), 5.42 (s, 1H, CH), 4.95 (s, 1H, CH), 2.99 (s, 3H, CH$_3$), 2.90 (s, 3H, CH$_3$); $^{13}$C-NMR (100 MHz, CDCl$_3$) ($\delta$, ppm): 170.20, 165.18, 149.91, 137.72, 136.24, 130.0, 129.83, 129.64, 128.96, 128.82, 128.67, 128.55, 128.36, 128.20, 126.77, 125.80, 120.63, 120.58, 64.71, 59.86, 59.85, 50.37; MS (MM-ES+APCI) 465.8 [M+H]$^+$. 

7,9-bis(4-chlorophenyl)-1',3'-dimethyl-3,6,7,9-tetrahydro-2'H-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione. (7b)

White solid, % purity (HPLC) = 99.3%, mp. 246-248°C; $^1$H-NMR (400 MHz, CDCl$_3$) ($\delta$, ppm): 7.48 ($d$, $J$ = 9.2 Hz, 1H, ArH), 7.27-7.36 (m, 4H, ArH), 7.09-7.20 (m, 4H, ArH), 5.39 (s, 1H, CH), 4.92 (s, 1H, CH), 3.04 (s, 3H, CH$_3$), 2.93 (s, 3H, CH$_3$); $^{13}$C-NMR (100 MHz, CDCl$_3$) ($\delta$, ppm): 169.74, 164.70,
1',3'-dimethyl-7,9-bis(4-nitrophenyl)-3,6,7,9-tetrahydro-2'H-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione. (7c)

Pale yellow solid, %purity (HPLC) =99.6%, mp. 264-266°C; 1H-NMR (400 MHz, CDCl3) (δ, ppm): 8.24 (d, J= 8.8 Hz, 3H, ArH), 8.0 (d, J= 8.8 Hz, 1H, ArH), 7.41-7.56 (m, 4H, ArH), 6.48 (s, 1H, ArH), 5.64 (s, 1H, CH), 5.08 (s, 1H, CH), 3.05 (s, 3H, CH3), 2.92 (s, 3H, CH3); 13C-NMR (100 MHz, CDCl3) (δ, ppm): 169.27, 164.13, 149.11, 148.65, 147.81, 145.20, 142.94, 131.34, 130.70, 128.13, 128.04, 124.25, 124.17, 123.90, 123.83, 123.62, 123.46, 119.57, 64.14, 59.75, 49.62, 49.55, 28.77, 27.99; MS(MM-ES+APCI) 535.8 [M+H]+.

7,9-bis(4-methoxyphenyl)-1',3'-dimethyl-3,6,7,9-tetrahydro-2'H-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione. (7d)

Off white solid, %purity (HPLC) =96.2%, mp. 244-246°C; 1H-NMR (400 MHz, CDCl3) (δ, ppm): 7.58 (d, J= 4.0 Hz, 1H, ArH), 7.16-7.25 (m, 4H, ArH), 6.73-6.83 (m, 4H, ArH), 5.34 (s, 1H, CH), 4.95 (s, 1H, CH), 3.81 (s, 6H, 2-OCH3), 3.02 (s, 3H, CH3), 2.95 (s, 3H, CH3); 13C-NMR (100 MHz, CDCl3) (δ, ppm): 170.15, 170.12, 160.43, 149.91, 131.16, 130.66, 128.03, 127.93, 127.84, 127.75, 114.50, 114.31, 114.17, 113.91, 63.85, 63.78, 63.72, 59.75, 55.31, 55.26, 49.47, 28.49, 27.81; MS(MM-ES+APCI) 525.8 [M+H]+.

1',3'-dimethyl-7,9-di-p-tolyl-3,6,7,9-tetrahydro-2'H-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione. (7e)

Off white solid, %purity (HPLC) =98.7%, mp. 178-180°C; 1H-NMR (400 MHz, CDCl3) (δ, ppm): 7.38 (d, J= 8.8 Hz, 1H, ArH), 7.06-7.25 (m, 8H, ArH), 6.92 (d, J= 8.0 Hz, 1H, ArH), 6.67 (d, J= 8.4 Hz, 1H, ArH), 5.35 (s, 1H, CH), 4.91 (s, 1H, CH), 3.0 (s, 3H, CH3), 2.92 (s, 3H, CH3), 2.33 (s, 6H, 2CH3); 13C-NMR (100 MHz, CDCl3) (δ, ppm): 170.31, 165.30, 150.09, 150.07, 139.52, 138.40, 138.12, 136.01, 134.45, 133.18, 132.67, 129.92, 129.62, 129.51, 129.44, 129.32, 126.63, 121.18, 64.36, 59.72, 59.69, 50.10, 38.27, 28.40, 27.70, 21.17, 21.15; MS(MM-ES+APCI) 493.8 [M+H]+.

7,9-bis(4-fluorophenyl)-1',3'-dimethyl-3,6,7,9-tetrahydro-2'H-spiro[pyrazolo[4,3-f]quinoline-8,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione. (7f)

White solid, %purity (HPLC) =99.4%, mp. 262-264°C; 1H-NMR (400 MHz, CDCl3) (δ, ppm): 7.22-7.37 (m, 4H, ArH), 7.01-7.13 (m, 4H, ArH), 6.81-6.86 (m, 2H, ArH), 6.53 (s, 1H, ArH), 5.42 (s, 1H,
CH), 4.93 (s, 1H, CH), 3.03 (s, 3H, CH$_3$), 2.93 (s, 3H, CH$_3$); $^{13}$C-NMR (100 MHz, CDCl$_3$) (δ, ppm):170.04, 164.97, 164.41, 163.75, 161.92, 161.28, 149.68, 133.46, 133.42, 132.08, 132.04, 131.72, 131.64, 131.54, 131.46, 128.67, 128.58, 120.35, 116.17, 115.96, 115.92, 115.71, 115.62, 115.41, 63.93, 60.04, 49.44, 28.50, 27.78; MS(MM-ES+APCI) 501.8 [M+H]$^+$. 

7,9-bis(4-bromophenyl)-1’,3’-dimethyl-3,6,7,9-tetrahydro-2’H-spiro[pyrazolo[4,3-f]quinoline-8,5’-pyrimidine]-2’,4’,6’(1’H,3’H)-trione. (7g) 

White solid, %purity (HPLC) = 98.8%, mp. 208-210°C; $^1$H-NMR (400 MHz, CDCl$_3$) (δ, ppm): 7.47-7.50 (m, 3H, ArH), 7.40 (d, $J$= 8.8 Hz, 1H, ArH), 7.20-7.26 (m, 2H, ArH), 7.05-7.13 (m, 3H, ArH), 6.69 (d, $J$= 8.4 Hz, 1H, ArH), 6.56 (s, 1H, ArH), 5.39 (s, 1H, CH), 4.90 (s, 1H, CH), 3.04 (s, 3H, CH$_3$), 2.93 (s, 3H, CH$_3$); $^{13}$C-NMR (100 MHz, CDCl$_3$) (δ, ppm):169.80, 160.73, 149.56, 138.28, 136.54, 135.04, 132.23, 131.94, 131.92, 131.60, 131.53, 128.44, 123.84, 122.71, 120.96, 111.84, 110.32, 63.99, 59.54, 49.51, 28.60, 27.86; MS(MM-ES+APCI) 623.6 [M+H]$^+$. 

7,9-bis(3-methoxyphenyl)-1’,3’-dimethyl-3,6,7,9-tetrahydro-2’H-spiro[pyrazolo[4,3-f]quinoline-8,5’-pyrimidine]-2’,4’,6’(1’H,3’H)-trione. (7h) 

White solid, %purity (HPLC) = 99.1%, mp. 234-236°C; $^{13}$C-NMR (100 MHz, CDCl$_3$) (δ, ppm):170.25, 170.12, 165.35, 165.14, 160.07, 159.75, 159.58, 150.04, 150.01, 139.19, 139.14, 138.07, 137.76, 130.01, 129.57, 122.38, 122.19, 120.72, 120.60, 118.98, 118.96, 116.0, 115.02, 114.78, 113.17, 112.68, 112.35, 112.33, 109.87, 64.53, 59.58, 59.47, 55.35, 55.28, 55.12, 50.29, 28.47, 28.44, 27.78, 27.73; MS(MM-ES+APCI) 525.8 [M+H]$^+$. 

7,9-di(1,1’-biphenyl)-4-yl)-1’,3’-dimethyl-3,6,7,9-tetrahydro-2’H-spiro[pyrazolo[4,3-f]quinoline-8,5’-pyrimidine]-2’,4’,6’(1’H,3’H)-trione. (7i) 

Off white solid, %purity (HPLC) = 98.3%, mp. 258-260°C; $^1$H-NMR (400 MHz, CDCl$_3$) (δ, ppm): 7.53-7.65 (m, 7H, ArH), 7.28-7.51 (m, 11H, ArH), 7.08 (d, $J$= 6.0 Hz, 1H, ArH), 6.88 (d, $J$= 8.4 Hz, 1H, ArH), 5.47 (s, 1H, CH), 5.02 (s, 1H, CH), 3.04 (s, 3H, CH$_3$), 2.95 (s, 3H, CH$_3$); $^{13}$C-NMR (100 MHz, CDCl$_3$) (δ, ppm):170.18, 165.19, 149.86, 142.55, 141.10, 140.10, 139.87, 136.59, 135.06, 134.95, 130.46, 130.22, 128.90, 128.81, 127.86, 127.56, 127.28, 127.22, 127.10, 127.06, 126.96, 121.23, 64.40, 64.33, 59.77, 50.10, 50.01, 49.94, 28.53, 27.82; MS(MM-ES+APCI) 617.8 [M+H]$^+$. 

Page | S10
Spectroscopic characterization of betaine based Deep Eutectic Mixtures (DEM) ($B_1$-$B_4$).

Figure: S4: $^1$H-NMR Spectra of Fresh catalyst $B_1$ (Betaine: Oxalic acid).

$^1$H-NMR (400 MHz, D$_2$O): δ (ppm): 3.99 (s, 2H, N-CH$_2$), 3.12 (s, 9H, N$^+$ (-CH$_3$)$_3$).
Figure: S5: $^{13}$C-NMR Spectra of Fresh catalyst B$_1$ (Betaine: Oxalic acid).

$^{13}$C-NMR (100 MHz, D$_2$O): $\delta$ (ppm): 167.42(CO), 164.23(CO), 64.08(N-CH$_2$), 53.65(N$^+$(-CH$_3$)$_3$).
Figure: S6: $^1$H-NMR Spectra of recycled catalyst B$_1$ (Betaine: Oxalic acid).

$^1$H-NMR (400 MHz, D$_2$O): $\delta$ (ppm): 3.77 (s, 2H, N-CH$_2$), 3.13 (s, 9H, N$^+$(-CH$_3$)$_3$).
Figure: S7: $^{13}$C-NMR Spectra of recycled catalyst B$_1$ (Betaine: Oxalic acid).

$^{13}$C-NMR (100 MHz, D$_2$O): $\delta$ (ppm): 64.08(N-CH$_2$), 53.65(N$^+$ (-CH$_3$)$_3$).
Figure: S8: $^1$H-NMR Spectra of catalyst B$_2$ (Betaine: Citric acid).

$^1$H-NMR (400 MHz, D$_2$O): $\delta$ (ppm): 3.82 (s, 2H, N-CH$_2$), 3.12 (s, 9H, N$^+$(-CH$_3$)$_3$), 2.87 (d, $J = 15.6$ Hz, 2H, COO-CH$_2$), 2.70 (d, $J = 15.6$ Hz, 2H, COO-CH$_2$).
Figure: S9: $^{13}$C-NMR Spectra of catalyst B₂ (Betaine: Citric acid).

$^{13}$C-NMR (100 MHz, D₂O); δ (ppm): 177.01(CO), 173.53(CO), 168.70(CO), 73.33(C-OH), 65.58(N-CH₂), 53.45(N⁺(-CH₃)), 53.41(N⁺(-CH₃)), 53.36(N⁺(-CH₃)), 43.29(-CH₂).
Figure: S10: $^1$H-NMR Spectra of catalyst B$_3$ (Betaine: Tartaric acid).

$^1$H-NMR (400 MHz, D$_2$O): $\delta$ (ppm): 4.53 (d, $J= 4.8$ Hz, 2H, -CH), 3.81 (s, 2H, N-CH$_2$), 3.09 (s, 9H, N$^+$(-CH$_3$)$_3$).
Figure: S11: $^{13}$C-NMR Spectra of catalyst B$_3$ (Betaine: Tartaric acid).

$^{13}$C-NMR (100 MHz, D$_2$O): $\delta$ (ppm): 174.79(CO), 168.63(CO), 71.98(C-OH), 65.47(N-CH$_2$), 53.42(N$^+$ (-CH$_3$)), 53.38(N$^+$ (-CH$_3$)), 53.34(N$^+$ (-CH$_3$)).
Figure: S12: $^1$H-NMR Spectra of catalyst B$_3$ (Betaine: Succinic acid)

$^1$H-NMR (400 MHz, D$_2$O): $\delta$ (ppm): 3.77 (s, 2H, N-CH$_2$), 3.11 (s, 9H, N$^+$(-CH$_3$)$_3$), 2.51 (d, $J = 2.8$ Hz, 4H, CH$_2$).
Figure: S13: $^{13}$C-NMR Spectra of catalyst B₄ (Betaine: Succinic acid)

$^{13}$C-NMR (100 MHz, D₂O): δ (ppm): 177.11(CO), 169.02(CO), 169.01(CO), 65.97(N-CH₂), 53.37(N⁺(-CH₃)), 53.32(N⁺(-CH₃)), 53.28(N⁺(-CH₃)), 28.86(-CH₂).
Figure: S14: LC report of compound 5a.
Figure: S15: HPLC report of compound 5a.
Figure: S16: LC-MS report of compound 5a.

Data File: C:\\CHEM32\data\SP University-04032020-NEW 2020-03-04 15-38-11\1.D
Sample Name: L1

Acq. Operator: SYSTEM
Acq. Instrument: LCMS
Injection Date: 3/4/2020 3:39:33 PM
Injection Volume: 5.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume: 2.000 µl
Acq. Method: C:\\Chem32\Data\SP University-04032020-NEW 2020-03-04 15-38-11\M26-FA.M
Last changed: 3/4/2020 3:38:11 PM by SYSTEM
Analysis Method: C:\\Chem32\Methods\MS-Washing-30min.M
Last changed: 3/2/2020 5:44:32 PM by SYSTEM
Method Info: Sulfur detection OQ/PV Method for the G6120B Quadrupole LC/MS System

Sample Info: L1

Sample-related custom fields:

Name | Value
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Additional Info: Peak(s) manually integrated

MS Signal: MSD3 TIC, MS File, MM-APCI, Neg, Fast Scan, Frag: 100
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%

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<th>Mol. Weight or Ion</th>
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<td>329.92 I</td>
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<tr>
<td>3.839</td>
<td>8779</td>
<td>347.75 I</td>
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<td></td>
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Graph: MSD3 SPC, time=0.729-3.797 of C:\CHEM32\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\1.D
MM-APCI Neg Pea
**Figure: S17: LC-MS report of compound 5b.**

Data File: C:\Chem32\Data\SP\UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L2.D
Sample Name: L2

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<td>Inj.</td>
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<td></td>
<td></td>
<td>Inj Volume</td>
<td>5.000 μl</td>
</tr>
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<td>Sulf drug OQ/PA Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test</td>
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Sample Info: L2

**Sample-related custom fields:**

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**Additional Info:** Peak(s) manually integrated

**MS Signal:** MSD3 TIC, MS File, MM-APCI, Neg, Fast Scan, Frag: 100
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

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![MSD3 SPC, SPC ID: 1724240 of C:\Chem32\1\Data\SP\UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L2.D MM-APCI, Neg_Peptide]
Figure: S18: LCMS report of compound 5c.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L3.D
Sample Name: L3

=================================================================================================
Acq. Operator : SYSTEM    Seq. Line : 3
Acq. Instrument : LCMS    Location : 44
Injection Date : 3/4/2020 4:01:50 PM    Inj : 1
                 Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 4:00:57 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
              MM-ES Positive Ion Sensitivity Test
Sample Info : L3

Sample-related custom fields:

Name | Value
-----------------------------------------------
Additional Info : Peak(s) manually integrated

=================================================================================================
MS Signal: MSD1 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 100
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

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Figure: S19: LC report of compound 5d.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L4.D
Sample Name: L4

-------------------------------------------------------------
Acq. Operator : SYSTEM
Acq. Instrument: LCMS
Injection Date : 3/4/2020 4:12:59 PM
Inj Volume : 5.000 µl
Inj: 1

Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 4:12:06 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulfa drug QQ/PV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : L4

Sample-related custom fields:
Name | Value
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Additional Info : Peak(s) manually integrated

-------------------------------------------------------------

![Chart Image]

-------------------------------------------------------------

![Chart Image]
Figure: S20: HPLC report of compound 5d.

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Totals

|        | 20239233 | 100.00  |
Figure: S21: LCMS report of compound 5d.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L4.D
Sample Name: L4

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Acq. Operator : SYSTEM  Seq. Line :  4
Acq. Instrument : LCMS  Location :  45
Injection Date : 3/4/2020 4:12:59 PM  Inj :  1
Inj Volume : 5.000 μl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 μl
Acq. Method : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 4:12:06 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : L4

Sample-related custom fields:

Name | Value
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Additional Info : Peak(s) manually integrated

MS Signal: MSD4 TIC, MS File, MM-APCI, Neg, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention | Mol. Weight
Time (MS) | MS Area or Ion
3.731 | 1248873 361.00 I
       | 359.80 I

MSD4 SPC, Time=3.765:3.773 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L4.D
MM-APCI, Neg, Fa
Max1: 149870

*** End of Report ***
Figure: S22: LC report of compound 5e.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L5.D
Sample Name: L5

================================================================================================
Acq. Operator : SYSTEM                                      Seq. Line : 5
Acq. Instrument : LCMS                                      Location : 46
Injection Date : 3/4/2020 4:24:09 PM                         Inj : 1
Inj Volume : 5.000 µl                                          Inj Volume : 2.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 4:23:14 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulfa drug OQ/PV Method for the GC120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test
Sample Info : L5

Sample-related custom fields:

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Additional Info: Peak(s) manually integrated

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![Diagram of LC report]

MSD4 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L5.D) MM-APCI, Neg, Fast Scan; F
Figure: S23: HPLC report of compound 5e.

Aether Industries Ltd

Sample ID : L5
Instruent ID : QCI04 (Offline)
Inj Vol : 1µl
Vial No : 46
Method : D:\HPLC DATA\2020\March\Method\MD\SP Uni-FA.met
Data File : D:\HPLC DATA\2020\March\Result\QC104\04032020\L5.dat
Acquired : 04/03/2020 19:44:46 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

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Figure: S24: LCMS report of compound 5e.

Data File: \C\HEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L5.D
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<td>C:\Chem32\1\Methods\MS-Washing-30min.M</td>
</tr>
<tr>
<td>Last changed</td>
<td>3/2/2020 5:44:32 PM by SYSTEM</td>
</tr>
<tr>
<td>Method Info</td>
<td>Sulf drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test</td>
</tr>
<tr>
<td>Sample Info</td>
<td>L5</td>
</tr>
</tbody>
</table>

Sample-related custom fields:

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<th>Name</th>
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</thead>
<tbody>
<tr>
<td>Additional Info</td>
<td>Peak(s) manually integrated</td>
</tr>
</tbody>
</table>

MS Signal: MSD4 TIC, MS File, MM-APCI, Neg, Fast Scan, Frag: 150 Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

<table>
<thead>
<tr>
<th>Retention Time (MS)</th>
<th>MS Area</th>
<th>Mol. Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.031</td>
<td>606430</td>
<td>345.00 I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>343.95 I</td>
</tr>
</tbody>
</table>

*** End of Report ***
Figure: S25: LC report of compound 5f.
Figure: S26: HPLC report of compound 5f.
Figure: S27: LCMS report of compound 5f.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-84032020-NEW 2020-03-04 15-38-11\L6.D
Sample Name: L6

==================================================================
Acq. Instrument : LCMS  Location : 47
Injection Date : 3/4/2020 4:35:19 PM  Inj : 1
Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\Chem32\1\Data\SP University-84032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 4:34:24 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulfa drug OQ/PV Method for the GG1200 Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : L6

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Info</td>
<td>Peak(s) manually integrated</td>
</tr>
</tbody>
</table>

MS Signal: MSD1 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 100
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention  Mol. Weight
Time (MS)  MS Area or Ion
3.980  1763041  350.80 I
       349.80 I

*** End of Report ***
Figure: S28: LCMS report of compound 5g.

Data File C:\\CHEM321\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L7.D
Sample Name: L7

Acq. Operator : SYSTEM
Acq. Instrument : LCMS
Injection Date : 3/4/2020 4:46:30 PM
Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Inj : 1
Seq. Line : 7
Location : 48

Acq. Method : C:\Chem321\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 4:45:35 PM by SYSTEM
(modified after loading)

Analysis Method : C:\Chem321\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM

Method Info : Sulfa drug Q/UV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : L7

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Info : Peak(s) manually integrated</td>
<td></td>
</tr>
</tbody>
</table>

MS Signal: MSD4 TIC, MS File, MM-APCI, Neg, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS) | MS Area | Mol. Weight or Ion |
-------------------|---------|-------------------|
4.290  | 863708  | 410.95 I          |
        |         | 409.80 I          |
        |         | 408.80 I          |
        |         | 407.80 I          |
4.430  | 694703  | 428.90 I          |
        |         | 427.80 I          |
        |         | 425.80 I          |
        |         | 418.60 I          |
        |         | 408.80 I          |
        |         | 407.65 I          |
        |         | 385.80 I          |
        |         | 384.80 I          |
        |         | 382.80 I          |
        |         | 367.70 I          |
        |         | 341.75 I          |
        |         | 339.80 I          |

MSD4 SPC, t ime=4.2514.319 of C:\CHEM321\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L7.D
MM-APCI, Neg, Fa
**Figure: S29: LC report of compound 5h.**

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L8.D
Sample Name: L8

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acq. Operator</td>
<td>SYSTEM</td>
</tr>
<tr>
<td>Acq. Instrument</td>
<td>LCMS</td>
</tr>
<tr>
<td>Injection Date</td>
<td>3/4/2020 4:57:41 PM</td>
</tr>
<tr>
<td>Injection Volume</td>
<td>5.000 μl</td>
</tr>
<tr>
<td>Sample Info</td>
<td>L8</td>
</tr>
<tr>
<td>Acq. Method</td>
<td>C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M</td>
</tr>
<tr>
<td>Last changed</td>
<td>3/4/2020 4:56:45 PM by SYSTEM</td>
</tr>
<tr>
<td>Analysis Method</td>
<td>C:\Chem32\1\Methods\MS-Kashing-30min.M</td>
</tr>
<tr>
<td>Last changed</td>
<td>3/2/2020 5:44:32 PM by SYSTEM</td>
</tr>
<tr>
<td>Method Info</td>
<td>Sulfur drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test</td>
</tr>
</tbody>
</table>

**Sample-related custom fields:**

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Info</td>
<td>Peak(s) manually integrated</td>
</tr>
</tbody>
</table>

---

**Graphs:**

- DAD1 A, Sign=254.4 Reflower (C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L8.D)
- MSD4 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L8.D) MM-APCI, Neg. Fast Scan; F
Figure: S30: HPLC report of compound 5h.

Aether Industries Ltd

Sample ID : L8        Instruunt ID : QC104 (Offline)
Inj Vol : 1ul
Vial No : 49
Method : D:\HPLC DATA\2020\March\Method\MD\SP Uni-FA.met
Data File : D:\HPLC DATA\2020\March\Result\QC\04032020\L8.dat
Acquired : 04/03/2020 20:24:55 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.38</td>
<td>882.39</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3.05</td>
<td>187621</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.80</td>
<td>76108132</td>
<td>99.64</td>
<td>L8</td>
</tr>
</tbody>
</table>

Totals        | 76383992 | 100.00   |
Figure: S31: LCMS report of compound 5h.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L8.D
Sample Name: L8

Acq. Operator : SYSTEM Seq. Line : 8
Acq. Instrument : LCMS Location : 49
Injection Date : 3/4/2020 4:57:41 PM Inj : 1
  Inj Volume : 5.000 μl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 μl
Acq. Method : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 4:56:45 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulf drug OQ/PV Method for the G6120B Quadrupole LC/MS System
  MM-ES Positive Ion Sensitivity Test

Sample Info : L8

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Info</td>
<td>Peak(s) manually integrated</td>
</tr>
</tbody>
</table>

MS Signal: MSD4 TIC, MS File, MM-APCI, Neg, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS) MS Area or Ion
3.780 635193 361.00 I
360.00 I

*** End of Report ***
Figure: S32: LCMS report of compound 5i.

Data File: C:\CHEM32\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L0.D
Sample Name: L9

Acq. Operator : SYSTEM
Acq. Instrument : LCMS
Injection Date : 3/4/2020 5:08:55 PM
Inj Volume : 5.000 µl

Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl

Acq. Method : C:\Chem32\DATA\SP University-04032020-NEW 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 5:07:59 PM by SYSTEM
(modified after loading)

Analysis Method : C:\Chem32\DATA\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM

Method Info : Sulfa drug O/Q/PV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : L9

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Info</td>
<td>Peak(s) manually integrated</td>
</tr>
</tbody>
</table>

MS Signal: MSD3 TIC, MS File, MM-APCI, Neg, Fast Scan, Frag: 100
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

<table>
<thead>
<tr>
<th>Retention Time (MS)</th>
<th>MS Area</th>
<th>Mol. Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.757</td>
<td>310489</td>
<td>407.00 I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>406.00 I</td>
</tr>
<tr>
<td>4.961</td>
<td>16897</td>
<td>425.00 I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>423.80 I</td>
</tr>
</tbody>
</table>

![MSD3 SPC plot](image)
Figure: S33: LC report of compound 5j.

Data File: C:\CHEM321\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L10.D
Sample Name: L10

Acq. Operator: SYSTEM
Seq. Line: 10
Acq. Instrument: LCMS
Location: SI
Injection Date: 3/4/2020 5:20:09 PM
Inj: 1
Inj Volume: 5.000 μl

Different Inj Volume from Sample Entry! Actual Inj Volume: 2.000 μl
Acq. Method: C:\Chem321\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed: 3/4/2020 5:19:12 PM by SYSTEM
(modified after loading)
Analysis Method: C:\Chem321\Methods\MS-Washing-30min.M
Last changed: 3/2/2020 5:44:32 PM by SYSTEM
Method Info: Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info: L10

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
</table>

Additional Info: Peak(s) manually integrated

---

DAD1 A, S(4g=254,4 Reflow (C:\CHEM321\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L10.D)

MSD1 TIC, MS File (C:\CHEM321\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L10.D) MM-APCI Pos, Fast Scan
Figure: S34: HPLC report of compound 5j.

Aether Industries Ltd

Sample ID : L10
Inj Vol : 1µl
Vial No : 51
Method : D:\HPLC DATA\2020\March\Method\MDSP Uni-FA.met
Data File : D:\HPLC DATA\2020\March\Result\QC04\04032020\L10.dat
Acquired : 04/03/2020 20:51:42 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.37</td>
<td>113771</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3.05</td>
<td>120485</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.93</td>
<td>57132</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4.03</td>
<td>225211776</td>
<td>99.58</td>
<td>110</td>
</tr>
<tr>
<td>5</td>
<td>4.32</td>
<td>365361</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>4.64</td>
<td>398230</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td>253566755</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>
Figure: S35: LCMS report of compound 5j.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L10.D
Sample Name: L10

================================================================================================
Acq. Operator : SYSTEM                         Seq. Line : 10
Acq. Instrument : LCMS                         Location : 51
Injection Date : 3/4/2020 5:20:09 PM         Inj. : 1
                Inj Volume : 5.000 μl
Different Inj Volume from Sample Entry!   Actual Inj Volume : 2.000 μl
Acq. Method : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 5:19:12 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulfur drug OQ/PV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : L10

Sample-related custom fields:

Name | Value
---------------------------------------------
Additional Info : Peak(s) manually integrated

MS Signal: MSD1 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 100
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS)  MS Area or Ion
4.138  1393262  367.80 I
         366.80 I
         365.80 I

*** End of Report ***
Figure: S36: LC report of compound 5k.
Figure: S37: HPLC report of compound 5k.

Aether Industries Ltd

Sample ID : L12  
Instruent ID : QC04 (Offline)  
Inj Vol : 1µl  
Vial No : 53  
Method : D:\HPLC DATA\2020\March\Method\MDSP Uni-FA.mat  
Data File : D:\HPLC DATA\2020\March\Result\QC04\04032020\L12.dat  
Acquired : 04/03/2020 21:18:27 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.37</td>
<td>79825</td>
<td>0.12</td>
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</tr>
<tr>
<td>2</td>
<td>3.79</td>
<td>67538275</td>
<td>99.03</td>
<td>L12</td>
</tr>
<tr>
<td>3</td>
<td>4.03</td>
<td>579816</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td>68197916</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>
Figure: S38: LCMS report of compound 5k.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L12.D
Sample Name: L12

====================================================================================================
Acq. Operator : SYSTEM                      Seq. Line : 12
Acq. Instrument : LCMS                        Location : 53
Injection Date : 3/4/2020 5:42:33 PM
                      Inj : 1
                      Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\CHEM32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Last changed : 3/4/2020 5:41:39 PM by SYSTEM
(modified after loading)
Analysis Method : C:\CHEM32\1\Methods\MS-Washing-30min.M
Last changed : 3/2/2020 5:44:32 PM by SYSTEM
Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
               MM-ES Positive Ion Sensitivity Test
Sample Info : L12

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
</table>

Additional Info : Peak(s) manually integrated

====================================================================================================

MS Signal: MS2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS)  | MS Area  | Mol. Weight or Ion
---------------------|----------|---------------------
3.912                | 519169   | 367.75 I            
                      |          | 366.80 I            
                      |          | 365.80 I            
                      |          | 363.65 I            
                      |          | 253.80 I            

*** End of Report ***
Figure: S39: LC report of compound 7a.
Figure: S40: HPLC report of compound 7a.

Aether Industries Ltd

Sample ID: CB1  Instrument ID: QC104 (Offline)
Inj Vol: 2µl  Vial No: 62
Method: D:\HPLC DATA\2019\November\Method\50 X 4.6 2.7µMDSP Uni-F.A.met
Data File: D:\HPLC DATA\2019\November\Result\QC104\14112019--CB1.dat

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
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<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.73</td>
<td>2056896</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.20</td>
<td>3716336</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.50</td>
<td>1109607</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3.83</td>
<td>718446573</td>
<td>98.74</td>
<td>CB1</td>
</tr>
<tr>
<td>5</td>
<td>4.43</td>
<td>762509</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>4.76</td>
<td>457205</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>5.85</td>
<td>668336</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>6.27</td>
<td>396042</td>
<td>0.05</td>
<td></td>
</tr>
</tbody>
</table>

Totals        | 72763504| 100.00 |
Figure: S41: LCMS report of compound 7a.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-14112019 2019-11-14 18-16-00\CB1.D
Sample Name: CB1

-------------------------------------------------------------------------------
Acq. Operator : SYSTEM                      Seq. Line :  2
Acq. Instrument : LCMS                      Location :  62
Injection Date : 11/14/2019 6:30:12 PM     Inj :  1
            Inj Volume: 1.000 µl           
Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
Acq. Method : C:\CHEM32\1\Data\SP University-14112019 2019-11-14 18-16-00\M206-FA.M
Last changed : 11/14/2019 6:29:18 PM by SYSTEM
(modified after loading)
Analysis Method : C:\CHEM32\1\Methods\MS-Washing-30min.M
Last changed : 11/14/2019 6:11:49 PM by SYSTEM
Method Info : Sulfa drug OQ/PV  Method for the G6120B Quadrupole LC/MS System
            MM-ES Positive Ion Sensitivity Test

Sample Info : CB1

Sample-related custom fields:

Name | Value
-----------------------|-----------------------
Additional Info : Peak(s) manually integrated

==============================================================================
MS Signal: MSD2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention  | Mol. Weight
Time (MS)   | MS Area or Ion
3.927       | 1992628 467.00 I
            | 465.80 I

MSD2 SPC, tms=0.892.3.970 of C:\CHEM32\1\DATA\SP UNIVERSITY-14112019 2019-11-14 18-16-00\CB1.D  MM-APCI, Pos, Fast
Max: 1638402

*** End of Report ***
Figure: S42: LC report of compound 7b.
Figure: S43: HPLC report of compound 7b.

Aether Industries Ltd

Sample ID: CB2#SP University
Inj Vol: 2µl
Vial No: 56
Method: D:\HPLC DATA\2020\January\Method\MD/SP Uni-FA.met
Data File: D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB2#SP University.dat
Acquired: 22/01/2020 22:48:22 (GMT +05:30)

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.25</td>
<td>203650</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4.27</td>
<td>1035499</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4.43</td>
<td>1205681</td>
<td>0.32</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4.77</td>
<td>368629438</td>
<td>99.34</td>
<td></td>
</tr>
</tbody>
</table>

Totals: 371074268 100.00
Figure: S44: LCMS report of compound 7b.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB2.D
Sample Name: CB2

<table>
<thead>
<tr>
<th>Acq. Operator</th>
<th>SYSTEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acq. Instrument</td>
<td>LCMS</td>
</tr>
<tr>
<td>Injection Date</td>
<td>1/22/2020 3:33:16 PM</td>
</tr>
<tr>
<td>Inj</td>
<td>1</td>
</tr>
<tr>
<td>Inj Volume</td>
<td>1.000 μl</td>
</tr>
<tr>
<td>Acq. Method</td>
<td>C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\MS206-FA.M</td>
</tr>
<tr>
<td>Last changed</td>
<td>1/22/2020 3:32:21 PM by SYSTEM</td>
</tr>
<tr>
<td>Analysis Method</td>
<td>C:\Chem32\1\Methods\MS-Washing-30min.M</td>
</tr>
<tr>
<td>Last changed</td>
<td>1/22/2020 4:03:07 PM by SYSTEM</td>
</tr>
<tr>
<td>Method Info</td>
<td>Sulf drug OQ/PS Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test</td>
</tr>
<tr>
<td>Sample Info</td>
<td>CB2</td>
</tr>
</tbody>
</table>

Sample-related custom fields:

- Name: |Value
- Additional Info: Peak(s) manually integrated

MS Signal: MSD2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

<table>
<thead>
<tr>
<th>Retention Time (MS)</th>
<th>MS Area</th>
<th>Mol. Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.847</td>
<td>5722229</td>
<td>537.80 I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>536.80 I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>535.80 I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>534.80 I</td>
</tr>
<tr>
<td></td>
<td></td>
<td>533.80 I</td>
</tr>
</tbody>
</table>

*** End of Report ***
Figure: S45: LC report of compound 7c.
Figure: S46: HPLC report of compound 7c.

Aether Industries Ltd

Sample ID: CB3#SP University  Instruent ID: QCI04 (Offline)
Inj Vol: 2µl
Vial No: 57
Method: D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met
Data File: D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB3#SP University.dat
Acquired: 22/01/2020 23:02:44 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.58</td>
<td>106788</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.74</td>
<td>116449</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.47</td>
<td>51248</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2.75</td>
<td>713974</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3.17</td>
<td>81969</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3.81</td>
<td>698626850</td>
<td>99.66</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>6.28</td>
<td>115377</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

Totals       |      | 699202655| 100.00 |
Figure: S47: LCMS report of compound 7c.
Figure: S48: LC report of compound 7d.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB4.D
Sample Name: CB4

Acq. Operator: SYSTEM
Acq. Instrument: LCMS
Injection Date: 1/22/2020 3:59:38 PM
Seq. Line: 18
Location: 58
Inj: 1
Inj Volume: 1.000 μl

Different Inj Volume from Sample Entry! Actual Inj Volume: 2.000 μl
Acq. Method: C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Last changed: 1/22/2020 3:58:44 PM by SYSTEM
(modified after loading)
Analysis Method: C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed: 1/22/2020 4:03:07 PM by SYSTEM
(modified after loading)
Method Info: Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info: CB4

Sample-related custom fields:

Name | Value
---------------------------------------------
Additional Info: Peak(s) manually integrated

=========================================================================

[Graphs showing chromatograms and mass spectra for compound 7d]
Figure: S49: HPLC report of compound 7d.

Aether Industries Ltd

Sample ID : CB4#SP University  Instruent ID : QCI04 (Offline)
Inj Vol : 2μl
Vial No : 58
Method : D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met
Data File : D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB4#SP University.dai
Acquired : 22/01/2020 23:17:07 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.23</td>
<td>4838605</td>
<td>1.77</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.27</td>
<td>1407902</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.48</td>
<td>240476</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2.75</td>
<td>127174</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2.95</td>
<td>489782</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3.16</td>
<td>422872</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>3.73</td>
<td>262931045</td>
<td>96.24</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>4.12</td>
<td>891607</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>4.20</td>
<td>1072338</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>5.87</td>
<td>397586</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>6.04</td>
<td>227911</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>6.27</td>
<td>151132</td>
<td>0.06</td>
<td></td>
</tr>
</tbody>
</table>

Totals      | 273199430 | 100.00  |
Figure: S50: LCMS report of compound 7d.

Data File: C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB4.D
Sample Name: CB4

-----------------------------------------------
Acq. Operator: SYSTEM                      Seq. Line: 18
Acq. Instrument: LCMS                       Location: 58
Injection Date: 1/22/2020 3:59:38 PM     Inj: 1
                                         Inj Volume: 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume: 2.000 µl
Acq. Method: C:\CHEM32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Last changed: 1/22/2020 3:58:44 PM by SYSTEM
             (modified after loading)
Analysis Method: C:\CHEM32\1\Methods\MS-Washing-30min.M
Last changed: 1/22/2020 4:03:07 PM by SYSTEM
             (modified after loading)
Method Info: Sulfs drug OQ/PR Method for the G61208 Quadrupole LC/MS System
             MM-ES Positive Ion Sensitivity Test
Sample Info: CB4

Sample-related custom fields:

Name            | Value
----------------|------------------
Additional Info: Peak(s) manually integrated

MS Signal: MSD2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS)  | Mol. Weight
---------------------|-------------
                      | or Ion
3.827                | 526.90 I
                      | 525.80 I

*** End of Report ***
Figure: S51: LC report of compound 7e.
Figure: S52: HPLC report of compound 7e.

Aether Industries Ltd

Sample ID : CB5#SP University
Instruent ID : QC104 (Offline)
Inj Vol : 2pl
Vial No : 59
Method : D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met
Data File : D:\HPLC DATA\2020\January\Result\QC104\22012020\CB5#SP University.dat
Acquired : 22/01/2020 23:31:29 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
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<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.45</td>
<td>1603852</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.96</td>
<td>499660</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.42</td>
<td>520939</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4.38</td>
<td>439523</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>4.62</td>
<td>30218966</td>
<td>98.79</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>7.00</td>
<td>651332</td>
<td>0.21</td>
<td></td>
</tr>
</tbody>
</table>

Totals | 305904966 | 100.00 |
Figure: S53: LCMS report of compound 7e.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CBS.D
Sample Name: CBS

Acq. Operator : SYSTEM    Seq. Line : 19
Acq. Instrument : LCMS    Location : 59
Injection Date : 1/22/2020 4:12:54 PM    Inj : 1
Inj Volume : 1.000 μl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 μl
Acq. Method : C:\Chem32\1\Data\SP University-2020-01-22 12-13-54\M206-FA.M
Last changed : 1/22/2020 4:11:56 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 1/22/2020 4:03:07 PM by SYSTEM
(modified after loading)
Method Info : Sulfa drug OQ/PV Method for the GG120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : CBS

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Info</td>
<td>Peak(s) manually integrated</td>
</tr>
</tbody>
</table>

MS Signal: MSD2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%

<table>
<thead>
<tr>
<th>Retention (MS)</th>
<th>Mol. Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.716</td>
<td>5116771</td>
</tr>
<tr>
<td></td>
<td>494.95 I</td>
</tr>
<tr>
<td></td>
<td>493.80 I</td>
</tr>
</tbody>
</table>

*** End of Report ***
Figure: S54: LC report of compound 7f.
Figure: S55: HPLC report of compound 7f.

Aether Industries Ltd

Sample ID: CB6#SP University  
Inj Vol: 2μl  
Vial No: 60  
Method: D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met  
Data File: D:\HPLC DATA\2020\January\Result\QC104\22012020\CB6#SP University.dat  
Acquired: 22/01/2020 23:45:52 (GMT +05:30)

DAD: Signal A, 254.0 nm/Bw:4.0 nm Results

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.29</td>
<td>151966</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.39</td>
<td>354255</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2.47</td>
<td>181695</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2.73</td>
<td>131381</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3.04</td>
<td>357397</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>3.53</td>
<td>118106</td>
<td>0.03</td>
<td></td>
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<td>7</td>
<td>3.71</td>
<td>83416</td>
<td>0.02</td>
<td></td>
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<td>395687459</td>
<td>99.48</td>
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<td>9</td>
<td>4.85</td>
<td>62560</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>4.96</td>
<td>59232</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>5.29</td>
<td>79810</td>
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</tr>
<tr>
<td>12</td>
<td>5.35</td>
<td>104893</td>
<td>0.03</td>
<td></td>
</tr>
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<td>5.88</td>
<td>88964</td>
<td>0.02</td>
<td></td>
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<tr>
<td>14</td>
<td>6.19</td>
<td>289507</td>
<td>0.07</td>
<td></td>
</tr>
</tbody>
</table>

Totals: 397750641 | 100.00
Figure: S56: LCMS report of compound 7f.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB6.D
Sample Name: CB6

<table>
<thead>
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<th>Acq. Operator</th>
<th>Acq. Instrument</th>
<th>Injection Date</th>
<th>Location</th>
<th>Inj Volume</th>
<th>Actual Inj Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYSTEM</td>
<td>LCMS</td>
<td>1/22/2020 4:26:05 PM</td>
<td>60</td>
<td>1.000 µl</td>
<td>2.000 µl</td>
</tr>
</tbody>
</table>

Acq. Method: C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Last changed: 1/22/2020 4:25:11 PM by SYSTEM (modified after loading)
Analysis Method: C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed: 1/22/2020 4:03:07 PM by SYSTEM (modified after loading)
Method Info: Sulf drug Qq/Py Method for the G6120B Quadrupole LC/MS System

Sample Info: CB6

Sample-related custom fields:

Name | Value
---|---
Additional Info: Peak(s) manually integrated

MS Signal: MSD2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention | Mol. Weight
---|---
Time (MS) | MS Area or Ion
4.119 | 6321377 502.80 I
| 501.80 I

*** End of Report ***
Figure: S57: LC report of compound 7g.
Figure: S58: HPLC report of compound 7g.
Figure: S59: LCMS report of compound 7g.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB7.D
Sample Name: CB7

Acq. Operator : SYSTEM
Acq. Instrument : LCMS
Injection Date : 1/22/2020 4:39:15 PM
Injection : 1
Inj Volume : 1.000 µl

Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Last changed : 1/22/2020 4:38:21 PM by SYSTEM
(modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 1/22/2020 4:03:07 PM by SYSTEM
(modified after loading)
Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
MM-ES Positive Ion Sensitivity Test

Sample Info : CB7

Sample-related custom fields:

<table>
<thead>
<tr>
<th>Name</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional Info</td>
<td>Peak(s) manually integrated</td>
</tr>
</tbody>
</table>

MS Signal: MS2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS) | MS Area | Mol. Weight |
-------------------|---------|-------------|
5.050             | 3944078 | 626.60 I    |
                   |         | 625.60 I    |
                   |         | 624.70 I    |
                   |         | 623.60 I    |
                   |         | 622.60 I    |
                   |         | 621.60 I    |

*** End of Report ***
Figure: S60: LC report of compound 7h.
Figure: S61: HPLC report of compound 7h.

### Aether Industries Ltd

Sample ID: CB8#SP University, Instrument ID: QCI04 (Offline)
Inj Vol: 2μl
Vial No: 62
Method: D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met
Data File: D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB8#SP University.dat
Acquired: 23/01/2020 00:14:33 (GMT +05:30)

![HPLC Graph]

<table>
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<th>RT</th>
<th>Area</th>
<th>Area %</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.23</td>
<td>916300</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2.60</td>
<td>1756597</td>
<td>0.32</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.25</td>
<td>72602</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>3.85</td>
<td>548706811</td>
<td>99.13</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>4.49</td>
<td>383380</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>4.96</td>
<td>132298</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>5.10</td>
<td>194416</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>5.19</td>
<td>190523</td>
<td>0.03</td>
<td></td>
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<td>9</td>
<td>5.37</td>
<td>53876</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>5.65</td>
<td>151640</td>
<td>0.03</td>
<td></td>
</tr>
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<td>11</td>
<td>5.99</td>
<td>547986</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>6.16</td>
<td>436298</td>
<td>0.08</td>
<td></td>
</tr>
</tbody>
</table>

Totals: 553542727 | 100.00
Figure: S62: LCMS report of compound 7h.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB8.D
Sample Name: CB8

Acq. Operator : SYSTEM
Acq. Instrument : LCMS
Injection Date : 1/22/2020 4:52:24 PM
Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Last changed : 1/22/2020 4:51:32 PM by SYSTEM (modified after loading)
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 1/22/2020 4:03:07 PM by SYSTEM (modified after loading)
Method Info : Sulfo drug OQ/PP Method for the GG1208 Quadrupole LC/MS System
Sample Info : CB8

Sample-related custom fields:
Name | Value
Additional Info : Peak(s) manually integrated

MS Signal: MS02 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS) MS Area or Ion
3.930 7845816 526.90 I
525.80 I

*** End of Report ***
Figure: S63: LC report of compound 7i.
Figure: S64: HPLC report of compound 7i.
Figure: S65: LCMS report of compound 7i.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB9.D
Sample Name: CB9

Acq. Operator : SYSTEM                  Seq. Line : 23
Acq. Instrument : LCMS                  Location : 63
Injection Date : 1/22/2020 5:05:37 PM   Inj : 1
Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
Acq. Method : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Last changed : 1/22/2020 5:04:42 PM by SYSTEM
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Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
Last changed : 1/22/2020 4:03:07 PM by SYSTEM
(modified after loading)
Method Info : Sulf drug Qq/Qq Method for the G6120B Quadrupole LC/MS System
             MM-ES Positive Ion Sensitivity Test

Sample Info : CB9

Sample-related custom fields:

Name | Value
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Additional Info : Peak(s) manually integrated

MS Signal: MS2 TIC, MS File, MM-APCI, Pos, Fast Scan, Frag: 150
Spectra averaged over upper half of peaks.
Noise Cutoff: 500 counts.
Reportable Ion Abundance: > 10%.

Retention Time (MS)      MS Area or Ion
------------------------  -------------
5.865                    4365161
                           618.90 I
                           617.80 I

*** End of Report ***
Figure S66: $^1$H-NMR Spectra of Compound 5a.
Figure S67: $^{13}$C-NMR Spectra of Compound 5a.
Figure S68: $^1$H-NMR Spectra of Compound 5b.
Figure S69: Extended $^1$H-NMR Spectra of Compound 5b.
Figure S70: $^{13}$C-NMR Spectra of Compound 5b.
Figure S71: $^{13}$C-NMR Spectra of Compound 5c.
Figure S72: $^1$H-NMR Spectra of Compound 5d.
Figure S73: $^{13}$C-NMR Spectra of Compound 5d.
Figure S74: $^1$H-NMR Spectra of Compound 5e.
Figure S75: Extended $^1$H-NMR Spectra of Compound 5e.
Figure S76: $^{13}$C-NMR Spectra of Compound 5e.
Figure S77: $^1$H-NMR Spectra of Compound 5f.
Figure S78: $^{13}$C-NMR Spectra of Compound 5f.
Figure S79: $^1$H-NMR Spectra of Compound 5g.
Figure S80: $^{13}$C-NMR Spectra of Compound 5g.
Figure S81: $^1$H-NMR Spectra of Compound 5h.
Figure S82: $^{13}$C-NMR Spectra of Compound 5h.
Figure S83: $^1$H-NMR Spectra of Compound 5i.
Figure S84: Extended $^1$H-NMR Spectra of Compound 5i.
Figure S85: $^{13}$C-NMR Spectra of Compound 5i.
Figure S86: $^1$H-NMR Spectra of Compound 5j.
Figure S87: $^{13}$C-NMR Spectra of Compound 5j.
Figure S88: $^1$H-NMR Spectra of Compound 5k.
Figure S89: $^{13}$C-NMR Spectra of Compound 5k.
Figure S90: $^1$H-NMR Spectra of Compound 7a.
Figure S91: Extended $^1$H-NMR Spectra of Compound 7a.
Figure S92: $^{13}$C-NMR Spectra of Compound 7a.
Figure S93: $^1$H-NMR Spectra of Compound 7b.
Figure S94: $^{13}$C-NMR Spectra of Compound 7b.
Figure S95: $^1$H-NMR Spectra of Compound 7c.
Figure S96: $^{13}$C-NMR Spectra of Compound 7c.
Figure S97: $^1$H-NMR Spectra of Compound 7d.
Figure S98: Extended $^1$H-NMR Spectra of Compound 7d.
Figure S99: $^{13}$C-NMR Spectra of Compound 7d.
Figure S100: $^1$H-NMR Spectra of Compound 7e.
Figure S101: $^{13}$C-NMR Spectra of Compound 7e.
Figure S102: $^1$H-NMR Spectra of Compound 7f.
Figure S103: $^{13}\text{C}$-NMR Spectra of Compound 7f.
Figure S104: $^1$H-NMR Spectra of Compound 7g.
Figure S105: $^{13}$C-NMR Spectra of Compound 7g.
Figure S106: $^{13}$C-NMR Spectra of Compound 7h.
Figure S107: $^1$H-NMR Spectra of Compound 7i.
Figure S108: Extended $^1$H-NMR Spectra of Compound 7i.
Figure S109: $^{13}$C-NMR Spectra of Compound 7i.
Validation of Green chemistry metrics for all newly synthesized compounds.

Materials used for green chemistry metrics calculations

5-aminoindazole (1, 1.0 mmol), barbituric acid (2a, 1.0 mmol), N, N-dimethyl barbituric acid (2b, 1.0 mmol) and aldehyde (3a-k, 1.0 mmol and 3a-i, 2.0mmol).

Respective amount of reagents:

5-aminoindazole (1): 0.133gm (Mol.wt.=133.15), barbituric acid (2a): 0.128gm (Mol.wt.=128.14), N, N-dimethyl barbituric acid (2b): 0.156gm (Mol.wt.=156.14), benzaldehyde (3a): 0.106gm (Mol.wt. = 106.12), 4-chlorobenzaldehyde (3b): 0.140gm (Mol.wt. = 140.56), 4-nitrobenzaldehyde (3c): 0.151gm (Mol.wt. = 151.12), 4-methoxybenzaldehyde (3d): 0.136gm (Mol.wt. = 136.15), 4-methylbenzaldehyde (3e): 0.120gm (Mol.wt. = 120.15), 4-fluorobenzaldehyde (3f): 0.124gm (Mol.wt. = 124.11), 4-bromobenzaldehyde (3g): 0.185gm, (Mol.wt.=185.02), 3-methoxybenzaldehyde (3h): 0.136gm (Mol. wt.=136.15), 4-phenylbenzaldehyde (3i): 0.182gm (Mol.wt.=182.22), 3-chlorobenzaldehyde (3j): 0.140gm (Mol.wt.=140.56), 2-chlorobenzaldehyde (3k): 0.140gm (Mol. wt.=140.56).

Note: For the synthesis of 7(a-i) series of compounds the respective amount of aldehydes 3(a-i) is doubled.

Solvents used:

Ethanol as a reaction media (5mL): 3.77gm
Water in reaction work-up process (15 mL): 14.6gm
Ethanol for washing purpose (5mL): 3.77gm

Products:

For 5(a-k) series of compounds:
5a: 0.26gm (Mol.wt.=331.34), 5b: 0.32gm (Mol.wt.=365.78), 5c: 0.28gm (Mol.wt.=376.33), 5d: 0.32gm (Mol.wt.=361.36), 5e: 0.28gm (Mol.wt.=346.36), 5f: 0.24gm (Mol.wt.=349.33), 5g: 0.3gm (Mol.wt.=410.23), 5h: 0.28gm (Mol.wt. = 361.36), 5i: 0.32gm (Mol.wt.=407.43), 5j: 0.23gm (Mol.wt.=365.78), 5k: 0.3gm (Mol.wt=365.78).

For 7(a-i) series of compounds:
7a: 0.4gm (Mol.wt.=465.51), 7b: 0.44gm (Mol.wt.=534.40), 7c: 0.49gm (Mol.wt.=555.51), 7d: 0.48gm (Mol.wt.=525.57), 7e: 0.42gm (Mol.wt.=493.57), 7f: 0.39gm (Mol.wt.=501.49), 7g: 0.42gm (Mol.wt.=623.31), 7h: 0.47gm (Mol.wt.=525.57), 7i: 0.51gm (Mol.wt.=617.71).
Calculation of green chemistry metrics for one representative entry, viz. 5a.

✓ E-factor = (Total mass of wastes)/ (Mass of product)

E-factor = ((0.133gm+0.128gm+0.106gm)-0.26)/0.26 = 0.41

✓ AE (%) = (Molecular wt. of product)/ (Total molecular wt. of reactants) x 100

AE (%) = [(331.34)/ (133.15+128.09+106.12)] x 100 = 90.19%

✓ RME (%) = (Mass of isolated product)/ (Total mass of reactant) x 100

RME (%) = [(0.26gm)/(0.133gm+0.128gm+0.106gm)] x 100 = 70.84%

✓ OE (%) = RME/ AE x 100

OE (%) = (70.84/ 90.19) x 100 = 78.54%

✓ AEF (%) = AE x % yield

AEF (%) = (90.19 x 80)/100 = 72.15

Fig S110: Radar chart for green metrics evaluation of compounds 5(a-i)
### Table S4:

<table>
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<th>Sr. No.</th>
<th>Product (5(a-k))</th>
<th>E-factor</th>
<th>AE (%)</th>
<th>RME (%)</th>
<th>OE (%)</th>
<th>AEF (%)</th>
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<td>1</td>
<td>5a</td>
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<tr>
<td>2</td>
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### Table S5:

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<th>RME (%)</th>
<th>OE (%)</th>
<th>AEF (%)</th>
</tr>
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