A novel substrate directed multicomponent reaction for the synthesis of tetrahydro-spiro[pyrazolo[4,3-*f*]quinoline-8,5'-pyrimidines and tetrahydropyrazolo[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.

Identification code	5g	
Empirical formula	C18 H12 Br N5 O2	
Formula weight	410.23	
Temperature	298 K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 10.1063(13) Å	$\alpha = 94.851^{\circ}$ (4).
	b = 10.6214(12) Å	β= 97.256° (4).
	c = 12.8286(16) Å	$\gamma = 111.253^{\circ}$ (3).
Volume	1260.4(3) Å ³	
Density (calculated)	1.081 g/Cm ³	

Crystal X-ray report of compound 7b [CCDC:1978229].



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

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

Identification code	7b
Empirical formula	C27 H21 Cl2 N5 O3
Formula weight	534.39
Temperature	293 K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c

Unit cell dimensions	a = 9.6991 (4) Å	<i>α</i> = 90°.
	b = 15.1736 (7) Å	β=101.750° (2).
	c = 18.5825 (9) Å	$\gamma = 90^{\circ}$.
Volume	2677.5(2)Å ³	
Density (calculated)	1.326 g/Cm ³	
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.

Identification code	7h
Empirical formula	C27 H27 N5 O5
Formula weight	525.55

Temperature	293 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	12.2814(14)Å	$\alpha = 90^{\circ}$.
	b = 12.4871(16) Å	β= 90°.
	c = 16.249(2)Å	$\gamma = 90^{\circ}$.
Volume	2492.0(5) Å ³	
Density (calculated)	1.401g/Cm ³	
F(000)	1104.0	
Data completeness	1.76/0.99	

Characterizations details of 11-aryl-3,6,7,11-tetrahydro-8*H*-pyrazolo[4,3-*f*]pyrimido[4,5*b*]quinoline-8,10(9*H*)-diones 5(a-k) and 7,9-diaryl-3,6,7,9-tetrahydro-2'*H*-spiro[pyrazolo[4,3-*f*] quinoline-8,5'-pyrimidine]-2',4',6'(3'*H*)-triones (7a-i).

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

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

Light pink solid, %purity (HPLC) =88.1%, mp. 282-284°C; ¹H-NMR (400 MHz, DMSO-d₆) (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); ¹³C-NMR (100 MHz, DMSO-d₆) (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]⁺.

$\label{eq:constraint} 11-(4-chlorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione.~(5b)$

Off white solid, mp. 280-282°C; ¹H-NMR (400 MHz, DMSO-d₆) (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);¹³C-NMR (100 MHz, DMSO-d₆) (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-d₆) (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-8*H*-pyrazolo[4,3-*f*]pyrimido[4,5-*b*]quinoline-8,10(9*H*)-dione. (5d)

Off white solid, %purity (HPLC) =98.7%, mp. 278-280°C; ¹H-NMR (400 MHz, DMSO-d₆) (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), 7.22 (*d*, *J*= 8.8 Hz, 2H, ArH), 7.13 (*d*, *J*= 8.8 Hz, 1H, ArH), 6.72 (*d*, *J*= 8.8 Hz, 2H, ArH), 5.36 (s, 1H, CH), 3.63 (s, 1H, OCH₃); ¹³C-NMR (100 MHz, DMSO-d₆) (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]⁺.

$\label{eq:constraint} 11-(p-tolyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. \eqref{eq:constraint} (5e)$

Off white solid, %purity (HPLC) =98.5%, mp. >300°C; ¹H-NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.97 (s, 1H, NH), 10.54 (s, 1H, NH), 10.29 (s, 1H, NH), 8.82 (*s*, 1H, ArH), 8.01 (*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, CH₃); ¹³C-NMR (100 MHz, DMSO-d₆) (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]⁺.

$\label{eq:constraint} 11-(4-fluorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione.~(5f)$

Off white solid, %purity (HPLC) =99.5%, mp. >300°C; ¹H-NMR (400 MHz, DMSO-d₆) (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-d₆) (δ, ppm):162.77, 161.69, 159.29, 150.16, 145.53, 143.33, 143.29, 137.25, 131.73, 131.71, 129.27,129.19, 128.19, 121.39, 117.12, 114.66, 114.45, 113.66, 109.59, 85.16, 37.35; MS(MM-ES+APCI) 349.8 [M+H]⁺.

$\label{eq:constraint} 11-(4-bromophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione.~(5g)$

Off white solid, mp. 290-292°C; ¹H-NMR (400 MHz, DMSO-d₆) (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); ¹³C-NMR (100 MHz, DMSO-d₆) (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-8*H*-pyrazolo[4,3-*f*]pyrimido[4,5-*b*]quinoline-8,10(9*H*)-dione. (5h)

White solid, %purity (HPLC) =99.6%, mp. >300°C; ¹H-NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.98 (s, 1H, NH), 10.56 (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, OCH₃); ¹³C-NMR (100 MHz, DMSO-d₆) (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-8*H*-pyrazolo[4,3-*f*]pyrimido[4,5-*b*]quinoline-8,10(9*H*)-dione. (5i)

Off white solid, mp. >300°C; ¹H-NMR (400 MHz, DMSO-d₆) (δ, ppm): 12.97 (s, 1H, NH), 10.54 (s, 1H, NH), 10.34 (s, 1H, NH), 8.88 (*s*, 1H, ArH), 8.06 (*d*, *J*= 16.8 Hz, 1H, ArH), 7.26-7.79(*m*, 10H, ArH), 5.44 (s, 1H, CH); ¹³C-NMR (100 MHz, DMSO-d₆) (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]⁺.

$\label{eq:constraint} 11-(3-chlorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione.~(5j)$

Off white solid, %purity (HPLC) =99.5%, mp. >300°C; ¹H-NMR (400 MHz, DMSO-d₆) (δ, 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); ¹³C-NMR (100 MHz, DMSO-d₆) (δ, 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, 109.81, 109.61, 107.35, 84.77, 79.21; MS(MM-ES+APCI) 365.8 [M+H]⁺.

$\label{eq:chlorophenyl} 11-(2-chlorophenyl)-3,6,7,11-tetrahydro-8H-pyrazolo[4,3-f]pyrimido[4,5-b]quinoline-8,10(9H)-dione. (5k)$

Off white solid, %purity (HPLC) =99.0%, mp. >300°C; ¹H-NMR (400 MHz, DMSO-d₆) (δ, 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);¹³C-NMR (100 MHz, DMSO-d₆) (δ, 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; ¹H-NMR (400 MHz, CDCl₃) (δ, 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, CH₃), 2.90 (s, 3H, CH₃); ¹³C-NMR (100 MHz, CDCl₃) (δ, 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, 120.62, 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; ¹H-NMR (400 MHz, CDCl₃) (δ, 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, CH₃), 2.93 (s, 3H, CH₃); ¹³C-NMR (100 MHz, CDCl₃) (δ, ppm):169.74, 164.70,

149.53, 135.84, 135.76, 134.63, 134.41, 131.24, 131.20, 129.29, 129.05, 128.17, 121.83, 63.83, 59.59, 49.37; MS(MM-ES+APCI) 535.8 [M+H]⁺.

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) 555.8 [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, CH₃), 2.93 (s, 3H, CH₃); ¹³C-NMR (100 MHz, CDCl₃) (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; ¹H-NMR (400 MHz, CDCl₃) (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, CH₃), 2.93 (s, 3H, CH₃); ¹³C-NMR (100 MHz, CDCl₃) (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; ¹³C-NMR (100 MHz, CDCl₃) (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, 50.59, 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; ¹H-NMR (400 MHz, CDCl₃) (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, CH₃), 2.95 (s, 3H, CH₃); ¹³C-NMR (100 MHz, CDCl₃) (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]⁺. # Spectroscopic characterization of betaine based Deep Eutectic Mixtures (DEMs) (B₁-B₄).

Figure: S4: ¹H-NMR Spectra of Fresh catalyst B₁ (Betaine: Oxalic acid).





Figure: S5: ¹³C-NMR Spectra of Fresh catalyst B₁ (Betaine: Oxalic acid).



¹³C-NMR (100 MHz, D₂O): δ (ppm): 167.42(CO), 164.23(CO), 64.08(N-CH₂), 53.65(N⁺(-CH₃)₃).

Figure: S6: ¹H-NMR Spectra of recycled catalyst B₁ (Betaine: Oxalic acid).



¹H-NMR (400 MHz, D₂O): δ (ppm): 3.77(s, 2H, N-CH₂), 3.13 (s, 9H, N⁺(-CH₃)₃).

Figure: S7: ¹³C-NMR Spectra of recycled catalyst B₁ (Betaine: Oxalic acid).



¹³C-NMR (100 MHz, D₂O): δ (ppm): 64.08(N-CH₂), 53.65(N⁺(-CH₃)₃).

Figure: S8: ¹H-NMR Spectra of catalyst B₂ (Betaine: Citric acid).



¹H-NMR (400 MHz, D₂O): δ (ppm): 3.82 (s, 2H, N-CH₂), 3.12 (s, 9H, N⁺ (-CH₃)₃), 2.87 (d, *J* = 15.6 Hz, 2H, COO-CH₂), 2.70 (d, *J* = 15.6 Hz, 2H, COO-CH₂).



Figure: S9: ¹³C-NMR Spectra of catalyst B₂ (Betaine: Citric acid).

¹³C-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: ¹H-NMR Spectra of catalyst B₃ (Betaine: Tartaric acid).



¹H-NMR (400 MHz, D₂O): δ (ppm): 4.53 (d, *J*= 4.8 Hz, 2H, -CH), 3.81 (s, 2H, N-CH₂), 3.09 (s, 9H, N⁺ (-CH₃)₃).





¹³C-NMR (100 MHz, D₂O): δ (ppm): 174.79(CO), 168.63(CO), 71.98(C-OH), 65.47(N-CH₂), 53.42(N⁺(-CH₃)), 53.38(N⁺(-CH₃)), 53.34(N⁺(-CH₃)).

Figure: S12: ¹H-NMR Spectra of catalyst B₃ (Betaine: Succinic acid)



¹H-NMR (400 MHz, D₂O): δ (ppm): 3.77 (s, 2H, N-CH₂), 3.11 (s, 9H, N⁺ (-CH₃)₃), 2.51 (d, J = 2.8 Hz, 4H, CH₂).

Figure: S13: ¹³C-NMR Spectra of catalyst B₄ (Betaine: Succinic acid)



 $\label{eq:constraint} ^{13}\text{C-NMR} \ (100 \ \text{MHz}, D_2\text{O}): \ \delta \ (\text{ppm}): \ 177.11(\text{CO}), \ 169.02(\text{CO}), \ 169.01(\text{CO}), \ 65.97(\text{N-CH}_2), \ 53.37(\text{N}^+(\text{-CH}_3)), \ 53.32(\text{N}^+(\text{-CH}_3)), \ 53.28(\text{N}^+(\text{-CH}_3)), \ 28.86\ (\text{-CH}_2).$

Figure: S14: LC report of compound 5a.

0

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

```
-----
Acq. Operator : SYSTEM
                                            Seq. Line : 1
                                            Location : 42
Acq. Instrument : LCMS
Injection Date : 3/4/2020 3:39:33 PM
                                                 Inj: 1
                                           Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 \mu l
             : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Acq. Method
Last changed
             : 3/4/2020 3:38:11 PM by SYSTEM
Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M
             : 3/2/2020 5:44:32 PM by SYSTEM
Last changed
Method Info
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
               MM-ES Positive Ion Sensitivity Test
              : L1
Sample Info
Sample-related custom fields:
Name
                           Value
Additional Info : Peak(s) manually integrated
DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L1.D)
                                         868.051
   mAU
    200
                                                  38.755
    150
                                           shin .
    100
    50
     0 -
       2 4 6 8
MSD3 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L1.D) MM-APCI, Neg, Fast Scan, F
                                        1883. 1839L
                                       3.758
  60000
                                                44829
4829
4829
                                          estite.
  40000
  20000
```

mir

mir

Q

Figure: S15: HPLC report of compound 5a.



	Aethe	er Industrie	es Ltd				
Sample ID : L1	Instruent ID	: QCI04 (Offline)					
Inj Vol : 1µl							
Vial No : 42							
Method : D:W	HPLC DATA\2020\Mar	ch\Method\MD\SP Uni	-FA.met				
Data File : D:\	HPLC DATA\2020\Mar	ch\Result\QCI04\04032	2020\L1.dat				
Acquired : 04/)3/2020 18:51:21 (GMT	r +05:30)					
DAD:	Signal A, 254.0 nm/Bw:4-0 nm						
L1 Retention	Time			-			
100	Time			- 100			
Fe 50 -	A	~		- 50 E			
60	533	.02					
	4.52	4		-			
0				0			
0	2 4	6 Minutes	8 10	12			
DAD: Signal A.		initiates of					
254.0 nm/Bw:4.0							
nm Results							
Peak Number	RT	Area	Area %	Name			
1	1.49	323316	0.51				
2	2.23	139971	0.22				
3	3.63	56312824	88.19	L1			
4	3.76	3190555	5.00				
5	3.88	1269614	1.99				
6	4.02	83331	0.13				
7	7 4.71 2536643 3.97						
Totals	Totals						
		63856254	100.00				

Figure: S16: LC-MS report of compound 5a.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L1.D Sample Name: L1 -----Acq. Operator : SYSTEM Seq. Line : 1 Acq. Instrument : LCMS Location : 42 Injection Date : 3/4/2020 3:39:33 PM Inj : 1 Inj Volume : 5.000 µl Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M Acq. Method Last changed : 3/4/2020 3:38:11 PM by SYSTEM Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M : 3/2/2020 5:44:32 PM by SYSTEM Last changed Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test Sample Info : L1 Sample-related custom fields: Name Value ------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%. Retention Mol. Weight Time (MS) MS Area or Ion 3.758 283922 331.00 I 329.90 I 3.839 8779 347.75 I 329.80 I 327.80 I 8751 3.891 347.80 I 327.80 I 4.829 38771 436.80 I 435.80 I MSD3 SPC, time=3.729:3.797 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L1,D MM-APCI, Neg, Fa Max: 35669 329.9 30000 20000 331.0 10000 0 250 100 150 200 300 350 400 450

Figure: S17: LC-MS report of compound 5b.

5000 0

100

150

200

250

300

350

400

450

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L2.D Sample Name: L2

```
_____
Acq. Operator : SYSTEM
                                           Seq. Line : 2
                                            Location : 43
Acq. Instrument : LCMS
Injection Date : 3/4/2020 3:50:41 PM
                                                Inj: 1
                                          Inj Volume : 5.000 μl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 \mu l
             : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M
Acq. Method
             : 3/4/2020 3:49:45 PM by SYSTEM
Last changed
                (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 In<del>f</del>o
              : Sulfa drug OQ/PV \, Method for the G6120B Quadrupole LC/MS System \,
               MM-ES Positive Ion Sensitivity Test
Sample Info
             : L2
Sample-related custom fields:
Name
                           Value
-----
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%.
Retention
                         Mol. Weight
Time (MS)
             MS Area
                         or Ion
  4.205
              296116
                          365.80 I
                          364.85 I
                          363.80 I
             1293902
                          383.95 I
  4.347
                          383.00 I
                          381.80 I
                          364.80 I
      MSD3 SPC, time=4.172:4.240 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L2.D MM-APCI, Neg, Fa
                                                                             Max: 25352
                                                           363.8
 20000
 15000
 10000
                                                           366.8
                                                                             461.7
```

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 Inj: 1 Injection Date : 3/4/2020 4:01:50 PM 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: Value Name ------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 Mol. Weight Time (MS) MS Area or Ion 465.80 I 3.883 150577 464.80 I 376.80 I 3.919 112787 464.80 I 377.80 I 376.80 I 4.051 418266 395.80 I 394.80 I 377.60 I 352.80 I 351.80 I 308.80 I 306.75 I MSD1 SPC, time=3.844:3.903 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L3.D MM-APCI, Pos, Fa Max: 021523 20000 464 15000 165.8 376.8 10000 5000 0 250 350 400 450 100 150 200 300

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 Seq. Line : 4 Acq. Instrument : LCMS Location : 45 Inj: 1 Injection Date : 3/4/2020 4:12:59 PM 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 : 3/2/2020 5:44:32 PM by SYSTEM Last changed Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test

Sample Info : L4

100000

50000 0

Sample-related custom fields:

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



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min

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Figure: S20: HPLC report of compound 5d.



	Aethe	er Industrie	es Ltd	
Sample ID : L4	Instruent ID	: QCI04 (Offline)		
Inj Vol : 1µl				
Vial No : 45				
Method : D:\H	IPLC DATA\2020\Mar	ch\Method\MD\SP Uni-	-FA.met	
Data File : D:\H	IPLC DATA\2020\Mar	ch\Result\QCI04\04032	020\L4.dat	
Acquired : 04/0	3/2020 19:31:23 (GMT	7+05:30)		
DAD: S	ignal A. 254.0 nm/Bw:4.0 nm			
400 L4	·····			400
Retention	ime			-
200 -				- 200 E
£29	153 167			
	3.0 3.8			-
0				0
0	2 4	6	8 10	12
DAD, Signal A		Minutes		
DAD: Signal A, 254.0 nm/Bw:4.0				
234.0 IIII/DW.4.0 nm Results				
Peak Number	RT	Area	Area %	Name
1	1.37	53282	0.03	. (white
2	1.50	92229	0.05	
3	3.05	162604	0.08	
4	3.61	199815557	98.77	L4
5	3.91	282440	0.14	
6	3.96	1893121	0.94	
Totala				
TOTAIS		202299233	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 -----Acq. Operator : SYSTEM Seq. Line : 4 Acq. Instrument : LCMS Location : 45 Inj: 1 Injection Date : 3/4/2020 4:12:59 PM 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 : 3/2/2020 5:44:32 PM by SYSTEM Last changed 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: Value Name ------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=3.705:3.773 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L4.D MM-APCI, Neg, Fa 359.8 100000 361.0 50000 0 100 150 200 250 300 350 400 450 m/z

*** 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 Inj: 1 Injection Date : 3/4/2020 4:24:09 PM 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 4:23:14 PM by SYSTEM (modified after loading) Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M : 3/2/2020 5:44:32 PM by SYSTEM Last changed Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test

Sample Info : L5

Sample-related custom fields:





Figure: S23: HPLC report of compound 5e.



		Aethe	r Industrie	<u>es Ltd</u>			
Sample ID Inj Vol Vial No Method Data File Acquired	: L5 : 1μl : 46 : D:\HPLC : D:\HPLC : 04/03/202	Instruent ID DATA\2020\MarcH DATA\2020\MarcH 0 19:44:46 (GMT -	: QCI04 (Offline) h\Method\MD\SP Uni h\Result\QCI04\04032 +05:30)	-FA.met 2020\L5.dat			
150	DAD: Signal A, L5 Retention Time	254.0 nm/Bw:4.0 <u>, np</u>			- 150		
100 -					- 100 F		
50	1.353	327 4.233 4.493			- 50		
0					0		
0	2	4	6 Minutes	8	10 12		
DAD: 254.0 m n	DAD: Signal A, 254.0 nm/Bw:4.0 nm Results						
Peak N	lumber	RT	Area	Area %	Name		
	1	1.35	76935	0.10			
2	2	3.93	77227417	98.57	L5		
2	3 4	4.23 4.49	920248 121160	1.17 0.15			
То	tals		78345760	100.00			

Figure: S24: LCMS 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 Inj: 1 Injection Date : 3/4/2020 4:24:09 PM 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 4:23:14 PM by SYSTEM (modified after loading) Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M : 3/2/2020 5:44:32 PM by SYSTEM Last changed Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test Sample Info : L5 Sample-related custom fields: Value Name -----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 4.031 606430 345.00 I 343.95 I MSD4 SPC, time=4.003:4.071 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L5.D MM-APCI, Neg, Fa Max: 77491 344.0 60000 345.0 40000 20000 0 100 150 200 250 300 350 400 450 500 m/z

*** End of Report ***

Figure: S25: LC report of compound 5f.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L6.D Sample Name: L6

-----Acq. Operator : SYSTEM Seq. Line : 6 Acq. Instrument : LCMS Location : 47 Inj: 1 Injection Date : 3/4/2020 4:35:19 PM 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 4:34:24 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 G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test

Sample Info : L6

0

Sample-related custom fields:



6

mir

min

9

8

Figure: S26: HPLC report of compound 5f.



	Aeth	er Industrie	es Ltd	
Sample ID:L6Inj Vol:1µlVial No:47Method:D:\IData File:D:\IAcquired:04/0	Instruent ID HPLC DATA\2020\Ma HPLC DATA\2020\Ma 03/2020 19:58:06 (GM	: QCI04 (Offline) rch\Method\MD\SP Un rch\Result\QCI04\04032 T +05:30)	i-FA.met 2020\L6.dat	
0 0	Signal A, 254.0 nm/Bw:40.4m Time <u> <u> <u> </u> <u></u></u></u>	6 Minutes	8	600 400 200 10 12
DAD: Signal A, 254.0 nm/Bw:4.0				
nm Results				
Peak Number	RT	Area	Area %	Name
1	3.05	118786	0.04	
2	3.63	354838	0.11	
3	3.78	318974440	99.58	L6
4 4.01 859275 0.27				
Totals		320307339	100.00	

Figure: S27: LCMS report of compound 5f.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L6.D Sample Name: L6 -----Acq. Operator : SYSTEM Seq. Line : 6 Acq. Instrument : LCMS Location : 47 Inj: 1 Injection Date : 3/4/2020 4:35:19 PM 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 4:34:24 PM by SYSTEM (modified after loading) Analysis Method : C:\Chem32\1\Methods\MS-Washing-30min.M : 3/2/2020 5:44:32 PM by SYSTEM Last changed Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test Sample Info : L6 Sample-related custom fields: Value Name -----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 Mol. Weight Time (MS) MS Area or Ion 350.80 I 3.900 1763041 349.80 I MSD1 SPC, time=3.869:3.937 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L6.D MM-APCI, Pos, Fa 349.8 150000 100000 347.8 50000 0 100 150 200 250 300 350 400 450 *** End of Report ***

Figure: S28: LCMS report of compound 5g.

20000 -

150

200

250

300

350

400

450

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L7.D Sample Name: L7 -----Acq. Operator : SYSTEM Seq. Line : 7 Acq. Instrument : LCMS Location : 48 Inj: 1 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 Acq. Method : C:\Chem32\1\Data\SP University-04032020-New 2020-03-04 15-38-11\M206-FA.M Last changed : 3/4/2020 4:45:35 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 : L7 Sample-related custom fields: Value Name -----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 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 410.60 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, time=4.251:4.319 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L7.D MM-APCI, Neg, Fa Max: 60808 409.8 40000 408.8

. m∕z

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

-----Acq. Operator : SYSTEM Seq. Line : 8 Acq. Instrument : LCMS Location : 49 Inj: 1 Injection Date : 3/4/2020 4:57:41 PM 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 : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test

Sample Info : L8

Sample-related custom fields:

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




Figure: S30: HPLC report of compound 5h.





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 Inj: 1 Injection Date : 3/4/2020 4:57:41 PM 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 : 3/2/2020 5:44:32 PM by SYSTEM Last changed Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test Sample Info : L8 Sample-related custom fields: Value Name -----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 3.780 635193 361.00 I 360.00 I MSD4 SPC, time=3.756:3.816 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L8.D MM-APCI, Neg, Fa Max: 84893 360.0 80000 60000 9 40000 361 20000 0 100 150 200 250 300 350 400 *** End of Report ***

450 m/z

Figure: S32: LCMS report of compound 5i.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L9.D Sample Name: L9 -----Acq. Operator : SYSTEM Seq. Line : 9 Acq. Instrument : LCMS Location : 50 Inj: 1 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\1\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\1\Methods\MS-Washing-30min.M : 3/2/2020 5:44:32 PM by SYSTEM Last changed Method Info : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System MM-ES Positive Ion Sensitivity Test Sample Info : L9 Sample-related custom fields: Value Name -----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%. Retention Mol. Weight Time (MS) MS Area or Ion 407.00 I 4.757 310489 406.00 I 4.961 **168**97 425.00 I 423.80 I MSD3 SPC, time=4.726:4.794 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L9.D MM-APCI, Neg, Fa Max: 39784 406.0 30000 407.0 20000 10000 0 200 250 300 350 400 450 100 150

m/z

Figure: S33: LC 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 Inj: 1 Injection Date : 3/4/2020 5:20:09 PM 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 : 3/2/2020 5:44:32 PM by SYSTEM Last changed 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:

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



Figure: S34: HPLC report of compound 5j.



		Aeth	ner Industrie	es Ltd	
Sample ID	: L10	Instruent 1	ID : QCI04 (Offline)		
Inj Ŷol	: 1µl				
Vial No	: 51				
Method	: D:\HPLC	DATA\2020\M	arch\Method\MD\SP Uni	-FA.met	
Data File	: D:\HPLC	DATA\2020\M	arch\Result\QCI04\04032	2020\L10.dat	
Acquired	: 04/03/202	20 20:51:42 (GN	AT +05:30)		
-	DAD: Signal A	, 254.0 nm/Bw:4.0 pm			
	L10 Retention Time				-
400					400
D					- D
an an					200
200	73	153 127	220		200
-	,	-3.0 02∲5	4 4		-
0	~~	4			0
0	2	4	6 Minutes	8 10	12
DAD:	Signal A,				
254.0 ni	n/Bw:4.0				
n	m Results				
Peak N	umber	RT	Area	Area %	Name
1		1.37	113771	0.04	
2	2	3.05	120485	0.05	
3		3.93	57132	0.02	
4	ł	4.03	252511776	99.58	110
5	5	4.32	365361	0.14	
6)	4.64	398230	0.16	
Tot	als				
			253566755	100.00	

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 Inj: 1 Injection Date : 3/4/2020 5:20:09 PM 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 : 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: Value Name -----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 Mol. Weight Time (MS) MS Area or Ion 367.80 I 4.138 1393262 366.80 I 365.80 I 365.8 100000 75000 50000 368.8 25000 0 100 150 200 250 300 350 400 450 m/z

*** End of Report ***

Figure: S36: LC 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 Inj: 1 Injection Date : 3/4/2020 5:42:33 PM 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 : 3/2/2020 5:44:32 PM by SYSTEM Last changed 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:

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



Figure: S37: HPLC report of compound 5k.



		Aether	r Industrie	es Ltd	
Sample ID Inj Vol Vial No Method Data File Acquired	 L12 1μl 53 D:\HPLC D:\HPLC 04/03/20 	Instruent ID DATA\2020\March DATA\2020\March 20 21:18:27 (GMT +	: QCI04 (Offline) \\Method\\MD\SP Un \\Result\QCI04\0403; -05:30)	i-FA.met 2020\L12.dat	
150	DAD: Signal A	, 254.0 nm/Bw:4 <mark>,0 n</mark> m			150
100					- 100
50 0	1.373	3,793 4.033			- 50 0
 0	2	4	6 Minutes	8	10 12
DAD: 254.0 n	: Signal A, 1m/Bw:4.0 1m Results				
Peak 1	Number	RT	Area	Area %	Name
	1	1.37	79825	0.12	
	2	3.79	67538275	99.03	L12
	3	4.03	579816	0.85	
Тс	otals		68197916	100.00	

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 Inj: 1 Injection Date : 3/4/2020 5:42:33 PM 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 : 3/2/2020 5:44:32 PM by SYSTEM Last changed 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: Value Name ------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 3.912 367.75 I 519169 366.80 I 365.80 I 363.65 I 253.80 I MSD2 SPC, time=3.888:3.947 of C:\CHEM32\1\DATA\SP UNIVERSITY-04032020-NEW 2020-03-04 15-38-11\L12.D MM-APCI, Pos, F Max: 36347 365.8 253.8 30000 20000 254.8 368.8 10000 0 150 200 250 300 350 400 450 100

*** End of Report ***

m/z

Figure: S39: LC 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 0Q/PV Method for the G6120B Quadrupole LC/MS System

MM-ES Positive Ion Sensitivity Test
```

Sample Info : CB1

Sample-related custom fields:



DAI	D1 A, Sig=254,4 Ref=off (C:\CHEM3)	211DATASP UNIVE	RSITY-14112019 2019-1	1-14 18-16-00\CB1.D)		
mAU _		35				
75		8. 8.				
50 -						
25						
0						~
	2	4	6	8	10	min
MS	D2 TIC, MS File (C:\CHEM32\1\DAT	AISP UNIVERSITY-	14112019 2019-11-14 18	-16-00\CB1.D) MM-APCI	, Pos, Fast Scan, Frag	
300000		927				
200000		ب				
100000						
0-[
	2	4	6	8	10	min

Figure: S40: HPLC report of compound 7a.



Sample ID : CB1 Inj Vol : 2µl Vial No : 62 Method : D:\H Data File : D:\H Acquired : 14/1	Aethe Instruent II IPLC DATA\2019\Nov IPLC DATA\2019\Nov 1/2019 23:55:21 (GMT	er Industrie D : QCI04 (Offline) rember\Method\50 X 4.6 rember\Result\QCI04\14 Γ+05:30)	<u>es Ltd</u> 5 2.7u\MD\SP Uni-FA.: 112019\CB1.dat	met
1000 DAD: S CB1 Retention T	ignal A, 254.0 nm/Bwe40 nm			- 1000
0 000	3.333 3.333 4.433 7 4.433	6.267 6.267	3 10	0 12
DAD: Signal A		Minutes		
254.0 nm/Bw:4.0				
nm Results			5 5536	
Peak Number	RT	Area	Area %	Name
1	0.73	2056896	0.28	
2	3.50	1109607	0.51	
4	3.83	718446573	98.74	CB1
5	4.43	762509	0.10	021
6	4.76	457205	0.06	
7	5.85	668336	0.09	
8	6.27	396042	0.05	
Totals		727633504	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 \mu l
           : C:\Chem32\1\Data\SP University-14112019 2019-11-14 18-16-00\M206-FA.M
Acq. Method
             : 11/14/2019 6:29:18 PM by SYSTEM
Last changed
               (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
                          467.00 I
  3.927
             1992628
                          465.80 I
      MSD2 SPC, time=3.892:3.970 of C:\CHEM32\1\DATA\SP UNIVERSITY-14112019 2019-11-14 18-16-00\CB1.D MM-APCI, Pos, Fast
                                                                           Max: 163892
                                                  465.8
150000
100000
                                                  468.0
 50000
    0
                                       400
                                                       500
                                                                      600
        200
                        300
```

*** End of Report ***

m/z

Figure: S42: LC report of compound 7b.

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

```
.....
Acq. Operator : SYSTEM
                                            Seq. Line : 16
Acq. Instrument : LCMS
                                            Location : 56
                                                 Inj: 1
Injection Date : 1/22/2020 3:33:16 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 3:32:21 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)
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
             : CB2
Sample-related custom fields:
Name
                           Value
 Additional Info : Peak(s) manually integrated
_____
       DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB2.D)
   mAU
                                         200
    400
    200
     0
                                                                               10
       2 4 6 8 10
MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB2.D) MM-APCI, Pos, Fast Scan, Frag
                                                                                            mir
 600000
                                          847
 400000
  200000
     0.
                                                                               10
                                                                                            min
```

Figure: S43: HPLC report of compound 7b.



Aether Industries Ltd : CB2#SP University Instruent ID : QCI04 (Offline) Sample ID Inj Vol : 2µl Vial No : 56 Method : D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met : D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB2#SP University.dat Data File Acquired : 22/01/2020 22:48:22 (GMT +05:30) DAD: Signal A, 254.0 nm/Bw:4.0 nm CB2#SP University Retention Time 400 400 mAU mAU 200 200 4:433 3.247 797.1 0 0 10 0 2 4 6 8 12 Minutes DAD: Signal A, 254.0 nm/Bw:4.0 nm Results Peak Number RT Area Area % Name 3.25 203650 0.05 1 4.27 1035499 2 0.28 3 4.43 1205681 0.32 4 4.77 368629438 99.34 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

```
.....
Acq. Operator : SYSTEM
                                           Seq. Line : 16
Acq. Instrument : LCMS
                                            Location : 56
Injection Date : 1/22/2020 3:33:16 PM
                                                Inj: 1
                                          Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 \mu l
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
Last changed
             : 1/22/2020 3:32:21 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)
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
              : CB2
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
                          537.80 I
  4.847
             5722229
                          536.80 I
                          535.80 I
                          534.80 I
                          533.80 I
      MSD2 SPC, time=4.802:4.913 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB2.D MM-APCI, Pos, Fast
                                                                           Max: 218397
200000
                                                      535.8
150000
100000
                                                      531.8
 50000
    0 -
```

*** End of Report ***

400

500

600

700

m/z

300

200

Figure: S45: LC report of compound 7c.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB3.D Sample Name: CB3

```
.....
Acq. Operator : SYSTEM
                                           Seq. Line : 17
Acq. Instrument : LCMS
                                           Location : 57
                                                Inj: 1
Injection Date : 1/22/2020 3:46:27 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
             : 1/22/2020 3:45:33 PM by SYSTEM
Last changed
              (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)
             : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
              MM-ES Positive Ion Sensitivity Test
Sample Info
             : CB3
Sample-related custom fields:
Name
                          Value
------
Additional Info : Peak(s) manually integrated
_____
       DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB3.D)
   mAU
                                  80
    800
    600
    400
    200
     0
                                                                             10
       2 4 6 8 10
MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB3.D) MM-APCI, Pos, Fast Scan, Frag
                                                                                          mir
                                  3.916
 400000
  200000
     0
                                                                             10
                                                                                          min
```

Figure: S46: HPLC report of compound 7c.



Aether Industries Ltd : CB3#SP University Instruent ID : QCI04 (Offline) Sample ID Inj Vol : 2µl Vial No : 57 Method : D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met : D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB3#SP University.dat Data File Acquired : 22/01/2020 23:02:44 (GMT +05:30) DAD: Signal A, 254.0 nm/Bw:4.0 nm CB3#SP University 1000 1000 Retention Time mAU mAU 500 500 2.473 2.747 3.167 6.280 1.588 807 0 0 0 2 4 6 8 10 12 Minutes DAD: Signal A, 254.0 nm/Bw:4.0 nm Results Peak Number RT Area Area % Name 1.58 106788 0.02 1 116449 2 1.74 0.02 3 2.47 511248 0.07 4 2.75 713974 0.10 811969 5 3.17 0.12 6 3.81 696826850 99.66 7 6.28 115377 0.02 Totals 699202655 100.00

Figure: S47: LCMS report of compound 7c.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB3.D Sample Name: CB3

```
.....
Acq. Operator : SYSTEM
                                          Seq. Line : 17
Acq. Instrument : LCMS
                                           Location : 57
Injection Date : 1/22/2020 3:46:27 PM
                                               Inj: 1
                                          Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
Last changed
             : 1/22/2020 3:45:33 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)
             : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
             : CB3
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
                         556.80 I
  3.916
             3807850
                         555.80 I
      MSD2 SPC, time=3.859:3.959 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB3.D MM-APCI, Pos, Fast
                                                                          Max: 323194
                                                       555.8
300000
200000
                                                       556.8
100000
```

*** End of Report ***

400

500

600

700

300

0

200

m/z

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
                                             Seq. Line : 18
Acq. Instrument : LCMS
                                              Location : 58
                                                  Inj: 1
Injection Date : 1/22/2020 3:59:38 PM
                                            Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
            : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
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)
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
              : CB4
Sample-related custom fields:
Name
                            Value
 .----|-----
Additional Info : Peak(s) manually integrated
_____
       DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB4.D)
                                      180<sup>A.O.</sup>
   mAU
                                   3.743
    200
    100
     0
                                                                                 10
       2 4 6 8 10
MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-2201202 02020-01-22 12-13-54\CB4.D) MM-APCI, Pos, Fast Scan, Frag
                                                                                              mir
                                   .827
  400000
  200000
     0.
                      2
                                                                                 10
                                                                                              min
```

Figure: S49: HPLC report of compound 7d.



	Aethe	er Industrie	es Ltd	
Sample ID : CB4 Inj Vol : 2µl Vial No : 58	#SP University	Instruent ID : QC	CI04 (Offline)	
Data File : D:\F Acquired : 22/0	IPLC DATA\2020\Janu IPLC DATA\2020\Janu 01/2020 23:17:07 (GMT	ary\Result\QCI04\2201 1+05:30)	2020\CB4#SP Univers	ity.dat
400 DAD: CB4#5 Retention	Signal A, 254.0 nm/Bw:4.0 nm SP University Fime			- 400
Den 200	N0 KN0 (8)	70%		- 200 Pe
0	2 4 2 4 2 4 2 4 2 4 2 4 2 4 2 4	6.26 6.26 6.26 78 78 78 78 78 78 78 78 78 78 78 78 78	3 10	0
DAD: Signal A, 254.0 nm/Bw:4.0	2 7	Minutes	5	12
nm Results Book Number	рт	4	A ros 9/	Namo
1	1.23	4839605	1 77	Name
2	2.27	1407902	0.52	
3	2.48	240476	0.09	
4	2.75	127174	0.05	
5	2.95	489782	0.18	
6	3.16	422872	0.15	
7	3.73	262931045	96.24	
8	4.12	891607	0.33	
9	4.20	1072338	0.39	
10	5.87	397586	0.15	
11	6.04	227911	0.08	
12	6.27	151132	0.06	
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
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
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)
             : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               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
                        Mol. Weight
Time (MS)
             MS Area
                        or Ion
  3.827
             4320049
                         526.90 I
                         525.80 I
      MSD2 SPC, time=3.781:3.881 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB4.D MM-APCI, Pos, Fast
                                                                          Max: 324621
                                                      525.8
300000
200000
100000
                                                      527.9
```

*** End of Report ***

400

500

600

700

m/z

300

0

200

Figure: S51: LC report of compound 7e.

Data File C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB5.D Sample Name: CB5

```
.....
Acq. Operator : SYSTEM
                                             Seq. Line : 19
Acq. Instrument : LCMS
                                              Location : 59
                                                  Inj: 1
Injection Date : 1/22/2020 4:12:54 PM
                                            Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
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)
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
                MM-ES Positive Ion Sensitivity Test
Sample Info
              : CB5
Sample-related custom fields:
Name
                            Value
 -----|-----|------
Additional Info : Peak(s) manually integrated
_____
        DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB5.D)
                                          see. 2059.16
   mAU
                                         .623
    300
    200
    100
     0
                                                                                 10
        2 4 6 8 10
MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-2201202 02020-01-22 12-13-54\CB5.D) MM-APCI, Pos, Fast Scan, Frag
                                                                                               mir
  600000
                                          1716
  400000
  200000
     0
                                                                                 10
                                     4
                                                                                               min
```

Figure: S52: HPLC report of compound 7e.



Aether Industries Ltd : CB5#SP University Instruent ID : QCI04 (Offline) Sample ID Inj Vol : 2µl Vial No : 59 Method : D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB5#SP University.dat Data File : Acquired : 22/01/2020 23:31:29 (GMT +05:30) DAD: Signal A, 254.0 nm/Bw:4.0 nm CB5#SP University 400 400 Retention Time mAU mAU 200 200 1.447 3.420 4.380 7.000 2.960 0 0 0 2 4 6 8 10 12 Minutes DAD: Signal A, 254.0 nm/Bw:4.0 nm Results Peak Number RT Area Area % Name 1.45 1603852 0.52 1 499660 2 2.96 0.16 3 3.42 520939 0.17 4 4.38 439523 0.14 5 302189660 98.79 4.62 6 7.00 651332 0.21 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\CB5.D Sample Name: CB5

```
.....
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
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
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)
             : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
             : CB5
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
  4.716
             5116771
                         494.95 I
                         493.80 I
      MSD2 SPC, time=4.658:4.769 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB5.D MM-APCI, Pos, Fast
                                                                          Max: 330903
                                              493.8
300000
200000
                                               496.0
100000
```

*** End of Report ***

400

500

600

700

300

0

200

m/z

Figure: S54: LC report of compound 7f.

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

```
.....
Acq. Operator : SYSTEM
                                           Seq. Line : 20
Acq. Instrument : LCMS
                                            Location : 60
Injection Date : 1/22/2020 4:26:05 PM
                                                Inj: 1
                                          Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
           : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
             : 1/22/2020 4:25:11 PM by SYSTEM
Last changed
                (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)
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
             : CB6
Sample-related custom fields:
Name
                           Value
------
Additional Info : Peak(s) manually integrated
_____
       DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB6.D)
                                     ea: 2704.31
   mAU
    400
    200
     0
       2 4 6 8 10
MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB6.D) MM-APCI, Pos, Fast Scan, Frag
                                                                                           mir
                                    4.119
 600000
 400000
 200000
     0 -
                                                                              10
                     5
                                                                                           min
```

Figure: S55: HPLC report of compound 7f.



	Aeth	er Industrie	es Ltd	
Sample ID:CInj Vol:2Vial No:6Method:1Data File:1Acquired:2	2B6#SP University 4µl 00 D:\HPLC DATA\2020\Jar D:\HPLC DATA\2020\Jar 22/01/2020 23:45:52 (GM	Instruent ID : QC nuary\Method\MD\SP Ur nuary\Result\QCI04\2201 IT +05:30)	CI04 (Offline) hi-FA.met 2020\CB6#SP Univers	ity.dat
500 - Retenti	AD: Signal A, 254.0 nm/Bw:4.0 nm B6#SP University on Time			- 500
	7.27.7 3.040 3.040 3.040 3.040 4.033 4.033 4.033	6 Minutes	8 10	0
DAD: Signal	Α,	Winutes		
254.0 nm/Bw:4	.0			
254.0 nm/Bw:4 nm Resu Book Number	.0 lts PT	A 100	A rog 9/	Namo
254.0 nm/Bw:4 nm Resu Peak Number	.0 lts 1 29	Area	Area %	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2	.0 lts 1.29 1.39	Area 151966 354255	Area % 0.04 0.09	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3	.0 Its <u>RT</u> 1.29 1.39 2.47	Area 151966 354255 181695	Area % 0.04 0.09 0.05	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4	.0 Its <u>RT</u> 1.29 1.39 2.47 2.73	Area 151966 354255 181695 131381	Area % 0.04 0.09 0.05 0.03	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5	.0 Its <u>RT</u> 1.29 1.39 2.47 2.73 3.04	Area 151966 354255 181695 131381 357397	Area % 0.04 0.09 0.05 0.03 0.09	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6	.0 Its <u>RT</u> 1.29 1.39 2.47 2.73 3.04 3.53	Area 151966 354255 181695 131381 357397 118106	Area % 0.04 0.09 0.05 0.03 0.09 0.03	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7	.0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71	Area 151966 354255 181695 131381 357397 118106 83416	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7 8	.0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71 4.03	Area 151966 354255 181695 131381 357397 118106 83416 395687459	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02 99.48	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7 8 9	.0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71 4.03 4.85	Area 151966 354255 181695 131381 357397 118106 83416 395687459 62560	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02 99.48 0.02	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7 8 9 10	.0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71 4.03 4.85 4.96	Area 151966 354255 181695 131381 357397 118106 83416 395687459 62560 59232	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02 99.48 0.02 0.01	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7 8 9 10 11	.0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71 4.03 4.85 4.96 5.29	Area 151966 354255 181695 131381 357397 118106 83416 395687459 62560 59232 79810	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02 99.48 0.02 0.01 0.02	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7 8 9 10 11 12	.0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71 4.03 4.85 4.96 5.29 5.35	Area 151966 354255 181695 131381 357397 118106 83416 395687459 62560 59232 79810 104893	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02 99.48 0.02 0.01 0.02 0.01 0.02 0.03	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7 8 9 10 11 12 13	0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71 4.03 4.85 4.96 5.29 5.35 5.88	Area 151966 354255 181695 131381 357397 118106 83416 395687459 62560 59232 79810 104893 88964	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02 99.48 0.02 0.01 0.02 0.01 0.02 0.03 0.02	Name
254.0 nm/Bw:4 nm Resu Peak Number 1 2 3 4 5 6 7 8 9 10 11 12 13 14	.0 Its RT 1.29 1.39 2.47 2.73 3.04 3.53 3.71 4.03 4.85 4.96 5.29 5.35 5.88 6.19	Area 151966 354255 181695 131381 357397 118106 83416 395687459 62560 59232 79810 104893 88964 289507	Area % 0.04 0.09 0.05 0.03 0.09 0.03 0.02 99.48 0.02 0.01 0.02 0.01 0.02 0.03 0.02 0.07 0.03 0.02 0.07 0.02 0.07 0.02 0.03 0.02 0.07 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.03 0.07 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.02 0.07 0.07 0.02 0.07 0.0	Name

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

```
.....
Acq. Operator : SYSTEM
                                          Seq. Line : 20
Acq. Instrument : LCMS
                                           Location :
                                                      60
Injection Date : 1/22/2020 4:26:05 PM
                                               Inj: 1
                                          Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
             : 1/22/2020 4:25:11 PM by SYSTEM
Last changed
               (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)
             : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
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
                         502.80 I
  4.119
             6321377
                         501.80 I
      MSD2 SPC, time=4.070:4.181 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB6.D MM-APCI, Pos, Fast
                                                                          Max: 415843
400000
                                               501.8
300000
200000
                                               499.8
100000
```

*** End of Report ***

400

500

600

700

300

0

200

m/z

Figure: S57: LC 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
                                               Seq. Line : 21
Acq. Instrument : LCMS
                                               Location : 61
                                                    Inj: 1
Injection Date : 1/22/2020 4:39:15 PM
                                              Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 \mu l
              : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
              : 1/22/2020 4:38:21 PM by SYSTEM
Last changed
                 (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)
               : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
                MM-ES Positive Ion Sensitivity Test
Sample Info
               : CB7
Sample-related custom fields:
Name
                             Value
------
Additional Info : Peak(s) manually integrated
_____
        DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB7.D)
                                              Nea: 21,602
    mAU
                                              .963
    300
    200
    100
     0
                                                                                    10
                                                                                                  min

        2
        4
        6
        8
        10

        MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB7.D)
        MM-APCI, Pos, Fast Scan, Frag

                                              5.050
  400000
  200000
      0
                                                                                    10
                                                                                                  min
```

Figure: S58: HPLC report of compound 7g.



Aether Industries Ltd : CB7#SP University Instruent ID : QCI04 (Offline) Sample ID Inj Vol : 2µl Vial No : 61 Method : D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met : D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB7#SP University.dat Data File Acquired : 23/01/2020 00:00:12 (GMT +05:30) DAD: Signal A, 254.0 nm/Bw:4.0 nm CB7#SP University 400 400 Retention Time mAU mAU 200 200 4.033 3.353 6.273 967 0 0 0 2 4 6 8 10 12 Minutes DAD: Signal A, 254.0 nm/Bw:4.0 nm Results Peak Number RT Area Area % Name 3.35 50049 0.02 1 81288 2 4.03 0.03 3 4.46 98871 0.04 4 4.97 280783304 99.88 5 6.27 97903 0.03 Totals 281111415 100.00

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
                                           Seq. Line : 21
Acq. Instrument : LCMS
                                            Location : 61
Injection Date : 1/22/2020 4:39:15 PM
                                                 Inj: 1
                                          Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 \mu l
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
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)
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
              : CB7
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
   5.050
             3944078
                          626.60 I
                          625.60 I
                          624.70 I
                          623.60 I
                          622.60 I
                          621.60 I
      MSD2 SPC, time=5.002:5.102 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB7.D MM-APCI, Pos, Fast
                                                                            Max: 157510
                                                              626.6 626.28.6
150000
100000
 50000
    0
        200
                     300
                                 400
                                              500
                                                           600
                                                                       700
                                                                                    800 m/z
```

*** End of Report ***

Figure: S60: LC 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
                                            Seq. Line : 22
Acq. Instrument : LCMS
                                            Location : 62
Injection Date : 1/22/2020 4:52:24 PM
                                                 Inj: 1
                                           Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 \mu l
           : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
             : 1/22/2020 4:51:32 PM by SYSTEM
Last changed
                (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)
              : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
              : CB8
Sample-related custom fields:
Name
                           Value
------
Additional Info : Peak(s) manually integrated
_____
       DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB8.D)
                                     3901.27
   mAU
600
    400
    200
     0
       2 4 6 8 10
MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB8.D) MM-APCI, Pos, Fast Scan, Frag
                                                                                            mir
  800000 -
                                   3.939
 600000
 400000 -
 200000
     0 -
                                                                               10
                                                                                            min
```

Figure: S61: HPLC report of compound 7h.



	Aeth	er Industrie	es Ltd	
Sample ID : CB8 Inj Vol : 2µl	8#SP University	Instruent ID : QC	CI04 (Offline)	
Vial No : 62				
Method : D:\	HPLC DATA\2020\Jan	uary\Method\MD\SP Un	ni-FA.met	
Data File : D:\	HPLC DATA\2020\Janı	uary\Result\QCI04\2201	2020\CB8#SP Univers	ity.dat
Acquired : 23/	01/2020 00:14:33 (GM)	Г +05:30)		
750 - DAD: CB8#	Signal A, 254.0 nm/Bw:4.0 nm SP University			- 750
Retention	Time			-
500 -				- 500
mAU T				U MAU
250	93			- 250
1.2	2.6(3.24 4.49	400 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		-
0				0
<u> </u>				
0	2 4	6 Minutes	5 10	12
DAD: Signal A.				
254.0 nm/Bw:4.0				
nm Results				
Peak Number	RT	Area	Area %	Name
1	1.23	916300	0.17	
2	2.60	1756597	0.32	
3	3.25	72602	0.01	
4	3.85	548706811	99.13	
5	4.49	383380	0.07	
6	4.96	132298	0.02	
7	5.10	194416	0.04	
8	5.19	190523	0.03	
9	5.37	53876	0.01	
10	5.65	151640	0.03	
11	5.99	547986	0.10	
12	6.16	436298	0.08	
Totala				
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
                                          Seq. Line : 22
Acq. Instrument : LCMS
                                           Location : 62
Injection Date : 1/22/2020 4:52:24 PM
                                               Inj: 1
                                          Inj Volume : 1.000 µl
Different Inj Volume from Sample Entry! Actual Inj Volume : 2.000 µl
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
             : 1/22/2020 4:51:32 PM by SYSTEM
Last changed
               (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)
             : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
             : CB8
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
                         526.90 I
  3.939
             7845816
                         525.80 I
      MSD2 SPC, time=3.881:4.003 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB8.D MM-APCI, Pos, Fast
                                                                          Max: 483141
                                                      525.8
400000
300000
200000
                                                      528.0
100000
```

300 400

500

600

700

m/z

*** End of Report ***

0

200

Figure: S63: LC 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
                (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)
               : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
                MM-ES Positive Ion Sensitivity Test
Sample Info
              : CB9
Sample-related custom fields:
Name
                             Value
Additional Info : Peak(s) manually integrated
_____
        DAD1 A, Sig=254,4 Ref=off (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB9.D)
                                                      N2569.A
    mAU
                                                   5.775
   1500
   1000
    500
     0
                                                                                   10

        2
        4
        6
        8
        10

        MSD2 TIC, MS File (C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB9.D)
        MM-APCI, Pos, Fast Scan, Frag

                                                                                                 mir
                                                    .865
  400000
  200000
     0
                                                                                   10
                                                                                                 min
                                                     6
```

Figure: S64: HPLC report of compound 7i.



Aether Industries Ltd : CB9#SP University Instruent ID : QCI04 (Offline) Sample ID Inj Vol : 2µl Vial No : 63 Method D:\HPLC DATA\2020\January\Method\MD\SP Uni-FA.met : D:\HPLC DATA\2020\January\Result\QCI04\22012020\CB9#SP University.dat Data File : 23/01/2020 00:28:56 (GMT +05:30) Acquired : DAD: Signal A, 254.0 nm/Bw:4.0 nm CB9#SP University **Retention Time** 2000 2000 mAU mAU 1000 1000 1.460 3.900 2.699 3.180 3.467 4.393 4.960 5.180 5.460 793 ¥:889 8.627 0 0 0 2 4 6 8 10 12 Minutes DAD: Signal A, 254.0 nm/Bw:4.0 nm Results Peak Number RT Area Area % Name 1.46 15973285 0.95 1 942949 2 2.60 0.06 3 2.67 861794 0.05 4 351213 3.18 0.02 5 3.47 370160 0.02 6 3.90 1468987 0.09 7 4.39 2653316 0.16 4.96 245439 0.01 8 9 5.18 2160883 0.13 615815 10 5.46 0.04 11 5.79 1659459204 98.38 487405 6.52 0.03 12 13 6.72 139304 0.01 14 6.82 65032 0.00 221573 7.01 0.01 15 16 7.27 113591 0.01 17 7.78 305065 0.02 323334 18 7.87 0.02 19 8.63 57243 0.00 Totals 1686815592 100.00

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
             : C:\Chem32\1\Data\SP University-22012020 2020-01-22 12-13-54\M206-FA.M
Acq. Method
Last changed
             : 1/22/2020 5:04:42 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)
             : Sulfa drug OQ/PV Method for the G6120B Quadrupole LC/MS System
Method Info
               MM-ES Positive Ion Sensitivity Test
Sample Info
             : CB9
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
                         618.90 I
   5.865
             4365161
                         617.80 I
      MSD2 SPC, time=5.812:5.922 of C:\CHEM32\1\DATA\SP UNIVERSITY-22012020 2020-01-22 12-13-54\CB9.D MM-APCI, Pos, Fast
                                                                          Max: 278342
                                                                   617.8
200000
                                                                   620.0
100000
```

*** End of Report ***

400

500

600

700

m/z

300

0 -

200
Figure S66: ¹H-NMR Spectra of Compound 5a.









Figure S68: ¹H-NMR Spectra of Compound 5b.







Figure S69: Extended ¹H-NMR Spectra of Compound 5b.





Figure S71: ¹³C-NMR Spectra of Compound 5c.





Figure S72: ¹H-NMR Spectra of Compound 5d.







Figure S73: ¹³C-NMR Spectra of Compound 5d.

Figure S74: ¹H-NMR Spectra of Compound 5e.







Figure S75: Extended ¹H-NMR Spectra of Compound 5e.





Figure S77: ¹H-NMR Spectra of Compound 5f.









Figure S79: ¹H-NMR Spectra of Compound 5g.









Figure S81: ¹H-NMR Spectra of Compound 5h.







Figure S82: ¹³C-NMR Spectra of Compound 5h.

Figure S83: ¹H-NMR Spectra of Compound 5i.













Figure S86: ¹H-NMR Spectra of Compound 5j.









Figure S88: ¹H-NMR Spectra of Compound 5k.









Figure S90: ¹H-NMR Spectra of Compound 7a.





Figure S91: Extended ¹H-NMR Spectra of Compound 7a.







Figure S93: ¹H-NMR Spectra of Compound 7b.





Figure S94: ¹³C-NMR Spectra of Compound 7b.



Figure S95: ¹H-NMR Spectra of Compound 7c.





Figure S96: ¹³C-NMR Spectra of Compound 7c.



Figure S97: ¹H-NMR Spectra of Compound 7d.









.





Figure S100: ¹H-NMR Spectra of Compound 7e.





Figure S101: ¹³C-NMR Spectra of Compound 7e.


Figure S102: ¹H-NMR Spectra of Compound 7f.





Figure S103: ¹³C-NMR Spectra of Compound 7f.



Figure S104: ¹H-NMR Spectra of Compound 7g.









Figure S106: ¹³C-NMR Spectra of Compound 7h.





Figure S107: ¹H-NMR Spectra of Compound 7i.





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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 (3(a-k), 1.0 mmol and 3(a-i), 2.0 mmol).

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 (%) = $[(0.26\text{gm})/(0.133\text{gm}+0.128\text{gm}+0.106\text{gm})] \times 100 = 70.84\%$

✓ OE (%) = RME/ AE x 100

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

 \checkmark 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:

Sr.	Product (5(a-k))	E-factor	AE (%)	RME (%)	OE (%)	AEF (%)
No.						
1	5a	0.41	90.19	70.84	78.54	72.15
2	5b	0.25	91.03	79.80	87.66	70.22
3	5c	0.47	91.26	68.0	74.51	69.35
4	5d	0.24	90.93	80.60	88.63	80.92
5	5e	0.36	90.81	73.49	80.92	74.46
6	5f	0.60	90.65	62.33	68.76	63.45
7	5g	0.49	91.92	67.26	73.17	68.02
8	5h	0.41	90.93	70.53	77.56	72.74
9	5i	0.38	91.87	72.23	76.62	71.65
10	5j	0.74	91.03	57.36	63.01	58.25
11	5k	0.33	91.03	74.81	82.18	75.55

Table S5:

Sr.	Product (7(a-i))	E-factor	AE (%)	RME (%)	OE (%)	AEF (%)
No.						
1	7a	0.25	96.67	79.84	82.59	82.16
2	7b	0.29	93.70	77.19	82.38	77.77
3	7c	0.20	93.91	82.91	88.29	82.64
4	7d	0.17	93.58	85.56	91.43	85.15
5	7e	0.26	93.19	79.39	85.19	79.21
6	7f	0.38	93.29	72.63	77.85	71.83
7	7g	0.56	94.54	63.73	67.41	64.28
8	7h	0.19	93.58	83.78	89.53	84.22
9	7i	0.28	94.49	78.10	82.65	77.48