Supplementary information

Table S1. Crystal data and structure refinement of crystals **1** and **2.**

	1	**2**
Crystal data		
Chemical formula	$C_{14}H_{20}ClN_3O_3S$	$C_{28}H_{42}Cl_2N_6O_7S_2$
Moiety formula	$C_{14}H_{20}ClN_3O_3S$	$(C_{14}H_{20}ClN_3O_3S)_2 \cdot H_2O$
Melting point	248.3 °C	251.3 °C
M_r	345.84	709.69
Colour / Shape	Colourless / Needle	Colourless / Prism
Crystal size (mm)	0.5 x 0.1 x 0.1	0.5 x 0.2 x 0.1
Crystal system, space group	Monoclinic, $P2_1/n$	Monoclinic, $C2/c$
Z, Z'	8, 2	4, 1
a (Å)	18.7914(4)	14.5166(8)
b (Å)	9.2921(4)	9.3747(7)
c (Å)	19.0621(4)	24.7064(17)
α (°)	90	90
β (°)	99.322(7)	100.965(2)
γ (°)	90	90
V (Å^3)	3284.51(18)	3300.9(4)
D_x (Mg m^{-3})	1.399	1.428
Radiation type	Cu-Kα	Mo-Kα
μ (mm $^{-1}$)	3.389	0.377
Temperature (K)	128(2)	103(2)
F(000)	1456	1496
T_{min}, T_{max}	0.919, 0.978	0.8179, 0.9450
θ–range for data collection (°)	$3.063 \le \theta \le 68.225$	$3.028 \le \theta \le 27.485$
Index ranges	$-22 \le h \le 22$;$-11 \le k \le 10$;	$-18 \le h \le 18$;$-12 \le k \le 12$;
Reflections collected	42764	45688
Completeness to 2θ	0.988	0.998
Independent reflections	5936	3762
R_{int}	0.0740	0.0564
Reflections $I>2\sigma(I)$	5039	3253
Data / restraints / parameters	5936 /0 /401	3762 /0 /210
Goodness-of-fit on *F*2	1.214	1.055
Final *R* indices [$I>2\sigma(I)$]	*R*1 =0.0998, *wR*2 =0.2229	*R*1 =0.0440, *wR*2 =0.1076
R indices (all data)	*R*1 =0.1199, *wR*2 =0.2315	*R*1 =0.0510, *wR*2 =0.1122
Max. and mean shift/esd	0.000; 0.000	0.000; 0.000
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.617, -0.494	0.376, -0.412

Table S2. Comparison of bond lengths (Å) in the Clopamide molecules in crystals **1** and **2.**

1A		**1B**		**2**	
Cl1-C3	1.733(7)	Cl2-C23	1.730(7)	Cl1-C3	1.727(2)
S1-O2	1.427(5)	S2-O5	1.431(5)	S1-O2	1.436(1)
S1-C2	1.790(7)	S2-C22	1.782(7)	S1-C2	1.788(2)
S1-O1	1.416(5)	S2-O4	1.425(5)	S1-O1	1.429(1)
S1-N1	1.599(6)	S2-N2	1.605(6)	S1-N1	1.601(2)
C1-C2	1.378(9)	C21-C22	1.383(9)	C1-C2	1.393(2)
C2-C3	1.41(1)	C22-C23	1.38(1)	C2-C3	1.398(3)
C3-C4	1.38(1)	C23-C24	1.40(1)	C3-C4	1.392(3)
C4-C5	1.377(9)	C24-C25	1.372(9)	C4-C5	1.385(3)
C5-C6	1.402(9)	C25-C26	1.400(9)	C5-C6	1.393(3)
C6-C1	1.377(9)	C26-C21	1.374(9)	C6-C1	1.393(3)
C6-C7	1.493(9)	C26-C27	1.503(9)	C6-C7	1.508(3)
C7-O3	1.232(8)	C27-O6	1.222(8)	C7-O3	1.219(3)
C7-N8	1.339(9)	C27-N28	1.344(9)	C7-C8	1.338(3)
N8-N9	1.423(7)	N28-N29	1.412(7)	N8-N9	1.414(2)
N9-C10	1.475(9)	N29-C30	1.493(9)	N9-C10	1.485(3)
C10-C11	1.518(9)	C30-C31	1.53(1)	C10-C16	1.520(3)
C11-C12	1.52(1)	C31-C32	1.52(1)	C11-C12	1.505(5)
C12-C13	1.52(1)	C32-C33	1.52(1)	C12-C13	1.505(5)
C13-C14	1.53(1)	C33-C34	1.53(1)	C13-C14	1.517(4)
C14-C15	1.52(1)	C34-C35	1.51(1)	C14-C15	1.517(4)
C14-N9	1.492(9)	C34-N29	1.488(9)	C14-N9	1.491(3)
C10-C16	1.52(1)	C30-C36	1.51(1)	C10-C11	1.519(3)

Table S3. Comparison of bond angles (°) in the Clopamide molecules in crystals **1** and **2.**

1A		**1B**		**2**	
S1-O1-O2	118.2(3)	S2-O4-O5	118.1(3)	S1-O1-O2	119.06(8)
S1-O1-N1	109.2(3)	S2-O4-N2	109.3(3)	S1-O1-N1	108.37(9)
S1-O2-N1	107.8(3)	S2-O5-N2	107.6(3)	S1-O2-N1	107.53(8)
S1-N1-C2	107.7(3)	S2-N2-C22	106.1(3)	S1-N1-C2	107.20(8)
S1-O1-C2	105.1(3)	S2-O4-C22	105.6(3)	S1-O1-C2	105.27(8)
S1-O2-C2	108.4(3)	S2-O5-C22	109.6(3)	S1-O2-C2	108.87(8)
S1-C1-C2	117.1(5)	S2-C21-C22	116.9(5)	S1-C1-C2	117.2(1)
S1-C2-C3	123.8(5)	S2-C22-C23	124.0(5)	S1-C2-C3	123.7(1)
Cl1-C2-C3	121.4(5)	Cl2-C22-C23	122.2(5)	Cl1-C2-C3	121.3(1)
Cl1-C3-Cl4	118.7(5)	Cl2-C23-Cl24	117.6(5)	Cl1-C3-Cl4	118.2(2)
C1-C2-C3	119.0(6)	C21-C22-C23	119.0(6)	C1-C2-C3	119.1(2)
C2-C3-C4	119.9(6)	C22-C23-C24	120.2(6)	C2-C3-C4	120.5(2)
C3-C4-C5	120.3(6)	C23-C24-C25	119.8(6)	C3-C4-C5	120.0(2)
C4-C5-C6	120.1(6)	C24-C25-C26	120.3(6)	C4-C5-C6	120.1(2)
C5-C6-C1	119.3(6)	C25-C26-C21	118.9(6)	C5-C6-C1	119.8(2)
C6-C1-C2	121.3(6)	C26-C21-C22	121.7(6)	C6-C1-C2	120.5(2)
C1-C6-C7	121.5(6)	C21-C26-C27	122.7(6)	C1-C6-C7	121.3(2)
C5-C6-C7	119.2(6)	C25-C26-C27	118.4(6)	C5-C6-C7	118.8(2)
C6-C7-O3	121.1(7)	C26-C27-O6	121.4(6)	C6-C7-O3	121.9(2)
C6-C7-N8	114.4(6)	C26-C27-N28	113.8(6)	C6-C7-N8	114.4(2)
C7-N8-O3	124.5(6)	C27-N28-O6	124.8(6)	C7-N8-O3	123.6(2)
C7-N8-N9	120.9(6)	C27-N28-N29	121.1(6)	C7-N8-N9	121.6(2)
N8-N9-C10	107.9(5)	N28-N29-C30	107.0(5)	N8-N9-C10	107.3(2)
N8-N9-C14	107.0(5)	N28-N29-C34	108.7(5)	N8-N9-C14	107.7(2)
N9-C10-C11	109.8(6)	N29-C30-C31	108.8(6)	N9-C10-C11	109.2(2)
N9-C10-C14	111.7(6)	N29-C30-C34	113.1(6)	N9-C10-C14	111.5(2)
N9-C10-C16	110.0(6)	N29-C30-C36	111.3(6)	N9-C10-C16	110.5(2)
N9-C13-C14	109.9(6)	N29-C33-C34	108.8(6)	N9-C13-C14	108.8(2)
N9-C14-C15	111.1(6)	N29-C34-C35	110.1(6)	N9-C14-C15	110.2(2)
C10-C11-C12	112.5(6)	C30-C31-C32	112.6(6)	C10-C11-C12	112.4(2)
C10-C11-C16	110.6(6)	C30-C31-C36	110.4(6)	C10-C11-C16	111.0(2)
C11-C12-C13	109.9(7)	C31-C32-C33	109.0(7)	C11-C12-C13	110.3(2)
C12-C13-C14	110.3(6)	C32-C33-C34	110.2(6)	C12-C13-C14	111.7(2)
C11-C12-C13	109.9(6)	C33-C34-C35	111.1(6)	C13-C14-C15	112.2(3)

Table S4. Selected hydrogen, halogen and chalcogen bond distances (Å) and angles (°) in crystals **1** and **2**

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*	Symmetry codes
1					
N1—H1A···N9$^{(i)}$	0.80	2.47	3.213(9)	154	3/2–x, 1/2+y, 1/2–z
N1—H1B···*O2*$^{(ii)}$	0.87	2.13	2.942(8)	155	2–x, 1–y, 1–z
N2—H2A···O5$^{(iii)}$	0.92	2.06	2.959(7)	165	–x, –y, –z
N2—H2B···N29$^{(iv)}$	0.99	2.29	3.204(8)	153	1/2–x, –1/2+y, 1/2–z
C10-H10…Ph$_{C1-C6}$	1.00	2.56	3.544(8)	168	3/2-X,1/2+Y,1/2-Z
C15-H15A…Ph$_{C1-C6}$	0.98	3.00	3.884(9)	151	3/2-X,-1/2+Y,1/2-Z
C30-H30…Ph$_{C21-C26}$	1.00	2.50	3.466(8)	163	1/2-X,-1/2+Y,1/2-Z
C35-H35A…Ph$_{C21-C26}$	0.98	2.89	3.798(9)	154	1/2-X,1/2+Y,1/2-Z
Cl1…O2 halogen bond			3.148(6)		intra
O3…O1 chalcogen bond			3.036(7)		3/2-x,-1/2+y,1/2-z
Cl2…O5 halogen bond			3.096(4)		intra
O6…O4 chalcogen bond			3.233(7)		1/2-x,1/2+y,1/2-z
2					
N1—H1A···N9$^{(i)}$	0.84	2.33	3.094(2)	151	1/2–x, 1/2+y, 1/2–z
N1—H1B···*O2*$^{(ii)}$	0.86	2.32	3.169(2)	167	1/2–x, 1/2–y, 1–z
O7—H7A···O3$^{(i)}$	0.87	2.01	2.762(5)	145	1/2–x, 1/2+y, 1/2–z
O7—H7B···O1$^{(iii)}$	0.87	2.27	3.054(4)	150	–x, y, 1/2–z
N8—H8···O7	0.86	2.56	3.195(5)	131	
C10-H10…Ph$_{C1-C6}$	1.00	2.58	3.530(2)	159	1/2-X,1/2+Y,1/2-Z
C15-H15B…Ph$_{C1-C6}$	0.98	2.75	3.634(3)	151	1/2-X,-1/2+Y,1/2-Z
Cl1…O2 halogen bond			3.0581(16)		intra

Table S5. Crystal data and refinement parameters of crystals **3-6**

	3	**4**	**5**	**6**
Crystal data				
Chemical formula	$C_{30}H_{50}Cl_2CuN_6O_{10}S_2$	$C_{32}H_{54}Cl_2CuN_6O_{10}S_2$	$C_{34}H_{58}Cl_2CuN_6O_{10}S_2$	$C_{34}H_{58}Cl_2CuN_6O_{10}S_2$
Moiety formula	$C_{28}H_{38}Cl_2CuN_6O_6S_2\cdot(CH_4O)_2\cdot(H_2O)_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2\cdot(C_2H_6O)_2\cdot(H_2O)_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2\cdot(C_3H_8O)_2\cdot(H_2O)_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2\cdot(C_3H_8O)_2\cdot(H_2O)_2$
Melting point	No evident melting endotherm	231.8 °C	229.3 °C	239.925 °C
M_r	853.32	881.37	909.42	909.42
Colour / Shape	Brown / Prism	Brown / Prism	Brown / Platelet	Brown / Platelet
Crystal size (mm)	0.5 x 0.25 x 0.25	0.3 x 0.1 x 0.1	0.5 x 0.25 x 0.05	0.5 x 0.5 x 0.05
Crystal system, space group	Triclinic, $P\ \bar{1}$	Triclinic, $P\ \bar{1}$	Triclinic, $P\ \bar{1}$	Triclinic, $P\ \bar{1}$
Z, Z'	1, 0.5	1, 0.5	1, 0.5	1, 0.5
a (Å)	7.7518(3)	8.2195(7)	8.404(4)	8.3107(14)
b (Å)	8.0901(4)	8.2439(7)	8.497(5)	8.7469(14)
c (Å)	16.3683(7)	16.4822(14)	16.310(8)	16.387(3)
α (°)	83.1130(10)	85.598(2)	79.445(10)	79.713(5)
β (°)	78.8210(10)	78.212(2)	83.113(12)	87.099(4)
γ (°)	71.6590(10)	68.273(2)	67.366(10)	65.629(4)
V (Å^3)	953.96(7)	1015.62(15)	1055.2(10)	1067.3(3)
D_x (Mg m^{-3})	1.485	1.441	1.431	1.415
Radiation type	Mo-Kα	Mo-Kα	Mo-Kα	Mo-Kα
μ (mm $^{-1}$)	0.883	0.831	0.803	0.794
Temperature (K)	103(2)	103(2)	103(2)	103(2)
F(000)	447	463	479	479
T_{min}, T_{max}	0.7746, 0.9182	0.7534, 0.8767	0.6700, 0.9604	0.5771, 1.0000
θ–range for data collection (°)	$3.018 \le \theta \le 32.525$	$3.035 \le \theta \le 27.478$	$2.989 \le \theta \le 25.348$	$3.003 \le \theta \le 28.698$
Index ranges	$-11 \le h \le 11$;$-12 \le k \le 12$;$-24 \le l \le 24$	$-10 \le h \le 10$;$-10 \le k \le 10$;$-21 \le l \le 21$	$-10 \le h \le 10$;$-10 \le k \le 10$;$-19 \le l \le 19$	$-11 \le h \le 11$;$-11 \le k \le 11$;$-22 \le l \le 22$
Reflections collected	41399	43872	16943	51848
Completeness to 2θ	0.998	0.998	0.997	0.998
Independent reflections	6813	4634	3846	5523
R_{int}	0.0600	0.0918	0.1536	0.0884
Reflections $I>2\sigma(I)$	5424	3687	2585	4481
Data / restraints / parameters	6813 /0 /236	4634 /0 /244	3846 /0 /253	5523 /0 /368
Goodness-of-fit on *F*2	1.102	1.094	1.069	1.099
Final *R* indices [$I>2\sigma(I)$]	*R*1 =0.0472, *wR*2 =0.1021	*R*1 =0.0972, *wR*2 =0.2386	*R*1 =0.0849, *wR*2 =0.2092	*R*1 =0.0690, *wR*2 =0.1530
R indices (all data)	*R*1 =0.0684, *wR*2 =0.1284	*R*1 =0.1179, *wR*2 =0.2561	*R*1 =0.1143, *wR*2 =0.2328	*R*1 =0.0816, *wR*2 =0.1599
Max. and mean shift/esd	0.000; 0.000	0.000; 0.000	0.000; 0.000	0.000; 0.000
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.832, -0.888	1.573, -1.098	0.852, -0.963	0.644, -0.708

Table S6. Selected interatomic distances (Å) and angles (°) for the coordination sphere in crystals **3-10**

Crystal number	Distance of Cu-O3	Distance of Cu-N9	Distance of Cu-O6	Distance of Cu-N29	Angle of O3-Cu-N9	Angle of O6-Cu-N29
3	1.916(1)	2.019(2)			83.49(7)	
4	1.909(4)	1.997(6)			83.5(2)	
5	1.906(4)	1.994(6)			83.6(2)	
6	1.904(2)	2.006(4)			83.4(1)	
7	1.922(8)	2.01(1)	1.923(8)	2.02(1)	83.0(4)	83.1(4)
8A	1.878(4)	2.070(5)	1.863(4)	2.057(5)	82.6(2)	83.0(2)
8B	1.874(3)	2.072(4)			82.6(2)	
8C			1.875(4)	2.078(5)		82.6(2)
9	1.866(5)	2.041(6)			82.3(2)	
10	1.876(6)	2.061(1)			83.0(3)	

Table S7. Cell similarity indexes calculated for pairs of **3**-**6** isostructural crystals

	4	5	6
3	0.02	0.03	0.04
4	-	0.01	0.01
5	-	-	0.01

Table S8. Selected N/O-H…O/N hydrogen bond distances and angles of crystals **3-6**

	D-H (Å)	H…A (Å)	D…A (Å)	D-H…A (°)	Symmetry codes
		N1-H1A…O8			
Crystal **3**	0,84	2,11	2.883(2)	154	1–x, 1–y, –z
Crystal **4**	0,89	2,14	2.976(6)	156	1–x, –y, –z
Crystal **5**	0,91	1,93	2.807(6)	160	1–x, 1–y, –z
Crystal **6**	0.77(5)	2.10(5)	2.868(4)	175(5)	1–x, 1–y, –z
		N1-H1B…O8			
Crystal **3**	0,76	2,10	2.861(3)	172	x, –1+y, z
Crystal **4**	0,88	1,99	2.862(7)	174	
Crystal **5**	0,87	2,02	2.831(6)	155	–1+x, y, z
Crystal **6**	0.91(3)	2.15(3)	3.001(4)	156(4)	–1+x, y, z
		O8-H8…O7			
Crystal **3**	0,82	1,83	2.642(2)	170	
Crystal **4**	0,84	1,85	2.673(6)	168	x, –1+y, z
Crystal **5**	0,81	1,72	2.532(6)	176	
Crystal **6**	0,84	1,88	2.708(4)	170	
		O7-H7B….O2			
Crystal **3**	0,81	2,06	2.871(2)	173	1+x, y, z
Crystal **4**	0,84	2,13	2.915(6)	156	1+x, y, z
Crystal **5**	0,86	2,00	2.833(6)	163	x, 1+y, z
Crystal **6**	0.83(4)	2.04(5)	2.859(4)	169(4)	x, 1+y, z
		O7-H7A….N8			
Crystal **3**	0,82	2,02	2.846(3)	175	
Crystal **4**	0,84	2,02	2.857(7)	177	
Crystal **5**	0,86	2,09	2.938(6)	168	
Crystal **6**	0.84(2)	2.05(2)	2.885(4)	173(4)	

Table S9. Crystal data and refinement parameters of crystals **7-10**

	7	**8**	**9**	**10**
Chemical formula	$C_{28}H_{38}Cl_2CuN_6O_6S_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2$	$C_{30}H_{42}Cl_6CuN_6O_{10}S_2$
Moiety formula	$C_{28}H_{38}Cl_2CuN_6O_6S_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2$	$C_{28}H_{38}Cl_2CuN_6O_6S_2 \cdot (CH_2Cl_2)_2$
Melting point	222.6 °C	245.4 °C	240.4 °C	-
M_r	753.20	753.20	753.20	923.05
Colour / Shape	Brown / Chunk	Brown / Chunk	Brown / Chunk	Brown / Prism
Crystal size (mm)	0.2 x 0.1 x 0.05	0.1 x 0.1 x 0.1	0.1 x 0.1 x 0.05	0.25 x 0.15 x 0.1
Crystal system, space group	Triclinic, $P\ \bar{1}$	Triclinic, $P\ \bar{1}$	Trigonal, $R\ \bar{3}$	Monoclinic, $C2/c$
Z, Z'	2	4	9	4
a (Å)	7.8247(14)	13.4600(10)	23.078(3)	26.699(2)
b (Å)	13.829(2)	15.2424(11)	23.078(3)	9.8941(8)
c (Å)	15.156(3)	18.1855(16)	18.3291(12)	15.6876(14)
α (°)	78.981(4)	114.627(6)	90	90
β (°)	81.309(4)	93.362(8)	90	104.750(7)
γ (°)	85.041(4)	90.021(6)	120	90
V (Å^3)	1588.5(5)	3384.5(5)	8454(2)	4007.5(6)
D_x (Mg m^{-3})	1.575	1.478	1.331	1.530
Radiation type	Mo-Kα	Mo-Kα	Cu-Kα	Cu-Kα
μ (mm $^{-1}$)	1.040	0.976	3.544	5.833
Temperature (K)	103(2)	123(2)	153(2)	128(2)
F(000)	782	1564	3519	1900
T_{min}, T_{max}	0.7778, 0.9414	0.970, 0.987	0.962, 0.982	0.783, 0.892
θ–range for data collection (°)	$2.984 \le \theta \le 25.349$	$3.033 \le \theta \le 25.308$	$3.272 \le \theta \le 68.152$	$3.424 \le \theta \le 68.186$
Index ranges	$-9 \le h \le 9$;$-16 \le k \le 16$;$-18 \le l \le 18$	$-16 \le h \le 16$;$-18 \le k \le 18$;$-21 \le l \le 21$	$-26 \le h \le 26$;$-26 \le k \le 27$;$-21 \le l \le 20$	$-32 \le h \le 32$;$-11 \le k \le 11$;$-18 \le l \le 18$
Reflections collected	20566	51524	18855	24441
Completeness to 2θ	0.998	0.997	0.998	0.999
Independent reflections	5798	12256	3429	3661
R_{int}	0.1852	0.1301	0.1176	0.0901
Reflections $I>2\sigma(I)$	3000	7883	1580	2601
Data / restraints / parameters	5798 /0 /410	12256 /0 /822	3429 /0 /207	3661 /0 /234
Goodness-of-fit on F^2	1.111	1.054	1.094	1.151
Final *R* indices [$I>2\sigma(I)$]	*R*1 =0.1495, *wR*2 =0.3073	*R*1 =0.0777, *wR*2 =0.1198	*R*1 =0.1033, *wR*2 =0.1672	*R*1 =0.1231, *wR*2 =0.2351
R indices (all data)	*R*1 =0.2415, *wR*2 =0.3583	*R*1 =0.1375, *wR*2 =0.1366	*R*1 =0.2142, *wR*2 =0.2052	*R*1 =0.1623, *wR*2 =0.2539
Max. and mean shift/esd	0.000; 0.000	0.001; 0.000	0.000; 0.000	0.000; 0.000
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.205, -0.647	0.564, -0.576	0.553, -0.264	0.887, -0.619

Table S10. Comparison of molecular conformations: root-mean-square deviation (rmsD) values (Å) of [CuL_2] complexes (high similarity values are marked with gray).

Cryst. Nr.	**3**	**4**	**5**	**6**	**7**	**8A**	**8B**	**8C**	**9**	**10**
3		0.0889	0.1599	0.1538	0.6089	0.8649	0.8212	0.8418	0.8257	0.9978
4			0.1183	0.0826	0.6199	0.8647	0.8124	0.8453	0.8139	0.9879
5				0.1008	0.6481	0.8659	0.7930	0.8372	0.7937	0.9712
6					0.6393	0.8728	0.8107	0.8522	0.8081	0.9819
7						1.0187	1.0246	1.0284	1.0312	0.9168
8A							0.2434	0.1878	0.2516	0.5737
8B								0.1635	0.0777	0.6500
8C									0.1878	0.5142
9										0.6771

Table S11. Comparison of molecular conformations: maximum atomic distance (maxD) values (Å) of [CuL_2] complexes (high similarity values are marked with gray).

Cryst. Nr.	**3**	**4**	**5**	**6**	**7**	**8A**	**8B**	**8C**	**9**	**10**
3		0.1765	0.2569	0.2419	3.0863	2.1343	2.1284	2.0599	2.1563	2.7058
4			0.2427	0.1489	3.1388	2.0892	2.0693	2.0054	2.0969	2.7780
5				0.2380	3.2499	2.0264	1.9893	1.9314	2.0164	2.8848
6					3.2371	2.0564	2.0149	1.9579	2.0421	2.8888
7						2.4873	2.7187	2.6089	2.8167	2.8209
8A							0.5322	0.3915	0.5907	1.3423
8B								0.3301	0.1941	1.4561
8C									0.3210	1.1943
9										1.4488

Table S12. Selected hydrogen bond distances (Å) and angles (°) in crystals **7**-**10**

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*	Symmetry codes
7					
N1—H1A···O2	0.79	2.18	2.934(15)	161	–x, –y, 1–z
N1—H1B···N8	0.89	2.51	3.350(16)	157	–1+x, y, z
N2—H2B···O4	0.71	2.29	2.916(15)	147	–x, –y, –z
8					
C13-H13B…O6	0.99	2.43	3.184(8)	133	
C11-H11B…O6	0.99	2.37	3.128(8)	133	
C33-H33B…O3	0.99	2.34	3.082(8)	131	
C31-H11A…O3	0.99	2.44	3.168(8)	130	
C13'-H13C'…O3'	0.99	2.34	3.117(8)	135	1–x, 1–y, –z
C11'-H11D…O3'	0.99	2.46	3.196(8)	131	1–x, 1–y, –z
C33'-H33D…O6'	0.99	2.42	3,195(9)	135	1–x, 1–y, –z
C31'-H31C'…O6'	0.99	2.55	3.284(9)	131	1–x, 1–y, –z
N1—H1A···O5	0.93	2.13	2.990(6)	154	x, 1+y, 1+z
N1—H1B···*N28'*	0.79	2.43	3.195(7)	163	1–x, 1–y, 1–z
N2—H2A···O4	0.86	2.18	3.032(7)	173	2–x, –1–y, –z
N2—H2B···O2	0.88	2.11	2.971(6)	165	x, –1+y, –1+z
N1'—H1'A···*O2'*	0.79	2.16	2.901(6)	156	1–x, 2–y, 1–z
N1'—H1'B···*N8*	0.84	2.06	2.895(7)	169	x, 1+y, z
N2'—H2'A···N8'	0.87	2.19	3.012(7)	165	1–x, 1–y, –z
N2'—H2'B···O5'	0.81	2.18	2.929(6)	155	1–x, –y, 1–z
9					
C13-H13A…O3	0.99	2.40	3.140(14)	131	2/3–x, 1/3–y, –2/3–z
C11-H11B…O3	0.99	2.31	3.085(12)	135	2/3–x, 1/3–y, –2/3–z
N1—H1A···O2	0.94	1.95	2.882(7)	172	2/3–x, 1/3–y, 1/3–z
N1—H1B···N8(	0.92	2.03	2.926(12)	163	2/3–x+y, 1/3–x, 1/3+z
10					
C13-H13A…O3	0.99	2.59	3.340(19)	132	1/2–x, 1/2–y, –z
C11-H11B…O3	0.99	2.57	3.306(17)	131	1/2–x, 1/2–y, –z
N1—H1A···O2	0.88	2.39	2.995(12)	126	x, –y, 1/2+z
N1—H1B···N8	0.88	2.22	2.945(10)	139	1–x,–y, 1–z

Table S13. Frequencies of major IR bands of compounds **1** and **2** with tentative assignments

(1) HL	**(2) HL×0.5H2O**	**Tentative assignment** [29–31]
	3629	ν-OH
3299	***3312***	ν_{sym} (NH2) sulfonamide + ν-NH piperidine
3147	3085 3064	ν-CH arom
2971 2931 2861	2973 2932 2861	ν-CH piperidine
1666 s	***1661 s***	νC=O amide
1596 m	***1593 m***	νC=C ring
1561 m	***1556 m***	δNH amide
1525	1532	
1459	1457	
1382	1381	
1337 s	***1342 s***	$\nu_{asym}SO_2$
1323 1291	1328 1293	νC-C
1263	1265	νC-N
1230	1228	
1177 ***1166***	***1177 sh*** ***1165***	$\nu_{asym}SO_2$
1134	1134	νS-N
1102	1106	
1091	1090	
1057	1056	
1042	***1040***	νCC+δCH ring
979 929 911	981 928 914	νC-C + νC-N
849	***853***	νS-N
839		
809	811	
764 s	***762 s***	νC-N
709	708	
682	683	
663		
620	612	
593 s	***591 s***	νCC+δCH ring
552	554	

Abbreviations: ν-stretching vibration; δ-bending vibration; sym-symmetric; asym-antisymmetric; s-strong; m-medium; sh-shoulder

Table 14: Frequencies of major IR bands of compounds (**3-6**) with tentative assignments

(3)	**(4)**	**(5)**	**(6)**	**Tentative assigment** [29–31]
3475 sh	3475 sh	3475 sh	3475 sh	ν-OH
3240	3339	3339	3240	ν_{sym} (NH2) sulfonamide + ν-NH piperidine
3068	3091 3068	3091 3068	3071	ν-CH arom
2969 2932 2858	2962 2928 2859	2962 2928 2858	2969 2932 2859	ν-CH piperidine
1653 br, ↘	***1649, 1634 br, ↘↘***	***1656, 1634 br, ↘↘***	***1652 br, ↘***	***νC=O amide***
1589	1587	1587	1590	δ-NH
1544	1546	1544	1546	δ-NH amide
1373 1353	***1373 sh, 1355 ↗***	***1373 sh, 1355 ↗***	***1373 1353***	$\nu_{asym}SO_2$
1241 1226	***1245***	***1244***	***1240 1228***	***νC-O+δO-H alcool***
1156 1129 1103	***1156 1127***	***1156 1126***	***1156 1128 1104***	$\nu_{sym}SO_2$
1040	1040	1040	1040	νC-C+δC-H ring
971 950 920	***966 943***	***966 939***	***973 950 922***	***νC-O+δO-H alcool***
836	834	834	834	
744	744	744	744	νC-N
680	680	680	680	
591	591	591	591	νC-C+δC-H ring

Abbreviations: ν-stretching vibration; δ-bending vibration; sym-symmetric; asym-antisymmetric; br-broad; sh-shoulder

Table 15: Frequencies of major IR bands of compounds (**7**-**10**) with tentative assignments

(7)	**(8)**	**(9)**	**(10)**	**Tentative assigment** [29–32]
3426 sh				ν-OH
3309 br 3247 br	3299	3303	3299	ν_{sym} (NH2) sulfonamide + ν-NH piperidine
3086	3098 3068	3068	3098 3068	ν-CH arom
			3060 w *2979 w*	*CH2Cl2*
2971 2946 2929 2860	2968 2926 2860	2929 2869 2860	2968 2926 2860	ν-CH piperidine
1662 m	***1661 w, br***	***1667 m***	***1667 w, br***	***νC=O amide***
1593 m 1574 m	1587 s	1595 m 1574 m	1590	δ-NH
1531	***1550 m***	***1536 m***	***1550 m***	***δ-NH amide***
1372 ***1340 s***	***1357 s*** ***1335 s*** ***1327 s***	***1363*** ***1337***	***1357 s*** ***1335 s*** ***1327 s***	$\nu_{asym}SO_2$
1247	1247	1247	1247	
			1266	*CH2Cl2*
1169 1150	1156 1150	1156 1150	1168 1150	$\nu_{sym}SO_2$
1040	1040	1040	1040	νC-C+δC-H ring
922	947 922	922	947 922	νC-O+δO-H alcohol
847	847	847	847	
744	744	744	744	νC-N
			730	*CH2Cl2*
591	591	591	591	νC-C+δC-H ring

Abbreviations: ν-stretching vibration; δ-bending vibration; sym-symmetric; asym-antisymmetric; s-strong; m-medium; br-broad; sh-shoulder; w-weak

29. Socrates G (2010) Infrared and Raman characteristic group frequencies: tables and charts, 3. ed., repr. as paperback. Wiley, Chichester

30. Topacli C, Topacli A (2002) INFRARED SPECTRA SIMULATION FOR SOME SULFONAMIDES BY USING SEMI-EMPIRICAL METHODS. Spectroscopy Letters 35:207–217 . https://doi.org/10.1081/SL-120003806

31. Bellamy LJ (2013) Infra-red Spectra of Complex Molecules. Springer Netherlands, Dordrecht

32. Breda S, Reva ID, Lapinski L, Nowak MJ, Fausto R (2006) Infrared spectra of pyrazine, pyrimidine and pyridazine in solid argon. Journal of Molecular Structure 786:193–206 . https://doi.org/10.1016/j.molstruc.2005.09.010

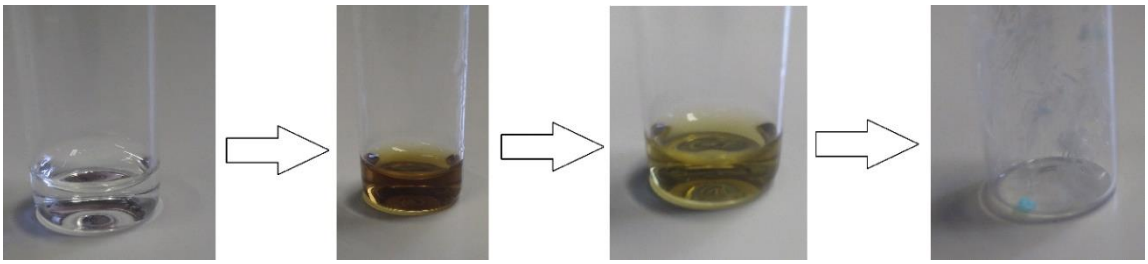
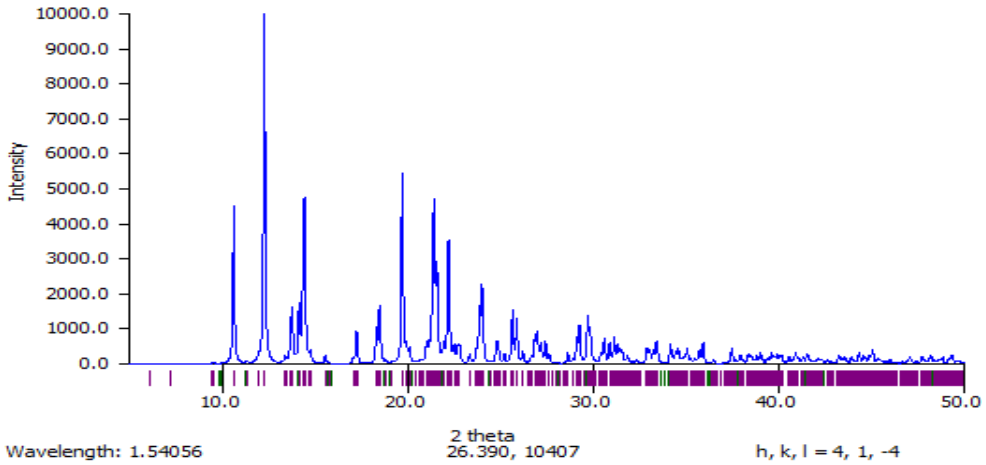
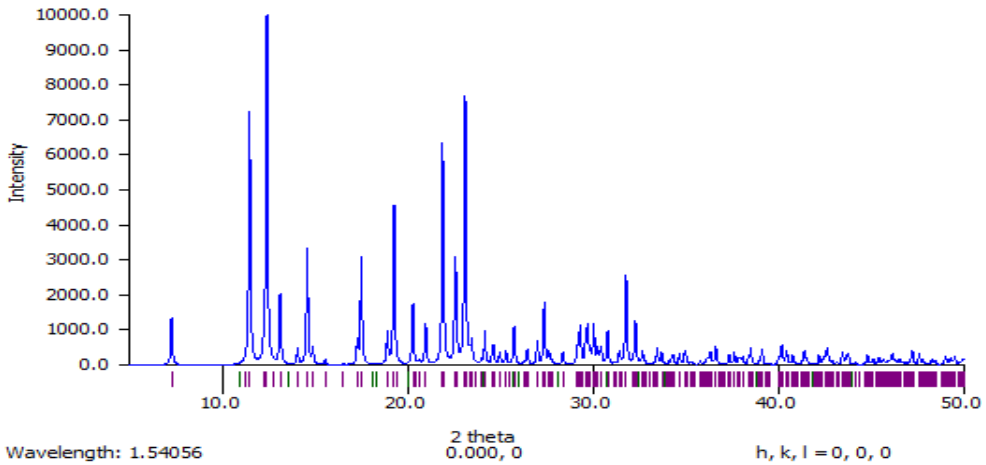


Figure S1. Crystallisation of Clopamide LH (**1**) from methanol solution. The colourless Clopamide solution becomes brown by adding $CuSO_4$ indicating complex formation in solution. As the temperature decreases or the solvent evaporates from the system, the complex decomposes, which results in solvent free crystals of Clopamide LH (**1**) and blue $CuSO_4 \cdot 5H_2O$ crystals.

(a)



(b)



(c)

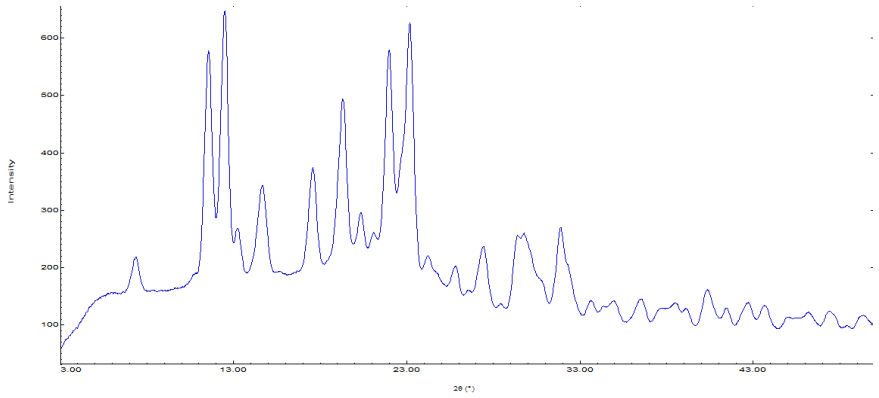
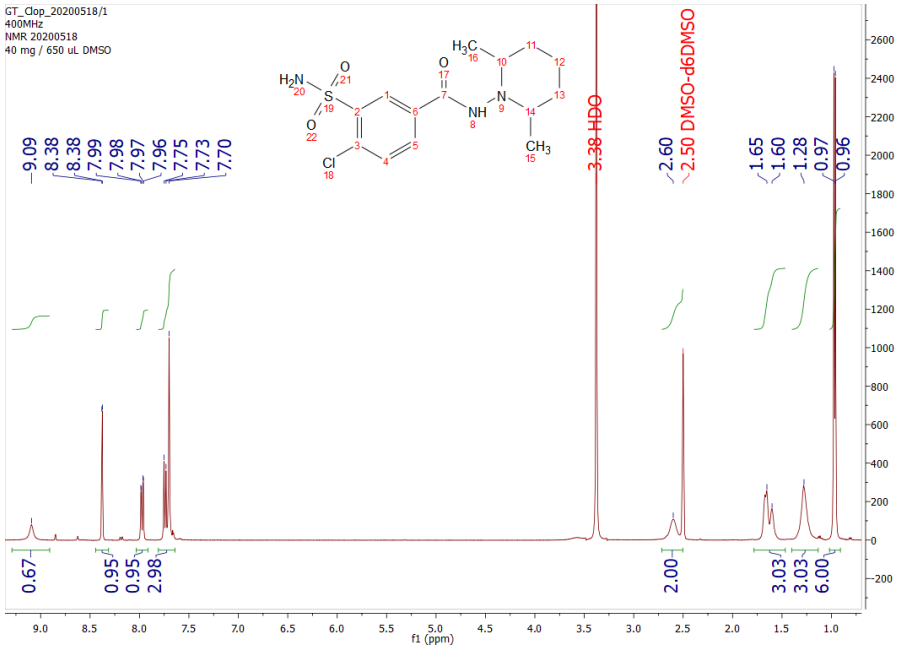


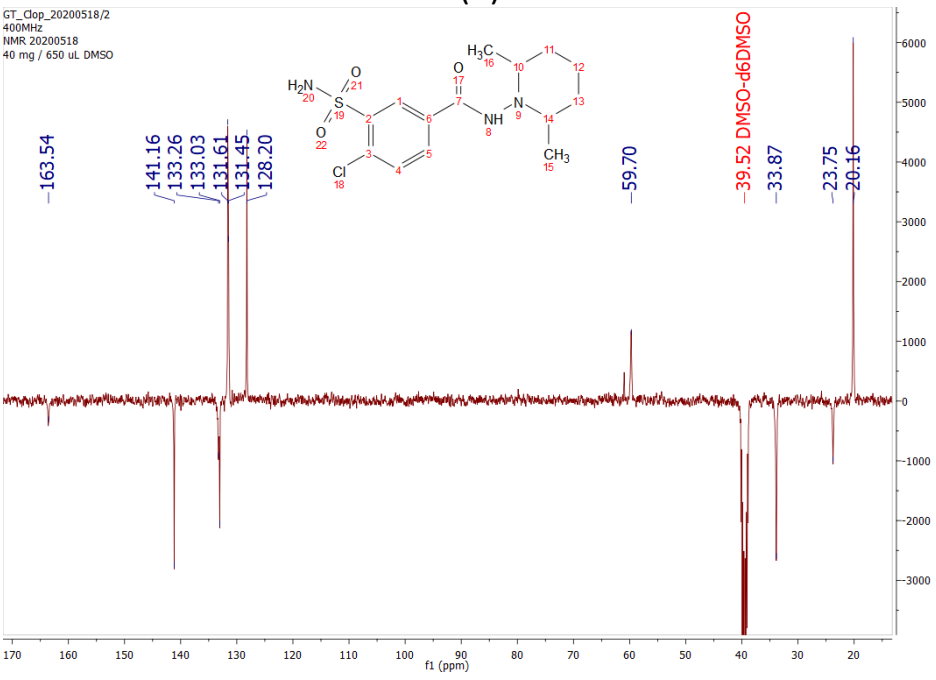
Figure S2. Calculated powder diffractograms of Clopamide: (a) anhydrate crystal **1** (b) hemihydrate crystal **2** and (c) measured PXRD of Clopamide API powder used as starting material in the crystallization experiments. The powder diffractogram of Clopamide sample used in the crystallization experiments agrees well with the calculated pattern based on the Clopamide hemihydrate structure **2.**

(a)



^{1}H-NMR (400.13 MHz, DMSO, 25 °C) δ 0.97 (*d*, *J*=6.1 Hz, 6H, C15/C16–CH_3), 1.28, 1.60, 1.65 (*m*, 6H, C11/C12/C13–CH_2), 2.60 (*m*, 2H, C10/C14–C*H*), 7.70 (*s*, 2H, SO_2NH_2), 7.74 (*d*, *J*=8.3 Hz, 1H, C4–C$_{ar}$*H*), 7.97 (*dd*, *J*=8.3, 2.2 Hz, 1H, C5-C$_{ar}$H), 8.38 (*d*, *J*=2.1 Hz, 1H, C1-C$_{ar}$H), 9.09 (*s*, 1H, N8-H), ppm.

(b)



^{13}C NMR (100.62 MHz, DMSO, 25 °C) δ: 20.16 (C2, C15/16-CH_3), 23.75 (C1, C12-CH_2), 33.87 (C2, C11/13-CH_2), 59.70 (C2, C10/14-CH), 128.20 (C1, C6-C$_{ar}$H), 131.45 (C1, C5-C$_{ar}$H), 131.61 (C1, C4-C$_{ar}$H), 133.03 (C1, C3-C$_{ar}$Cl), 133.26 (C1, C6-C$_q$), 141.16 (C1, C6-C$_{SO2NH2}$), 163.54 (C1, C7-C=O), ppm.

Figure S3. (a) ^{1}H-NMR and (b) ^{13}C-NMR spectrum of Clopamide powder used for the crystallization experiments**.** ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 (400 MHz spectrometer at 25 °C in deuterated dimethyl sulfoxide (DMSO).

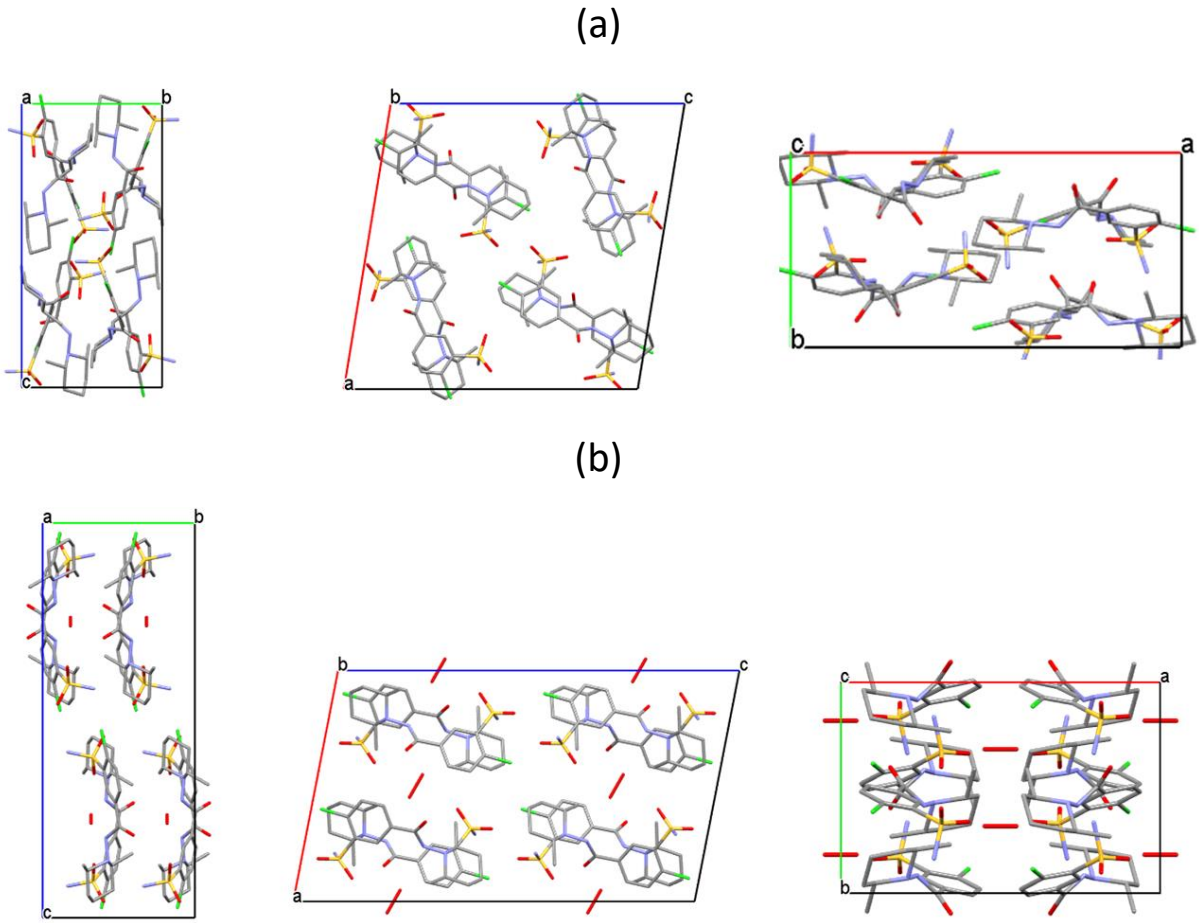


Figure S4. Comparison of the unit cells of crystals **1** (a) and **2** (b) viewed from crystallographic *a, b* and *c* axes, respectively.

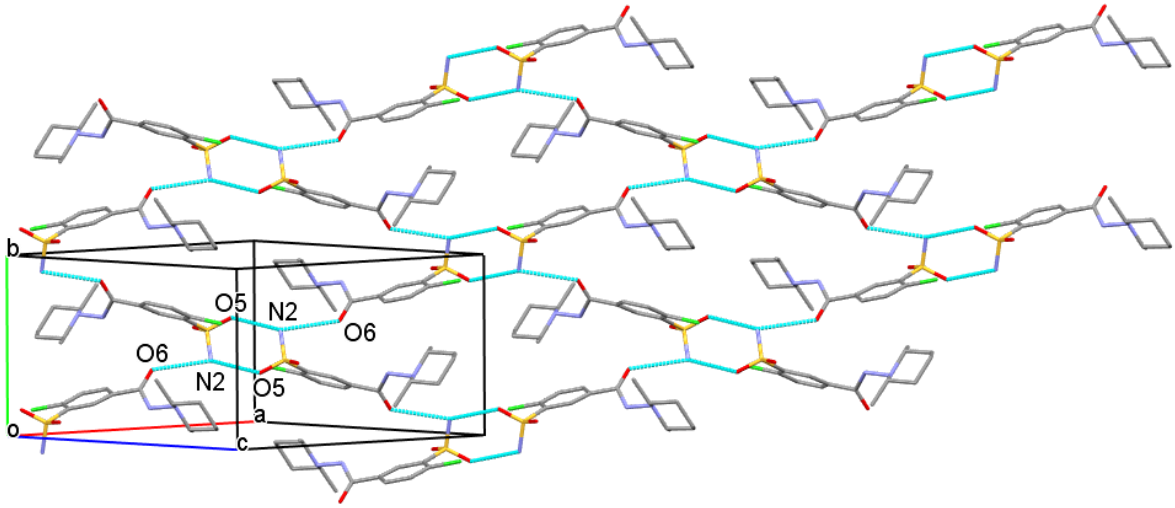


Figure S5. Layer of molecules B of **1** in ac diagonal with H-bonds.

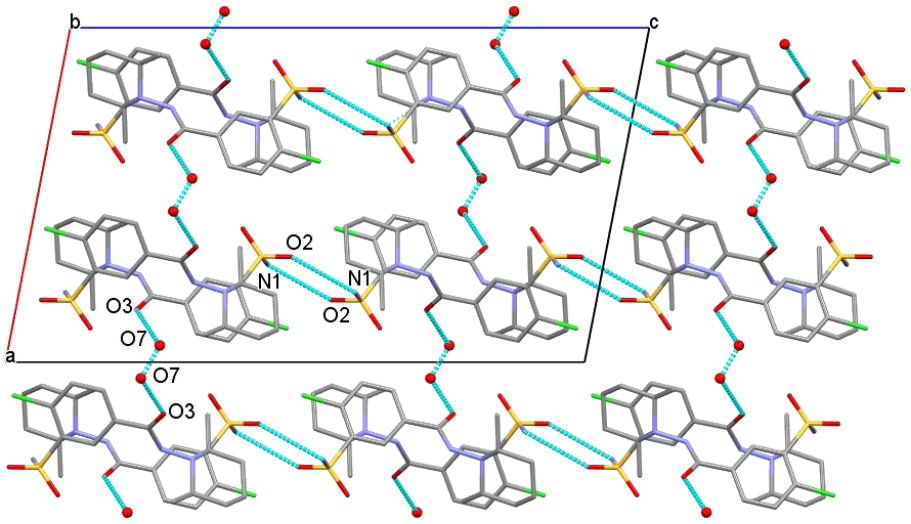


Figure S6. Layer of molecules **2** viewing from the crystallographic *b* axis. The disordered water molecules are drawn as red balls. The neighbouring water molecules are actually one water molecule in two disordered positions.

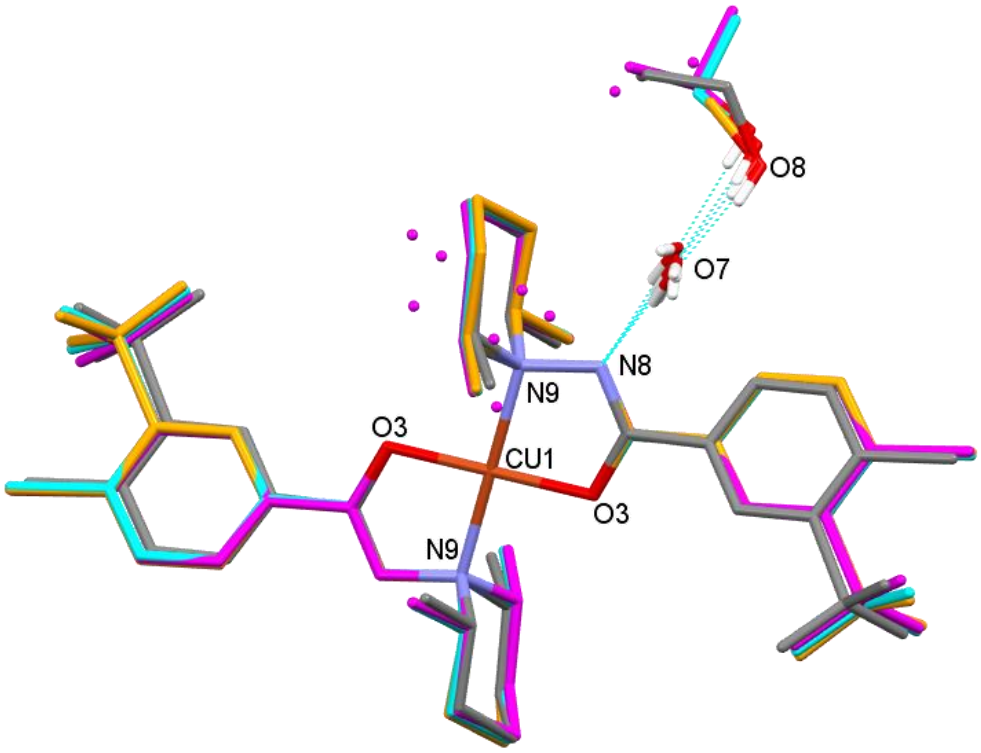


Figure S7: Structural overlay of the complex molecules in crystal (**3**) (**orange**), (**4**) (**cyan**), (**5**) (**grey**) and (**6**) (**magenta**). The whole complex molecules are symmetry generated by an inversion centre from the asymmetric unit which contains only half of the complex molecule, one water and one alcohol molecules.

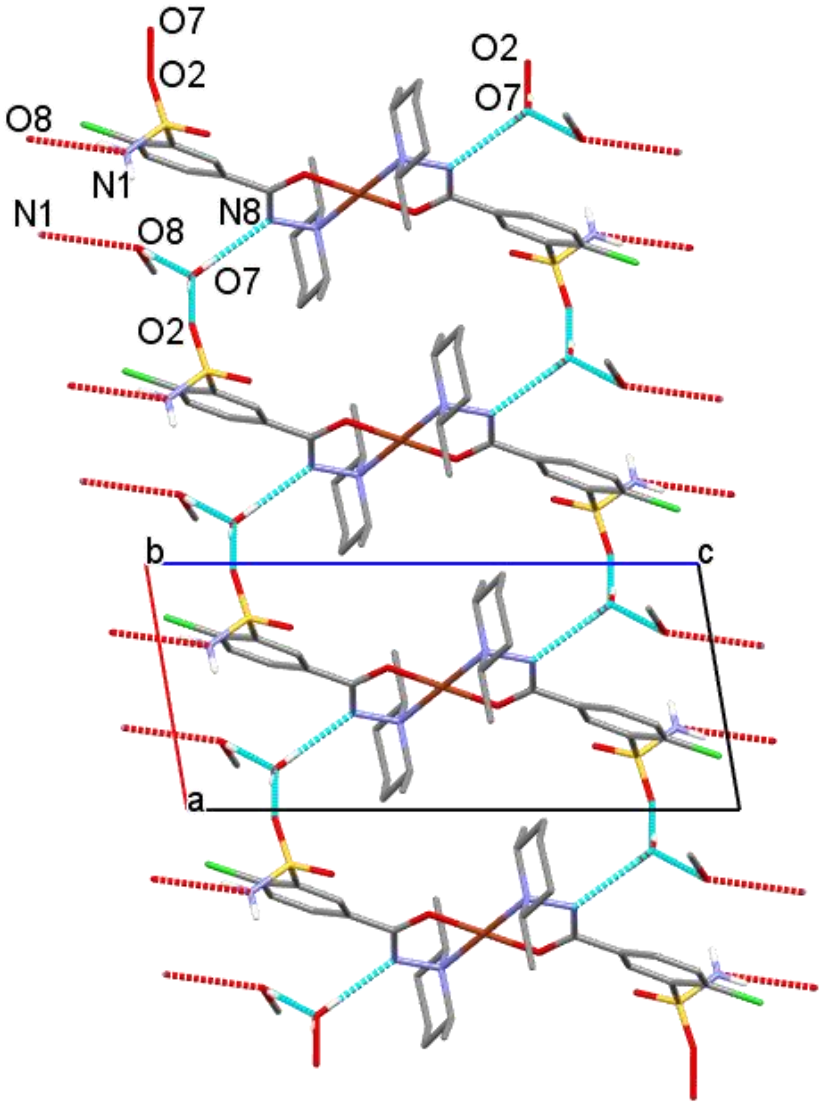


Figure S8. Viewed from the crystallographic direction ‘a’, molecular columns running along the ‘b’ axis are found in the solvatomorphic (**3**-**6**) series. The columns then form a sheet, the sheets form 3D network by secondary interactions. Here structure of crystal **3** is presented as typical example.

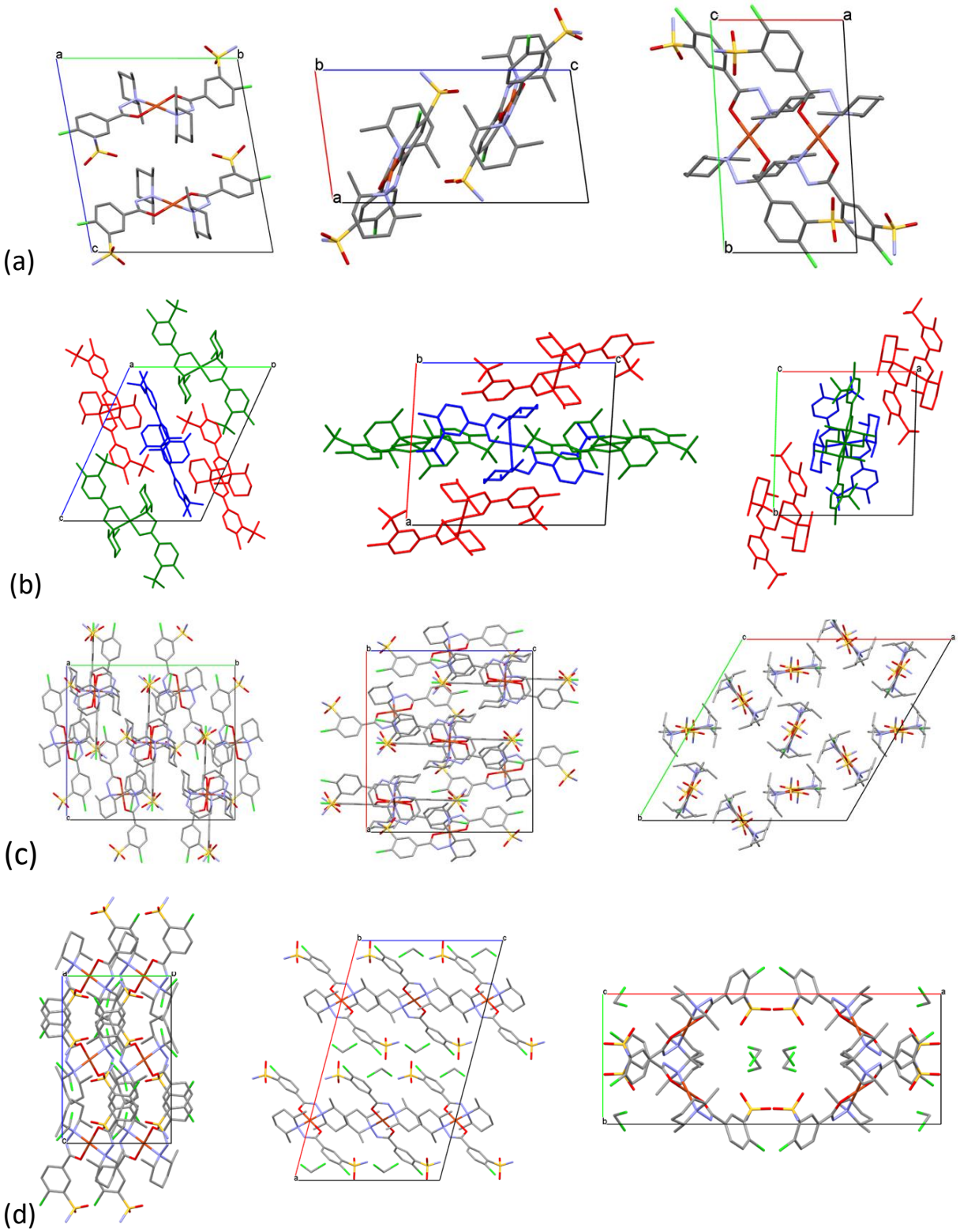


Figure S9. Unit cell of crystals **7** (a), **8**(b), **9** (c) and **10** (d) viewed from the crystallographic *a, b* and *c* axes. In case of crystal **8** the three molecules of the asymmetric unit are indicated by different colours: molecule A is red, molecule B is blue and molecule C is green

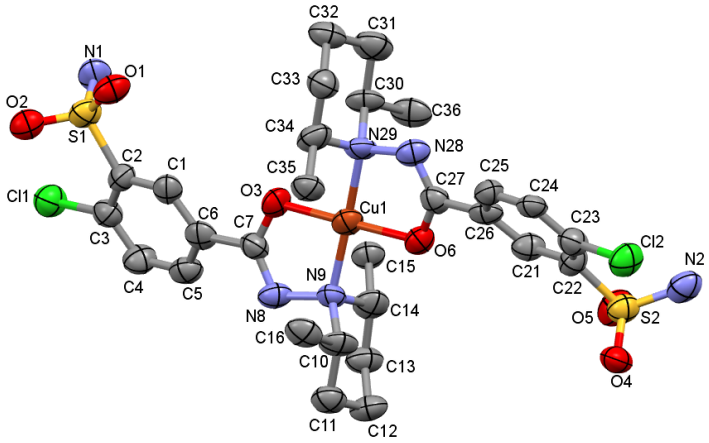


Figure S10. The molecular structure of **7** with atom labelling. Displacement ellipsoids are drawn at 50% probability level. The asymmetric unit contains a whole bis-complex molecule. H atoms have been omitted for clarity.

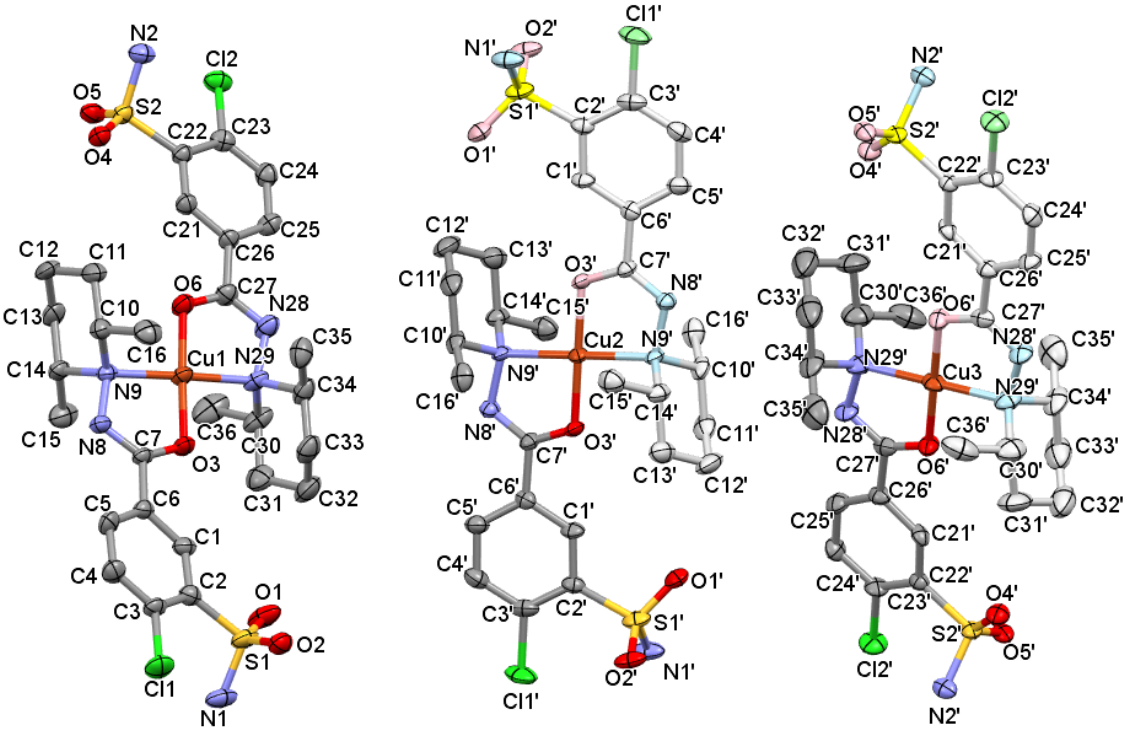


Figure S11. Molecular structure of **8** with atom labelling. Displacement ellipsoids are drawn at 50% probability level. The asymmetric unit consists of a whole bis-complex molecule and two halves of complex molecules. H atoms have been omitted for clarity.

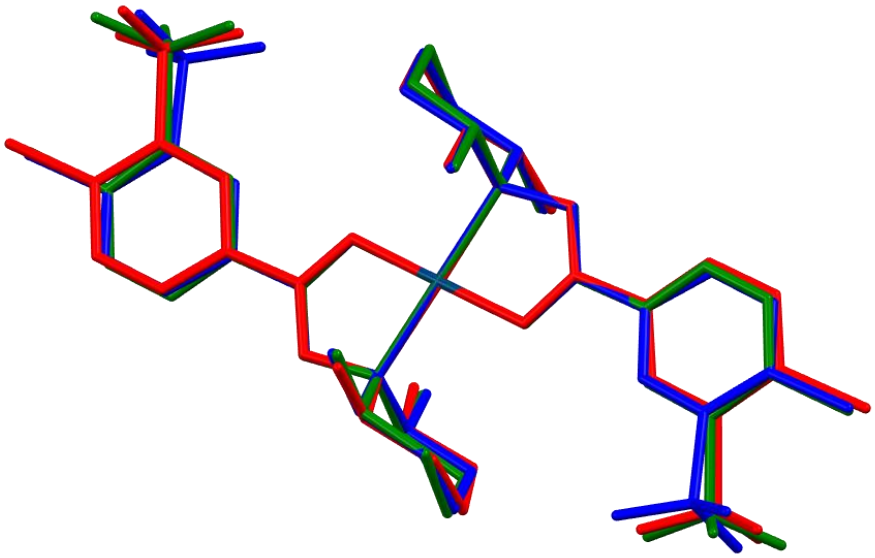


Figure S12. Structural overlay of the molecules of the asymmetric unit of crystal **8**. The superimposed atoms belong to the coordination sphere of the Cu(II) showing the conformational differences between the molecules: molecule A (**red**), molecule B (**blue**), and molecule C (**green**). The asymmetric unit contains the entire complex A (red) and the halves of the omplexes B and C. Hydrogen atoms are removed for clarity.

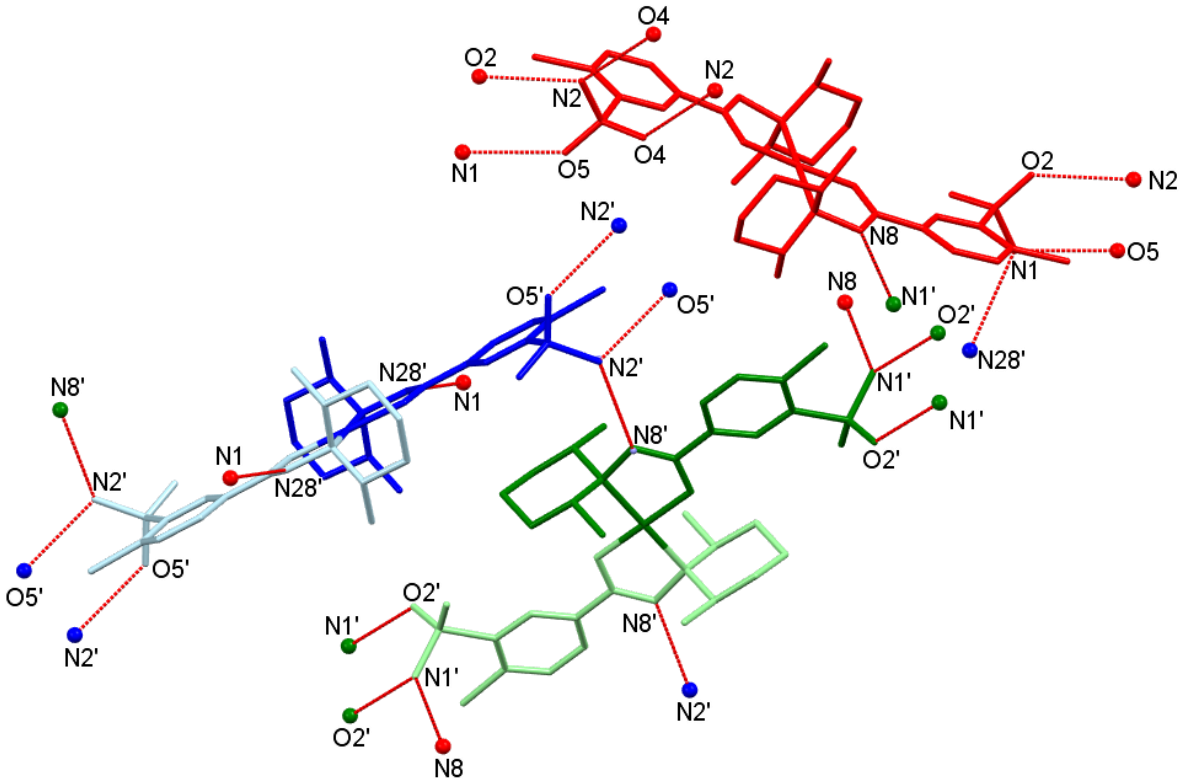


Figure S13. The asymmetric unit of crystal **8** showing the main H-bond interactions with neighbouring atoms. Molecule A is red, molecule B is blue and molecule C is green. The atoms at the ends of the hanging contacts are coloured according to the colour codes of the molecules.

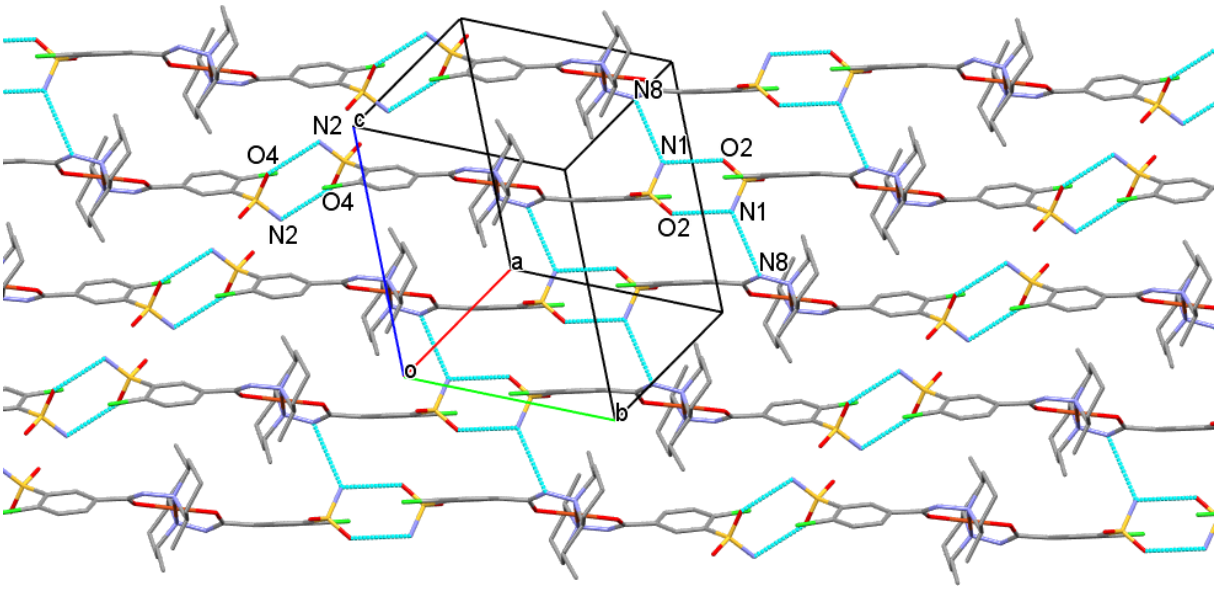


Figure S14. The molecules form planes in the crystal lattice, which are stabilized by strong N—H···O type interactions. N—H···N type H bonds also stabilize the crystal structure of **7**.

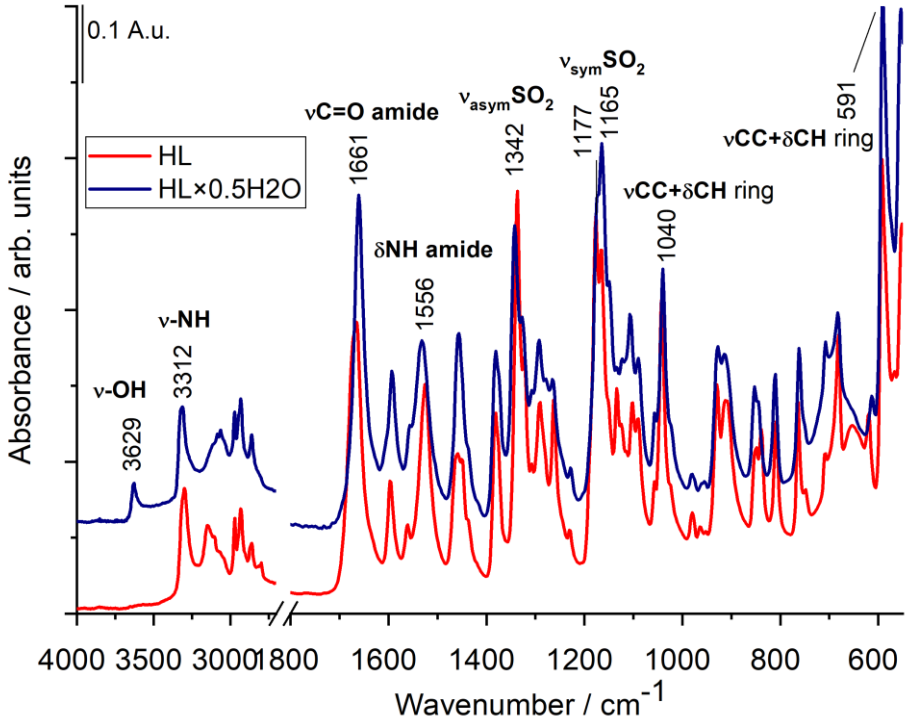


Figure S15. IR spectra of the anhydrate and hemihydrate forms (**1** and **2**) of clopamide.

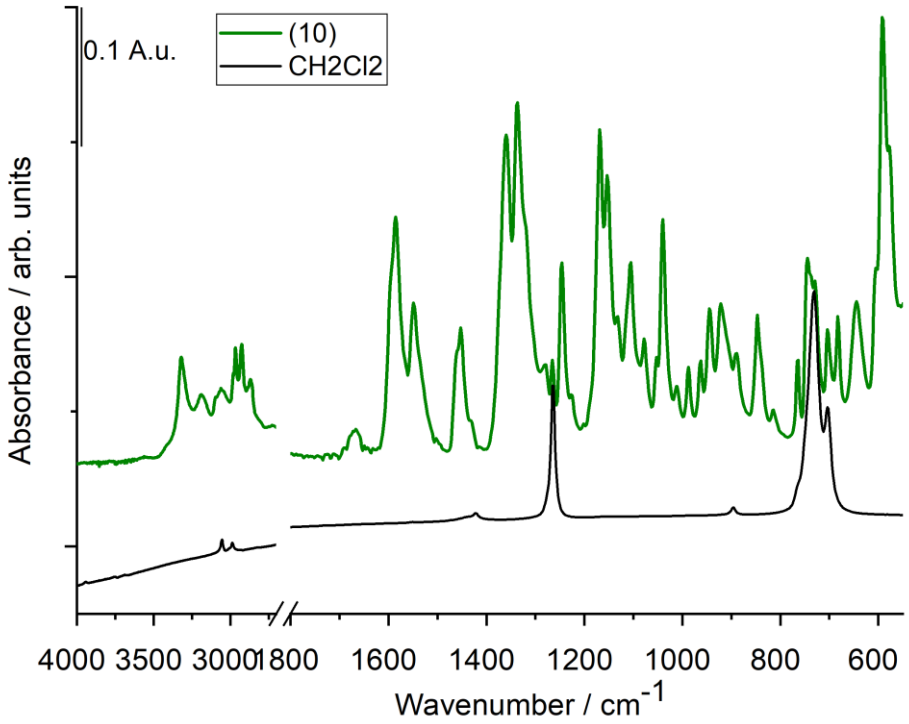


Figure S16. IR spectrum of compound **10** showing the presence of the DCM in the crystal.

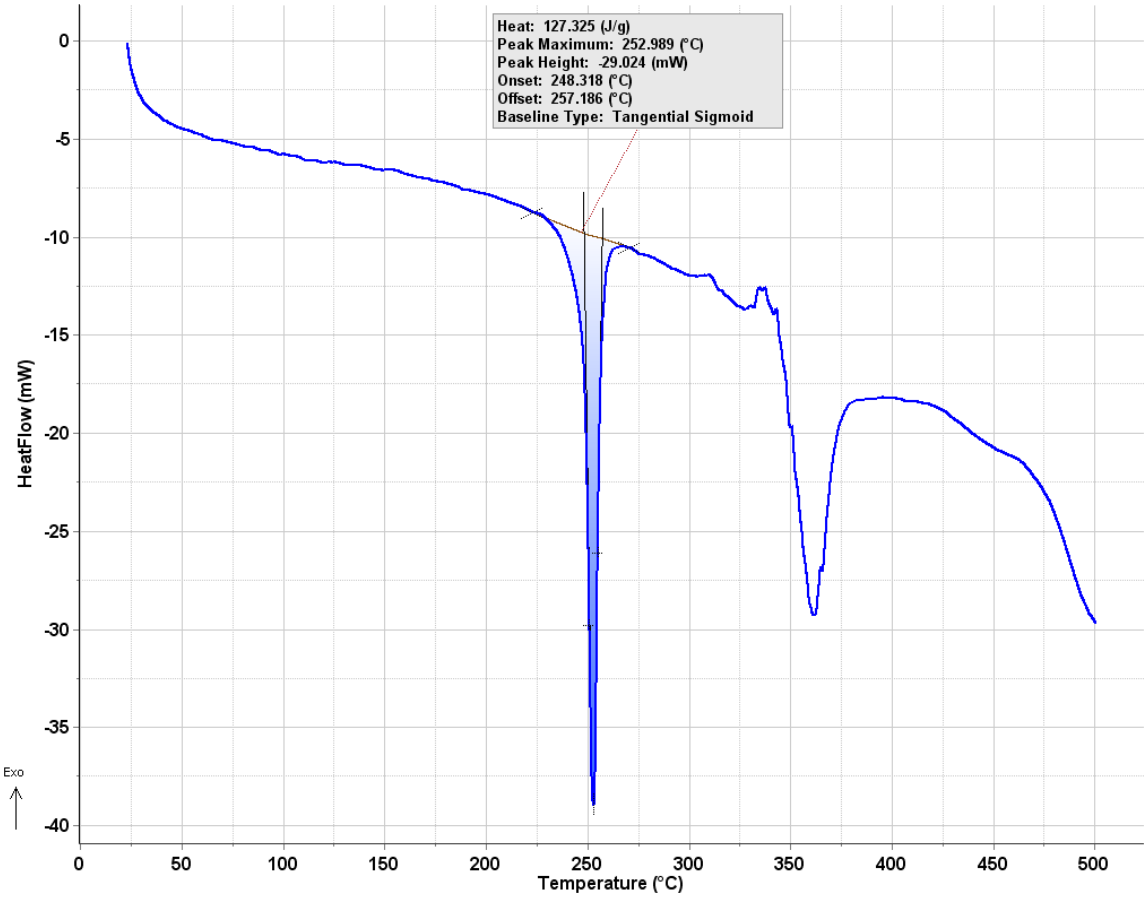


Figure S17. DSC curve of compound **1** in inert atmosphere.

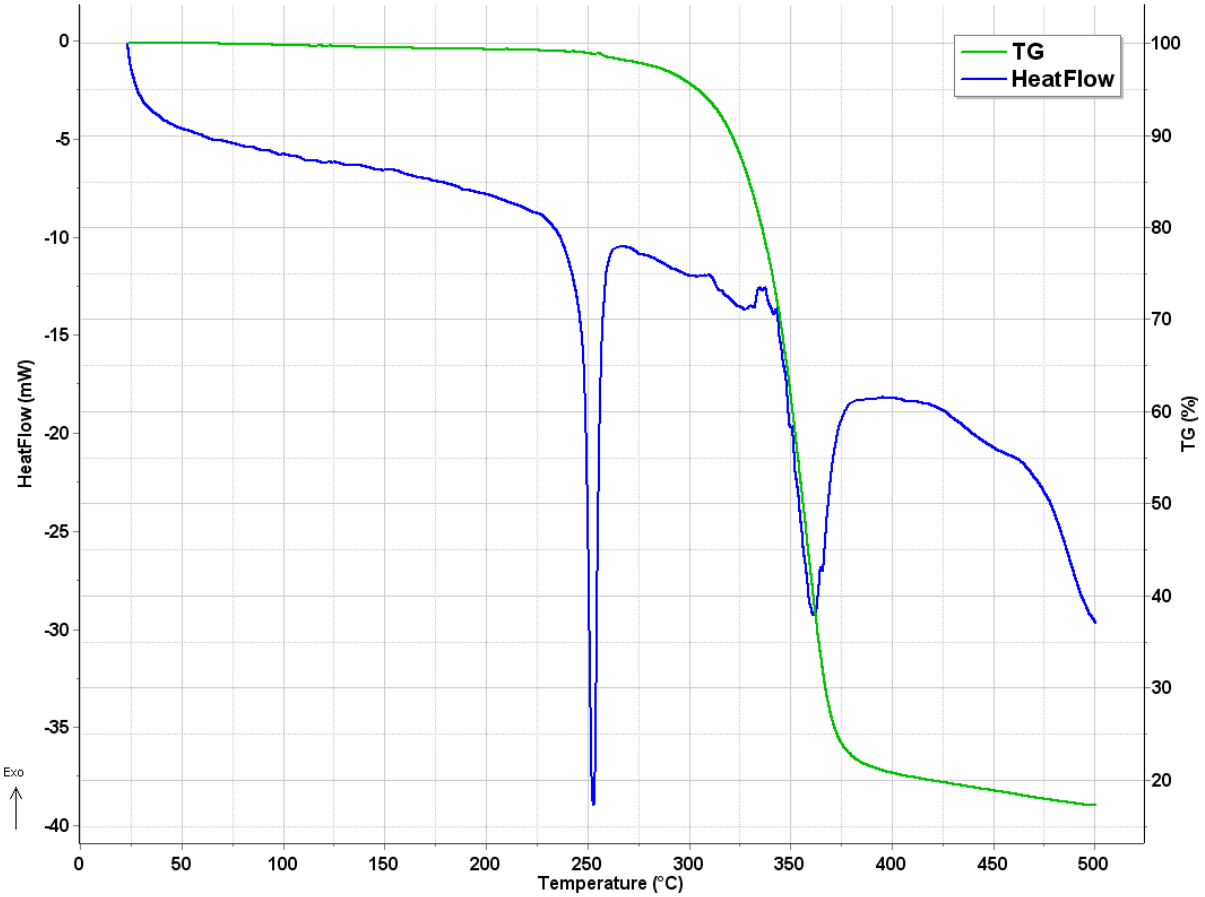


Figure S18. TG and DSC curves of compound **1** in inert atmosphere.

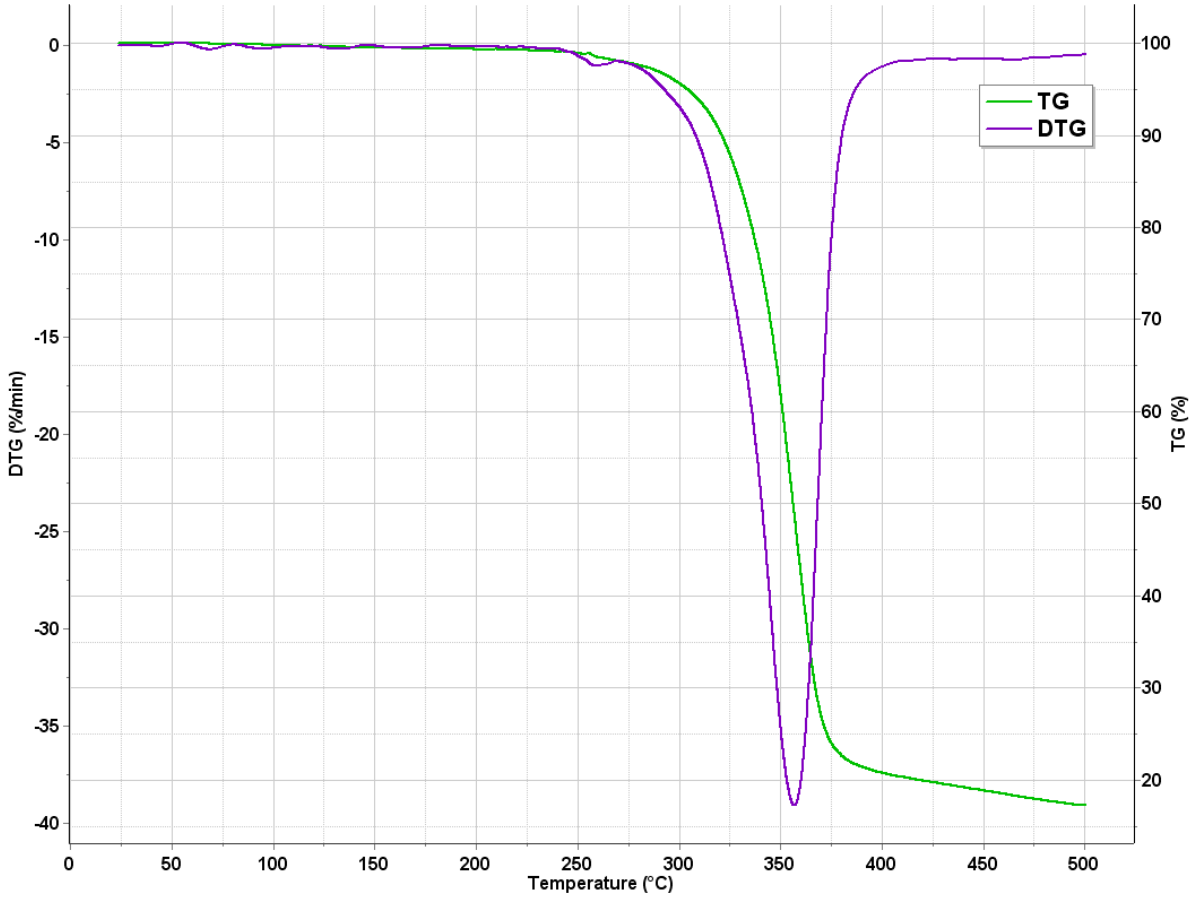


Figure S19. TG and DTG curves of compound **1** in synthetic air atmosphere.

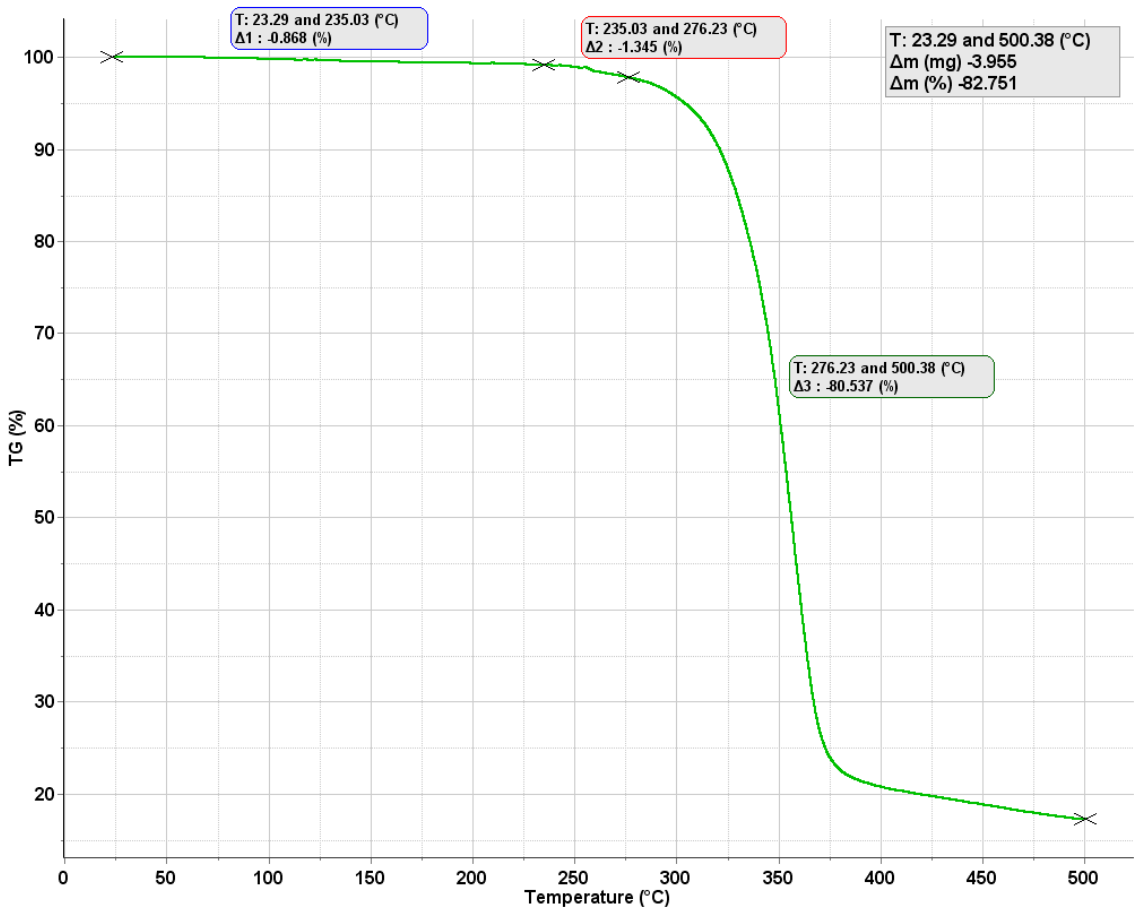


Figure S20. TG curves of compound **1** in He atmosphere.

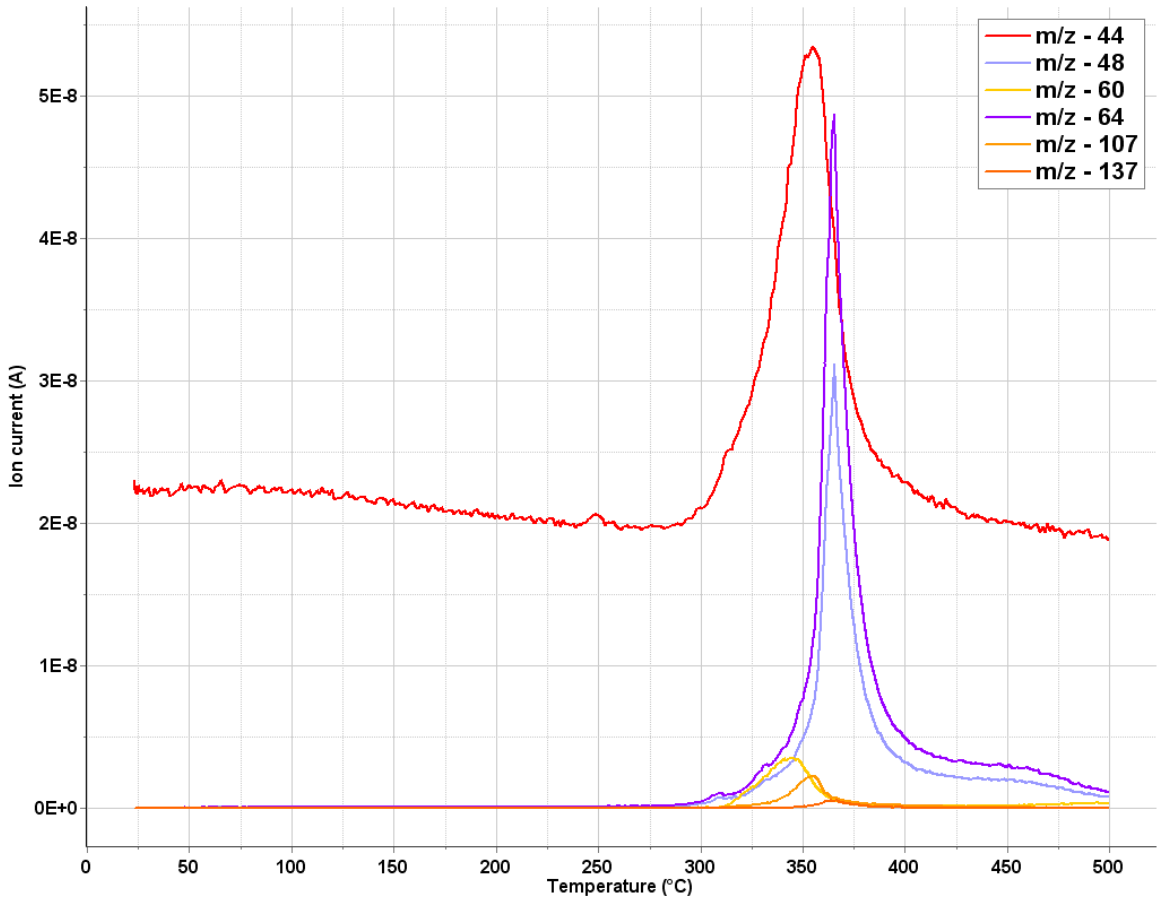


Figure S21. TG -MS curves of the fragments measured during thermal decomposition of compound **1** in inert atmosphere. The m/z=64 shows the mass of SO_2 as one of the products of degradation.

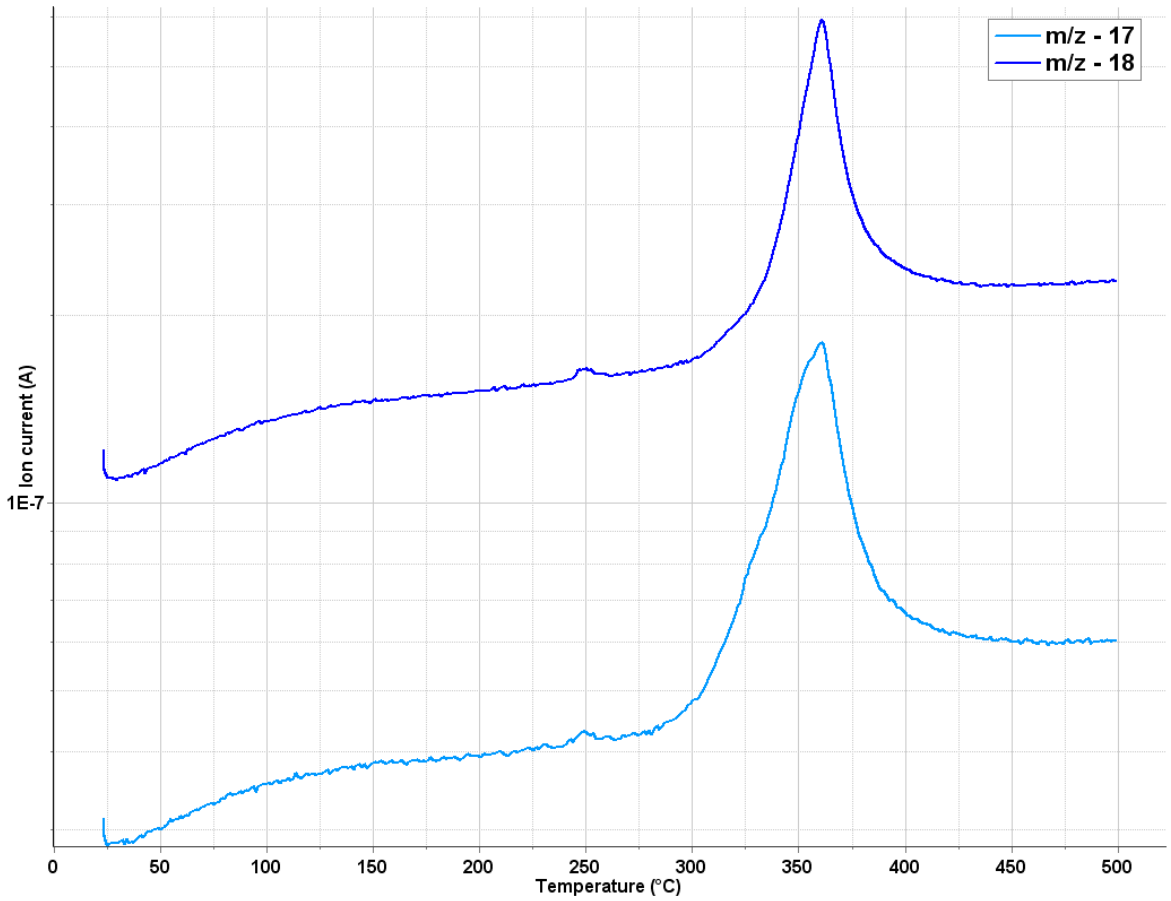


Figure S22. TG -MS curves of the water fragments measured during thermal decomposition of compound **1** under inert atmosphere.

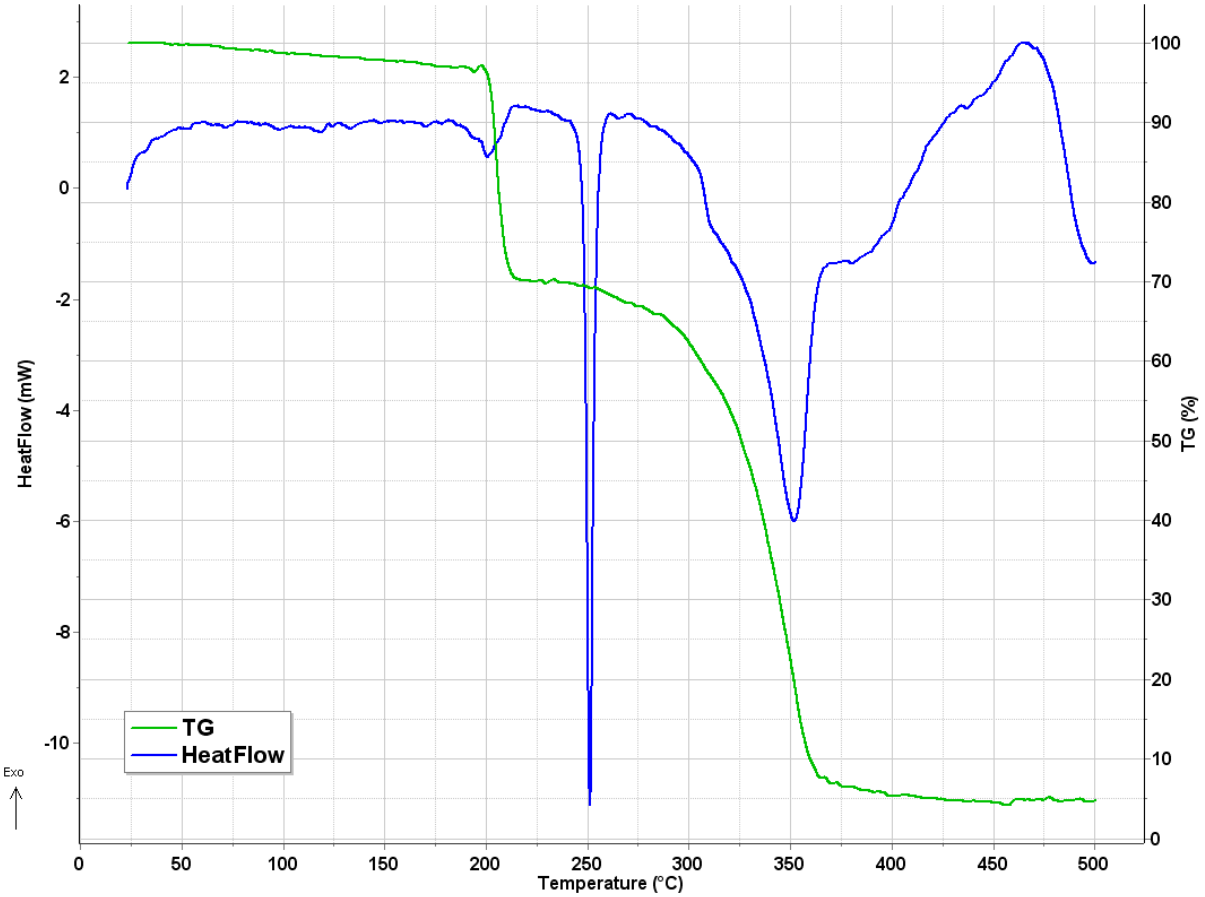


Figure S23. TG and DSC curves of compound **2** in inert atmosphere.

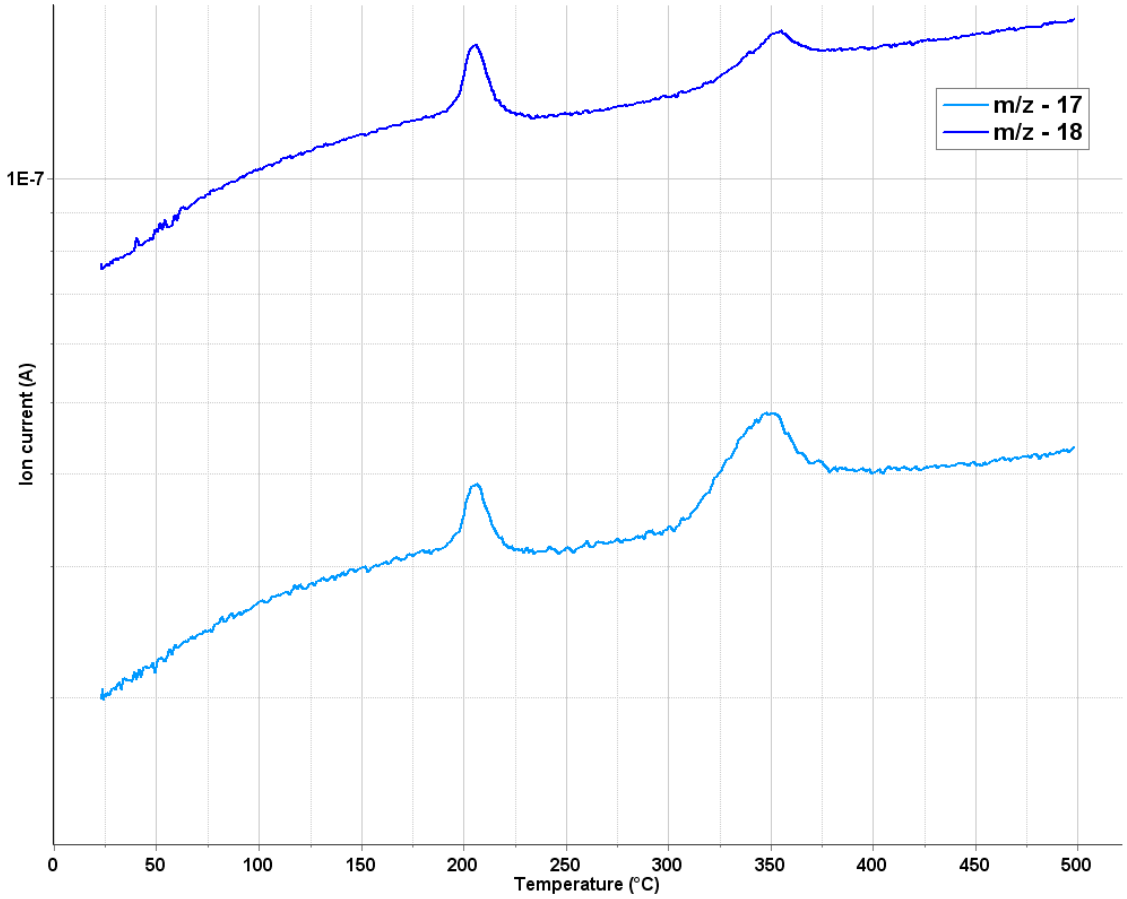


Figure S24. TG -MS curves of the water fragments measured during thermal decomposition of compound **2** under inert atmosphere.

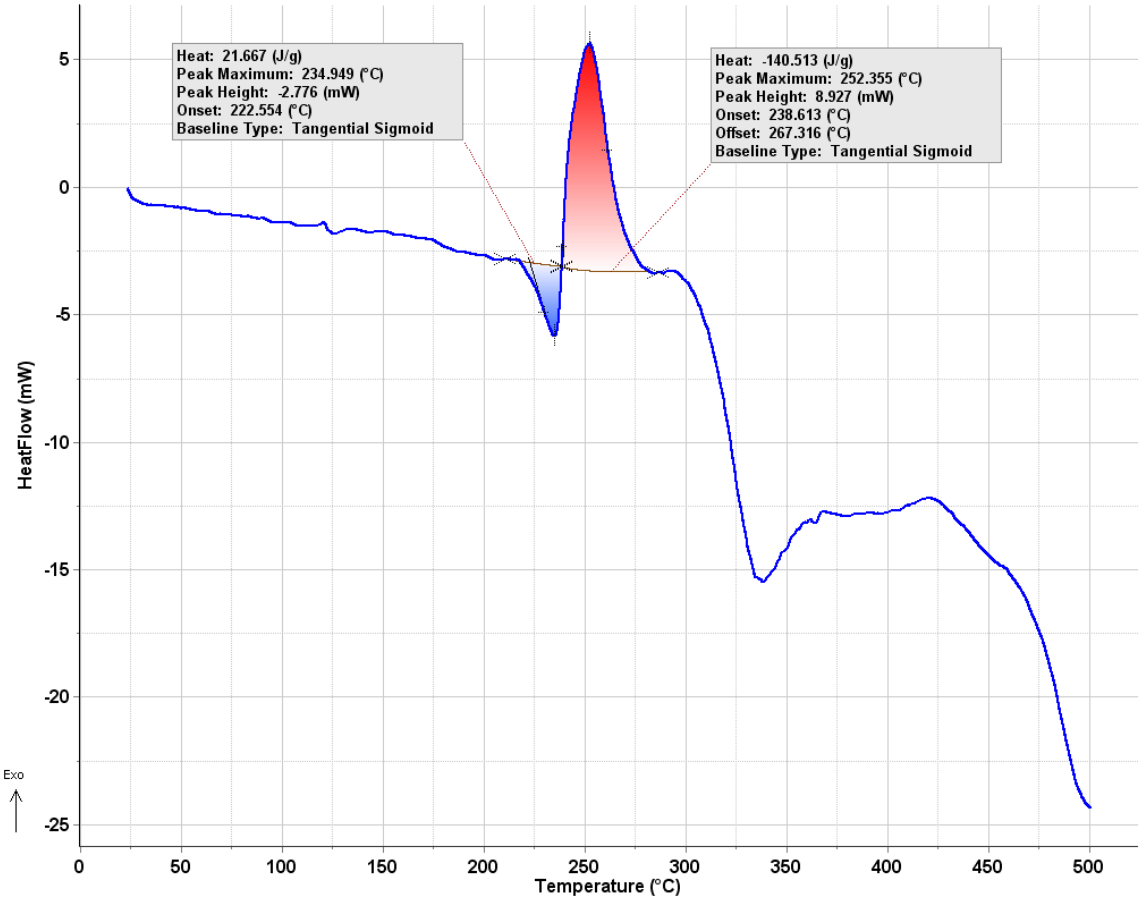


Figure S25. DSC results of compound **7** in inert atmosphere.

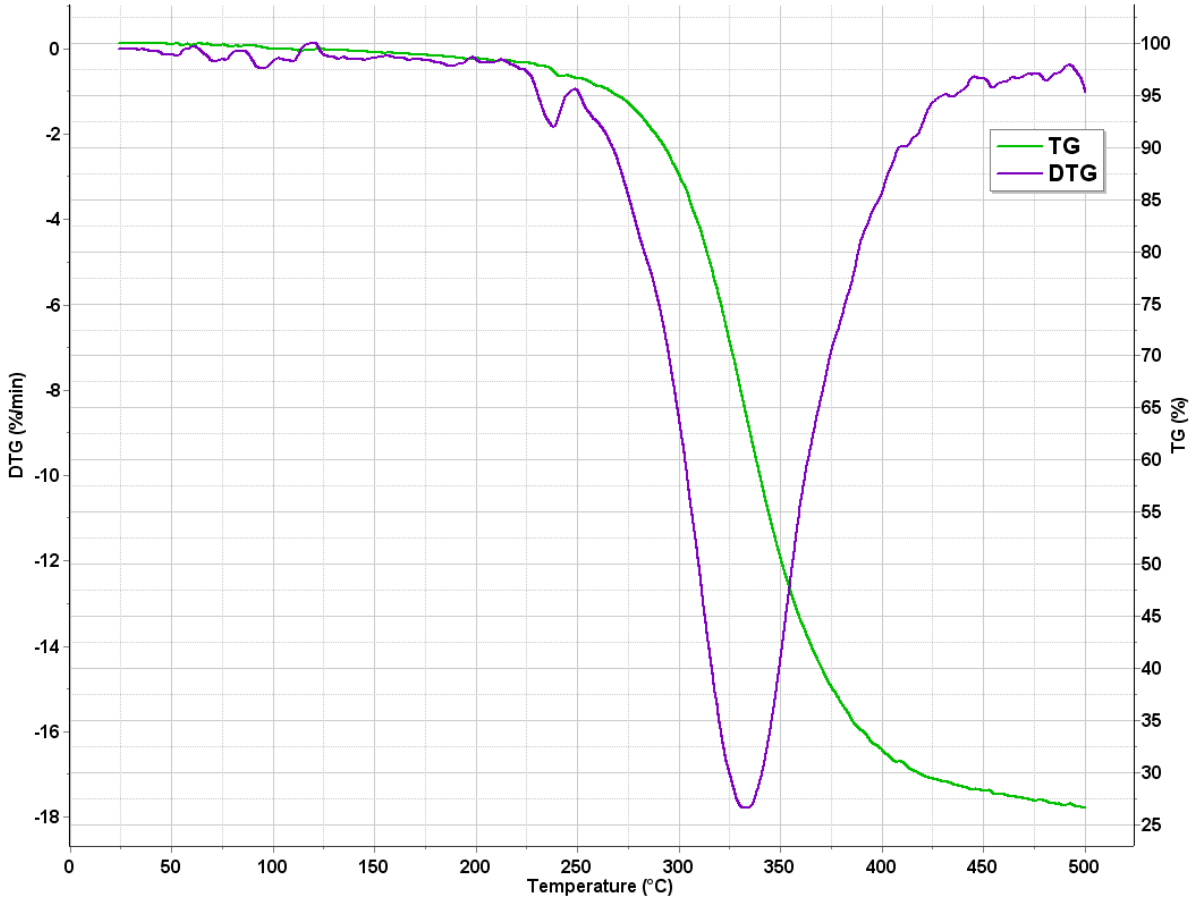


Figure S26. TG and DTG curves of compound **7** in synthetic air atmosphere.

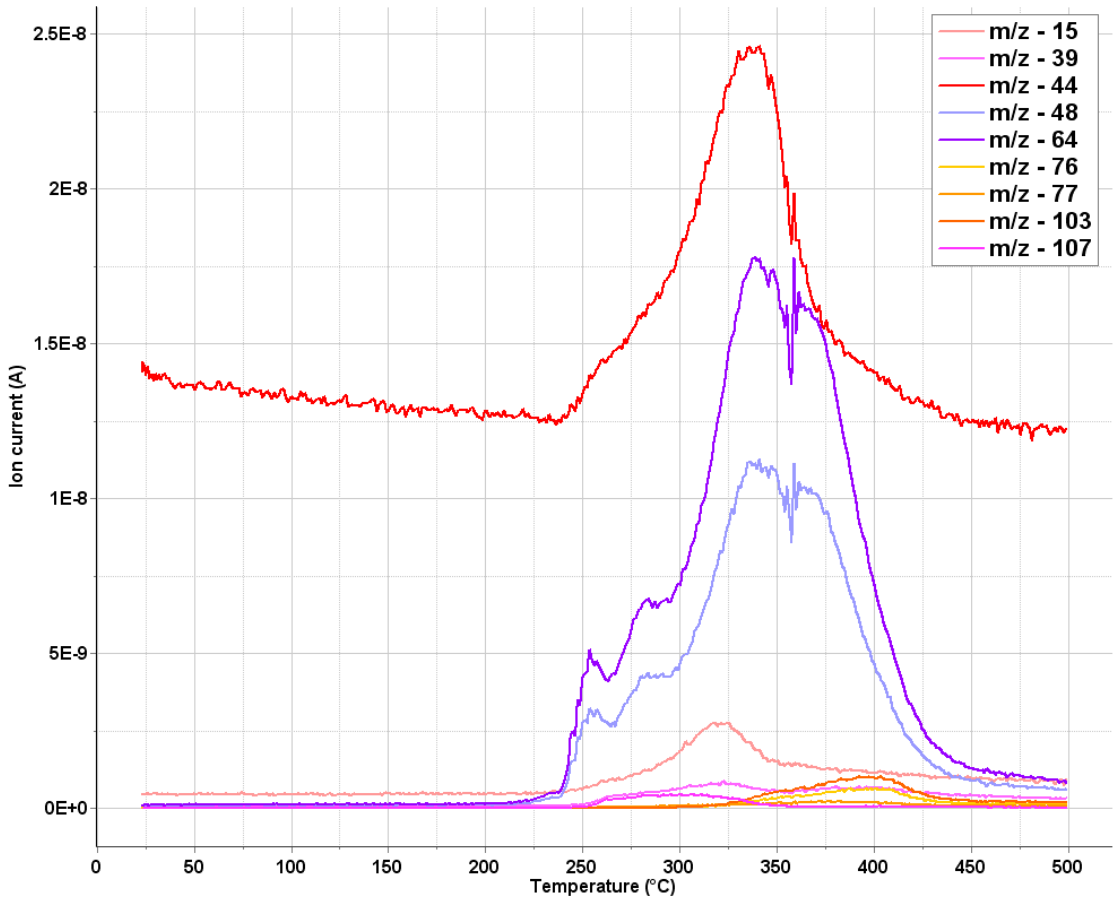


Figure S27. TG -MS curves of the fragments measured during thermal decomposition of compound **7** under inert atmosphere. The m/z=64 shows the mass of SO_2 as one of the products of degradation.

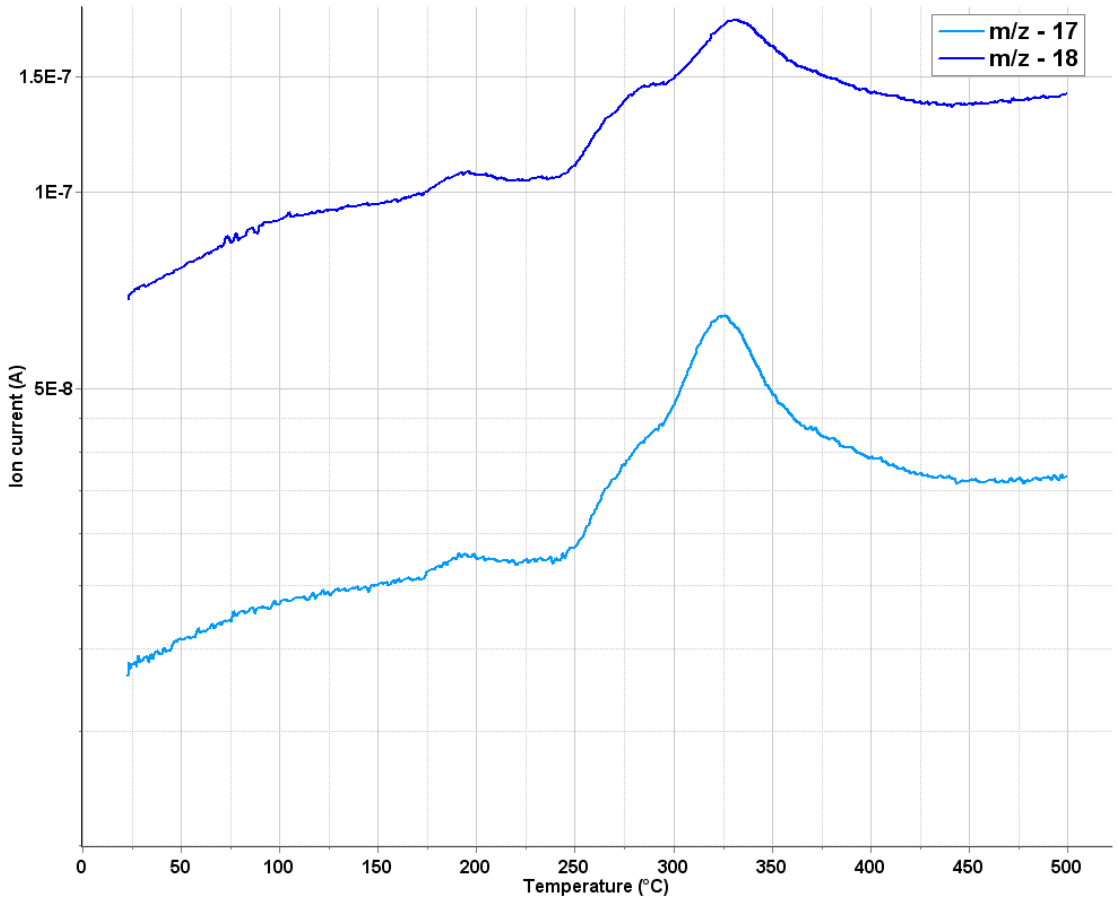


Figure S28. TG -MS curves of the water fragments measured during thermal decomposition of compound **7** under inert atmosphere.

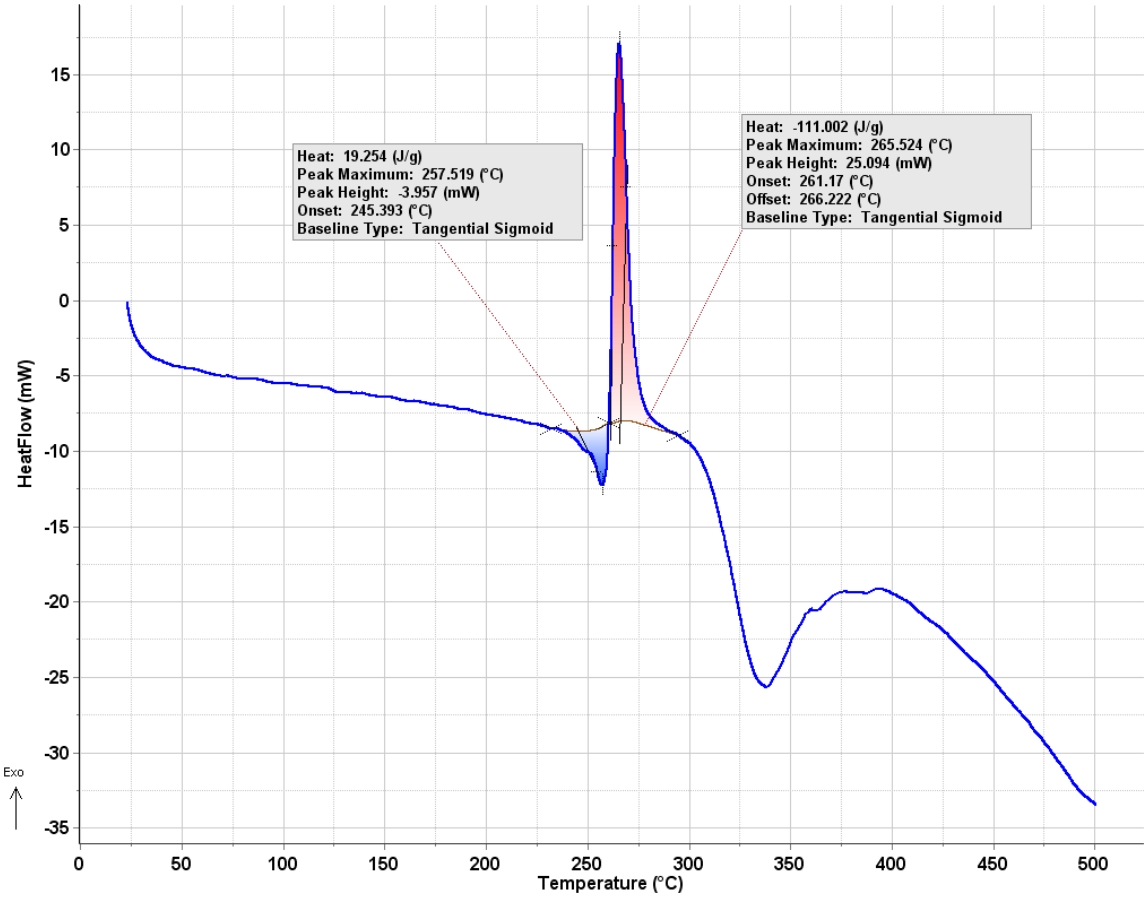


Figure S29. DSC curve of compound **8** in inert atmosphere.

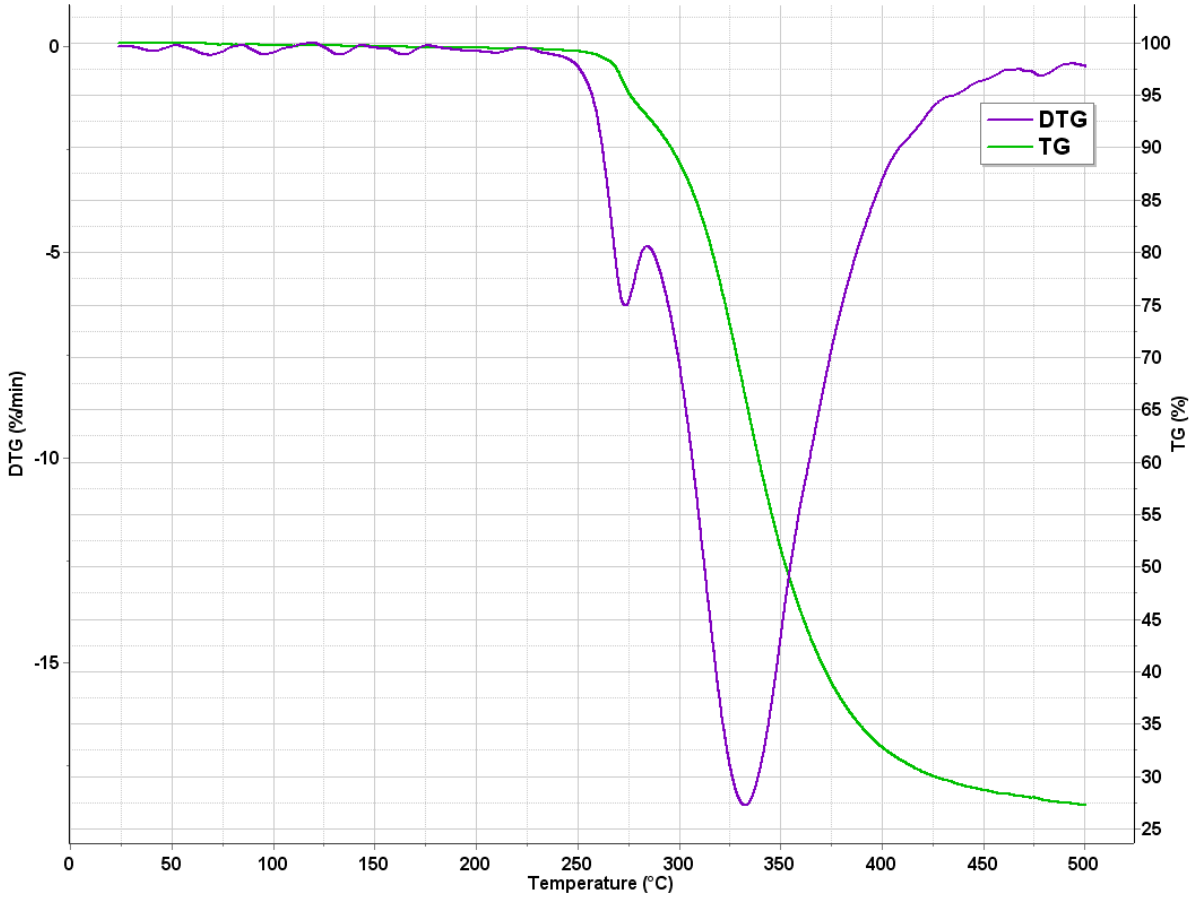


Figure S30. TG and DTG curves of compound **8** in synthetic air atmosphere.

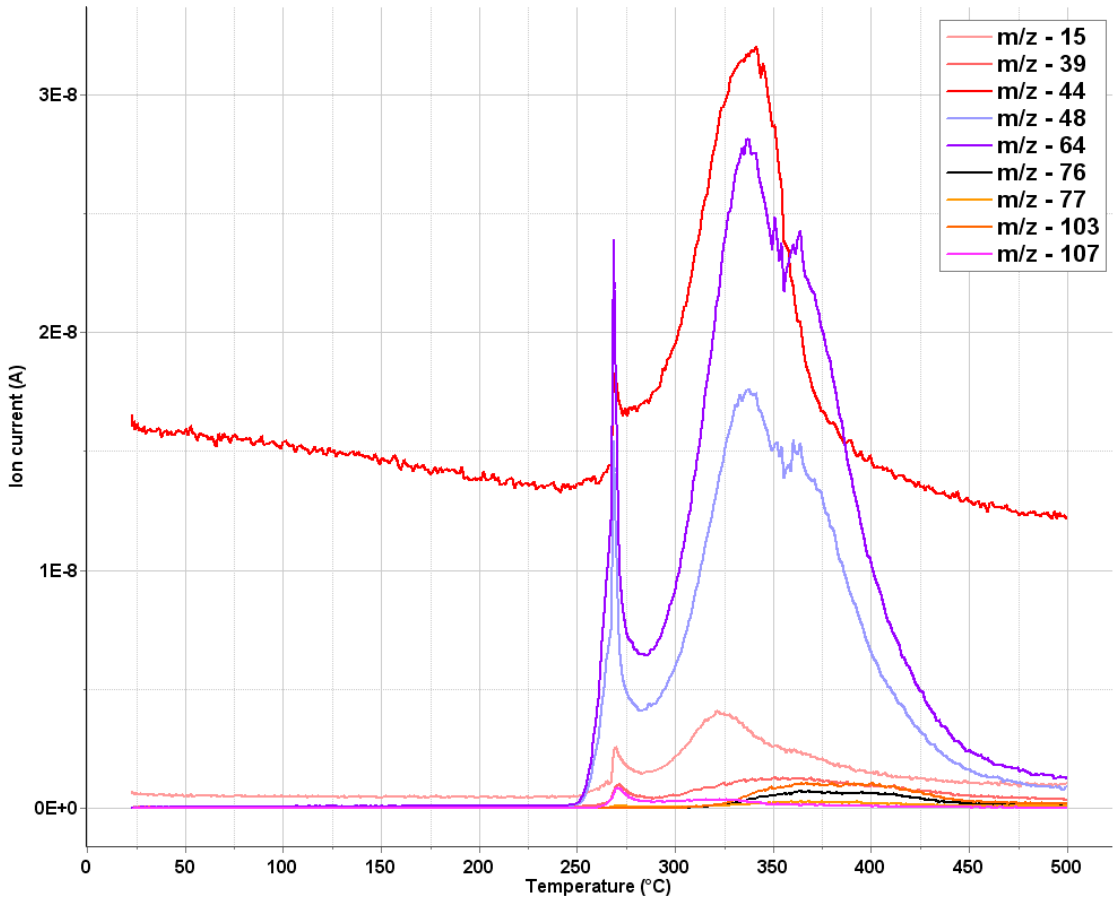


Figure S31. TG -MS curves of the fragments measured during thermal decomposition of compound **8** under inert atmosphere. The m/z=64 shows the mass of SO_2 as one of the products of degradation.

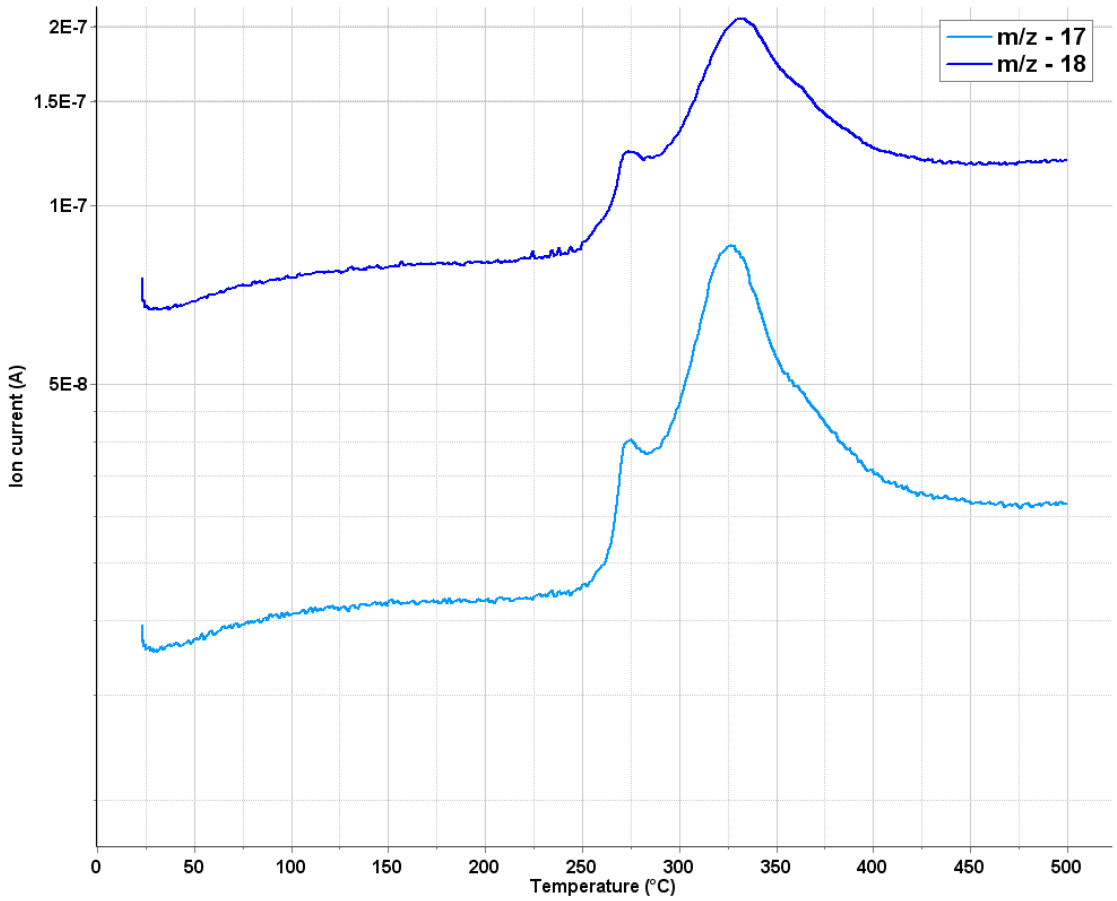


Figure S32. TG -MS curves of the water fragments measured during thermal decomposition of compound **8** under inert atmosphere.