STRUCTURAL CHEMISTRY

Volume 75 (2019)

Supporting information for article:

The design of novel metronidazole benzoate structures: exploring stoichiometric diversity

Yara Santiago de Oliveira, Wendell Saraiva Costa, Poliana Ferreira Borges, Maria Silmara Alves de Santana and Alejandro Pedro Ayala

Table S1 Crystallographic Data and Structure Refinement Parameters for the BZMD Structures.

Identification code	**BZMDBZC**	**BZMDNAF**	**BZMDMAC**	**BZMD3,5DNZ**	**BZMDABN**
Empirical formula	$C_{20}H_{19}N_3O_6$	$C_{23}H_{21}N_3O_5$	$C_{21}H_{21}N_3O_7$	$C_{20}H_{17}N_5O_{10}$	$C_{20}H_{20}N_4O_6$
Formula weight	397.38	419.43	427.41	487.39	412.4
Temperature/K	300.39	300	300	300	300
Crystal system	monoclinic	monoclinic	triclinic	monoclinic	triclinic
Space group	$P2_1/n$	$P2_1/c$	P-1	$P2_1/c$	P-1
a/Å	13.5997(6)	8.5105(8)	9.1309(4)	21.0988(13)	7.9316(7)
b/Å	9.0354(4)	22.387(2)	11.1274(4)	8.4322(5)	11.9585(12)
c/Å	16.5974(8)	11.7752(11)	11.8538(5)	12.0341(8)	12.1978(12)
α/°	90	90	107.3650(10)	90	76.362(3)
β/°	108.646(2)	108.664(4)	103.2700(10)	99.505(2)	78.927(3)
γ/°	90	90	110.0910(10)	90	79.583(3)
Volume/Å^3	1932.42(15)	2125.4(3)	1002.73(7)	2111.6(2)	1092.21(18)
Z	4	4	2	4	2
ρ_{calc}g/cm^3	1.366	1.311	1.416	1.533	1.254
μ/mm^{-1}	0.86	0.775	0.108	0.126	0.094
F(000)	832	880	448	1008	432
Crystal size/mm^3	0.8 × 0.2 × 0.2	0.418 × 0.089 × 0.067	0.734 × 0.487 × 0.212	0.456 × 0.398 × 0.064	0.914 × 0.089 × 0.048
Radiation	CuKα (λ = 1.54178)	CuKα (λ = 1.54178)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)
2Θ range for data collection/°	7.348 to 136.622	7.898 to 136.666	7.11 to 55.022	5.212 to 54.988	5.288 to 54.97
Index ranges	-16 ≤ h ≤ 16, -10 ≤ k ≤ 10, -19 ≤ l ≤ 20	-10 ≤ h ≤ 10, -26 ≤ k ≤ 26, -14 ≤ l ≤ 13	-11 ≤ h ≤ 11, -14 ≤ k ≤ 14, -15 ≤ l ≤ 15	-27 ≤ h ≤ 27, -10 ≤ k ≤ 10, -15 ≤ l ≤ 15	-10 ≤ h ≤ 10, -15 ≤ k ≤ 15, -15 ≤ l ≤ 15
Reflections collected	60527	39131	32021	71598	38219
Independent reflections	3542 [R_{int} = 0.0527, R_{sigma} = 0.0191]	3884 [R_{int} = 0.0839, R_{sigma} = 0.0469]	4583 [R_{int} = 0.0632, R_{sigma} = 0.0493]	4820 [R_{int} = 0.1084, R_{sigma} = 0.0433]	5008 [R_{int} = 0.0898, R_{sigma} = 0.0532]
Data/restraints/parameters	3542/0/339	3884/0/365	4583/0/364	4820/0/385	5008/0/340
Goodness-of-fit on F^2	1.069	1.068	1.049	1.142	1.005
Final R indexes [I>=2σ (I)]	R_1 = 0.0453, wR_2 = 0.1043	R_1 = 0.0585, wR_2 = 0.1560	R_1 = 0.0586, wR_2 = 0.1509	R_1 = 0.0645, wR_2 = 0.1783	R1 = 0.0536, wR2 = 0.1353
Final R indexes [all data]	R_1 = 0.0653, wR_2 = 0.1295	R_1 = 0.0799, wR_2 = 0.1939	R_1 = 0.0689, wR_2 = 0.1647	R_1 = 0.0975, wR_2 = 0.2129	R1 = 0.1051, wR2 = 0.1679
Largest diff. peak/hole / e Å^{-3}	0.16/-0.14	0.30/-0.23	0.76/-0.24	0.40/-0.35	0.25/-0.19

Identification code	**BZMDSLC**	**BZMDMLC**	**BZMDIAC**	**BZMDRES**	**BZMDFMA**
Empirical formula	$C_{20}H_{19}N_3O_7$	$C_{17}H_{17}N_3O_8$	$C_{21}H_{19}N_3O_8$	$C_{32}H_{32}N_6O_{10}$	$C_{15}H_{15}N_3O_6$
Formula weight	413.38	391.33	441.39	660.63	333.3
Temperature/K	301.34	302.34	304	300.39	300
Crystal system	monoclinic	monoclinic	monoclinic	orthorhombic	monoclinic
Space group	$P2_1/c$	C2/c	$P2_1/c$	Pbca	$P2_1/c$
a/Å	9.5055(6)	43.130(3)	8.8300(3)	26.3241(4)	9.0358(5)
b/Å	31.2239(19)	5.7944(4)	33.7182(10)	7.16120(10)	26.6419(14)
c/Å	6.8578(4)	15.2645(11)	7.3199(2)	33.8433(5)	6.8796(3)
α/°	90	90	90	90	90
β/°	102.628(2)	109.600(3)	107.8780(10)	90	102.419(2)
γ/°	90	90	90	90	90
Volume/Å^3	1986.2(2)	3593.7(5)	2074.13(11)	6379.87(16)	1617.38(14)
Z	4	8	4	8	4
ρ_{calc}g/cm^3	1.382	1.447	1.414	1.376	1.369
μ/mm^{-1}	0.106	0.117	0.11	0.875	0.108
F(000)	864	1632	920	2768	696
Crystal size/mm^3	0.678 × 0.244 × 0.16	0.571 × 0.231 × 0.05	0.954 × 0.3 × 0.11	0.254 × 0.116 × 0.11	0.632 × 0.172 × 0.168
Radiation	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	MoKα (λ = 0.71073)	CuKα (λ = 1.54178)	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.884 to 55.016	5.338 to 55.024	5.972 to 61.04	5.222 to 136.67	5.538 to 55.056
Index ranges	-12 ≤ h ≤ 12, -40 ≤ k ≤ 40, -8 ≤ l ≤ 8	-56 ≤ h ≤ 49, -7 ≤ k ≤ 7, -19 ≤ l ≤ 19	-12 ≤ h ≤ 12, -48 ≤ k ≤ 48, -10 ≤ l ≤ 10	-31 ≤ h ≤ 31, -8 ≤ k ≤ 8, -40 ≤ l ≤ 40	-11 ≤ h ≤ 11, -34 ≤ k ≤ 34, -8 ≤ l ≤ 8
Reflections collected	69959	20803	38842	121051	46849
Independent reflections	4553 [R_{int} = 0.0348, R_{sigma} = 0.0177]	4130 [R_{int} = 0.0894, R_{sigma} = 0.0690]	6344 [R_{int} = 0.0365, R_{sigma} = 0.0260]	5865 [R_{int} = 0.0657, R_{sigma} = 0.0254]	3705 [R_{int} = 0.0658, R_{sigma} = 0.0313]
Data/restraints/parameters	4553/100/347	4130/0/322	6344/0/365	5865/0/540	3705/0/267
Goodness-of-fit on F^2	1.055	1.019	1.035	1.033	1.046
Final R indexes [I>=2σ (I)]	R_1 = 0.0417, wR_2 = 0.1079	R_1 = 0.0557, wR_2 = 0.1173	R_1 = 0.0502, wR_2 = 0.1313	R_1 = 0.0484, wR_2 = 0.1329	R_1 = 0.0514, wR_2 = 0.1298
Final R indexes [all data]	R_1 = 0.0484, wR_2 = 0.1150	R_1 = 0.1237, wR_2 = 0.1465	R_1 = 0.0668, wR_2 = 0.1445	R_1 = 0.0579, wR_2 = 0.1466	R_1 = 0.0752, wR_2 = 0.1507
Largest diff. peak/hole / e Å^{-3}	0.17/-0.20	0.18/-0.21	0.20/-0.21	0.30/-0.31	0.39/-0.33

Identification code	**BZMDMLN**	**BZMD2,6DBA**	**BZMD3,5DBA**
Empirical formula	$C_{29}H_{28}N_6O_{12}$	$C_{20}H_{19}N_3O_8$	$C_{46}H_{45}N_9O_{16}$
Formula weight	652.57	429.38	979.91
Temperature/K	300	301.07	300
Crystal system	orthorhombic	monoclinic	monoclinic
Space group	Pbcn	$P2_1/n$	$P2_1/n$
a/Å	26.1542(4)	8.2443(4)	7.1481(2)
b/Å	7.27080(10)	15.9009(7)	36.7892(8)
c/Å	16.6719(3)	15.4526(8)	18.0584(4)
α/°	90	90	90
β/°	90	102.454(2)	100.4510(10)
γ/°	90	90	90
Volume/Å^3	3170.36(9)	1978.04(17)	4670.1(2)
Z	4	4	4
ρ_{calc}g/cm^3	1.367	1.442	1.394
μ/mm^{-1}	0.922	0.113	0.907
F(000)	1360	896	2048
Crystal size/mm^3	0.455 × 0.29 × 0.13	0.834 × 0.665 × 0.274	0.284 × 0.141 × 0.058
Radiation	CuKα (λ = 1.54178)	MoKα (λ = 0.71073)	CuKα (λ = 1.54178)
2Θ range for data collection/°	11.14 to 136.416	5.672 to 55.078	5.526 to 137.306
Index ranges	-31 ≤ h ≤ 31, -8 ≤ k ≤ 8, -20 ≤ l ≤ 20	-10 ≤ h ≤ 10, -20 ≤ k ≤ 20, -20 ≤ l ≤ 19	-7 ≤ h ≤ 8, -44 ≤ k ≤ 44, -21 ≤ l ≤ 21
Reflections collected	54755	27674	56516
Independent reflections	2893 [R_{int} = 0.0383, R_{sigma} = 0.0196]	4348 [R_{int} = 0.0757, R_{sigma} = 0.0603]	8547 [R_{int} = 0.0581, R_{sigma} = 0.0362]
Data/restraints/parameters	2893/36/244	4348/0/356	8547/1/855
Goodness-of-fit on F^2	1.128	1.1	1.062
Final R indexes [I>=2σ (I)]	R_1 = 0.0779, wR_2 = 0.2572	R_1 = 0.0691, wR_2 = 0.1670	R1 = 0.0516, wR2 = 0.1322
Final R indexes [all data]	R_1 = 0.0834, wR_2 = 0.2678	R_1 = 0.0847, wR_2 = 0.1853	R1 = 0.0865, wR2 = 0.1757
Largest diff. peak/hole / e Å^{-3}	0.33/-0.27	0.37/-0.27	0.27/-0.21

Table S2 Hydrogen bonds of the BZMD structures

BZMDBZC					
Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1'--H1'...N2		0.99(3)	1.67(3)	2.645(2)	169(3)
C5 --H5A...O1		0.99(3)	2.53(3)	3.281(3)	132.7(19)'
C12--H12...O2'		0.99(3)	2.40(3)	3.334(3)	157(2)
C4 --H4C...O2'		0.97(4)	2.51(4)	3.463(3)	166(2)
C4 --H4A...O2'		1.02(3)	2.58(3)	3.553(3)	160(2)
C9 --H9...O4	Intra	0.95(3)	2.47(3)	2.829(3)	102.2(18)
C5 --H5A...O2	Intra	0.99(3)	2.22(3)	2.910(3)	126(2)

BZMDNAF					
Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1'--H1'...N2		0.92(4)	1.90(4)	2.794(3)	166(3)
C8'--H8'...O4		1.02(4)	2.43(4)	3.397(4)	159(3)
C9 --H9...O3	Intra	0.96(3)	2.42(3)	2.767(3)	101(2)
C13--H13...O4	Intra	0.98(3)	2.49(3)	2.819(3)	100(2)
C5 --H5A...O2	Intra	0.96(3)	2.44(3)	2.857(3)	106(2)
C6 --H6B...O2	Intra	0.97(2)	2.52(2)	3.069(3)	115.7(19)

BZMDMAC					
Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1' --H1'...N2		0.84(4)	1.88(4)	2.718(3)	172(3)
C6 --H6B...O1		1.04(2)	2.58(2)	3.435(2)	139(2)
C4 --H4A...O2'		0.92(3)	2.58(3)	3.462(4)	162.9(19)
C6' --H6'...O1'	Intra	0.94(3)	2.41(3)	2.739(3)	100.3(15)
C13 --H13...O3	Intra	0.88(3)	2.45(3)	2.742(3)	100(2)
C5 --H5B...O2	Intra	1.00(3)	2.39(2)	2.856(2)	108.0(15)
C5 --H5A...O4	Intra	0.99(2)	2.58(2)	3.090(3)	111.8(16)

BZMD3,5DNZ					
Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1'—H1'...N2		1.00(4)	1.65(4)	2.635(3)	168(4)
C5 --H5B...O4		1.02(4)	2.47(4)	3.189(4)	127(3)'
C2 --H2...O5'		0.91(4)	2.59(4)	3.324(4)	138(3)
C5 --H5A...O1		0.97(3)	2.56(4)	3.351(5)	140(3)
C4'--H4'...O6'		1.04(3)	2.50(3)	3.440(4)	149(3)'
C6'--H6'...O6'	Intra	0.97(4)	2.36(3)	2.721(4)	101(2)
C4'--H4'...O3'	Intra	1.04(3)	2.35(3)	2.730(4)	100(2)
C5 --H5B...O2	Intra	1.02(4)	2.29(3)	2.842(4)	112(2)

BZMDABN					
Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1' --H1'...N2		0.99(3)	1.72(4)	2.694(3)	165(3)
N1' --H1'B...O2'		0.89(4)	2.26(4)	3.071(4)	151(3)
N1' --H1'A...O4		0.89(4)	2.28(4)	3.140(4)	164(3)
C6 --H6B...O2		0.98(2)	2.51(2)	3.222(3)	128.8(18)
C6' --H6'...O2'		1.01(2)	2.59(2)	3.435(3)	141.1(17)
C5 --H5A...O2	Intra	0.94(2)	2.48(2)	2.847(3)	103.4(17)
C6 --H6A...O2	Intra	0.98(2)	2.51(2)	3.083(3)	117.1(17)

BZMDSLC

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1' --H1'...N2		0.91(2)	1.76(2)	2.6600(18)	172.0(18)
C3' --H3'A...O1		0.95(2)	2.413(19)	3.270(2)	150.0(16)
C11 --H11...O1		1.02(3)	2.54(2)	3.327(3)	133.7(17)
C2 --H2...O3'		0.95(2)	2.530(19)	3.4488(19)	163.4(15)
C10 --H10...O2		0.98(3)	2.53(3)	3.484(2)	163(2)
O3' --H3'...O2'	Intra	0.92(2)	1.80(2)	2.6219(18)	148(2)
C5 --H5A...O2	Intra	0.969(16)	2.438(15)	2.8286(19)	103.7(9)
C13 --H13...O4	Intra	0.923(19)	2.525(19)	2.845(2)	100.7(13)
C6 --H6A...O2	Intra	0.990(19)	2.428(17)	3.006(2)	116.8(12)

BZMDMLC

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
N2 --H2...O1'		1.00(3)	1.65(3)	2.644(3)	172(3)
C5 --H5B...O4		0.98(2)	2.46(2)	3.141(3)	125.9(17)'
N2 --H2...O2'		1.00(3)	2.59(3)	3.254(3)	124(2)'
C4 --H4B...O3'		0.95(3)	2.55(3)	3.303(4)	136(2)
C2 --H2A...O4'		0.92(2)	2.56(2)	3.347(3)	144(2)
C4 --H4A...O2'		1.00(4)	2.48(4)	3.373(4)	148(2)
C6 --H6A...O1		1.02(3)	2.58(3)	3.482(4)	148(2)
C3' --H3'A...O3'		0.97(3)	2.60(3)	3.505(3)	157(2)
O2' --H3'...O3'	Intra	1.35(5)	1.10(5)	2.427(4)	166(4)
C5 --H5B...O2	Intra	0.98(2)	2.24(2)	2.925(4)	126.2(18)

BZMDIAC

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O3' --H3'...O4'		1.01(3)	1.63(3)	2.6334(17)	171(3)
O1' --H1'...N2		0.94(2)	1.79(3)	2.7207(18)	172(2)
C2 --H2...O2'		0.98(2)	2.53(2)	3.110(2)	117.9(14)
C5 --H5A...O1		0.99(2)	2.56(2)	3.418(2)	145.0(15)
C4' --H4'...O3'		0.98(2)	2.54(2)	3.4617(19)	156.7(16)
C6' --H6'...O1'	Intra	0.965(14)	2.418(17)	2.7562(18)	100.1(12)
C5 --H5B...O2	Intra	0.979(19)	2.37(2)	2.847(2)	109.5(15)
C13 --H13...O4	Intra	0.94(3)	2.52(3)	2.854(2)	100.8(17)

BZMDRES

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1' --H1'...N2B		1.05(4)	1.75(4)	2.758(2)	159(3)
O2' --H2'...N2A		1.04(4)	1.79(4)	2.761(2)	155(3)
C11B --H11B...O1A		1.07(3)	2.43(2)	3.252(3)	132.2(18)
C2B --H2B...O1'		0.92(3)	2.52(3)	3.326(3)	148(2)
C10B --H10B...O2A		1.08(3)	2.50(3)	3.465(3)	149(2)
C5B --H5BB ..O2B	Intra	0.93(3)	2.37(2)	2.823(3)	109.9(16)
C5A --H5AA ..O2A	Intra	0.95(3)	2.42(3)	2.864(3)	109(2)
C13A --H13A ..O4A	Intra	0.93(2)	2.51(2)	2.860(3)	102.6(16)
C13B --H13B ..O4B	Intra	0.95(3)	2.52(3)	2.851(3)	100.4(18)
C6A --H6AB ..O2A	Intra	0.92(3)	2.54(3)	3.105(3)	120(2)
C6B --H6BB ..O2B	Intra	1.06(3)	2.58(2)	3.086(3)	108.6(16)
C5B --H5BB ..O2B	Intra	0.93(3)	2.37(2)	2.823(3)	109.9(16)

BZMDFMA

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)

O1'--H1'...N2		1.00(4)	1.66(4)	2.652(3)	174(3)
C2'--H2'...O1		0.96(3)	2.45(3)	3.285(3)	145(2)
C2 --H2...O2'		0.96(3)	2.54(3)	3.495(3)	176(2)
C4 --H4A...O2'		0.96	2.58	3.439(3)	149
C9 --H9...O3	Intra	0.95(3)	2.39(3)	2.736(3)	100.9(19)
C2'--H2'...O1'	Intra	0.96(3)	2.40(3)	2.747(3)	101.2(19)'
C5 --H5B...O2	Intra	0.97(3)	2.40(2)	2.831(3)	106.4(14)
C13--H13...O4	Intra	0.96(3)	2.52(3)	2.854(3)	100.6(19)

BZMDMLN

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1' --H1'...N2		0.82	1.92	2.715(9)	164
O1" --H1"...N2		0.82	2.31	2.736(8)	113
C2 --H2...O2"		0.93	2.41	3.334(8)	177
C13 –H13...O3	Intra	0.93	2.41	2.724(3)	100
C5 --H5B...O1	Intra	0.97	2.43	2.827(5)	104
C6 --H6A...O1	Intra	0.97	2.43	3.034(5)	125

BZMD2,6DBA

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
N2 --H1'...O1'		1.24(5)	1.33(5)	2.564(2)	171(4)
O4' --H4'...O1		1.04(4)	2.55(3)	3.069(3)	110(3)
C6 --H6B...O4		0.98(3)	2.45(3)	3.307(3)	146(2)
C5' --H5'...N2		0.99(3)	2.59(3)	3.487(3)	150(3)
O2' --H3'...O3'	Intra	1.14(5)	1.39(5)	2.513(3)	167(4)
O4' --H4'...O1'	Intra	1.04(4)	1.64(4)	2.588(2)	149(3)'
C9 --H9...O3	Intra	0.92(3)	2.42(3)	2.772(3)	103.1(19)
C5 --H5B...O2	Intra	0.94(2)	2.40(2)	2.809(3)	105.7(17)
C6 --H6A...O2	Intra	1.02(2)	2.51(2)	3.036(3)	111.1(16)

BZMD3,5DBA

Donor-H…Acceptor	Type	D…H(Å)	H...A(Å)	D...A(Å)	D-H...A(º)
O1' --H1'...N2C		0.99(4)	1.73(4)	2.715(3)	174(3)
O3' --H3'...N2B		0.98(4)	1.78(4)	2.751(3)	175(3)
O4' --H4'...N2A		0.94(4)	1.83(4)	2.764(3)	172(3)
C6A --H6AA...O4A		1.00(3)	2.38(3)	3.209(4)	140(2)
C2B --H2B...O4'		0.96(3)	2.46(3)	3.288(4)	145(2)
C6A --H6AB...O2'		1.02(4)	2.57(4)	3.302(4)	129(3)'
C11A --H11A...O1C		1.00(4)	2.58(4)	3.374(5)	136(3)
C2' --H2'...O3A		0.98(3)	2.58(3)	3.501(3)	157(2)
C13A --H13A...O4A	Intra	0.97(4)	2.40(4)	2.795(5)	104(3)
C9B --H9B...O3B	Intra	0.93(3)	2.47(3)	2.797(4)	101(2)
C5B --H5BA...O2B	Intra	0.97(3)	2.42(3)	2.829(5)	105(2)
C5C --H5CA...O2C	Intra	0.97(3)	2.47(3)	2.830(4)	102(2)
C5A --H5AA...O2A	Intra	0.96(3)	2.47(3)	2.885(4)	106(2)
C6C --H6CA...O2C	Intra	1.00(4)	2.49(3)	3.074(4)	117(2)
C6B --H6BB...O2B	Intra	1.02(4)	2.50(3)	3.076(4)	115(2)
C6A --H6AB...O2A	Intra	1.02(4)	2.49(4)	3.091(4)	118(3)

Table S3 Selected π-π interactions

Code	Cg1	Cg2	Cg-Cg (Å)	α (°)	β (°)	γ (°)	Slippage (Å)
BZC	Imid	Phen	3.9455(14)	6.10(12)	25.4	31.1	1.691
	Phen	Imid	3.9455(14)	6.10(12)	31.1	25.4	2.04
NAF	Cof	Imid	3.6418(18)	6.87(15)	21.1	24	1.308
	Imid	Cof	3.6418(18)	6.87(15)	24	21.1	1.478
	Cof	Imid	4.0431(16)	7.02(14)	33.1	26.5	2.206
	Imid	Cof	4.0431(16)	7.02(14)	26.5	33.1	1.805
MAC	Cof	Imid	3.6911(13)	6.43(11)	17.8	23.8	1.128
	Imid	Cof	3.6912(13)	6.43(11)	23.8	17.8	1.487
	Cof	Phen	4.0761(15)	9.95(12)	21	28.8	1.46
	Phen	Cof	4.0761(15)	9.95(12)	28.8	21	1.962
	Imid	Phen	4.3227(15)	16.35(13)	29.2	19.9	2.109
	Phen	Imid	4.3227(15)	16.35(13)	19.9	29.2	1.474
3,5DNZ	Imid	Phen	3.889(2)	15.88(19)	32.3	28.2	2.076
	Phen	Imid	3.889(2)	15.88(19)	28.2	32.3	1.836
ABN	Cof	Imid	3.6656(17)	3.73(14)	22.8	24.9	1.42
	Imid	Cof	3.6657(17)	3.75(14)	24.9	22.8	1.544
	Phen	Phen	4.0390(19)	0.00(14)	32.9	32.9	2.191
SLC	Cof	Cof	3.5958(9)	0.00(7)	12	12	0.748
	Imid	Cof	3.6278(9)	5.23(8)	21.2	19.9	1.314
	Cof	Imid	3.6279(9)	5.23(8)	19.9	21.2	1.235
	Phen	Phen	4.0722(11)	11.36(8)	27.6	38.8	1.885
	Phen	Phen	4.0723(11)	11.36(8)	38.8	27.6	2.55
MLC	Phen	Phen	4.1470(17)	0.00(14)	37.3	37.3	2.513
IAC	Cof	Imid	3.8502(9)	16.51(8)	31.1	15.2	1.987
	Imid	Cof	3.8502(9)	16.51(8)	15.2	31.1	1.009
	Phen	Phen	4.0147(11)	4.74(10)	31.6	27.7	2.104
	Phen	Phen	4.0148(11)	4.74(10)	27.7	31.6	1.864
RES	PhenA	PhenA	4.0344(13)	7.67(11)	29.4	35.9	1.98
	PhenA	PhenA	4.0344(13)	7.67(11)	35.9	29.4	2.367
	ImidB	Cof	4.0361(12)	17.42(10)	22.7	38.9	1.561
	Cof	ImidB	4.0362(12)	17.42(10)	38.9	22.7	2.533
	PhenB	PhenB	4.0656(14)	4.61(12)	30.1	34.2	2.039
	PhenB	PhenB	4.0657(14)	4.61(12)	34.2	30.1	2.285
FMA	Phen	Phen	4.0004(15)	6.38(12)	34.8	28.6	2.281
	Phen	Phen	4.0004(15)	6.38(12)	28.6	34.8	1.913
MLN	Phen	Phen	4.155(2)	9.89(18)	38.1	29.5	2.563
	Phen	Phen	4.156(2)	9.89(18)	29.5	38.1	2.043
2,6DBA	Phen	Cof	4.0421(15)	5.36(12)	28.9	24.9	1.954
	Cof	Phen	4.0422(15)	5.36(12)	24.9	28.9	1.702
3,5DBA	Cof	ImidA	3.6373(16)	7.20(15)	22	15.3	1.361
	ImidA	Cof	3.6373(16)	7.20(15)	15.3	22	0.962
	Cof	ImidA	3.7439(16)	7.20(15)	27.9	24.1	1.751
	ImidA	Cof	3.7438(16)	7.20(15)	24.1	27.9	1.53
	ImidC	PhenA	3.840(2)	3.46(18)	29	25.6	1.862
	PhenA	ImidC	3.840(2)	3.46(18)	25.6	29	1.658

PhenB	PhenC'	4.069(10)	18.4(8)	15.9	33.5	1.112
PhenC'	PhenB	4.069(10)	18.4(8)	33.5	15.9	2.245
PhenB	PhenC'	4.109(10)	18.4(8)	26.8	42.3	1.851
PhenC'	PhenB	4.110(10)	18.4(8)	42.3	26.8	2.764
PhenC	PhenB	4.163(11)	19	22	41.1	1.561
PhenB	PhenC	4.163(11)	19	41.1	22	2.736

Table S4 Calculated ΔpKa between BZMD and coformers.

Code	**pKa (API)**	**pKa (Coformer)**	**ΔpKa**	**Novel form**
BZMDNAF		9.51	-6.96	Cocrystal
BZMDRES		9.15	-6.6	Cocrystal
BZMDMAC		4.47	-1.92	Cocrystal
BZMDBZC		4.2	-1.65	Cocrystal
BZMD3,5DBA		4.04	-1.49	Cocrystal
BZMDIAC		3.7	-1.15	Cocrystal
BZMDABN	2.55	3.11	-0.56	Cocrystal (Solvate)
BZMDFMA		3.02	-0.47	Cocrystal
BZMDSLC		2.97	-0.42	Cocrystal
BZMDMLN		2.85	-0.3	Cocrystal
BZMD3,5DNZ		2.77	-0.22	Cocrystal
BZMD2,6DBA		2.77	-0.22	Salt
BZMDMLC		1.83	0.72	Salt

Table S5 List of coformers and used stoichiometry in the unsuccessful crystallization attempts. In all attempts 2 mL of ethanol were used as solvent and the crystallization method was slow evaporation at room temperature.

Coformer	**Stoichiometry**
2,4-Dihydroxybenzoic acid	1:3
2-picolinic	1:1
4-Aminobenzoic acid	1:1
Oxalic acid	1:2
Caffeic acid	1:3
p-Coumaric acid	1:2
Phthalic acid	1:2
Propyl 4- hydroxybenzoate	1:1
Propyl gallate	1:3
Pyridoxine	1:3
Trans-Acotinic acid	1:3
Acetylsalicylic acid	1:1
Adipic acid	1:2
Methyl 3,4,5-trihydroxybenzoate	1:3
Boric acid	1:3
DL-Glutamic acid monohydrate	1:2
DL-Malic acid	1:3
Sarcosine	1:1
Succinic acid	1:2
Terephthalic acid	1:2
Trans-Ferulic acid	1:2
Triethanolamine	1:3
Umbelliferone	1:1
L-Glutamic acid	1:1
Glutaric acid	1:2
Glycolic acid	1:2
Nicotinic acid	1:1
Vanillic acid	1:2
Vanillin	1:1
α-Naftol	1:1
Mandelic acid	1:2
Phenol	1:1

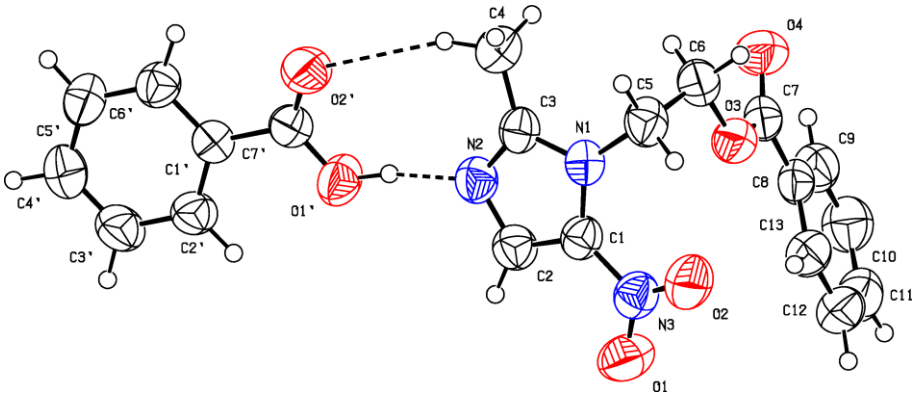

Figure S1 - Representation of the asymmetric unit of the BZMDBZC cocrystal with software ORTEP3.

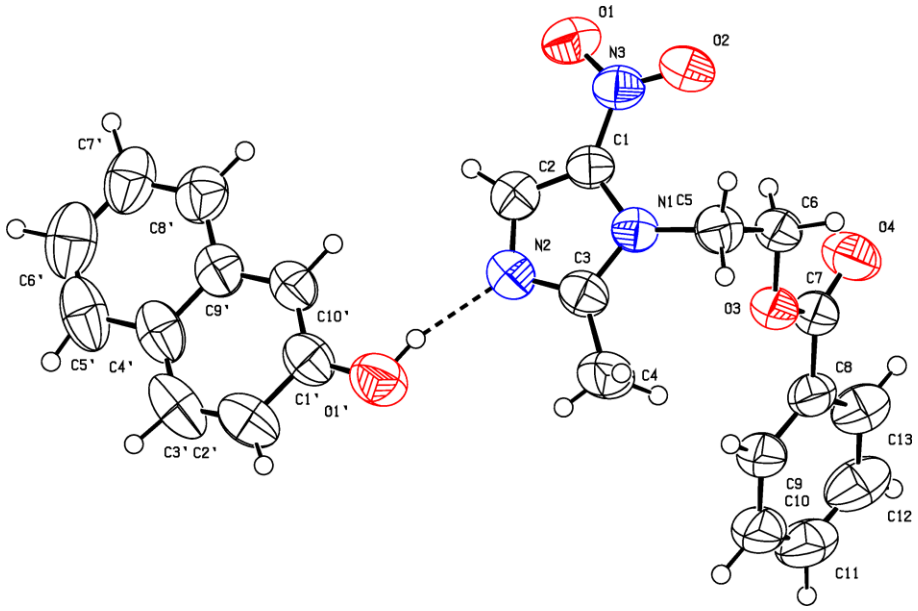

Figure S2 - Representation of the asymmetric unit of the BZMDNAF cocrystal with software ORTEP3.

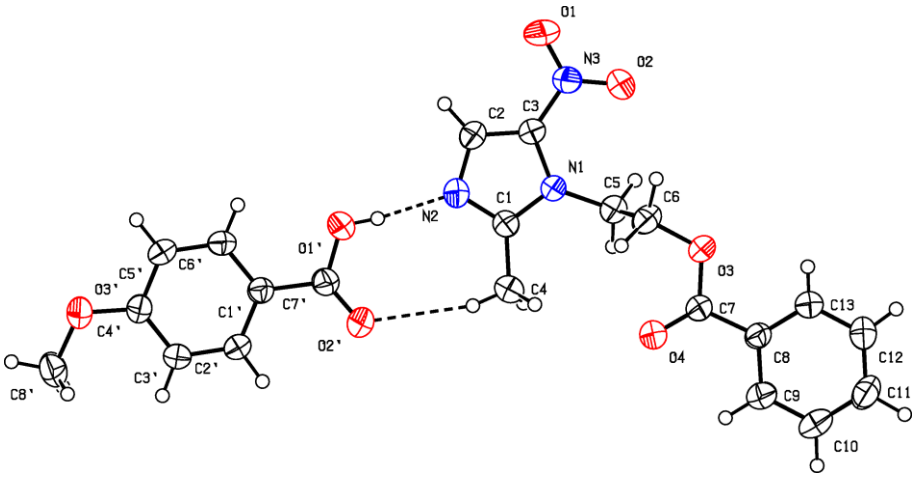

Figure S3 - Representation of the asymmetric unit of the BZMDMAC cocrystal with software ORTEP3.

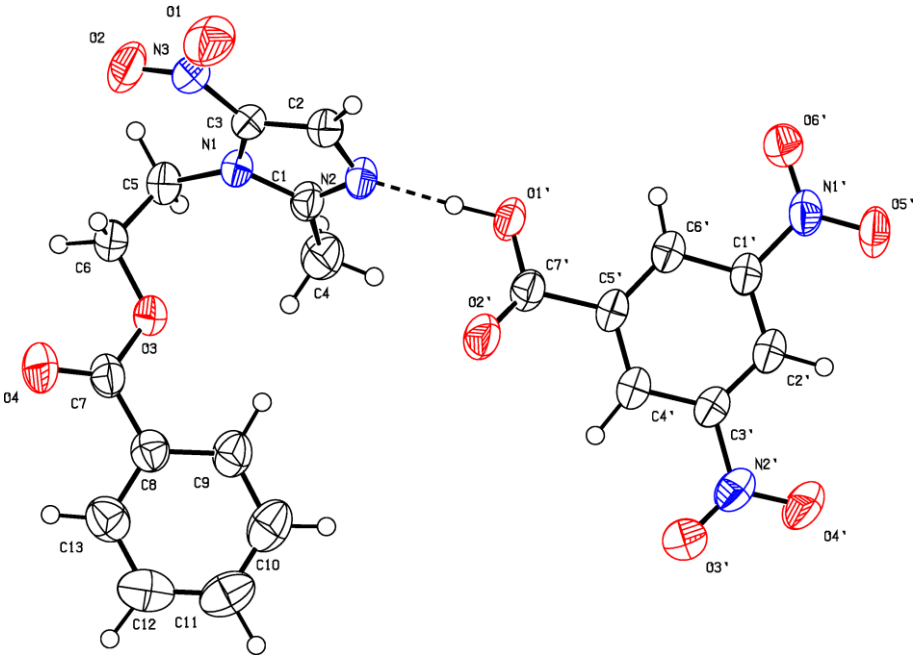

Figure S1 - Representation of the asymmetric unit of the BZMD3,5DNZ cocrystal with software ORTEP3.

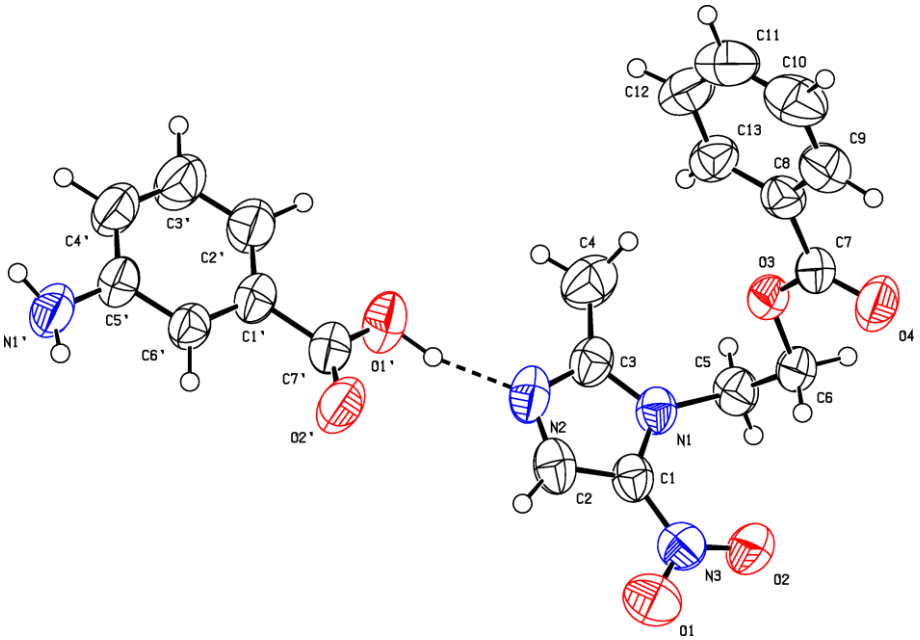

Figure S5 - Representation of the asymmetric unit of the BZMDABN cocrystal with software ORTEP3.

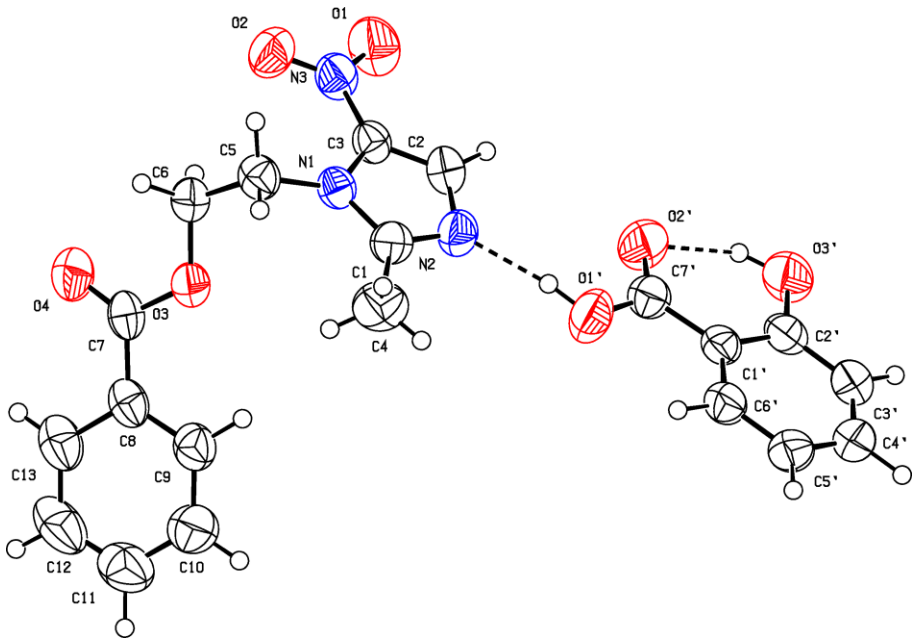

Figure S6 - Representation of the asymmetric unit of the BZMDSLC cocrystal with software ORTEP3.

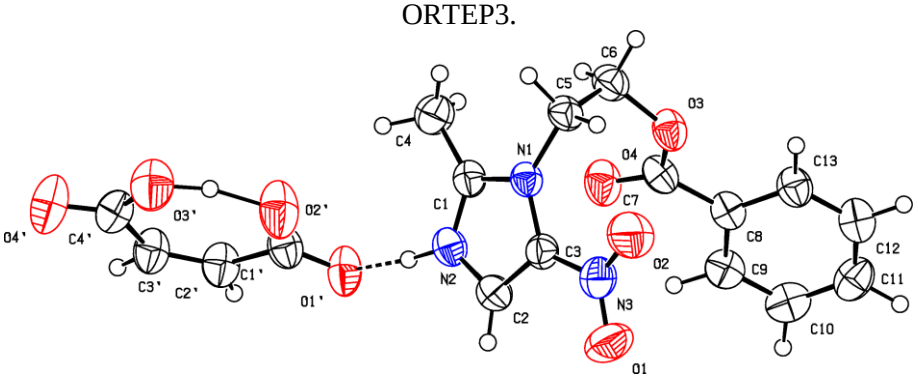

Figure S2 - Representation of the asymmetric unit of the BZMDMLC cocrystal with software ORTEP3.

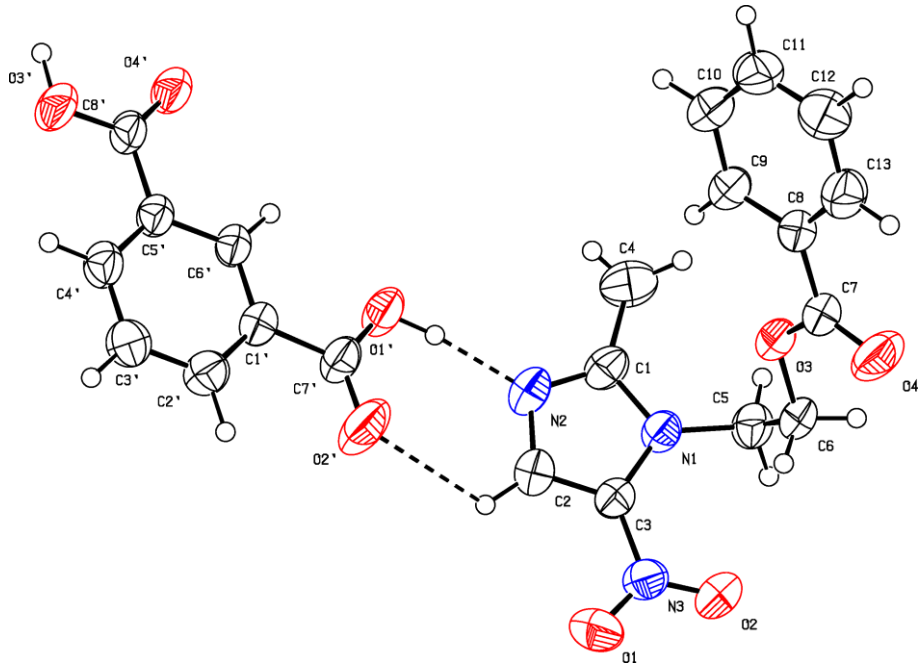

Figure S3 - Representation of the asymmetric unit of the BZMDIAC cocrystal with software ORTEP3.

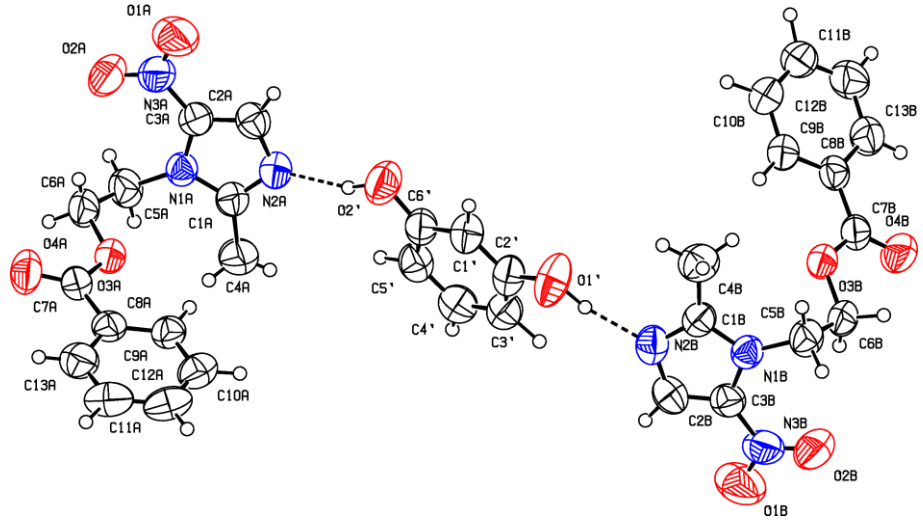

Figure S9 - Representation of the asymmetric unit of the BZMDRES cocrystal with software ORTEP3.

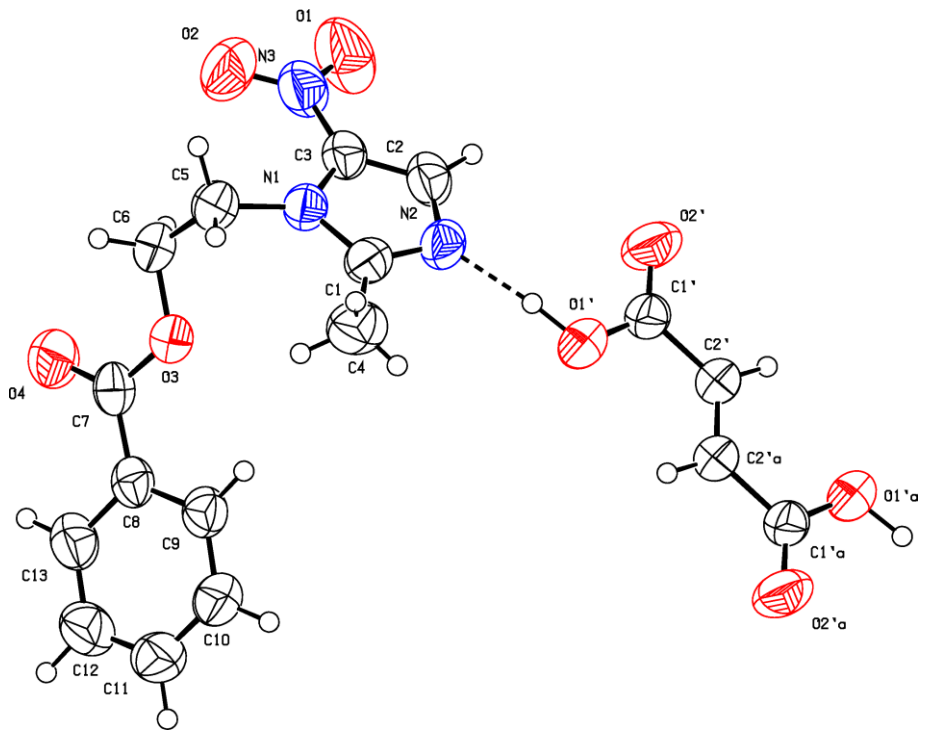

Figure S10 - Representation of the asymmetric unit of the BZMDFMA cocrystal with software ORTEP3.

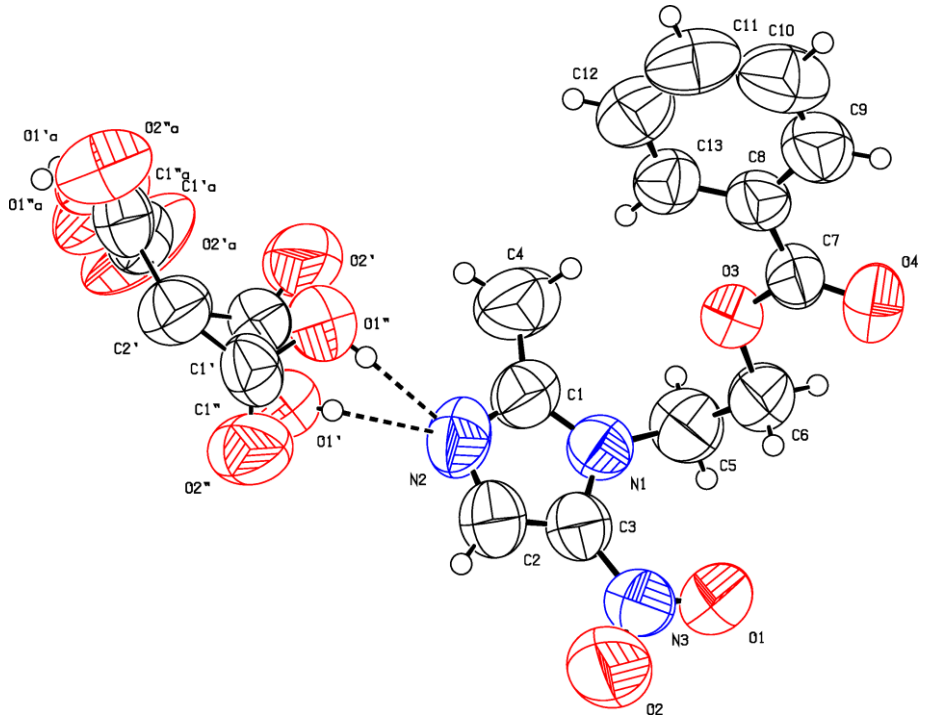

Figure S11 - Representation of the asymmetric unit of the BZMDMLN cocrystal with software ORTEP3.

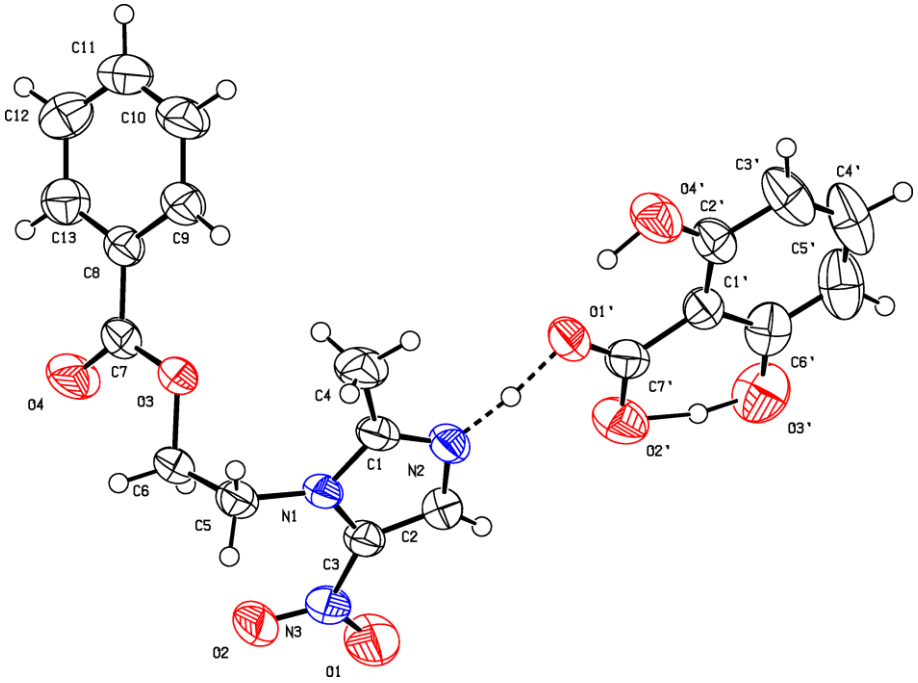

Figure S12 - Representation of the asymmetric unit of the BZMD2,6DBA cocrystal with software ORTEP3.

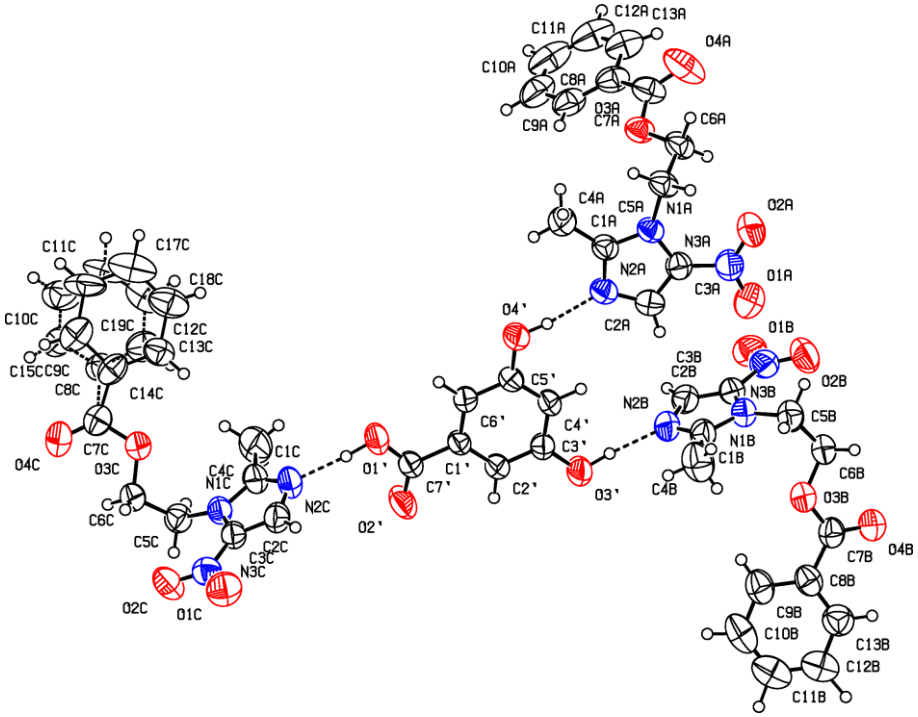

Figure S13 - Representation of the asymmetric unit of the BZMD3,5DBA cocrystal with software ORTEP3.