Electronic Supplementary Information

Proteasome inhibition and cytostatic effects to human cancer cells by pyrazolone-enamines: a combined crystallographic, structural and computational study

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Characterization of the position of the hydrogen atom

In the crystal structures, the hydrogen atoms involved in tautomeric reactions were found in the final difference Fourier map and participated in the refinement, which confirms the establishment of the keto-enamine forms in the solid state. Then the ^{1}H NMR spectra were recorded in [D_6]DMSO to confirm the positions of the hydrogen atoms in solution. As the nine compounds are very similar, compounds **1** and **6** were selected to make the detailed discussions. For compound **1**, the chemical shift at 13.34 ppm is assigned to the resonance of the hydrogen in carboxyl. The chemical shift at 12.77 ppm is assigned to the resonance of H1, which confirms the existence of the keto-enamine forms in DMSO solution. The signals in the range of 8.17 ~ 7.18 ppm are assigned to the resonance of the hydrogen in phenyl rings. The signal at 1.48 ppm is ascribed to the resonance of the hydrogen in methyl. For compound **6**, the chemical shift at 12.67 ppm is assigned to the resonance of H3, which also confirms the existence of the keto-enamine forms in DMSO solution. The chemical shift at 9.52 ppm is assigned to the resonance of the hydrogen in hydroxyl. The signals in the range of 8.01 ~ 6.24 ppm are assigned to the resonance of the hydrogen in phenyl rings. The signal at 2.00 ppm is ascribed to the resonance of the hydrogen in the methyl connected with the phenyl ring. The signal at 1.44 ppm is attributed to the resonance of the hydrogen the methyl connected with the pyrazolone ring.

Table S1. Crystallographic data and structure refinement for compounds **1** ~ **6**

Compound	**1**	**2**	**3**
Empirical formula	$C_{27}H_{25}N_3O_6$	$C_{32}H_{34}N_4O_3$	$C_{26}H_{25}N_3O_4$
Formula weight	487.50	522.63	443.49
Temperature (K)	298(2)	298(2)	298(2)
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	Triclinic	Triclinic	Triclinic
Space group	P^{-1}	P^{-1}	P^{-1}
a (Å)	8.4482(7)	9.5274(8)	10.1589(11)
b (Å)	10.4238(11)	10.4205(9)	11.3338(12)
c (Å)	13.9303(12)	14.7518(13)	11.6688(14)
α (˚)	86.458(2)	77.2540(10)	68.3220(10)
β (˚)	77.2390(10)	82.0960(10)	67.3960(10)
γ (˚)	86.317(2)	84.377(2)	82.841(2)
Volume (Å^3)	1192.54(19)	1411.4(2)	1152.4(2)
Z	2	2	2
Calculated density (g/cm^3)	1.358	1.227	1.278
Absorption coefficient (mm^{-1})	0.097	0.080	0.087
F(000)	512	556	468
Crystal size (mm)	0.42 × 0.30 × 0.27	0.42 × 0.37 × 0.18	0.43 × 0.38 × 0.23
θ range for data collection (˚)	3.00 to 25.02	2.44 to 25.02	2.60 to 25.02
Limiting indices	$-10 \le h \le 9$	$-11 \le h \le 11$	$-12 \le h \le 11$
	$-12 \le k \le 9$	$-8 \le k \le 12$	$-13 \le k \le 13$
	$-16 \le l \le 16$	$-16 \le l \le 17$	$-13 \le l \le 13$
Reflections collected / unique	6035 / 4140 [R_{int} = 0.0413]	7082 / 4894 [R_{int} = 0.0636]	6007 / 4003 [R_{int} = 0.0284]
Completeness to θ = 25.02	0.982	0.980	0.982
Max. and min. transmission	0.9742 and 0.9603	0.9857 and 0.9672	0.9802 and 0.9634
Data / restraints / parameters	4140 / 0 / 327	4894 / 0 / 355	4003 / 0 / 298
Goodness of fit on F^2	0.995	1.010	0.973
R_1[a], wR_2[b] [$I > 2\sigma(I)$]	R_1 = 0.0640	R_1 = 0.0729	R_1 = 0.0513
	wR_2 = 0.1427	wR_2 = 0.1616	wR_2 = 0.1346
R_1[a], wR_2[b] (all data)	R_1 = 0.1562	R_1 = 0.2033	R_1 = 0.0931
	wR_2 = 0.1892	wR_2 = 0.2464	wR_2 = 0.1720
Largest diff. peak and hole (e. Å^3)	0.329 and -0.279	0.347 and -0.236	0.499 and -0.263
Compound	**4**	**5**	**6**
Empirical formula	$C_{25}H_{24}N_4O_3$	$C_{24}H_{21}N_3O_2$	$C_{24}H_{21}N_3O_2$
Formula weight	428.48	383.44	383.44
Temperature (K)	298(2)	298(2)	298(2)
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	Triclinic	Triclinic	Triclinic
Space group	P^{-1}	P^{-1}	P^{-1}

a (Å)	7.3752(6)	7.7356(7)	7.2287(6)
b (Å)	10.9275(9)	10.8256(8)	11.0934(9)
c (Å)	14.5614(12)	13.5508(11)	14.0509(14)
α (˚)	101.707(2)	112.683(2)	107.981(2)
β (˚)	92.7690(10)	90.9070(10)	99.5340(10)
γ (˚)	98.5440(10)	107.7410(10)	105.1460(10)
Volume (Å^3)	1132.64(16)	985.67(14)	996.58(15)
Z	2	2	2
Calculated density (g/cm^3)	1.253	1.292	1.278
Absorption coefficient (mm^{-1})	0.084	0.088	0.083
F(000)	452	404	404
Crystal size (mm)	0.42 × 0.40 × 0.23	0.46 × 0.44 × 0.35	0.50 × 0.48 × 0.40
θ range for data collection (˚)	2.64 to 25.02	2.80 to 25.02	3.02 to 25.02
Limiting indices	$-8 \le h \le 8$	$-9 \le h \le 9$	$-8 \le h \le 8$
	$-12 \le k \le 12$	$-12 \le k \le 12$	$-13 \le k \le 12$
	$-17 \le l \le 12$	$-16 \le l \le 11$	$-16 \le l \le 11$
Reflections collected / unique	5528 / 3936 [R_{int} = 0.0437]	4952 / 3429 [R_{int} = 0.0237]	4993 / 3457 [R_{int} = 0.0255]
Completeness to θ = 25.02	0.983	0.984	0.982
Max. and min. transmission	0.9809 and 0.9654	0.9699 and 0.9607	0.9676 and 0.9597
Data / restraints / parameters	3936 / 0 / 291	3429 / 0 / 264	3457 / 0 / 263
Goodness of fit on F^2	1.025	1.044	0.971
R_1[a], wR_2[b] [$I > 2\sigma(I)$]	R_1 = 0.0721	R_1 = 0.0446	R_1 = 0.0427
	wR_2 = 0.1896	wR_2 = 0.1076	wR_2 = 0.1076
R_1[a], wR_2[b] (all data)	R_1 = 0.1387	R_1 = 0.0735	R_1 = 0.0627
	wR_2 = 0.2453	wR_2 = 0.1320	wR_2 = 0.1258
Largest diff. peak and hole (e. Å^3)	0.484 and -0.298	0.536 and -0.481	0.206 and -0.192

[a] $R = \Sigma(||F_0|-|F_C||)/\Sigma|F_0|$

[b] $wR = [\Sigma w(|F_0|^2-|F_C|^2)^2/\Sigma w(F_0^2)]^{1/2}$.

Table S2. Selected bond lengths and angles for compound **1** (Å, °)

Bond	Dist.	Bond	Dist.
N1–C9	1.334(4)	C7–C8	1.383(5)
N1–C7	1.416(5)	C9–C17	1.384(5)
N2–C16	1.365(4)	C9–C10	1.482(5)
N2–N3	1.396(4)	C10–C15	1.374(6)
N2–C20	1.417(4)	C10–C11	1.383(5)
N3–C18	1.305(4)	C11–C12	1.374(5)
O1–C1	1.200(5)	C12–C13	1.374(6)
O2–C1	1.306(5)	C13–C14	1.362(6)
O3–C2	1.323(4)	C14–C15	1.372(5)
O4–C2	1.186(4)	C16–C17	1.442(5)
O5–C16	1.245(4)	C17–C18	1.434(5)
O6–C26	1.407(7)	C18–C19	1.490(5)
C1–C3	1.479(5)	C20–C25	1.372(5)
C2–C5	1.490(5)	C20–C21	1.378(5)
C3–C4	1.378(5)	C21–C22	1.375(5)
C3–C8	1.381(5)	C22–C23	1.369(6)
C4–C5	1.387(5)	C23–C24	1.372(6)
C5–C6	1.383(5)	C24–C25	1.387(5)
C6–C7	1.376(5)	C26–C27	1.396(8)
Bond	Angle	Bond	Angle
C9–N1–C7	132.3(3)	C15–C10–C11	119.4(4)
C16–N2–N3	111.8(3)	C15–C10–C9	119.8(4)
C16–N2–C20	127.4(3)	C11–C10–C9	120.7(4)
N3–N2–C20	119.6(3)	C12–C11–C10	119.7(4)
C18–N3–N2	106.6(3)	C13–C12–C11	120.0(4)
O1–C1–O2	122.5(4)	C14–C13–C12	120.7(4)
O1–C1–C3	123.2(4)	C13–C14–C15	119.5(5)
O2–C1–C3	114.2(4)	C14–C15–C10	120.8(4)
O4–C2–O3	124.1(4)	O5–C16–N2	126.5(3)
O4–C2–C5	125.1(4)	O5–C16–C17	128.1(3)
O3–C2–C5	110.8(3)	N2–C16–C17	105.4(3)
C4–C3–C8	120.7(4)	C9–C17–C18	133.2(3)
C4–C3–C1	121.9(4)	C9–C17–C16	122.2(3)
C8–C3–C1	117.4(4)	C18–C17–C16	104.6(3)
C3–C4–C5	119.4(4)	N3–C18–C17	111.7(3)
C6–C5–C4	119.5(4)	N3–C18–C19	119.6(3)
C6–C5–C2	120.0(3)	C17–C18–C19	128.8(4)
C4–C5–C2	120.5(4)	C25–C20–C21	119.8(4)
C7–C6–C5	121.3(3)	C25–C20–N2	120.2(4)
C6–C7–C8	118.9(4)	C21–C20–N2	120.0(4)
C6–C7–N1	116.6(3)	C22–C21–C20	119.4(4)
C8–C7–N1	124.4(3)	C23–C22–C21	121.3(4)

C3–C8–C7	120.2(4)	C22–C23–C24	119.4(4)
N1–C9–C17	117.8(3)	C23–C24–C25	119.9(4)
N1–C9–C10	119.6(3)	C20–C25–C24	120.2(4)
C17–C9–C10	122.6(3)	C27–C26–O6	114.9(6)

Table S3. Selected bond lengths and angles for compound **2** (Å, °)

Bond	Dist.	Bond	Dist.
N1–C3	1.361(6)	C12–C17	1.383(6)
N1–N2	1.395(5)	C12–C13	1.391(6)
N1–C4	1.412(6)	C13–C14	1.362(7)
N2–C1	1.308(6)	C14–C15	1.373(8)
N3–C11	1.344(6)	C15–C16	1.365(8)
N3–C18	1.412(6)	C16–C17	1.371(7)
N4–C28	1.375(7)	C18–C19	1.363(7)
O1–C3	1.249(5)	C18–C23	1.378(6)
O2–C31	1.315(8)	C19–C20	1.380(7)
O3–C32	1.395(8)	C20–C21	1.384(6)
C1–C2	1.431(6)	C21–C22	1.367(7)
C1–C10	1.500(6)	C21–C24	1.506(7)
C2–C11	1.377(7)	C22–C23	1.377(7)
C2–C3	1.436(6)	C24–C25	1.507(7)
C4–C5	1.359(6)	C25–C30	1.356(7)
C4–C9	1.387(6)	C25–C26	1.378(7)
C5–C6	1.373(7)	C26–C27	1.382(7)
C6–C7	1.388(7)	C27–C28	1.367(8)
C7–C8	1.350(8)	C28–C29	1.368(8)
C8–C9	1.360(7)	C29–C30	1.386(8)
C11–C12	1.460(6)		
Bond	Angle	Bond	Angle
C3–N1–N2	111.2(4)	C13–C12–C11	119.1(5)
C3–N1–C4	129.9(4)	C14–C13–C12	120.0(5)
N2–N1–C4	118.9(4)	C13–C14–C15	120.3(5)
C1–N2–N1	106.9(4)	C16–C15–C14	120.0(6)
C11–N3–C18	131.1(5)	C15–C16–C17	120.6(6)
N2–C1–C2	111.3(4)	C16–C17–C12	119.6(5)
N2–C1–C10	118.4(4)	C19–C18–C23	118.8(5)
C2–C1–C10	130.3(5)	C19–C18–N3	124.8(4)
C11–C2–C1	131.8(5)	C23–C18–N3	116.3(5)
C11–C2–C3	123.5(4)	C18–C19–C20	120.6(5)
C1–C2–C3	104.5(5)	C19–C20–C21	121.4(5)
O1–C3–N1	125.9(5)	C22–C21–C20	117.0(5)
O1–C3–C2	128.2(5)	C22–C21–C24	122.5(5)
N1–C3–C2	105.9(4)	C20–C21–C24	120.5(6)
C5–C4–C9	120.1(5)	C21–C22–C23	122.2(5)
C5–C4–N1	120.7(4)	C22–C23–C18	120.0(5)
C9–C4–N1	119.3(5)	C21–C24–C25	113.8(4)
C4–C5–C6	120.0(5)	C30–C25–C26	117.8(6)
C5–C6–C7	120.0(6)	C30–C25–C24	121.6(6)
C8–C7–C6	118.9(6)	C26–C25–C24	120.5(6)

C7–C8–C9	121.9(5)	C25–C26–C27	121.3(6)
C8–C9–C4	119.1(5)	C28–C27–C26	120.9(6)
N3–C11–C2	116.9(5)	C27–C28–C29	117.3(6)
N3–C11–C12	120.7(5)	C27–C28–N4	120.5(6)
C2–C11–C12	122.3(4)	C29–C28–N4	122.2(7)
C17–C12–C13	119.4(5)	C28–C29–C30	121.9(6)
C17–C12–C11	121.5(4)	C25–C30–C29	120.7(6)

Table S4. Selected bond lengths and angles for compound **3** (Å, °)

Bond	Dist.	Bond	Dist.
N1–C19	1.331(3)	C9–C10	1.429(3)
N1–C6	1.424(3)	C9–C18	1.495(4)
N2–C11	1.368(3)	C10–C19	1.396(3)
N2–N3	1.396(3)	C10–C11	1.437(3)
N2–C12	1.414(3)	C12–C17	1.366(4)
N3–C9	1.308(3)	C12–C13	1.383(4)
O1–C1	1.305(3)	C13–C14	1.373(4)
O2–C1	1.191(4)	C14–C15	1.372(5)
O3–C11	1.251(3)	C15–C16	1.350(5)
O4–C26	1.419(4)	C16–C17	1.379(4)
C1–C2	1.496(4)	C19–C20	1.475(3)
C2–C3	1.510(4)	C20–C25	1.384(4)
C3–C8	1.369(4)	C20–C21	1.388(4)
C3–C4	1.384(4)	C21–C22	1.379(4)
C4–C5	1.378(4)	C22–C23	1.370(5)
C5–C6	1.373(4)	C23–C24	1.365(5)
C6–C7	1.374(4)	C24–C25	1.372(4)
C7–C8	1.382(4)		
Bond	Angle	Bond	Angle
C19–N1–C6	129.0(2)	C9–C10–C11	104.8(2)
C11–N2–N3	110.52(19)	O3–C11–N2	125.4(2)
C11–N2–C12	128.6(2)	O3–C11–C10	128.6(2)
N3–N2–C12	120.6(2)	N2–C11–C10	106.0(2)
C9–N3–N2	107.5(2)	C17–C12–C13	119.3(3)
O2–C1–O1	122.1(3)	C17–C12–N2	121.0(2)
O2–C1–C2	125.6(3)	C13–C12–N2	119.6(2)
O1–C1–C2	112.2(3)	C14–C13–C12	119.3(3)
C1–C2–C3	114.0(2)	C15–C14–C13	121.3(3)
C8–C3–C4	118.1(2)	C16–C15–C14	118.7(3)
C8–C3–C2	121.4(3)	C15–C16–C17	121.2(3)
C4–C3–C2	120.5(3)	C12–C17–C16	120.1(3)
C5–C4–C3	121.1(3)	N1–C19–C10	117.2(2)
C6–C5–C4	119.9(3)	N1–C19–C20	118.5(2)
C5–C6–C7	119.7(2)	C10–C19–C20	124.3(2)
C5–C6–N1	122.1(2)	C25–C20–C21	119.1(2)
C7–C6–N1	118.0(2)	C25–C20–C19	121.3(2)
C6–C7–C8	119.7(3)	C21–C20–C19	119.5(2)
C3–C8–C7	121.4(3)	C22–C21–C20	119.8(3)
N3–C9–C10	111.0(2)	C23–C22–C21	120.2(3)
N3–C9–C18	118.8(2)	C24–C23–C22	120.3(3)
C10–C9–C18	130.2(2)	C23–C24–C25	120.2(3)
C19–C10–C9	133.4(2)	C24–C25–C20	120.3(3)

Table S5. Selected bond lengths and angles for compound **4** (Å, °)

Bond	Dist.	Bond	Dist.
N1–C3	1.383(5)	C7–C8	1.386(6)
N1–N2	1.406(4)	C8–C9	1.368(6)
N1–C5	1.426(5)	C9–C10	1.384(6)
N2–C1	1.309(5)	C11–C12	1.479(5)
N3–C11	1.340(5)	C12–C13	1.389(6)
N3–C22	1.435(5)	C12–C17	1.391(5)
N4–C18	1.327(5)	C13–C14	1.385(6)
O1–C3	1.253(4)	C14–C15	1.369(7)
O2–C18	1.244(4)	C15–C16	1.371(7)
O3–C25	1.401(6)	C16–C17	1.372(6)
C1–C2	1.445(5)	C18–C19	1.498(5)
C1–C4	1.492(5)	C19–C24	1.380(5)
C2–C11	1.410(5)	C19–C20	1.400(5)
C2–C3	1.439(5)	C20–C21	1.387(5)
C5–C6	1.380(6)	C21–C22	1.378(5)
C5–C10	1.387(6)	C22–C23	1.388(6)
C6–C7	1.388(6)	C23–C24	1.387(5)
Bond	Angle	Bond	Angle
C3–N1–N2	112.1(3)	N3–C11–C12	120.4(3)
C3–N1–C5	129.0(3)	C2–C11–C12	122.5(3)
N2–N1–C5	118.8(3)	C13–C12–C17	119.3(4)
C1–N2–N1	106.8(3)	C13–C12–C11	121.4(4)
C11–N3–C22	130.5(4)	C17–C12–C11	119.3(4)
N2–C1–C2	110.8(3)	C12–C13–C14	120.2(4)
N2–C1–C4	118.5(3)	C15–C14–C13	119.7(5)
C2–C1–C4	130.7(4)	C14–C15–C16	120.3(5)
C11–C2–C3	122.1(3)	C15–C16–C17	121.0(5)
C11–C2–C1	131.7(3)	C16–C17–C12	119.5(4)
C3–C2–C1	106.0(3)	O2–C18–N4	123.0(4)
O1–C3–N1	125.3(4)	O2–C18–C19	119.3(3)
O1–C3–C2	130.4(3)	N4–C18–C19	117.7(4)
N1–C3–C2	104.3(3)	C24–C19–C20	119.0(3)
C6–C5–C10	120.1(4)	C24–C19–C18	118.6(3)
C6–C5–N1	120.5(4)	C20–C19–C18	122.4(3)
C10–C5–N1	119.3(4)	C21–C20–C19	120.0(4)
C5–C6–C7	120.0(4)	C22–C21–C20	120.4(4)
C6–C7–C8	120.0(4)	C21–C22–C23	119.9(3)
C9–C8–C7	119.3(4)	C21–C22–N3	116.5(4)
C8–C9–C10	121.5(5)	C23–C22–N3	123.5(4)
C9–C10–C5	119.0(4)	C24–C23–C22	119.7(4)
N3–C11–C2	116.9(3)	C19–C24–C23	120.9(4)

Table S6. Selected bond lengths and angles for compound **5** (Å, °)

Bond	Dist.	Bond	Dist.
N1–C1	1.368(3)	C6–C7	1.387(3)
N1–N2	1.399(2)	C7–C8	1.377(4)
N1–C5	1.417(2)	C8–C9	1.365(4)
N2–C3	1.314(3)	C9–C10	1.373(3)
C18–C23	1.383(3)	C11–C12	1.489(3)
C18–C19	1.392(3)	C12–C13	1.385(3)
C18–N3	1.423(3)	C12–C17	1.388(3)
O1–C1	1.259(2)	C13–C14	1.381(3)
N3–C11	1.334(3)	C14–C15	1.373(4)
O2–C19	1.357(2)	C15–C16	1.370(4)
C1–C2	1.434(3)	C16–C17	1.377(3)
C2–C11	1.395(3)	C19–C20	1.379(3)
C2–C3	1.437(3)	C20–C21	1.373(3)
C3–C4	1.490(3)	C21–C22	1.387(3)
C5–C6	1.374(3)	C22–C23	1.382(3)
C5–C10	1.379(3)	C22–C24	1.506(3)
Bond	Angle	Bond	Angle
C1–N1–N2	112.46(16)	C8–C9–C10	120.6(2)
C1–N1–C5	127.18(17)	C9–C10–C5	119.7(2)
N2–N1–C5	120.03(17)	N3–C11–C2	118.29(18)
C3–N2–N1	105.74(17)	N3–C11–C12	118.55(18)
C23–C18–C19	120.00(19)	C2–C11–C12	123.11(19)
C23–C18–N3	124.65(19)	C13–C12–C17	119.8(2)
C19–C18–N3	115.32(18)	C13–C12–C11	121.03(18)
C11–N3–C18	131.09(17)	C17–C12–C11	119.20(19)
O1–C1–N1	125.27(18)	C14–C13–C12	119.5(2)
O1–C1–C2	129.74(19)	C15–C14–C13	120.6(2)
N1–C1–C2	104.96(17)	C16–C15–C14	119.8(2)
C11–C2–C1	122.73(19)	C15–C16–C17	120.6(2)
C11–C2–C3	131.56(18)	C16–C17–C12	119.7(2)
C1–C2–C3	105.04(17)	O2–C19–C20	124.8(2)
N2–C3–C2	111.64(18)	O2–C19–C18	116.22(19)
N2–C3–C4	118.45(19)	C20–C19–C18	119.0(2)
C2–C3–C4	129.88(19)	C21–C20–C19	120.5(2)
C6–C5–C10	120.4(2)	C20–C21–C22	121.4(2)
C6–C5–N1	120.40(19)	C23–C22–C21	118.1(2)
C10–C5–N1	119.15(19)	C23–C22–C24	121.2(2)
C5–C6–C7	119.2(2)	C21–C22–C24	120.8(2)
C8–C7–C6	120.2(2)	C22–C23–C18	121.1(2)
C9–C8–C7	119.9(2)		

Table S7. Selected bond lengths and angles for compound **6** (Å, °)

Bond	Dist.	Bond	Dist.
N1–C1	1.367(2)	C8–C9	1.376(4)
N1–N2	1.400(2)	C9–C10	1.372(3)
N1–C19	1.419(2)	C10–C11	1.378(3)
N2–C3	1.308(2)	C12–C17	1.382(3)
N3–C5	1.328(2)	C12–C13	1.384(3)
N3–C12	1.426(2)	C13–C14	1.382(2)
O1–C1	1.261(2)	C14–C15	1.391(3)
O2–C14	1.354(2)	C15–C16	1.376(3)
C1–C2	1.435(2)	C15–C18	1.511(3)
C2–C5	1.400(2)	C16–C17	1.381(3)
C2–C3	1.439(3)	C19–C20	1.371(3)
C3–C4	1.487(3)	C19–C24	1.376(3)
C5–C6	1.487(2)	C20–C21	1.380(3)
C6–C7	1.384(3)	C21–C22	1.367(3)
C6–C11	1.385(3)	C22–C23	1.373(3)
C7–C8	1.378(3)	C23–C24	1.385(3)
Bond	Angle	Bond	Angle
C1–N1–N2	112.03(14)	C9–C10–C11	120.2(2)
C1–N1–C19	127.40(16)	C10–C11–C6	119.90(19)
N2–N1–C19	119.95(14)	C17–C12–C13	119.93(17)
C3–N2–N1	106.46(15)	C17–C12–N3	122.36(17)
C5–N3–C12	129.35(15)	C13–C12–N3	117.67(16)
O1–C1–N1	125.60(16)	C14–C13–C12	120.33(16)
O1–C1–C2	129.44(16)	O2–C14–C13	122.83(17)
N1–C1–C2	104.92(15)	O2–C14–C15	116.47(16)
C5–C2–C1	121.96(17)	C13–C14–C15	120.68(17)
C5–C2–C3	132.47(17)	C16–C15–C14	117.52(17)
C1–C2–C3	105.29(15)	C16–C15–C18	122.42(18)
N2–C3–C2	111.08(16)	C14–C15–C18	120.06(19)
N2–C3–C4	118.35(17)	C15–C16–C17	123.00(18)
C2–C3–C4	130.52(17)	C16–C17–C12	118.50(18)
N3–C5–C2	118.59(16)	C20–C19–C24	120.41(18)
N3–C5–C6	119.05(15)	C20–C19–N1	119.46(17)
C2–C5–C6	122.30(17)	C24–C19–N1	120.12(17)
C7–C6–C11	119.68(18)	C19–C20–C21	120.00(19)
C7–C6–C5	119.06(17)	C22–C21–C20	120.1(2)
C11–C6–C5	121.24(16)	C21–C22–C23	119.8(2)
C8–C7–C6	119.9(2)	C22–C23–C24	120.6(2)
C9–C8–C7	120.1(2)	C19–C24–C23	119.0(2)
C10–C9–C8	120.2(2)		

Table S8. Hydrogen bonding geometry for compound **1** (Å, °)

D–H···*A*	*D*–H	H···*A*	*D*···*A*	*D*–H···*A*
N1–H1···O5	0.84(4)	1.92(4)	2.649(4)	145(4)
O2–H2···O6[a]	0.82	1.80	2.611(4)	171.4
O3–H3···N3[b]	0.82	2.05	2.741(4)	141.6
O6–H6···O1	0.82	1.92	2.712(5)	160.6
C15–H15···O5[c]	0.93	2.39	3.296(5)	164.3
C19–H19A···O3[d]	0.96	2.40	3.169(5)	137.4
C21–H21···N3	0.93	2.50	2.816(5)	100.1
C25–H25···O5	0.93	2.36	2.910(5)	117.4

Symmetry codes: (a) −*x*+2, −*y*+1, −*z*+2; (b) *x*+1, *y*−1, *z*; (c) −*x*+1, −*y*+1, −*z*+1; (d) *x*−1, *y*+1, *z*.

Table S9. Hydrogen bonding geometry for compound **2** (Å, °)

D–H⋯*A*	*D*–H	H⋯*A*	*D*⋯*A*	*D*–H⋯*A*
O2–H2⋯N2[a]	0.82	2.07	2.822(6)	152
O3–H3⋯O2[b]	0.82	1.88	2.676(7)	165
N3–H3A⋯O1	0.91(5)	1.86(5)	2.680(6)	149(4)
N4–H4A⋯O3[c]	0.86	2.30	3.158(8)	172
N4–H4B⋯O3[d]	0.86	2.25	3.057(8)	155
C9–H9⋯O1	0.93	2.42	2.957(6)	117

Symmetry codes: (a) $x+1, y, z$; (b) $x-1, y, z+1$; (c) $x, y-1, z$; (d) $-x+1, -y, -z+2$.

Table S10. Hydrogen bonding geometry for compound **3** (Å, °)

D–H⋯*A*	*D*–H	H⋯*A*	*D*⋯*A*	*D*–H⋯*A*
O1–H1⋯O4[a]	0.82	1.81	2.591(3)	159.3
O4–H4⋯N3	0.82	2.00	2.810(3)	172.2
N1–H1A⋯O3	0.96(3)	1.79(3)	2.628(3)	145(2)
C7–H7⋯O2[b]	0.93	2.59	3.502(4)	166.0
C2–H2B⋯O1[c]	0.97	2.57	3.503(4)	162.4
C26–H26B⋯O3[d]	0.96	2.47	3.400(4)	164.6

Symmetry codes:(a) *x*−1, *y*−1, *z*;(b) −*x*, −*y*, *z*+2;(c) −*x*, −*y*, −*z*+1;(d) *x*+1, *y*, *z*.

Table S11. Hydrogen bonding geometry for compound **4** (Å, °)

D–H⋯*A*	*D*–H	H⋯*A*	*D*⋯*A*	*D*–H⋯*A*
O3–H3⋯O1	0.82	2.13	2.914(5)	161.2
N3–H2a⋯O1	0.89(4)	1.95(4)	2.696(4)	141(3)
N4–H4A⋯O2[a]	0.86	2.04	2.895(4)	171.5
N4–H4B⋯O3[b]	0.86	2.19	2.943(5)	146.8
C7–H7⋯O2[c]	0.93	2.49	3.414(6)	176.1
C17–H17⋯O2[d]	0.93	2.56	3.480(6)	172.0

Symmetry codes: (a) −*x*+3, −*y*, −*z*; (b) −*x*+2, −*y*+1, −*z*; (c) *x*−1, *y*+1, *z*; (d) *x*−1, *y*, *z*.

Table S12. Hydrogen bonding geometry for compound **5** (Å, °)

D–H⋯*A*	*D*–H	H⋯*A*	*D*⋯*A*	*D*–H⋯*A*
N3–H3⋯O1	0.94(3)	1.92(3)	2.718(2)	143(2)
O2–H2⋯O1[a]	0.82	1.98	2.762(2)	158.4

Symmetry codes: (a) −*x*+1, −*y*+1, −*z*+1.

Table S13. Hydrogen bonding geometry for compound **6** (Å, °)

D–H⋯*A*	*D*–H	H⋯*A*	*D*⋯*A*	*D*–H⋯*A*
N3–H3⋯O1	0.97(2)	1.88(2)	2.696(2)	140.3(19)
O2–H2⋯O1[a]	0.82	1.96	2.7485(19)	162.0

Symmetry codes: (a) −*x*, −*y*, −*z*+1.

Table S14. The experimental bond lengths and torsion angles for tautomer **6c**, and the corresponding calculated values for tautomers **6a**, **6b** and **6c** (Å, º)

Bond	**6a** Calculated	**6b** Calculated	**6c** Calculated	**6c** Experimental
O1–C1	1.241	1.228	1.257	1.261(2)
C1–C2	1.460	1.534	1.454	1.435(2)
C2–C3	1.388	1.509	1.444	1.439(3)
C2–C5	1.473	1.527	1.405	1.400(2)
N1–C1	1.406	1.381	1.386	1.367(2)
N1–N2	1.389	1.409	1.397	1.400(2)
N2–C3	1.360	1.288	1.314	1.308(2)
N3–C5	1.292	1.283	1.343	1.328(2)
Torsion angle	**6a** Calculated	**6b** Calculated	**6c** Calculated	**6c** Experimental
C1–N1–C19–C20	-55.1	1.5	-16.2	-44.1(3)
C1–C2–C5–C6	143.1	71.1	177.5	-176.97(16)
C2–C5–C6–C7	127.8	120.8	111.8	113.9(2)
C1–C2–C5–N3	-37.0	-112.4	-4.6	0.0(3)
C2–C5–N3–C12	170.8	175.2	173.9	174.18(17)
C5–N3–C12–C13	130.2	-55.6	131.4	144.01(19)