Study of molecular structure, chemical reactivity and H-bonding interactions in the cocrystal of nitrofurantoin with urea

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New Journal of Chemistry

†Electronic Supplementary Information

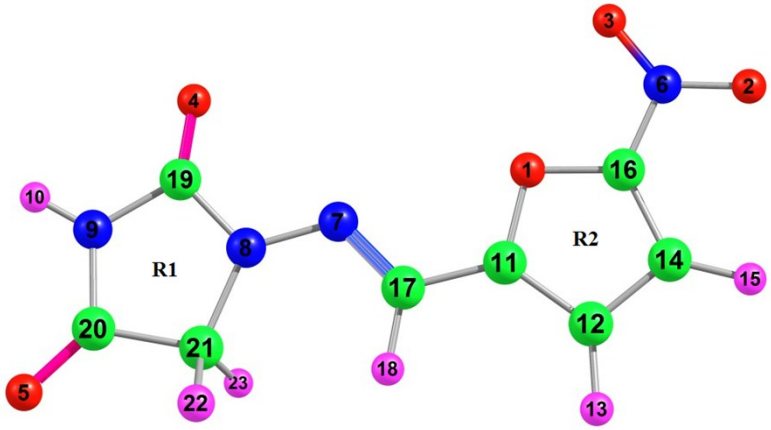

Fig.S1 Optimized structure for NF.

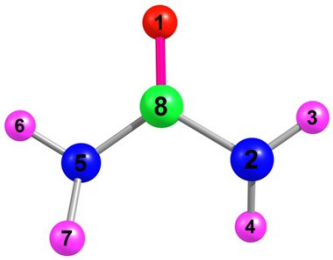

Fig. S2. Optimized structure for urea.

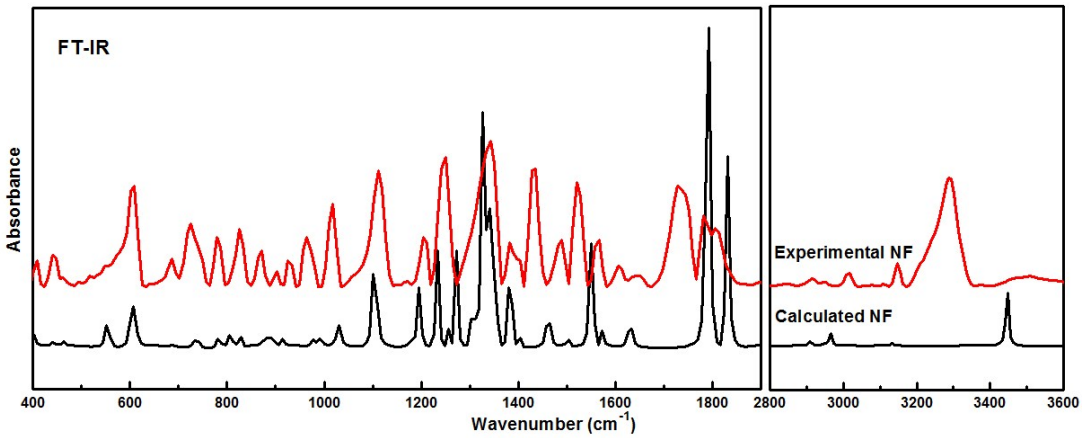

Fig. S3. Experimental and calculated FT-IR absorbance spectra of NF in the region, 400-3600 cm^{-1}.

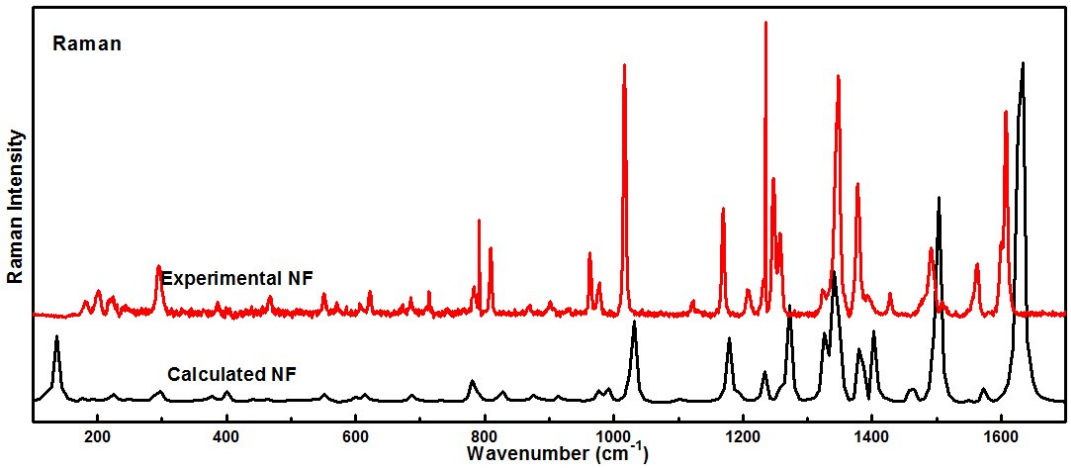

Fig. S4. Experimental and calculated Raman spectra of NF in the region, 100-1700 cm^{-1}.

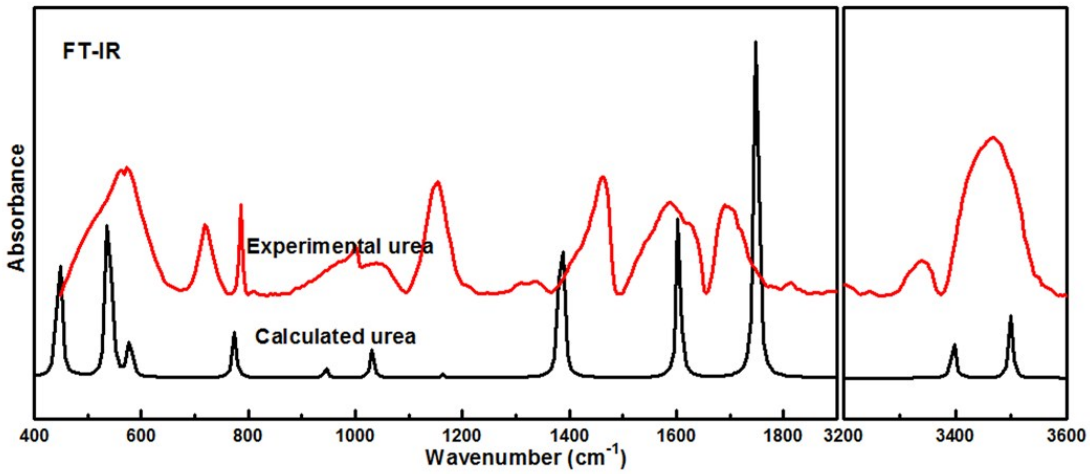

Fig. S5. Experimental and calculated IR absorbance spectra of urea in the region, 400-3600 cm^{-1}.

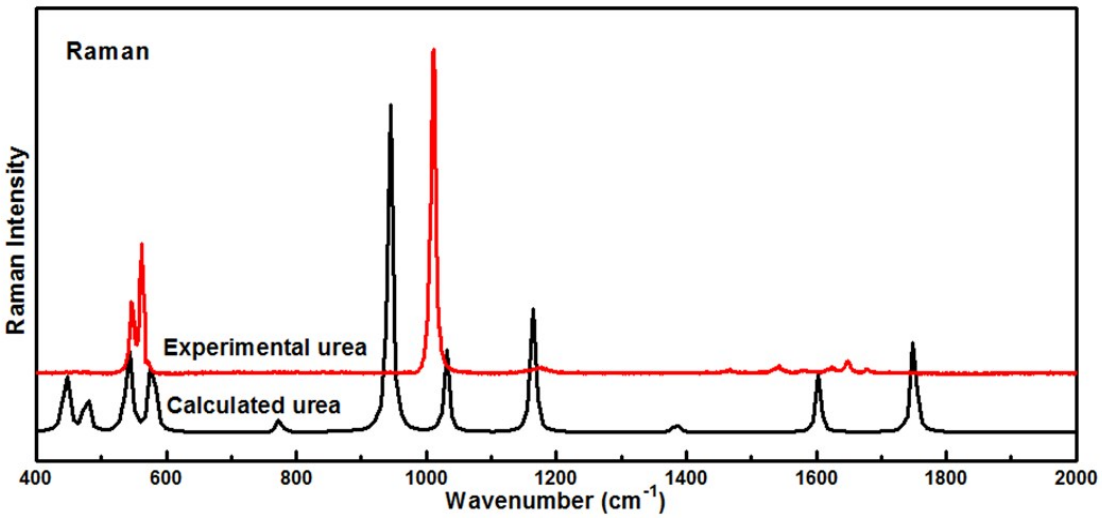

Fig. S6. Experimental and calculated Raman spectra of urea in the region, 400-2000 cm^{-1}.

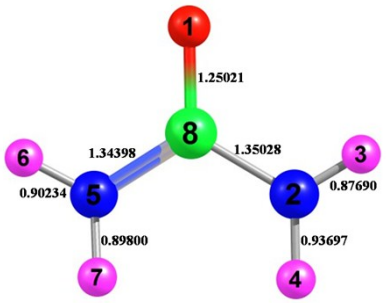

Fig. S7. Experimental structure of urea.

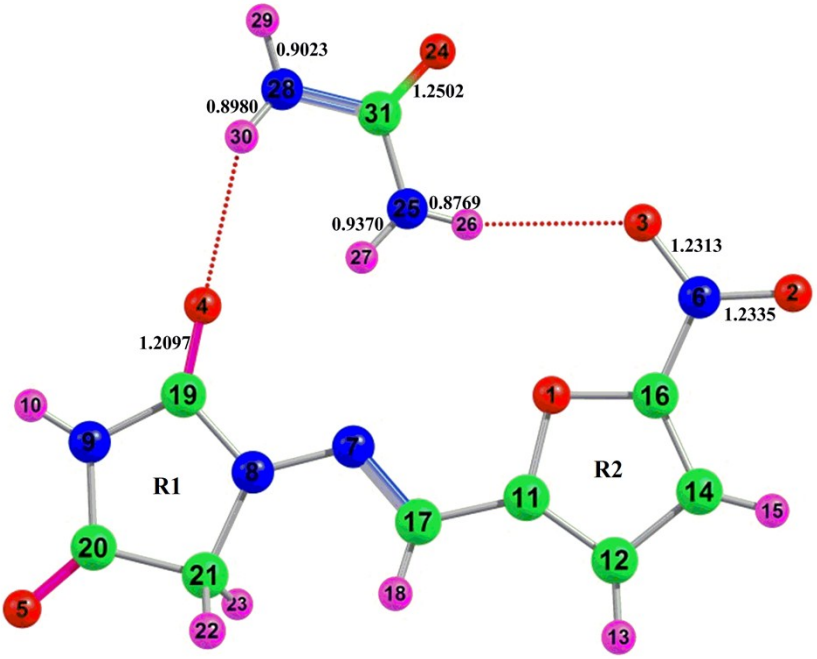

Fig. S8. Experimental structure of NF-urea.

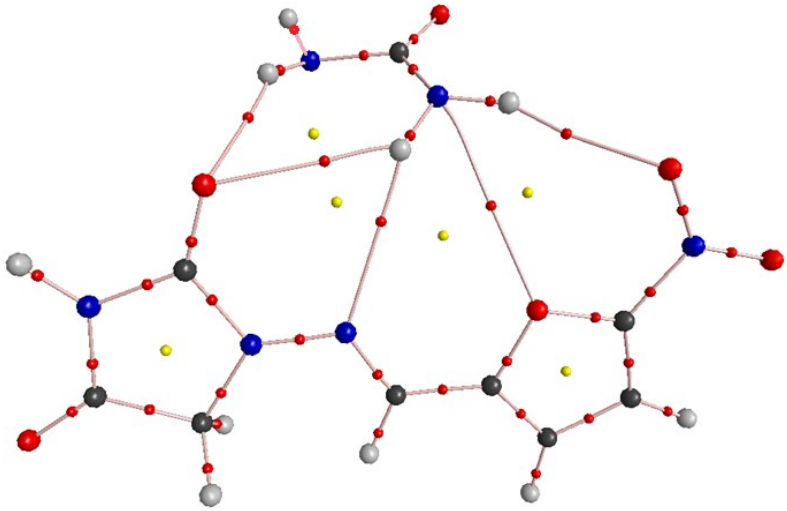

Fig. S9. Molecular graph of the NF-urea (monomer): bond critical points (small red spheres), ring critical points (small yellow sphere), bond paths (pink lines).

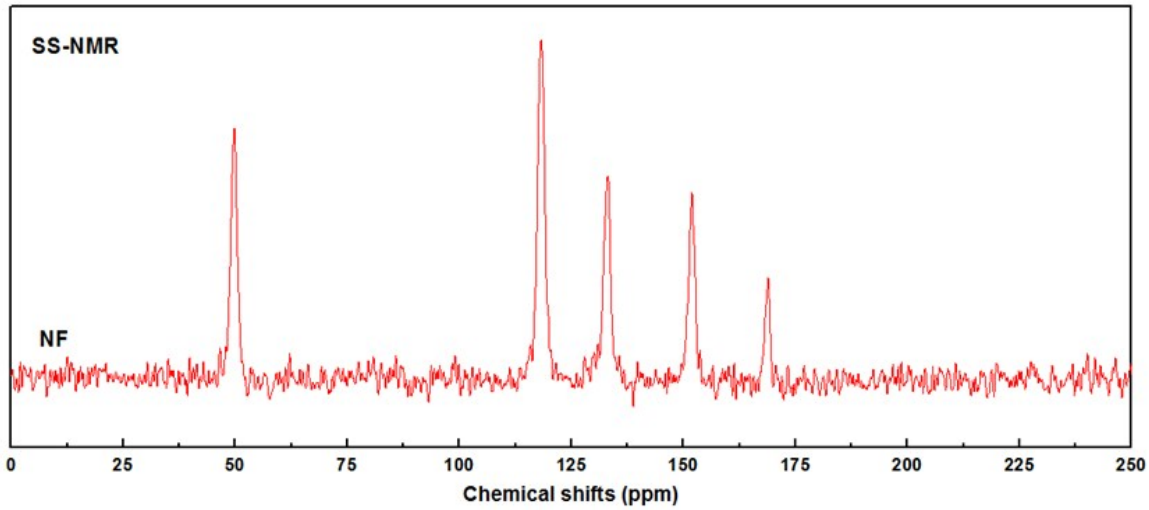

Fig. S10. Experimental ^{13}C NMR spectrum of NF.

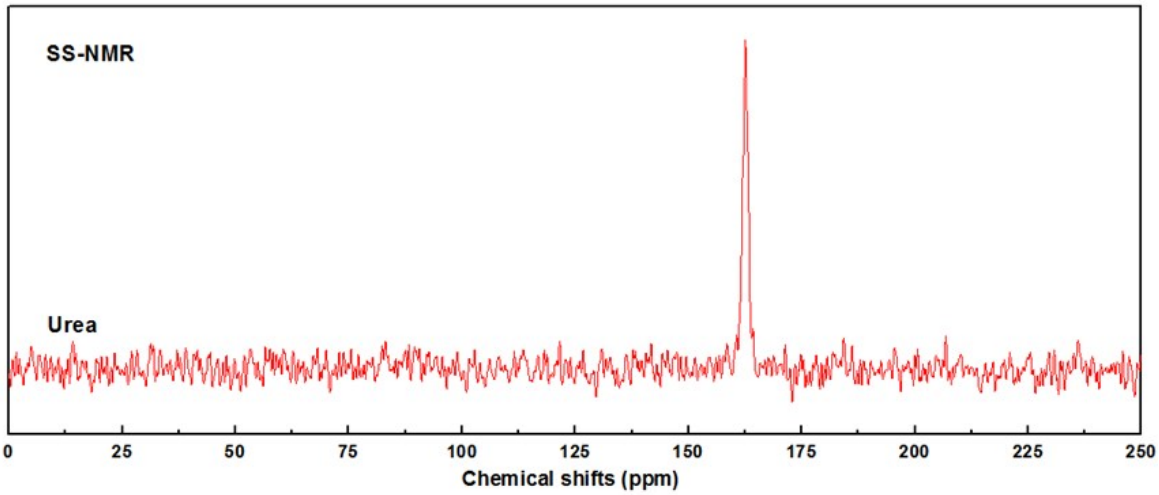

Fig. S11. Experimental ^{13}C NMR spectrum of urea.

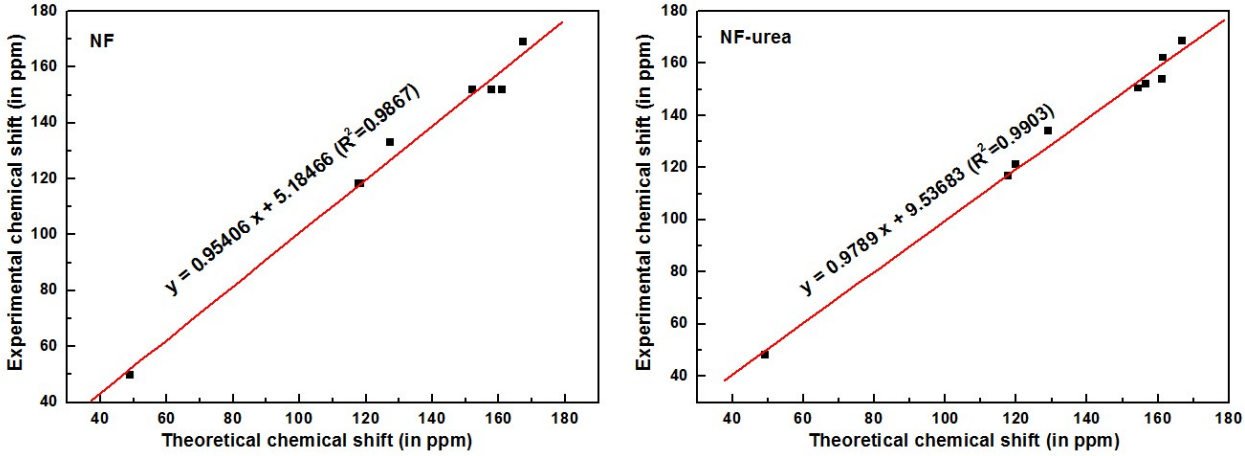

Fig. S12. The 13C NMR correlation graph of NF-urea and NF.

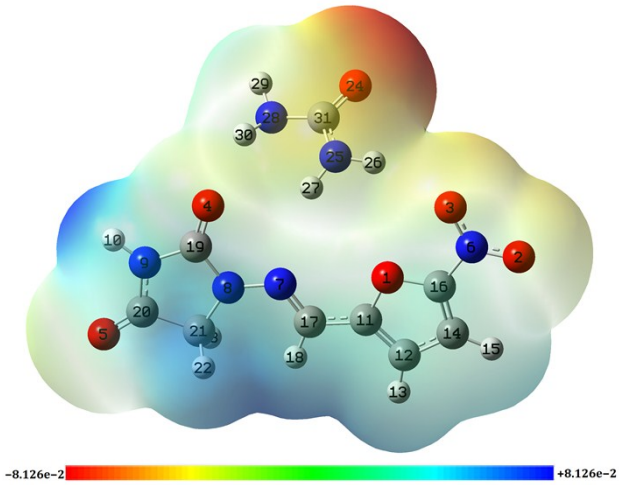

Fig. S13. Molecular electrostatic potential (MEP) formed by mapping of the total density over electrostatic potential in gas phase for NF-urea (monomer).

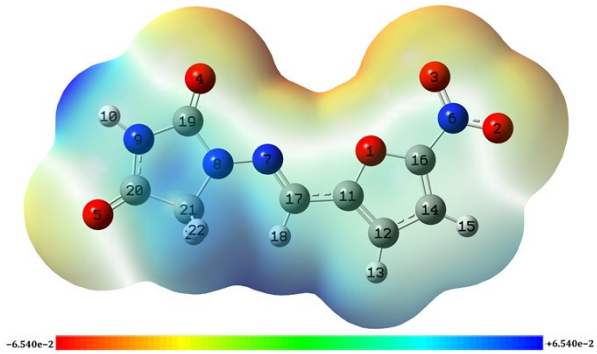

Fig. S14. Molecular electrostatic potential (MEP) formed by mapping of the total density over electrostatic potential in gas phase for NF.

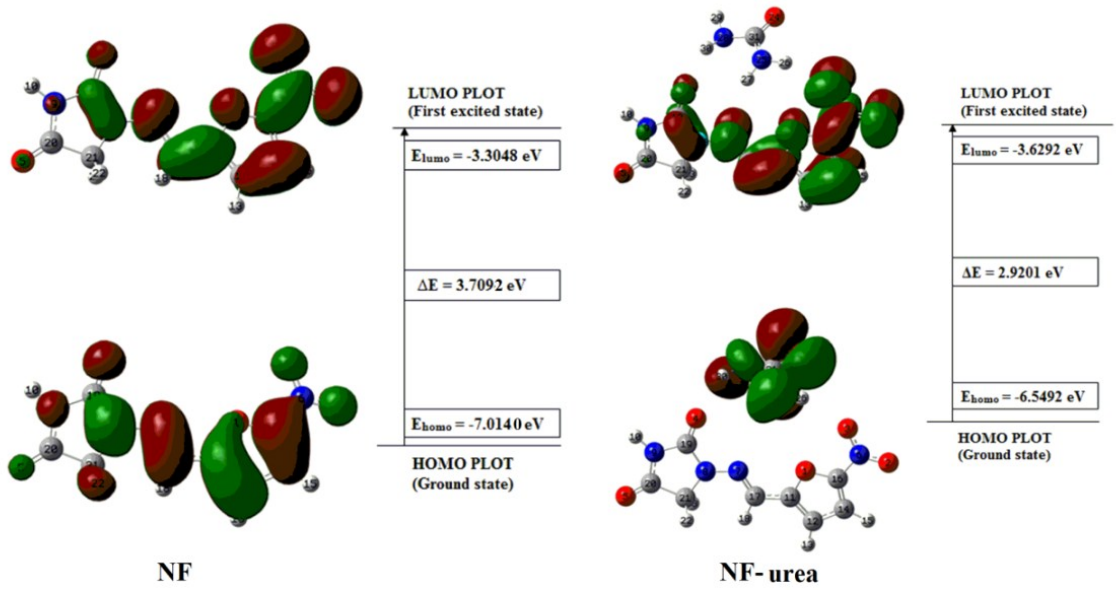

Fig. S15 HOMO-LUMO energy gap of NF and NF-urea (monomer) with orbitals involved in electronic transitions.

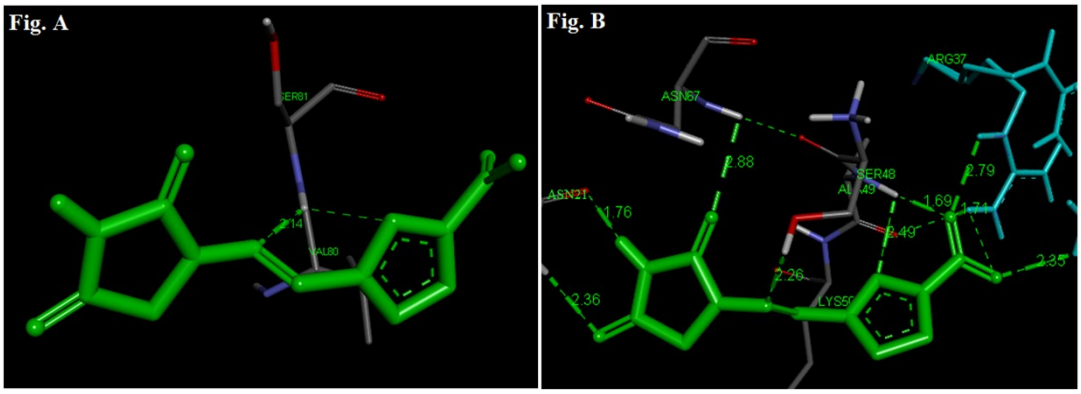

Fig. S16 The interaction of NF against drug targets- Hu Alpha2 Protein (1MULA)(Fig. A) and ELAV like protein 1 (3HI9)(Fig. B) generated by computer aided docking.

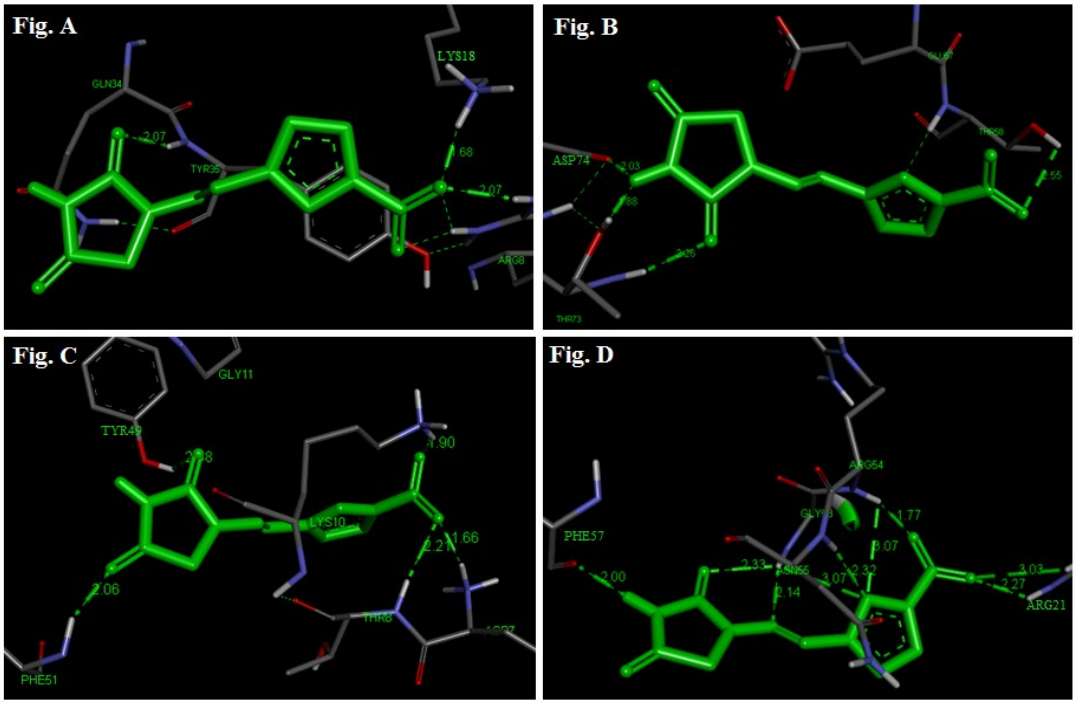

Fig. S17 The interaction of NF against drug targets-Glutaredoxin protein: 1GRXA (Fig. A), 1EGO (Fig. B), 5CAX (Fig. C) and 2MZC (Fig. D).

Table S1 The experimental and calculated geometric parameters of NF-urea and calculated geometric parameters of NF and NF-urea (monomer +3urea) using DFT/6-311++g(d,p), bond lengths in angstrom (Å) and bond angles in degrees (º).

Geometrical Parameters	Experimental	Calculated		
		Optimized parameters		
	NF-urea cocrystal	NF-urea (monomer + 3urea)	NF-urea (monomer)	NF (monomer)
		B3LYP/6-311++G(d,p)		
Bond lengths(Å)				
O1-C11	1.3748(19)	1.361	1.359	1.359
O1-C16	1.3564(19)	1.350	1.348	1.349
O2-N6	1.2334(18)	1.229	1.228	1.231
O3-N6	1.2313(18)	1.226	1.225	1.222
O4-C19	1.2100(2)	1.207	1.202	1.196
O5-C20	1.2093(19)	1.208	1.202	1.204
N6-C16	1.4220(2)	1.430	1.434	1.434
N7-N8	1.3605(18)	1.337	1.344	1.340
N7-C17	1.2870(2)	1.286	1.285	1.285
N8-C19	1.3800(2)	1.405	1.397	1.404
N8-C21	1.4542(19)	1.460	1.461	1.461
N9-H10	0.9259	1.049	1.010	1.010
N9-C19	1.3850(2)	1.387	1.401	1.408
N9-C20	1.3710(2)	1.373	1.381	1.377
C11-C12	1.3650(2)	1.379	1.378	1.379
C11-C17	1.4410(2)	1.442	1.441	1.442
C12-H13	0.9500	1.078	1.079	1.079
C12-C14	1.4170(2)	1.417	1.418	1.417
C14-H15	0.9500	1.077	1.077	1.077
C14-C16	1.3450(2)	1.365	1.365	1.365
C17-H18	0.9500	1.090	1.090	1.091
C20-C21	1.5210(2)	1.534	1.530	1.530
C21-H22	0.9900	1.095	1.094	1.094
C21-H23	0.9900	1.094	1.094	1.095
O24-C31	1.2503(19)	1.240	1.222	-
N25-H26	0.8764	1.006	1.008	-
N25-H27	0.9369	1.008	1.009	-
N25-C31	1.350(2)	1.366	1.372	-
N28-H29	0.9030	1.015	1.008	-
N28-H30	0.8980	1.012	1.011	-
N28-C31	1.3440(2)	1.364	1.390	-
Bond angle(°)				
C11-O1-C16	104.53(12)	106.24	106.19	106.19
O2-N6-O3	124.33(13)	125.83	126.03	126.04
O2-N6-C16	117.40(13)	116.09	115.89	115.67
O3-N6-C16	118.26(13)	118.08	118.07	118.29
N8-N7-C17	117.24(13)	119.65	118.97	119.022
N7-N8-C19	118.70(12)	119.25	119.50	119.76
N7-N8-C21	128.48(12)	128.38	128.13	127.83
C19-N8-C21	112.82(13)	111.46	112.36	112.40
H10-N9-C19	121.90	119.63	121.74	121.45
H10-N9-C20	125.50	125.58	124.05	124.03
C19-N9-C20	112.57(13)	113.21	114.21	114.51
O1-C11-C12	110.52(14)	109.96	110.02	110.05
O1-C11-C17	117.17(13)	119.08	119.41	119.79
C12-C11-C17	132.29(15)	130.95	130.57	130.16
C11-C12-H13	126.70	126.09	126.16	126.12

C11-C12-C14	106.65(14)	106.71	106.66	106.64
H13-C12-C14	126.70	127.20	127.18	127.24
C12-C14-H15	127.40	128.87	128.91	128.97
C12-C14-C16	105.18(14)	105.6	104.95	104.98
H15-C14-C16	127.40	126.06	126.13	126.05
O1-C16-N6	114.69(13)	117.35	117.25	117.63
O1-C16-C14	113.11(13)	112.03	112.16	112.14
N6-C16-C14	132.11(15)	130.61	130.58	130.23
N7-C17-C11	119.01(14)	120.22	121.10	121.20
N7-C17-H18	120.50	124.09	123.80	123.91
C11-C17-H18	120.50	115.69	115.10	114.88
O4-C19-N8	126.10(14)	126.66	128.12	128.68
O4-C19-N9	127.71(14)	126.87	126.66	126.65
N8-C19-N9	106.20(13)	106.46	105.22	104.67
O5-C20-N9	126.65(15)	127.77	127.45	127.59
O5-C20-C21	126.02(14)	125.65	126.96	126.77
N9-C20-C21	107.32(12)	106.58	105.59	105.63
N8-C21-C20	101.08(12)	102.17	102.62	102.78
N8-C21-H22	111.60	112.02	112.36	112.39
N8-C21-H23	111.60	112.74	112.38	112.37
C20-C21-H22	111.60	109.98	110.09	110.02
C20-C21-H23	111.60	110.42	109.97	110.01
H22-C21-H23	109.40	109.32	109.25	109.12
H26-N25-H27	120.90	117.23	116.86	-
H26-N25-C31	118.40	117.70	116.59	-
H27-N25-C31	120.70	122.00	120.38	-
H29-N28-H30	122.90	116.95	115.95	-
H29-N28-C31	117.70	116.24	113.27	-
H30-N28-C31	116.20	120.31	118.21	-
O24-C31-N25	121.54(15)	121.48	123.46	-
O24-C31-N28	121.37(14)	122.43	122.19	-
N25-C31-N28	117.08(14)	116.08	114.34	-
Dihedral angle(°)				
C16-O1-C11-C12	0.44(17)	0.16	0.04	−0.0
C16-O1-C11-C17	179.01(13)	179.73	−179.90	179.99
C11-O1-C16-N6	−177.13(12)	-179.11	179.84	179.98
C11-O1-C16-C14	−0.21(17)	-0.07	−0.04	0.00
O2-N6-C16-O1	−178.70(13)	-17891	177.88	179.9
O2-N6-C16-C14	5.10(3)	2.26	−2.25	−0.07
O3-N6-C16-O1	2.30(2)	1.21	−2.02	−0.04
O3-N6-C16-C14	−173.86(16)	-177.63	177.84	179.92
C17-N7-N8-C19	178.02(13)	176.94	−179.00	−179.93
C17-N7-N8-C21	−1.80(2)	8.81	0.99	−0.07
N8-N7-C17-C11	179.46(13)	-178.30	−179.97	−180.00
N7-N8-C19-O4	−0.70(2)	8.16	0.72	−0.09
N7-N8-C19-N9	179.08(12)	-171.75	−179.35	179.92
C21-N8-C19-O4	179.16(15)	178.18	−179.27	−179.98
C21-N8-C19-N9	−1.070(17)	-1.73	0.65	0.03
N7-N8-C21-C20	−178.73(14)	168.58	179.34	−179.94
C19-N8-C21-C20	1.44(16)	-0.30	−0.66	−0.07
C20-N9-C19-O4	179.91(15)	-176.53	179.55	−179.97
C20-N9-C19-N8	0.15(17)	3.38	−0.37	0.02
C19-N9-C20-O5	179.97(15)	176.17	179.99	179.95
C19-N9-C20-C21	0.76(17)	-3.57	−0.03	−0.06
O1-C11-C12-C14	−0.50(18)	-0.19	−0.02	−0.00
C17-C11-C12-C14	−178.78(16)	-179.69	179.91	−180.00
O1-C11-C17-N7	1.90(2)	4.39	1.10	0.00

C12-C11-C17-N7	−179.92(16)	-176.15	−178.83	180.00
C11-C12-C14-C16	0.35(18)	0.14	−0.00	0.01
C12-C14-C16-O1	−0.09(18)	-0.04	0.03	−0.01
C12-C14-C16-N6	176.15(16)	178.84	−179.84	−179.98
O5-C20-C21-N8	179.51(15)	-177.50	−179.62	−179.93
N9-C20-C21-N8	−1.27(15)	2.24	0.41	0.07

Table S2 Theoretical and experimental vibrational wavenumbers (cm^{-1}) of NF with PED.

Unscaled DFT	Scaled DFT	Raman	IR	Assignment
3630	3513	-	3503,3287	R1[υ(NH)](100)
3279	3174	-	3148	R2[υ(CH)](99)
3248	3144	-	3109	R2[υ(CH)](99)
3094	2995	-	3017	υ(CH)(99)
3077	2978	-	2947	R1[$\upsilon_a(CH_2)$](100)
3035	2937	-	2916	R1[$\upsilon_s(CH_2)$](49)
1871	1811	-	1830	R1[υ(C=O)(79)+δ'_{ring}(6)+υ(C19N)(9)]
1830	1771	-	1782	R1[υ(C=O5)(78)+υ(CN9)(7)
1660	1607	1608	1605	υ(CN7)(55)+ρ(CH)(15)+υ(CC)(15)+R2[υ(C11C12)](6)
1601	1550	1601	1566	R2[υ(CC)(45)+δ_{in}(CH)(9)]+$\upsilon(NO_2)$(20)+υ(CN7)(8)+$\rho(NO_2)$(5)
1577	1527	1562	1520	$\upsilon(NO_2)$(74)+R2[υ(C11C12)](9)
1526	1477	1492	1489	R2[υ(CC)(41)+δ_{ring}(13)+υ(CN)(5)]+υ(CC)(12)+υ(CN7)(5)
1484	1437		1435	R1[$\delta(CH_2)$](92)
1425	1379	1428	1404	R2[υ(CC)(23)+υ(OC)(31)+δ_{in}(CH15)](15)+δ_{in}(CC17)(5)]+ρ(CH)(6)
1403	1358	1378	1381	ρ(CH)(12)+R1[υ(C19N8)(11)+$\omega(CH_2)$(8)+υ(NN)(6)]+R2[υ(C11C12)(18)+δ_{in}(CH13)(5)]
1375	1331			R1[δ_{in}(NH)(36)+υ(CN9)](17)+ρ(CH)(7)+$\upsilon(NO_2)$(7)
1363	1319	1348	1342	ρ(CH)(22)+$\upsilon(NO_2)$(30)+R2[υ(CN)(14)+υ(C12C14)(10)+δ_{in}(CH15)(5)+δ(NO2)(9)
1346	1303	1323		R1[$\omega(CH_2)$](21)+δ_{in}(NH)(20)+υ(C19N9)(13)+υ(C19N8)(10)]+ρ(CH)(5)
1323	1281			R1[υ(CN)(26)+υ(CC)(19)+ω(CH2)(16)+δ_{in}(C=O)(14)+δ_{ring}(6)
1287	1246	1258	1250	R2[υ(C12C14)(28)+R2υ(OC11)(10)+δ_{in}(CH13)(7)]+υ(CC)(11)+$\upsilon(NO_2)$(14)+ρ(CH)(5)
1270	1229	1247	1250	R1[υ(NN)(26)+υ(C21N)(13)]+R2[υ(OC)(18)+δ_{in}(CH15)(5)+δ'_{ring}(5)]+δ(NNC)(6)
1248	1208	1235		R2[υ(OC)(34)+δ'_{ring}(10)+υ(CN)(8)+υ(C11C12)(5)]+R1[υ(NN)(16)+υ(C21N)(5)]
1209	1170	1207	1204	R1[ω(CH2)(23)+υ(C19N8)(21)+υ(C21N)(21)+υ(CN9)(5)]
1192	1154		1173	R2[δ_{in}(CH13)(31)+δ_{in}(CH15)(21)+υ(CN)(9)+δ'_{ring}(7)+υ(OC16)(5)+υ(CC)(5)]
1191	1153	1169	1173	R1[γ(CH2)](96)
1115	1079		1111	R1[υ(CN)(54)+δ_{in}(C=O4)(10)+δ_{in}(NH)(10)+υ(C21N)(7)+υ(CC)(5)]
1038	1005	1017		R2[δ_{in}(CH15)(64)+υ(C12C14)(24)]
1014	982	1017	1018	R1[ρ(CH2)(71)+OOP(C=O5)(15)+τ(6)]
1000	968	977		R2[υ(OC)(53)+δ'_{ring}(13)+υ(CC)(8)+δ_{in}(CH15)(4)
986	955	963	964	R2(δ_{ring})(42)+υ(OC)(18)+υ(CC16)(9)+υ(CN)(8)+υ(C11C12)(5)]
921	892			ω(CH)(54)+ τ(CN)(24)+R2[OOP(CH)](11)
904	875	902	903	R2[OOP(CH)(78)+τ(12)]+ω(CH)(5)
892	864			R1[υ(CC)(54)+υ(CN9)(18)+δ_{in}(NH)(7)]
879	851	870	872	R2(δ'_{ring})(17)+δ(NNC)(17)+δ_s(CH)(14)+R1[υ(C21N)(12)+δ'_{ring}(9)+υ(NN)(8)+υ(C19N8)(7)]
830	804		825	δ(NO2)(59)+R2[δ'_{ring}(17)+δ_{ring}(7)]
811	785	809		R2[OOP(CH)](88)
786	761	791	779	R1[υ(C19N8)(22)+δ'_{ring}(8)+δ_{in}(C=O4)(5)+R2[δ'_{ring}(15)+δ_{ring}(12)]+υ(CC)(7)+δ(N

				O2)(5)
741	717	783		R1[OOP(C=O4)(70)+τ'(13)+τ(8)]
738	714	714	725	ω(CN6)(66)+R2[OOP(C16N)(15)+τ'(10)
690	668			R1[δ_{ring}(26)+υ(C21N)(16)+δ_{in}(C=O)(17)+δ'_{ring}(10)+δ_{in}(NN)(10)+υ(CC)(5)]
688	666	685	687	R2[τ'(35)+OOP(CC17)(33)+τ(24)]
616	596	622		R1[δ_{in}(C=O)(32)+δ'_{ring}(15)+δ_{ring}(11)+δ_{in}(NN)(9)]+δ(NNC)(6)
608	588	606	609	R1[OOP(C=O5)(40)+OOP(NH)(38)+τ(12)+ρ(CH_2)(7)]
602	583		602	R1[δ'_{ring}(25)+δ_{ring}(19)+υ(C19N9)(10)]+υ(CC)(5)
594	575	585		R2[τ(53)+τ'(24)+OOP(C16N)(17)]
554	536			R1[OOP(NH)(54)+OOP(C=O5)(26)+ρ(CH_2)(10)+γ(CH_2)(5)]
553	535	551	548	ρ(NO2)(43)+R2[δ_{in}(C16N)(20)+δ_{in}(CC17)(10)+υ(CC16)(5)]+R1[δ_{in}(C=O)](8)
463	448	467	463	δ(NNC)(17)+ρ(NO_2)(12)+R2[δ_{in}(CC17)(15)+υ(CN)(11)+δ_{ring}(6)]+δ_s(CH)(6)+R1[δ_{in}(NN)(5)+δ_{in}(C=O)(9)]
441	427	438	440	R2[υ(CN)(19)+δ_{in}(CC17)(7)+δ'_{ring}(5)]+R1[δ_{in}(C=O5)(12)+δ_{in}(C=O4)(7)+υ(C19N9)(5)]+δ(NO_2)(8)+δ_s(CH)(6)
400	387	399	409	R1[δ_{in}(C=O)(43)+υ(C19N9)(6)+υ(CC)(6)+υ(C21N)(5)]+R2[υ(CN)(11)+δ_{ring}(5)]
378	366	386		τ(CN)(28)+R2[τ'(17)+τ(13)+OOP(CC17)(10)+OOP(C16N)(8)]+ω(CH)(9)+R1[OOP(NN)](6)
298	289		-	R1[τ(NN)(41)+OOP(NN)(20)+τ'(9)]+R2[τ(CC)](12)+τ(CN)(8)
293	283	295	-	R1[δ_{in}(NN)(18)+δ_{in}(C=O4)(17)+υ(C19N8)(6)]+R2[δ_{in}(C16N)(13)+δ_{in}(CC17)(12)]+ρ(NO_2)(7)+υ(CC)(6)
222	214	223	-	R2[δ_{in}(C16N)(33)+δ_{ring}(5)+ρ(NO_2)(17)+δ_s(CH)(12)+υ(CC)(6)
194	188	202	-	R2[OOP(C16N)(56)+OOP(CC17)(6)]+R1[τ(NN)](13)+τ(CN)(7)
178	173	181	-	R1[τ'(77)+OOP(NN)(16)]
142	137	-	-	R1[τ(54)+OOP(NH)(36)]
136	132	-	-	R1[δ_{in}(NN)](30)+δ(NNC)(21)+R2[δ_{in}(C16N)(18)+δ_{in}(CC17)(13)]
121	117	-	-	R1[τ(34)+OOP(NH)(21)+OOP(NN)(5)]+R2[OOP(CC17)(10)+τ(CN)(10)+OOP(C16N)(9)]
75	73	-	-	R2[τ(CN)](42)+R1[OOP(NN)(31)+τ'(9)]
50	49	-	-	δ_s(CH)(36)+R2[δ_{in}(CC17)(29)+δ_{in}(C16N)(5)]+δ(NNC)(17)+R1[δ_{in}(NN)](6)
44	43	-	-	R1[OOP(NN)(30)+τ'(11)]+R2[τ(CN)(20)+τ(CC)(18)+OOP(CC17)(8)]
24	23	-	-	R1[OOP(NN)(37)+τ(NN)(19)+τ(5)]+R2[τ(CC)](20)+τ(CN)(7)

Table S3 Theoretical and experimental vibrational wavenumbers (cm^{-1}) of urea with PED.

Unscaled DFT	Scaled DFT	Raman	IR	Assignment
3690	3571	-	3468	$\nu_a(N2H_2)$(96)
3688	3570	-	3468	$\nu_a(N5H_2)$(96)
3579	3464	-	3340	$\nu_s(N2H_2)$(58)+$\nu_s(N5H_2)$(41)
3573	3459	-	3340	$\nu_s(N5H_2)$(59)+$\nu_s(N2H_2)$(41)
1786	1729	1649	1690	ν(C=O)(68)+ν(CN)(12)+ δ(NCN)(6)
1633	1581	1624	1626	δ(NH_2)(89)+ν(CN)(10)
1632	1580	1542	1588	δ(NH_2)(90)+ν(C=O)(7)
1404	1359	-	1464	ν(CN2)(58)+ρ(OCN)(15)+ρ(CN5)(8)+ρ(CN2)(8)+δ(NCN)(5)
1177	1139	1176	1153	ρ(NH_2)(77)+ν(C=O)(17)
1040	1006	1011	1051	ρ(NH_2)(68)+$\nu_a(CN_2)$(28)
950	920	-	1000	ν(CN)(91)
777	752	-	786	ω(C=O)(85)
579	561	562	573	ρ(OCN)(58)+δ(NCN)(19)+ρ(CN2)(5)+ρ(CN5)(5)
545	527	546	560	ω(CN5)(49)+ω(CN2)(32)+ν(CN5)(5)
538	520			ω(CN2)(31)+τ(CN2)(15)+τ(CN5)(11)+ω(CN5)(10)+ρ(OCN)(8)+ω(NCN)(7)+ν(CN2)(5)
477	462	-	-	δ(NCN)(59)+ρ(CN5)(20)+ρ(CN2)(9)+ρ(CN5)(9)

445	431	-	-	ω(CN2)(26)+ρ(OCN)(24)+τ(CN5)(18)+τ(CN2)(17)+ν(CN2)(6)+ν(CN5)(6)
364	352	-	-	τ(CN2)(39)+τ(CN5)(39)+ω(CN2)(6)+ω(CN5)(6)+δ(NCN)(5)

Table S4 Theoretical and experimental vibrational wavenumbers (cm^{-1}) of NF-urea with PED.

Frequency NF-urea (monomer)				Experimental						
Calculated		Experimental		NF		urea		Assignment	Cal. Scaled Freq. (cm^{-1})	Simplified description of modes of dimer
Unscaled DFT	Scaled DFT	Raman	IR	Raman	IR	Raman	IR		Monomer + 3urea	
3690	3571	-	3485	-	3503	-	3468	$\upsilon_a(N25H_2)(98)$	3606,3588,3576,3558	NH_2asym stretch
3684	3566	-		-		-		$\upsilon_a(N28H_2)(99)$	3545,3507,3497,3480	NH_2asym stretch
3627	3511	-	3466	-	3287	-	-	R1[υ(NH)](99)	2862	Ring1 NH stretch
3572	3457	-		-	-	-	3340	$\upsilon_s(N25H_2)(89)+\upsilon_s(N28H_2)(11)$	3486,3476,3465,	NH_2sym stretch
3558	3444	-	3364	-	-	-		$\upsilon_s(N28H_2)(88)+\upsilon_s(N25H_2)(11)$	3411,3374,3308,3264	NH_2sym stretch
3279	3174	3156	3157	-	3148	-	-	R2[υ(CH)](99)	3172	Ring2 CH stretch
3250	3146	3122	3121	-	3109	-	-	R2[υ(CH)](99)	3122	Ring2 CH stretch
3104	3004	3026	3024	-	3017	-	-	υ(CH)(99)	3003	CH stretch
3081	2982	2947	2947	-	2947	-	-	$R1[\upsilon_a(CH_2)](100)$	2983	Ring1 CH_2asym stretch
3038	2940	2912	2912	-	2916	-	-	$R1[\upsilon_s(CH_2)](99)$	2940	Ring1 CH_2 sym stretch
1860	1800	1781	1782	1979	1830	-	-	$R1[\upsilon_s(C=O)(80)+\delta'_{ring}(8)]$	1781	Ring1 C=O stretch
1827	1768		1732		1780	-	-	$R1[\upsilon_a(C=O)(75)+\delta_{ring}(5)]$	1746	Ring1 C=O stretch
1765	1719		1732	-	-	1649	1690	υ(C=O)(64)+υ(C31N)(14)+ρ(C=O)(6)	1692	C=O stretch
1662	1609		1620	1608	1605	-	-	υ(CN7)(54)+υ(CC)(15)+ρ(CH)(15)+R2[υ(C11C12)](6)	1602	CN stretch
1642	1589	1611	1620	-	-	1624	1626	$\delta(NH_2)(72)+\delta$(O4HN25)(17)	1668,1650,1618,	NH_2 deformation
1636	1583		1593	-	-	1542	1588	$\delta(NH_2)(85)+\upsilon$(C31N)(10)	1614,1602,1580	NH_2 deformation
1603	1552	1571	1570	1601	1566	-	-	$R2[\upsilon(CC)(45)+\delta_{in}(CH13)(6)+\delta_{in}(C16N)(5)]+\upsilon_a(NO_2)(18)+\upsilon$(CN7)(8)+$\rho(NO_2)(5)$	1549	Ring2 CC stretch
1579	1528	1571	1549	1562	1520	-	-	$\upsilon_a(NO_2)(72)$+R2[υ(C11C12)](9)+$\rho(NO_2)(5)$	1520	NO_2 stretch
1527	1478	1499	1524	1492	1489	-	-	$R2[\upsilon(CC16)(29)+\upsilon(C11C12)(12)+\delta_{ring}(13)+\upsilon(CN)(5)]+\upsilon(CC)(12)+\upsilon(CN7)(5)$	1478	Ring2 CC stretch
1484	1436	1437	1439		1435	-	-	$R1[\delta(CH_2)](90)$	1434	Ring1 CH_2 sym stretch
1425	1379	1397	1402	1428	1404	-	-	$R2[\upsilon(CC)(21)+\upsilon(OC)(26)+\delta_{in}(CH)(14)+\delta_{in}(C16N)(5)+\delta_{in}(CC17)(7)]$	1436,1376	Ring2 CC stretch
1411	1366	1375	1381	-	-		1464	$\upsilon(C31N)(44)+\delta_s(C=O24)(12)+\rho(NH_2)(14)$	1450,1429,1410,1401	CN stretch
1406	1361	1349	1358	1378	1381	-	-	$R1[\upsilon(C19N8)(11)+\omega(CH_2)(7)]+\rho$(CH)(10)+R2[υ(C12C14)(8)+δ_{in}(CH13)(5)]+υ(NN)(5)	1356	Ring1 CN stretch
1374	1330	1338	1342			-	-	$R1[\delta_{in}(NH)(33)+\upsilon(CN9)(13)]+\rho(CH)(6)+\upsilon_S(NO_2)(12)$	1436	Ring1 NH in plane bend
1364	1320	1334		1348	1342	-	-	$\rho(CH)(25)+\upsilon_s(NO_2)(27)$+R2[υ(CN)(12)+υ(C12C14)(5)]+$\delta(NO_2)(9)$	1316	NO_2 stretch
1352	1309	1313	1313			-	-	$R1[\delta_{in}(NH)(25)+\upsilon(C19N9)(25)+\omega(CH_2)(12)]+\upsilon$	1316	Ring1 NH in

								$(NO_2)(8)$		plane bend
1322	1280	1260	1261	1323		-	-	R1[$\omega(CH_2)(22)+\upsilon(CC)(18)+\upsilon(CN9)(23)+\delta_{in}(C=O)(11)+\delta_{ring}(7)]+\rho(CH)(5)$	1283	Ring1 CH_2 wagging
1287	1246	1250	1248	1258		-	-	R2[$\upsilon(C12C14)(28)+\upsilon(OC11)(11)+\delta_{in}(CH13)(6)]+\upsilon(CC)(12)+\upsilon(NO_2)(13)+\rho(CH)(6)$	1242	Ring2 NN stretch
1272	1231	1237	1236	1247	1250	-	-	R1[$\upsilon(NN)(25)+\upsilon(C21N)(13)]$+R2[$\upsilon(OC16)(11)+\upsilon(OC11)(7)]+\delta_s(NNC)(7)+\delta_s(CH18)(6)$	1236,1209	Ring1 NN stretch
1248	1208	1207	1209	1207	1204	-	-	R2[$\upsilon(OC)(34)+\delta'_{ring}(10)+\upsilon(CN)(7)]$+R1[$\upsilon(NN)(16)+\upsilon(C21N)(6)]$	1176	Ring2 OC stretch
1213	1174	1181	1178	1169	1173	-	-	R1[$\omega(CH_2)(24)+\upsilon(CN8)(39)+\upsilon(CN9)(7)]$	1152	Ring1 CH_2 wagging
1193	1155		1134			-	-	R2[$\delta_{in}(CH)(47)+\upsilon(CN)(10)+\delta'_{ring}(7)+\upsilon(OC16)(6)]+\upsilon(CC)(5)$+R1[$\gamma(CH_2)](5)$	1157	Ring2CH in plane bend
1192	1154					-	-	R1[$\gamma(CH_2)](91)$	1152	Ring1 CH_2 twisting
1186	1148			-	-	1176	1153	$\rho(NH_2)(67)+\upsilon(C=O)(15)+\delta(O4HN25)(11)$	1169,1136,1145	NH_2 rocking
1122	1086	1041	1055	1123	1111	-	-	R1[$\upsilon(CN9)(52)+\delta_{in}(NH)(10)+\delta_{in}(C=O4)(9)+\upsilon(C21N)(6)+\upsilon(CC)(6)]$	1126	Ring1 CN stretch
1054	1020		1034	-	-	1011	1051	$\rho(NH_2)(61)+\upsilon(C31N)(22)+\delta(O4HN25)(13)$	1075,1037,1029,1018	NH_2 rocking
1040	1007	1007				-	-	R2[$\delta_{in}(CH)(62)+\upsilon(C12C14)(25)$	1006	Ring2 CH in plane bend
1012	980			1017	1018	-	-	R1[$\rho(CH_2)(71)+OOP(C=O5)(15)+\tau(6)]$	987	Ring1 CH_2 rocking
1002	969	991		977		-	-	R2[$\upsilon(OC)(52)+\delta'_{ring}(12)]+\upsilon(CC)(8)$	980	Ring2 OC stretch
988	956	979	978	963	964	-	-	R2[$\delta_{ring}(41)+\upsilon(OC)(17)+\upsilon(CC16)(9)+\upsilon(CN)(8)+\upsilon(C11C12)(5)]$	968	Ring2 deformation
958	928	920	920	-	-	-	1000	$\upsilon(C31N)(84)+\rho(N25H_2)(8)$	967,962,949	CN stretch
926	896				926	-	-	$\omega(CH)(54)+\tau(CN)(25)$+R2[$OOP(CH)](10)$	890,879	CH wagging
907	878	898	893	902	903	-	-	R2[$OOP(CH)](78)+\tau(12)]+\omega(CH)(5)$	955	Ring2 CH out of plane bend
889	860		893			-	-	R1[$\upsilon(CC)(53)+\upsilon(CN9)(18)+\delta_{in}(NH)(7)]$	876	Ring CC stretch
881	853	876	872, 862	870	872	-	-	$\delta_s(CH)(19)+\delta_s(NNC)(18)$+R2($\delta'_{ring}$)(14)+R1[$\upsilon(CN8)(18)+\delta'_{ring}(8)+\upsilon(NN)(8)]$	847	CH symmetric deformation
832	805		816		825	-	-	$\delta(NO_2)(59)$+R2[$\delta'_{ring}(17)+\delta_{ring}(7)]+\upsilon(NO_2)(8)$	804	NO_2 deformation
816	790	817	816	809		-	-	R2[$OOP(CH)](87)$	790	Ring1 CN stretch
791	765	791	785	783	779	-	-	R1[$\upsilon(C19N8)(19)+\delta'_{ring}(8)+\delta_{in}(C=O4)(5)]$+R2[$\delta'_{ring}(15)+\delta_{ring}(12)]+\upsilon(CC)(6)+\delta_s(CH)(6)+\delta(NO_2)(5)$	769	Ring1 CN stretch
779	754			-	-	-	786	$\omega(C=O24)(89)$	786,756,751	C=O wagging
744	720	748	748			-	-	R1[$OOP(C=O4)(71)+\tau'(14)+\tau(8)]$	761	Ring1 C=O out of plane bend
735	711	737	737	714	725	-	-	$\omega(CN6)(67)$+R2[$OOP(C16N)(16)+\tau'(11)]$	714	CN wagging
692	670	690	689			-	-	R1[$\delta_{ring}(25)+\upsilon(C21N)(15)+\delta'_{ring}(10)+\delta_{in}(C=O4)(10)+\delta_{in}(NN)(9)+\upsilon(CC)(5)+\delta_{in}(C=O5)(5)]+\delta_s(CH)(5)$	734	Ring1 deformation
685	663	665	669	685	687	-	-	R2[$\tau'(35)+OOP(CC17)(34)+\tau(23)]+\tau(CN)(4)$	665	Ring2 torsion
619	599	625	617	622		-	-	R1[$\delta_{in}(C=O)(30)+\delta'_{ring}(16)+\delta_{in}(NN)(10)+\delta_{ring}(7)]+\delta_s(NNC)(7)$	669	Ring1 C=O in plane bend
609	590	609	609					$\tau(C31N)(37)+\delta_s(C=O24)(16)+\delta(O4HN25)(14)+\delta(N25HN7)(6)+\rho(C=O24)(5)$	640	CN torsion
606	587			606	609	-	-	R1[$OOP(C=O5)(24)+OOP(NH)(23)+\delta_{ring}(8)+\tau(7)+\delta'_{ring})(7)]$	611	Ring1 out of plane bend

604	585				602	-	-	R1[OOP(C=O5)(23)+OOP(NH)(22)+δ'$_{ring}$(10)+δ$_{ring}$(8)+τ(7)]	595	Ring1 out of plane bend
593	573	584	596	585		-	-	R2[τ(52)+τ'(24)+OOP(C16N)(17)]	574	Ring2 torsion
562	544	578	561	-	-	562	573	δ$_s$(C=O24)(29)+δ(O4HN25)(18)+ρ(C=O24)(11)+τ(N25C)(11)+ρ(NH$_2$)(12)+δ(O3HN25)(5)	587	C=O symmetric deformation
554	536		555	570		-	-	R1[OOP(NH)(33)+OOP(C=O5)(18)+ρ(CH$_2$)(7)]+ρ(NO$_2$)(12)+R2[δ$_{in}$(C16N)](6)	572,571	Ring1 NH out of plane bend
553	536	553	544	551	548	-	-	ρ(NO$_2$)(29)+R2[δ$_{in}$(C16N)(15)+δ$_{in}$(CC17)(8)]+R1[OOP(NH)(13)+OOP(C=O5)(7)]	537	NO$_2$ rocking
535	518		525	-	-	546	560	ω(CN28)(73)+υ(CN28)(12)+R1[OOP(NH)](5)	583,582,575	CN wagging
500	484	470	507	-	-			ρ(C=O)(36)+δ(O4HN25)(19)+δ$_s$(C=O)(15)+τ(N28C)(7)+ρ(N25H$_2$)(6)	532,530	C=O rocking
483	468		480	-	-			ω(CN25)(26)+τ(N28C)(25)+δ(N25HN7)(19)+ρ(C=O)(9)	518,510,489	CN wagging
464	450	470	459	467	463	-	-	δ$_s$(NNC)(17)+R2[δ$_{in}$(CC17)(16)+υ(CN)(9)+δ$_{ring}$(5)]+ρ(NO$_2$)(11)+δ$_s$(CH)(7)+R1[δ$_{in}$(NN)](5)	450,288	NNC deformation
442	428		444	438	440	-	-	R2[υ(CN)(17)+δ$_{in}$(CC17)(7)+δ'$_{ring}$(5)]+R1[δ$_{in}$(C=O)(18)]+δ$_s$(CH)(8)+δ(NO$_2$)(8)	472	Ring1 C=O in plane bend
429	415	409	418	-	-			δ(O4HN25)(34)+δ(N25HN7)(33)+τ(N25C)(11)+τ(N28C)(8)+ω(CN25)(8)	398,388	OHN deformation
402	389	409	409	399	409	-	-	R1[δ$_{in}$(C=O)(41)+υ(CC)(6)+υ(CN9)(10)+υ(C21N)(5)]+R2[υ(CN)(11)+δ$_{ring}$(5)]	349	Ring1 C=O in plane bend
379	366	386		386		-	-	τ(CN)(29)+R2[τ'(16)+τ(13)+OOP(CC17)(9)+OOP(C16N)(8)]+ω(CH)(8)+R1[OOP(NN)](7)	368,223	CN torsion
299	290	305	-		-	-	-	R1[τ(NN)(33)+OOP(NN)(16)+τ'(7)]+R2[τ(CC)](14)+τ(CN)(7)+δ(N8NH27)(5)	301,205	Ring1 NN torsion
295	285	296	-	295	-	-	-	R1[δ$_{in}$(NN)(12)+δ$_{in}$(C=O4)(10)+τ(NN)(8)]+R2[δ$_{in}$(CC17)(10)+δ$_{in}$(C16N)(10)]+δ(O4HN25)(5)+ρ(NO$_2$)(5)	191	Ring1 NN in plane bend
224	217	212	-	223	-	-	-	R2[δ$_{in}$(C16N)](32)+ρ(NO$_2$)(15)+δ$_s$(CH)(14)+υ(CC)(5)+δ(N6OH26)(5)	186,169	Ring2 CN in plane bend
193	187	196	-	202	-	-	-	R2[OOP(C16N)(52)+OOP(CC17)(5)]+R1[τ(NN)](14)+τ(CN)(6)	162,159	Ring2 CN out of plane bend
189	183		-	181	-	-	-	R1[τ'(71)+OOP(NN)(15)+OOP(NH)(5)]	145,140	Ring1 torsion
150	145	156	-	-	-	-	-	R1[τ(50)+OOP(NH)(29)+OOP(NN)(6)+τ'(5)]	137,129	Ring1 torsion
139	135	149	-	-	-	-	-	R1[δ$_{in}$(NN)](25)+δ$_s$(NNC)(19)+R2[δ$_{in}$(C16N)(15)+δ$_{in}$(CC17)(14)]+δ(N6OH26)(5)	140,137	Ring1 NN in plane bend
124	120	119	-	-	-	-	-	R1[τ(18)+OOP(NN)(6)+OOP(NH)(10)]+R2[τ(CN)(16)+OOP(CC17)(12)+OOP(C16N)(10)+τ(CC)(6)]	108,100	Ring1 torsion
97	94	109	-	-	-	-	-	δ(O4HN25)(41)+R1[τ(15)+OOP(NH)(10)]+δ(N8NH27)(5)+δ(O3HN25)(5)	94,86	OHN deformation
80	77		-	-	-	-	-	R2[τ(CN)](35)+R1[OOP(NN)(20)+τ(10)+δ(N6OH26)(16)	83,81	Ring2 CN torsion
72	69	70	-	-	-	-	-	δ(O4HN25)(40)+ω(CN25)(10)+δ(N25HN7)(9)+ω(CN28)(7)+δ(N6OH26)(7)+τ(N28C)(6)+δ(COH30)(5)	76,73	OHN deformation
65	63		-	-	-	-	-	δ(N6OH26)(29)+δ(O4HN25)(17)+ω(CN25)(14)+δ(COH30)(9)+δ(O3HN25)(5)	73,64	NOH deformation
61	59	-	-	-	-	-	-	δ$_s$(CH)(14)+δ(N8NH27)(14)+δ(N25HN7)(11)+δ(O4HN25)(10)+δ(N6OH26)(9)+R2[δ$_{in}$(CC17)](9)+δ$_s$(NNC)(6)+δ(O3HN25)(5)	60,56	CH deformation
51	50	-	-	-	-	-	-	δ(O3HN25)(30)+R1[OOP(NN)](13)+R2[τ(CC)](10)+δ(N25HN7)(10)+δ(O4HN25)(9)	49,44	OHN deformation

42	41	-	-	-	-	-	-	δ(O4HN25)(45)+δ(N8NH27)(29)+δ(N25HN7)(15)	38,36	OHN deformation
33	32	-	-	-	-	-	-	δ(O3HN25)(34)+R1[OOP(NN)](17)+δ(O4HN25)(13)+R2[τ(CN)](7)+ω(CN25)(5)	31,24	OHN deformation
22	21	-	-	-	-	-	-	δ(N8NH27)(21)+δ(O4HN25)(16)+R2[τ(CC)](16)+R1[τ(NN)(12)+OOP(NN)](11)]+δ(N25HN7)(7)	22,18	NNH deformation
13	13	-	-	-	-	-	-	δ(N25HN7)(39)+δ(O4HN25)(21)+δ(COH30)(19)+δ(N6OH26)(7)+δ(N8NH27)(7)	15,12	NHN deformation

Table S5 Geometrical parameters (bond length) and topological parameters for hydrogen bonds of interacting atoms of cocrystal (monomer + 3urea): electron density (ρ_{BCP}), Laplacian of electron density ($\nabla^2\rho_{BCP}$), electron kinetic energy density (G_{BCP}), electron potential energy density (V_{BCP}), total electron energy density (H_{BCP}) at bond critical point (BCP) and estimated interaction energy (E_{int}).

Interactions	Bond length	ρ_{BCP}	$\nabla^2\rho_{BCP}$	G_{BCP}	V_{BCP}	H_{BCP}	E_{int}
O32···H10	1.67082	0.04761	0.13818	−0.00525	−0.04505	−0.05030	−31.5637
O24···H53	1.79262	0.03602	0.11629	−0.00046	−0.02999	−0.03045	−19.1077
O32···H45	1.93082	0.02663	0.09375	−0.00173	−0.01997	−0.02170	−13.6170
O40···H37	1.91980	0.02642	0.09289	−0.00189	−0.01944	−0.02133	−13.3848
O48···H35	2.04629	0.01896	0.07606	−0.00278	−0.01345	−0.01623	−10.1845
O4···H30	2.03885	0.01842	0.07363	−0.00292	−0.01256	−0.01548	−9.7138
O48···H29	2.08743	0.01887	0.06508	−0.00194	−0.01238	−0.01432	−8.9859
O48···H38	2.20677	0.01442	0.05183	−0.00186	−0.00924	−0.01110	−6.9653
O5···H46	2.45626	0.00889	0.02948	−0.00099	−0.00539	−0.00638	−4.0035
O4···H34	2.57557	0.00770	0.02505	−0.00079	−0.00469	−0.00548	−3.4387
O3···H26	2.64432	0.00571	0.02327	−0.00099	−0.00384	−0.00483	−3.0308
O1···H27	2.94638	0.00262	0.01103	−0.00060	−0.00156	−0.00216	−1.3554
N7···H27	3.35510	0.00149	0.00555	−0.00035	−0.00069	−0.00104	−0.6526

Bond length (in Å); ρ_{BCP}, $\nabla^2\rho_{BCP}$, G_{BCP}, V_{BCP}, H_{BCP} (in a.u.); E_{int} (in kcal mol^{-1}).

Table S6 Geometrical parameters for intermolecular hydrogen bond in NF-urea (monomer + 3urea): bond length (Å), bond angle (◦) and sum of van der Waals radii of interacting atoms (Å).

D-H···A	D-H	H···A	D-H···A	(r_H+ r_A) (Å)
N9-H10···O32	1.04860	1.67082	166.87133	2.72
N52-H53···O24	1.03213	1.79262	176.58883	2.72
N44-H45···O32	1.02046	1.93082	166.52778	2.72
N36-H37···O40	1.02201	1.91980	174.15750	2.72
N33-H35···O48	1.01346	2.04629	150.19926	2.72
N28-H30···O4	1.01159	2.03885	167.18286	2.72
N28-H29···O48	1.01492	2.08743	170.63755	2.72
N36-H38···O48	1.01187	2.20677	144.85794	2.72
N44-H46···O5	1.01045	2.45626	134.10930	2.72
N33-H34···O4	1.00811	2.57557	128.25881	2.72
N25-H26···O3	1.00624	2.64432	113.75347	2.72

Table S7 Geometrical parameters (bond length) and topological parameters for hydrogen bonds of interacting atoms of NF-urea (monomer): electron density (ρ_{BCP}), Laplacian of electron density ($\nabla^2\rho_{BCP}$), electron kinetic energy density (G_{BCP}), electron potential energy density (V_{BCP}), total electron energy density (H_{BCP}) at bond critical point (BCP) and estimated interaction energy (E_{int}).

Interactions	Bond length	ρ_{BCP}	$\nabla^2\rho_{BCP}$	G_{BCP}	V_{BCP}	H_{BCP}	E_{int}
O4···H30	2.21754	0.01272	0.04853	−0.00203	−0.00808	−0.01011	−4.7754
O4···H27	2.67752	0.00549	0.01959	−0.00080	−0.00330	−0.00410	−4.6513
N7···H27	2.66864	0.00655	0.01978	−0.00084	−0.00327	−0.00411	−3.8609
O1···N25	3.36319	0.00406	0.01636	−0.00076	−0.00257	−0.00333	−1.4859

O3···H26	2.38129	0.00878	0.03161	−0.00135	−0.00521	−0.00656	−1.2482

Table S8 Second order perturbation theory analysis of Fock matrix in NBO basis for intramolecular interactions for monomer unit 1 and 2 within NF-urea (monomer + 3urea).

Donor NBO (i)	ED(i)/e	Acceptor NBO (j)	ED(j)/e	E(2)[a] kcal mol^{-1}	E(j)−E(i)[b]	F(i,j)[c]
within unit 1						
πO3-N6	1.98264	n(3)O2	1.46522	11.55	0.18	0.077
		π*O3-N6	0.66610	8.08	0.31	0.055
		π*C14-C16	0.31455	5.35	0.45	0.048
πN7-C17	1.91207	π*C11-C12	0.32461	12.01	0.35	0.062
πC11-C12	1.74905	π*N7-C17	0.24494	14.21	0.34	0.062
		π*C14-C16	0.31455	18.82	0.29	0.067
σC12-C14	1.96704	σ*N6-C16	0.10014	7.93	1.00	0.081
		σ*C11-C17	0.03050	5.56	1.16	0.072
πC14-C16	1.77379	π*O3-N6	0.66610	24.76	0.17	0.065
		π*C11-C12	0.32461	14.31	0.30	0.060
σC17-H18	1.97829	σ*O1-C11	0.02859	5.77	0.90	0.064
n(2)O1	1.70147	π*C11-C12	0.32461	29.14	0.36	0.092
		π*C14-C16	0.31455	28.04	0.36	0.090
n(2)O2	1.89341	σ*O3-N6	0.05638	18.70	0.72	0.105
		σ*N6-C16	0.10014	11.16	0.59	0.073
n(3)O2	1.46522	π*O3-N6	0.66610	161.19	0.14	0.137
n(2)O3	1.89491	σ*O2-N6	0.05533	18.54	0.72	0.104
		σ*N6-C16	0.10014	12.63	0.59	0.077
n(2)O4	1.83839	σ*N8-C19	0.10051	28.64	0.64	0.123
		σ*N9-C19	0.07473	23.94	0.71	0.119
n(2)O5	1.85256	σ*N9-C20	0.07810	25.50	0.71	0.122
		σ*C20-C21	0.07419	22.88	0.60	0.107
n(1)N7	1.91282	σ*N8-C21	0.04131	12.13	0.70	0.083
		σ*C17-H18	0.03128	10.37	0.76	0.080
n(1)N8	1.64034	π*O4-C19	0.33698	49.90	0.29	0.108
		π*N7-C17	0.24494	30.87	0.34	0.094
		σ*C21-H23	0.01813	5.66	0.66	0.060
n(1)N9	1.60179	π*O4-C19	0.33698	56.80	0.27	0.112
		π*O5-C20	0.25278	58.25	0.27	0.116
π*O3-N6	0.66610	π*C14-C16	0.31455	19.20	0.14	0.066
π*C11-C12	0.32461	π*N7-C17	0.24494	29.18	0.05	0.063
within unit 2						
n(2)O24	1.85765	σ*N25-C31	0.05874	21.93	0.73	0.115
		σ*N28-C31	0.05714	16.17	0.74	0.100
n(1)N25	1.78458	σ*O24-C31	0.30077	21.04	0.46	0.089
		π*O24-C31	0.14940	9.08	0.67	0.071
n(1)N28	1.77923	σ*O24-C31	0.30077	27.30	0.46	0.102
σ*O24-C31	0.30077	π*O24-C31	0.14940	91.70	0.21	0.263
π*O24-C31	0.14940	σ*N25-H26	0.00540	7.60	0.03	0.052
		σ*N28-H30	0.01859	5.74	0.05	0.050

[a]E(2) means energy of hyper conjugative interaction (stabilization energy). [b]Energy difference between donor (i) and acceptor (j) NBO orbitals.

[c]F(i,j) is the Fock matrix element between i and j NBO orbitals.

Table S9 Second order perturbation theory analysis of Fock matrix in NBO basis for the intermolecular interactions for NF-urea (monomer + 3urea).

Donor NBO (i)	ED(i)/e	Acceptor NBO (j)	ED(j)/e	E(2)[a] kcal mol^{-1}	E(j)−E(i)[b]	F(i,j)[c]
From unit 1 to unit 2						
n(1)O4	1.97316	σ*N28-H30	0.01859	2.72	1.19	0.051
From unit 1 to unit 3						
σN9-H10	1.98125	π*O32-C39	0.45779	0.67	0.71	0.022
From unit 1 to unit 4						
π*N7-C17	0.24494	π*O40-C47	0.36294	1.52	0.04	0.012

From unit 1 to unit 5						
π*N7-C17	0.24494	σ*N49-H51	0.00818	7.49	3.02	0.377
From unit 2 to unit 5						
n(1)O24	1.96539	σ*N52-H53	0.04783	5.80	1.15	0.073
n(2)O24	1.85765	σ*N52-H53	0.04783	13.44	0.74	0.091
π*O24-C31	0.14940	σ*N52-H53	0.04783	4.11	0.07	0.048
From unit 3 to unit 1						
πO32-C39	1.97310	σ*N9-H10	0.07402	7.15	0.76	0.067
n(1)O32	1.94169	σ*N9-H10	0.07402	13.60	1.08	0.109
n(2)O32	1.87746	σ*N9-H10	0.07402	5.39	0.65	0.053
π*O32-C39	0.45779	σ*N9-H10	0.07402	3.01	0.36	0.057
From unit 3 to unit 4						
n(1)O32	1.94169	σ*N44-H45	0.02929	4.79	1.16	0.067
n(2)O32	1.87746	σ*N44-H45	0.02929	5.47	0.73	0.058
From unit 4 to unit 3						
n(1)O40	1.96954	σ*N36-H37	0.03213	3.95	1.14	0.060
n(2)O40	1.86134	σ*N36-H37	0.03213	7.86	0.72	0.069
From unit 4 to unit 5						
π*O40-C47	0.36294	σ*N49-H51	0.00818	0.57	2.98	0.086
From unit 5 to unit 1						
σO48-C55	1.99224	σ*N9-C19	0.07473	2.44	1.43	0.054
		σ*C12-H13	0.01167	5.73	1.50	0.083
		σ*C14-H15	0.01081	2.18	1.44	0.050
σN49-H51	1.98771	π*N7-C17	0.24494	2.12	0.71	0.037
σN49-C55	1.99323	π*N7-C17	0.24494	2.80	0.85	0.046
		σ*C14-C16	0.01834	2.49	1.39	0.053
σN52-H53	1.98592	σ*C12-H13	0.01167	2.35	1.14	0.046
σN52-C55	1.99288	π*N7-C17	0.24494	4.53	0.87	0.060
		σ*C12-H13	0.01167	4.61	1.33	0.070
		σ*C12-C14	0.00890	2.61	1.38	0.054
n(1)O48	1.96520	σ*C12-H13	0.01167	3.18	1.20	0.055
n(2)O48	1.87387	π*N7-C17	0.24494	8.07	0.29	0.045
		σ*C12-H13	0.01167	2.97	0.76	0.044
		σ*C12-C14	0.00890	2.46	0.80	0.041
From unit 5 to unit 2						
n(1)O48	1.96520	σ*N28-H29	0.02088	2.37	1.17	0.047
n(2)O48	1.87387	σ*N28-H29	0.02088	3.96	0.73	0.049
From unit 5 to unit 3						
n(1)O48	1.96520	σ*N33-H35	0.01786	3.08	1.16	0.054
From unit 5 to unit 4						
σO48-C55	1.99129	σ*N44-H46	0.01071	3.77	1.47	0.067
n(1)O48	1.96520	σ*N44-H46	0.01071	2.24	1.17	0.046

Table S10 Selected Lewis orbitals (occupied bond orbital) with percentage ED over bonded atoms (ED_X, ED_Y in %), hybrid NBOs with s and p character in % for NF-urea (monomer).

Bond (X-Y) (ED_{X-Y})	ED_X (%) ED_Y (%)	Hybrid NBOs	s (%)	p (%)
σ(O1-C11)	68.91	$0.8301(sp^{2.13})_O$ +	31.94	67.98
(1.98555)	31.09	$0.5576(sp^{3.35})_C$	22.93	76.82
σ(O1-C16)	68.37	$0.8269(sp^{2.23})_O$ +	30.98	68.94
(1.98847)	31.63	$0.5624(sp^{2.87})_C$	25.78	73.95
σ(O2-N6)	50.27	$0.7090(sp^{3.15})_O$+	24.08	75.78
(1.99540)	49.73	$0.7052(sp^{2.07})_N$	32.54	67.33
σ(O3-N6)	50.35	$0.7096(sp^{3.10})_O$ +	24.36	75.50
(1.99624)	49.65	$0.7046(sp^{2.06})_N$	32.59	67.29
σ(O4-C19)	63.86	$0.7991(sp^{1.47})_O$ +	40.42	59.45
(1.99349)	36.14	$0.6012(sp^{1.71})_C$	36.81	63.06
σ(O5-C20)	64.24	$0.8015(sp^{1.42})_O$ +	41.30	58.57
(1.99583)	35.76	$0.5980(sp^{1.81})_C$	35.53	64..33
σ(N6-C16)	61.81	$0.7862(sp^{1.89})_N$ +	34.60	65.35
(1.98989)	38.19	$0.6180(sp^{2.40})_C$	29.42	70.47

σ(N7-N8)	45.81	$0.6769(sp^{2.97})_N$ +	25.18	74.68
(1.98790)	54.19	$0.73361(sp^{2.11})_N$	32.18	67.76
σ(N7-C17)	59.57	$0.7718(sp^{1.40})_N$ +	41.70	58.21
(1.98298)	40.43	$0.6358(sp^{2.03})_C$	33.02	66.89
σ(N8-C19)	63.26	$0.7953(sp^{1.97})_N$ +	33.71	66.24
(1.98342)	36.74	$0.6062(sp^{2.16})_C$	31.61	68.27
σ(N8-C21)	62.81	$0.7925(sp^{1.94})_N$ +	34.05	65.92
(1.98801)	37.19	$0.6098(sp^{3.51})_C$	22.16	77.70
σ(N9-H10)	72.04	$0.8488(sp^{2.24})_N$ +	30.88	69.08
(1.98732)	27.96	$0.5287(sp^{0.00})_H$	99.93	0.07
σ(N9-C19)	62.42	$0.7901(sp^{1.98})_N$ +	33.53	66.41
(1.98411)	37.58	$0.6130(sp^{2.18})_C$	31.36	68.51
σ(N9-C20)	62.90	$0.7931(sp^{1.82})_N$ +	35.46	64.49
(1.98846)	37.10	$0.6091(sp^{2.29})_C$	30.39	69.50
σ(O24-C31)	64.22	$0.8014(sp^{1.67})_O$ +	37.36	62.52
(1.99368)	35.78	$0.5981(sp^{2.01})_C$	33.18	66.66
σ(N25-H26)	70.55	$0.8400(sp^{2.40})_N$ +	29.39	70.56
(1.98799)	29.45	$0.5427(sp^{0.00})_H$	99.94	0.06
σ(N25-H27)	70.14	$0.8375(sp^{2.36})_N$ +	29.73	70.22
(1.98744)	29.86	$0.5464(sp^{0.00})_H$	99.93	0.07
σ(N25-C31)	60.79	$0.7797(sp^{1.73})_N$ +	36.61	63.33
(1.99359)	39.21	$0.6262(sp^{2.03})_C$	33.01	66.90
σ(N28-H29)	69.40	$0.8330(sp^{2.66})_N$ +	27.34	72.60
(1.98802)	30.60	$0.5532(sp^{0.00})_H$	99.94	0.06
σ(N28-H30)	69.94	$0.8363(sp^{2.46})_N$ +	28.86	71.08
(1.98682)	30.06	$0.5482(sp^{0.00})_H$	99.93	0.07
σ(N28-C31)	60.98	$0.7809(sp^{1.82})_N$ +	35.40	64.53
(1.99332)	39.02	$0.6247(sp^{2.12})_C$	32.06	67.84

Table S11 Calculated and observed ^{13}C NMR chemical shifts (δ/ppm) of NF-Urea, NF and Urea.

Atom	**δ_{cal}**	**δ_{exp}**	**Atom**	**δ_{cal}**	**δ_{exp}**
	NF-Urea			**NF**	
C21	49.2	48.1	C21	48.87	49.8
C14	117.7	116.8	C14	117.65	118.2
C12	119.9	121.2	C12	118.57	118.2
C17	129.1	134.1	C17	127.24	133.1
C19	154.4	150.4	C19	152.09	151.9
C11	156.6	152.0	C11	157.89	151.9
C16	161.1	154.0	C16	160.98	151.9
C31	161.5	162.1	C20	167.4	168.9
C20	166.9	168.5		**Urea**	
			C8	160.62	162.6

Table S12 Calculated local reactivity properties of the atoms of NF-urea (monomer + 3urea) using Hirshfeld derived charges.

Atom No.	**f_k^+**	**S_k^+**	**ω_k^+**	**f_k^-**	**S_k^-**	**ω_k^-**	**f_k^0**	**S_k^0**	**ω_k^0**
1 O	0.0062	0.0018	0.0494	0.0340	0.0097	0.2712	0.0201	0.0058	0.1603
2 O	0.0408	0.0117	0.3256	0.1330	0.0381	1.0604	0.0869	0.0249	0.6930
3 O	0.0187	0.0054	0.1495	0.1232	0.0353	0.9828	0.0710	0.0203	0.5661
4 O	0.0143	0.0041	0.1140	0.0318	0.0091	0.2535	0.0230	0.0066	0.1837
5 O	0.0233	0.0067	0.1861	0.0374	0.0107	0.2920	0.0303	0.0087	0.2420
6 N	0.0085	0.0024	0.0678	0.0718	0.0206	0.5730	0.0402	0.0115	0.3204
7 N	0.0182	0.0052	0.1451	0.0708	0.0203	0.5647	0.0445	0.0127	0.3549
8 N	0.0320	0.0091	0.2550	0.0177	0.0051	0.1413	0.0248	0.0071	0.1982
9 N	0.0087	0.0025	0.0693	0.0143	0.0041	0.1139	0.0115	0.0033	0.0916
10 H	0.0040	0.0011	0.0317	0.0083	0.0024	0.0666	0.0062	0.0018	0.0492
11 C	0.0178	0.0051	0.1422	0.0555	0.0159	0.4428	0.0367	0.0105	0.2925
12 C	0.0401	0.0115	0.3199	0.0455	0.0130	0.3629	0.0428	0.0123	0.3414
13 H	0.0186	0.0053	0.1484	0.0305	0.0087	0.2433	0.0245	0.0070	0.1958
14 C	0.0247	0.0071	0.1974	0.0658	0.0188	0.5247	0.0453	0.0130	0.3611

15 H	0.0165	0.0047	0.1319	0.0342	0.0098	0.2730	0.0254	0.0073	0.2025
16 C	0.0362	0.0104	0.2888	0.0343	0.0098	0.2734	0.0352	0.0101	0.2811
17 C	0.0318	0.0091	0.2537	0.0455	0.0130	0.3632	0.0387	0.0111	0.3085
18 H	0.0146	0.0042	0.1169	0.0268	0.0077	0.2139	0.0207	0.0059	0.1654
19 C	0.0084	0.0024	0.0673	0.0257	0.0073	0.2046	0.0170	0.0049	0.1359
20 C	0.0070	0.0020	0.0558	0.0131	0.0037	0.1045	0.0100	0.0029	0.0802
21 C	0.0092	0.0026	0.0737	0.0087	0.0025	0.0695	0.0090	0.0026	0.0716
22 H	0.0109	0.0031	0.0868	0.0092	0.0026	0.0731	0.0100	0.0029	0.0799
23 H	0.0146	0.0042	0.1161	0.0112	0.0032	0.0897	0.0129	0.0037	0.1029
24 O	0.0644	0.0184	0.5139	0.0173	0.0049	0.1377	0.0408	0.0117	0.3258
25 N	0.0121	0.0035	0.0968	−0.0075	−0.0021	−0.0594	0.0023	0.0007	0.0187
26 H	0.0121	0.0034	0.0962	−0.0001	−0.0000	−0.0004	0.0060	0.0017	0.0479
27 H	0.0050	0.0014	0.0397	−0.0092	−0.0026	−0.0735	−0.0021	−0.0006	−0.0169
28 N	0.0408	0.0117	0.3253	0.0018	0.0005	0.0143	0.0213	0.0061	0.1698
29 H	0.0093	0.0026	0.0739	0.0062	0.0018	0.0495	0.0077	0.0022	0.0617
30 H	0.0097	0.0028	0.0777	−0.0025	−0.0007	−0.0198	0.0036	0.0010	0.0290
31 C	0.0194	0.0055	0.1546	0.0039	0.0011	0.0309	0.0116	0.0033	0.0927
32 O	0.0230	0.0066	0.1838	−0.0009	−0.0002	−0.0070	0.0111	0.0032	0.0884
33 N	0.0247	0.0071	0.1968	0.0015	0.0004	0.0122	0.0131	0.0037	0.1045
34 H	0.0109	0.0031	0.0870	−0.0017	−0.0005	−0.0134	0.0046	0.0013	0.0368
35 H	0.0075	0.0022	0.0601	0.0017	0.0005	0.0134	0.0046	0.0013	0.0367
36 N	0.0493	0.0141	0.3932	0.0059	0.0017	0.0474	0.0276	0.0079	0.2203
37 H	0.0122	0.0035	0.0971	0.0029	0.0008	0.0230	0.0075	0.0021	0.0601
38 H	0.0155	0.0044	0.1236	0.0032	0.0009	0.0256	0.0093	0.0027	0.0746
39 C	0.0133	0.0038	0.1063	0.0012	0.0003	0.0097	0.0073	0.0021	0.0580
40 O	0.0539	0.0154	0.4302	0.0039	0.0011	0.0313	0.0289	0.0083	0.2308
41 N	0.0170	0.0049	0.1357	0.0015	0.0004	0.0118	0.0092	0.0026	0.0737
42 H	0.0147	0.0042	0.1174	0.0049	0.0014	0.0388	0.0098	0.0028	0.0781
43 H	0.0146	0.0042	0.1163	0.0028	0.0008	0.0221	0.0087	0.0025	0.0692
44 N	0.0403	0.0115	0.3217	−0.0009	−0.0003	−0.0072	0.0197	0.0057	0.1572
45 H	0.0075	0.0021	0.0597	−0.0014	−0.0004	−0.0111	0.0030	0.0009	0.0243
46 H	0.0157	0.0045	0.1251	−0.0011	−0.0003	−0.0089	0.0073	0.0021	0.0581
47 C	0.0187	0.0054	0.1495	0.0010	0.0003	0.0077	0.0098	0.0028	0.0786
48 O	−0.0061	−0.0018	−0.0490	−0.0053	−0.0015	−0.0420	−0.0057	−0.0016	−0.0455
49 N	0.0123	0.0035	0.0984	0.0056	0.0016	0.0443	0.0090	0.0026	0.0713
50 H	0.0061	0.0018	0.0490	0.0041	0.0012	0.0325	0.0051	0.0015	0.0408
51 H	0.0113	0.0032	0.0901	0.0057	0.0016	0.0458	0.0085	0.0024	0.0679
52 N	0.0156	0.0045	0.1248	0.0004	0.0001	0.0033	0.0080	0.0023	0.0640
53 H	0.0035	0.0010	0.0280	−0.0002	−0.0001	−0.0018	0.0016	0.0005	0.0131
54 H	0.0132	0.0038	0.1051	0.0047	0.0013	0.0374	0.0089	0.0026	0.0712
55 C	0.0067	0.0019	0.0539	0.0020	0.0006	0.0163	0.0044	0.0013	0.0351

Table S13 Calculated local reactivity properties of the atoms of NF-urea (monomer) using Hirshfeld derived charges.

Atom No.	f_k^+	S_k^+	ω_k^+	f_k^-	S_k^-	ω_k^-	f_k^0	S_k^0	ω_k^0
1 O	0.0026	0.0009	0.0228	0.0336	0.0115	0.2977	0.0181	0.0062	0.1603
2 O	0.0515	0.0176	0.4564	0.1263	0.0433	1.1204	0.0889	0.0304	0.7884
3 O	0.0141	0.0048	0.1250	0.1145	0.0392	1.0155	0.0643	0.0220	0.5703
4 O	0.0163	0.0056	0.1445	0.0388	0.0133	0.3441	0.0276	0.0094	0.2443
5 O	0.0401	0.0137	0.3555	0.0433	0.0148	0.3837	0.0417	0.0143	0.3696
6 N	0.0103	0.0035	0.0912	0.0697	0.0239	0.6179	0.0400	0.0137	0.3546
7 N	0.0211	0.0072	0.1870	0.0728	0.0249	0.6458	0.0469	0.0161	0.4164
8 N	0.0382	0.0131	0.3389	0.0163	0.0056	0.1448	0.0273	0.0093	0.2419
9 N	0.0151	0.0052	0.1336	0.0155	0.0053	0.1375	0.0153	0.0052	0.1356
10 H	0.0143	0.0049	0.1271	0.0174	0.0060	0.1543	0.0159	0.0054	0.1407
11 C	0.0253	0.0087	0.2246	0.0509	0.0174	0.4515	0.0381	0.0130	0.3381
12 C	0.0503	0.0172	0.4461	0.0482	0.0165	0.4276	0.0492	0.0169	0.4368
13 H	0.0243	0.0083	0.2152	0.0312	0.0107	0.2766	0.0277	0.0095	0.2459
14 C	0.0330	0.0113	0.2926	0.0613	0.0210	0.5439	0.0471	0.0161	0.4182
15 H	0.0212	0.0073	0.1882	0.0336	0.0115	0.2980	0.0274	0.0094	0.2431

16 C	0.0418	0.0143	0.3707	0.0368	0.0126	0.3262	0.0393	0.0134	0.3484
17 C	0.0324	0.0111	0.2878	0.0540	0.0185	0.4794	0.0432	0.0148	0.3836
18 H	0.0183	0.0063	0.1628	0.0288	0.0099	0.2558	0.0236	0.0081	0.2093
19 C	0.0135	0.0046	0.1197	0.0299	0.0102	0.2650	0.0217	0.0074	0.1923
20 C	0.0092	0.0031	0.0813	0.0155	0.0053	0.1378	0.0123	0.0042	0.1095
21 C	0.0107	0.0037	0.0950	0.0086	0.0029	0.0762	0.0096	0.0033	0.0856
22 H	0.0154	0.0053	0.1366	0.0109	0.0037	0.0967	0.0131	0.0045	0.1167
23 H	0.0138	0.0047	0.1221	0.0108	0.0037	0.0956	0.0123	0.0042	0.1089
24 O	0.1988	0.0681	1.7635	0.0197	0.0067	0.1744	0.1092	0.0374	0.9689
25 N	0.0592	0.0203	0.5248	−0.006	−0.0020	−0.0532	0.0266	0.0091	0.2358
26 H	0.0219	0.0075	0.1941	−0.0023	−0.0008	−0.0201	0.0098	0.0034	0.0870
27 H	0.0231	0.0079	0.2051	−0.0044	−0.0015	−0.0387	0.0094	0.0032	0.0832
28 N	0.0562	0.0192	0.4982	0.0042	0.0014	0.0374	0.0302	0.0103	0.2678
29 H	0.0314	0.0107	0.2784	0.0134	0.0046	0.1188	0.0224	0.0077	0.1986
30 H	0.0261	0.0089	0.2312	0.0024	0.0008	0.0213	0.0142	0.0049	0.1262
31 C	0.0507	0.0174	0.4499	0.0043	0.0015	0.0380	0.0275	0.0094	0.2439

Table S14 Calculated local reactivity properties of the atoms of NF using Hirshfeld derived charges.

Atom No.	f_k^+	S_k^+	ω_k^+	f_k^-	S_k^-	ω_k^-	f_k^0	S_k^0	ω_k^0
1 O	0.0715	0.0193	0.5135	0.5135	0.0096	0.2549	0.0535	0.0144	0.3842
2 O	0.2733	0.0737	1.9619	1.9619	0.0353	0.9410	0.2022	0.0545	1.4514
3 O	0.1986	0.0535	1.4254	1.4254	0.0340	0.9039	0.1623	0.0437	1.1647
4 O	0.3323	0.0896	2.3847	2.3847	0.0119	0.3157	0.1881	0.0507	1.3502
5 O	0.3021	0.0814	2.1678	2.1678	0.0115	0.3077	0.1725	0.0465	1.2378
6 N	−0.2200	−0.0593	−1.5787	−1.5787	0.0195	0.5188	−0.0738	−0.0199	−0.5299
7 N	0.1939	0.0523	1.3913	1.3913	0.0196	0.5226	0.1333	0.0359	0.9570
8 N	0.2481	0.0669	1.7807	1.7807	0.0048	0.1269	0.1329	0.0358	0.9538
9 N	0.1135	0.0306	0.8149	0.8149	0.0040	0.1073	0.0642	0.0173	0.4611
10 H	−0.1679	−0.0453	−1.2051	−1.2051	0.0048	0.1274	−0.0751	−0.0202	−0.5389
11 C	0.0083	0.0022	0.0595	0.0595	0.0143	0.3820	0.0308	0.0083	0.2207
12 C	0.1812	0.0488	1.3001	1.3001	0.0129	0.3440	0.1145	0.0309	0.8220
13 H	−0.0608	−0.0164	−0.4364	−0.4364	0.0086	0.2288	−0.0145	−0.0039	−0.1038
14 C	0.0491	0.0132	0.3524	0.3524	0.0173	0.4597	0.0566	0.0153	0.4061
15 H	−0.0779	−0.0210	−0.5588	−0.5588	0.0094	0.2515	−0.0214	−0.0058	−0.1536
16 C	0.0804	0.0217	0.5768	0.5768	0.0099	0.2642	0.0586	0.0158	0.4205
17 C	0.0525	0.0141	0.3770	0.3770	0.0137	0.3651	0.0517	0.0139	0.3710
18 H	−0.0497	−0.0134	−0.3565	−0.3565	0.0077	0.2056	−0.0105	−0.0028	−0.0754
19 C	−0.2264	−0.0610	−1.6249	−1.6249	0.0080	0.2138	−0.0983	−0.0265	−0.7056
20 C	−0.2010	−0.0542	−1.4422	−1.4422	0.0041	0.1096	−0.0928	−0.0250	−0.6663
21 C	0.0084	0.0023	0.0603	0.0603	0.0024	0.0648	0.0087	0.0023	0.0626
22 H	−0.0549	−0.0148	−0.3937	−0.3937	0.0030	0.0806	−0.0218	−0.0059	−0.1566
23 H	−0.0548	−0.0148	−0.3935	−0.3935	0.0030	0.0806	−0.0218	−0.0059	−0.1565

Table S15 Binding energies, inhibition constants and interaction energies of NF against protein targets of E. Coli. using Autodock 4.2.

Protein	Targets	Binding energy (kcal mol^{-1})	Inhibition costant Ki (μm)	Intermolecular energy (kcal mol^{-1})	Hydrogen bonds (Å) with binding sites
Hu Alpha2	1MULA	−4.89	260.95	−5.78	2.14 (N7) SerA 81
ELAV-like protein1	3HI9	−10.64	15.81	−11.54	2.36 (O5) AsnA 21 1.76 (H10) AsnA 21 2.26 (N7) SerA 48

					2.49 (O1) AlaA 49 2.35 (O2) ArgC 37 1.69 (O3) AlaA 49 1.71 (O3) ArgA 37
Glutaredoxin	IGRX	−6.09	34.56	−6.98	2.07 (O4) TyrA 35 1.68 (O3) LysA 18 2.07 (O3) ArgA 8
	1EGO	−5.56	84.72	−6.45	1.88 (H10) ThrA 73 2.03 (H10) AspA 74 2.26 (O5) ThrA 73
	5CAX	−8.26	886.31	−9.15	2.06 (O5) PheC 51 2.58 (O4) TyrB 49 1.90 (O3) LysC 10 1.66 (O2) AspC 7 2.21 (O2) ThrC 8
	2MZC	−6.59	14.78	−7.48	2.00 (H10) PheB 57 2.33 (O4) GlyB 53 2.14 (N7) GlyB 53 2.32 (O1) AsnB 55 1.77 (O3) ArgB 54 2.27 (O2) ArgA 21