Supplementary Material

Calculation of NMR chemical shifts

Chemical shieldings were computed for sulfathiazole (ST), sulfapyridine (SP), sulfamerazine (SMZ), sulfadimethoxine (SDM) and sulfadoxine (SDX) in monomer and dimer forms; according to the results discussed in the text, ST was considered in its imidic tautomeric form (with the heterocycle N atom protonated), while all the other drugs were considered in the amidic structure (characterized by the SO_2-NH moiety).

All the structures were optimized at the B3LYP/6-31G(d,p) level; NMR parameters were computed with the GIAO method using larger basis sets, namely 6-311+G(d,p) (hereafter BS1) and aug-cc-PVTZ (BS2), to verify the stability of the computed values; no environmental effects were included in the calculations. The calculations on dimers with the largest basis set raised convergency problems due to the huge computational weight, so that only BS1 results are reported for dimers: then in the text we shall refer to more accurate BS2 values for momoner drugs, and approximate the monomer-dimer differences at the BS1 level.

Conventional chemical shifts (δ, ppm) were obtained by subtracting the chemical shieldings (σ, ppm) of the various nuclei in sulfadrugs from the σ values computed at the same level for tetramethylsilane (TMS) for ^{1}H and ^{13}C, and ammonia for ^{15}N.

The isotropic chemical shifts for ^{1}H, ^{13}C and ^{15}N are reported in tables S1, S2 and S3, respectively: the atom numbering is referred to figures S1 to S5. For ^{15}N only the atoms directly bound to hydrogen are reported since they are detected by the experiments.

Table S1. Computed ^{1}H isotropic chemical shifts (referred to TMS, ♦ = 31.9 ppm with BS1, 31.6 ppm with BS2). Refer to figures S1-S5 for the atom numbering.

ST				SP				SMZ			
	monomer		dimer		monomer		dimer		monomer		dimer
	BS1	BS2	BS1		BS1	BS2	BS1		BS1	BS2	BS1
7H	6.6	6.5	6.9	7H	6.8	6.7	7.0	7H	6.6	6.5	6.4
8H	7.4	7.8	7.1	8H	7.4	8.2	8.0	8H	8.4	8.5	8.5
9H	8.2	8.1	7.0	9H	7.5	7.9	7.2	9H	7.8	8.1	7.4
10H	6.9	6.9	6.1	10H	6.4	6.6	5.8	10H	6.9	6.9	6.3
12H	3.2	3.7	3.8	12H	3.4	3.7	3.8	12H	3.8	3.6	3.5
13H	3.7	3.6	3.8	13H	3.4	3.6	3.8	13H	3.4	3.7	3.1
21H	6.4	6.6	6.8	18H[(a)]	6.2	6.8	12.7	18H[(a)]	7.2	7.2	10.7
22H	6.0	6.1	6.0	22H	7.9	8.1	7.4	22H	8.7	8.5	9.7
25H[(a)]	10.4	11.3	14.2	24H	7.5	7.8	8.0	24H	6.6	6.7	6.8
				26H	6.9	7.0	7.5	28H	1.8	2.2	1.7
				28H	8.3	8.4	9.4	29H	2.5	2.4	3.5
								30H	2.5	2.5	2.1

(a) this atom involved in H-bonding in dimers.

Table S1 (continued).

SDM				SDX			
	monomer		Dimer		monomer		dimer
	BS1	BS2	BS1		BS1	BS2	BS1
7H	6.8	6.9	6.5	7H	6.4	6.7	6.5
8H	7.9	8.1	8.0	8H	7.8	8.4	7.9
9H	7.5	7.9	8.7	9H	7.8	8.1	7.7
10H	6.6	6.7	6.6	10H	6.6	6.7	6.4
12H	3.4	3.8	3.3	12H	3.7	3.7	3.9
13H	3.4	3.6	3.5	13H	3.6	3.7	3.6
18H[(a)]	6.4	6.6	9.8	18H[(a)]	6.2	7.1	12.0

24H	6.9	6.9	7.2	27H	3.8	3.9	3.7
29H	3.7	3.8	3.7	28H	4.0	4.0	4.2
30H	3.9	3.9	3.9	29H	4.0	4.0	4.2
31H	3.9	3.9	4.0	30H	8.2	8.2	9.5
33H	3.8	3.9	3.8	33H	3.5	3.8	3.9
34H	3.7	3.7	4.4	34H	3.5	3.7	3.6
35H	3.8	3.9	3.8	35H	3.7	4.0	3.9

Table S2. Computed ^{13}C isotropic chemical shifts (referred to TMS, ♦ = 183.7 ppm with BS1, 183.4 ppm with BS2). Refer to figures S1-S5 for the atom numbering.

ST				SP				SMZ			
	monomer		dimer		monomer		dimer		monomer		dimer
	BS1	BS2	BS1		BS1	BS2	BS1		BS1	BS2	BS1
1C	116.3	129.8	121.5	1C	115.2	135.3	113.8	1C	115.3	118.8	116.6
2C	134.7	160.2	136.6	2C	138.4	142.3	137.1	2C	141.2	152.7	145.0
3C	142.2	155.4	145.6	3C	139.4	129.7	147.9	3C	140.9	150.2	152.8
4C	135.8	127.5	132.6	4C	136.6	122.3	138.8	4C	136.1	138.4	136.2
5C	117.6	90.4	118.4	5C	119.0	123.9	112.9	5C	117.3	93.6	116.1
6C	161.1	148.3	159.8	6C	156.6	168.2	169.5	6C	160.6	153.1	157.6
18C	175.9	177.7	178.0	19C	159.3	159.1	163.5	19C	167.6	165.9	169.3
19C	125.7	127.5	129.8	20C	115.8	124.2	117.0	20C	166.7	158.6	167.4
20C	114.0	112.6	118.0	21C	143.8	141.1	144.6	21C	117.7	117.5	118.5
				23C	124.1	122.8	124.6	25C	177.6	172.0	178.5
				27C	156.1	161.1	157.2	27C	25.9	26.0	25.1

Table S2 (continued).

SDM				SDX			
	monomer		dimer		monomer		dimer
	BS1	BS2	BS1		BS1	BS2	BS1

1C	115.3	132.4	114.6	1C	116.8	117.1	116.4
2C	136.4	137.5	133.4	2C	139.7	147.4	142.3
3C	141.9	126.7	145.7	3C	137.1	147.8	146.3
4C	135.5	122.0	137.8	4C	136.7	143.4	136.5
5C	118.2	124.3	119.2	5C	119.1	112.2	117.5
6C	157.1	169.3	156.5	6C	156.7	152.0	160.0
19C	167.5	157.3	171.6	19C	160.1	152.9	161.8
20C	179.6	172.0	180.6	20C	173.7	169.4	172.7
22C	172.1	176.9	172.4	22C	159.5	158.9	161.5
23C	88.2	98.6	92.4	23C	135.1	132.3	134.4
28C	55.9	56.1	54.4	26C	56.1	59.6	54.1
32C	55.7	57.2	55.7	32C	61.6	61.0	61.8

Table S3. Computed ^{15}N isotropic chemical shifts (referred to NH_3, ♦ = 258.7 ppm with BS1, 259.8 ppm with BS2).

	ST			SP			SMZ			SDM			SDX		
	monomer		dimer	monomer		dimer	monomer		dimer	monomer		dimer	monomer		dimer
	BS1	BS2	BS1	BS1	BS2	BS1	BS1	BS2	BS1	BS1	BS2	BS1	BS1	BS2	BS1
NH_2	85.8	75.1	86.8	71.5	77.5	87.6	83.4	76.9	80.6	73.6	79.5	72.4	71.0	73.8	82.3
NH[(a)]	162.5	163.4	184.0	178.6	178.6	174.7	179.8	175.6	185.7	180.0	176.8	179.6	186.1	181.1	185.8

(a) heterocycle N atom in ST (in imidic tautomeric form); amidic SO_2-NH atom in all the other drugs.

Figure S2. Sulfathiazole atom numbering.

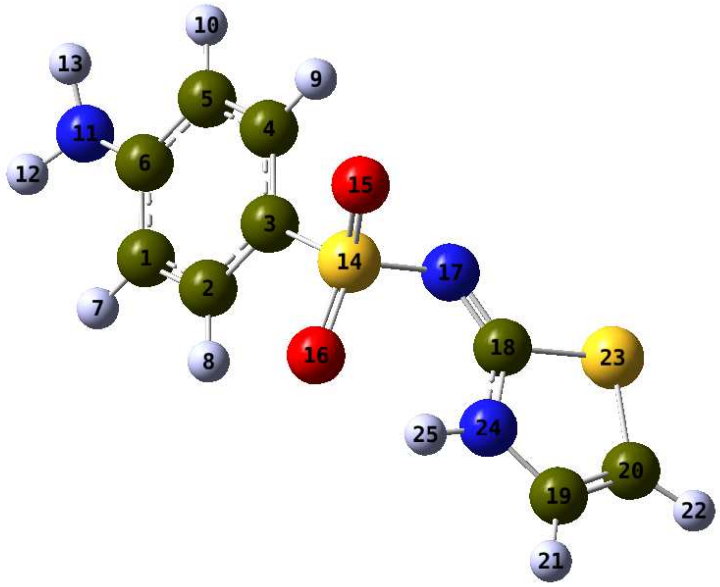


Figure S3. Sulfapyridine atom numbering.

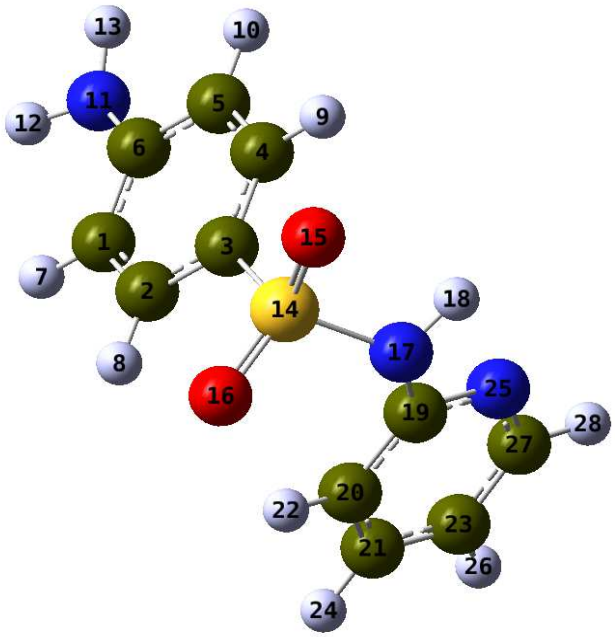


Figure S4. Sulfamerazine atom numbering.

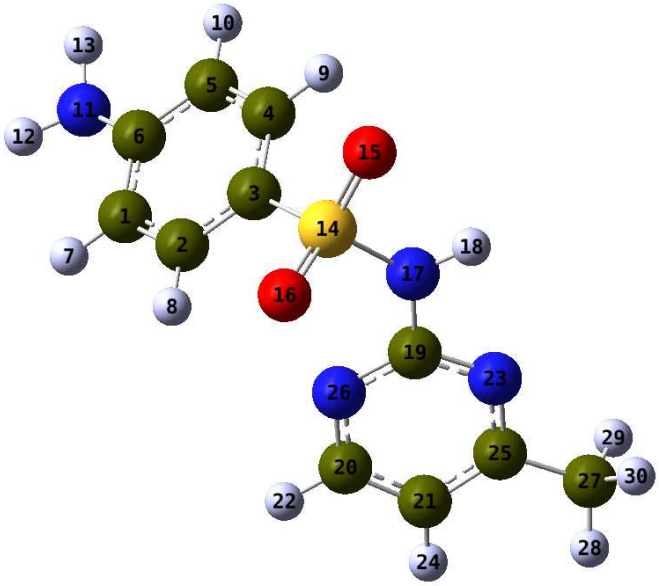
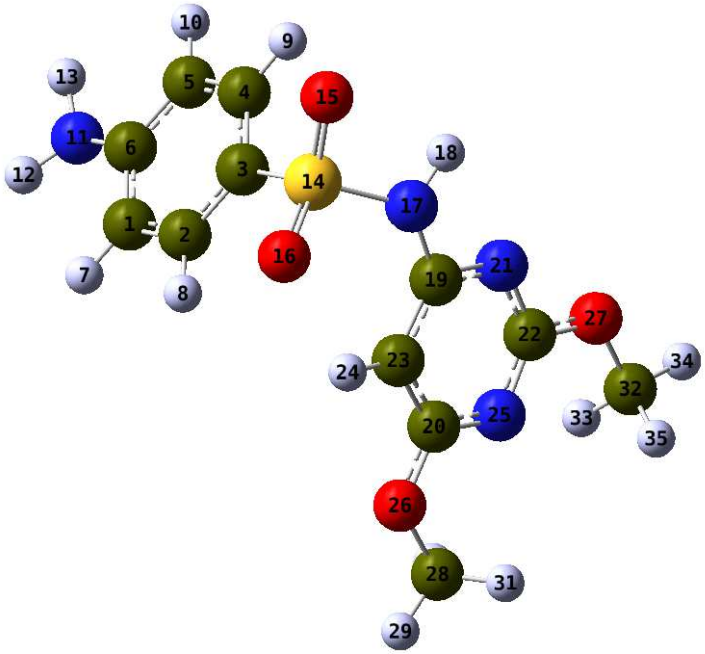
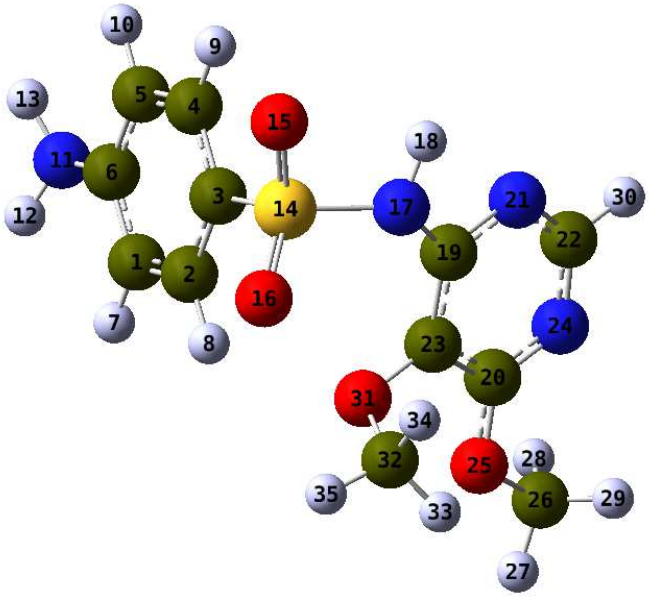


Figure S5. Sulfadimethoxine atom numbering.



1 Figure S6. Sulfadoxine atom numbering.



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