Text S1. Determination of Rate Law

The rate expression for the reaction of Fe(VI) with sulfonamide can be expressed as

$$-d[Fe(VI)]/dt = k[Fe(VI)]_{tot}^{m}[S]_{tot}^{n} \quad (1)$$

where [Fe(VI)] and $[S]_t$ are the concentrations of Fe(VI) and sulfonamide, m and n are the orders of the reaction, and k is the overall reaction rate constant. The kinetic studies were carried out under pseudo-order conditions with sulfonamide in excess i.e. $[S]_{ttot} >> [Fe(VI)]_{tot}$.. The Fe(VI) concentrations were ranged from 0.50 to 0.75 x 10^{-4} M while sulfonamide concentrations were at least ten times of Fe(VI) concentration. Equation (1) can thus be re-written under pseudo-order conditions as:

$$-d[Fe(VI)]/dt = k_1[Fe(VI)]^{m} \quad (2)$$

$$\text{where } k_1 = k[S]_{tot}^{n} \quad (3)$$

The rate law measurements were determined at pH 9.1 and 25 ^{o}C. Reactions were monitored by measuring the absorbance of Fe(VI) at 510 nm wavelength as a function of time. The reactions were followed for at least two half-lives. A successive integration model using the Global kinetic software for the absorbance of Fe(VI) as a function of time gave the best fit for an exponential value of 1, indicating the reaction is first-order with respect to Fe(VI). The k_1 values for the reaction were determined at various concentrations of sulfonamide under same conditions. The k_1 values were corrected for the spontaneous Fe(VI) decay in buffer solutions. The plots of k_1 values versus $[S]_{tot}$ were linear (*24*), which suggests that the rate law for this reaction is first-order with respect to sulfonamide.

Text S2

The observed activation enthalpy, $\Delta H^{\ddagger}_{obs}$, comprises enthalpy of the reaction, $\Delta H^{\ddagger}$, and enthalpies of dissociations of $HFeO_4^-$ and SH, $\Delta H^{\ddagger}_{HFeO4}$ and $\Delta H^{\ddagger}_{SH}$, respectively. The $\Delta H^{\ddagger}_{obs}$ in-terms of individual enthalpy can be written as

$$\Delta H^{\ddagger}_{obs} = \Delta H^{\ddagger} - \Delta H^{\ddagger}_{HFeO4} - \Delta H^{\ddagger}_{SH} \quad \text{(pH 7.0)} \qquad (4)$$

The values of $pK_{a,SH}$, except sulfamethazine are 3-4 orders of magnitude apart from pH 9.1. It is therefore possible that the contribution of $\Delta H^{\ddagger}_{obs}$ at pH 9.1 would be only from $\Delta H^{\ddagger}$ and $\Delta H^{\ddagger}_{HFeO4}$ (eq 5).

$$\Delta H^{\ddagger}_{obs} = \Delta H^{\ddagger} - \Delta H^{\ddagger}_{HFeO4} \quad \text{(pH 9.1)} \qquad (5)$$

Thus, the differences of observed enthalpies at pH 9.1 and 7.0 give values of $\Delta H^{\ddagger}_{SH}$ for sulfonamides except for sulfamethazine. The values of $\Delta H^{\ddagger}_{SH}$ were determined as 21.3±1.1, 39.4±2.4 and 36.9±3.0 kJ mol^{-1} for sulfisoxazole, sulfamethizole, and sulfamethoxazole, respectively. The value of $\Delta H^{\ddagger}_{SH}$ for sulfamethoxazole given in the literature (*34*) using solubility measurement is 33.76±0.25 kJ mol^{-1} and is in reasonable agreement with the value obtained in our study. A similar calculation could not be performed for sulfadimethoxine because it was not possible to perform temperature dependence measurements of its rates with Fe(VI) at pH 7.0. A solution of its powder could not be dissolved at this pH because of its low solubility. The values of pK_{SH} and pK_{HFeO4} for sulfamethazine are similar (Table 1) and the difference in $\Delta H^{\ddagger}_{obs}$ at pH 7.0 and 9.1 is most likely related to the difference in rate constants for the reactions of Fe(VI) species with sulfamethazine species (eqs 2-4 in manuscript). The pH dependence of the rates for the reaction of sulfamethazine with Fe(VI) at different temperature is needed to unravel the difference in $\Delta H^{\ddagger}_{obs}$ at the two pH conditions.

Table S1. Temperature Dependence of Rate Constants (k, $M^{-1}s^{-1}$) for oxidation of Sulfonamide Antimicrobials by Fe(VI) at pH 7.0 and 9.1.

Compound	pH	Temperature 15 °C	25 °C	35 °C	45 °C
Sulfisoxazole	7.0	1296±31.6	1504±32.0	1763±47.4	1981±37.0
	9.1	22.8±1.10	33.6±5.77	52.0±1.02	81.6±2.21
Sulfamethazine	7.0	736±19.6	869±33.3	892±23.3	1143±45.8
	9.1	7.79±0.79	14.7±0.61	20.3±0.75	28.9±0.94
Sulfamethiazole	7.0	672±10.1*	640±24.1	552±13.2	468±13.3
	9.1	1.84±0.08	3.13±0.57	3.75±0.57	5.89±0.21
Sulfadimethoxine	9.1	4.25±0.39	6.12±0.41	8.58±0.74	14.01±.83
Sulfamethoxazole	7.0	828±65.1	846±38.2	857±38.0	895±41.5
	9.1	7.68±0.10	13.54±0.80	20.71±0.10	-

*20 °C

Table S2. IR peaks of various functional groups present in SMX, A, B and C.

	SMX	A	B	C
CH_3, (2959, 2926 cm^{-1})	✓	✓	✓	✓
C=C-H (1600 cm^{-1})	✓	✓	✓	✓
N-H amide, (1528 cm^{-1})	✓	✓	✓	✓
SO_2 amide, (1348, 1398 cm^{-1})	✓	✓	✓	✓
SO_2NH, (1116 cm^{-1})	✓	✓	✓	✓
C=N, (1644 cm^{-1})	✓			
N-H amine, stretch, (3392 cm^{-1})	✓	✓		
N=O, (1592 cm^{-1})		✓	✓	✓
C=O stretch, (1720 cm^{-1})		✓	✓	✓

FIGURE S1. The temperature dependence of the observed second-order rate constants for the reaction between Fe(VI) and sulfonamides at different pH. ○- sulfamethazine, □- sulfamethoxazole (data at pH 7.0 were taken from (*24*)), Δ- sulfadimethoxine ●- sulfamethizole, ◊-sulfisoxazole)

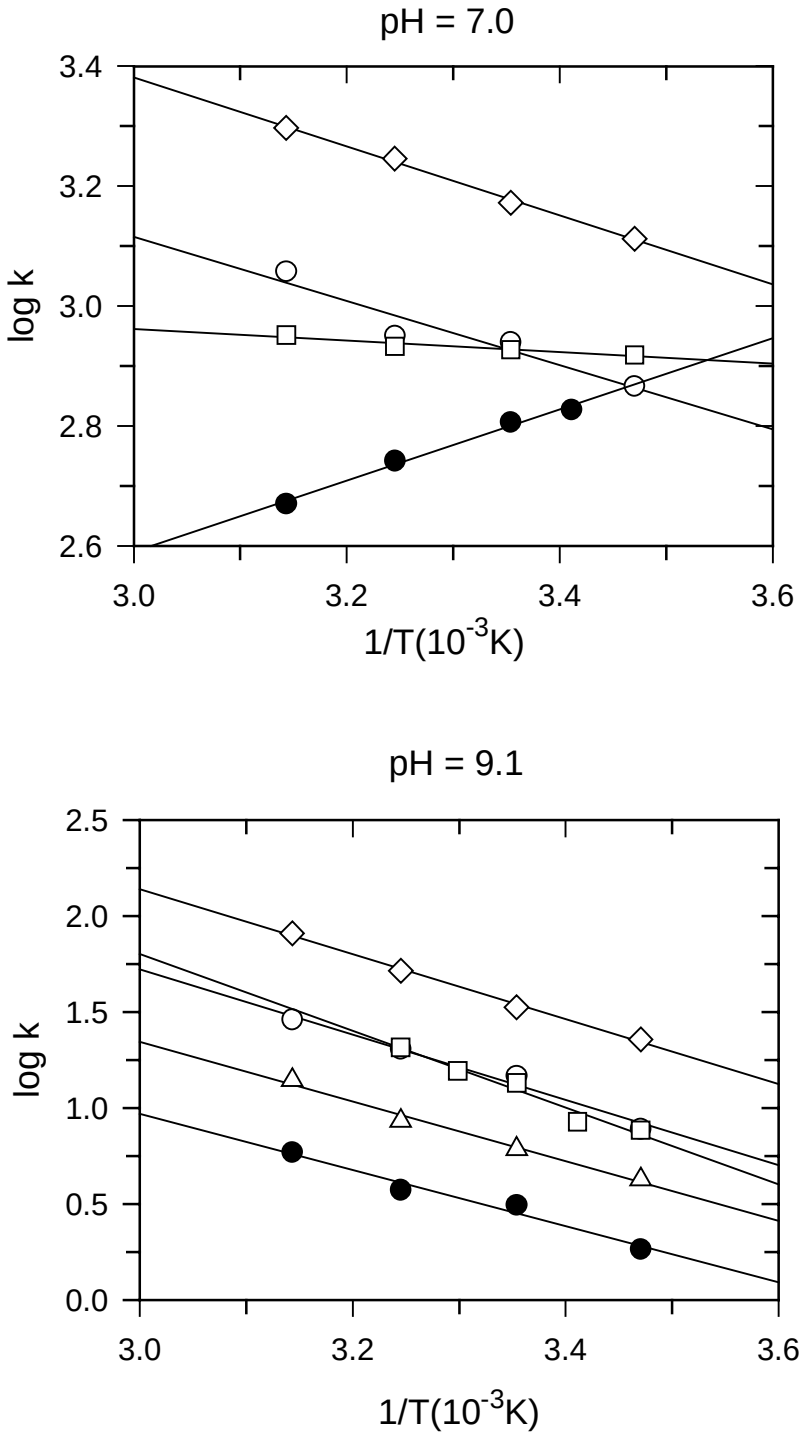


FIGURE S2. A plot of SMX decrease and formation of oxygen in the reaction of sulfamethoxazole with Fe(VI) under anoxic conditions (sulfamethoxazole (Δ -pH 7.0, □- pH 9.0), ●-oxygen (pH 9.0))

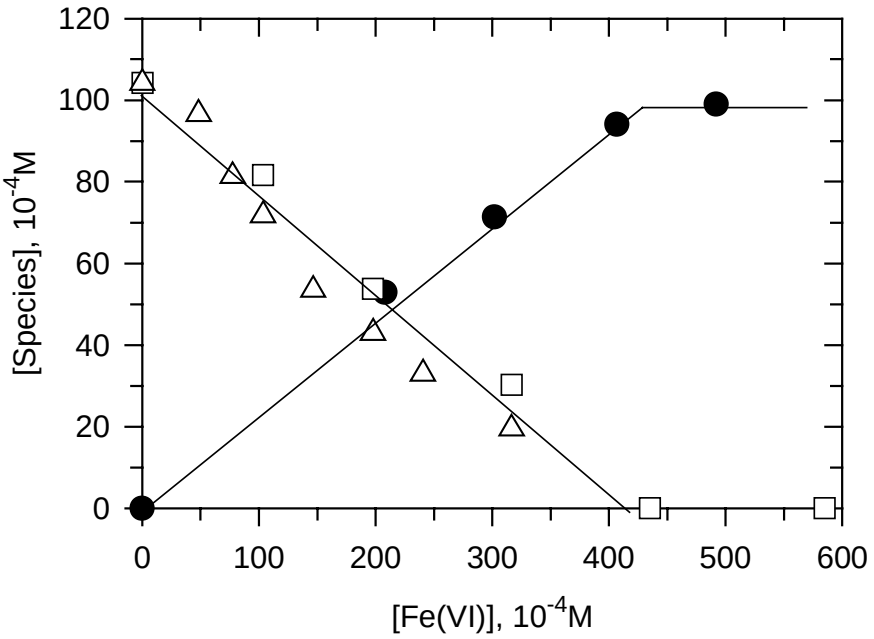


FIGURE S3. Various sub-structural models of SMX.

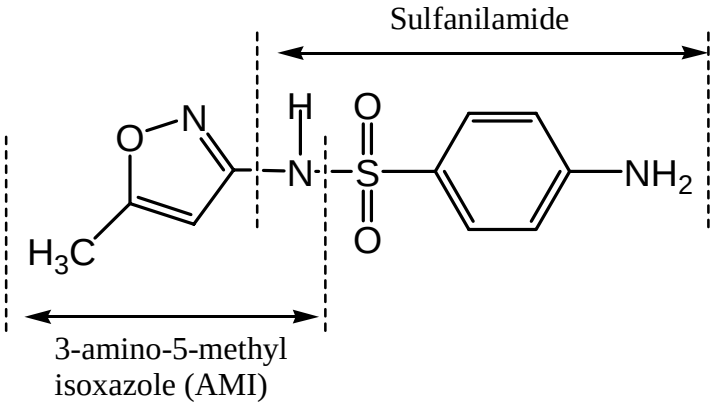
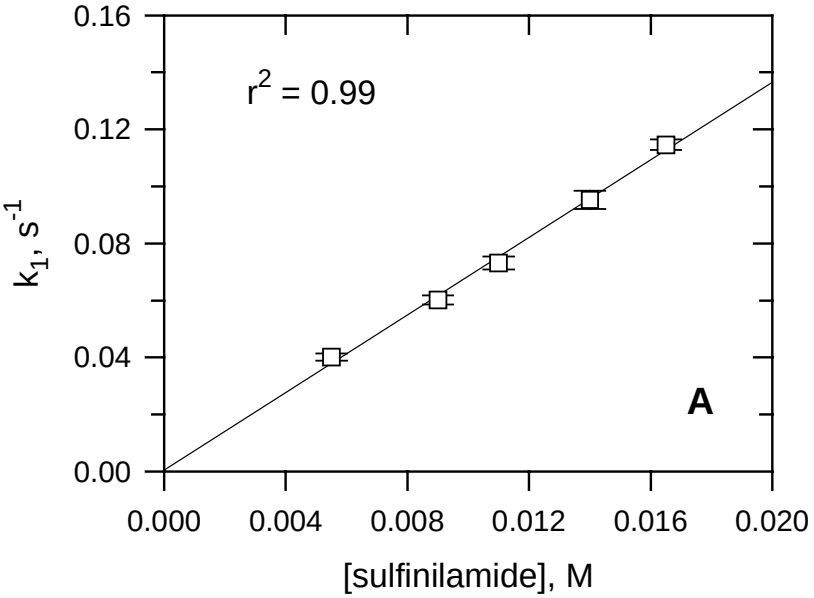


Figure S4. Plots of pseudo-first-order, k_1, s^{-1} versus concentrations of substructure compounds at pH 9.0 and 25 ^{o}C. A- sulfanilamide; B- 3-amino-5-methyl isoxazole (AMI) ([Fe(VI)]= 1.5 x 10^{-4} M).



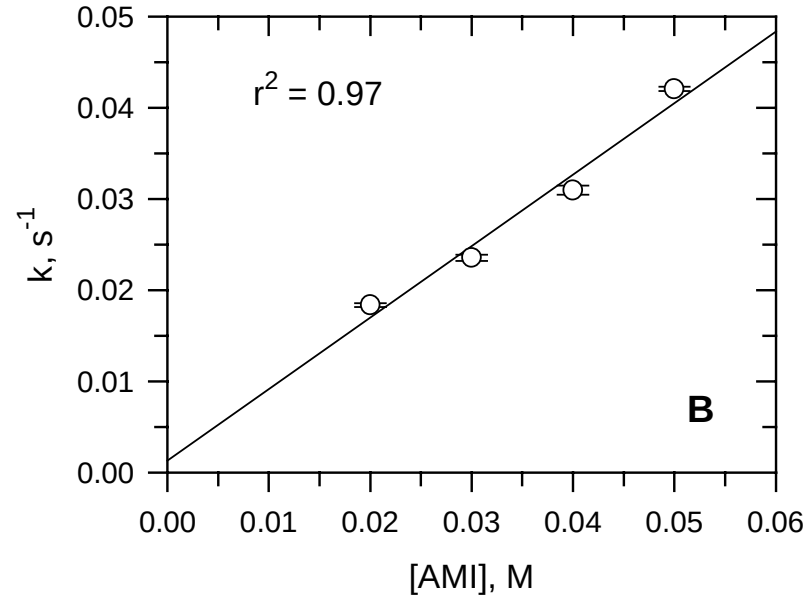
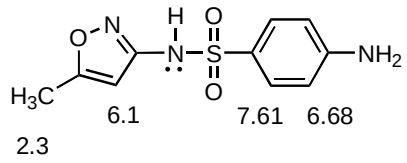
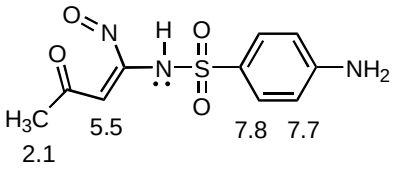


Figure S5. Chemical shifts of the non-exchangeable protons of SMX and the products from NMR spectra taken in CD_3OD.

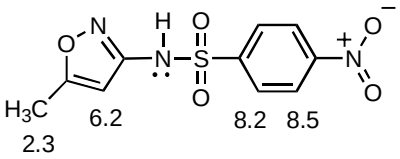
SMX :



Product A:



Product B:



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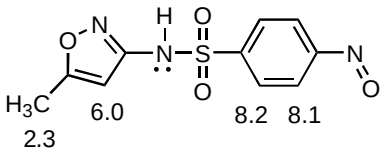
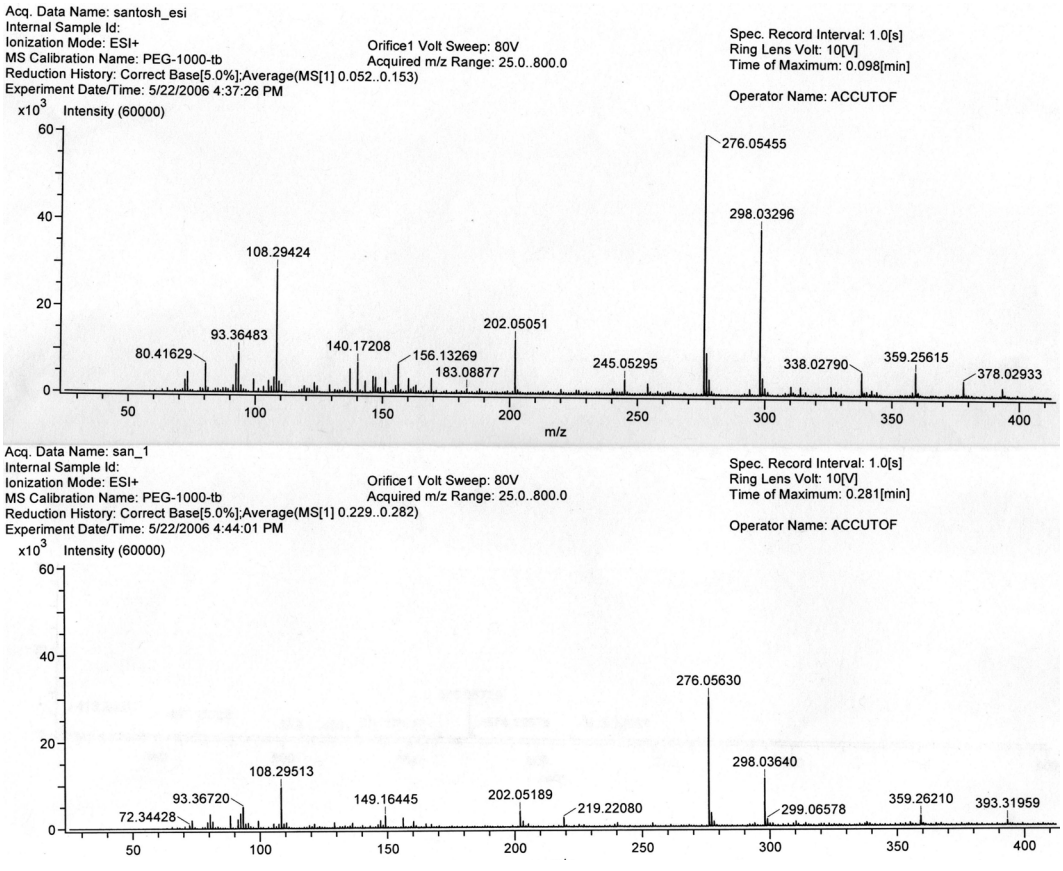
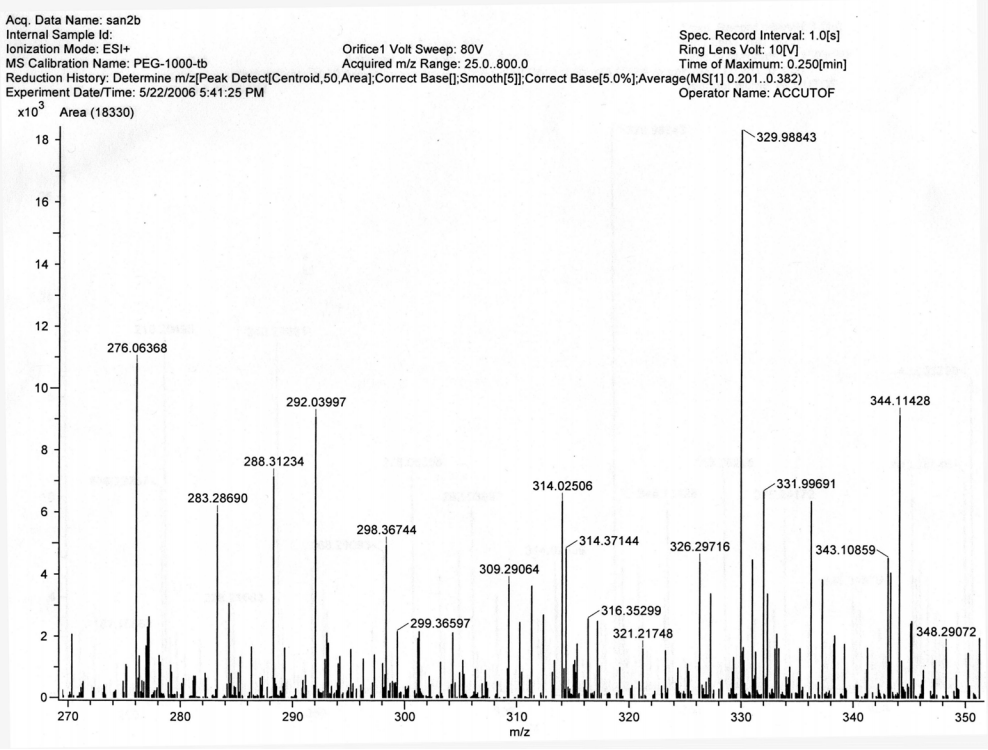


Figure S6. The three spectra are direct ESI measurements of (a) the SMX in aqueous solution at pH 9 (at 10 μM), (b) the addition of 5 equivalents of Fe(VI) at pH 9 after 7 min, and (c) an injection after 58 min of reaction time. Some minimal decrease in the SMX peak is observed in (b), and a substantial decrease of the SMX peak is observed in (c) with the appearance of a peak at 292.039 depicting product A+Na. Please note that the peaks with non-zero in the first decimal place (e.g. 288.312) do not correspond to SMX or any of its products. The AccuTOF instrument was calibrated for high resolution mass, and therefore 3 in the first decimal place corresponds to other impurities that are present at low concentrations (in the range of our SMX study).

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Internal Sample Id:
Ionization Mode: ESI+
MS Calibration Name: PEG-1000-tb
Orifice1 Volt Sweep: 80V
Acquired m/z Range: 25.0..800.0
Spec. Record Interval: 1.0[s]
Ring Lens Volt: 10[V]
Time of Maximum: 0.250[min]
Reduction History: Determine m/z[Peak Detect[Centroid,50,Area];Correct Base[];Smooth[5]];Correct Base[5.0%];Average(MS[1] 0.201..0.382)
Experiment Date/Time: 5/22/2006 5:41:25 PM
Operator Name: ACCUTOF
x10^3 Area (18330)
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276.06368
292.03997
344.11428
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321.21748
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m/z