Rapid and sensitive detection of sulfamethizole using a reusable molecularly imprinted electrochemical sensor

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Quantum chemical calculations

As the template molecule has multiple functional groups and has a certain flexibility, there will be multiple binding modes when they are combined. In order to obtain the low-lying binding mode of the system, we used the following scheme for conformational search. For the heterodimers formed by each monomer and template molecule, we created five different initial structures according to the possible binding sites and then used molecular dynamics for conformational sampling. The specific conditions of molecular dynamics (MD) are temperature=400 K, simulation time=100 ps, step size=2.0 fs, dumptime=50 fs, and other default values. In order to enhance the sampling effect, the temperature was set slightly higher than the normal temperature. The software used for MD calculations is xtb (version 6.3.2) [1]. For the ~10000 structures obtained, we use Crest to optimize them, and the level is gfn1 [2, 3]. For the optimized structure, deduplication is carried out according to the difference in energy and structure, and the program used is isostat [4]. The deduplication threshold for energy is 0.25 kcal/mol, and the structure deduplication threshold is 0.1Å. In order to obtain more accurate structures, the obtained structures were optimized using the B97-3c method, and was deduplicated further using isostat. For these final structures, in order to obtain more accurate electronic energies, the single-point energies were calculated using PWPB95(D3-BJ)/def2-QZVPP. The calculation programs used in the last two steps are orca [5] and molclus [4]. For monomers and template molecules, the search is performed in the same way.

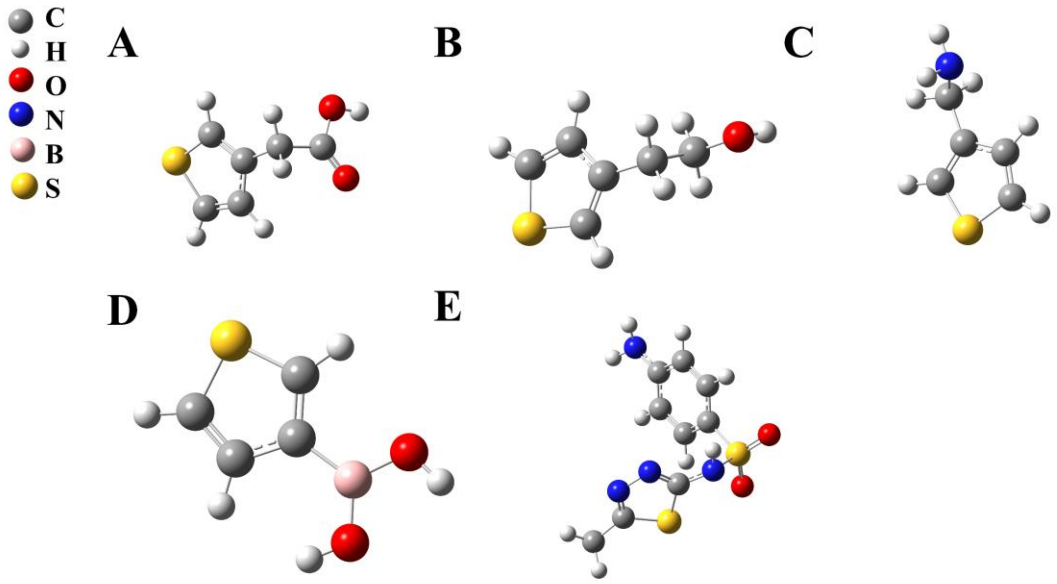

Figure. S1. The optimized structure for several monomers: (A) 3-thiopheneacetic acid (TAA), (B) 3-thiopheneethanol (TE), (C) 3-thiophenemethylamine (TM), (D) 3-thiopheneboronic acid (TBA), and (E) sulfamethizole (SMZ) molecule.

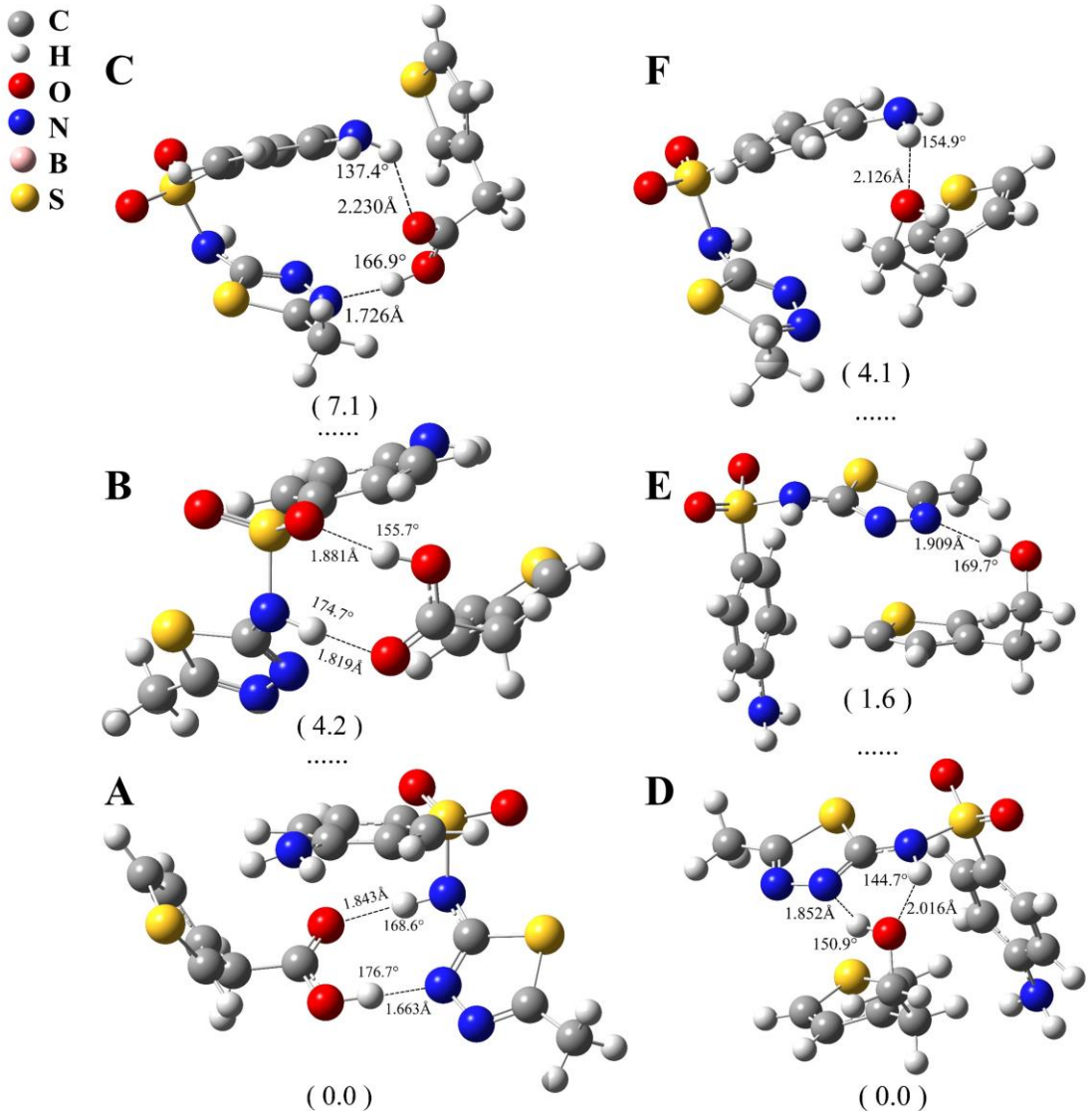

Figure. S2. Optimized geometric structures of several binding modes of the complexes between SMZ and TAA (A-C) or TE (D-F). Fig. S2 A, D is the lowest energy structures as shown in Fig. 1A and 1B. The presence of hydrogen bonds is indicated by the light black dashed lines. The values near the hydrogen bonds are the bond lengths and bond angles, and values in brackets are energies (unit: kcal/mol) relative to that of lowest energy structure. The ellipses indicate that there are many similar structures (the system below them), and their differences in energy and structure are very small, so only one representative structure was shown. Level of theory: PWPB95(D3-BJ)/def2-QZVPP//B97-3c.

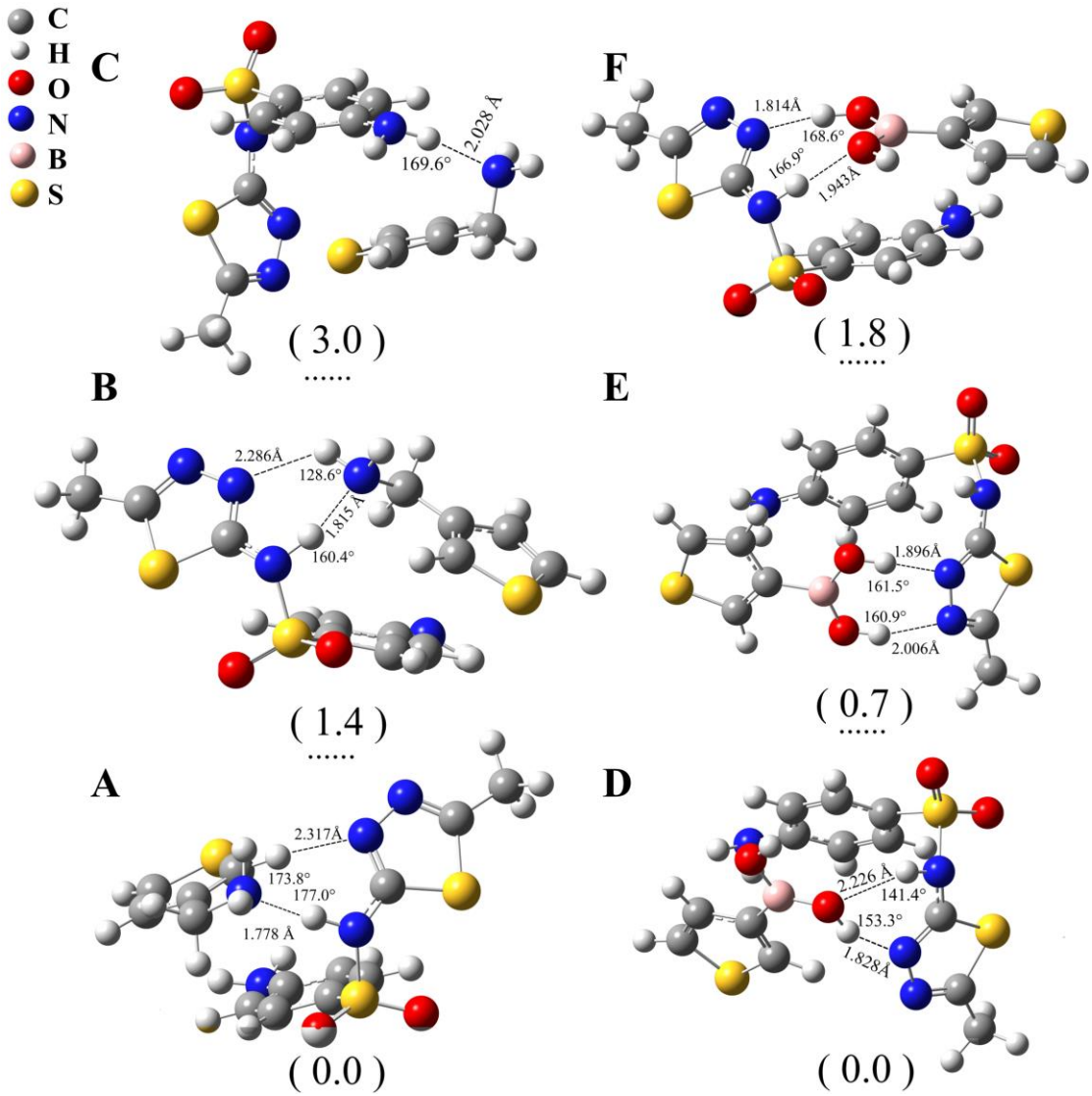

Figure. S3. Optimized geometric structures of several binding modes of the complexes between SMZ and TM (A-C) or TBA (D-F). Fig. S3 A, D is the lowest energy structures as shown in Fig. 1C and 1D. The presence of hydrogen bonds is indicated by the light black dashed lines. The values near the hydrogen bonds are the bond lengths and bond angles, and values in brackets are energies (unit: kcal/mol) relative to that of lowest energy structure. The ellipses indicate that there are many similar structures (the system below them), and their differences in energy and structure are very small, so only one representative structure was shown. Level of theory: PWPB95(D3-BJ)/def2-QZVPP//B97-3

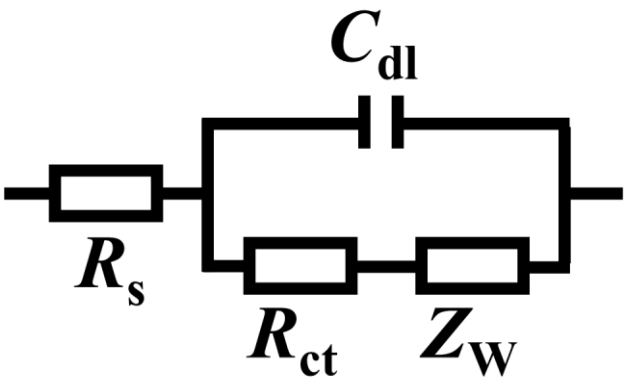

Figure. S4. The equivalent circuit model, where R_s, C_{dl}, and Z_w represent solution resistance, double-layer capacitance, and Warburg impedance, respectively.

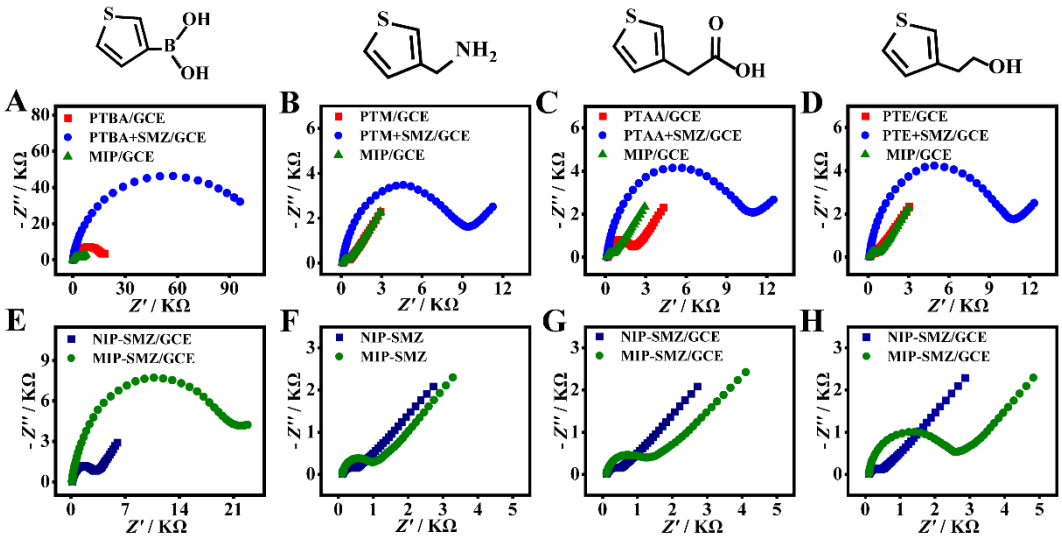

Figure. S5. (A-D) Electrochemical impedance spectroscopy (EIS) for each electropolymerized 3-substituted thiophene in the presence and absence of SMZ template, and the corresponding MIP film after template removal. (E-H) EIS response of each MIP and NIP towards target SMZ.

Table S1. Comparison of the proposed sensor with other reported molecularly imprinted electrochemical sensors for detecting sulfonamide antibiotics.

Sensor	Target	linear range (μM)	LOD (nM)	Sensor fabrication	Ref.
PDA-MIP/GE	sulfamethoxazole	8.0×10^{-1}-1.7×10^{2}	8×10^{2}	＞2.5 h	[6]
MIP/$Ni(OH)_2$ /NF	sulfapyridine	5.9×10^{-1}-1.34×10^{3}	3.57×10^{2}	＞11 h	[7]
MIP/MoS_2 /NH_2-MWCNT@COF/ GCE	sulfamerazine	3.0×10^{-1}-2.0×10^{2}	1.1×10^{2}	＞29 h	[8]
MIP/SPE	sulfamethizole	12.8×10^{-2}-1.6	9×10^{-1}	＞16 h	[9]
MIP/GE	sulphanilamide	5.8×10^{-3}-7.18×10^{-1}	5.8×10^{-1}	about 30 min	[10]
MIP/CuS/Au@COF/GCE	sulfathiazole	1.0×10^{-5}-1×10^{2}	4.3×10^{-3}	＞30 h	[11]
MIPs/UnZ-CCTF	sulfaquinoxaline	1.0×10^{-7}-2×10^{-6}	7.6×10^{-4}	＞27h	[12]
MIP/GCE	sulfamethizole	1.0×10^{-3}-1.0×10^{1}	1.8×10^{-1}	about 35min	This work

MIP: molecularly imprinted polymer**; GE**: Gold electrode; **PDA**: polydopamine; **$Ni(OH)_2$/NF**: $Ni(OH)_2$nanoarrays in situ grown on nickel foam; **GCE**: glassy carbon electrode; **CuS**: copper sulfide; **MoS_2:** disulfide; **NH_2-MWCNT**: amino-functionalized carbon nanotubes; **COF**: covalent organic frameworks; **H-GNs**: hybrid nanosheets; **SPE**: Screen-Printed Electrode; **UnZ-CCTF**: unzipped covalent triazine framework; **3D**: Three-dimensional.

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