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Mechanism for S_NAr reaction of atrazine and endogenous thiols: Experimental and theoretical study.

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Table S1. Kinetic data for the reaction of ATZ with CEE in aqueous solution at 25°C±0.1°C and pH=6.3

	$[CEE]_F$	k_{obs} / s^{-1}
1	0.0035	$1.8*10^{-6}$
2	0.0040	$2.5*10^{-6}$
3	0.0050	$5.0*10^{-6}$
4	0.0060	$6.4*10^{-6}$
5	0.0071	$7.3*10^{-6}$
6	0.0080	$8.7*10^{-6}$
7	0.0090	$9.5*10^{-6}$

Table S2. Kinetic data for the reaction of ATZ with CEE in aqueous solution at 25°C±0.1°C and pH=6.6

	$[CEE]_F$	k_{obs} / s^{-1}
1	0.0035	$3.5*10^{-6}$
2	0.0045	$5.5*10^{-6}$
3	0.0051	$6.6*10^{-6}$
4	0.0060	$8.2*10^{-6}$
5	0.0070	$9.1*10^{-6}$
6	0.0081	$1.1*10^{-5}$
7	0.0090	$1.3*10^{-5}$

Table S3. Kinetic data for the reaction of ATZ with CEE in aqueous solution at 25°C±0.1°C and pH=6.9

	$[CEE]_F$	k_{obs} / s^{-1}
1	0.0035	$5.8*10^{-6}$
2	0.0040	$7.1*10^{-6}$
3	0.0050	$8.9*10^{-6}$
4	0.0060	$1.1*10^{-5}$
5	0.0070	$1.5*10^{-5}$
6	0.0080	$1.7*10^{-5}$
7	0.0090	$1.8*10^{-5}$

Table S4. Kinetic data for the reaction of ATZ with CYS in aqueous solution at 25°C±0.1°C and pH=8.07

	$[CYS]_F$	k_{obs} / s^{-1}
1	0.0035	$2.1*10^{-6}$
2	0.0040	$4.1*10^{-6}$
3	0.0050	$5.7*10^{-6}$
4	0.0060	$8.3*10^{-6}$
5	0.0071	$1.3*10^{-5}$
6	0.0080	$1.6*10^{-5}$
7	0.0090	$1.8*10^{-5}$

Table S5. Kinetic data for the reaction of ATZ with CYS in aqueous solution at 25°C±0.1°C and pH=8.37

	$[CYS]_F$	k_{obs} / s^{-1}
1	0.0035	$2.5*10^{-6}$
2	0.0045	$4.3*10^{-6}$
3	0.0051	$4.8*10^{-6}$
4	0.0060	$5.5*10^{-6}$
5	0.0070	$7.0*10^{-5}$
6	0.0081	$8.2*10^{-5}$
7	0.0090	$9.4*10^{-5}$

Table S6. Kinetic data for the reaction of ATZ with CYS in aqueous solution at 25°C±0.1°C and pH=8.67

	$[CYS]_F$	k_{obs} / s^{-1}
1	0.0035	$6.7*10^{-6}$
2	0.0040	$8.1*10^{-6}$
3	0.0050	$9.0*10^{-6}$
4	0.0060	$1.0*10^{-5}$
5	0.0070	$1.2*10^{-5}$
6	0.0080	$1.3*10^{-5}$
7	0.0090	$1.5*10^{-5}$

Table S7. Kinetic data for the reaction of ATZ with GSH in aqueous solution at 25°C±0.1°C and pH=8.45

	$[GSH]_F$	k_{obs} / s^{-1}
1	0.0034	$5.2*10^{-6}$
2	0.0040	$7.3*10^{-6}$
3	0.0051	$9.1*10^{-6}$
4	0.0061	$1.2*10^{-5}$
5	0.0071	$1.5*10^{-5}$
6	0.0080	$1.9*10^{-5}$
7	0.0090	$2.2*10^{-5}$

Table S8. Kinetic data for the reaction of ATZ with GSH in aqueous solution at 25°C±0.1°C and pH= 8.75

	$[GSH]_F$	k_{obs} / s^{-1}
1	0.0036	$1.8*10^{-6}$
2	0.0040	$3.5*10^{-6}$
3	0.0050	$5.2*10^{-6}$
4	0.0061	$8.0*10^{-6}$
5	0.0070	$1.0*10^{-5}$
6	0.0081	$1.4*10^{-5}$
7	0.0090	$1.8*10^{-5}$

Table S9. Kinetic data for the reaction of ATZ with GSH in aqueous solution at 25°C±0.1°C and pH=9.05

	$[GSH]_F$	k_{obs} / s^{-1}
1	0.0036	$1.7*10^{-6}$
2	0.0040	$4.4*10^{-6}$
3	0.0050	$6.5*10^{-6}$
4	0.0061	$1.0*10^{-5}$
5	0.0070	$1.2*10^{-5}$
6	0.0080	$1.8*10^{-5}$
7	0.0090	$2.0*10^{-5}$

Table S10. Kinetic data for the reaction of ATZ with NAC in aqueous solution at 25°C±0.1°C and pH=9.22

	$[NAC]_F$	k_{obs} / s^{-1}
1	0.0036	$6.0*10^{-6}$
2	0.0043	$6.1*10^{-6}$
3	0.0049	$7.7*10^{-6}$
4	0.0060	$8.8*10^{-6}$
5	0.0072	$9.7*10^{-6}$
6	0.0085	$1.1*10^{-5}$
7	0.0092	$1.2*10^{-5}$

Table S11. Kinetic data for the reaction of ATZ with NAC in aqueous solution at 25°C±0.1°C and pH= 9.52

	$[NAC]_F$	k_{obs} / s^{-1}
1	0.0036	$5.0*10^{-6}$
2	0.0041	$7.8*10^{-6}$
3	0.0051	$8.9*10^{-6}$
4	0.0060	$1.2*10^{-5}$
5	0.0071	$1.3*10^{-5}$
6	0.0081	$1.5*10^{-5}$
7	0.0092	$1.9*10^{-5}$

Table S12. Kinetic data for the reaction of ATZ with NAC in aqueous solution at 25°C±0.1°C and pH=9.82

	$[NAC]_F$	k_{obs} / s^{-1}
1	0.0036	$9.2*10^{-6}$
2	0.0043	$1.4*10^{-5}$
3	0.0051	$1.5*10^{-5}$
4	0.0060	$1.7*10^{-5}$
5	0.0065	$2.0*10^{-5}$
6	0.0070	$2.5*10^{-5}$
7	0.0080	$2.9*10^{-5}$
8	0.0090	$3.2*10^{-5}$

Table S13: Cartesian coordinates TS-1a

C	0.31176300	0.37253900	-0.25890300
C	0.10323800	0.53461800	1.99195200
C	2.11939200	0.10529700	1.07942100
N	1.62189500	0.07368300	-0.16374900
N	1.40729000	0.36330700	2.20165200
N	-0.49843700	0.62644800	0.78345800
C	-2.18113000	2.30215700	3.31702500
H	-2.30305000	3.19356500	3.93562900
S	-0.37829200	2.20450000	3.01331700
H	-0.02186500	1.77500800	4.24101800
N	3.43746600	-0.10006900	1.25604500
N	-0.19542500	0.44765300	-1.50233500
H	3.74662400	-0.17446800	2.21613400
C	-1.59782900	0.65045000	-1.83011700
H	-1.62769800	0.99308500	-2.86626700
H	-1.98623600	1.47290700	-1.22367400
C	4.36774400	-0.54061400	0.21809400
H	4.09996500	-0.00892000	-0.69802600
C	4.26003500	-2.04535700	-0.02831900
H	4.55536800	-2.60084400	0.86892900
H	3.23616500	-2.32793700	-0.28911100
H	4.91949900	-2.34293800	-0.84967600
C	-2.45280500	-0.60184500	-1.67171300
H	-2.39491700	-0.99726300	-0.65289700
H	-3.49968500	-0.37036500	-1.89117600
H	-2.12074300	-1.38400800	-2.36094700
C	5.77967400	-0.13998800	0.62847000
H	6.06211500	-0.62904000	1.56814700
H	6.49311700	-0.44971300	-0.13993900
H	5.86338100	0.94254100	0.76170000
C	-3.00461200	2.47865700	2.04983500
H	-2.51463300	3.16123500	1.34837700
H	-2.48987200	1.42399100	3.88770100
H	0.43228500	0.16968600	-2.24314900
Cl	-0.94742800	-0.81405200	3.10682800
N	-3.17977900	1.18797600	1.33791600
H	-3.59009400	0.47971100	1.95121100
H	-3.82566700	1.31671900	0.55491000
C	-4.39500500	3.10006700	2.36798700
O	-5.38542400	2.56353100	1.81530400
O	-4.38580000	4.10449700	3.11715800
H	-2.24887900	0.84714500	0.97589900

Energy=-1768.5160891 a.u NIMAG=1 ; ν= 334 icm^{-1}

Table S14: Cartesian coordinates TS-1b

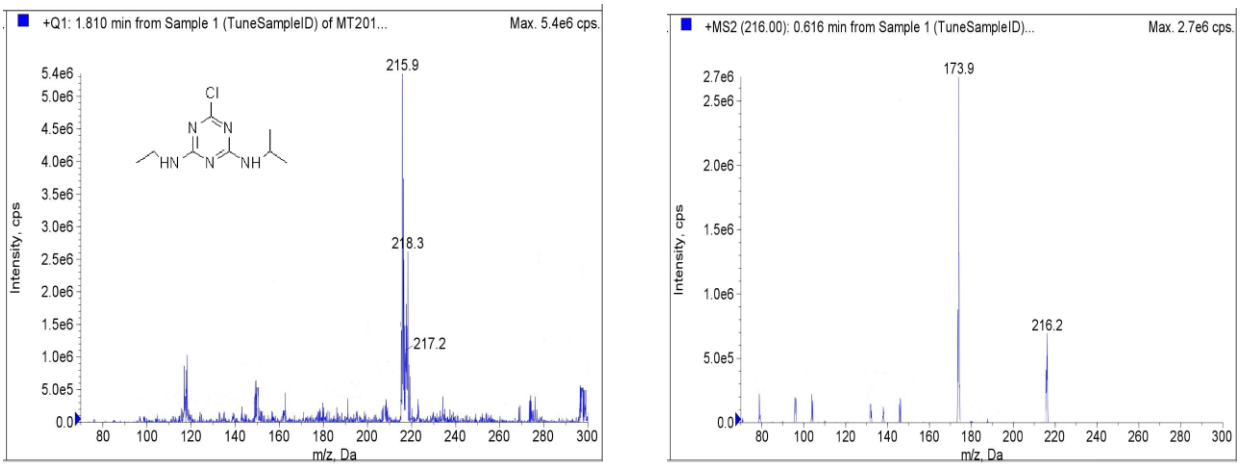
C	-0.05651600	0.11345500	0.01479200
C	-0.04444000	0.06979300	2.24601300
C	1.90273700	0.03787900	1.14215000
N	1.28391900	0.24144000	-0.03531200
N	1.29035700	-0.14317300	2.31818300
N	-0.77977600	-0.08179800	1.11850500
C	-1.74079900	2.76892800	1.83525200
H	-2.46915500	3.18720600	2.53230200
S	-0.17930300	2.36787700	2.67500000
N	3.26557500	0.05142900	1.16089700
N	-0.70750600	0.25292200	-1.17698200
H	3.65293000	-0.24756700	2.04833200
C	-2.11681200	-0.07701300	-1.35116800
H	-2.45377300	0.43371800	-2.25651300
H	-2.66971800	0.34977100	-0.51171200
C	4.08409400	-0.29896600	-0.00228100
H	3.66556500	0.23090900	-0.85978100
C	4.04500500	-1.80258000	-0.27450400
H	4.49068200	-2.35150500	0.56315200
H	3.01588900	-2.15146900	-0.40572000
H	4.60697300	-2.04566500	-1.18206200
C	-2.37990300	-1.57427200	-1.46869300
H	-2.05339500	-2.10368100	-0.56884100
H	-3.44974500	-1.75807500	-1.60899700
H	-1.84691000	-1.99370700	-2.32818900
C	5.50699900	0.19109400	0.23569700
H	5.93583600	-0.28434500	1.12596400
H	6.14087900	-0.06217300	-0.61904800
H	5.53520200	1.27544300	0.37772400
C	-1.57117000	3.76591500	0.67865400
H	-1.26120400	4.73962300	1.06202200
H	-2.14723200	1.83042400	1.43315600
H	-0.11569500	0.11481600	-1.98606100
Cl	-0.91218900	-0.56240400	3.69180600
N	-0.48540200	3.28552200	-0.21431000
H	0.28981600	2.96030300	0.38788700
H	-0.81542300	2.49507000	-0.78577900
C	-2.87774000	3.91487000	-0.11661900
O	-2.92935300	3.38267500	-1.25653600
O	-3.80328900	4.53962700	0.46408800
H	-0.15519000	4.01729800	-0.84432000

Energy= -1768.5341418 a.u NIMAG= 1 ; ν= 290 icm^{-1}

Table S15: Cartesian coordinates TS-1c

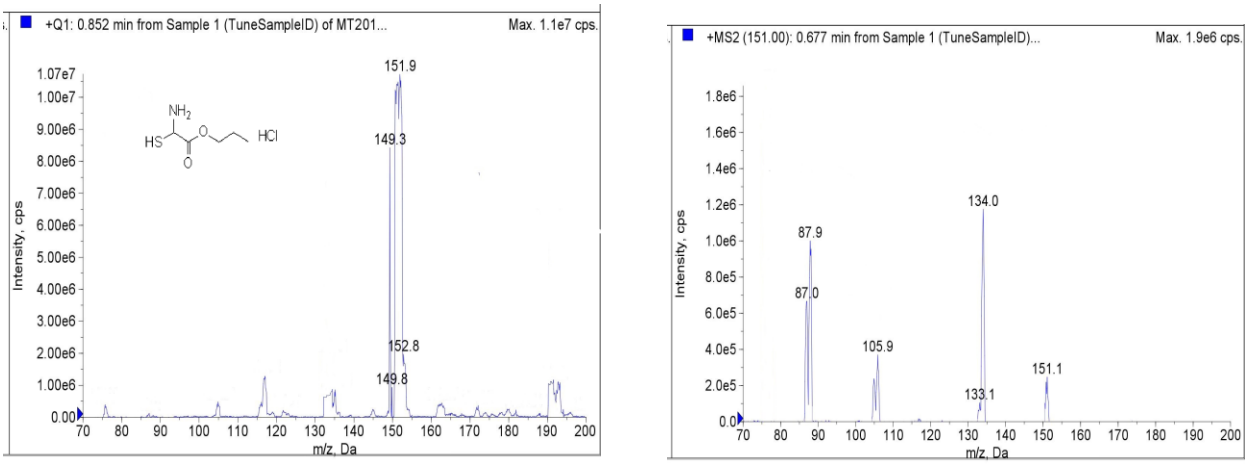
C	-0.35309602	-0.72301432	-0.20898212
C	-0.35309602	-0.72301432	2.02603988
C	1.59952098	-0.72301432	0.93171088
N	0.98830198	-0.57119132	-0.25385712
N	0.98566598	-0.89419632	2.10978688
N	-1.07930202	-0.89240432	0.90197488
C	-2.09796202	1.98627368	1.59017188
H	-2.85432502	2.36955068	2.28110188
S	-0.55438802	1.61219668	2.47005188
N	2.96356898	-0.66603032	0.96323688
N	-0.99276402	-0.70825932	-1.39988612
H	3.34648998	-0.93619232	1.86188388
C	-2.43291102	-0.78937332	-1.57344412
H	-2.67809102	-0.23301032	-2.48200212
H	-2.90779902	-0.27184532	-0.73618712
C	3.80119098	-1.02845932	-0.18296912
H	3.37302898	-0.53919332	-1.05995612
C	3.81177698	-2.54002032	-0.41115612
H	4.25402998	-3.05241532	0.45121688
H	2.79687798	-2.92323732	-0.55551712
H	4.40045798	-2.79009432	-1.29956312
C	-2.95825102	-2.21694732	-1.67991912
H	-2.73829102	-2.78605332	-0.77172912
H	-4.04351502	-2.20792532	-1.82375712
H	-2.50602902	-2.73645232	-2.53077712
C	5.20779798	-0.48803532	0.04317988
H	5.64484998	-0.91387532	0.95431988
H	5.85226398	-0.75681932	-0.79858812
H	5.20195698	0.60178668	0.13860288
C	-1.90415902	2.99911468	0.43199388
H	-1.60844902	3.95987968	0.86306688
H	-2.46406402	1.04137268	1.16321688
H	-0.40740902	-0.65859632	-2.22025912
Cl	-1.21646802	-1.36357732	3.47372088
N	-0.91444202	2.60220268	-0.55934512
H	-0.10336702	2.28513368	-0.02703312
H	-1.25736802	1.76986968	-1.03722212
C	-3.24132302	3.19762368	-0.23860312
O	-3.59115702	2.66171368	-1.27738712
O	-4.05304502	4.00355968	0.45740088
H	-4.91670802	4.04296968	0.01546288

Energy= -1768.9717124a.u NIMAG= 1 ; ν= 240 icm^{-1}



A **B**

Figure S1: MS of ATZ (A) and its corresponding fragmentation pattern (B).



A **B**

Figure S2: MS of CEE (A) and its corresponding fragmentation pattern (B).

Table S16. Kinetic data for the reaction of ATZ with CEE in aqueous solution at 25°C±0.1°C and pH= 9.06

	$[CEE]_F$	k_{obs} / s^{-1}
1	0.0036	$1.2*10^{-6}$
2	0.0041	$2.3*10^{-6}$
3	0.0050	$4.7*10^{-6}$
4	0.0060	$7.2*10^{-6}$
5	0.0070	$1.0*10^{-5}$
6	0.0081	$1.3*10^{-5}$
7	0.0090	$1.5*10^{-5}$

Table S17. Kinetic data for the reaction of ATZ with CEE in aqueous solution at 25°C±0.1°C and pH=9.36

	$[CEE]_F$	k_{obs} / s^{-1}
1	0.0035	$1.3*10^{-6}$
2	0.0040	$4.2*10^{-6}$
3	0.0050	$7.5*10^{-6}$
4	0.0061	$1.0*10^{-5}$
5	0.0071	$1.3*10^{-5}$
6	0.0080	$1.6*10^{-5}$
7	0.0091	$1.8*10^{-5}$

Table S18. Kinetic data for the reaction of ATZ with CEE in aqueous solution at 25°C±0.1°C and pH= 9.66

	$[CEE]_F$	k_{obs} / s^{-1}
1	0.0035	$3.6*10^{-7}$
2	0.0040	$5.4*10^{-6}$
3	0.0050	$8.2*10^{-6}$
4	0.0060	$1.3*10^{-5}$
5	0.0071	$1.6*10^{-5}$
6	0.0080	$2.1*10^{-5}$
7	0.0091	$2.6*10^{-5}$

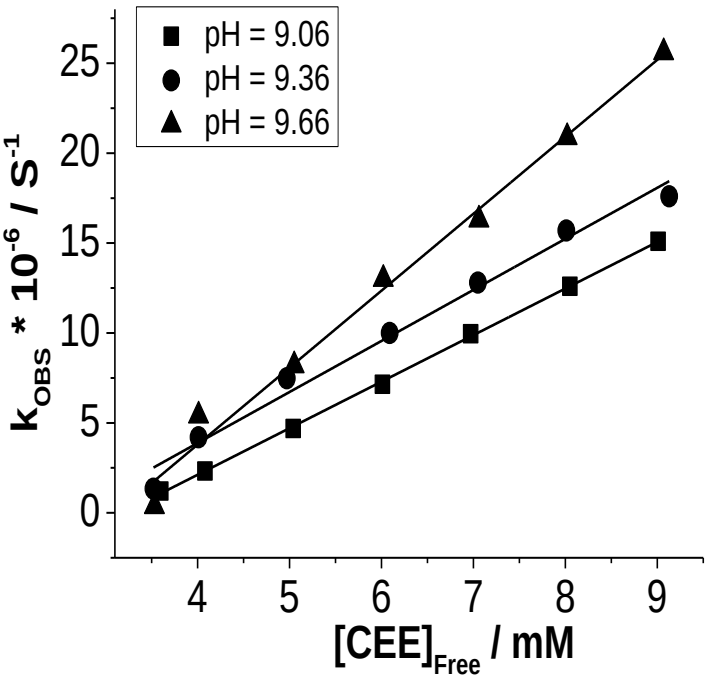


Figure S3: Plot of k_{obs} *vs.* free CEE concentration in water.

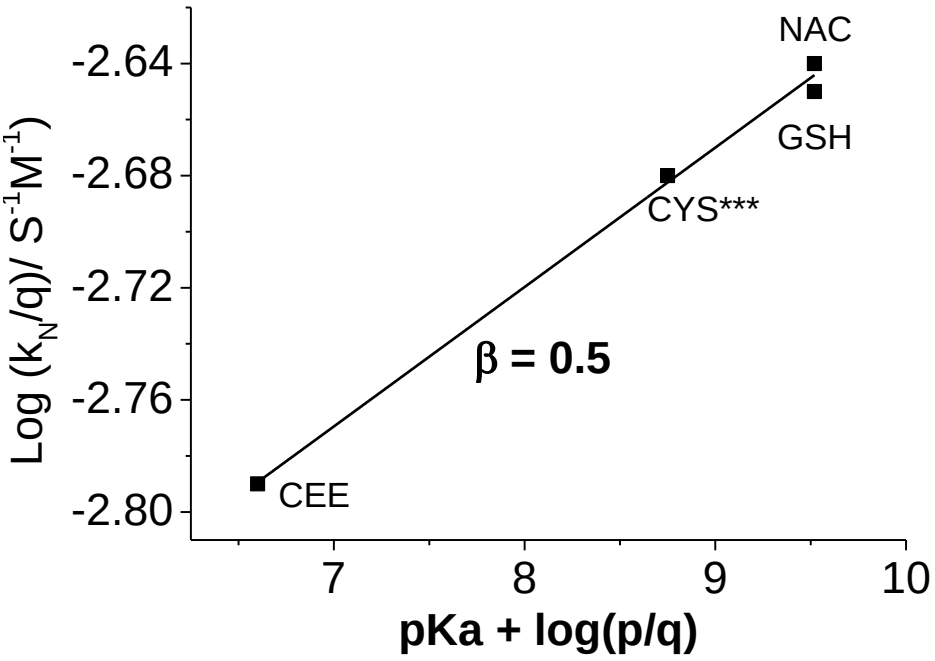


Figure S4: Brönsted type plots (CYS*** value adjusted according to its pKa).

Table S19: **ΔG#** values for the reactions between ATZ and biothiol series carried out in aqueous media.

Biothiols	pH	[a]ΔG# Kcal/mol
CYSTEINE ETHYL ESTER		
pKa - 0.3	6.30	16.3
pKa	6.60	15.9
pKa + 0.3	6.90	15.0
CYSTEINE		
pKa- 0.3	8.07	14.4
pKa	8.37	16.7
pKa + 0.3	8.67	16.3
GLUTHATIONE		
pKa - 0.3	8.45	14.4
pKa	8.75	14.5
pKa + 0.3	9.05	14.2
N-ACETYLCYSTEINE		
pKa - 0.3	9.22	15.9
pKa	9.52	15.1
pKa +0.3	9.82	13.5

[a]**ΔG#** values were determined considered the transition-state theory (1M and 298,15K).