

Supporting Information

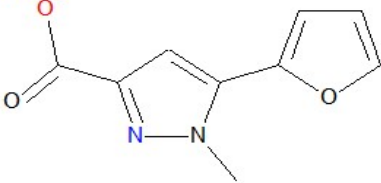
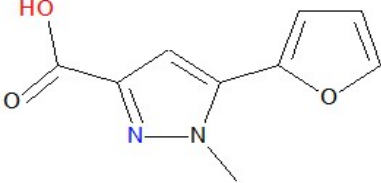
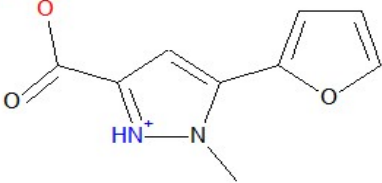
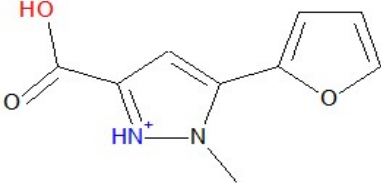
Thermodynamics-informed calculation and blind prediction of apparent pK_a values submitted to the euroSAMPL 1 challenge

Robert Fraczkiewicz

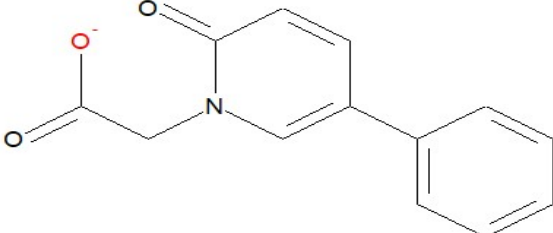
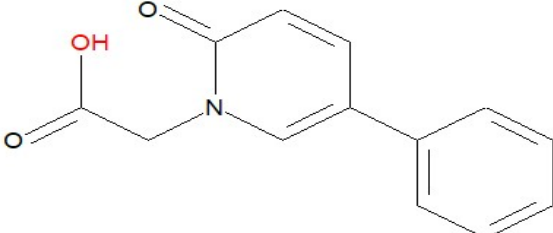
Simulations Plus, Inc. P.O. Box 12317, Research Triangle Park,
NC 27709, USA

Detailed microscopic ionization patterns for each of the 35 euroSAMPL compounds. The first column contains S+pKa predicted macroscopic pK_a values. The corresponding macrostate transitions are in the second columns. Third column contains structures of all microstates with relative contributions to their respective macrostates in %. The latter are determined from Boltzmann distribution of microstates relative to each macrostate.

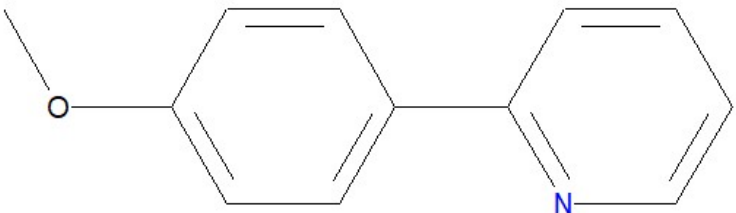
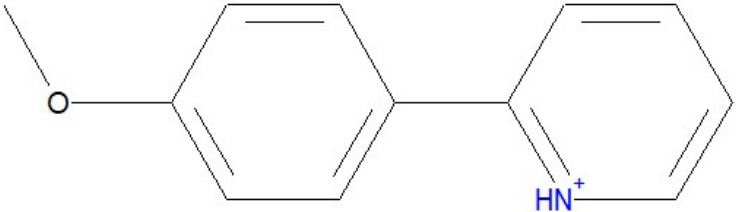
euroSAMPL-01

pK _a	Macrostates	Microstates
3.50	M^- $\rightleftharpoons$ HM $\rightleftharpoons$ H_2M^+	100.0% 
		99.2%  0.8% 
		100.0% 

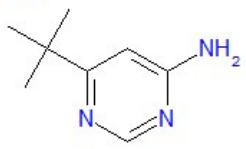
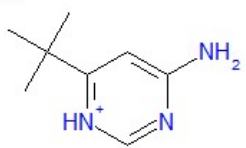
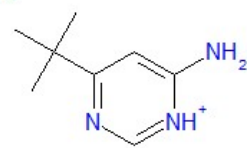
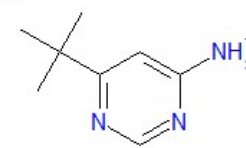
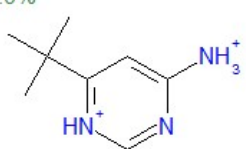
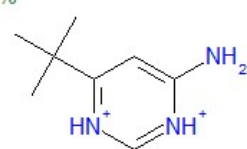
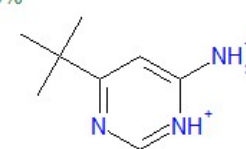
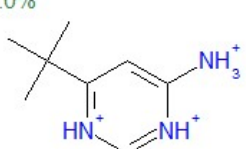
euroSAMPL-02

pK _a	Macrostates	Microstates
3.49	M^- $\rightleftharpoons$ HM	100.0% 
		100.0% 

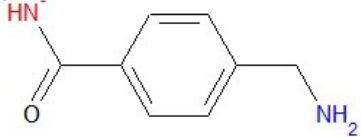
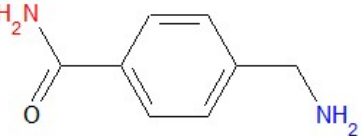
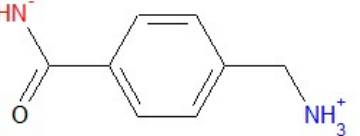
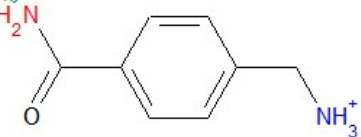
euroSAMPL-03

pK _a	Macrostates	Microstates
5.13	M	100.0% 
	HM ⁺	100.0% 

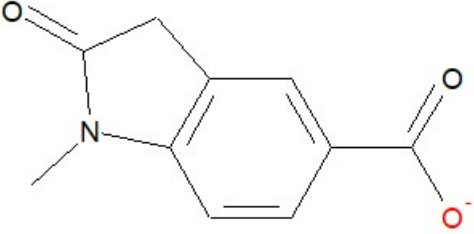
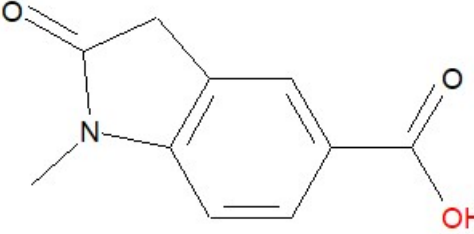
euroSAMPL-04

pK _a	Macrostates	Microstates
6.54	M	100.0% 
	HM ⁺	99.8%  0.2%  0.0% 
-1.09	H ₂ M ⁺²	100.0%  0.0%  0.0% 
-7.72	H ₃ M ⁺³	100.0% 

euroSAMPL-05

pK _a	Macrostates	Microstates	
12.16	M^-	100.0% 	
	HM	99.9% 	0.1% 
8.97	H_2M^+	100.0% 	

euroSAMPL-06

pK _a	Macrostates	Microstates	
3.91	M^-	100.0% 	
	HM	100.0% 	

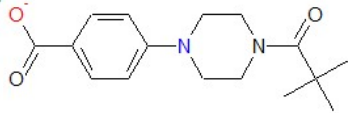
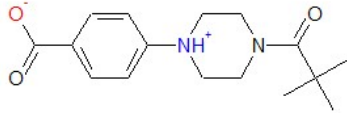
euroSAMPL-07

pK _a	Macrostates	Microstates	
4.68 -0.54	M	100.0% 	
	HM ⁺	99.5% 	0.5%
	H ₂ M ⁺²	100.0% 	

euroSAMPL-08

pK _a	Macrostates	Microstates	
11.65 8.91	M ⁻²	100.0%	
	HM ⁻	99.6%	0.4%
	H ₂ M	100.0%	

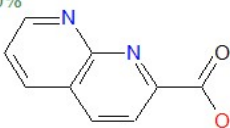
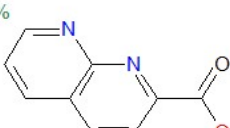
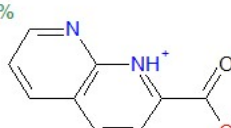
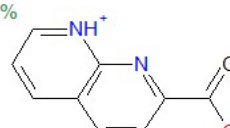
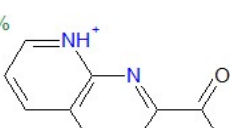
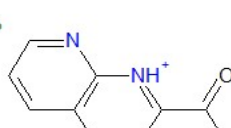
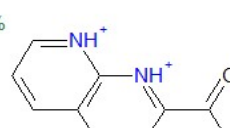
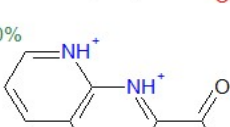
euroSAMPL-09

pK _a	Macrostates	Microstates	
4.41	M ⁻	100.0%	
	↕	95.0%	
2.62	HM	5.0%	
	↕	100.0%	
	H ₂ M ⁺		

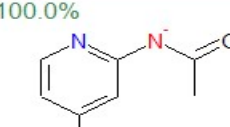
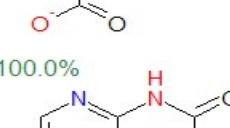
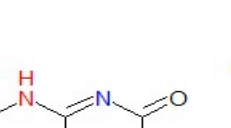
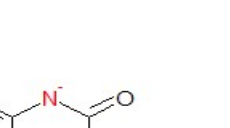
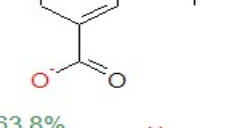
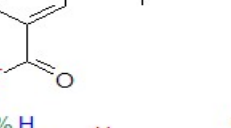
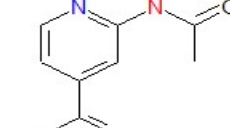
euroSAMPL-10

pK _a	Macrostates	Microstates	
4.84	M ⁻	100.0%	
	↕	99.9%	0.1%
	HM		
1.18	↕	100.0%	
	H ₂ M ⁺		

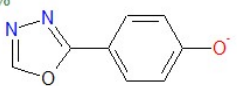
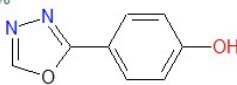
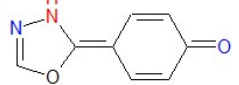
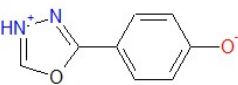
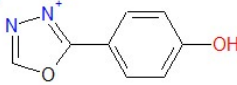
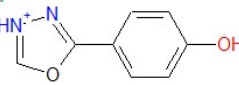
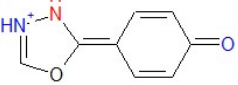
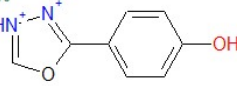
euroSAMPL-11

pK _a	Macrostates	Microstates		
3.45 1.36 -4.53	M ⁻	100.0% 		
	HM	68.4% 	19.8% 	11.8% 
	H ₂ M ⁺	92.0% 	8.0% 	0.0% 
	H ₃ M ⁺²	100.0% 		

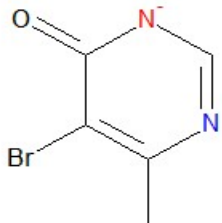
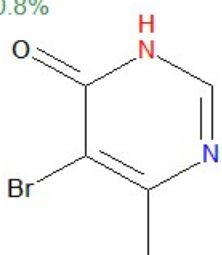
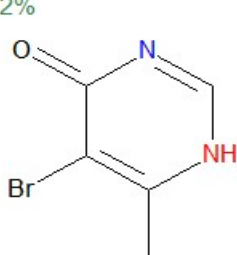
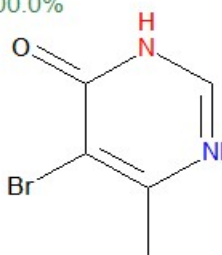
euroSAMPL-12

pK _a	Macrostates	Microstates		
11.96 3.59 2.03	M ⁻²	100.0% 		
	HM ⁻	100.0% 	0.0% 	0.0% 
	H ₂ M	63.8% 	36.2% 	0.0% 
	H ₃ M ⁺	100.0% 		

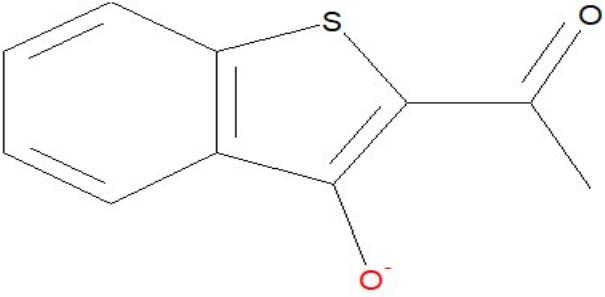
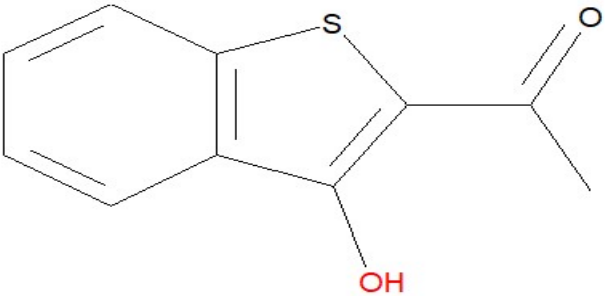
euroSAMPL-13

pK _a	Macrostates	Microstates		
8.25 -0.70 -3.97	M ⁻	100.0% 	0.0% 	0.0% 
	HM	100.0% 	0.0% 	0.0% 
	H ₂ M ⁺	85.9% 	14.1% 	0.0% 
	H ₃ M ⁺²	100.0% 		

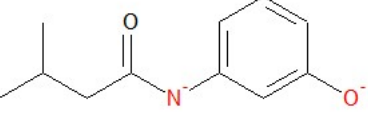
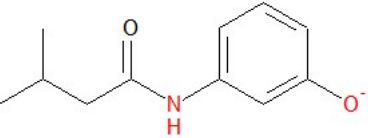
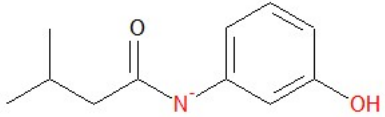
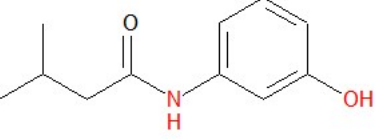
euroSAMPL-14

pK _a	Macrostates	Microstates	
7.96 1.02	M ⁻	100.0% 	
	HM	90.8% 	9.2% 
	H ₂ M ⁺	100.0% 	

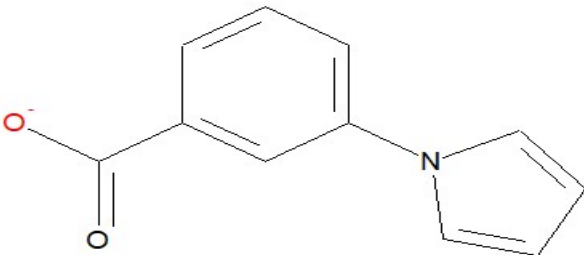
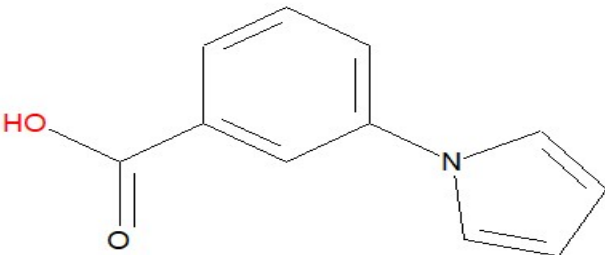
euroSAMPL-15

pK _a	Macrostates	Microstates
		100.0%
	M ⁻	
6.20	↕	100.0%
	HM	

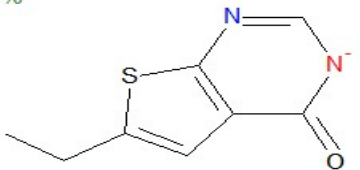
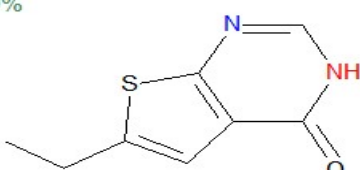
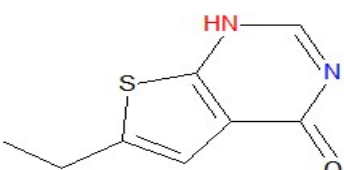
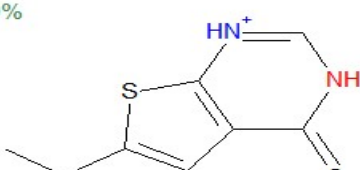
euroSAMPL-16

pK _a	Macrostates	Microstates
		100.0%
	M ⁻²	
12.18	↕	99.4%
	HM ⁻	
		0.6%
		
9.40	↕	100.0%
	H ₂ M	

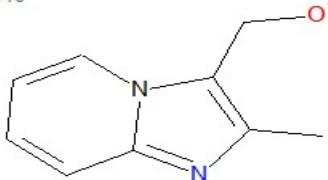
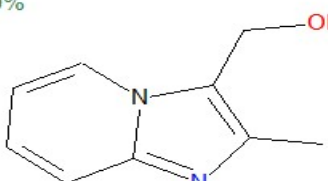
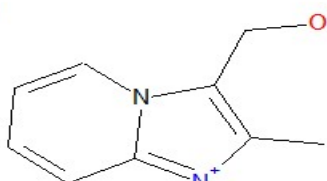
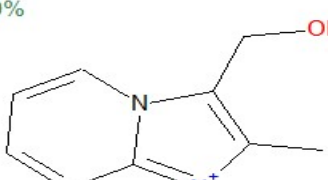
euroSAMPL-17

pK _a	Macrostates	Microstates
3.83	M ⁻	100.0% 
	HM	100.0% 

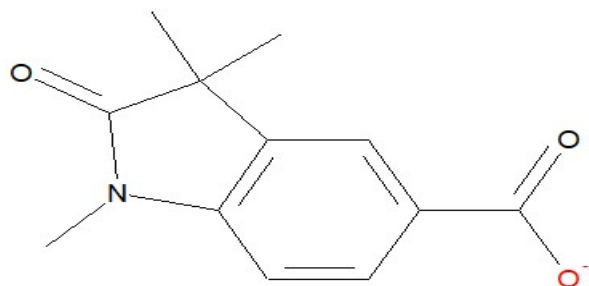
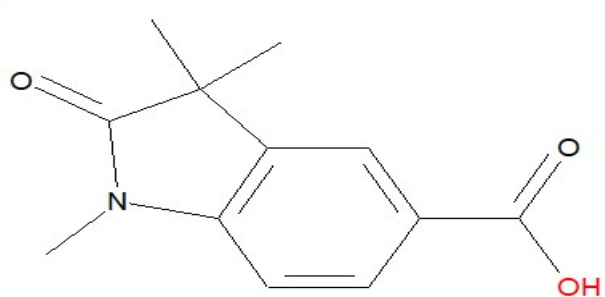
euroSAMPL-18

pK _a	Macrostates	Microstates
9.46	M ⁻	100.0% 
	HM	100.0% 
1.13	H ₂ M ⁺	0.0% 
		100.0% 

euroSAMPL-19

pK _a	Macrostates	Microstates		
12.21	M ⁻	100.0%		
	↕	100.0%		0.0% 
	HM			
7.57	↕	100.0%		
	H ₂ M ⁺			

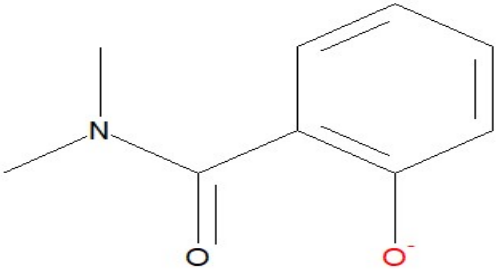
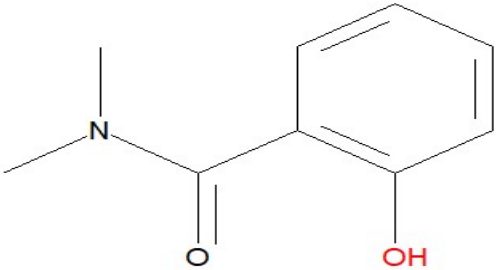
euroSAMPL-20

pK _a	Macrostates	Microstates
4.10	M ⁻	100.0% 
	↕	100.0% 
	HM	

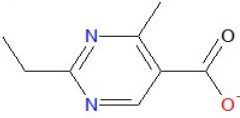
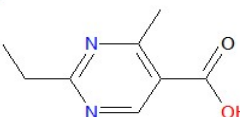
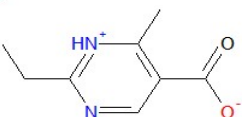
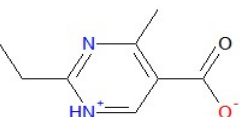
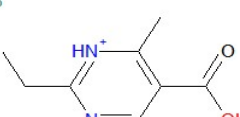
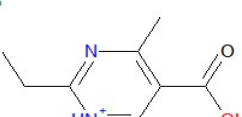
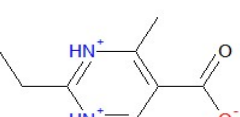
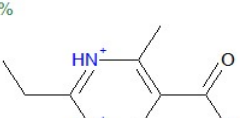
euroSAMPL-21

pK _a	Macrostates	Microstates		
3.02	M ⁻	100.0%		
	↕	50.1%	43.7%	6.2%
1.91	HM			
	↕	85.6%	13.3%	1.1%
0.40	H ₂ M ⁺			
	↕	100.0%		
	H ₃ M ⁺²			

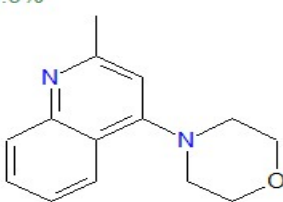
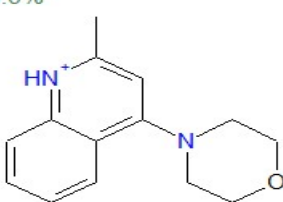
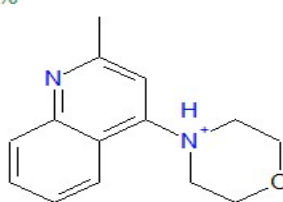
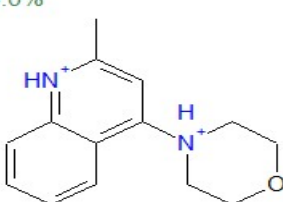
euroSAMPL-22

pK _a	Macrostates	Microstates	
9.37	M ⁻	100.0%	
	↕	100.0%	
	HM		

euroSAMPL-23

pK _a	Macrostates	Microstates		
		100.0%		
3.49	M ⁻			
	↕	74.8%	16.1%	9.1%
	HM			
1.06	↕	61.4%	38.6%	0.0%
	H ₂ M ⁺			
-5.14	↕	100.0%		
	H ₂ M ⁺²			

euroSAMPL-24

pK _a	Macrostates	Microstates	
		100.0%	
9.31	M		
	↕	100.0%	0.0%
0.98	HM ⁺		
	↕	100.0%	
	H ₂ M ⁺²		

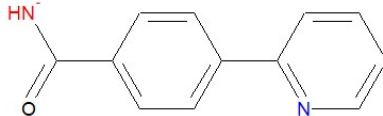
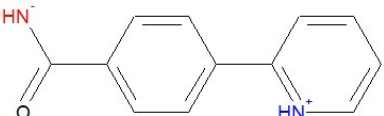
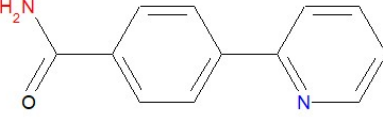
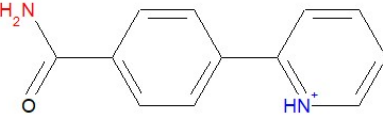
euroSAMPL-25

pK _a	Macrostates	Microstates	
11.85 4.90	M ⁻	100.0%	
	HM	100.0%	
	H ₂ M ⁺	100.0%	

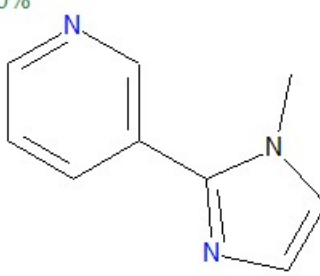
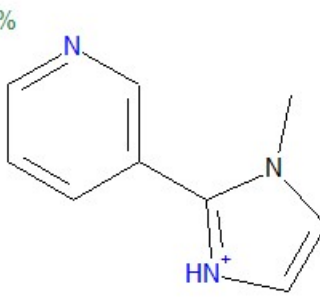
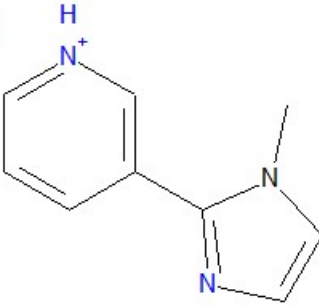
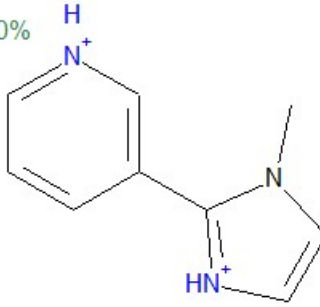
euroSAMPL-26

pK _a	Macrostates	Microstates	
9.51 1.84	M ⁻	100.0%	
	HM	97.4%	
	H ₂ M ⁺	100.0%	

euroSAMPL-27

pK _a	Macrostates	Microstates	
11.88 3.91	M ⁻	100.0% 	0.0% 
	HM	100.0% 	
	H ₂ M ⁺	100.0% 	

euroSAMPL-28

pK _a	Macrostates	Microstates	
6.10 2.16	M	100.0% 	
	HM ⁺	98.2% 	1.8% 
	H ₂ M ⁺²	100.0% 	

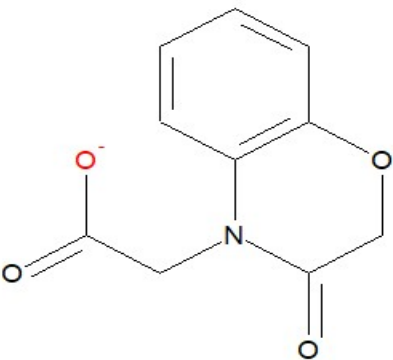
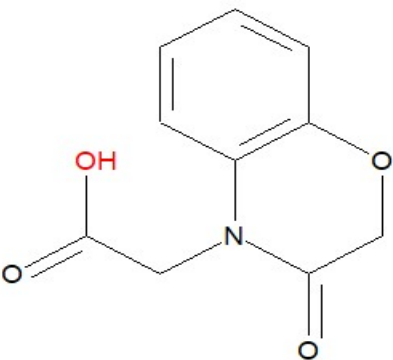
euroSAMPL-29

pK _a	Macrostates	Microstates		
3.63 -0.19 -2.12	M^-	100.0%		
	$\rightleftharpoons$			
	HM	99.8%	0.2%	0.0%
	$\rightleftharpoons$			
	H_2M^+	66.1%	33.9%	0.0%
	$\rightleftharpoons$			
	H_3M^{+2}	100.0%		

euroSAMPL-30

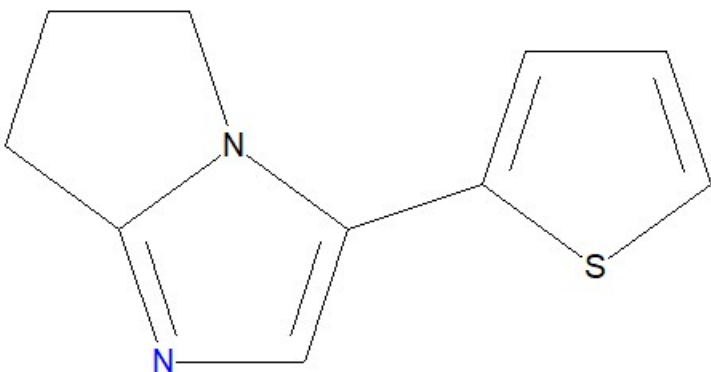
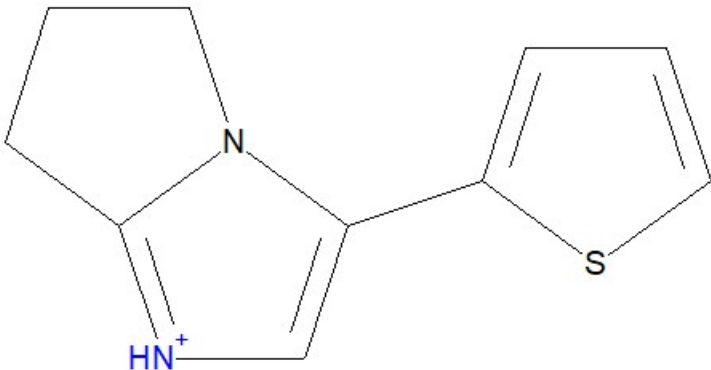
pK _a	Macrostates	Microstates		
12.77 11.68 9.06	M^{-3}	100.0%		
	$\rightleftharpoons$			
	HM^{-2}	79.2%	20.1%	0.7%
	$\rightleftharpoons$			
	H_2M^-	95.7%	4.2%	0.1%
	$\rightleftharpoons$			
	H_3M	100.0%		

euroSAMPL-31

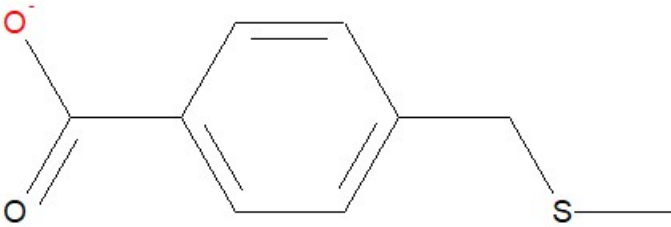
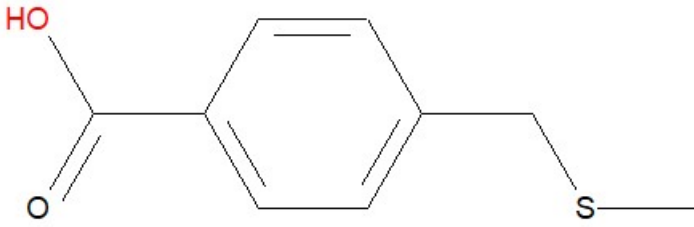
pK _a	Macrostates	Microstates
3.35	M ⁻	100.0% 
	HM	100.0% 

pK _s	Macrostates	Microstates
	M	100.0%
7.27	↕	
	HM ⁺	100.0% 0.0%
-3.77	↕	
	H ₂ M ⁺²	100.0%

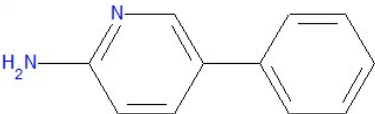
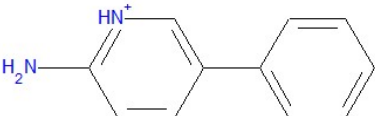
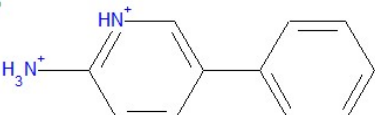
euroSAMPL-33

pK _a	Macrostates	Microstates
6.39	M	100.0% 
	HM ⁺	100.0% 

euroSAMPL-34

pK _a	Macrostates	Microstates
4.02	M ⁻	100.0% 
	HM	100.0% 

euroSAMPL-35

pK _a	Macrostates	Microstates
6.31 -2.02	M	100.0% 
	HM ⁺	99.9% 
	H ₂ M ⁺²	100.0% 
		0.1% 