Supplementary Information

Predicting the binding modes and sites of metabolism of xenobiotics

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Supplementary Table 1: Details of Statistical Test Formula performed for the validation of the empirical scoring function.

S. No.	Statistical Test Formula
1.	$$q^2 = 1 - \left(\frac{\sum_N \left(y_{pred} - y_{\exp} \right)^2}{\sum_N \left(y_{\exp} - \bar{y}_{\exp} \right)^2} \right)$$
2.	$$R = \frac{\sum_N \left(y_{\exp} - \bar{y}_{\exp} \right)\left(y_{pred} - \bar{y}_{pred} \right)}{\sqrt{\sum_N \left(y_{\exp} - \bar{y}_{\exp} \right)^2 \sum \left(y_{pred} - \bar{y}_{pred} \right)^2}}$$
3.	$$K = \frac{\sum_N y_{\exp} y_{pred}}{\sum_N y_{pred}^2}$$
4.	$$K' = \frac{\sum_N y_{\exp} y_{pred}}{\sum_N y_{\exp}^2}$$
5.	$$y_{\exp}^{r_0} = K\, y_{pred}$$
6.	$$y_{pred}^{r_0} = K'\, y_{\exp}$$
7.	$$R_0^2 = 1 - \frac{\sum_N \left(y_{pred} - y_{\exp}^{r_0} \right)^2}{\sum_N \left(y_{pred} - \bar{y}_{pred} \right)^2}$$
8.	$$R_0'^2 = 1 - \frac{\sum_N \left(y_{\exp} - y_{pred}^{r_0} \right)^2}{\sum_N \left(y_{\exp} - \bar{y}_{\exp} \right)^2}$$
9.	$$RMS\ error = \sqrt{\frac{\sum_N \left(y_{pred} - y_{\exp} \right)^2}{N}}$$
10.	$$S_{PRESS} = \sqrt{\frac{\sum_N \left(y_{pred} - y_{\exp} \right)^2}{N - c - 1}}$$

Supplementary Table 2: Experimental and predicted binding free energies (kcal/mol) of 58 training sets.

Sl. No.	Expt. B.E.#	Pred B. E.#	PDBID	Name of proteins
1	-4.78	-6.7	1AC8	Cytochrome c peroxidase
2	-3.96	-4.8	1AEE	Cytochrome c peroxidase
3	-4.92	-4.4	1AEM	Cytochrome c peroxidase
4	-7.07	-6.22	1AEN	Cytochrome c peroxidase
5	-6.23	-5.22	1CMP	Cytochrome c peroxidase
6	-5.59	-6.23	1IWJ	Cytochrome p450-cam
7	-8.97	-9.49	1JPZ	Bifunctional p-450:nadph-p450 reductase
8	-10.5	-10.19	1LWL	Cytochrome p450-cam
9	-7.32	-6.49	1M8D	Inducible nitric oxide synthase
10	-8.48	-6.56	1M9J	Inducible nitric oxide synthase
11	-6.41	-8.19	1N6B	Cytochrome p450 2c5
12	-8.89	-7.88	1P6H	Nitric oxide synthase, brain
13	-9.3	-7.74	1P6I	Nitric oxide synthase, brain
14	-5.69	-6.16	1P6K	Nitric oxide synthase, brain
15	-5.41	-5.73	1P6L	Nitric oxide synthase, brain
16	-5.59	-6.94	1P6M	Nitric oxide synthase, endothelial
17	-10.5	-9.42	1RE9	Cytochrome p450-cam
18	-9.88	-9.39	1Y4Z	Respiratory nitrate reductase
19	-6.41	-8.31	1ZZQ	Nitric oxide synthase, brain
20	-8.12	-8.66	1ZZT	Nitric oxide synthase, endothelial
21	-5.76	-6.13	2ANZ	Cytochrome c peroxidase
22	-6.41	-5.73	2AS1	Cytochrome c peroxidase
23	-3.25	-4.15	2AS3	Cytochrome c peroxidase
24	-2.88	-4.83	2AS4	Cytochrome c peroxidase
25	-7.23	-6.91	2CI0	Cytochrome p450 51
26	-5.95	-5.77	2D0E	Cytochrome p450 158a2
27	-5.86	-6.77	2EUN	Cytochrome c peroxidase
28	-5.86	-4.9	2EUQ	Cytochrome c peroxidase
29	-8.31	-7.32	2FDV	Cytochrome p450 2a6
30	-7.86	-9.31	2GQX	Cytochrome p450-cam
31	-5.8	-5.87	2H7R	Cytochrome p450-cam
32	-6.27	-6.53	2HI4	Cytochrome p450 1a2
33	-5.64	-5.22	2HX2	Nitric-oxide synthase
34	-8.87	-8.64	2HX4	Nitric-oxide synthase
35	-7.23	-8.62	2IJ7	Cytochrome p450 121
36	-9.61	-8.77	2NNJ	Cytochrome p450 2c8
37	-11.12	-10.7	2Q9F	Cytochrome p450 46a1
38	-8.13	-7.84	2WH8	Putative cytochrome p450 130
39	-7.25	-6.87	2WHF	Putative cytochrome p450 130

40	-5.81	-4.81	2Y5A	Cytochrome c peroxidase\, mitochondrial
41	-8.74	-7.46	3B3N	Nitric-oxide synthase
42	-9.64	-9.63	3B3O	Nitric-oxide synthase
43	-8.24	-6.85	3JT3	Nitric oxide synthase, brain
44	-6.91	-6.67	3JT9	Nitric oxide synthase, brain
45	-6.13	-6.62	3JTA	Nitric oxide synthase, brain
46	-10.53	-9.74	3JWV	Nitric oxide synthase, brain
47	-6.25	-7.92	3NLD	Nitric oxide synthase, endothelial
48	-9.46	-9.74	3NLK	Nitric oxide synthase, brain
49	-9.08	-8.98	3NNZ	Nitric oxide synthase, brain
50	-7.58	-6.96	8CPP	Cytochrome p450cam
51	-9.54	-8.27	1P6J	Nitric oxide synthase, brain
52	-7	-5.99	2D09	Cytochrome p450 158a2
53	-5.72	-6.62	1ZZU	Nitric oxide synthase, brain
54	-5.88	-7.53	3T3Q	Cytochrome P450 2A6
55	-11.32	-9.71	3MDT	Cytochrome P450 46A1
56	-8.74	-9.33	3DQR	Nitric oxide synthase, brain
57	-7	-7.6	3EKD	Cytochrome p450(bm-3)
58	-8.08	-8.95	3JX0	Nitric oxide synthase, brain

kcal/mol

Supplementary Table 3: *Experimental and predicted binding free energies (kcal/mol) of 63 test sets.*

Sl. No.	Expt. B.E.#	Pred B. E.#	PDBID	Name of proteins
1	-3.85	-5.7	1AC4	Cytochrome c peroxidase
2	-4.81	-4.97	1AEB	Cytochrome c peroxidase
3	-5.86	-5.81	1AED	Cytochrome c peroxidase
4	-6	-5.03	1AEF	Cytochrome c peroxidase
5	-5.99	-6.05	1AEG	Cytochrome c peroxidase
6	-4.96	-5.99	1AEH	Cytochrome c peroxidase
7	-5.21	-5.9	1AEJ	Cytochrome c peroxidase
8	-4.92	-4.92	1AEK	Cytochrome c peroxidase
9	-5.02	-4.82	1AEO	Cytochrome c peroxidase
10	-4.73	-5.17	1AEQ	Cytochrome c peroxidase
11	-4.33	-4.99	1AES	Cytochrome c peroxidase
12	-5.82	-5.48	1AET	Cytochrome c peroxidase
13	-5.94	-5.03	1AEU	Cytochrome c peroxidase
14	-6.06	-5.33	1AEV	Cytochrome c peroxidase
15	-6.35	-5.74	1IWI	Cytochrome p450-cam
16	-5.25	-5.2	1KXM	Cytochrome c peroxidase
17	-4.91	-5.76	1M9K	Nitric oxide synthase, endothelial
18	-5.86	-6.67	1NR6	Cytochrome p450 2c5
19	-5.4	-5.29	1P6N	Nitric oxide synthase, endothelial
20	-6.85	-6.09	1Q2O	Nitric oxide synthase, endothelial
21	-5.45	-7.23	1X8V	Cytochrome p450 51
22	-9.88	-8.94	1Y5N	Respiratory nitrate reductase
23	-7.8	-7.18	1Z11	Cytochrome p450 2a6
24	-5.97	-7.29	1ZZR	Nitric oxide synthase, brain
25	-7.22	-5.44	1ZZS	Nitric oxide synthase, endothelial
26	-14.35	-12.84	2A06	Bovine cytochrome bc1 complex
27	-7.01	-6.95	2CIB	Cytochrome p450 51
28	-6	-5.61	2EUP	Cytochrome c peroxidase
29	-6.61	-6.48	2FDU	Cytochrome p450 2a6
30	-6.79	-6.85	2NZ5	Cytochrome p450 cyp158a1
31	-12.48	-12.53	2QJY	Cytochrome bc1
32	-6.18	-5.53	2VKU	Cytochrome p450 51
33	-6.07	-6.65	2W09	Cytochrome p450 51
34	-5.77	-5.21	2W0B	Cytochrome p450 51
35	-5.89	-6.62	3B3M	Nitric-oxide synthase
36	-9	-8.1	3B3P	Nitric-oxide synthase
37	-7.46	-7.15	3B6H	Prostacyclin synthase(cyp 450)
38	-7.8	-7.54	3B99	Prostaglandin i2 synthase(cytochrome p450 8a1)
39	-8.86	-9.42	3BEN	Cytochrome p450 102

40	-6.38	-6.1	3EBS	Cytochrome p450 2a6
41	-6.72	-7.2	3IW2	Cytochrome p450 cyp125
42	-6.11	-6.13	3JT4	Nitric-oxide synthase
43	-6.91	-6.16	3JT5	Nitric-oxide synthase
44	-6.13	-6.21	3JT6	Nitric-oxide synthase
45	-5.77	-6.15	3JT7	Nitric-oxide synthase
46	-9.93	-9.23	3JWS	Nitric oxide synthase, brain
47	-9.23	-9.13	3JWU	Nitric oxide synthase, brain
48	-6.4	-7.37	3JWX	Nitric oxide synthase, endothelial
49	-5.79	-6.2	3JWZ	Nitric oxide synthase, endothelial
50	-8.91	-8.79	3JX1	Nitric oxide synthase, brain
51	-8.08	-7.72	3JX2	Nitric oxide synthase, brain
52	-9.2	-9.23	3JX3	Nitric oxide synthase, brain
53	-7.72	-9.12	3JX6	Nitric oxide synthase, brain
54	-7.53	-8.38	3N2R	Nitric oxide synthase
55	-6.43	-7.79	3NLE	Nitric oxide synthase, endothelial
56	-6.44	-6.56	3NLF	Nitric oxide synthase, endothelial
57	-6.06	-7.08	3NLG	Nitric oxide synthase, endothelial
58	-9.95	-8.57	3NNY	Nitric oxide synthase, brain
59	-7.41	-5.57	3QOA	Cytochrome P450 2B6
60	-5.45	-5.48	3T3R	Cytochrome P450 2A6
61	-5.95	-5.89	6CPP	Cytochrome p450cam
62	-5.25	-4.83	7CPP	Cytochrome p450cam
63	-8.77	-14.77	3UA1	Cytochrome P450 3A4

kcal/mol

Supplementary Table 4*: Names of the 60 CYP1A2 substrates along with their pose rank based on only docking and combined approach for predicting experimentally verified SOM, predicted binding free energy of the corresponding pose and energy gap between deep lying MO to HOMO (if applicable).*

	Pose rank based on			
Molecule#	**Only docking**	**Unique docked pose+knowledge based+QM approach**	**Predicted binding energy (kcal/mol) of the corresponding pose**	**Deep lying MO to HOMO energy gap (kcal/mol)***
3-Cyano-7-ethoxycoumarin	1	1	-9.2	
3-Methylether-estradiol	2	1	-8.7	
4-Chloromethyl-7-ethoxycoumarin	1	1	-8.3	
7-Methoxyresorufin	1	1	-8.9	
7-Ethoxycoumarin	1	1	-7.0	
Acenocoumarol	2	2	-7.1	
Aflatoxin	8	3	-9.2	-9.0
Amiodarone	3	2	-13.1	
Antipyrine	0	0	---	
Azelastine	2	2	-11.1	
BFC	2	2	-8.3	
BMAMC	1	1	-9.0	
Carvedilol	4	2	-9.6	
Chlorzoxazone	1	1	-6.7	
Cilostazol	7	3	-10.5	
Clomipramine	1	1	-11.3	-8.3
Cyclobenzaprine	1	1	-12.5	
Dacarbazine	1	1	-8.8	
Di-MMAMC	1	1	-10.6	
DMXAA	1	1	-6.5	
Doxepin	1	1	-10.4	
EFC	1	1	-8.1	
EMAMC	3	2	-8.2	
Fluoxetine	0	0	---	
Flutamide	3	1	-7.1	-12.1 (-0.8)
Furametpyr	3	3	-10.3	
Galangin	4	3	-7.4	
GTS-21	2	2	-10.5	

Kaempferide	2	2	-10.5	
MAMC	1	1	-7.4	
MBDB	1	1	-8.8	
MDE	1	1	-8.0	-10.06 (-2.9)
MDMA	1	1	-8.4	
Melatonin	6	2	-7.4	
Mephenytoin	3	2	-6.5	
Methoxychlor	1	1	-11.1	
MMAMC	2	2	-8.9	
Nordiazepam	0	0	---	
Nortriptyline	2	2	-8.6	
o-Phenylphenol	4	3	-5.3	
Pimozide	2	2	-12.0	-3.5
Pimobendan	7	3	-9.0	
Perphenazine	3	3	-11.0	
p-Isopropyloxyacetanilide	4	2	-6.7	
PMAMC	1	1	-8.8	
p-Methoxyacetanilide	1	1	-6.9	
Propofol	0	0	---	
Progesterone	5	2	-8.1	
Pranidipine	1	1	-11.6	
Proguanil	1	1	-9.6	-9.5 (-4.5)
Toremifene	0	0	---	
Propafenone	3	3	-8.8	
Ranitidine	4	3	-11.2	
Reduced diclofenac	4	2	-8.3	
Ropinirole	1	1	-7.9	
Selegiline	1	1	-9.3	
Ropivacaine	1	1	-7.6	
Thiabendazole	6	3	-6.8	
R-Warfarin	1	1	-7.4	
Zolpidem	1	1	-10.4	

2D representations of these molecules along with their experimentally verified SOM are given in supplementary (Supplementary Fig. 2); *BP86 values are in parentheses.

Supplementary Table 5*: Names of 70 CYP2C9 substrates along with their pose rank based on only docking and combined approach for predicting experimentally verified SOMs, predicted binding free energy of the corresponding pose and energy gap between deep lying MO to HOMO (if applicable).*

	Pose rank based on			
Molecule#	**Only docking**	**Unique docked pose+knowledge based+QM approach**	**Predicted binding energy (kcal/mol)of the corresponding pose**	**Deep lying MO to HOMO energy gap (kcal/mol)***
Flurbiprofen	7	3	-5.2	
Naproxen	1	1	-6.5	
Tienilic_acid	3	1	-7.5	
GV-150526	3	1	-9.1	
Fluvastatin	3	2	-8.8	
Indomethacin	1	1	-8.7	
Mefenamic acid	2	2	-6.1	
Zaltoprofen	4	3	-5.7	
Etodolac	0	0	---	
Aceclofenac	0	0	---	
Ibuprofen	3	1	-5.6	
Diclofenac	4	2	-7.2	
Valproic acid	2	1	-5.3	
Arachidonic acid	3	2	-9.3	
Seratrodast	3	2	-7.6	
Suprofen	1	1	-6.0	
TR-14035	1	1	-10.2	
Linoleic acid	2	1	-7.9	
Montelukast	0	0	---	
S_MTPPA	3	2	-6.0	
Rosuvastatin	3	1	-10.8	
Zolpidem	5	3	-8.6	
Sulprofos	4	3	-8.6	
Tolbutamide	0	0	---	
Desogestrel	2	2	-9.2	
Dapsone	1	1	-6.9	
Dibenzo[a,h]anthracene	1	1	-7.9	
Losartan	3	2	-11.5	
Piroxicam	3	2	-7.4	
Phorate	0	0	---	

Chlorpropamide	3	2	-7.2	
Amitriptyline	3	2	-9.1	
Celecoxib	1	1	-9.2	
Galangin	4	1	-6.8	
Mestranol	3	3	-8.9	
Methiocarb	6	3	-7.4	
17 Ethinyl Estradiol	1	1	-8.6	
Disulfoton	3	1	-8.3	
Sildenafil	2	1	-12.4	
Tolterodine	3	3	-7.6	
Meloxicam	3	3	-8.3	
Acenocoumarol	5	2	-6.6	
Methoxychlor	1	1	-10.3	
Clozapine	4	3	-10.2	-11.8 (-3.7)
Terbinafine	0	0	---	
Tenoxicam	3	2	-7.3	
Methyleugenol	0	0	---	
DMZ	1	1	-7.5	-10.2 (-5.6)
N-dehydroxyzileuton	2	2	-6.4	
Kaempferide	1	1	-9.5	
Limonene	1	1	-7.0	
Lansoprazole	6	2	-8.3	
Safrole	2	1	-7.1	
Warfarin	2	2	-6.8	
Lornoxicam	6	3	-8.1	
Fluoxetine	2	1	-9.1	
Phenytoin	0	0	---	
Zafirlukast	0	0	---	
Phenprocoumon	7	3	-6.1	
Ketamine	1	1	-7.9	
58C80	3	1	-7.0	
9 Tetrahydrocannabinol	6	3	-7.8	-6.1
Voriconazole	0	0	---	
Torsemide	6	3	-7.6	
Hydromorphone	3	3	-8.2	
Carvedilol	2	2	-9.6	-12.2 (-9.0)
Hexobarbital	1	1	-6.4	
Tamoxifen	1	1	-12.2	
Zopiclone	4	3	-11.1	
Phenobarbital	3	1	-5.7	

2D representations of these molecules along with their experimentally verified SOM are given in supplementary (Supplementary Fig. 3); *BP86 values are in parentheses.

Supplementary Table 6*: Names of 36 CYP2C19 substrates along with their pose rank based on only docking and combined approach for predicting experimentally verified SOMs, predicted binding free energy of the corresponding pose and energy gap between deep lying MO to HOMO (if applicable).*

	Pose rank based on			
Molecule#	**Only docking**	**Unique docked pose+knowledge based+QM approach**	**Predicted binding energy (kcal/mol) of the corresponding pose**	**Deep lying MO to HOMO energy gap (kcal/mol)***
Mephenytoin	1	1	-6.5	
Phenobarbital	3	2	-5.2	
Mephobarbital	3	3	-6.4	
Hexobarbital	5	2	-6.2	
Omeprazole	1	1	-10.5	
Lansoprazole	1	1	-9.5	
Warfarin	7	3	-6.5	
Moclobemide	1	1	-9.2	
Proguanil	1	1	-9.2	-9.5 (-4.5)
Propranolol	3	3	-6.8	-6.2
Diazepam	5	3	-8.0	
Benzbromarone	1	1	-9.2	
(2-ethylbenzofuran-3-yl)(4-hydroxy-3,5-dimethylphenyl)methanone	1	1	-8.6	
4-[(2-methyl-1-benzofuran-3-yl)carbonyl]phenol	5	2	-7.2	
Sertraline	8	2	-9.0	
N-3-benzyl-phenobarbital	3	2	-6.9	
Citalopram	3	3	-12.3	
Clomipramine	1	1	-11.1	-8.9
Pantoprazole	2	2	-10.4	-8.8
Clopidogrel	1	1	-8.7	
Cyclophosphamide	4	3	-8.3	
Amitriptyline	1	1	-9.3	
Imipramine	2	2	-9.5	-11.16 (-3.9)
Indomethacin	0	0	---	
Primidone	1	1	-6.4	-3.0
Progesterone	0	0	---	
Venlafaxine	2	1	-10.9	

Methadone	2	2	-9.4	
Clobazam	2	2	-7.8	
Arformoterol	0	0	---	
Rosuvastatin	1	1	-10.4	
Tamoxifen	1	1	-12.6	
Lumiracoxib	2	2	-7.4	
Carisoprodol	1	1	-8.9	
Escitalopram	4	3	-12.3	
Eletriptan	3	2	-9.3	

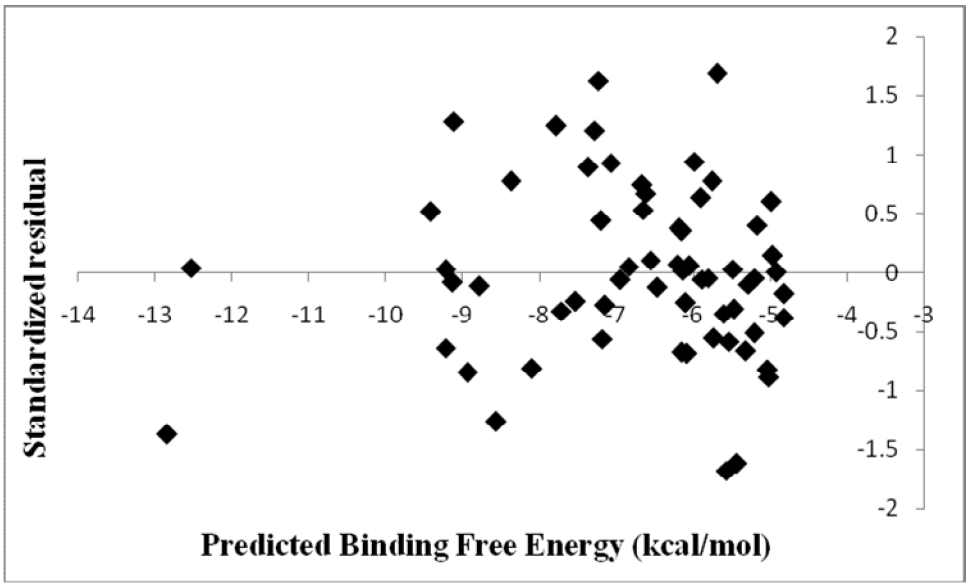
2D representations of these molecules along with their experimentally verified SOM are given in supplementary (Supplementary Fig. 4); *BP86 values are in parentheses.

Supplementary Table 7: Names of 47 CYP3A4 substrates along with their pose rank based on only docking and combined approach for predicting experimentally verified SOMs, predicted binding free energy of the corresponding pose and energy gap between deep lying MO to HOMO (if applicable).

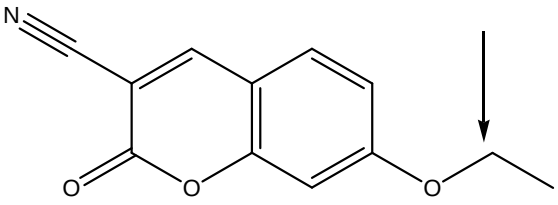
	Pose rank based on			
Molecule#	**Only docking**	**Unique docked pose+knowledge based+QM approach**	**Predicted binding energy (kcal/mol) of the corresponding pose**	**Deep lying MO to HOMO energy gap (kcal/mol)***
Adinazolam	2	2	-11.1	
Alfentanil	8	3	-8.7	
Amiodarone	1	1	-10.7	
Azelastine	2	2	-10.0	
Buprenorphine	2	2	-11.0	-2.0
Citalopram	5	2	-10.8	
Clarithromycin	1	1	-16.0	
Clozapine	4	2	-8.5	
Codeine	2	2	-9.6	-5.4
Dextromethorphan	3	3	-7.9	
Diazepam	1	1	-7.6	
Diltiazem	1	1	-11.0	
Erythromycin	3	3	-14.4	
Fentanyl	6	4	-7.5	
Halofantrine	1	1	-12.4	
Haloperidol	4	3	-8.7	
Indinavir	0	0	---	
LAAM	1	1	-10.0	
Lilopristone	0	0	---	
Onapristone	0	0	---	
Pimozide	5	3	-8.8	-4.2
Propafenone	7	3	-6.9	
Tamoxifen	0	0	---	
Terbinafine	1	1	-10.1	-3.0
Terfenadine	2	2	-9.2	
Verapamil	2	2	-14.8	-1.6
Zaleplon	6	3	-8.7	
β-Arteether	2	2	-7.9	
Pranidipine	1	1	-9.0	
Teniposide	3	2	-12.7	
Cortisol	1	1	-7.4	
Dexamethasone	1	1	-8.0	

Docetaxel	0	0	---	
Lovastatin	3	2	-8.2	
Midazolam	1	1	-8.0	
Quinidine	0	0	---	
Carbamazepine	7	3	-5.1	
Ebastine	8	3	-8.7	
Colchicine	2	2	-9.9	
Etoposide	1	1	-13.0	
Iloperidone	5	3	-10.0	
Loratadine	0	0	---	
Senecionine	2	2	-8.0	
Salmeterol	0	0	---	
Saquinavir	2	2	-11.4	
Seratrodast	2	2	-7.3	
Testosterone	2	2	-7.5	

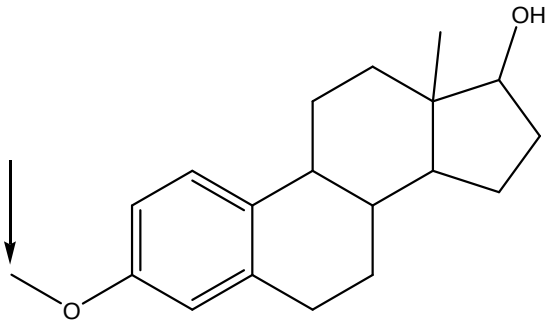
2D representations of these molecules along with their experimentally verified SOM are given in supplementary (Supplementary Fig. 5); *BP86 values are in parentheses.



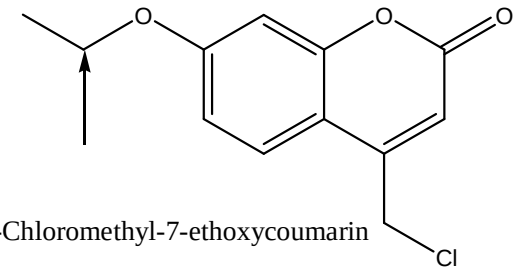
Supplementary Figure 1: Standardized residual errors shown against the predicted binding energies.



3-Cyano-7-ethoxycoumarin



3-Methylether-estradiol



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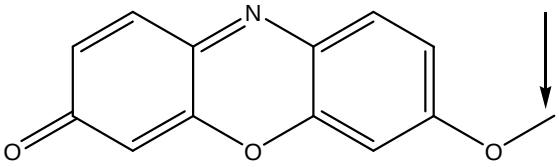
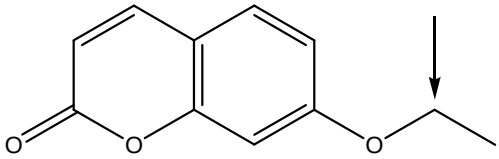
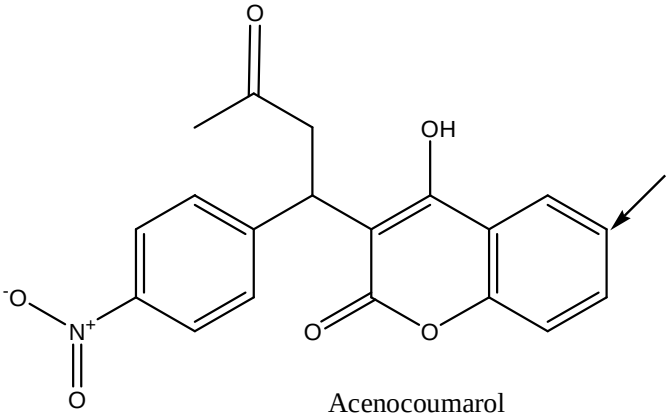


7-Methoxy-resorufin



7-Ethoxy-coumarin



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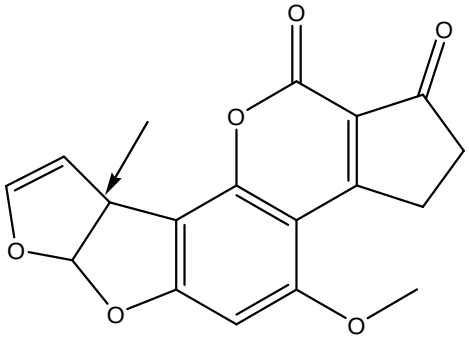

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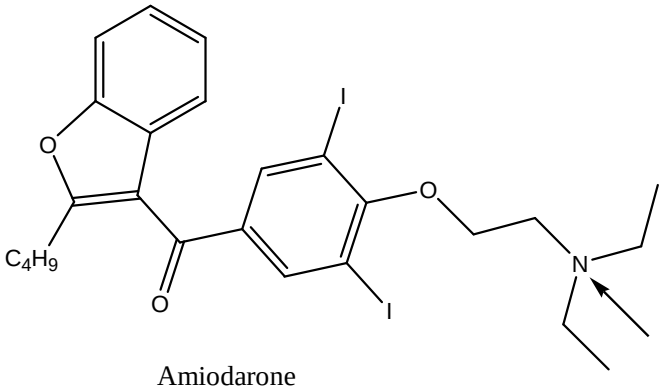

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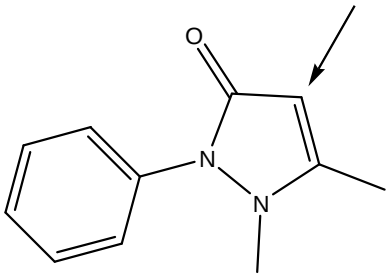
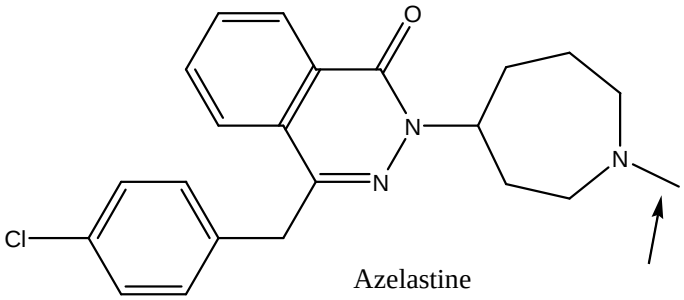


Antipyrine



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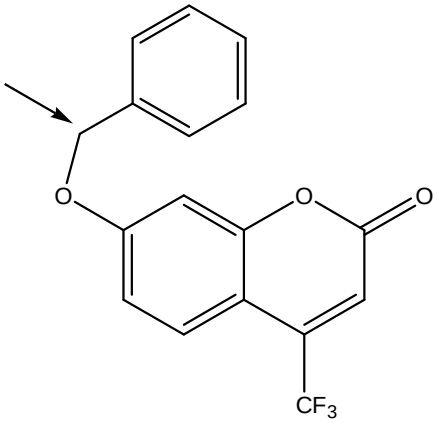

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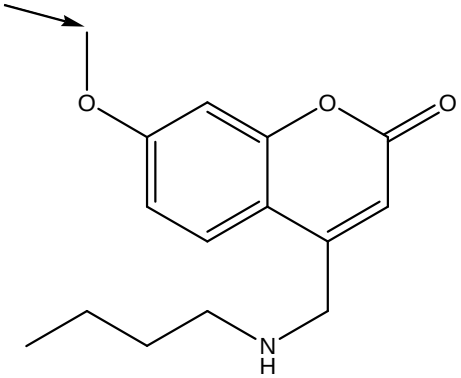

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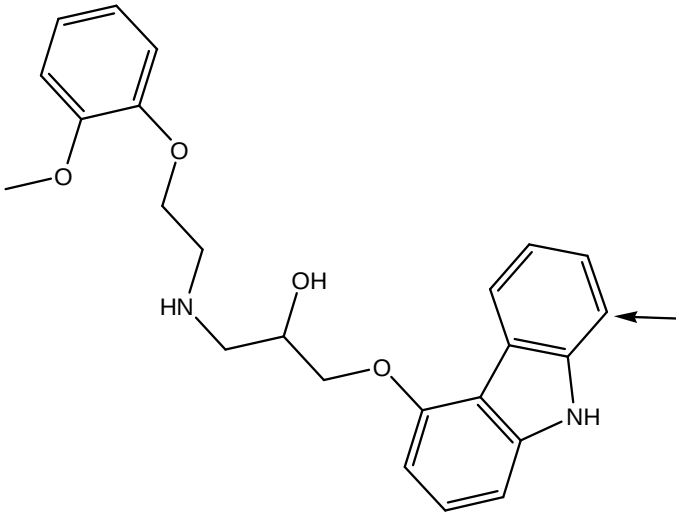

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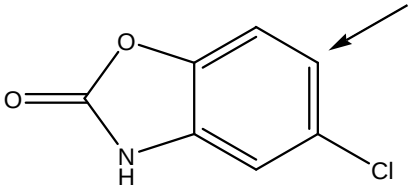

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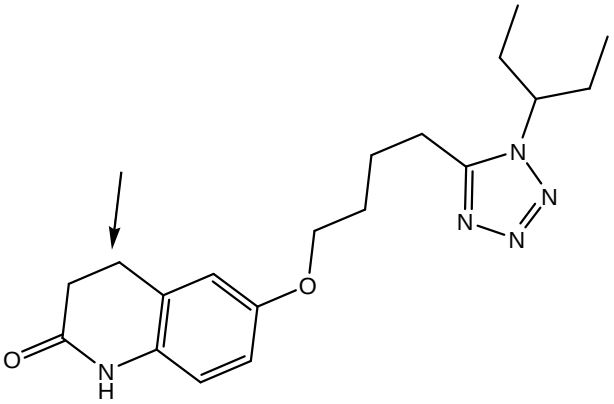
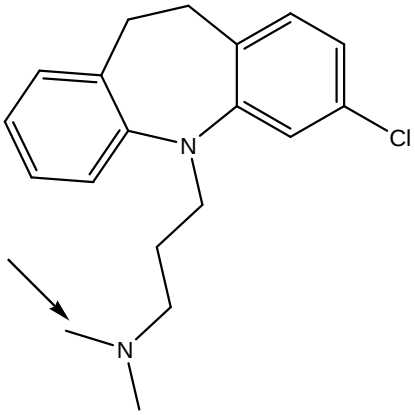
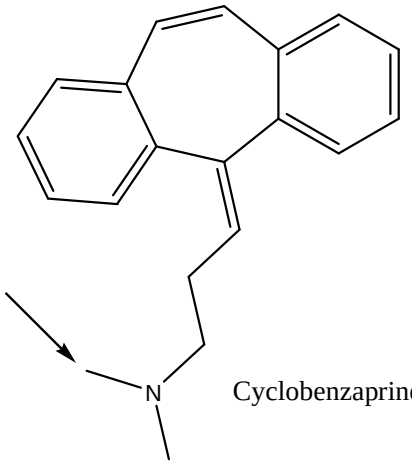


Cilostazol



Clomipramine



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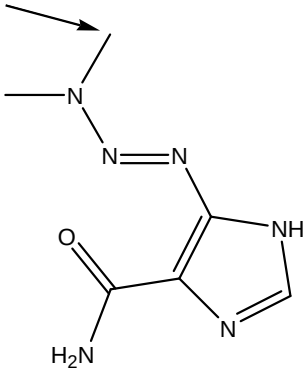

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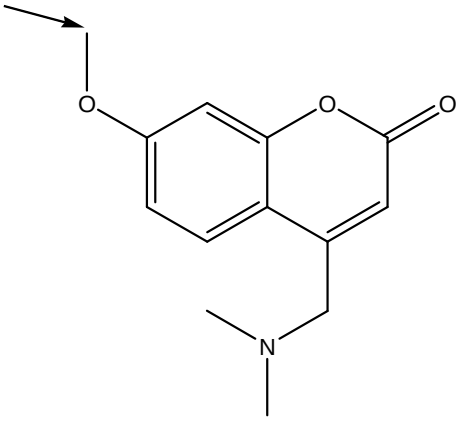

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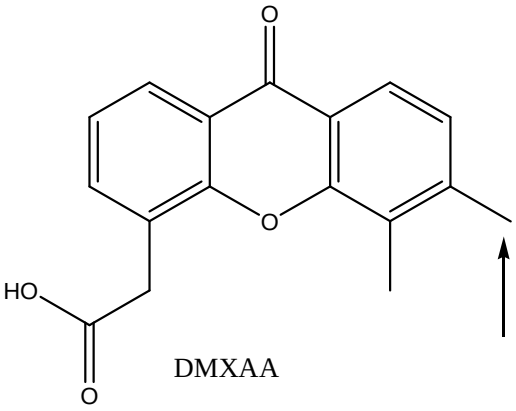

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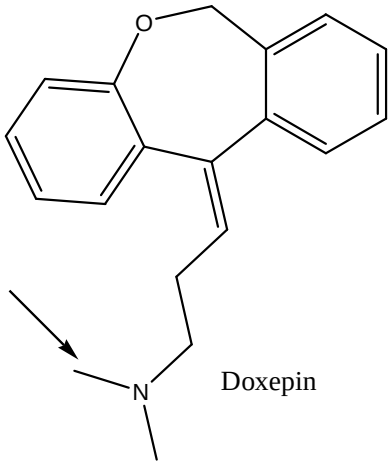

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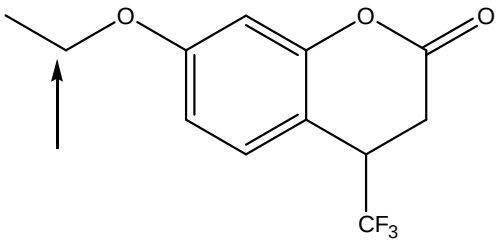

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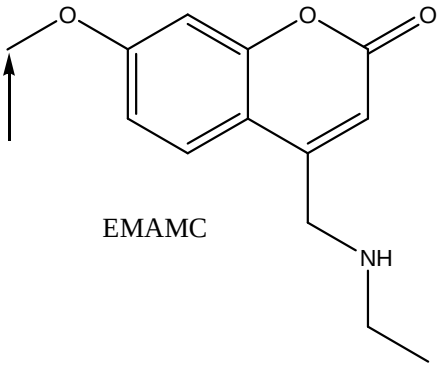

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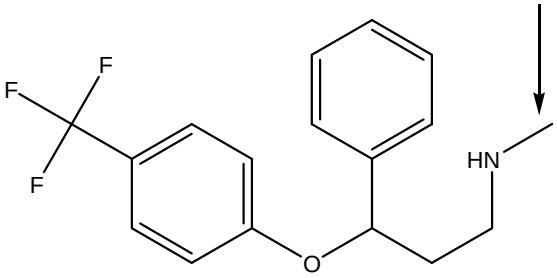

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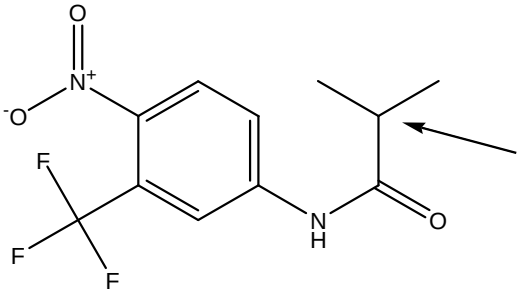

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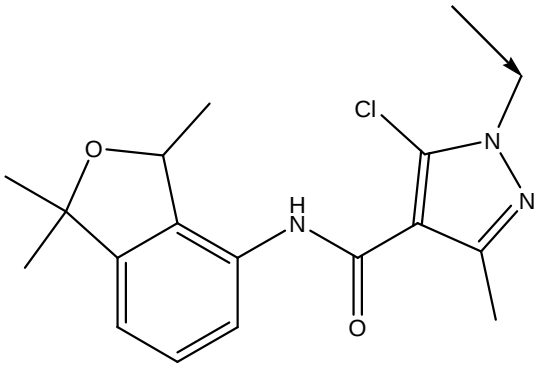

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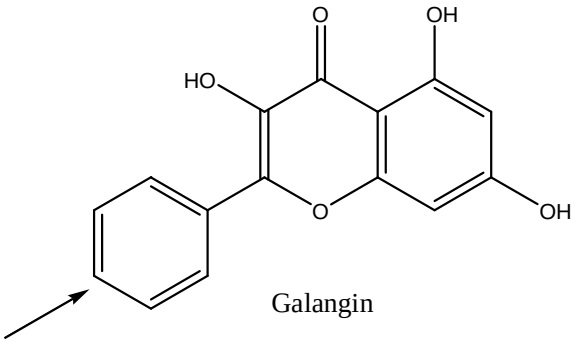

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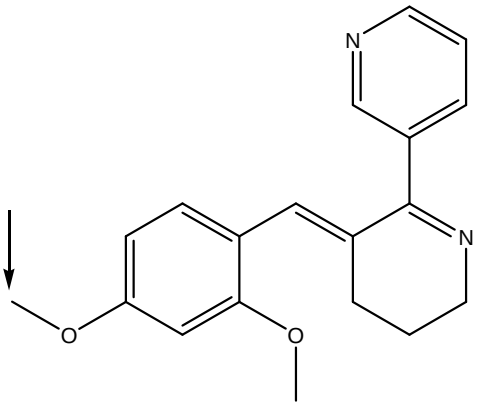

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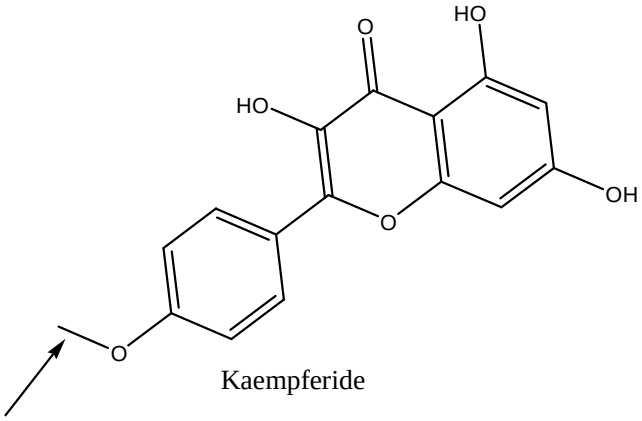

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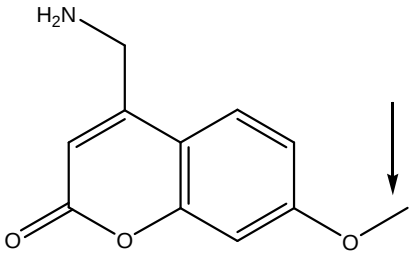

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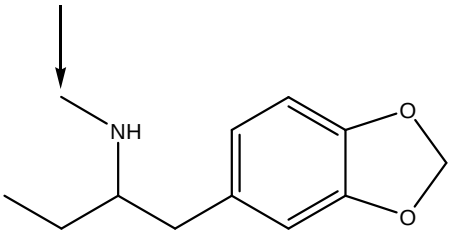

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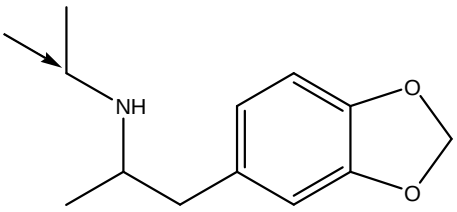

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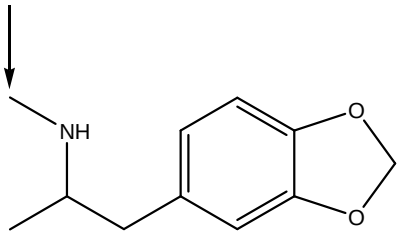

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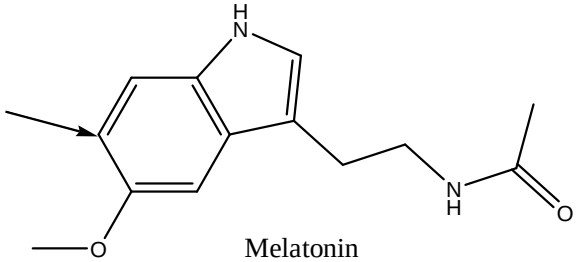

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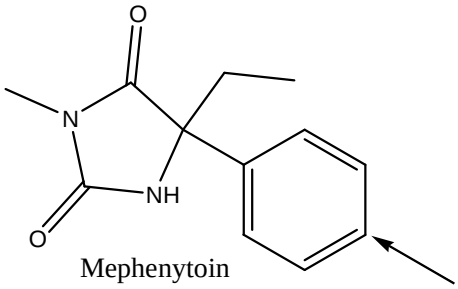

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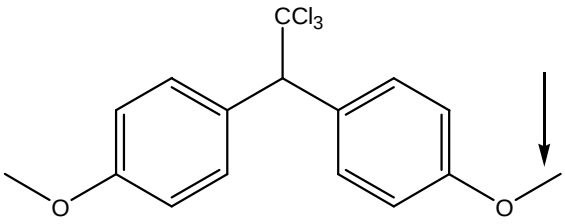

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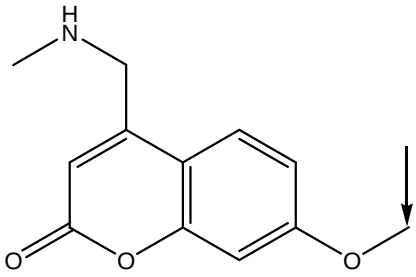

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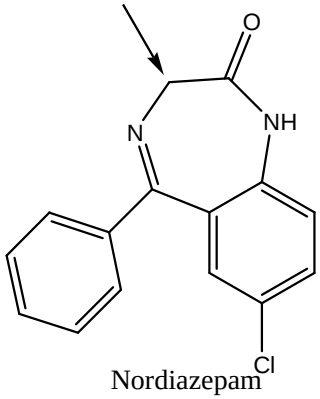
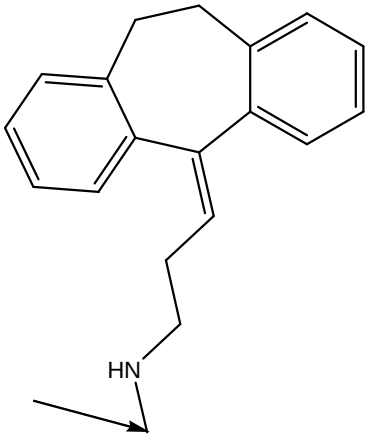


Nordiazepam



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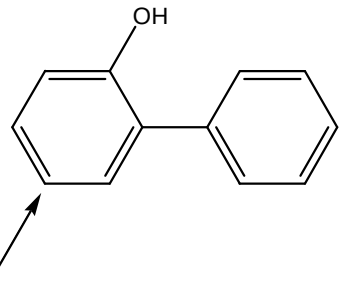
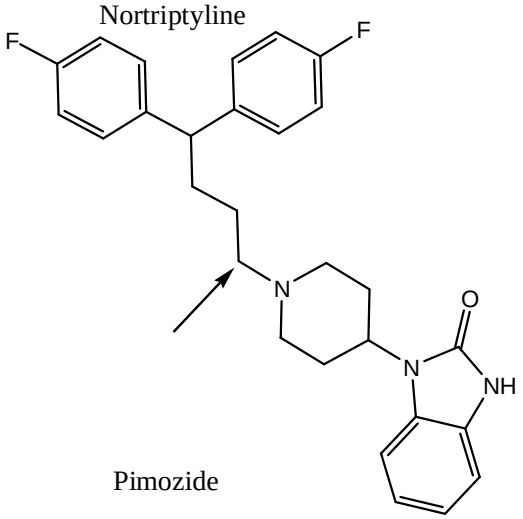


O-phenyl phenol



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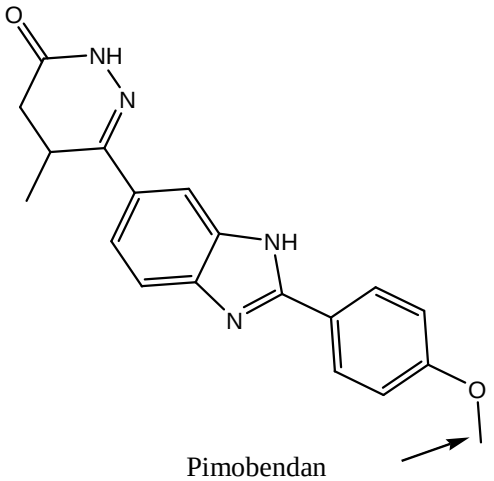

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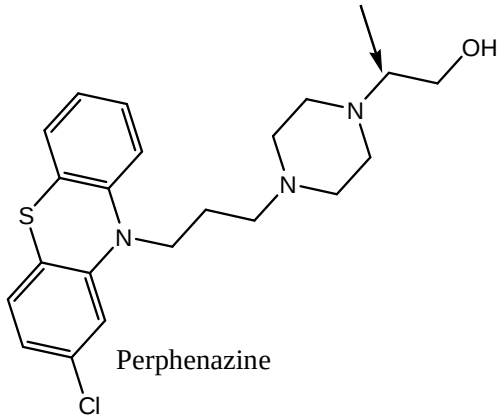

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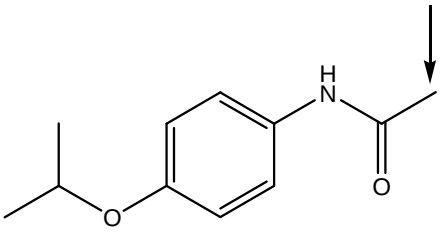
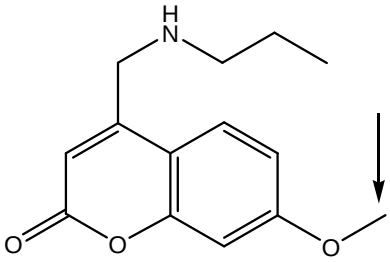


p-Isopropyloxyacetanilide



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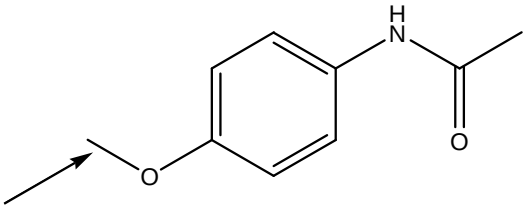
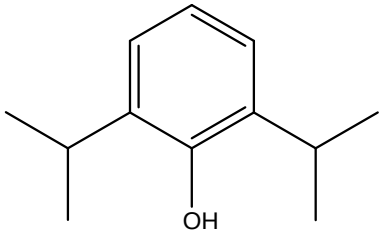
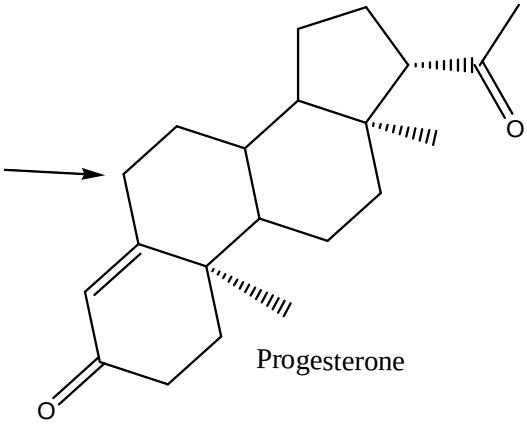


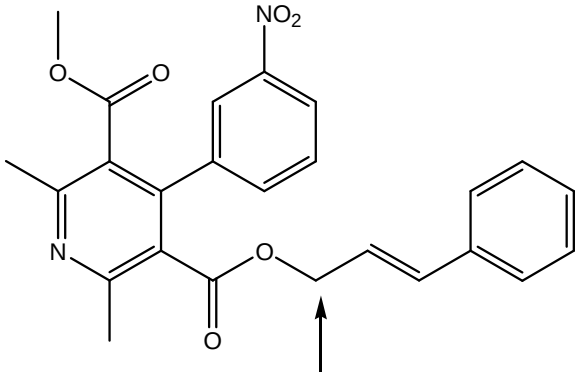
p-Methoxyacetanilide



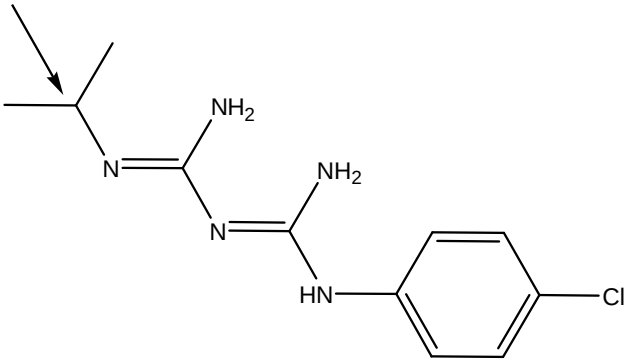
Propofol



Progesterone



Pranidipine



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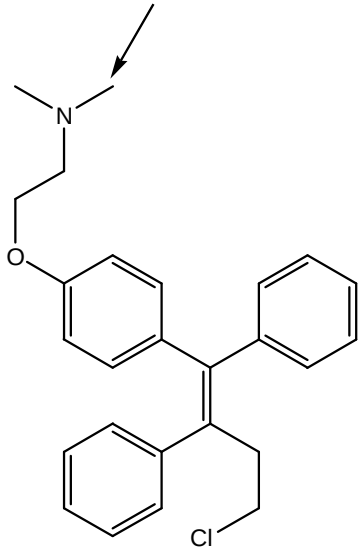

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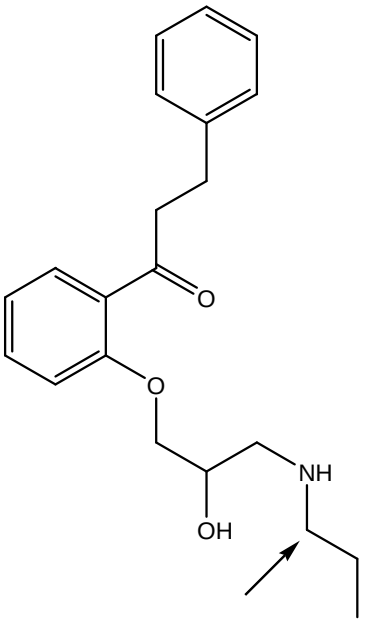

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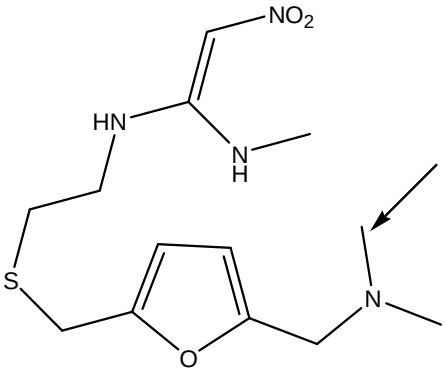
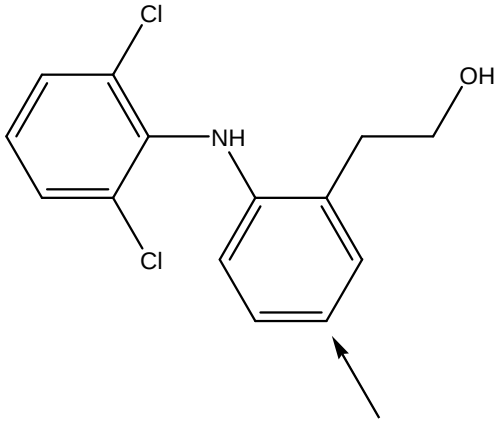
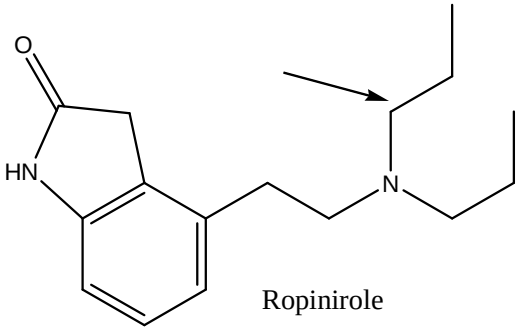


Ranitidine



reduced Diclofenac



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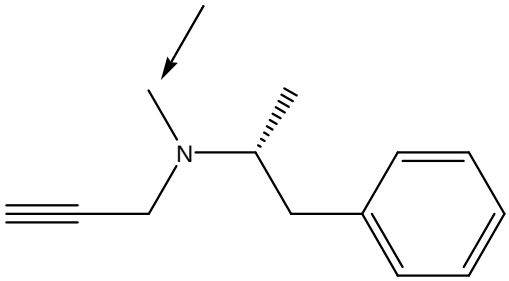

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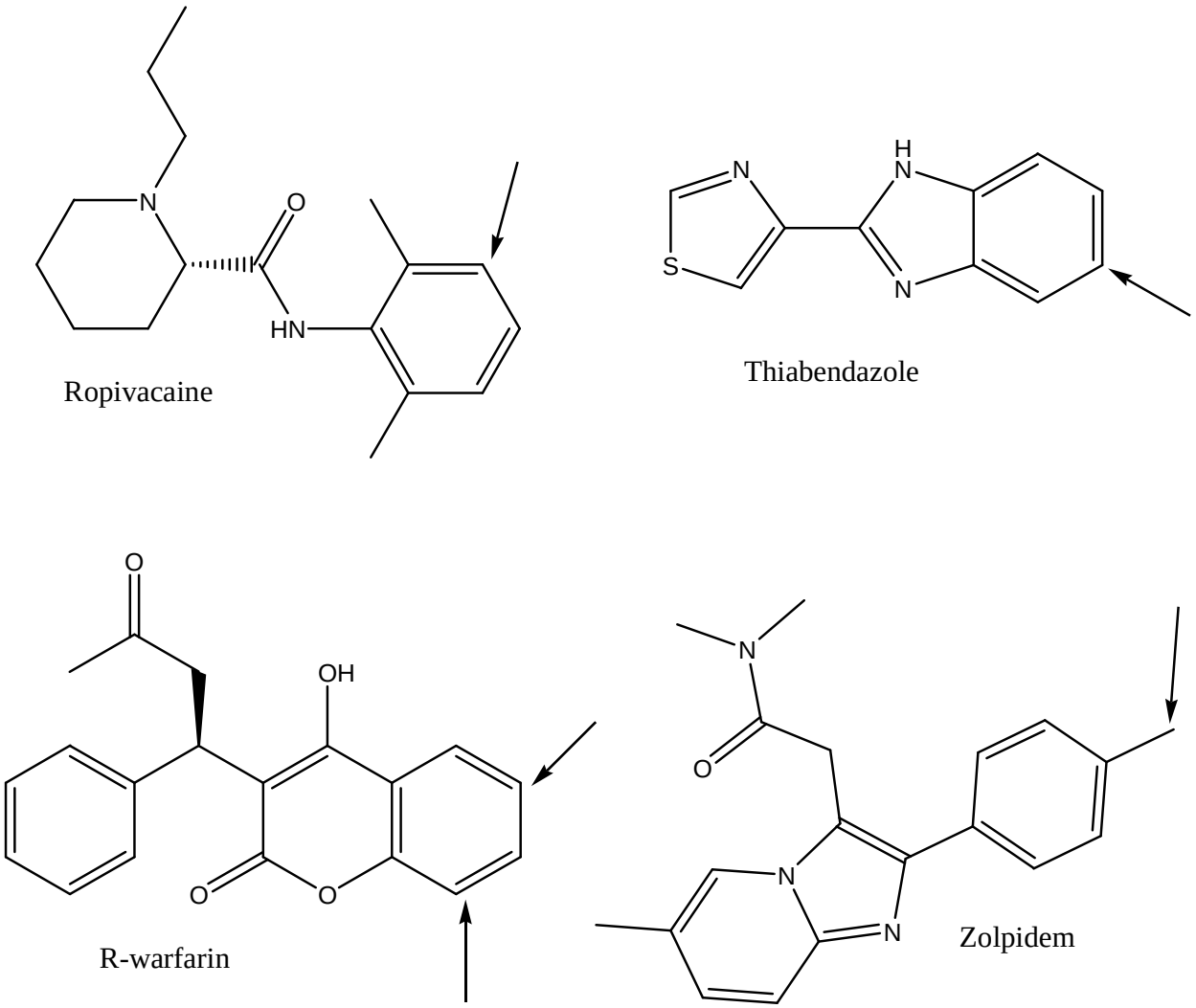
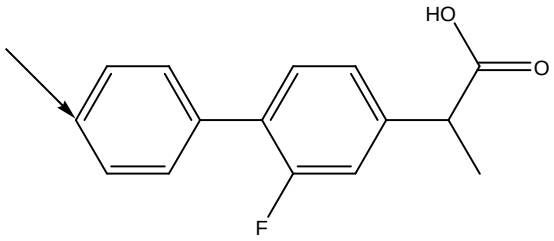
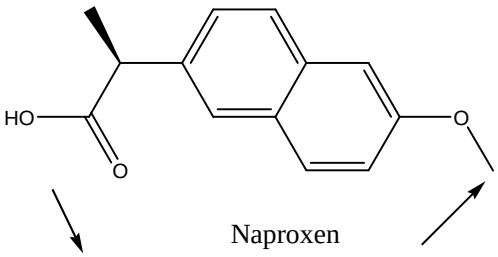


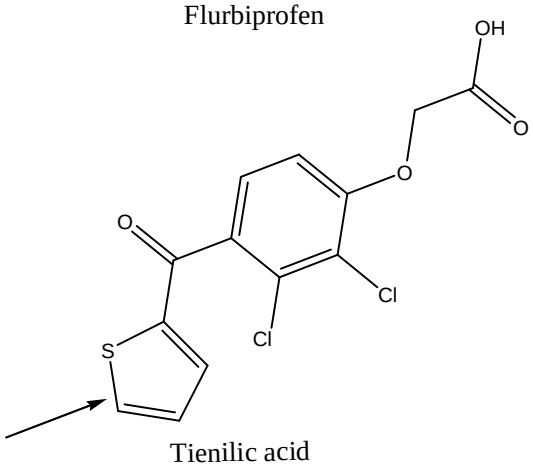
Supplementary Figure 2: 2D representations of 60 CYP1A2 substrates. SOM of these substrates are predicted by arrows.



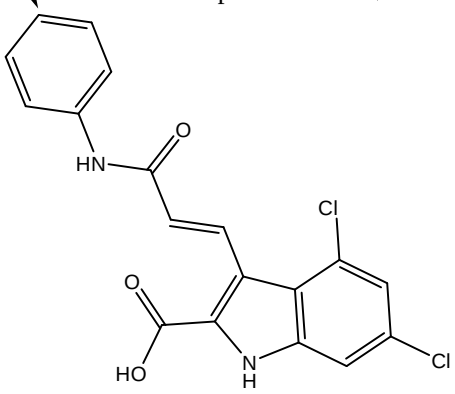
Flurbiprofen



Naproxen



Tienilic acid



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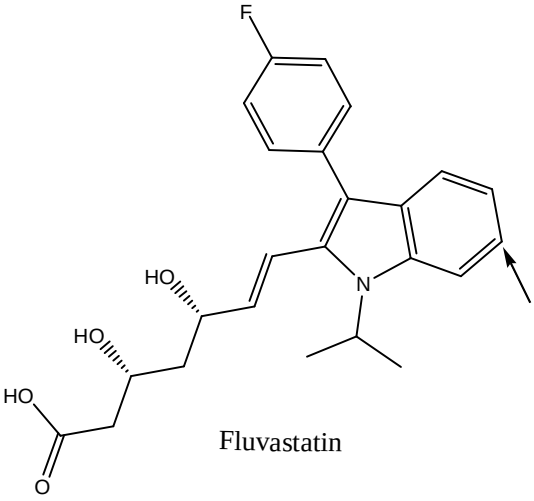

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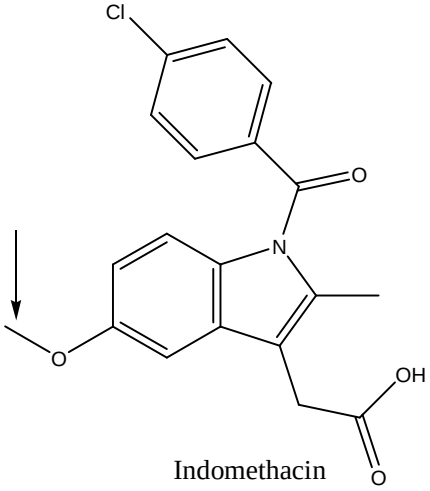

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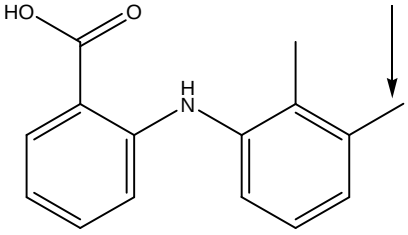
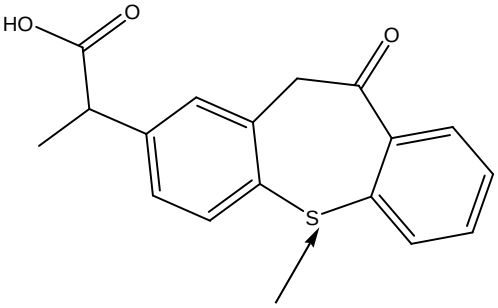
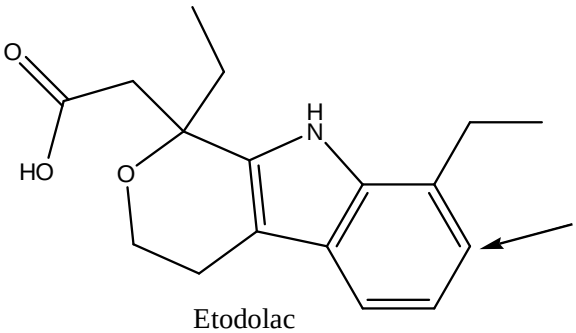


Mefenamic Acid



Zaltoprofen



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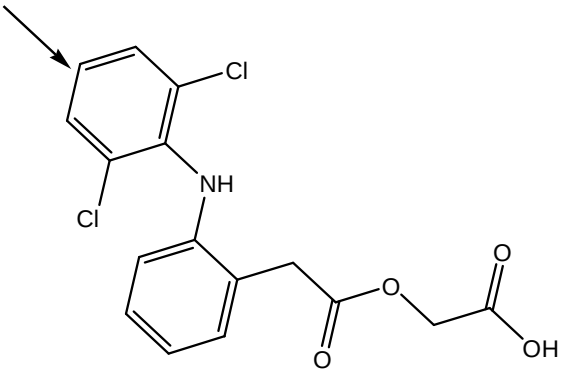

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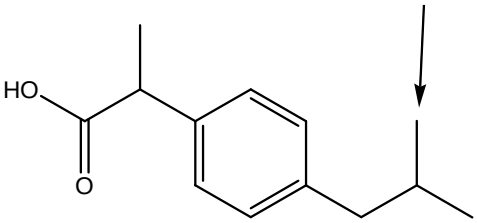
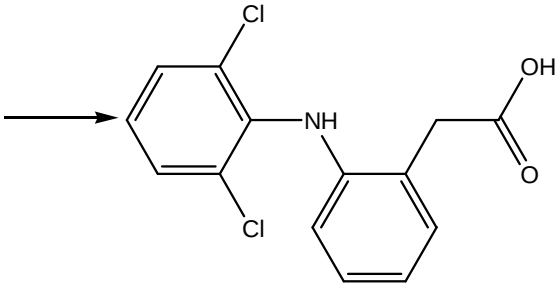
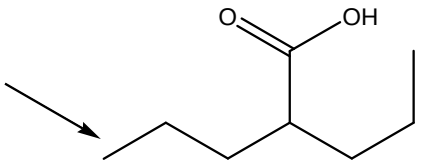


Ibuprofen



Diclofenac



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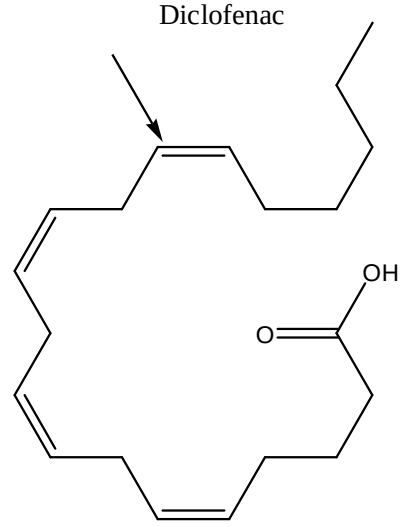

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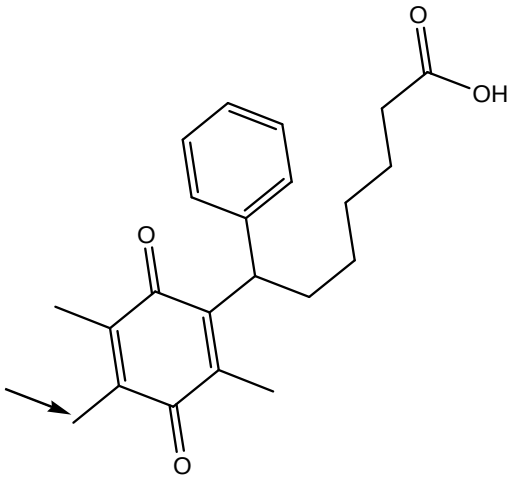

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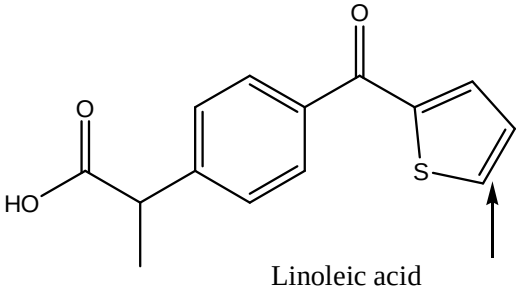
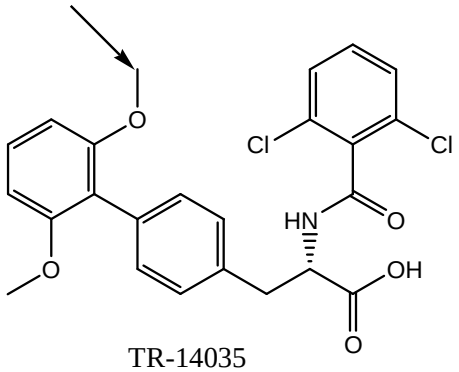
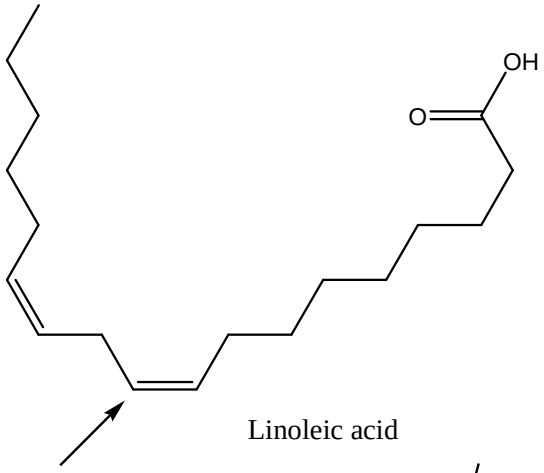


Linoleic acid



TR-14035



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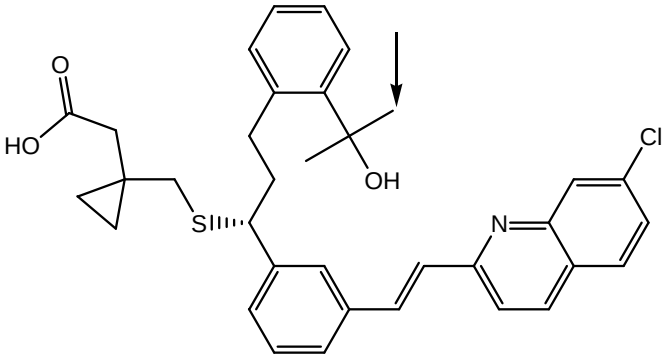

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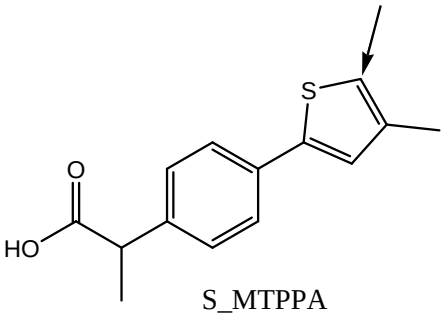
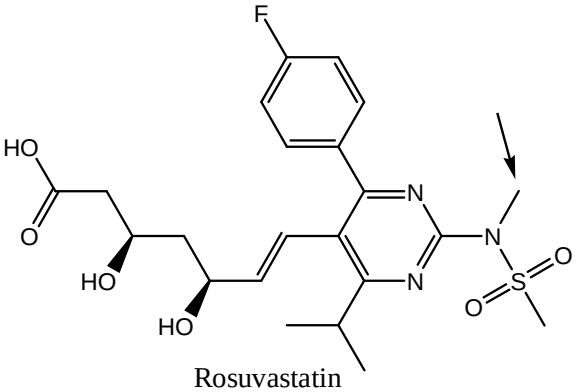


S_MTPPA



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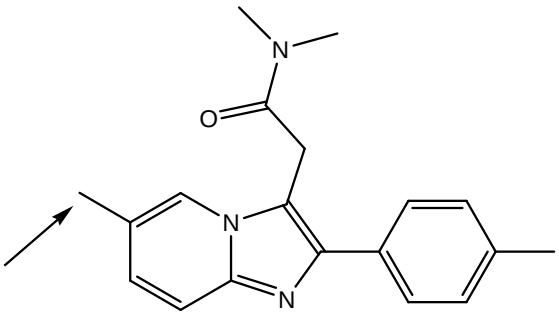

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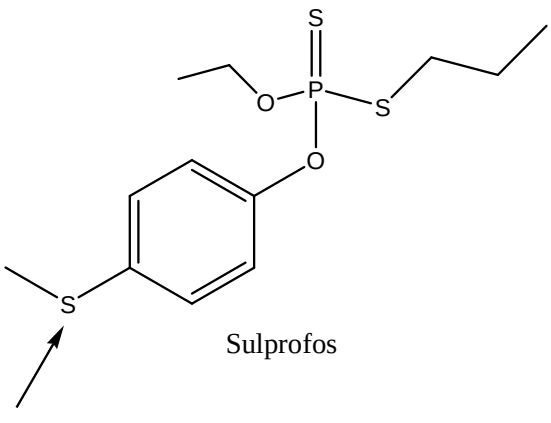
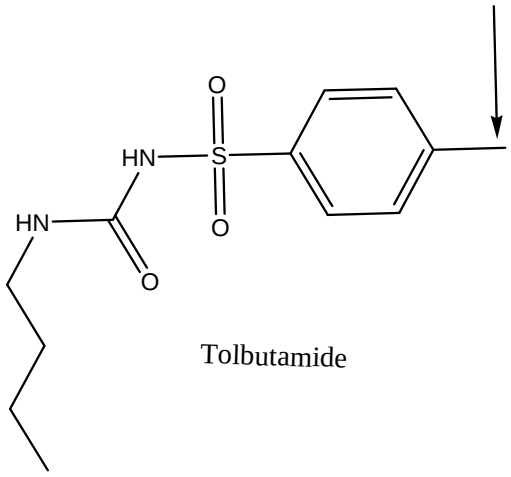


Sulprofos



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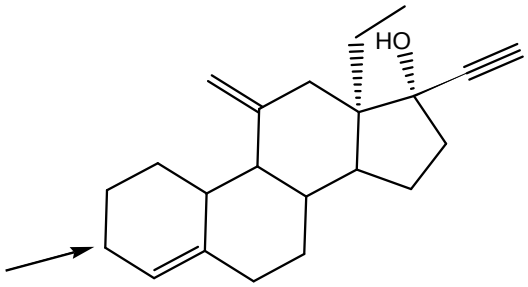

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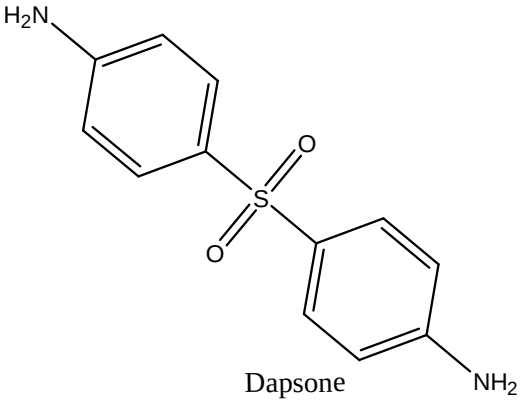

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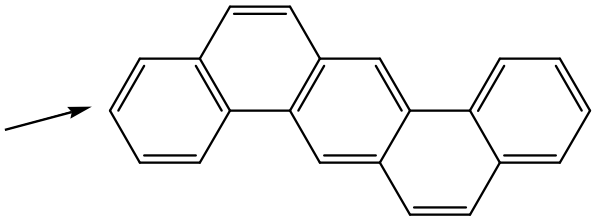

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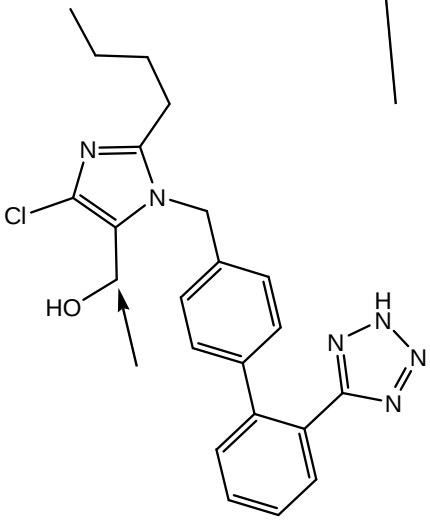

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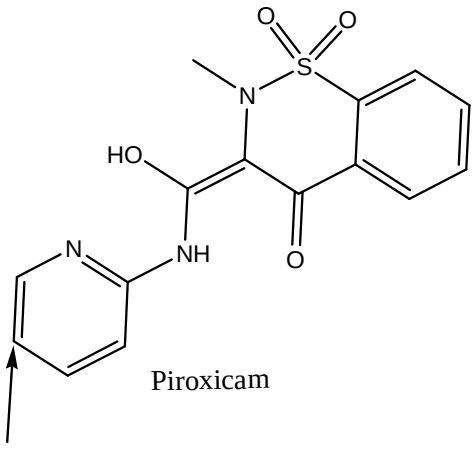

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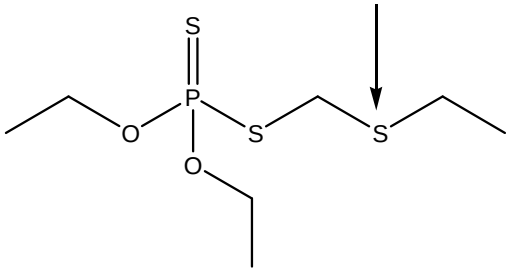

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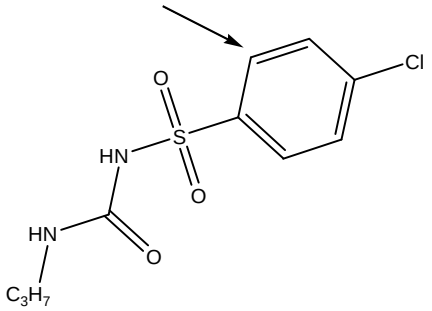

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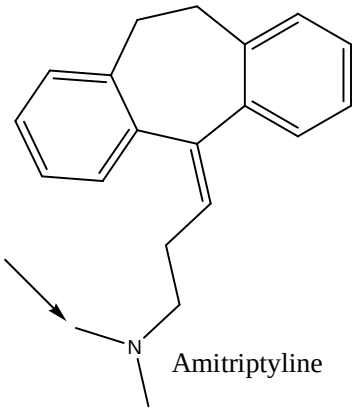

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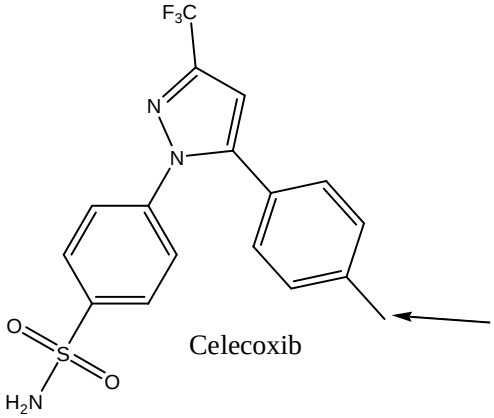
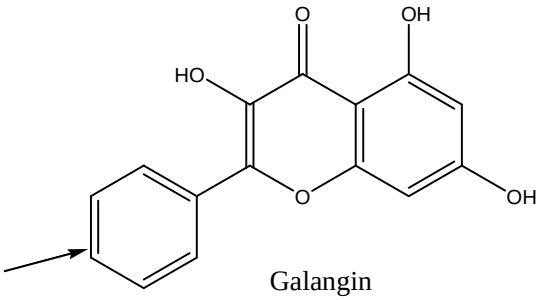
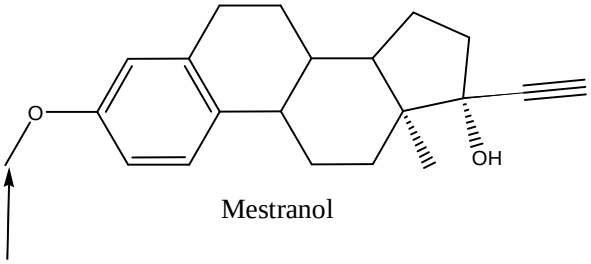


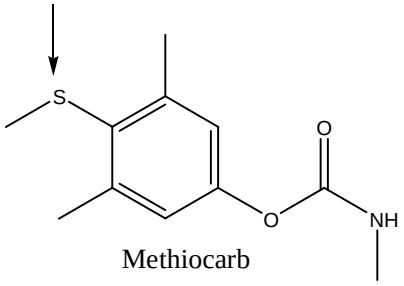
Celecoxib



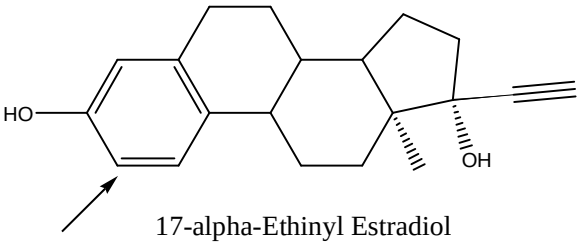
Galangin



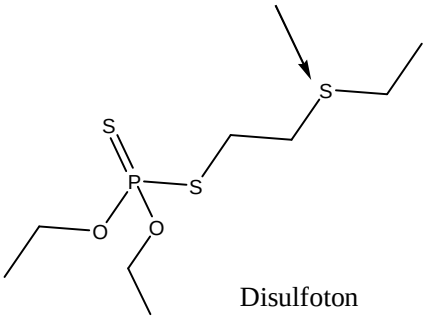
Mestranol



Methiocarb



17-alpha-Ethinyl Estradiol



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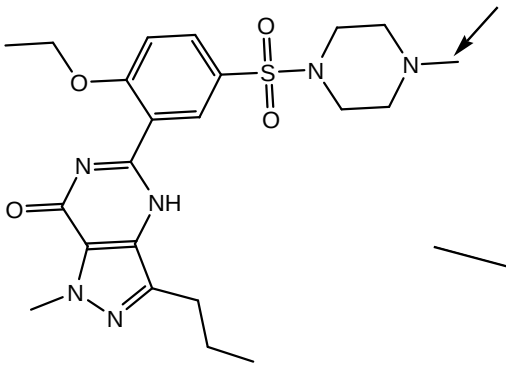
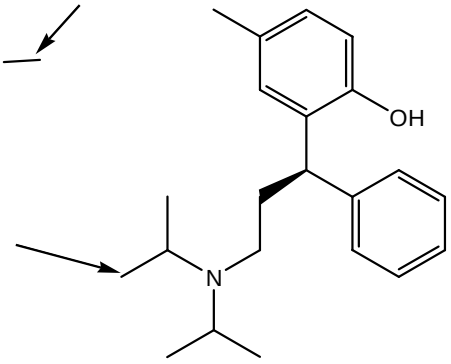


Sildenafil



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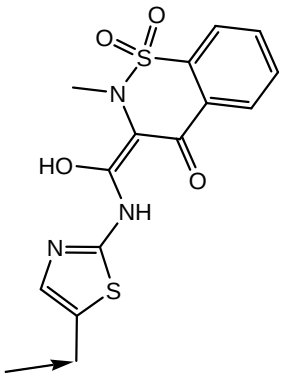
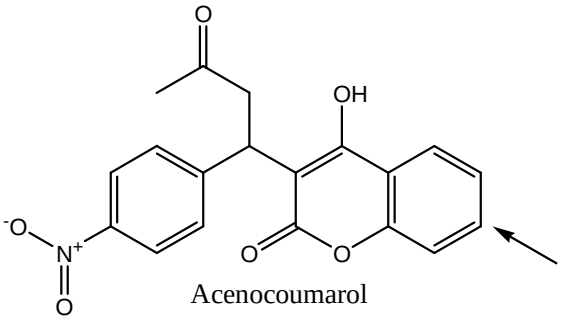
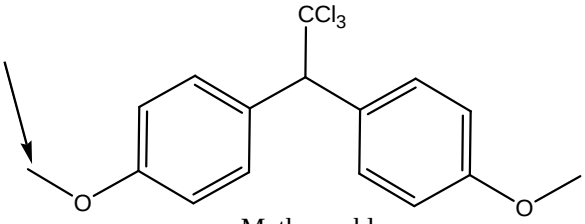


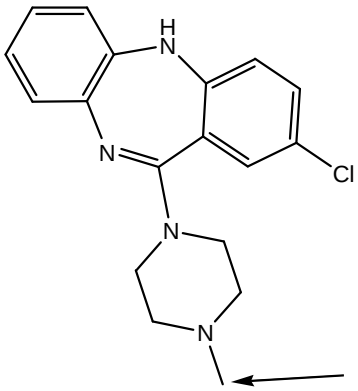
Meloxicam



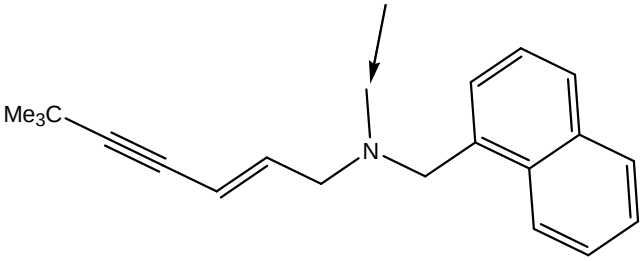
Acenocoumarol



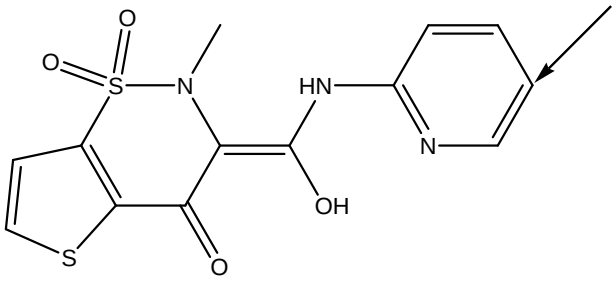
Methoxychlor



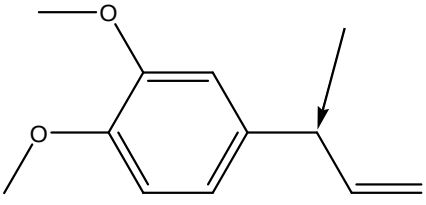
Clozapine



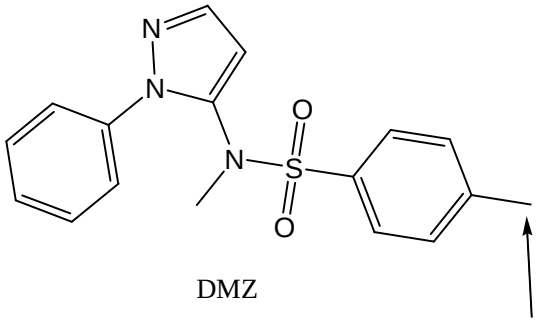
Terbinafine



Tenoxicam



Methyleugenol



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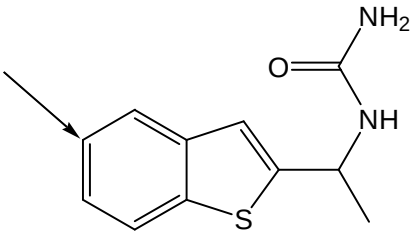
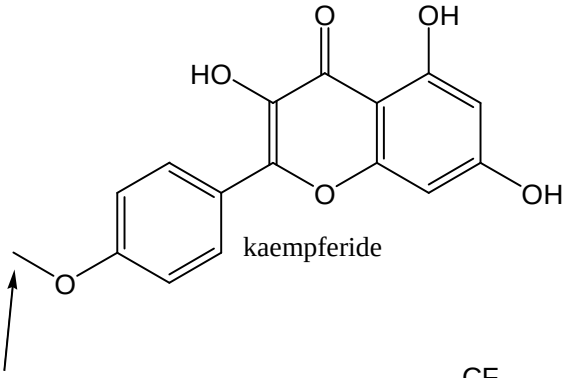
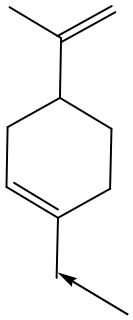


N-dehydroxy zileuton



kaempferide



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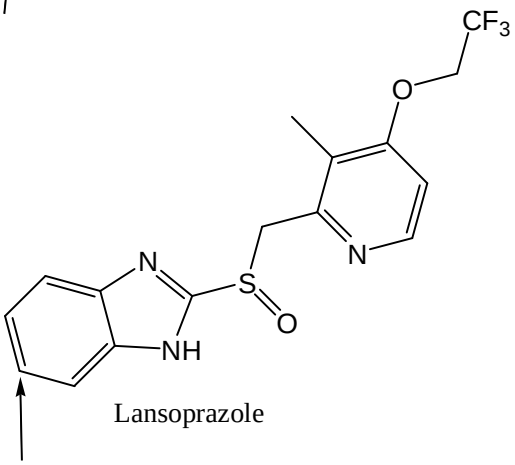

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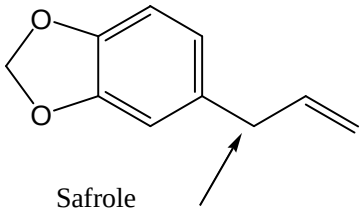

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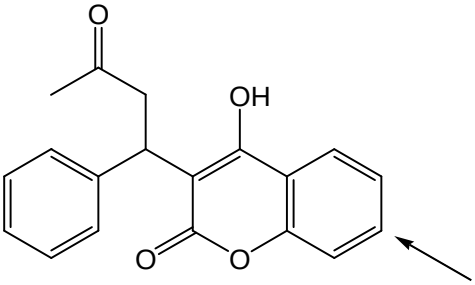

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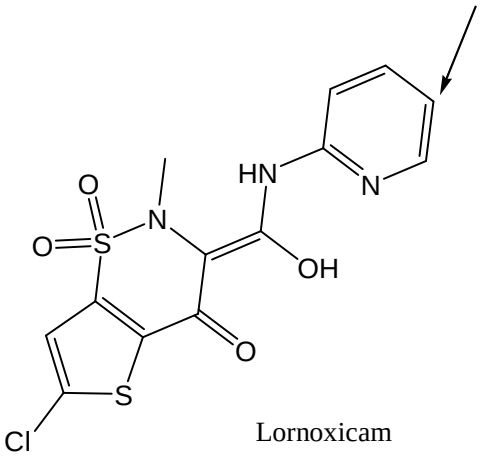

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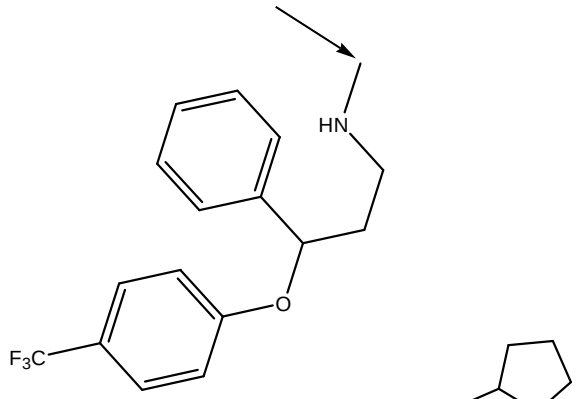

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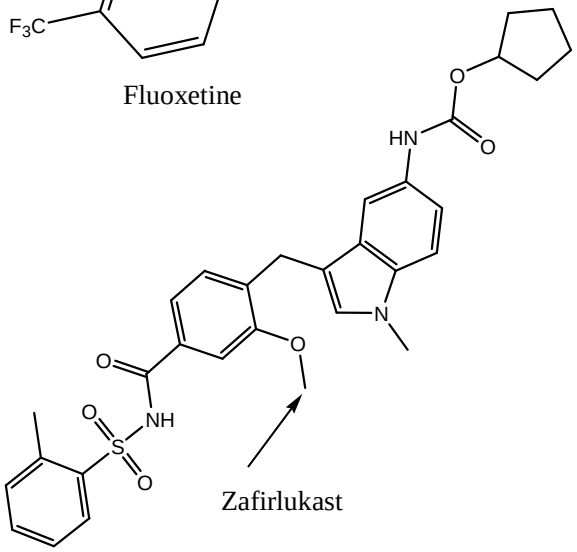
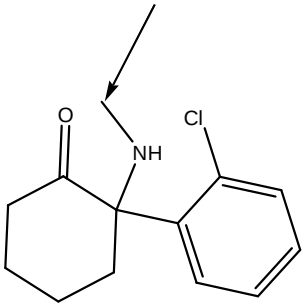
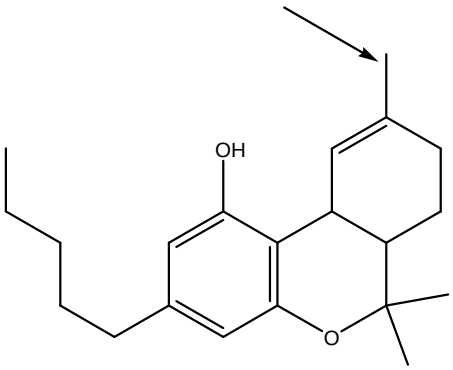


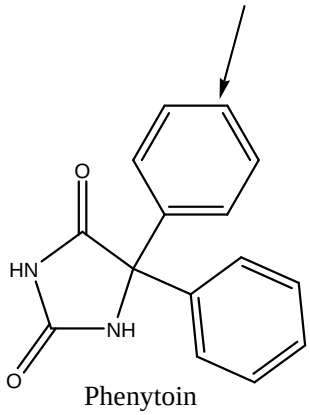
Zafirlukast



Ketamine



9-Tetrahydrocannabinol



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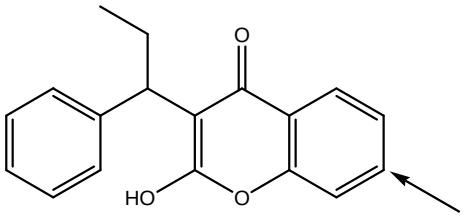

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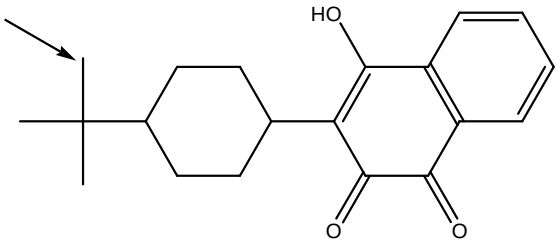
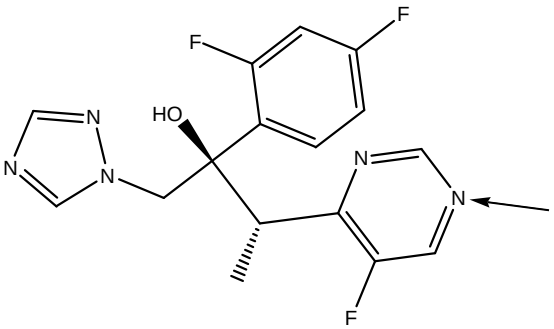
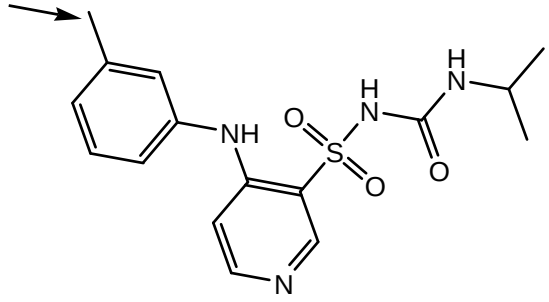


58C80



Voriconazole



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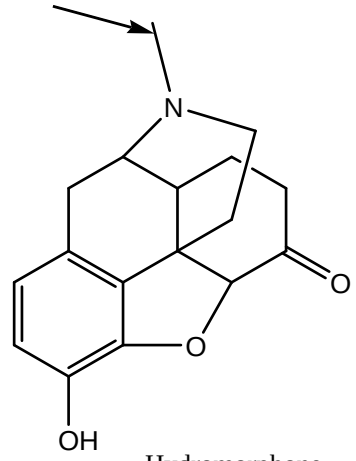
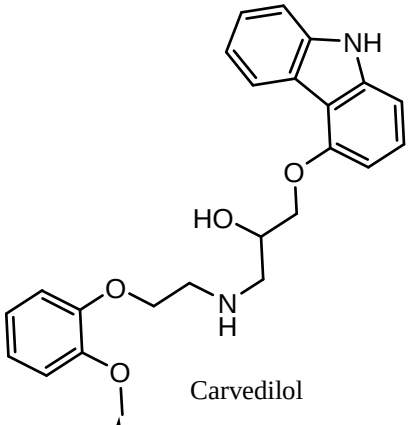
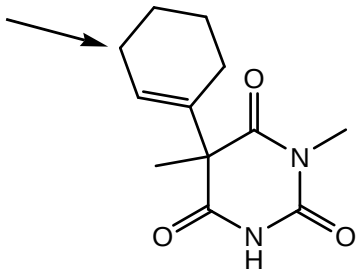


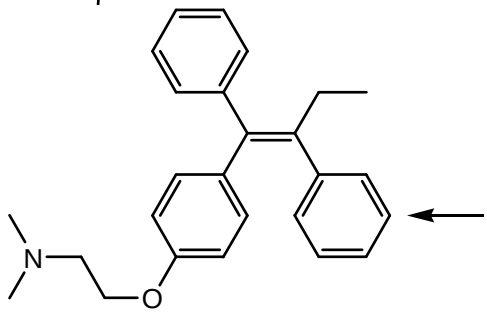
Hydromorphone



Carvedilol



Hexobarbital



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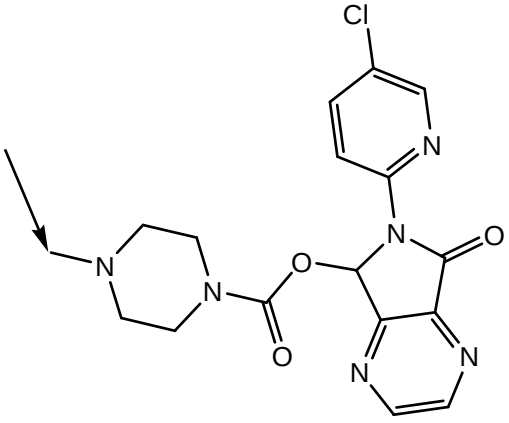

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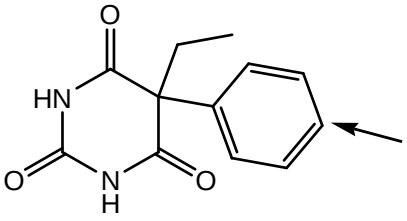
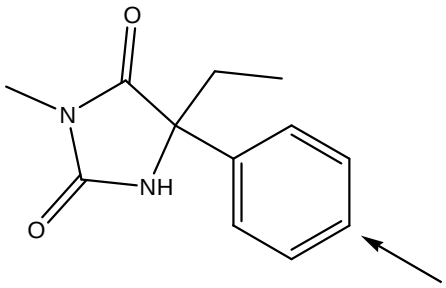
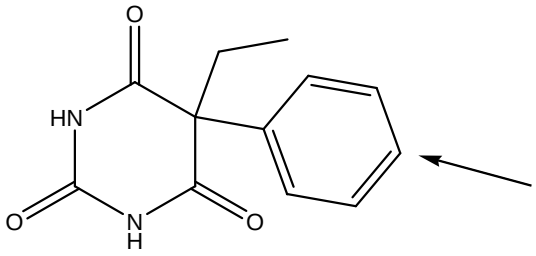


Phenobarbital

Supplementary Figure 3: 2D representations of 70 CYP2C9 substrates. SOM of these substrates are predicted by arrows.



Mephenytoin



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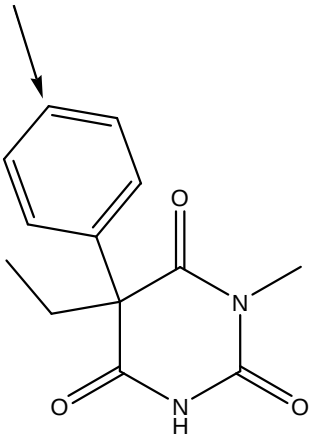
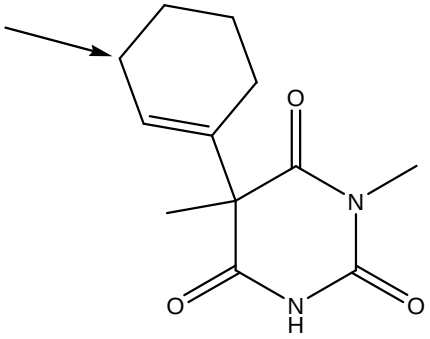


Mephobarbital



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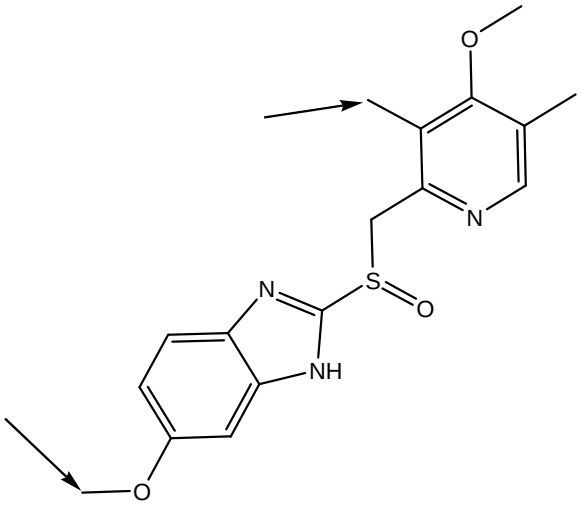
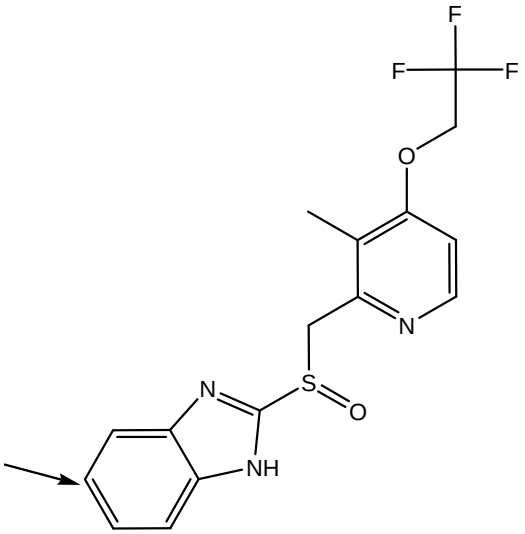


Omeprazole



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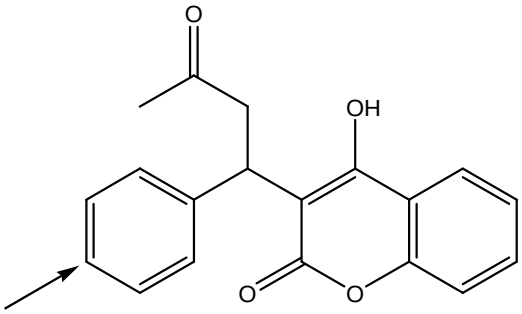
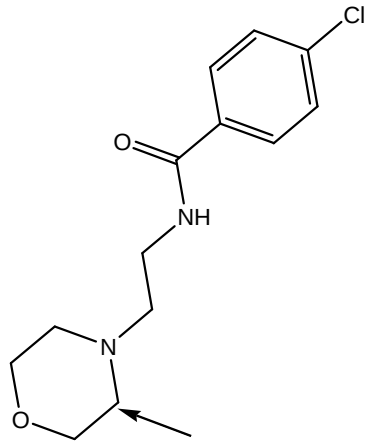


Warfarin



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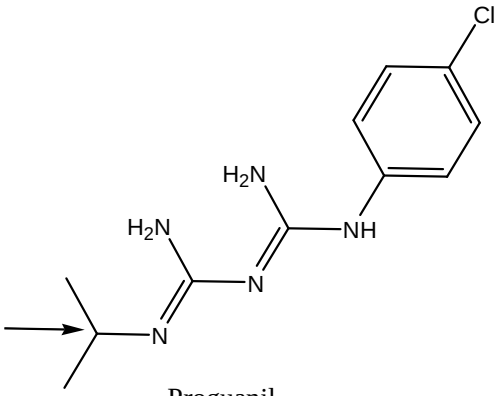

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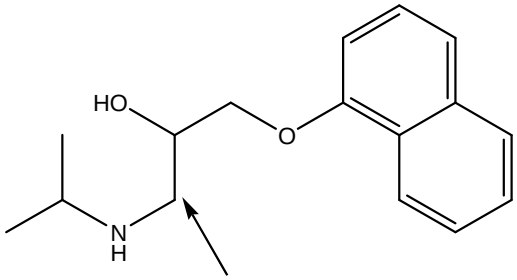

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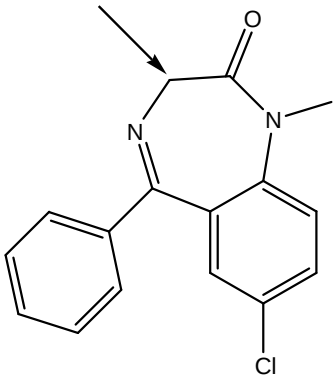
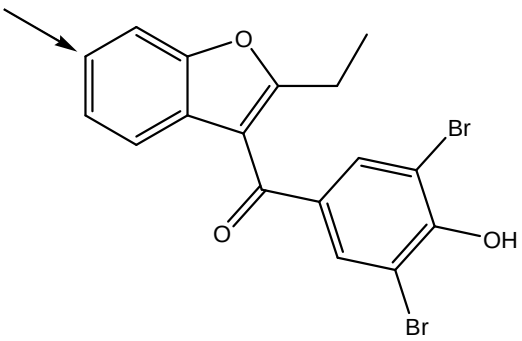
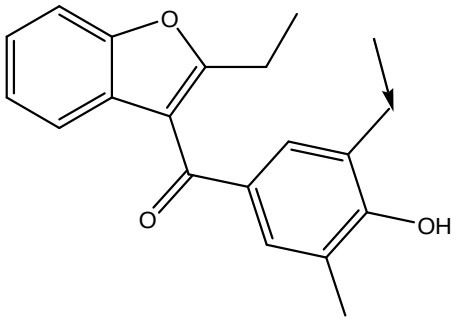
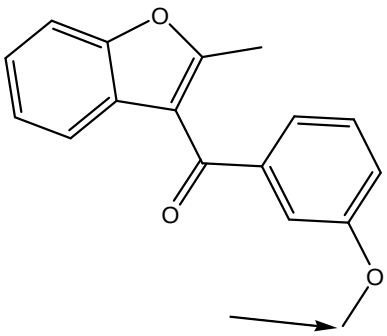
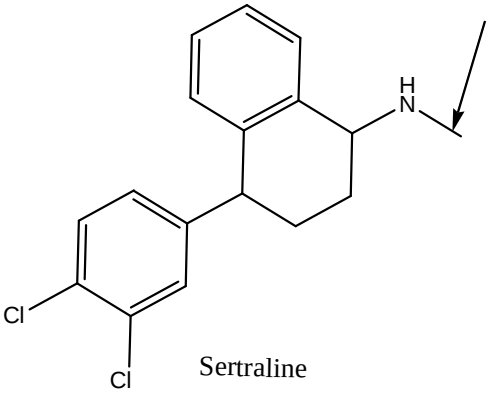


Diazepam

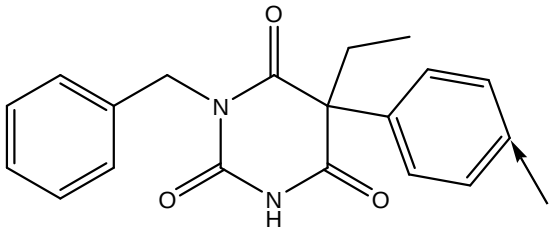








Sertraline



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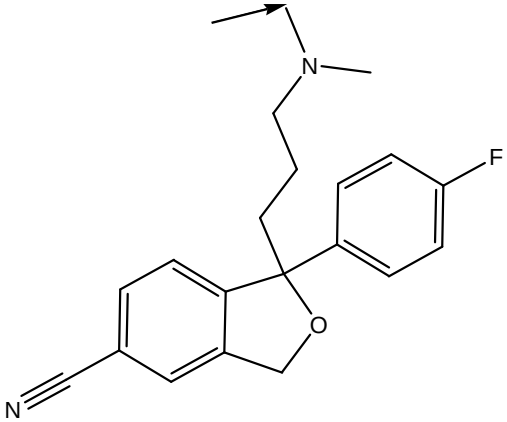
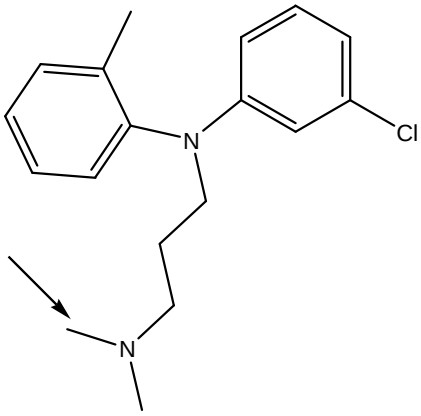
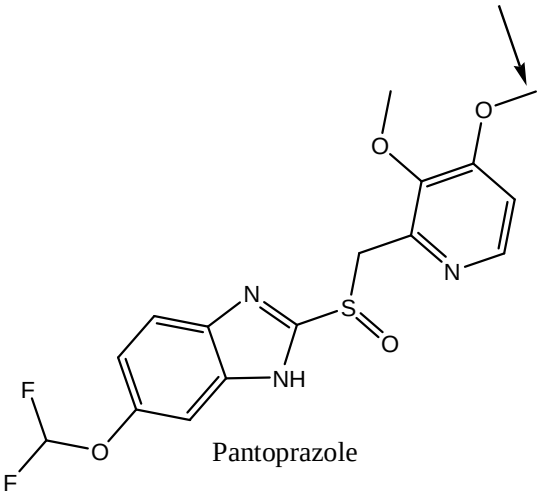


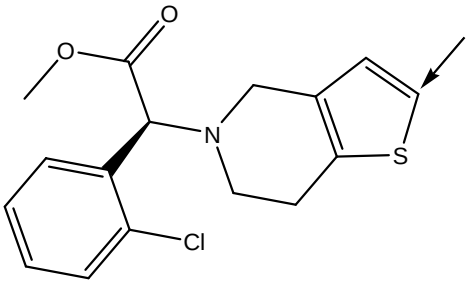
Citalopram



Clomipramine



Pantoprazole



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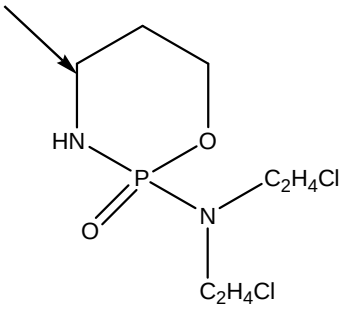
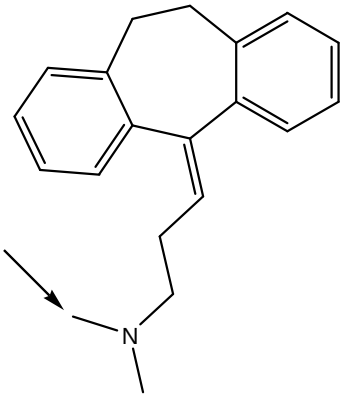


Cyclophosphamide



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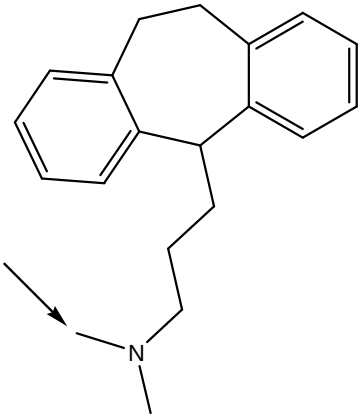
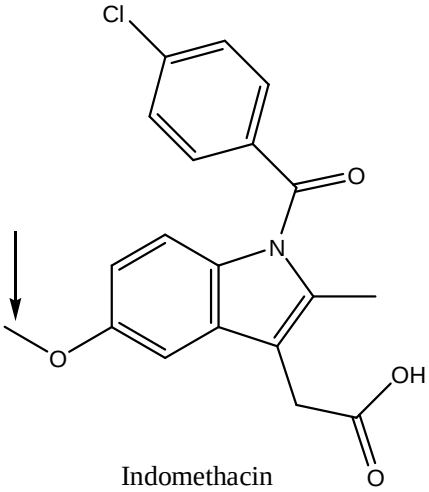


Imipramine



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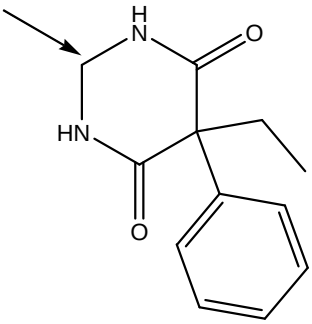
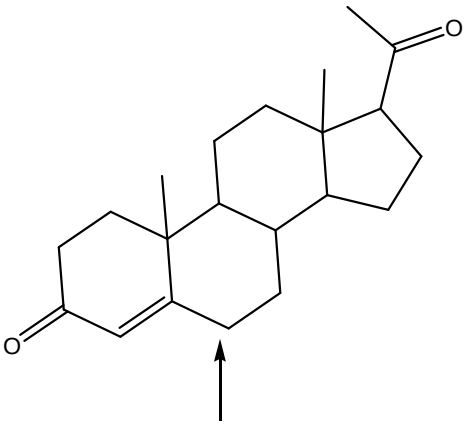
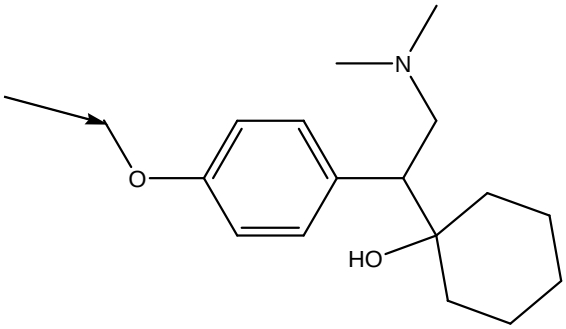


Primidone



Progesterone



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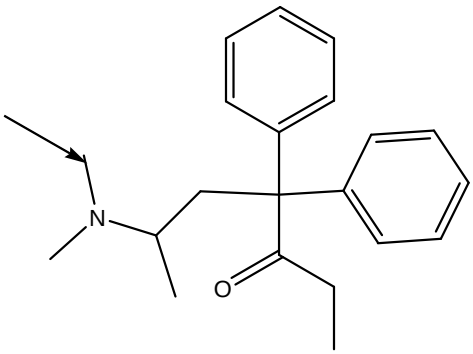

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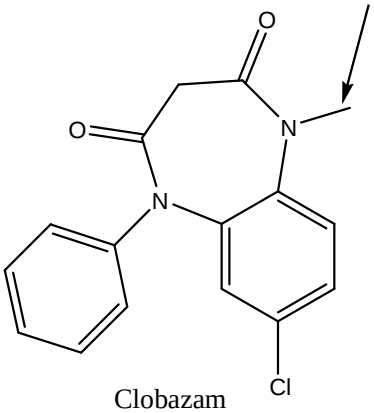

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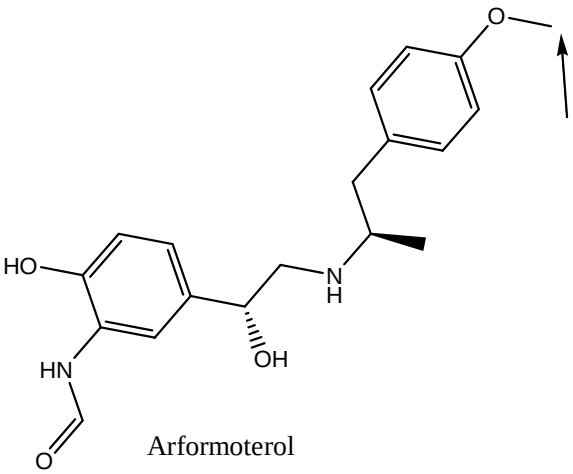
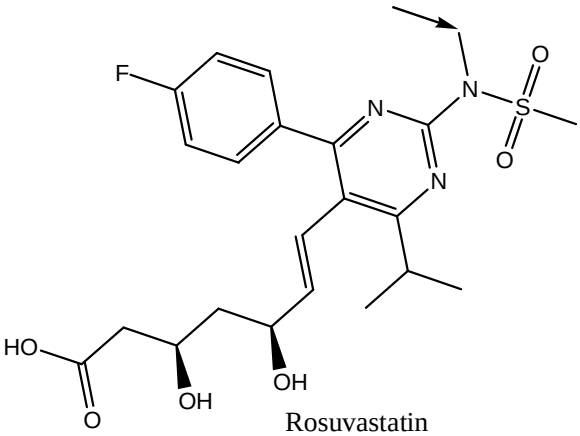


Arformoterol



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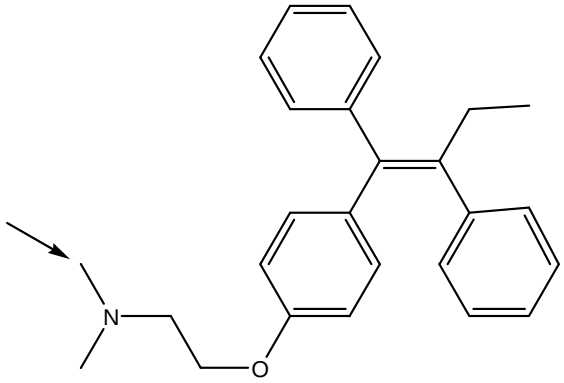
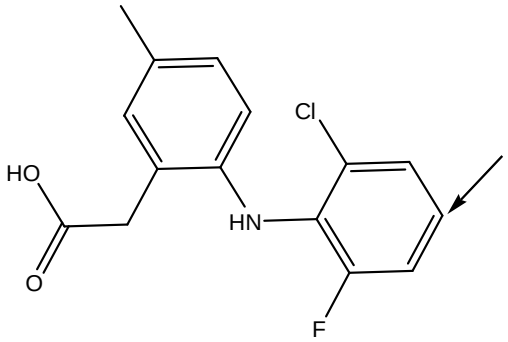
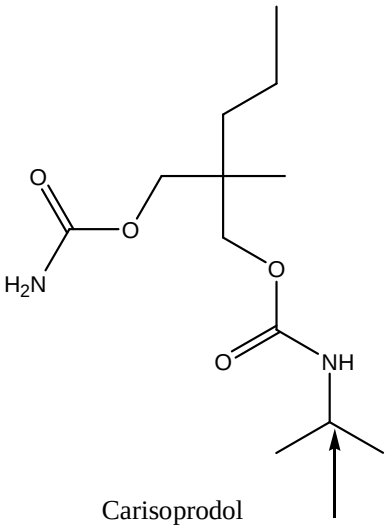


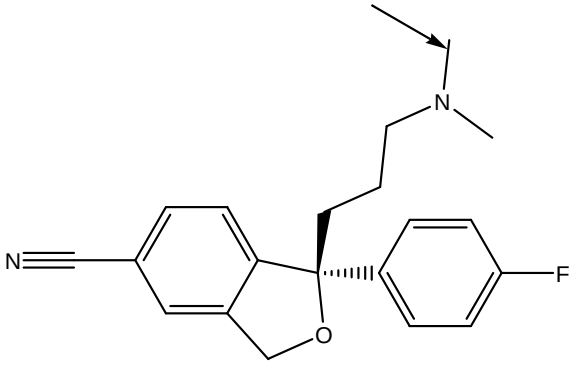
Tamoxifen



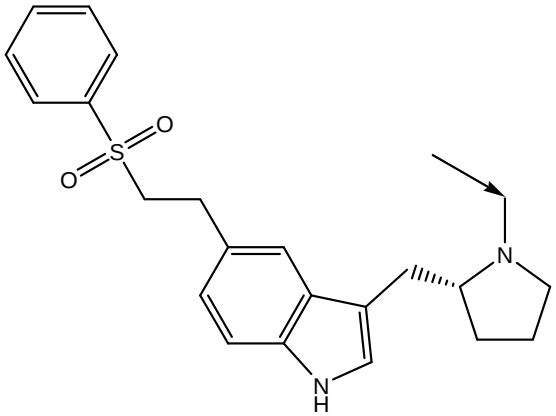
Lumaricoxib



Carisoprodol

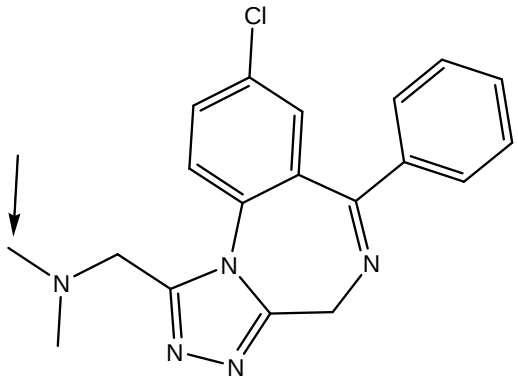


Escitalopram

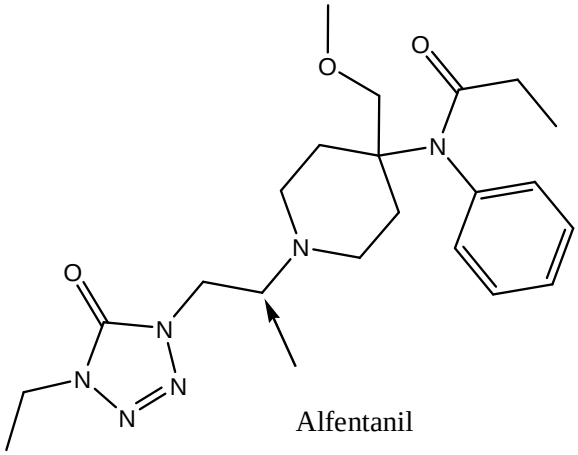


Eletriptan

Supplementary Figure 4: 2D representations of 36 CYP2C19 substrates. SOM of these substrates are predicted by arrows.



Adinazolam



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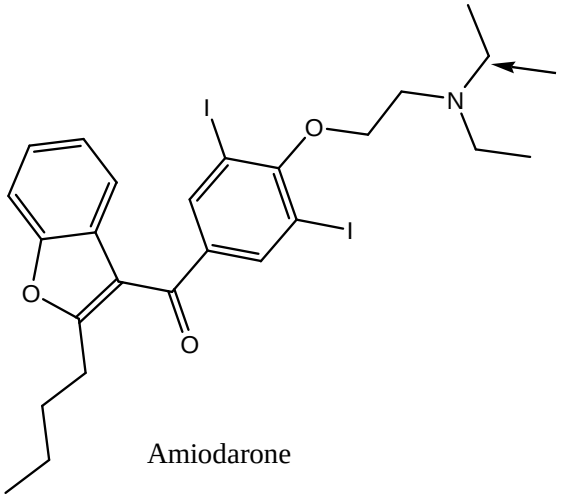
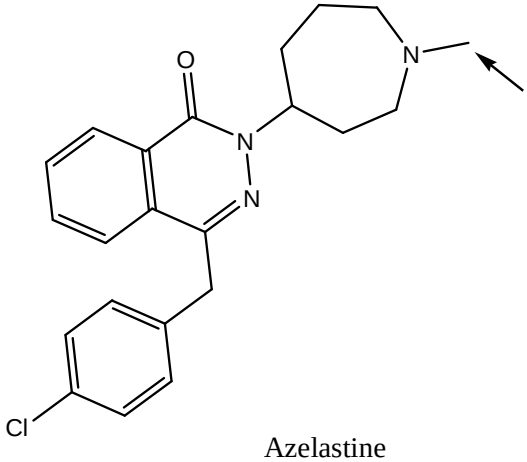
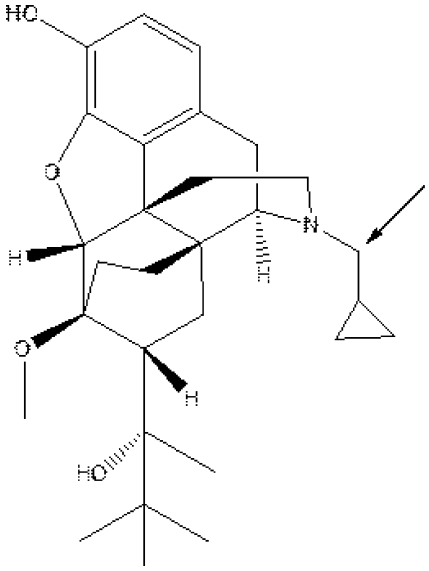


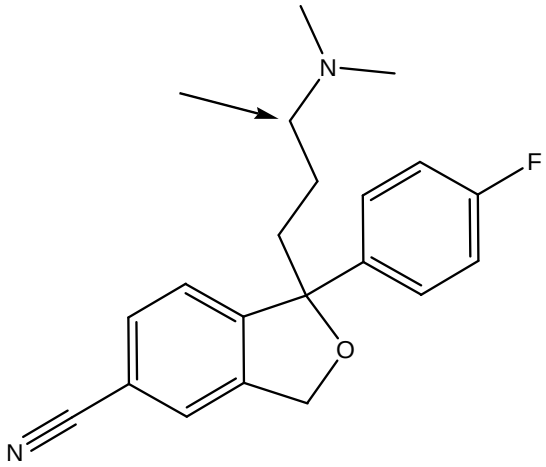
Amiodarone



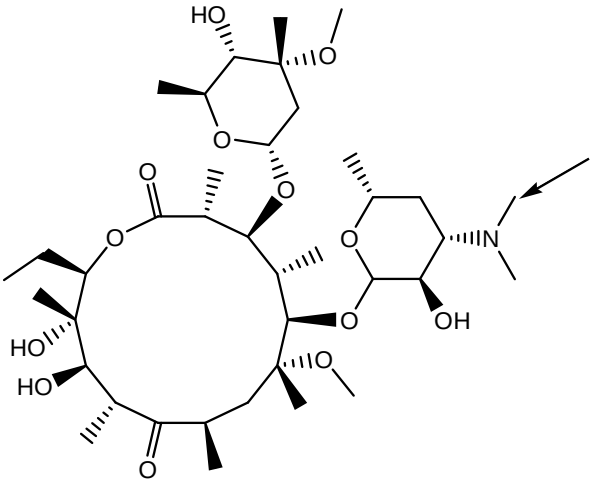
Azelastine



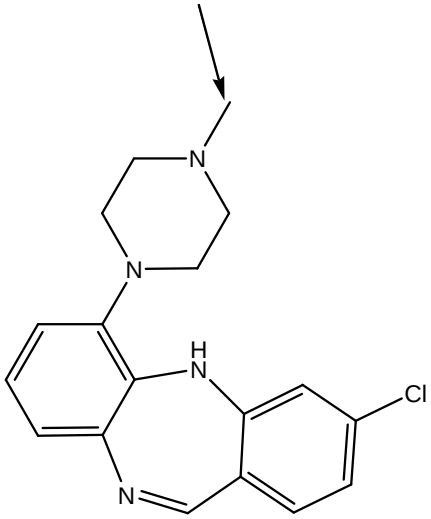
Buprenorphine



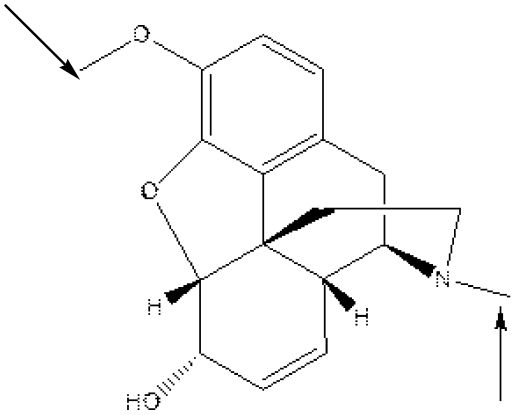
Citalopram



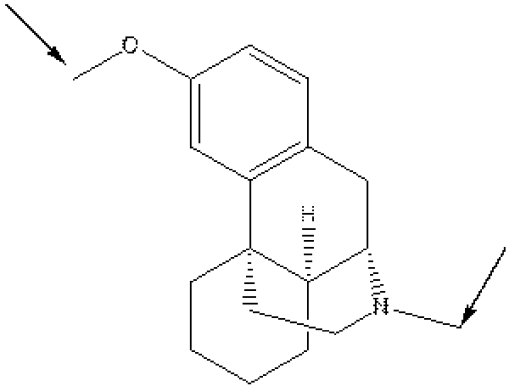
Clarithromycin



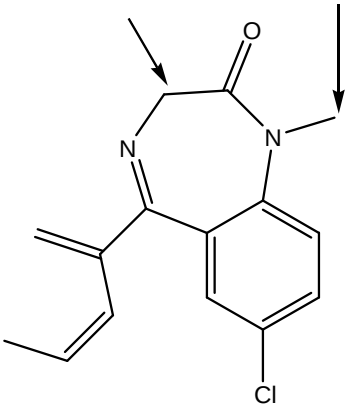
Clozapine



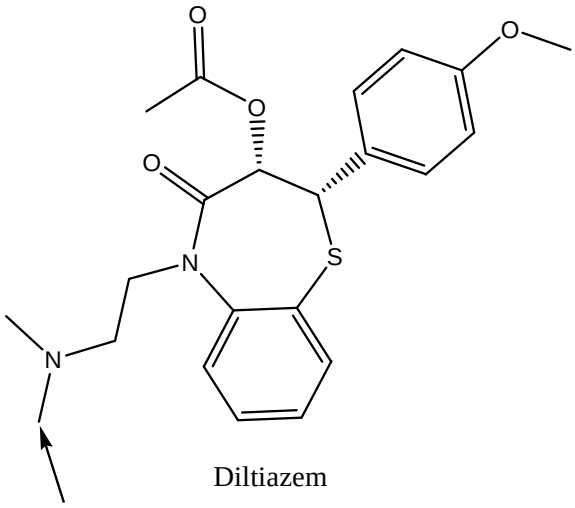
Codeine



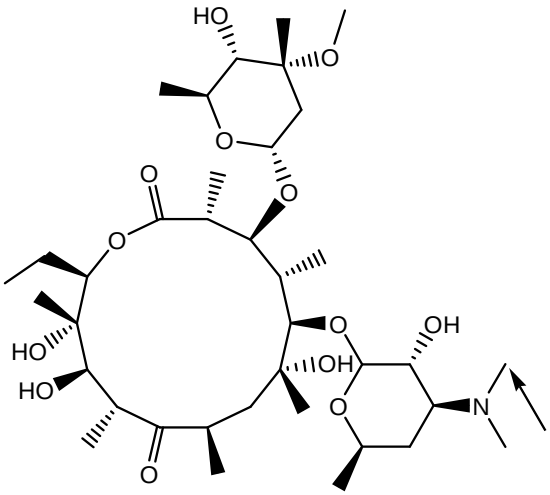
Dextromethorphan



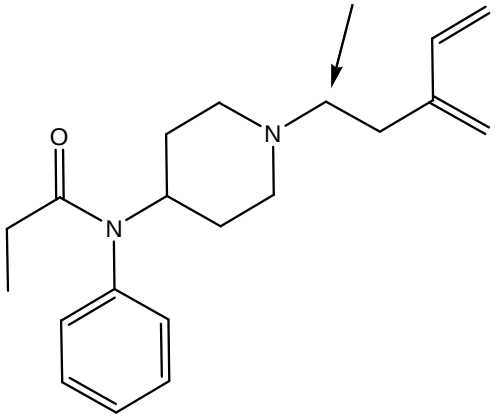
Diazepam



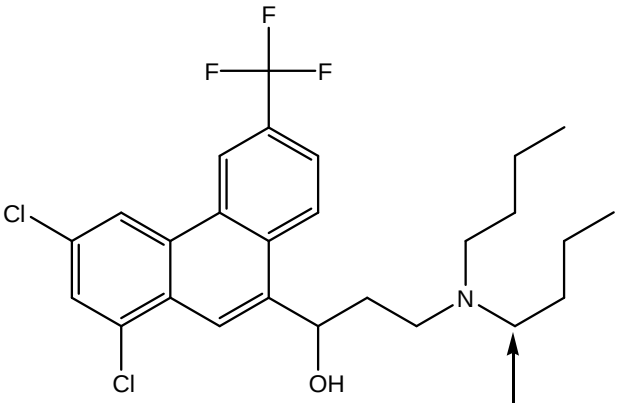
Diltiazem



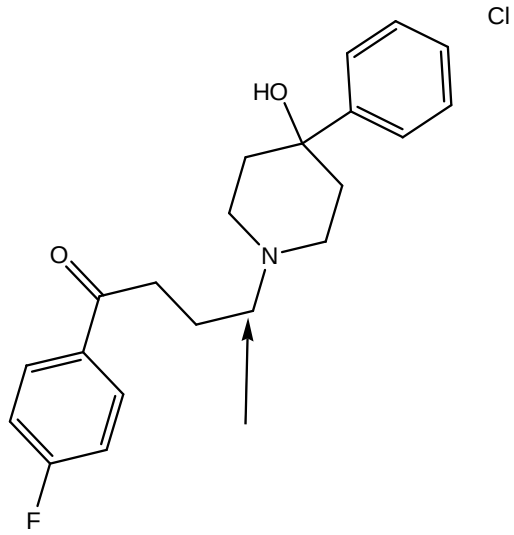
Erythromycin



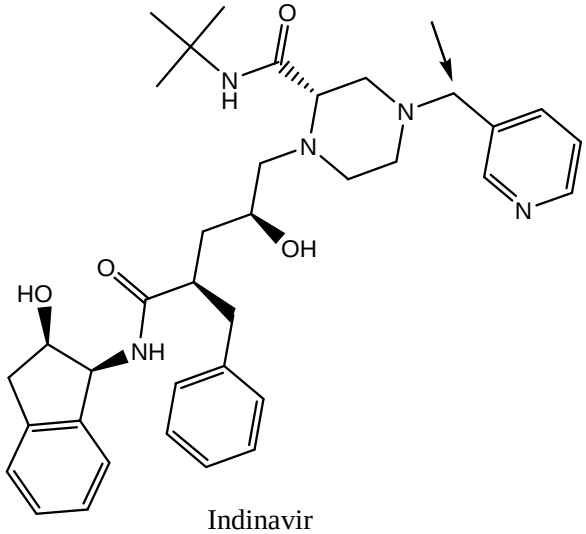
Fentanyl



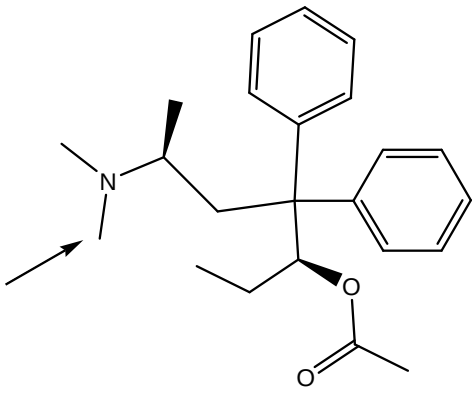
Halofantrine



Haloperidol



Indinavir



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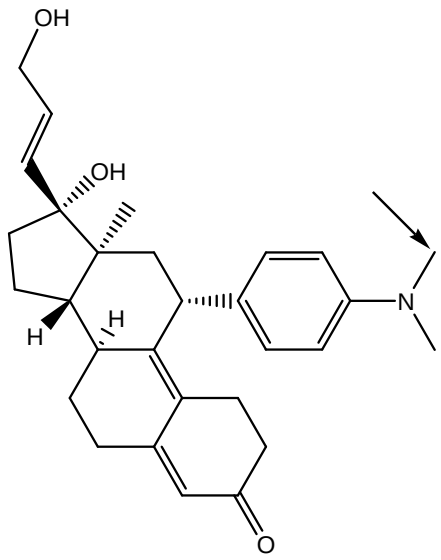
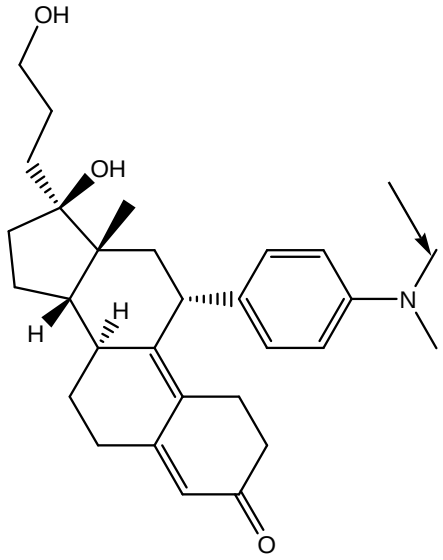
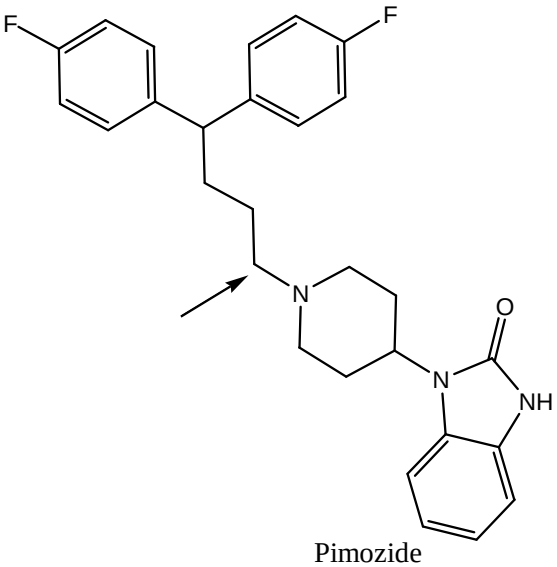


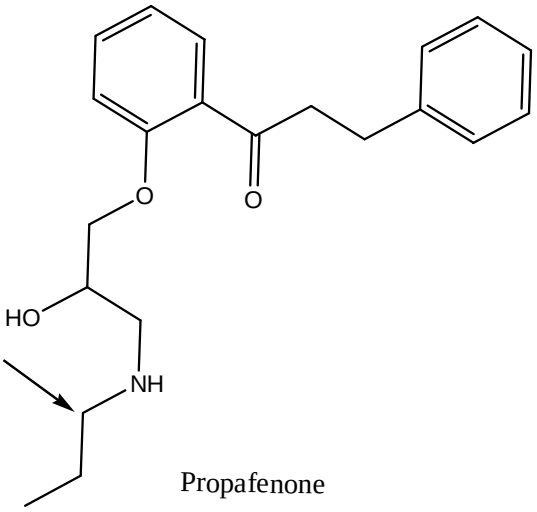
Lilopristone



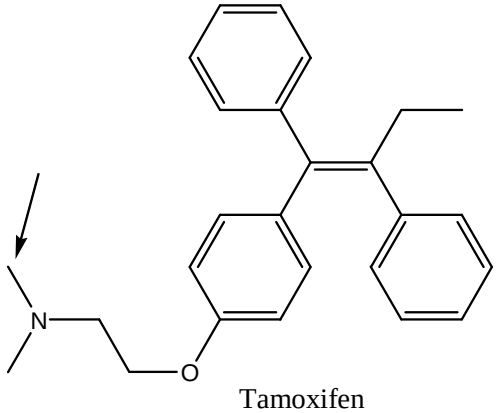
Onapristone



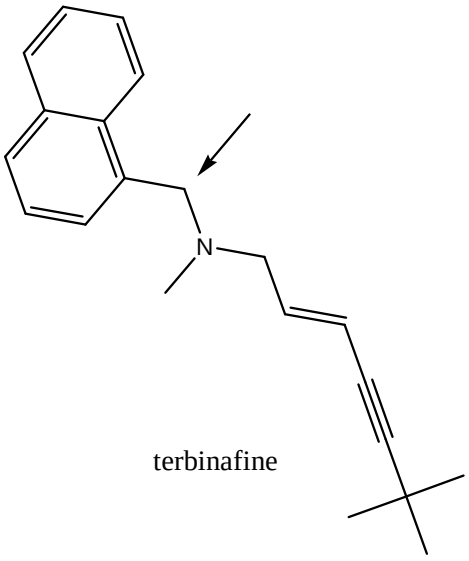
Pimozide



Propafenone



Tamoxifen



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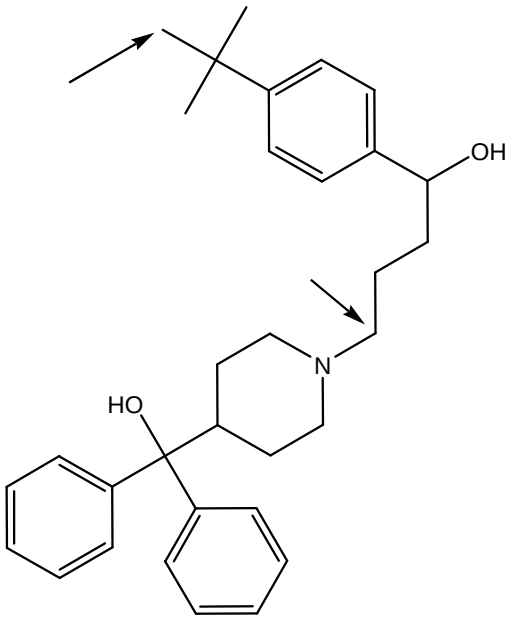
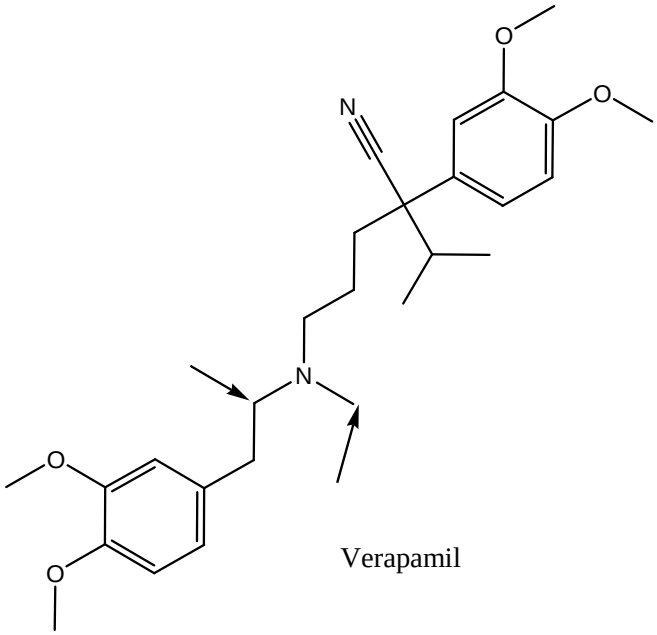


Terfinadine



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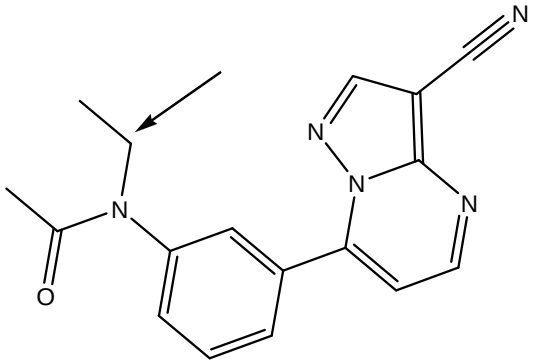
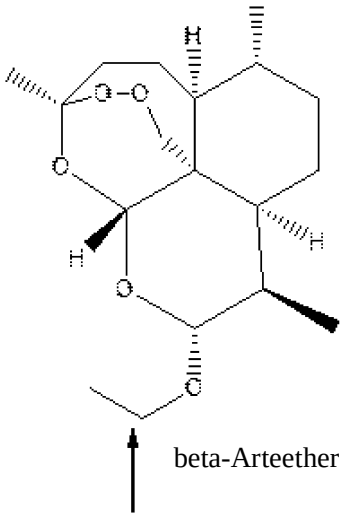


Zaleplon



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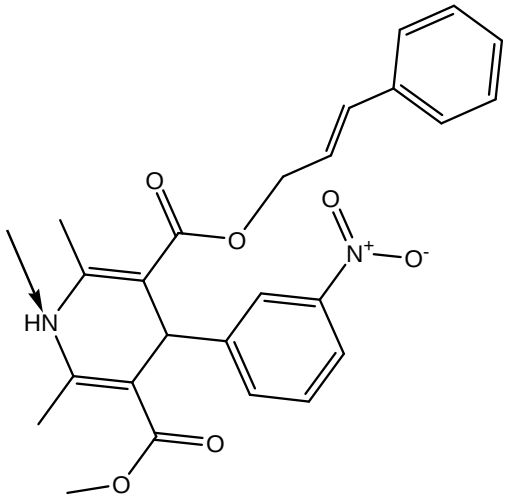
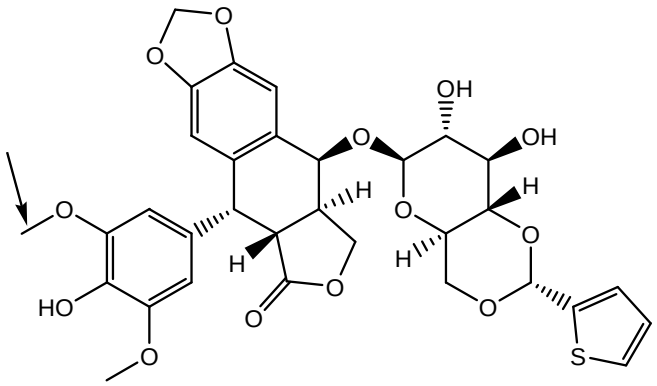
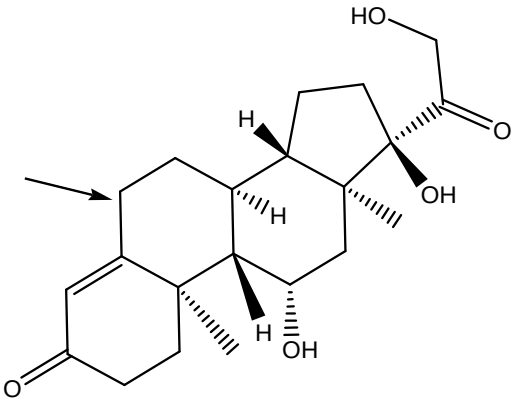


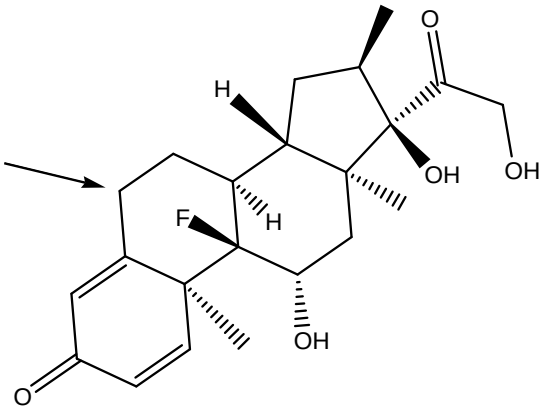
Pranidipine



Teniposide



Cortisol



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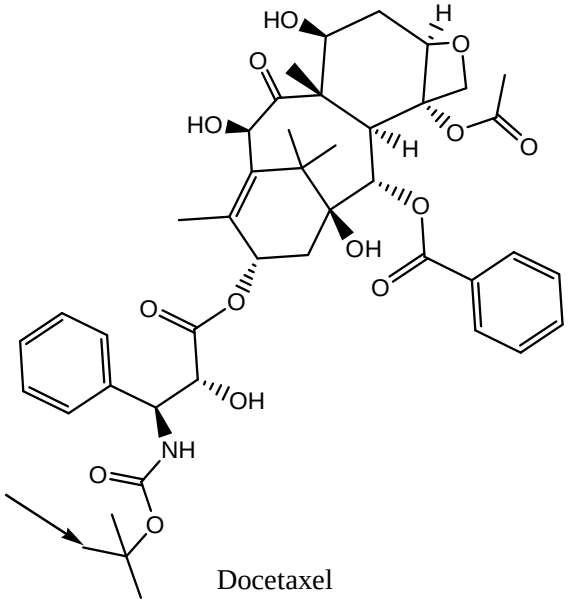

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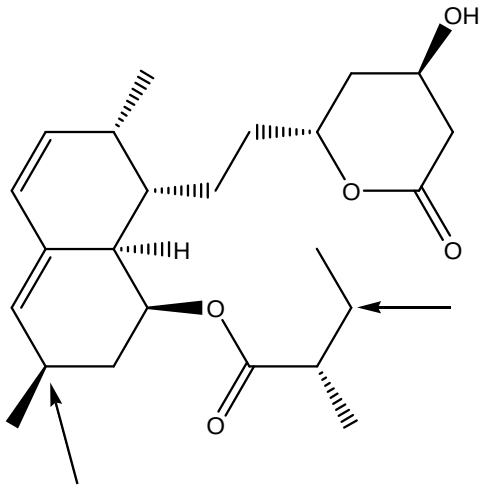
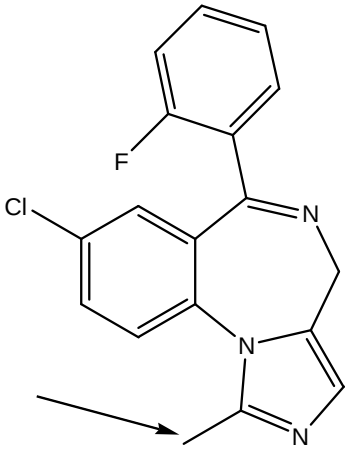
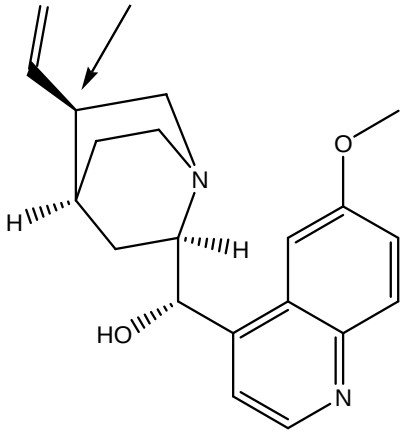


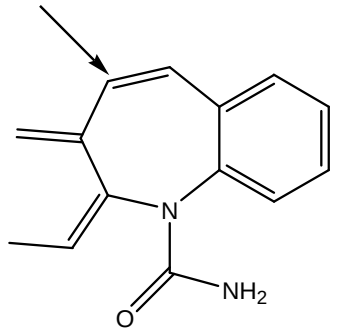
Lovastatin



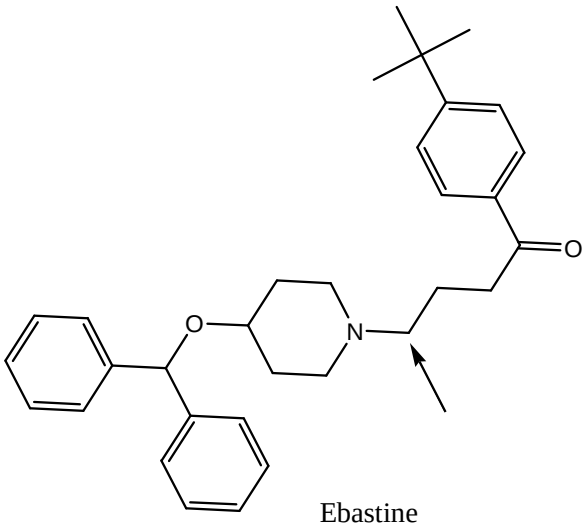
Midazolam



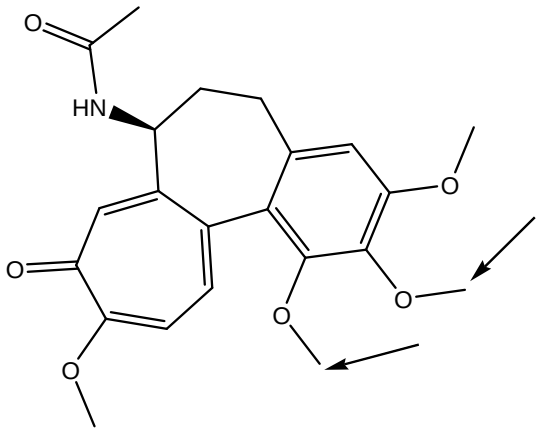
Quinidine



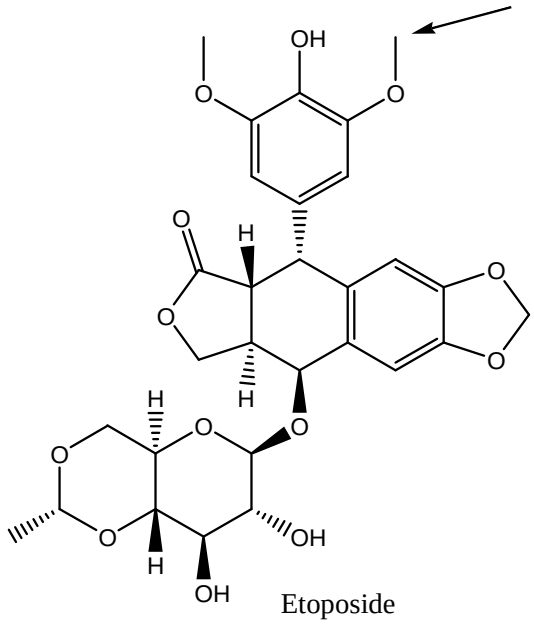
Carbamazepine



Ebastine



Colchicine



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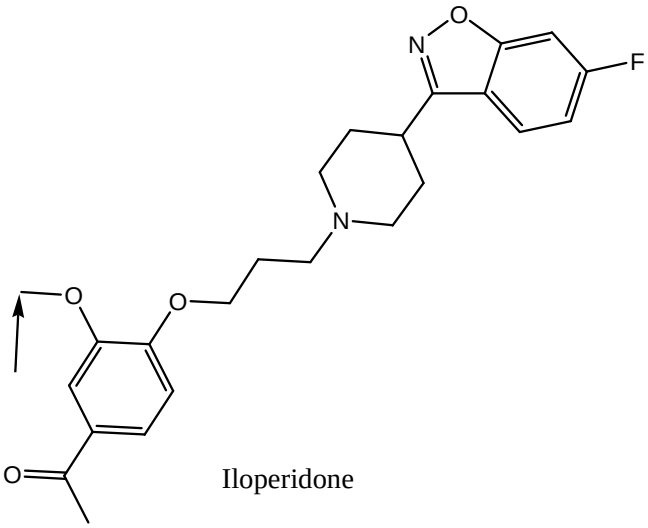
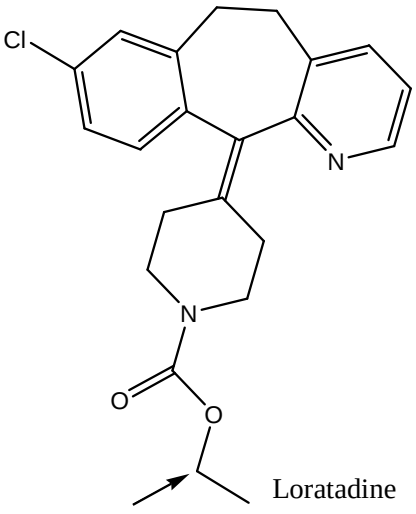
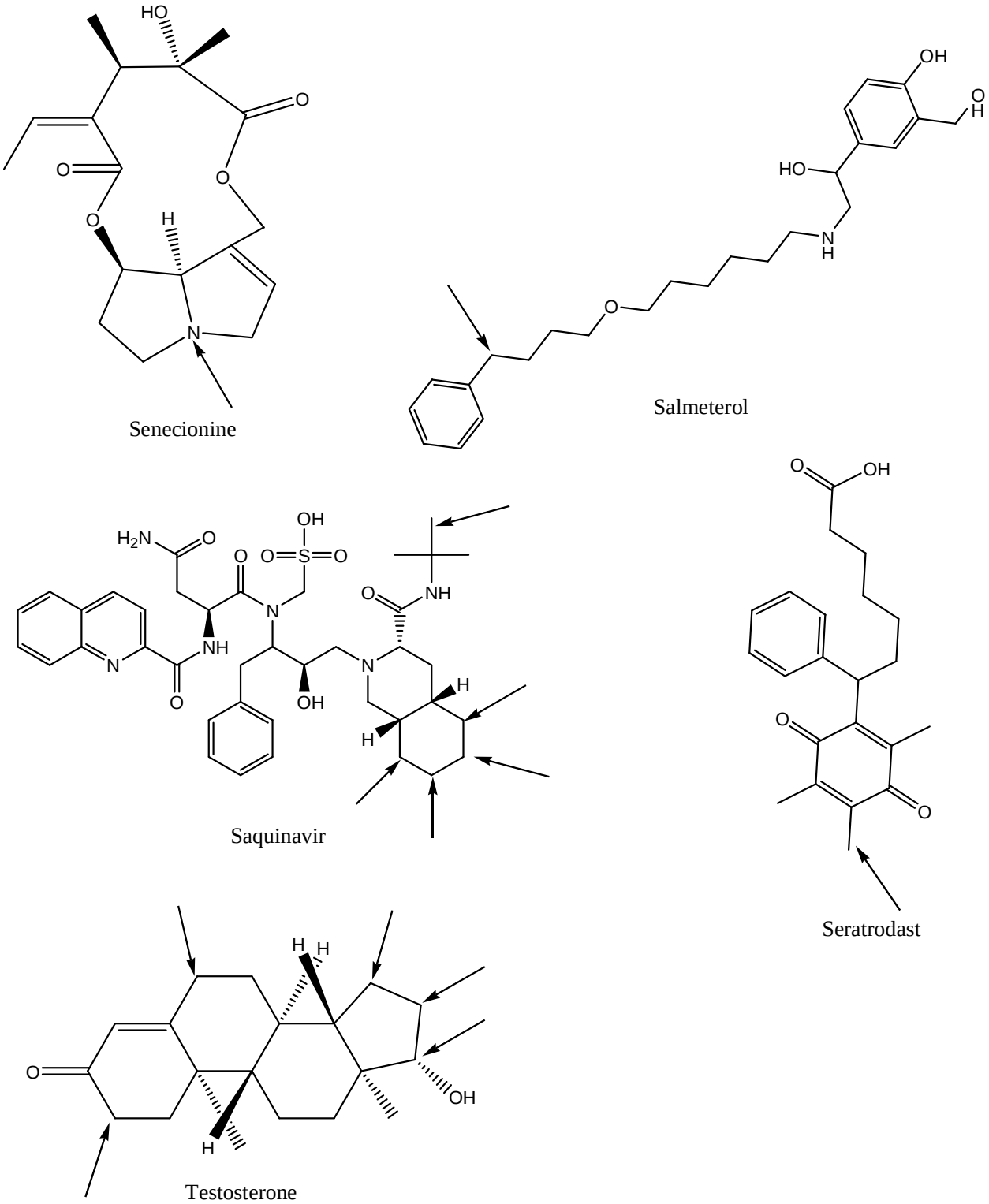


Iloperidone



Loratadine



Supplementary Figure 5: 2D representations of 47 CYP3A4 substrates. SOM of these substrates are predicted by arrows.