Metabolic profiles summary

Legends:

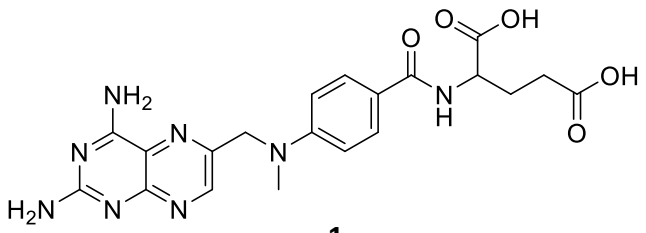
- Metabolite formed by **biomimetic** transformation at **pH 2.7**
- Metabolite formed by **biomimetic** transformation at **pH 4.5**
- Metabolite formed by **biomimetic** transformation at **pH 6.5**
- Metabolite formed by **biomimetic** transformation at **pH 7.4**
- Metabolite formed by **in vitro/in vivo biotransformation**

Átnézve

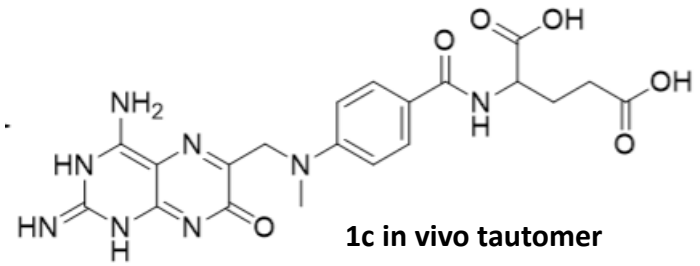
Kész

Problémás

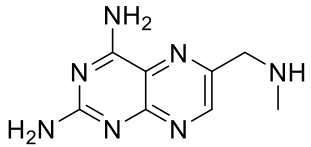
Amethopterin/Methotrexate **(1)** - **Biomimetic transformation**



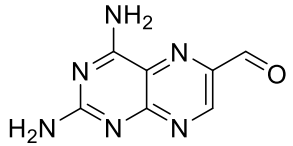
1
tR: 3.65
m/z: 455 (HPLC-MS)
m/z: (HRMS)



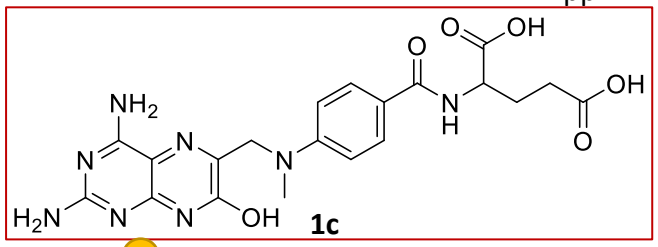
1c in vivo tautomer



1a
tR: 1.06
m/z: 206 (HPLC-MS)
m/z: 206.0742(HRMS)
deltam: -0.0412
ppm: -199.9



1b
tR: 1.34
m/z: 191 (HPLC-MS)
m/z: 191.0638(HRMS)
deltam: -0.0281
ppm: -147.1



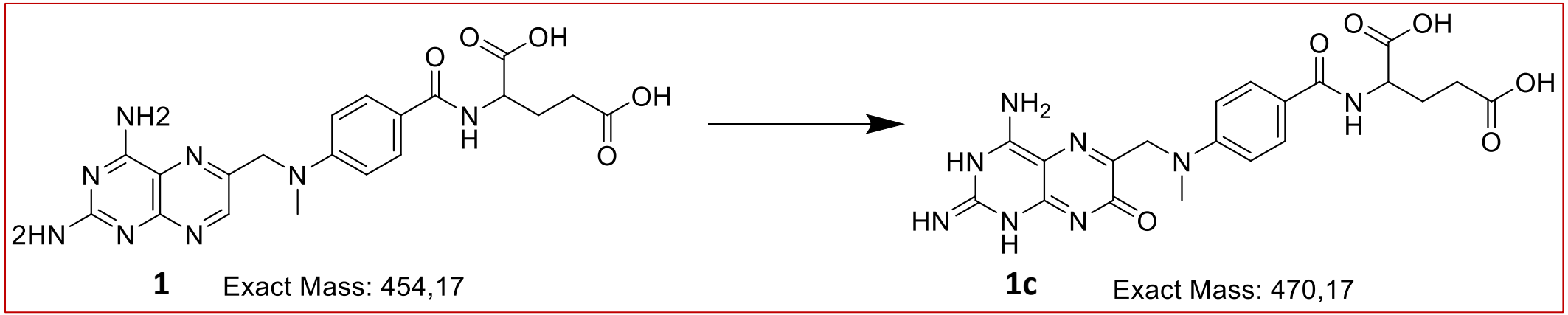
1c
tR: 3.02
m/z: 469 (HPLC-MS)
m/z: 469.1495(HRMS)
deltam: -0.0089
ppm: -19.0

1d
tR: 5.65
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	59.4	51.3
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			●	●	●	●	●	●	●	●
1a	1.06	-249	0	0	0	0	14.5	19.5	0	0
1b#	1.34	-264	0	0	0	0	**72.8**	**45.3**	27.6	0
1c*	3.02	+14	0	0	0	0	0	**24.2**	0	14.0
1d	5.65	NI	0	0	0	0	12.7	11.1	0	0

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non ionizable in positive mode of ESI

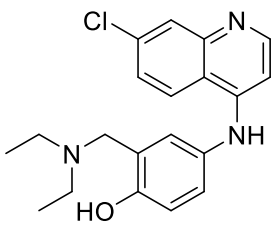
Amethopterin **(1)** – **in vitro/in vivo biotransformation**



https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/011719s125lbl.pdf

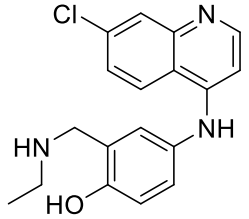
A metabolizmus nagyon kis mértékű és a metabolit 3-5-ször alacsonyabb az oldhatósága.

Amodiaquine **(2)** – **Biomimetic transformation**

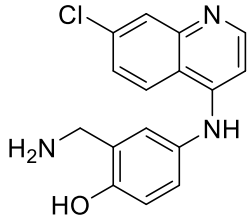


2
tR: 3.04
m/z: 356 (HPLC-MS)
m/z: (HRMS)

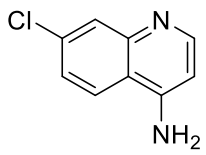
Primer v konszekutív reakció
2 ox -> 2d hidrl -> 2b (2b nem ox metabolit,
általánosságban kinonon keresztül)
milyen mechanizmus
csak azt amihez van szerkezetünk
Valahogy táblázatba
hanyadik generációs metabolit
artifical metabolit (metanol beépülése)



2i

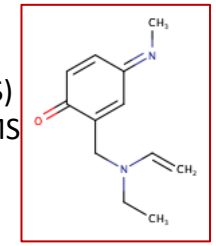


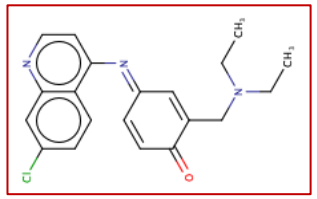
2a
tR: 2.88
m/z: 299 (HPLC-MS)
m/z: (HRMS)



2b
tR: 3.34
m/z: 179 (HPLC-MS)
m/z: 179.0374(HRMS)
deltam: -0.0002
ppm: -1.1

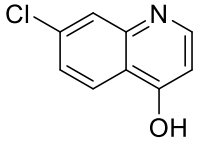
2c
tR: 3.62
m/z: 376 (HPLC-MS)
m/z: 376.1344 (HRMS





2d
tR: 4.20
m/z: 354 (HPLC-MS)
m/z: 354.1388(HRMS)
deltam: 0.0015
ppm: 4.2

2e
tR: 4.74
m/z: - (HPLC-MS)
m/z: (HRMS)



2f
tR: 5.32
m/z: 180 (HPLC-MS)
m/z: 180.0363(HRMS)
deltam: 0.0147
ppm: 81.7

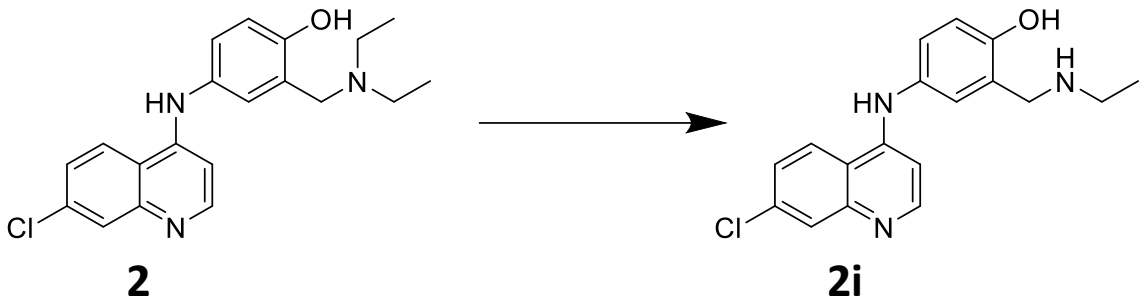
2g
tR: 6.12
m/z: 205 (HPLC-MS)
m/z: 205,0740(HRMS)
deltam: -0.0601
ppm: -293.1

2h
tR: 6.24
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	33.7	87.5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
2a	2.88	-57	0	0	0	0	0	0	0	11.7
2b#	3.34	-177	0	0	0	0	**57.2**	**61.1**	0	**57.4**
2c	3.62	+20	0	0	0	0	16.9	0	0	6.7
2d	4.20	-2	0	0	0	0	0	0	25.7	0
2e	4.74	NI	0	0	0	0	0	26.3	0	5.3
2f	5.32	-176	0	0	0	0	12.4	0	0	0
2g	6.12	-151	0	0	0	0	0	12.6	0	0
2h	6.24	NI	0	0	0	0	13.5	0	0	0

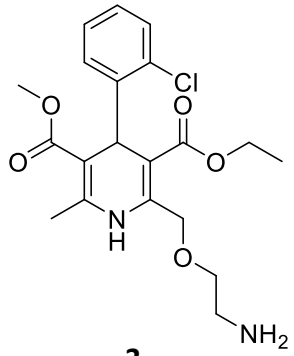
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Amodiaquine **(2)** – in vitro/ in vivo biotransformation

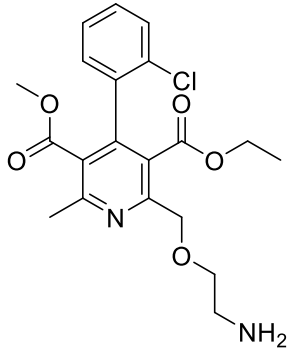


https://www.tandfonline.com/doi/abs/10.3109/00498259509061845

Amlodipine **(3)** - **Biomimetic transformation**



3
tR: 6.10
m/z: 409 (HPLC-MS)
m/z: (HRMS)

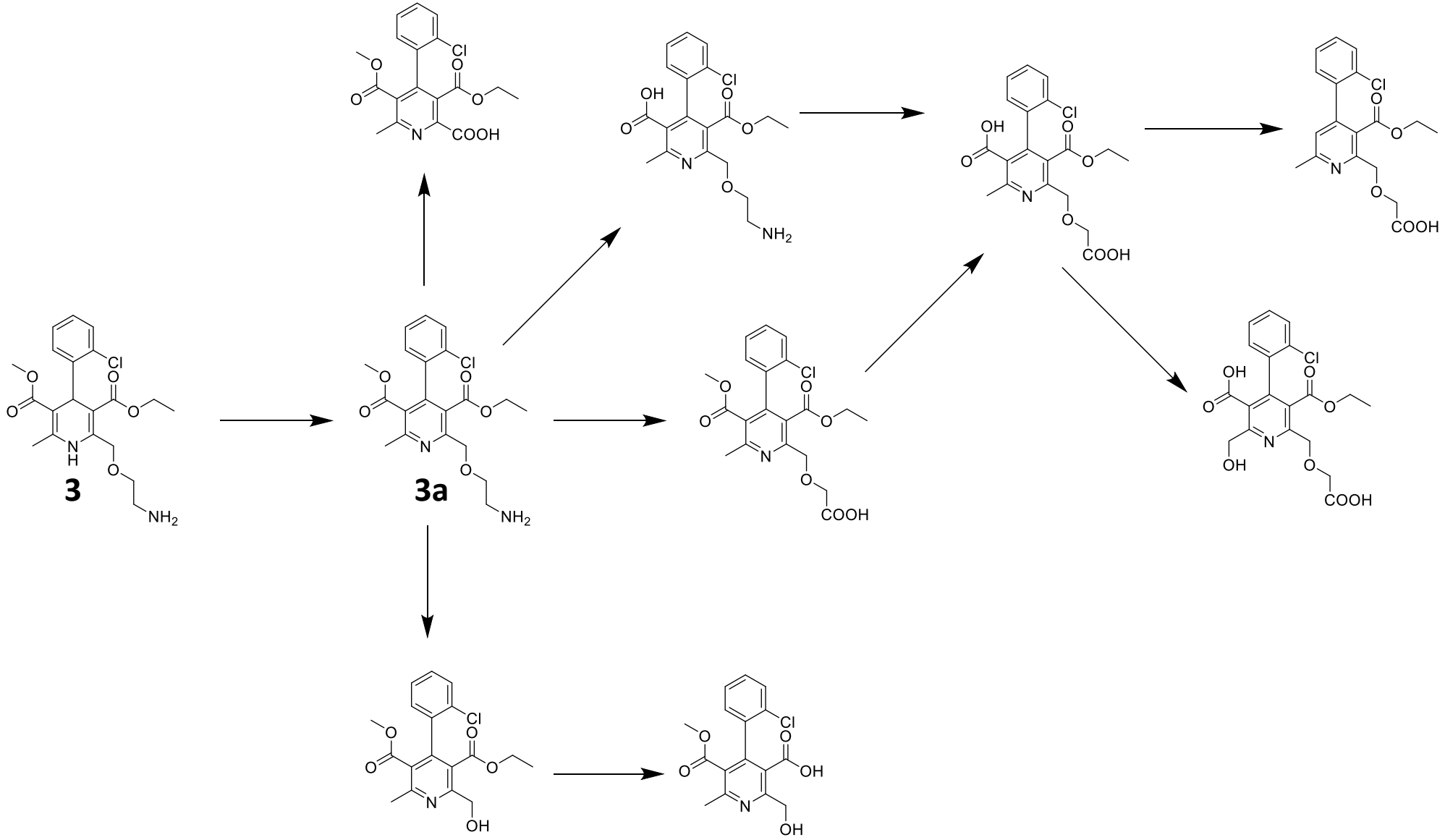


3a
tR: 5.60
m/z: 407 (HPLC-MS)
m/z: 407.2231(HRMS)
deltam: 0.0857
ppm: 210.4

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	5.6	0	100	100	100	38.9
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
3a*	5.60	-2	0	0	**9.4**	0	**100**	**100**	**100**	21.7

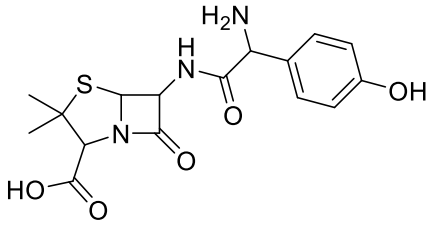
***in vivo/in vitro metabolite formed by biotransformation**
Non biomimetic metabolite

Amlodipine (**3**) - **in vitro/ in vivo biotransformation**

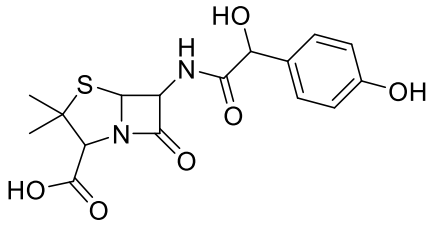


https://www.tandfonline.com/doi/abs/10.3109/00498258809041660

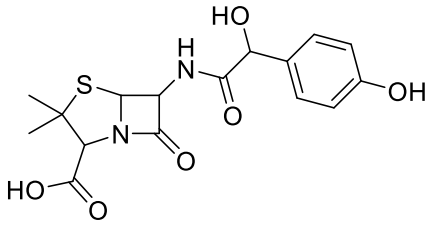
Amoxicillin **(4)** - **Biomimetic transformation**



4
tR: 3.10
m/z: 366 (HPLC-MS)
m/z: (HRMS)



4a
tR: 2.84
m/z: 367 (HPLC-MS)
m/z: (HRMS)



4b
tR: 2.94
m/z: 367 (HPLC-MS)
m/z: (HRMS)

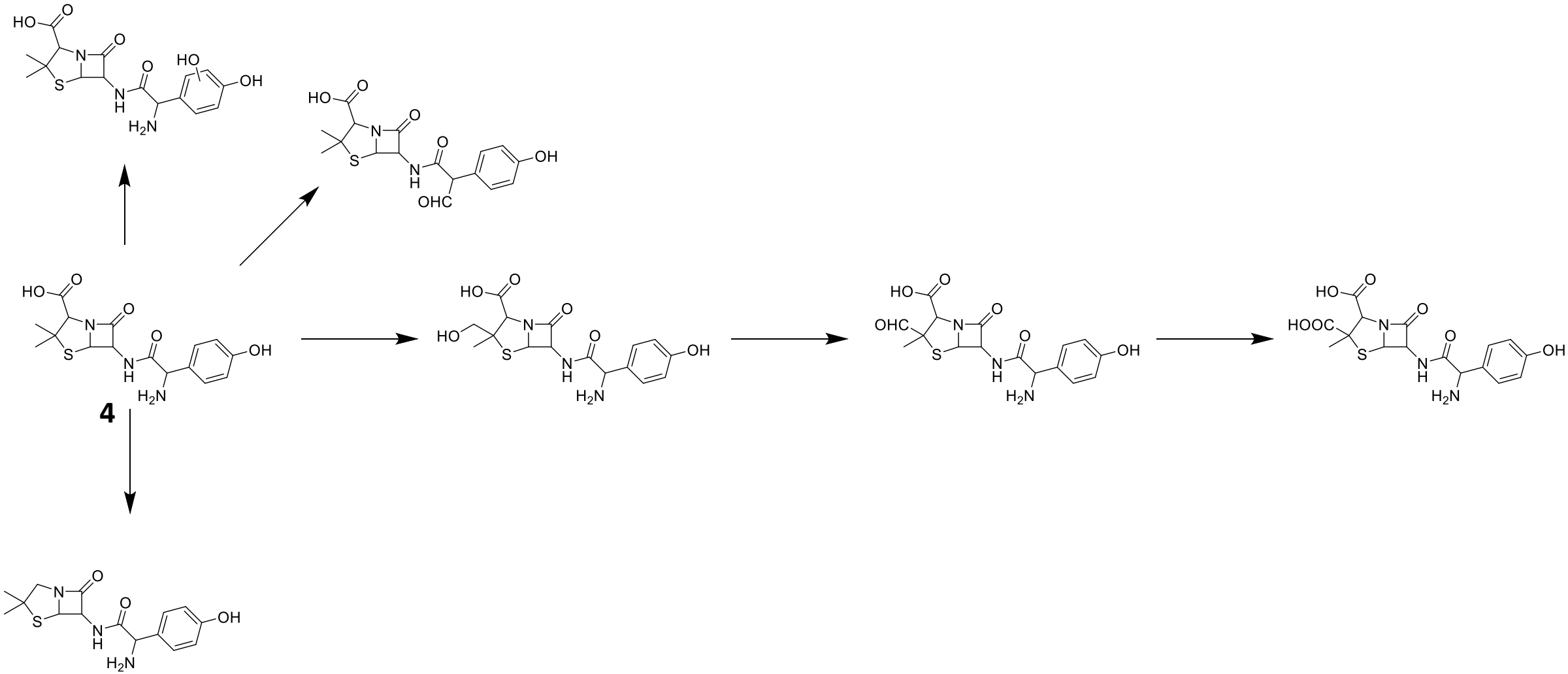
4c
tR: 4.84
m/z: 160/453 (HPLC-MS)
m/z: (HRMS)

(+)-ban látszik 219.1725; 157.0865; 159.1015
(-)-ban látszik 78.966;

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	100	83.7	100	55.1	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
4a[#]	2.84	+1	0	0	0	**23.8**	0	0	0	**61.0**
4b	2.94	+1	0	0	0	**18.1**	0	0	0	14.5
4c	4.84	NI	0	0	0	**58.1**	0	0	0	24.5

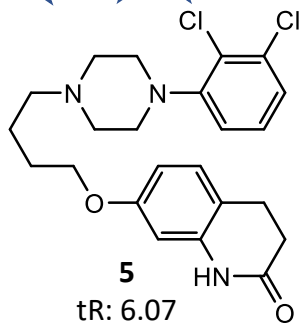
[#] **Major biomimetic metabolite**
Non biomimetic metabolite
NI: Non ionizable in positive mode of ESI

Amoxicillin **(4)** - in vitro/ in vivo biotransformation

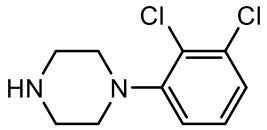


https://link.springer.com/article/10.1007/s10337-014-2648-2

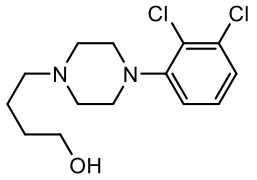
Aripiprazole **(5)** - Biomimetic transformation



5
tR: 6.07
m/z: 448 (HPLC-MS)
m/z: (HRMS)

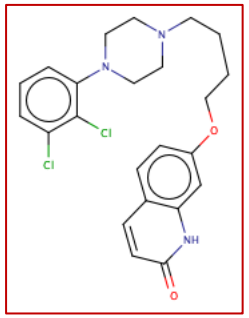


5b
tR: 4.85
m/z: 231 (HPLC-MS)
m/z: 231.0464(HRMS)
deltam: 0.0008
ppm: 3.5

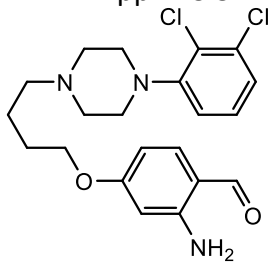


5c
tR: 4.99
m/z: 303 (HPLC-MS)
m/z: 303.1051(HRMS)
deltam: 0.0020
ppm: 6.6

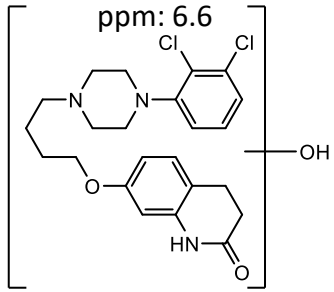
5a
tR: 3.45
m/z: - (HPLC-MS)
m/z: (HRMS)



5d
tR: 5.90
m/z: 446 (HPLC-MS)
m/z: 446.1407(HRMS)
deltam: 0.0005
ppm: 1.1



5e
tR: 5.92
m/z: 422 (HPLC-MS)
m/z: 422.1409(HRMS)
deltam: 0.0007
ppm: 1.7



5f
tR: 6.22
m/z: 464 (HPLC-MS)
m/z: 464.1474(HRMS)
deltam: -0,0034
ppm: -7.3

?

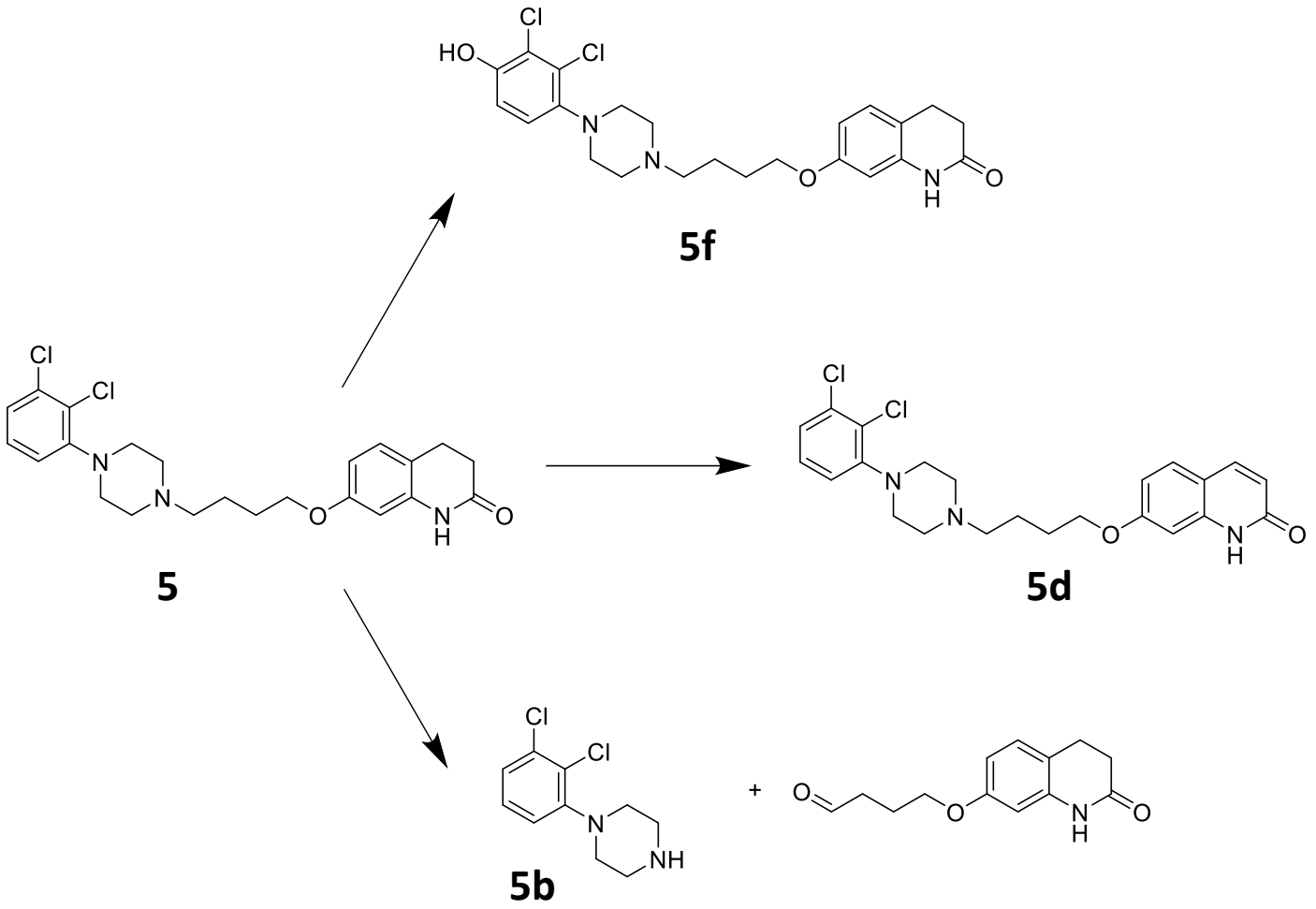
Aromás hidroxiláció

-ban látszik 214.8982

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	98.9	3.7	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
5a	3.45	NI	0	0	0	0	29.2	0	0	0
5b	4.85	-217	0	0	0	0	0	12.2	1.6	0
5c#	4.99	-145	0	0	0	0	**43.7**	0	0	0
5d*	5.90	-2	0	0	0	0	**11.7**	0	0	0
5e	5.92	-26	0	0	0	0	0	6.2	2.1	0
5f*	6.22	+16	0	0	0	0	0	**4.3**	0	0

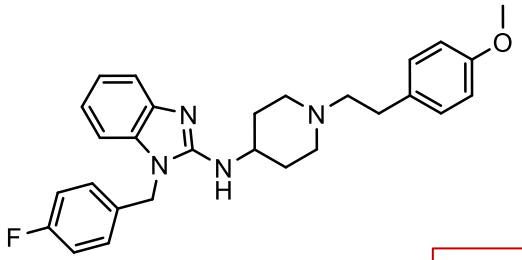
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Aripiprazole **(5)** - in vitro/ in vivo biotransformation

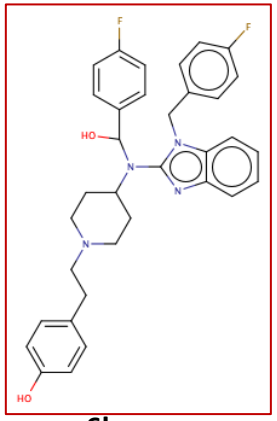


https://link.springer.com/article/10.2165/11208320-000000000-00000#Sec3

Astemizole **(6)** - **Biomimetic transformation**



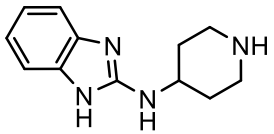
6
tR: 4.57
m/z: 459 (HPLC-MS)
m/z: (HRMS)



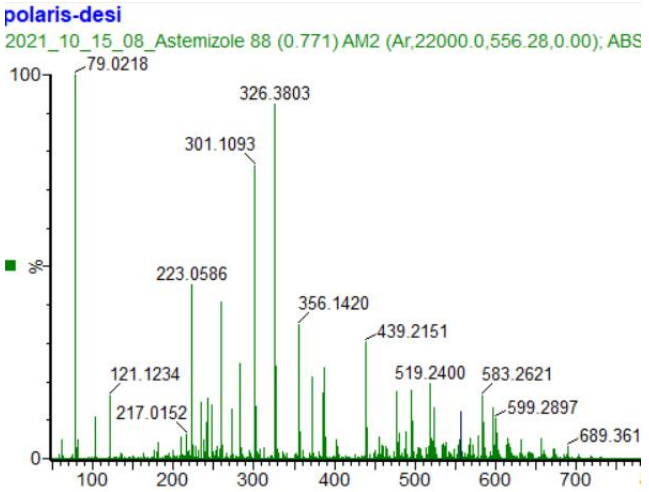
6a
tR: 4.65
m/z: - (HPLC-MS)
m/z: (HRMS)

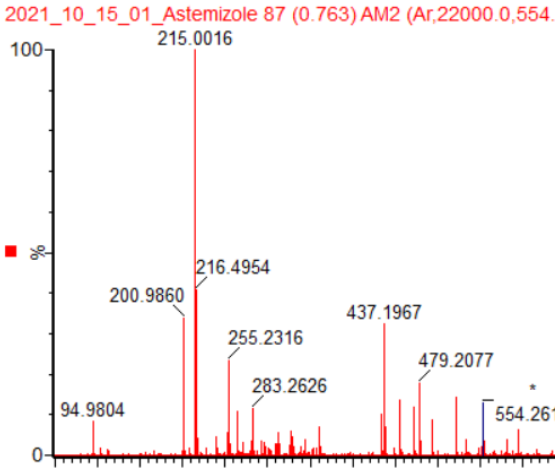
6b
tR: 5.14
m/z: 569 (HPLC-MS)
m/z: 569.2617(HRMS)
deltam: -0,0111
ppm: -19.5

6c
tR: 5.62
m/z: 439 (HPLC-MS)
m/z: 439.2152(HRMS)



6d
tR: 7.02
m/z: 216 (HPLC-MS)
m/z: 216.1392(HRMS)
deltam: 0,0017
ppm: 7.9

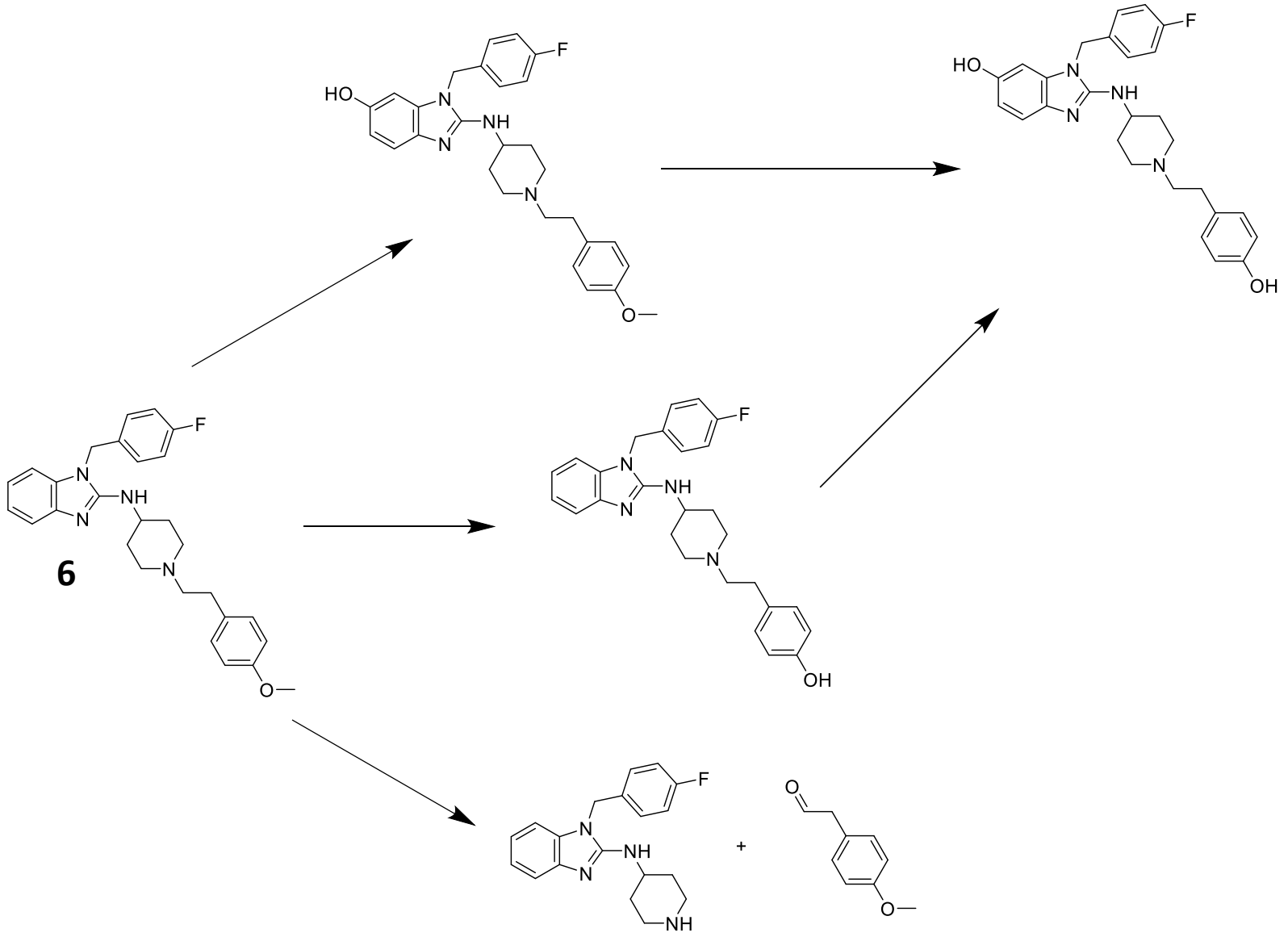




			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	96.3	100	0	38.1
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
6a	4.65	NI	0	0	0	0	17.7	0	0	0
6b	5.14	+110	0	0	0	0	13.1	0	0	0
6c	5.62	-20	0	0	0	0	24.1	0	0	0
6d#	7.02	-243	0	0	0	0	31.4	**100**	0	9.8

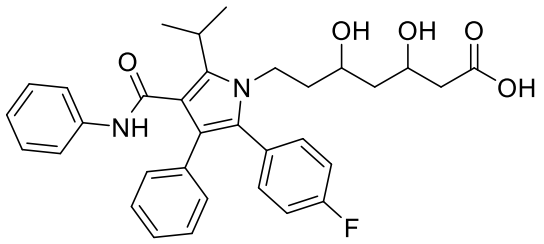
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Astemizole **(6)** - in vitro/ in vivo biotransformation

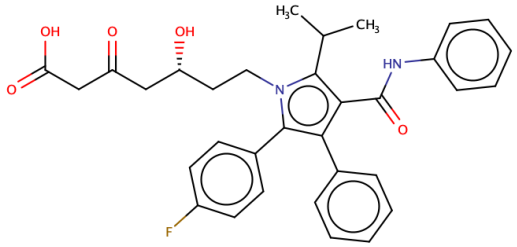


https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2125.2001.01292.x

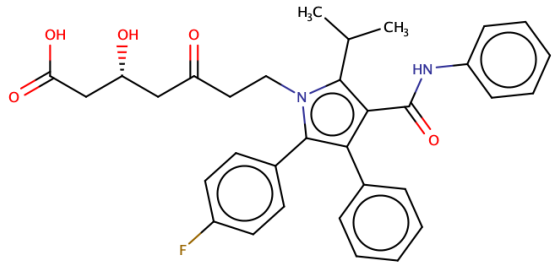
Atorvastatin **(7)** - **Biomimetic transformation**



7
tR: 9.62
m/z: 559 (HPLC-MS)
m/z: (HRMS)

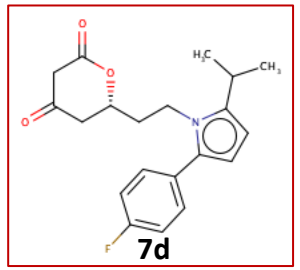


and



7a
tR: 9.60
m/z: 557 (HPLC-MS)
m/z: 557.2642(HRMS)
deltam: 0.0190
ppm: 3.4

7b
tR: 9.80
m/z: 557 (HPLC-MS)
m/z: 557.2642(HRMS)
deltam: 0.0190
ppm: 3.4



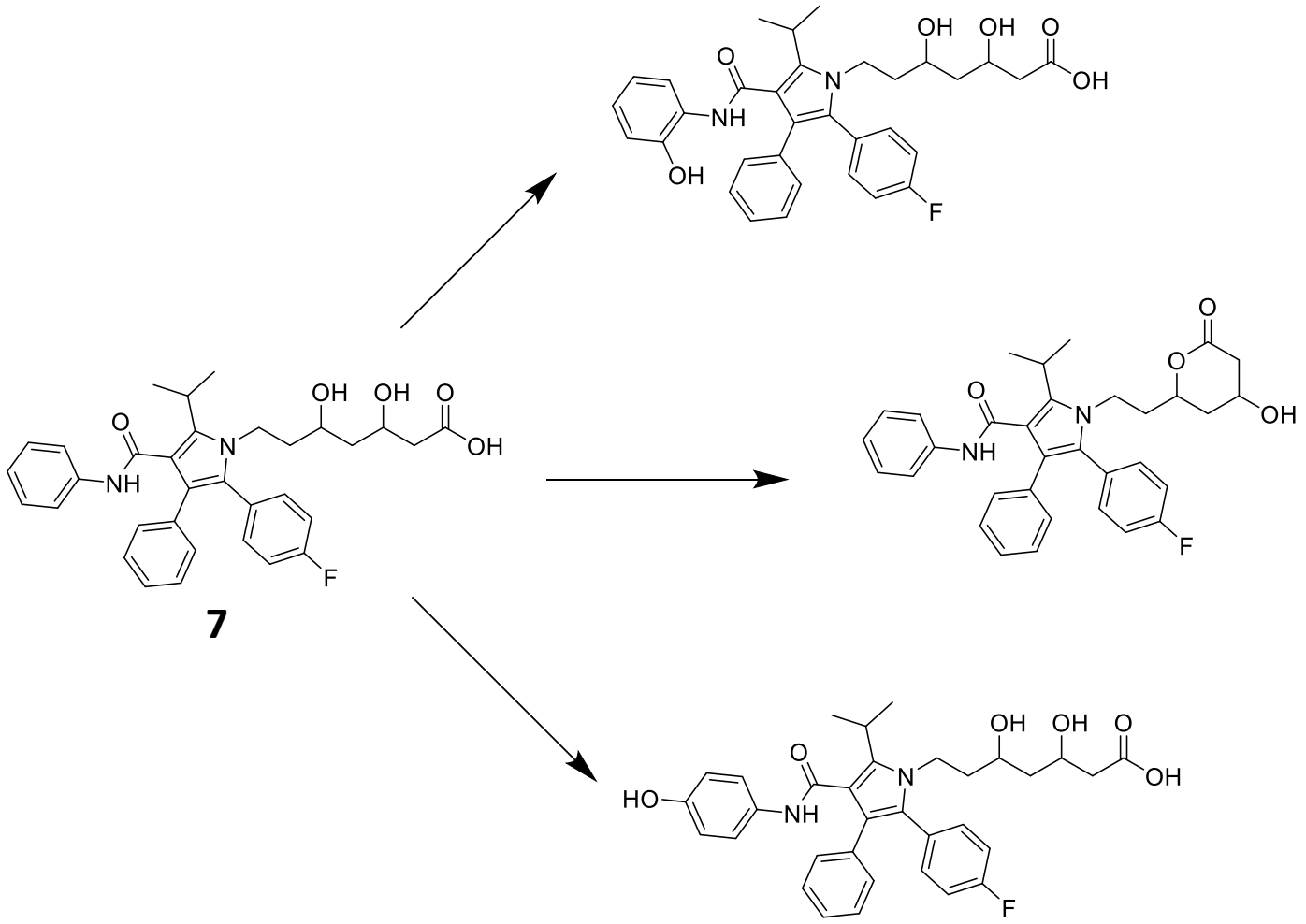
7d
tR: 11.22
m/z: 344 (HPLC-MS)
m/z: 344.1060 (HRMS)
deltam: -0,0602
ppm: -174,9

7c
tR: 10.27
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
7a#	9.60	-2	0	0	0	0	8.7	**68.2**	0	0
7b#	9.80	-2	0	0	0	0	**64.9**	0	0	0
7c	10.27	NI	0	0	0	0	19.7	0	0	0
7d	11.22	-215	0	0	0	0	0	18.3	0	0

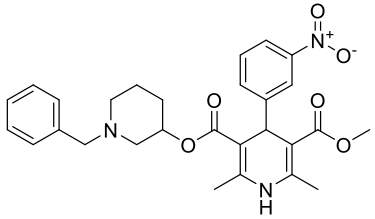
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Atorvastatin **(7)** - in vitro/ in vivo biotransformation

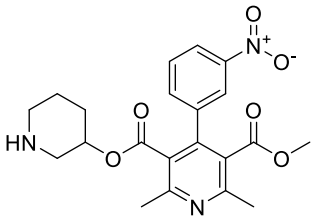


https://www.tandfonline.com/doi/abs/10.1080/00498250802334391

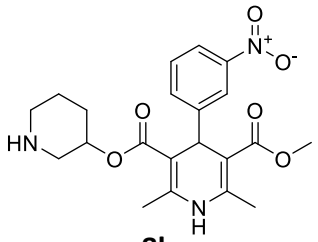
Benidipine **(8)** - **Biomimetic transformation**



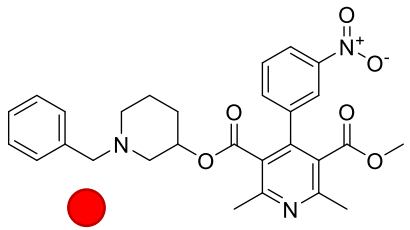
8
tR: 6.35
m/z: 506 (HPLC-MS)
m/z: (HRMS)



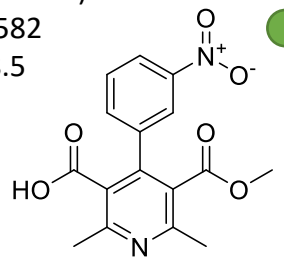
8a
tR: 5.20
m/z: 414 (HPLC-MS)
m/z: 414.1638(HRMS)
deltam: -0,0027
ppm: -6.5



8b
tR: 5.45
m/z: 416 (HPLC-MS)
m/z: 416.9404(HRMS)
deltam: 0.7582
ppm: 1818.5



8c
tR: 6.25
m/z: 504 (HPLC-MS)
m/z: 504.2167(HRMS)
deltam: 0.0032
ppm: 6.3



8e
tR: 6.68
m/z: 331 (HPLC-MS)
m/z: 331.0928(HRMS)
deltam: -0.0002
ppm: -0.6

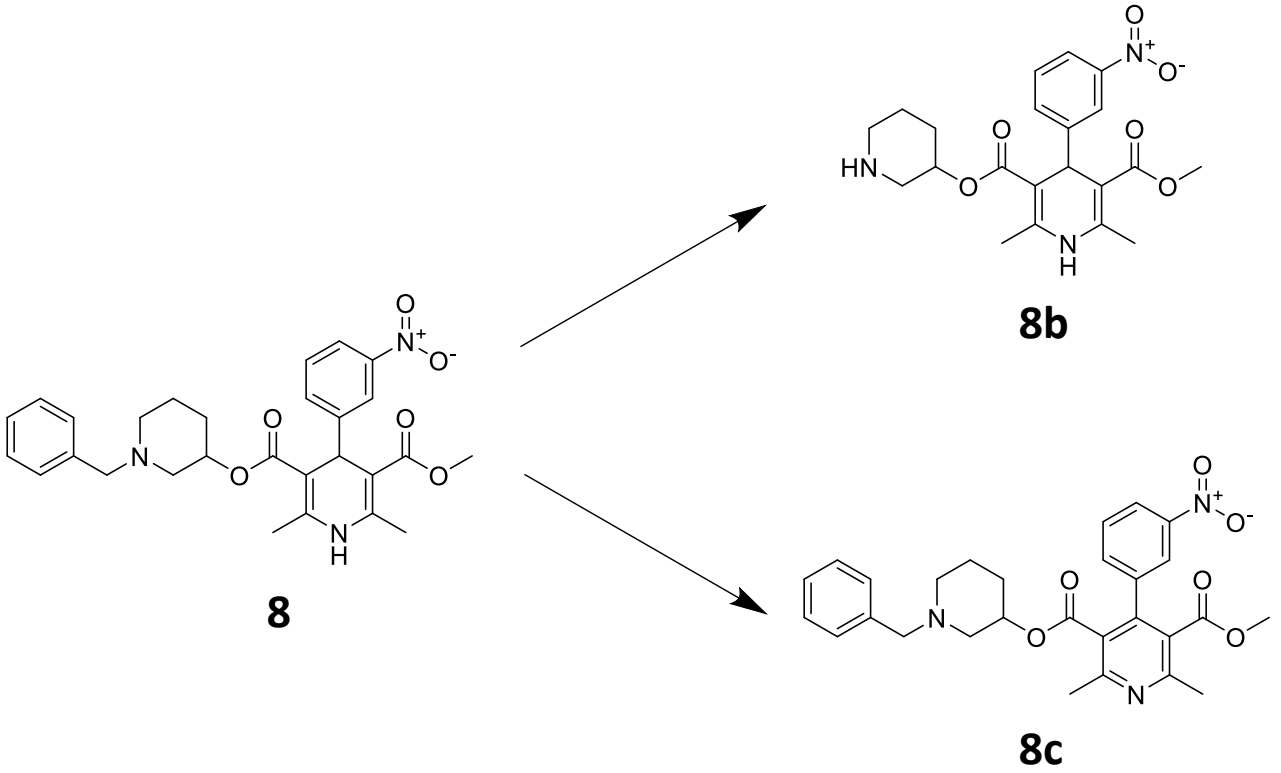
8d
tR: 6.47
m/z: 479 (HPLC-MS)
m/z: 479,1836(HRMS)
deltam:

8f
tR: 7.14
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	16.4	21.0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
8a#	5.20	-92	0	0	0	0	36.5	58.4	0	36.5
8b*	5.45	-90	0	0	0	0	0	0	0	2.7
8c*#	6.25	-2	0	0	0	0	43.6	23.1	13.4	5.3
8d	6.47	-27	0	0	0	0	10.7	0	0	0
8e	6.68	-175	0	0	0	0	0	5.7	0	0
8f	7.14	NI	0	0	0	0	0	12.9	0	0

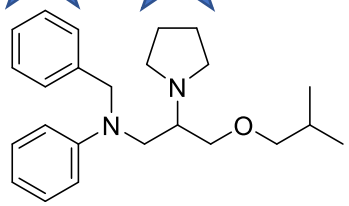
*in vivo/in vitro metabolite formed by biotransformation
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Benidipine **(8)** - in vitro/ in vivo biotransformation

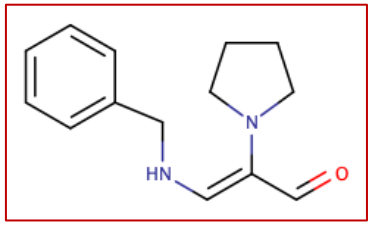


https://dmd.aspetjournals.org/content/35/9/1518

Bepridil **(9)** - **Biomimetic transformation (I)**



9
tR: 7.54
m/z: 367 (HPLC-MS)
m/z: (HRMS)

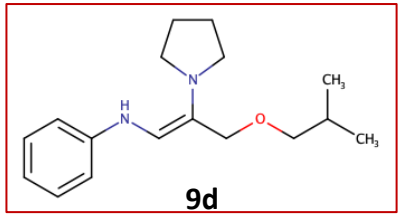


9a
tR: 4.85
m/z: 231 (HPLC-MS)
m/z: 231.0309(HRMS)
deltam: -0.1188
ppm: -514.2

9b
tR: 4.99
m/z: 303 (HPLC-MS)
m/z: 303.1094(HRMS)

9c
tR: 5.42
m/z: 494 (HPLC-MS)
m/z: 494.5681(HRMS)

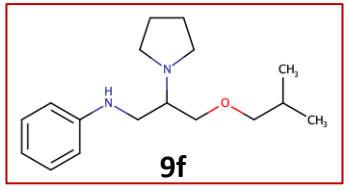
ox. alifás kettőskötés kialak.



9d
tR: 5.87
m/z: 275 (HPLC-MS)
m/z: 275.2110(HRMS)
deltam: -0.0013
ppm: -4.7

9e
tR: 5.90
m/z: 446 (HPLC-MS)
m/z: 445.9371(HRMS)

Debenzil (N-dealk)

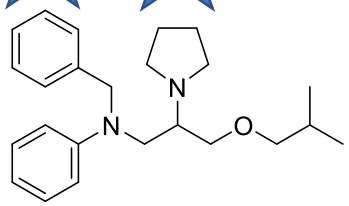


9f
tR: 6.00
m/z: 277 (HPLC-MS)
m/z: 277.2286(HRMS)
deltam: 0.0006
ppm: 2.2

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	100	70.8
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
9a	4.85	-166	0	0	0	0	8.32	11.4	0	0
9b#	4.99	-64	0	0	0	0	**70.6**	0	0	0
9c	5.42	+127	0	0	0	0	6.1	0	0	0
9d	5.87	-92	0	0	0	0	0	0	9.4	15.0
9e	5.90	+79	0	0	0	0	15.0	5.3	26.4	0
9f	6.00	-90	0	0	0	0	0	0	0	14.3
9g#	6.07	+81	0	0	0	0	0	**79.9**	0	0
9h#	7.10	NI	0	0	0	0	0	0	27.2	**44.6**
9i#	7.30	-2	0	0	0	0	0	0	**50.2**	0.9

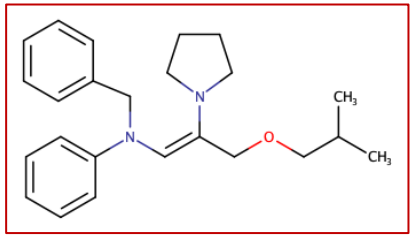
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Bepridil **(9)** - **Biomimetic transformation (II)**



9
tR: 7.54
m/z: 367 (HPLC-MS)
m/z: (HRMS)

ox. alifás kettőskötés kialak.



9g
tR: 6.07
m/z: 448 (HPLC-MS)
m/z: 447.9040(HRMS)

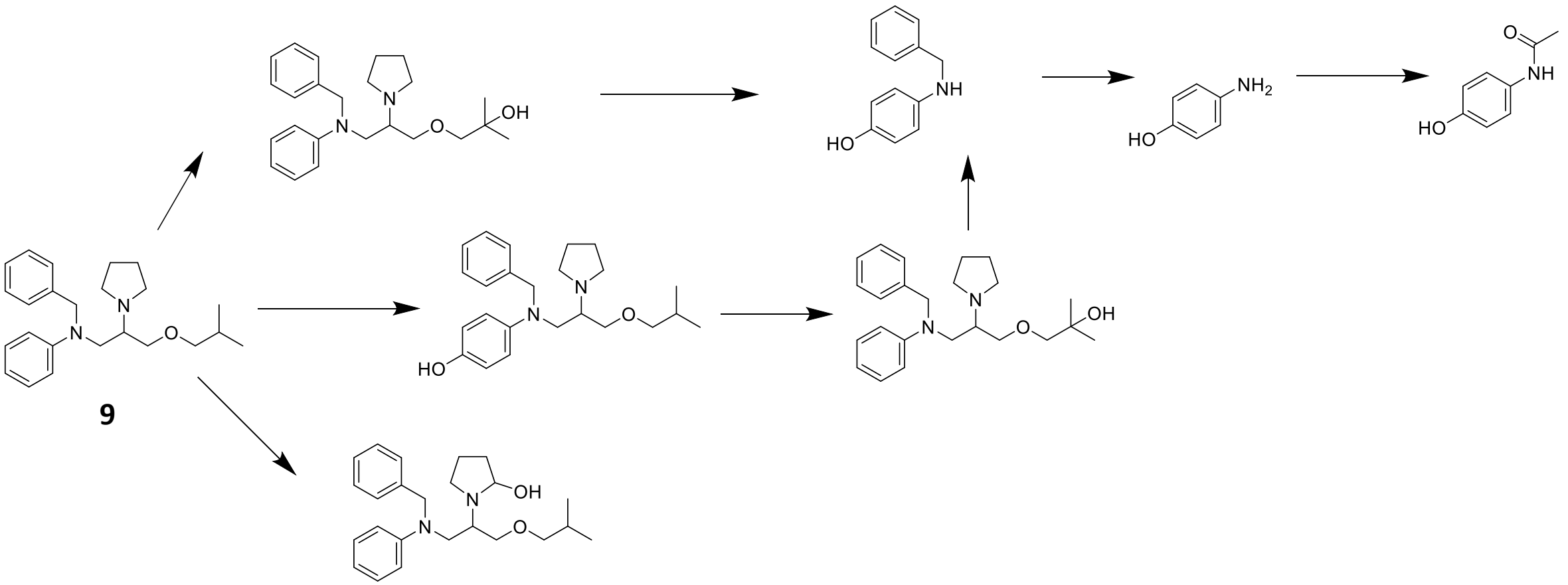
9h
tR: 7.10
m/z: - (HPLC-MS)
m/z: (HRMS)

9i
tR: 7.30
m/z: 365 (HPLC-MS)
m/z: 365.2605(HRMS)
deltam: 0,0012
ppm: 3.3

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	100	70.8
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
9a	4.85	-166	0	0	0	0	8.32	11.4	0	0
9b#	4.99	-64	0	0	0	0	**70.6**	0	0	0
9c	5.42	+127	0	0	0	0	6.1	0	0	0
9d	5.87	-92	0	0	0	0	0	0	9.4	15.0
9e	5.90	+79	0	0	0	0	15.0	5.3	26.4	0
9f	6.00	-90	0	0	0	0	0	0	0	14.3
9g#	6.07	+81	0	0	0	0	0	**79.9**	0	0
9h#	7.10	NI	0	0	0	0	0	0	27.2	**44.6**
9i#	7.30	-2	0	0	0	0	0	0	**50.2**	0.9

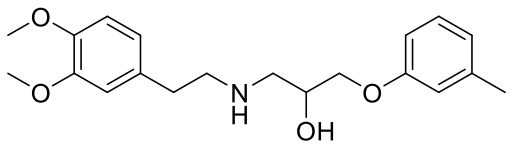
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Bepridil **(9)** - in vitro/ in vivo biotransformation



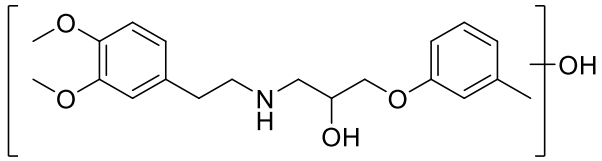
https://www.sciencedirect.com/science/article/abs/pii/0002914985907994
https://dmd.aspetjournals.org/content/16/1/69

Bevantolol **(10)** - **Biomimetic transformation**



10 (**Mw:345**)
tR: 5.43
m/z: 346 (HPLC-MS)
m/z: (HRMS)

Újra megcsinálni?



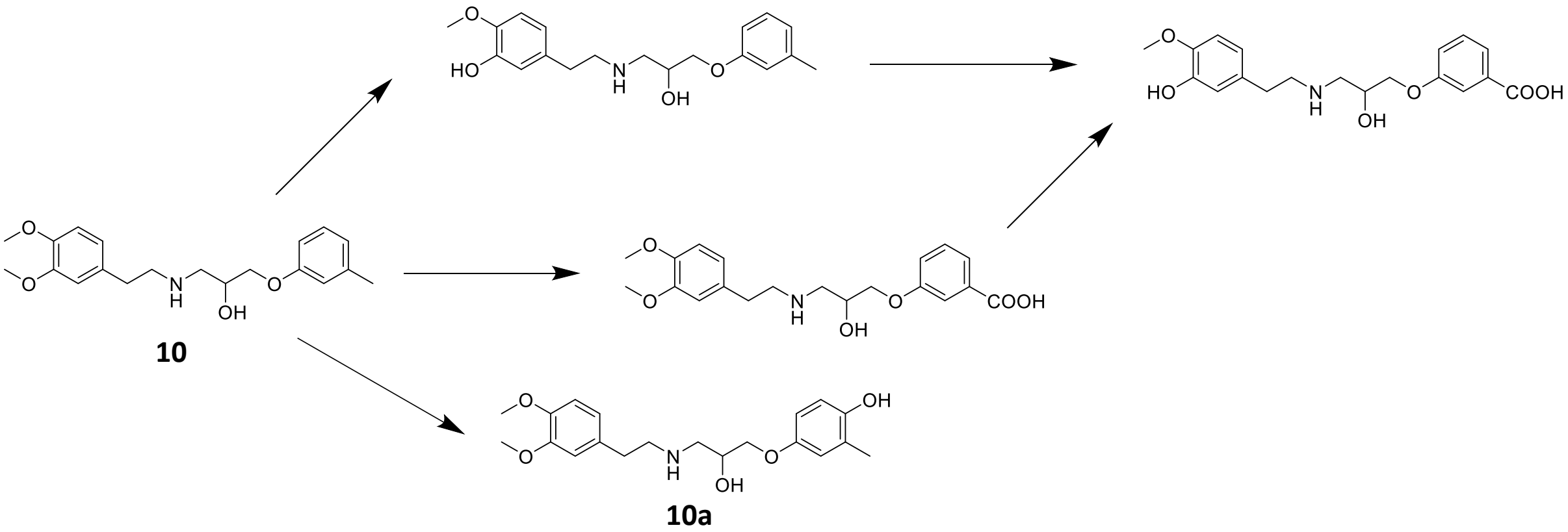
10a
tR: 6.32
m/z: **361**(HPLC-MS)
m/z: 361.1866(HRMS)
deltam: -0.0023
ppm: -6.4

10b
tR: 6.49
m/z: **343** (HPLC-MS)
m/z: 343.2018(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	40	0	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
10a*	6.32	**+15?**	0	0	0	0	**9.4**	0	0	0
10b#	6.49	**-3?**	0	0	0	0	**40.9**	0	0	0

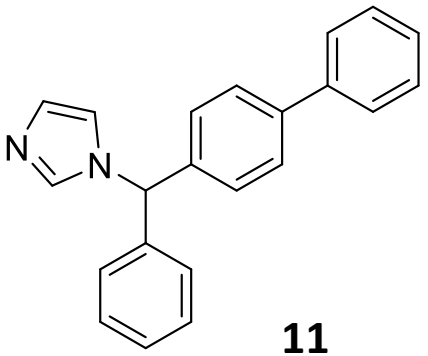
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Bevantolol **(10)** - in vitro/ in vivo biotransformation



https://journals.sagepub.com/doi/abs/10.1177/000331978603700313

Bifonazole **(11)** - **Biomimetic transformation**



11

NO biomimetic transformation

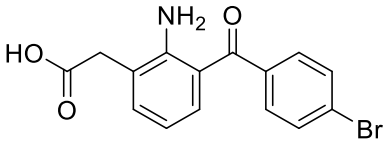
Bifonazole **(11)** - **in vitro/ in vivo biotransformation**

NO Hepatic (in vitro/ in vivo) biotransformation

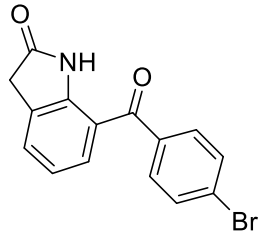
CYP450 inhibition

https://www.sciencedirect.com/science/article/pii/S0009279704000250#FIG4

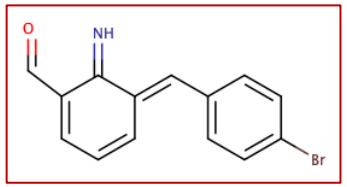
Bromfenac (**12**) - **Biomimetic transformation**



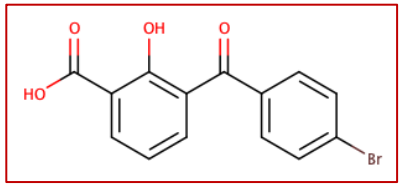
12
tR: 9.55
m/z: 334 (HPLC-MS)
m/z: (HRMS)



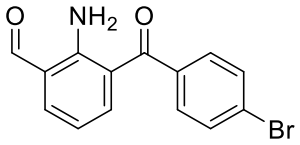
12a
tR: 9.28
m/z: 316 (HPLC-MS)
m/z: 315.9999(HRMS)
deltam: 0.0026
ppm: 8.2



12b
tR: 9.80
m/z: 288 (HPLC-MS)
m/z: 288.0040(HRMS)
deltam: 0.0016
ppm: 5.6



12c
tR: 10.19
m/z: **322** (HPLC-MS)
m/z: 319.9803(-HRMS)
deltam: 0.0119
ppm: 37.2

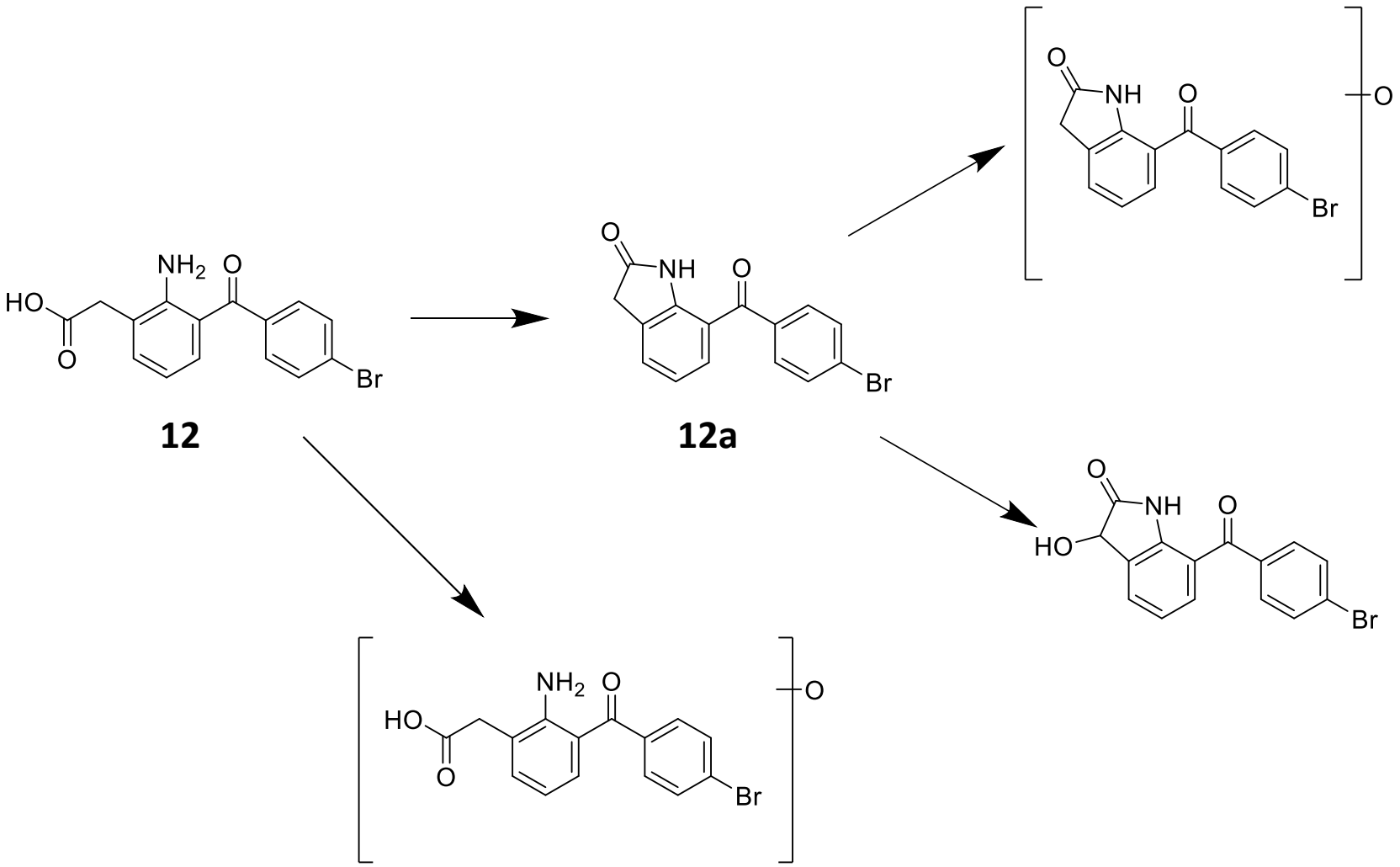


12d
tR: 10.85
m/z: 304 (HPLC-MS)
m/z: 303.9868(HRMS)
deltam: -0.0105
ppm: -34.5

			Non biomimetic				Biomimetic			
Conversion (%)			80.3	0	0	0	100	100	19.2	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
12a*	9.28	-18	**94.0**	0	0	0	34.5	**31.3**	0	0
12b	9.80	-46	0	0	0	0	0	0	7.3	0
12c	10.19	-12	0	0	0	0	0	0	5.1	0
12d#	10.85	-30	0	0	0	0	**65.5**	**68.7**	0	0

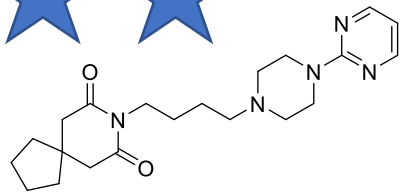
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
Non biomimetic metabolite

Bromfenac (**12**) - in vitro/ in vivo biotransformation

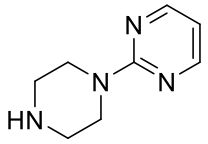


https://pubs.acs.org/doi/10.1021/acs.chemrestox.9b00268

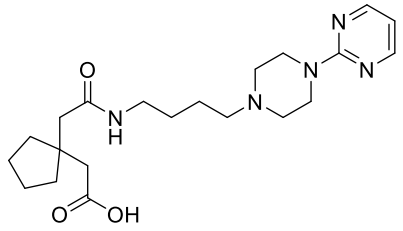
Buspirone (**16**) - **Biomimetic transformation**



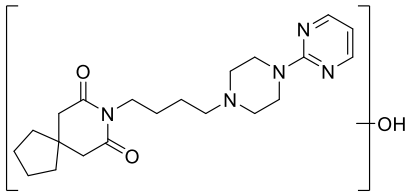
13
tR: 4.97
m/z: 386 (HPLC-MS)
m/z: (HRMS)



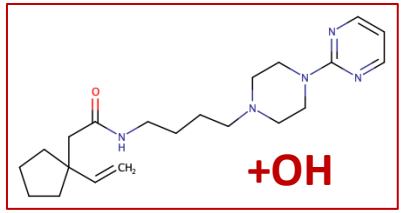
13a
tR: 1.60
m/z: 165 (HPLC-MS)
m/z: 165.1267(HRMS)
deltam. 0.0127
ppm: 76.9



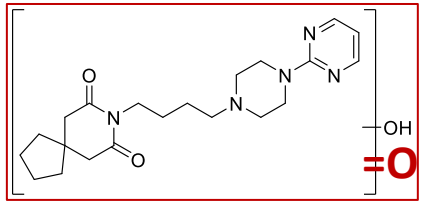
13b
tR: 4.30
m/z: 404 (HPLC-MS)
m/z: 404.2647(HRMS)
deltam: -0.0015
ppm: -3.7



13c
tR: 5.18
m/z: 402 (HPLC-MS)
m/z: 402.2509(HRMS)
deltam: 0.0004
ppm: 1.0



13d
tR: 6.75
m/z: 388 (HPLC-MS)
m/z: 388.2599(HRMS)
deltam: -0.0114
ppm: -29.4

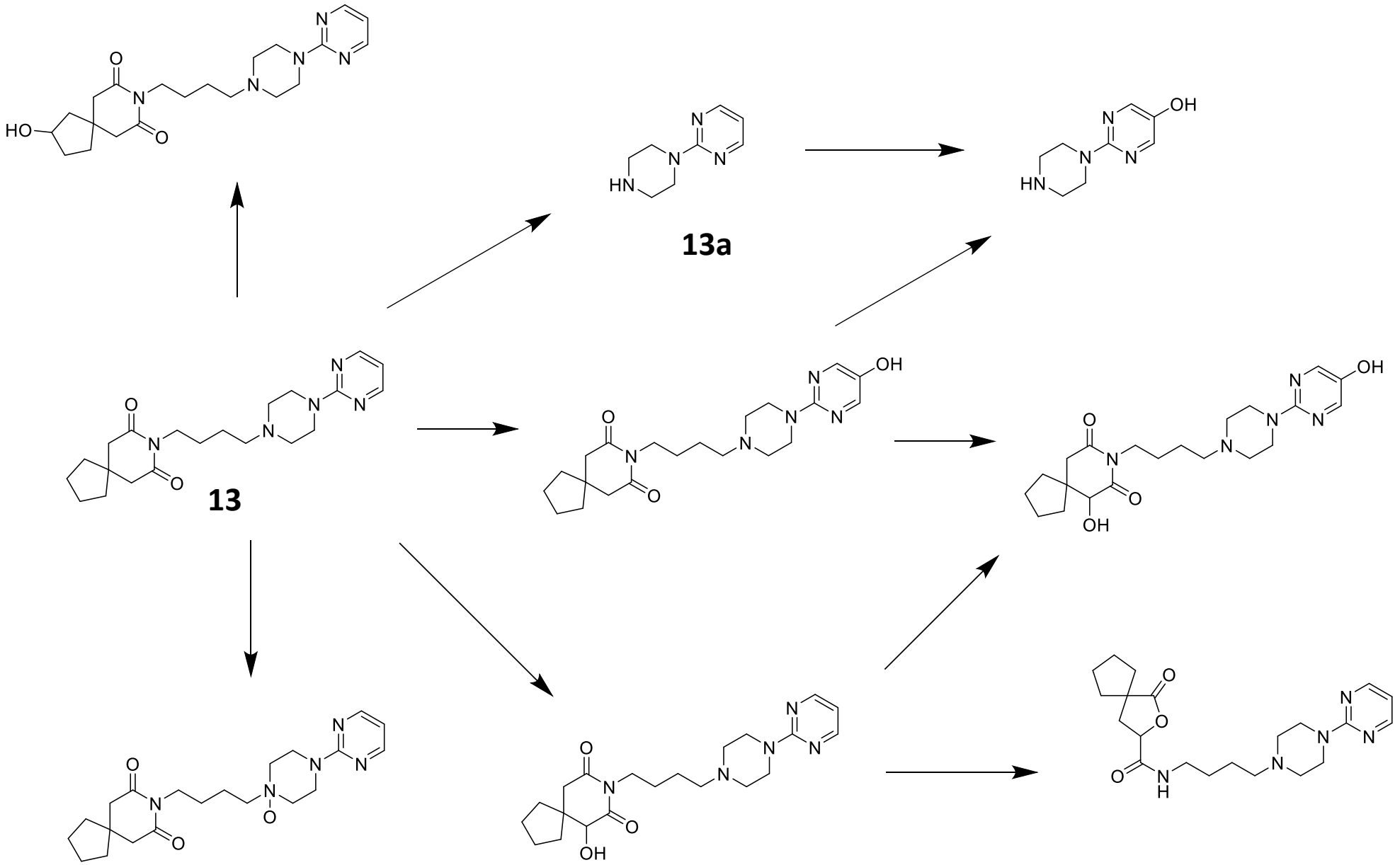


13e
tR: 7.70
m/z: 416 (HPLC-MS)
m/z: 416.2648 v 2662(HRMS)
deltam: 0.0350
ppm: 84,1

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	54.3	77.8	0	57.7
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
13a*	1.60	-221	0	0	0	0	**18.9**	**9.8**	0	0
13b	4.30	+18	0	0	0	0	0	0	0	6.4
13c#	5.18	+16	0	0	0	0	0	**50.0**	0	**41.6**
13d	6.75	+2	0	0	0	0	8.7	0	0	0
13e	7.70	+30	0	0	0	0	17.4	10.5	0	0

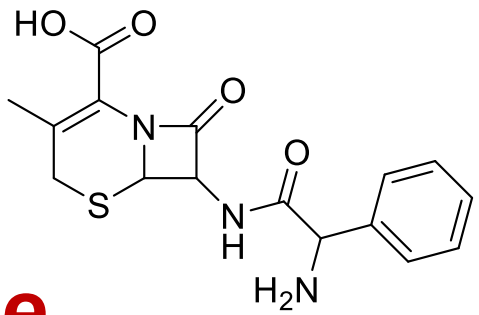
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Buspirone (**16**) - in vitro/ in vivo biotransformation



https://dmd.aspetjournals.org/content/33/4/500

L-Cephalexin (**14**) - **Biomimetic transformation**



14

No detectable metabolite

Az anyag valamilyen módon reagált, de nincsenek látható metabolit fragmensek

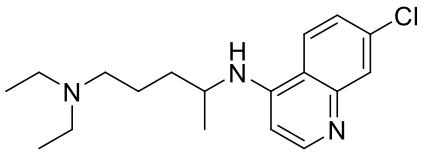
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	84	17.2	91.2	28.2
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵

L-Cephalexin (**14**) - **in vitro/ in vivo biotransformation**

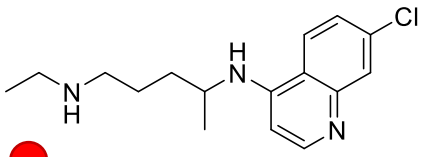
Not metabolized in the body

https://www.jstage.jst.go.jp/article/antibiotics1968/22/5/22_5_195/_article

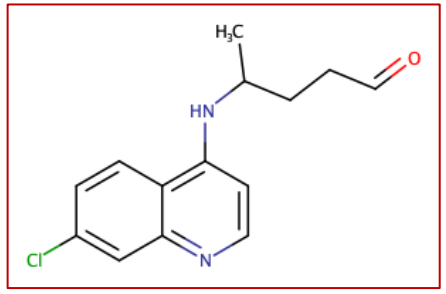
Chloroquine (**15**) - **Biomimetic transformation**



15
tR: 2.74
m/z: 320 (HPLC-MS)
m/z: (HRMS)



15a
tR: 2.27
m/z: 292 (HPLC-MS)
m/z: 292.1590(HRMS)
320.1921 K addukt
deltam: 0.0009
ppm: 3.1

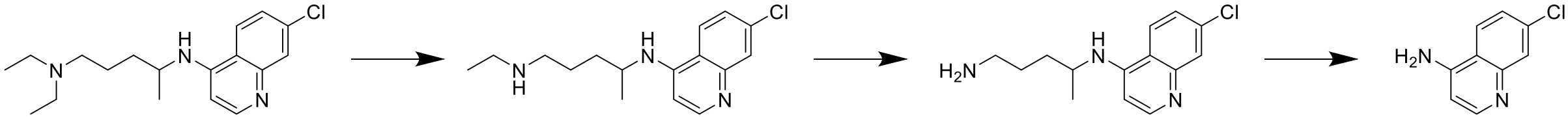


15b
tR: 4.05
m/z: 263 (HPLC-MS)
m/z: 263.0956(HRMS)
deltam: 0.0005
ppm: 1.9

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	10.8	57.0	86.3	53.7
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
15a*#	2.27	-28	0	0	0	0	7.5	**49.8**	31.8	31.6
15b	4.05	-57	0	0	0	0	3.3	42.8	35.8	14.6

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

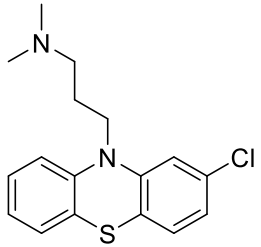
Chloroquine (**15**) - **in vitro/ in vivo biotransformation**



15 **15a**

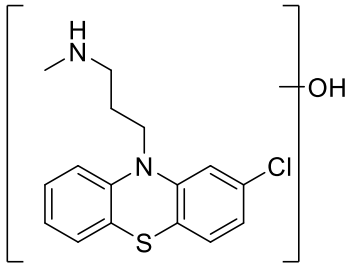
https://link.springer.com/article/10.2165/00003088-199631040-00003

Chlorpromazine (**16**) - **Biomimetic transformation**

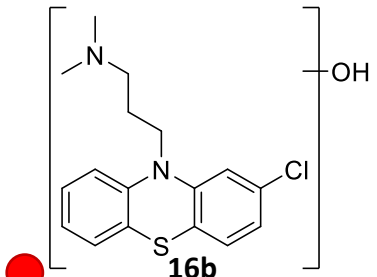


16
tR: 6.45
m/z: 319 (HPLC-MS)
m/z: (HRMS)

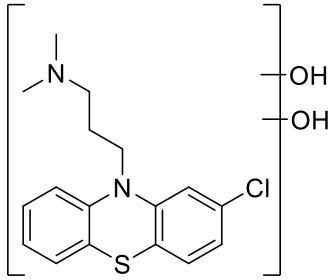
az –OH lehet
S=O vagy N-O is !!!



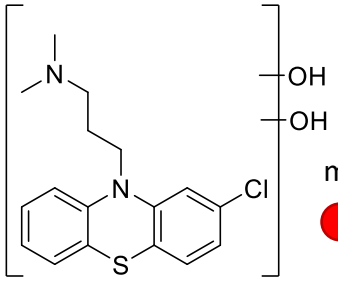
16a
tR: 4.74
m/z: 321 (HPLC-MS)
m/z: 321.0830(HRMS)
deltam: 0.0002
ppm: 0.6



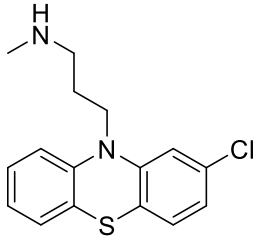
16b
tR: 4.79
m/z: 335 (HPLC-MS)
m/z: 335.1006(HRMS)
deltam: 0.0021
ppm: 6.3



16c
tR: 4.99
m/z: 351 (HPLC-MS)
m/z: 351.0938(HRMS)
deltam: 0.0004
ppm: 1.1



16d
tR: 5.20
m/z: 351 (HPLC-MS)
m/z: 351.0938(HRMS)
deltam: 0.0004
ppm: 1.1

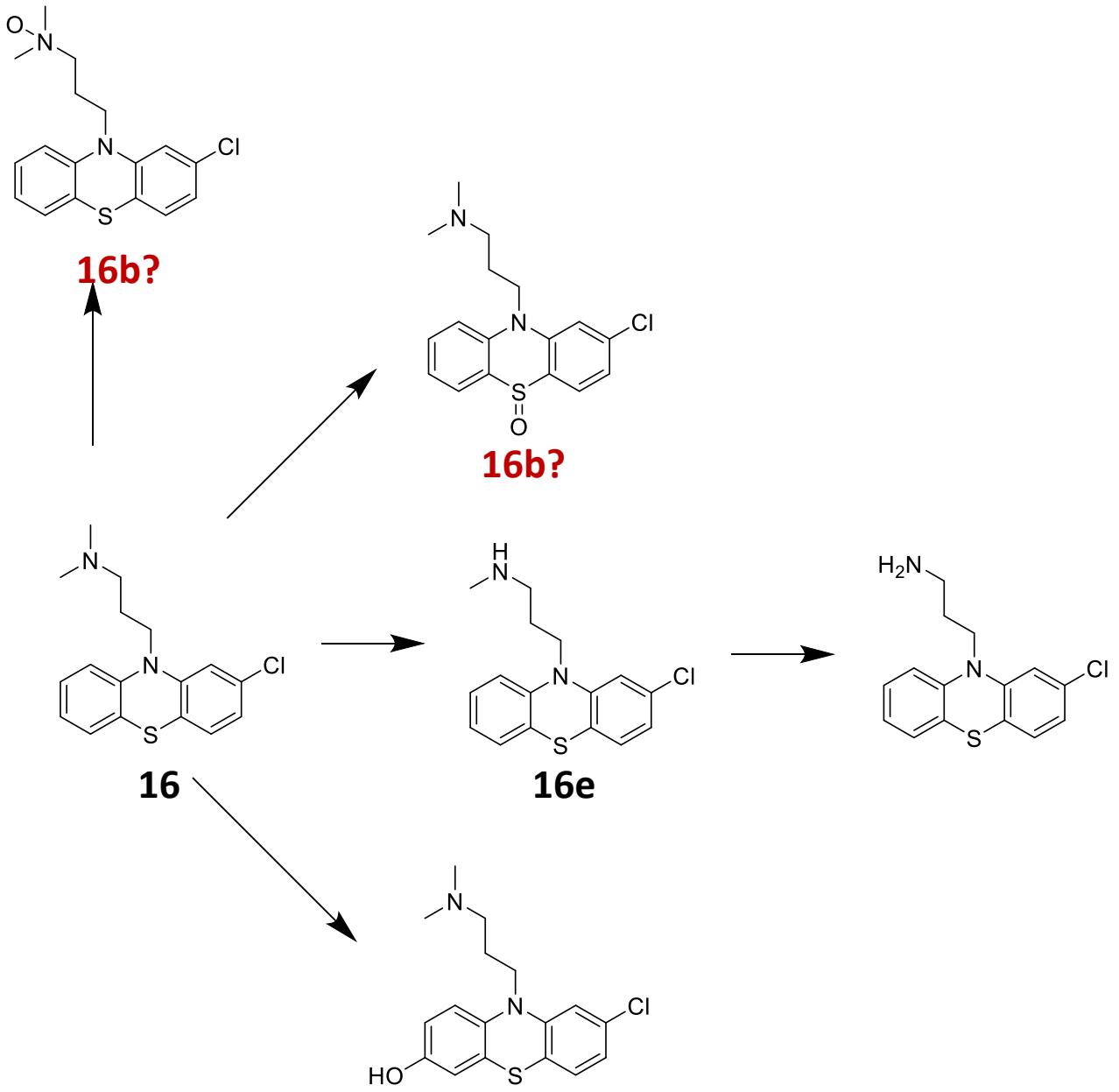


16e
tR: 6.34
m/z: 305 (HPLC-MS)
m/z: 305.1099(HRMS)
deltam: 0.0220
ppm: 72.1

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	71.2	27.8	34.8
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
16a	4.74	+2	0	0	0	0	0	5.8	0	0
16b*#	4.79	+16	0	0	0	0	**92.9**	**51.2**	**18.8**	**24.1**
16c	4.99	+32	0	0	0	0	0	31.0	0	0
16d	5.20	+32	0	0	0	0	7.1	0	0	0
16e*	6.34	-14	0	0	0	0	0	**0.7**	**9.0**	**5.9**

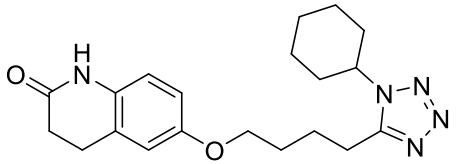
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Chlorpromazine (**16**) - **in vitro/ in vivo biotransformation**

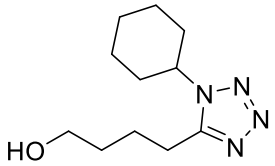


https://pubs.acs.org/doi/10.1021/acschemneuro.8b00258

Cilostazol (**17**) - **Biomimetic transformation**



17
tR: 3.10
m/z: 370 (HPLC-MS)
m/z: (HRMS)



17a
tR: 3.29
m/z: - (HPLC-MS)
m/z: (HRMS)

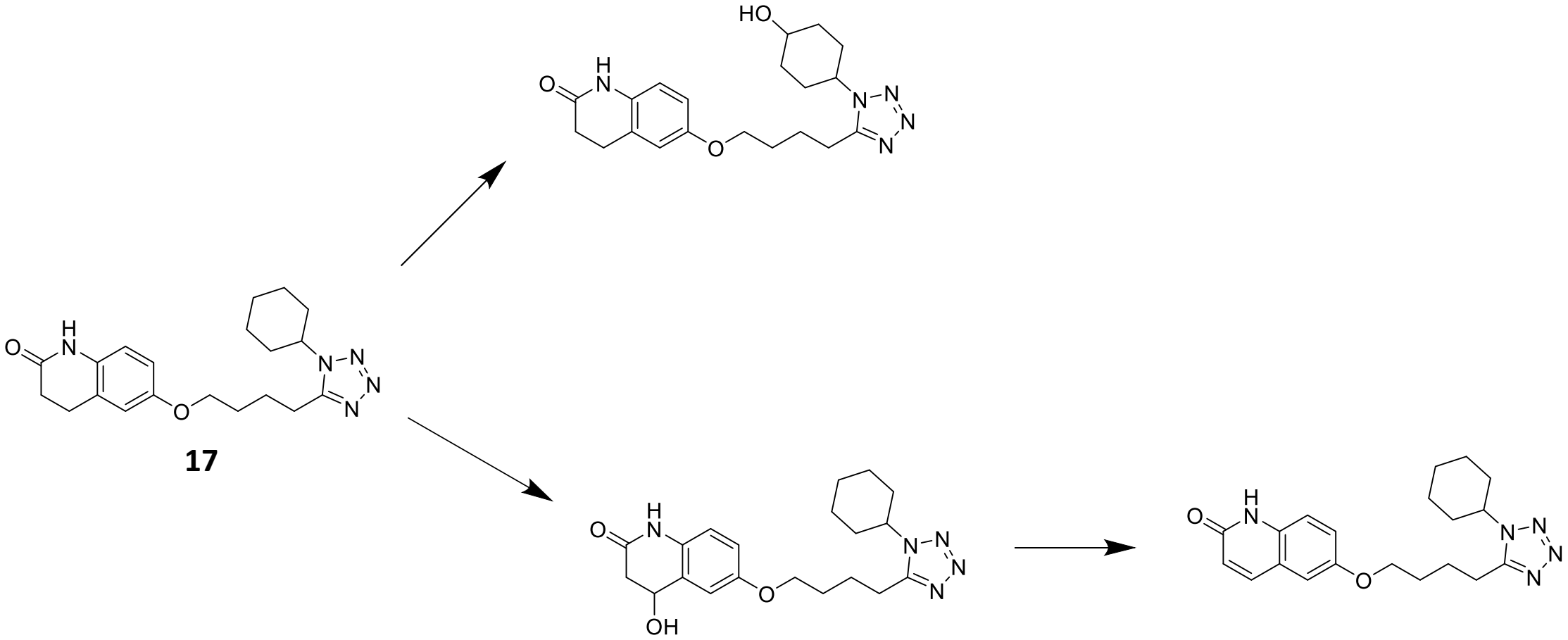
17b
tR: 3.82
m/z: - (HPLC-MS)
m/z: (HRMS)

17c
tR: 6.7*
m/z: 225 (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	95.0	64.8	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
17a#	**3.29**	**NI**	0	0	0	0	**64.3**	**13.8**	0	0
17b	**3.82**	**NI**	0	0	0	0	16.7	0	0	0
17c	**4.84**	-145	0	0	0	0	0	0	0	0

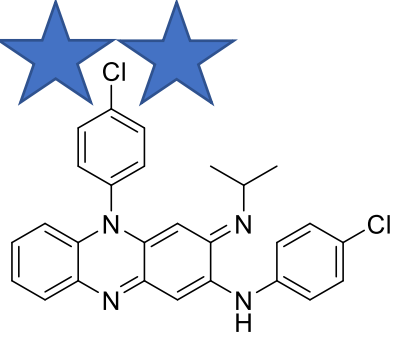
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Cilostazol (**17**) - in vitro/ in vivo biotransformation

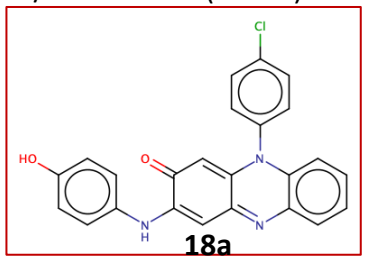


https://journals.sagepub.com/doi/10.1191/0960327006788277717

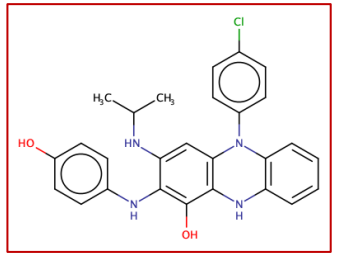
Clofazimine (**18**) - **Biomimetic transformation (I)**



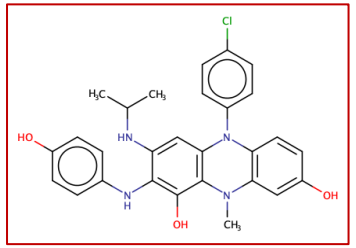
18
tR: 8.39
m/z: 473 (HPLC-MS)
m/z: 473.1315 (HRMS)



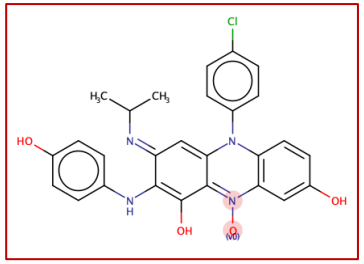
18a
tR: 5.29
m/z: 414 (HPLC-MS)
m/z: 414.122 (HRMS)
deltam: 0.0211
ppm: 51.0



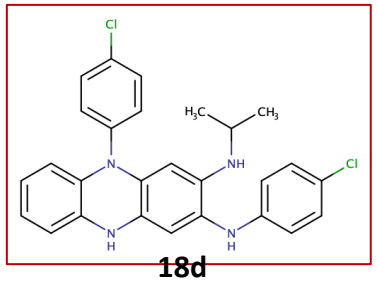
18b
tR: 7.09
m/z: 472 (HPLC-MS)
m/z: (HRMS)
ppm:



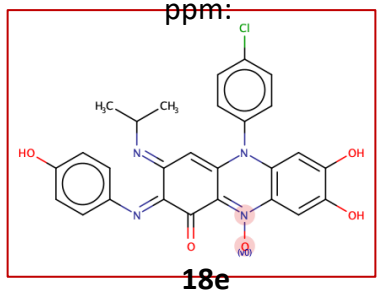
or



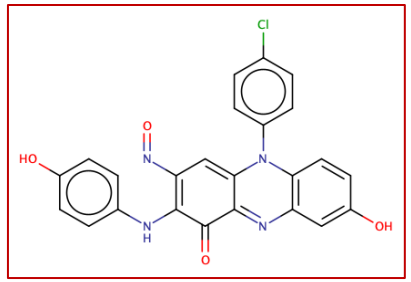
18c
tR: 7.18
m/z: 503 (HPLC-MS)
m/z: 503.1049(HRMS)
deltam: -0.0437
ppm: -86.9



18d
tR: 7.24
m/z: 475 (HPLC-MS)
m/z: 475.1061(HRMS)
deltam: -0.0395
ppm: -83.1



18e
tR: 7.67
m/z: 517 (HPLC-MS)
m/z: 517.1193 (HRMS)
deltam: -0.0086
ppm: -16.6

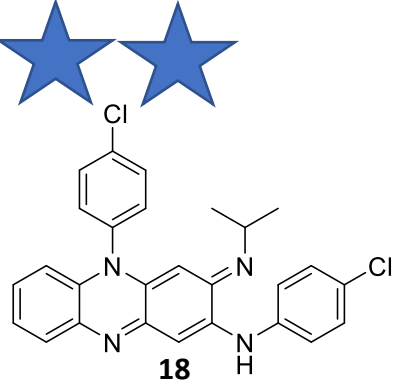


18f
tR: 7.85
m/z: 459 (HPLC-MS)
m/z: 459.1148 (HRMS)
deltam: 0.0288
ppm: 62.7

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	88	0	87.6
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
18a	**5.29**	-59	0	0	0	0	8.4	0	0	0
18b#	**7.09**	-1	0	0	0	0	**47.4**	5.8	0	0
18c	**7.18**	+30	0	0	0	0	0	27.7	0	0
18d	**7.24**	+2	0	0	0	0	23.5	0	0	7.7
18e	**7.67**	+44	0	0	0	0	16.7	5.8	0	1.5
18f	**7.85**	-14	0	0	0	0	0	5.3	0	0
18g	**10.97**	+23	0	0	0	0	0	21.3	0	0
18h	**11.65**	-135	0	0	0	0	0	0	0	6.0
18i	**13.47**	+44	0	0	0	0	0	26.8	0	0
18j	**13.56**	+2	0	0	0	0	0	0	0	23.3

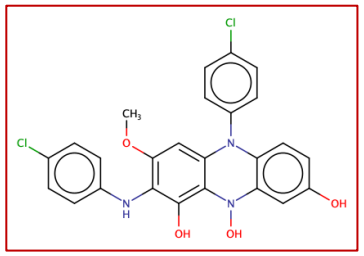
#Major biomimetic metabolite

Clofazimine (**18**) - **Biomimetic transformation (II)**



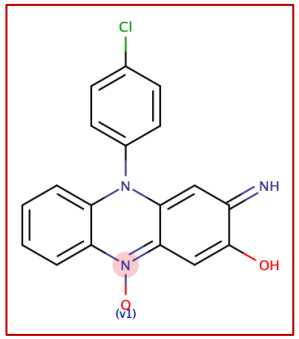
18

tR: 8.39
m/z: 473 (HPLC-MS)
m/z: 473.1315 (HRMS)



18g

tR: 10.97
m/z: 496 (HPLC-MS)
m/z: (HRMS)

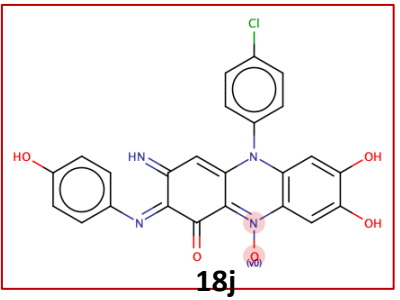


18h

tR: 11.65
m/z: 338 (HPLC-MS)
m/z: (HRMS)

18i

tR: 13.47
m/z: 517 (HPLC-MS)
m/z: 517.1193 (HRMS)
deltam: -0.0086
ppm: -16.6



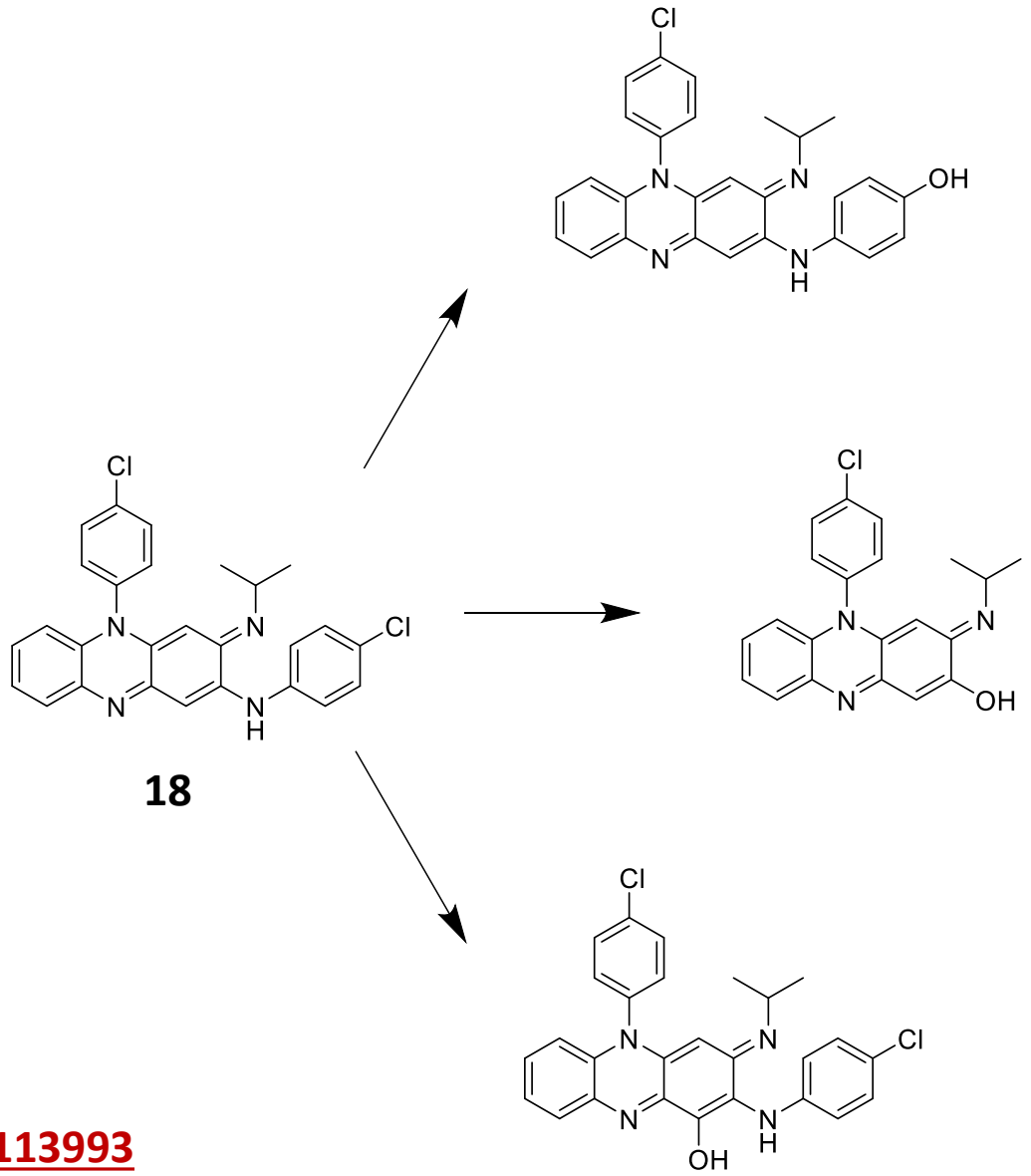
18j

tR: 13.56
m/z: 475 (HPLC-MS)
m/z: 475.1061 (HRMS)
deltam: 0.0252
ppm: 53.0

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	88	0	87.6
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
18a	**5.29**	-59	0	0	0	0	8.4	0	0	0
18b#	**7.09**	-1	0	0	0	0	**47.4**	5.8	0	0
18c	**7.18**	+30	0	0	0	0	0	27.7	0	0
18d	**7.24**	+2	0	0	0	0	23.5	0	0	7.7
18e	**7.67**	+44	0	0	0	0	16.7	5.8	0	1.5
18f	**7.85**	-14	0	0	0	0	0	5.3	0	0
18g	**10.97**	+23	0	0	0	0	0	21.3	0	0
18h	**11.65**	-135	0	0	0	0	0	0	0	6.0
18i	**13.47**	+44	0	0	0	0	0	26.8	0	0
18j	**13.56**	+2	0	0	0	0	0	0	0	23.3

#Major biomimetic metabolite

Clofazimine (**18**) - in vitro/ in vivo biotransformation

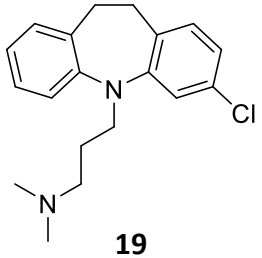


18

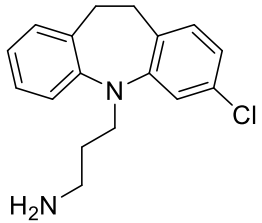
In vivo metabolism:
https://doi.org/10.1016/j.bcp.2020.113993

https://www.sciencedirect.com/science/article/pii/S0006295220302215?via%3Dihub#f0015

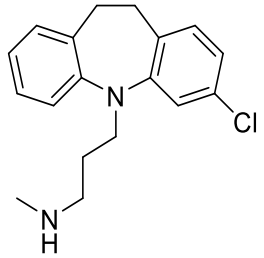
Clomipramine (**19**) - **Biomimetic transformation**



19
tR: 6.55
m/z: 315 (HPLC-MS)
m/z: (HRMS)



19a
tR: 6.32
m/z: 287 (HPLC-MS)
m/z: 287.1570(HRMS)
deltam: 0.0255
ppm: 88.8

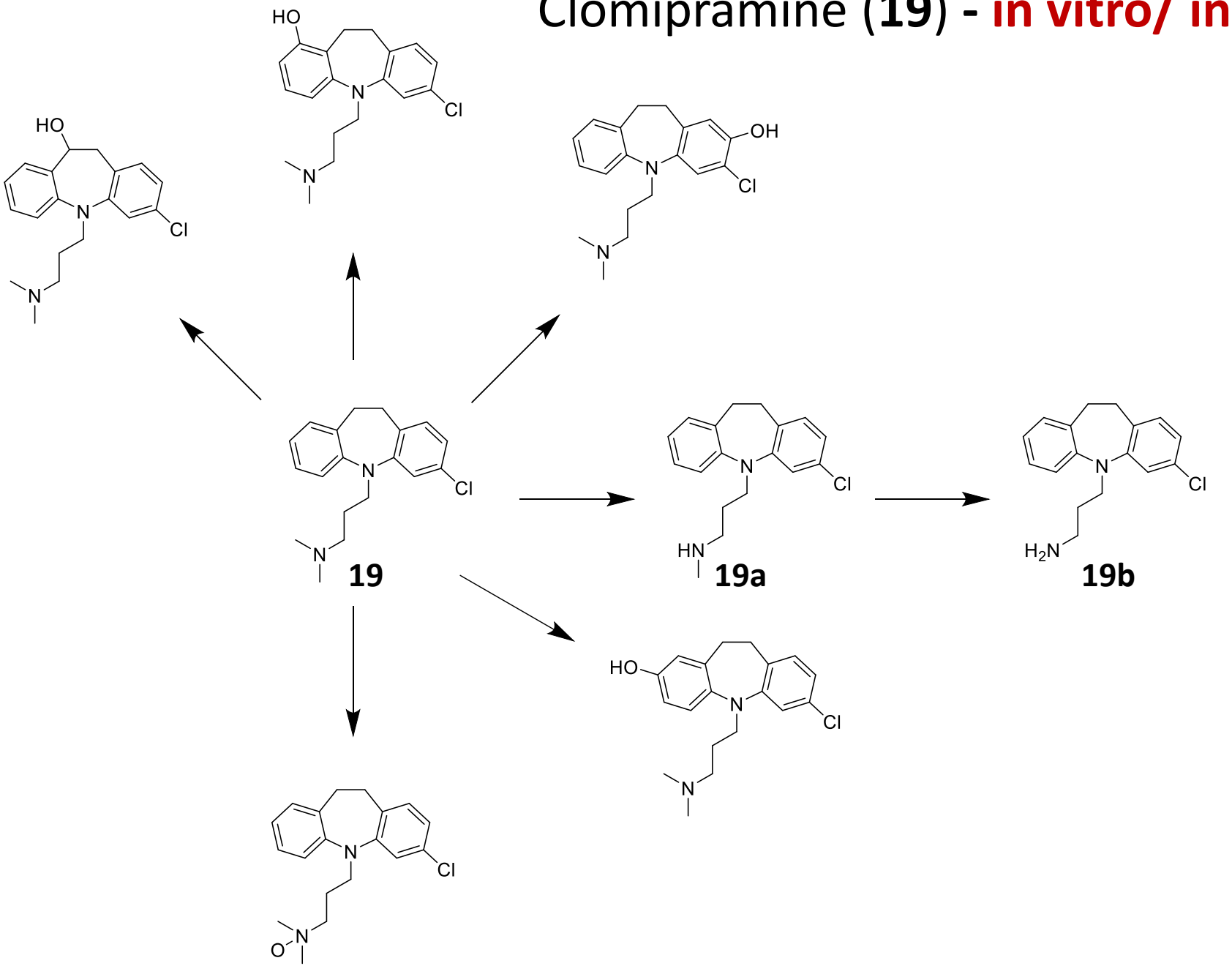


19b
tR: 6.43
m/z: 301 (HPLC-MS)
m/z: 301.1111(HRMS)
deltam: -0.0361
ppm: -119.9

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	59.7	81.1	87.9	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
19a*	6.32	-28	0	0	0	0	**10.7**	0	**8.7**	0
19b*#	6.43	-14	0	0	0	0	**75.2**	**34.8**	**73.6**	0

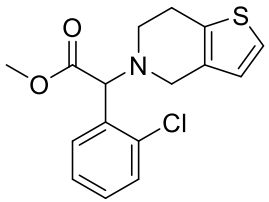
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Clomipramine (**19**) - **in vitro/ in vivo biotransformation**

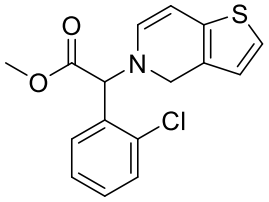


https://link.springer.com/article/10.2165/00003088-199120060-00002

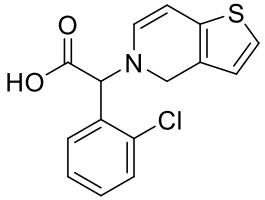
Clopidogrel (**20**) - **Biomimetic transformation**



20
tR: 9.80
m/z: 322 (HPLC-MS)
m/z: (HRMS)



20a
tR: 4.50
m/z: 320 (HPLC-MS)
m/z: 320.0445(HRMS)
deltam: -0.0067
ppm: -20.9

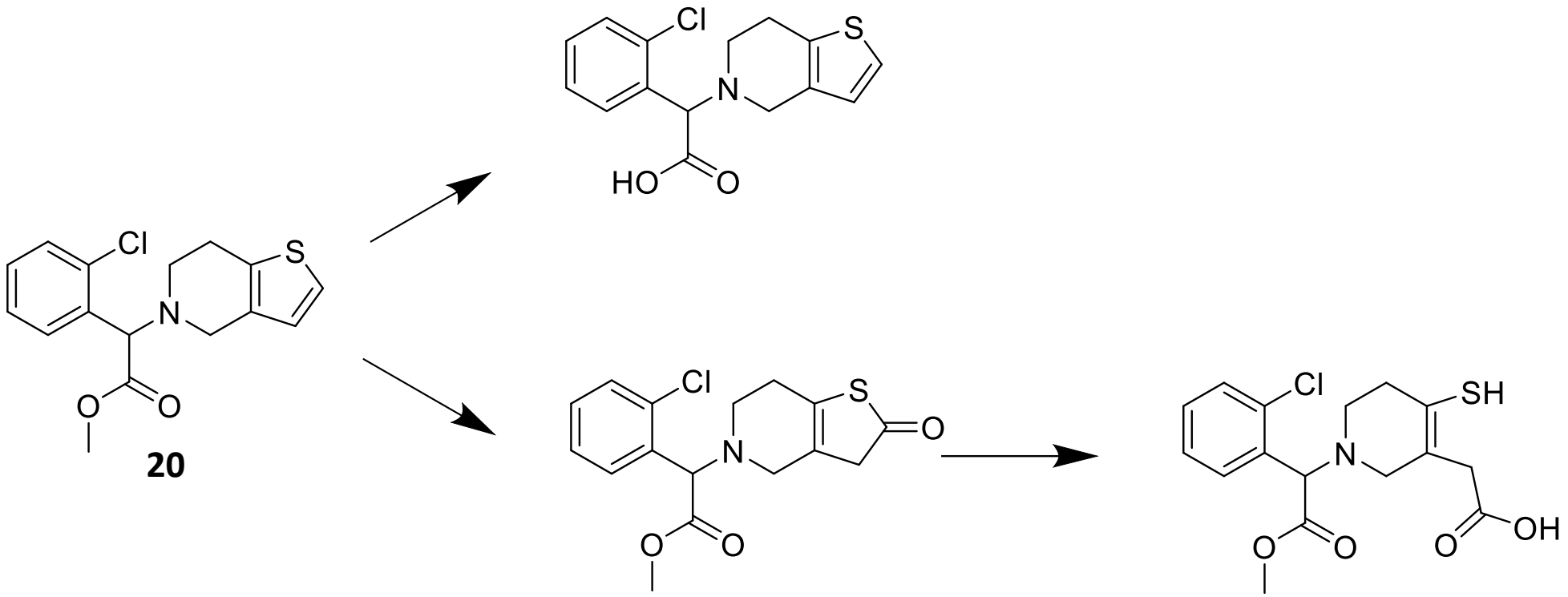


20b
tR: 5.04
m/z: 306 (HPLC-MS)
m/z: 344.0464(HRMS)
K addukt
deltam: 0,0550
ppm: 159.9

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	26.5	23.3	11.4	13.6
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
20a#	4.50	-2	0	0	0	0	**29.5**	**12.1**	**7.2**	5.5
20b	5.04	-16	0	0	0	0	0	0	0	7.3

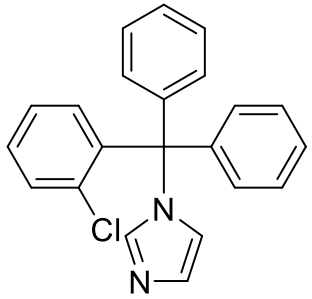
#Major biomimetic metabolite

Clopidogrel (**20**) - in vitro/ in vivo biotransformation



https://link.springer.com/article/10.1007/s40262-014-0230-6

Clotrimazole (**21**) - **Biomimetic transformation**



21

NO Biomimetic transformation

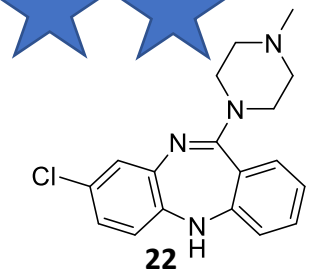
Clotrimazole (**21**) - **in vitro/ in vivo biotransformation**

NO Hepatic (in vitro/ in vivo) biotransformation

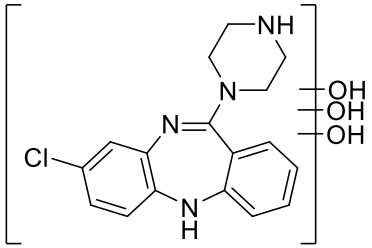
CYP450 inhibition

https://www.sciencedirect.com/science/article/pii/S0009279704000250#FIG4

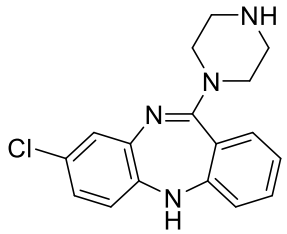
Clozapine (**22**) - **Biomimetic transformation**



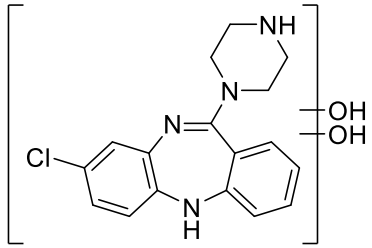
22
tR: 4.84
m/z: 327 (HPLC-MS)
m/z: (HRMS)



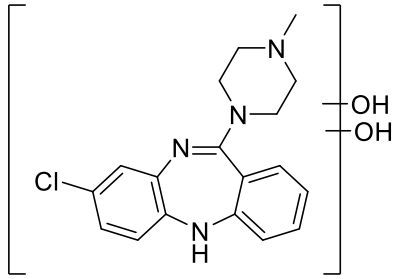
22a
tR: 2.18
m/z: 361 (HPLC-MS)
m/z: 361.0447(HRMS)
deltam: -0.0620
ppm: -171.7



22b
tR: 2.90
m/z: 313 (HPLC-MS)
m/z: 313.2742(HRMS)
deltam: 0.1522
ppm: 485.8

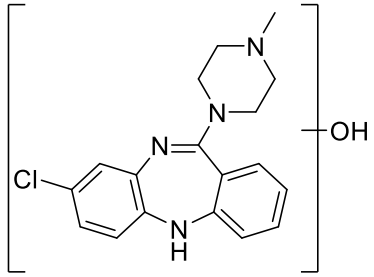


22c
tR: 3.29
m/z: 345 (HPLC-MS)
m/z: 345.1143(HRMS)
deltam: 0.0025



22d
tR: 3.32
m/z: 359 (HPLC-MS)
m/z: 359.0394(HRMS)
deltam: -0.0881

az –OH lehet N-O is !!!

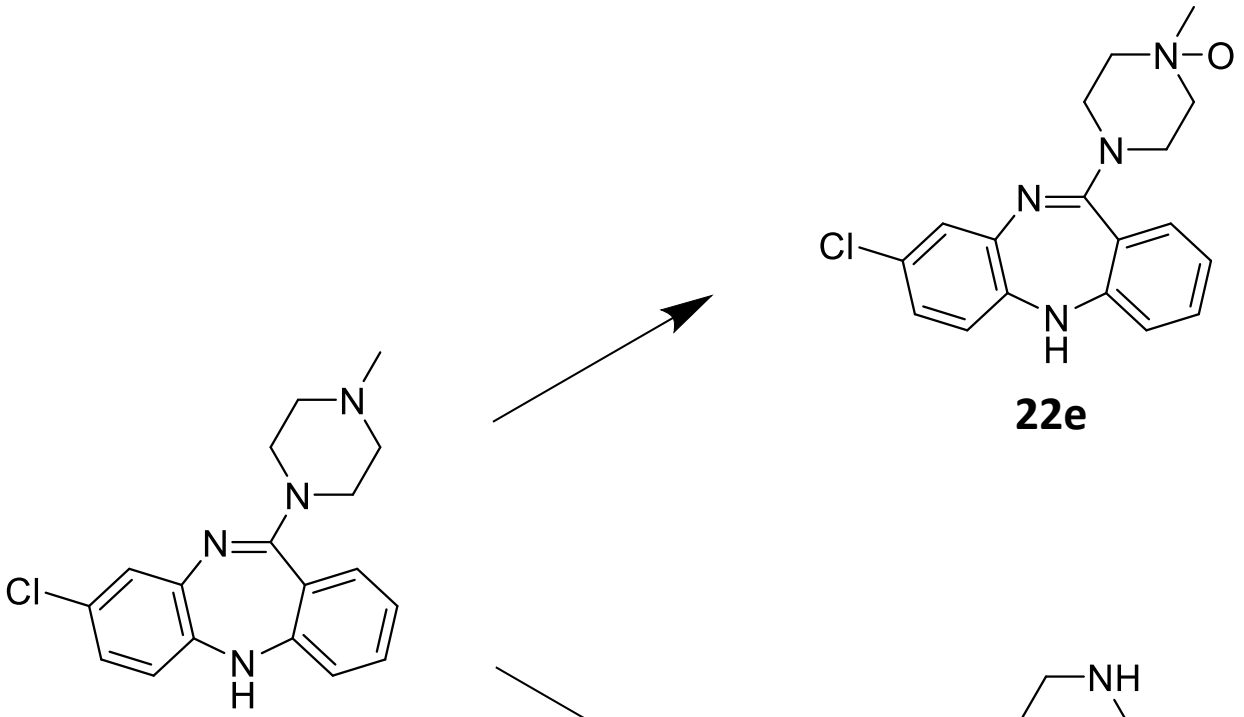


22e
tR: 3.52
m/z: 343 (HPLC-MS)
m/z: 343.2104(HRMS)
deltam: 0.0778

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	92.9	41.6	52.8
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
22a#	2.18	+34	0	0	0	0	**64.7**	**43.5**	0	0
22b*	2.9	-14	0	0	0	0	**14.5**	**4.2**	0	0
22c	3.29	+18	0	0	0	0	15.2	0	0	2.9
22d	3.32	+32	0	0	0	0	0	13.2	0	0
22e*	3.52	+16	0	0	0	0	0	5.13	0	0

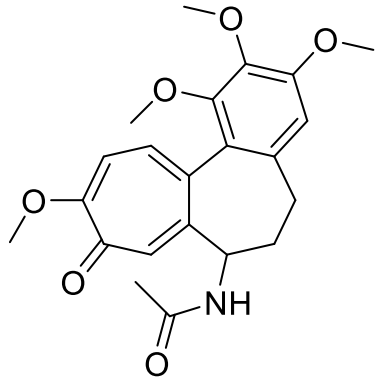
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Clozapine (**22**) - in vitro/ in vivo biotransformation



https://bpspubs.onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-2125.1997.t01-1-00605.x

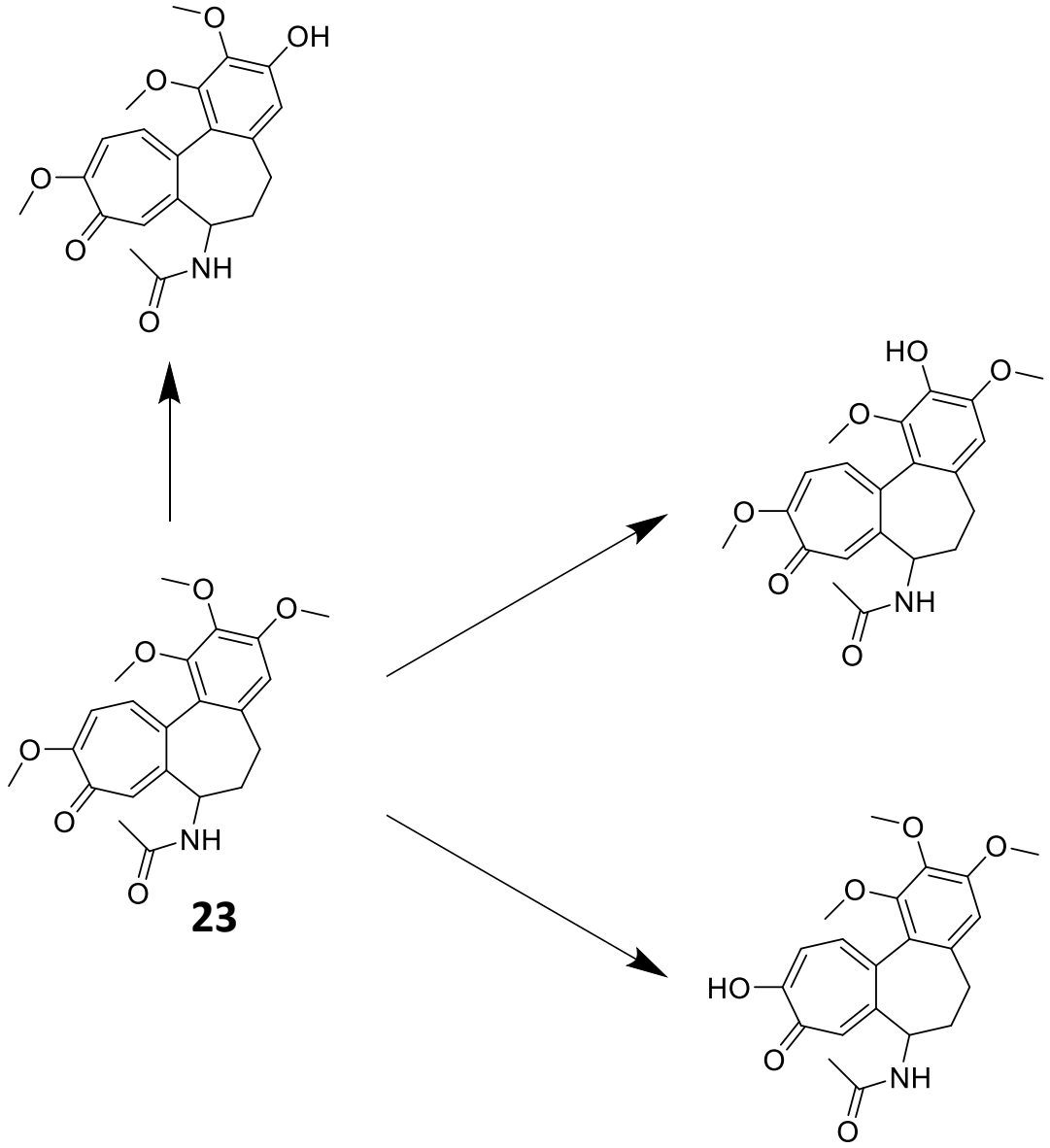
Colchicine (**23**) - **Biomimetic transformation**



23

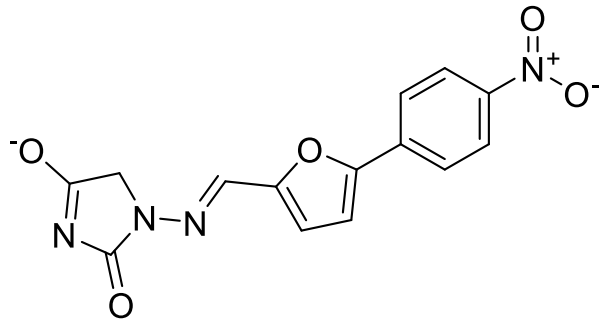
NO Biomimetic transformation

Colchicine (**23**) - in vitro/ in vivo biotransformation



https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/204820Orig1s000PharmR.pdf

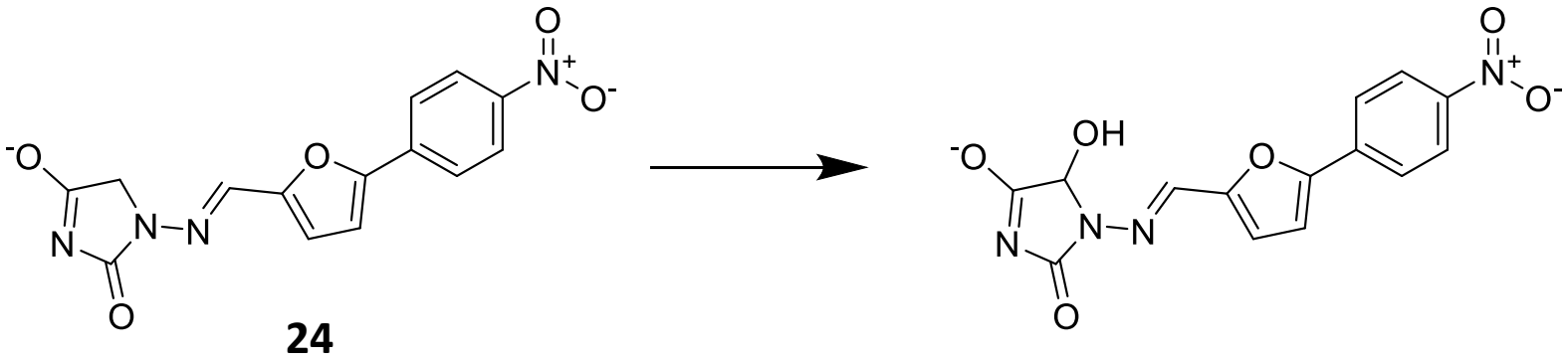
Dantrolene (**24**) - **Biomimetic transformation**



24

NO Biomimetic transformation

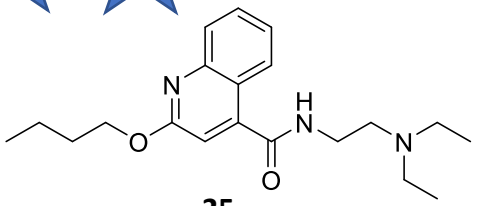
Dantrolene (**24**) - **in vitro/ in vivo biotransformation**



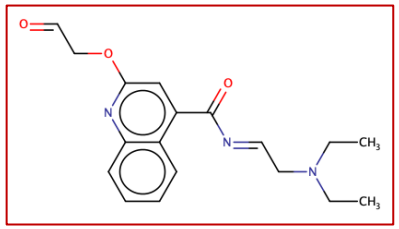
24

https://link.springer.com/article/10.2165/00003495-198632020-00003

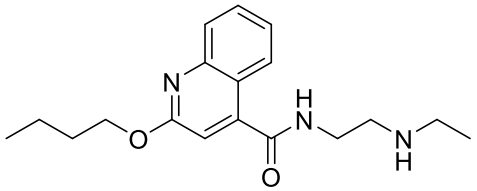
Dibucaine (**25**) - **Biomimetic transformation**



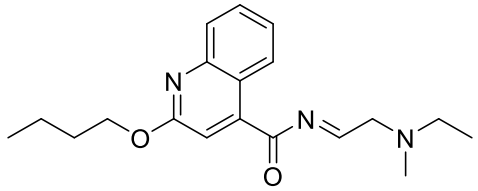
25
tR: 6.02
m/z: 344 (HPLC-MS)
m/z: 344.2338(HRMS)



or

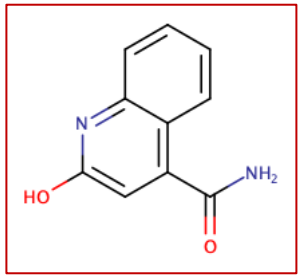


25a
tR: 5.18
m/z: 386 (HPLC-MS)
m/z: (HRMS)



25b
tR: 5.72
m/z: 316 (HPLC-MS)
m/z: 316.2028 (HRMS)
deltam: 0.0003
ppm: 0.9

25c
tR: 6.54
m/z: 328 (HPLC-MS)
m/z: (HRMS)

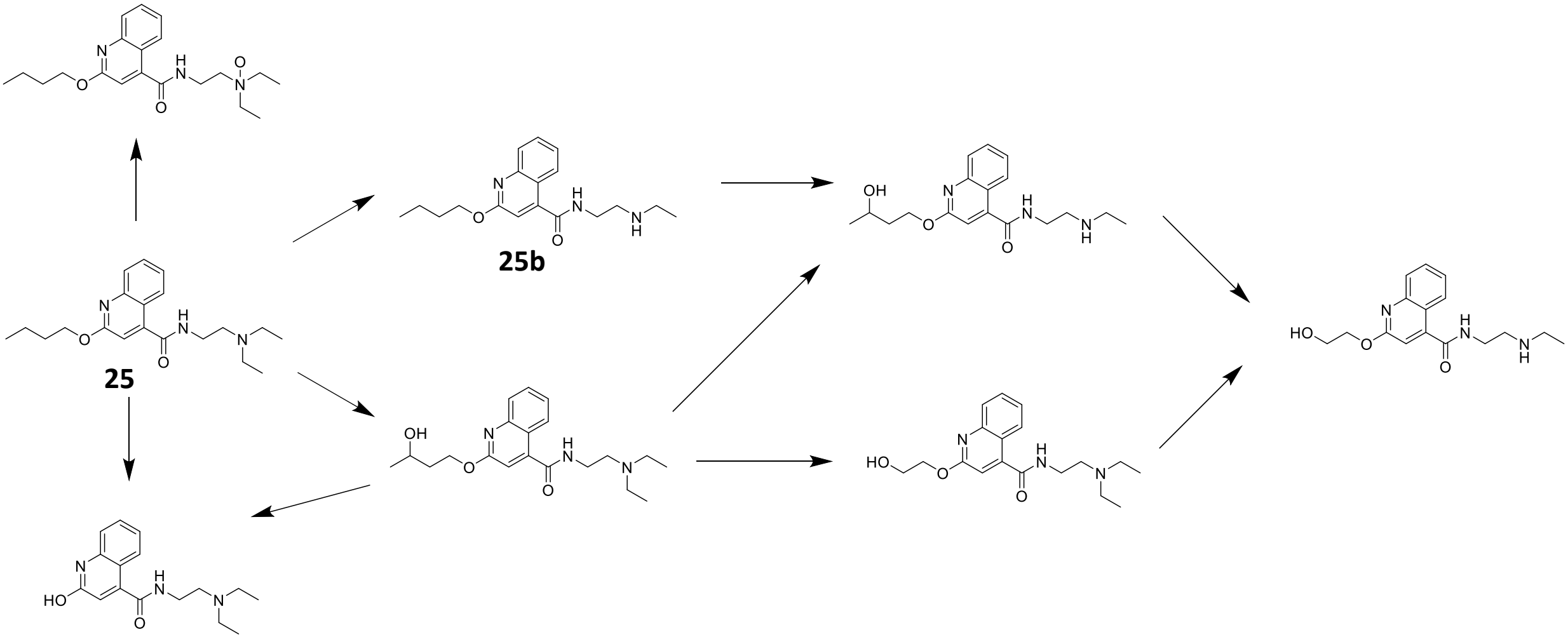


25d
tR: 9.30
m/z: 189 (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	0	61.7	94.4	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
25a	5.18	+42	0	0	0	0	0	0	2.5	0
25b*#	5.72	-28	0	0	0	0	0	**55.9**	**25.9**	0
25c#	6.54	-16	0	0	0	0	0	0	**59.5**	0
25d	9.30	-155	0	0	0	0	0	0	9.8	0

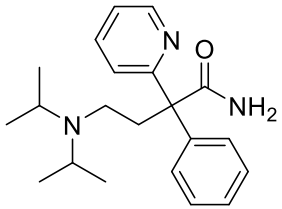
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Dibucaine (**25**) - in vitro/ in vivo biotransformation

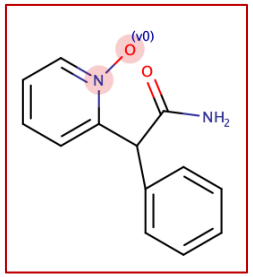


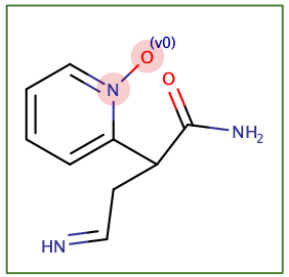
https://www.jstage.jst.go.jp/article/bpb1978/6/8/6_8_538/_article/-char/ja/

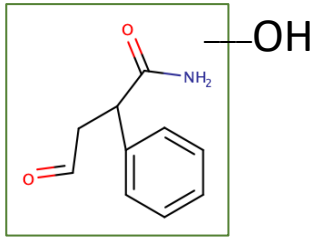
Disopyramide (**26**) - **Biomimetic transformation**



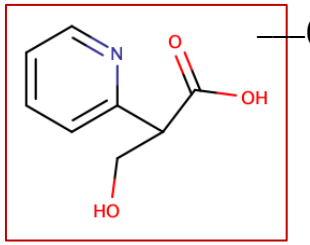
26
tR: 4.45
m/z: 340 (HPLC-MS)
m/z: (HRMS)

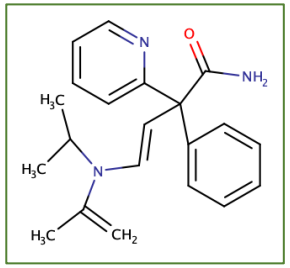




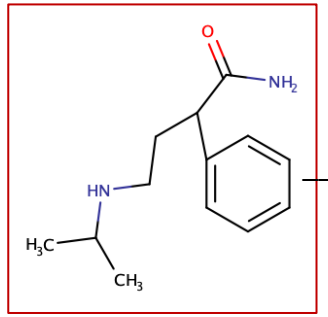


26a
tR: 4.79
m/z: 340/**229**/211/**194**/184/168 (HPLC-MS)
m/z: 340.2411/**229.1412**/211.1007/
194.0993/184.0781/168.0823(HRMS)
deltam: **0.0435**/**0.0063 v 0.0176**
ppm: **189.8**/**32.5 v 90.7**





26c
tR: 7.97
m/z: **184**/**336** (HPLC-MS)
m/z: 184.0781/336.2057(HRMS)
deltam: **0.0171**/**-0.0019**
ppm: **92.9**/ **-5.7**

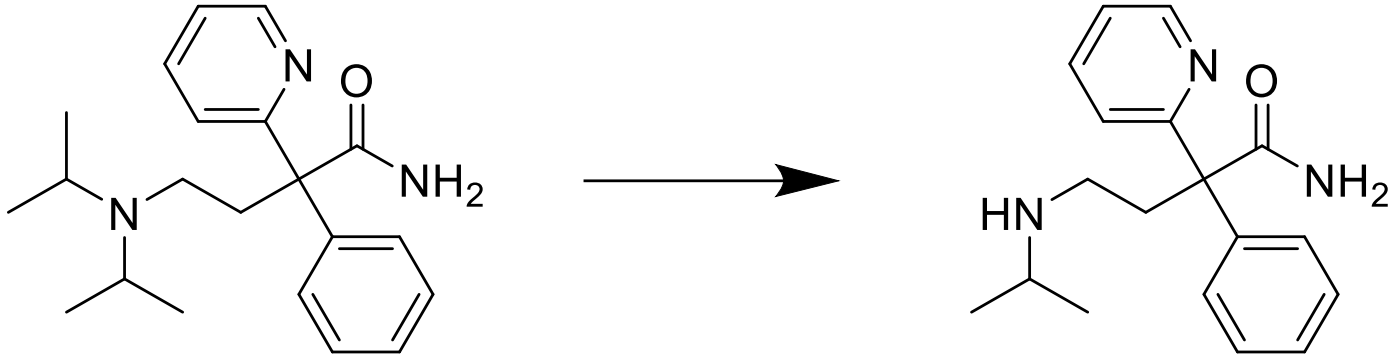


26b
tR: 6.14
m/z: **237**/209 (HPLC-MS)
m/z: 237.0843/
209.1061 (HRMS)
deltam:**-0.0760**
ppm: -320.6

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	0	4.8	70.1	87.3
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
26a	4.79	?	0	0	0	0	0	0	0	5.7
26b	6.14	-103 / -131	0	0	0	0	0	5.9	9.9	10.5
26c#	7.97	-4 / -156	0	0	0	0	0	**41.8**	**79.3**	**76.4**

#Major biomimetic metabolite

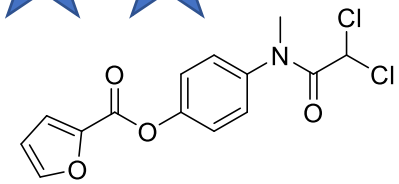
Disopyramide (**26**) - in vitro/ in vivo biotransformation



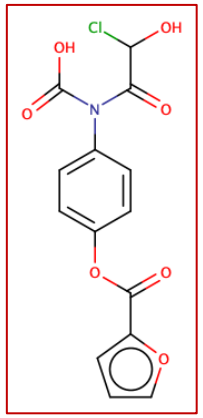
26

https://onlinelibrary.wiley.com/doi/10.1002/chir.530030505

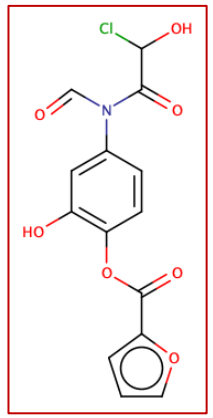
Diloxanide (**27**) - **Biomimetic transformation**



27
tR: 8.80
m/z: 328 (HPLC-MS)
m/z: (HRMS)

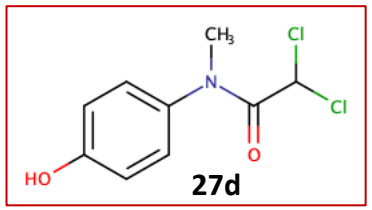


27a
tR: 4.55
m/z: 340/192 (HPLC-MS)
m/z: 192.0679(HRMS)



27b
tR: 4.59
m/z: 340/227 (HPLC-MS)
m/z: 226.8690(HRMS)

27c
tR: 6.67
m/z: - (HPLC-MS)
m/z: (HRMS)

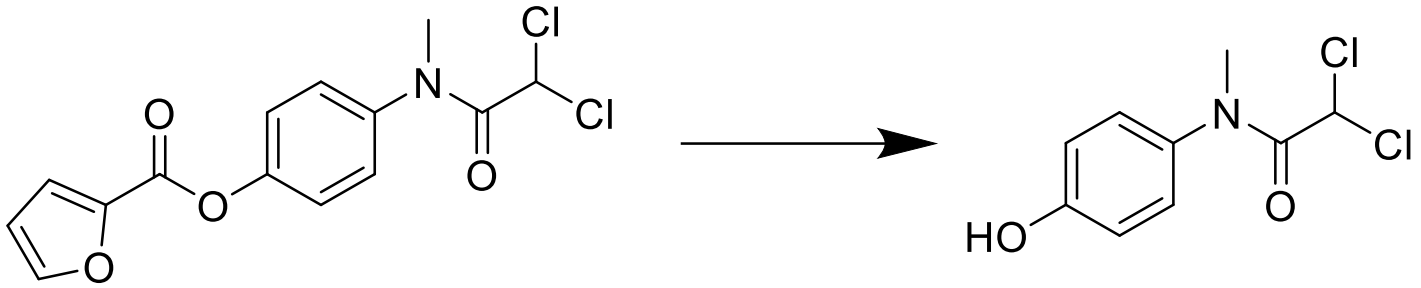


27d
tR: 6.84
m/z: **234** (HPLC-MS)
m/z: 234.0087(HRMS)
deltam: -0.0002
ppm: -0.9

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	100	100	0	0	100	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
27a	4.55	+12/ -136	0	0	0	**19.3**	0	0	0	16.7
27b	4.59	+12/ -101	0	0	0	**41.0**	0	0	0	47.3
27c	6.67	NI	0	0	**63.6**	0	0	0	68.3	0
27d*	6.84	-94	0	0	**32.5**	**32.0**	0	0	31.7	31.9

***in vivo/in vitro metabolite formed by biotransformation**
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

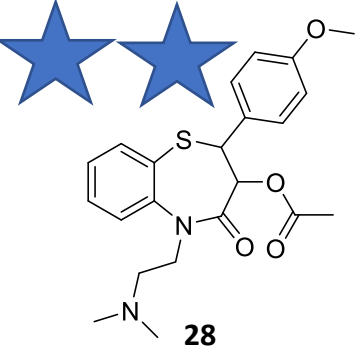
Diloxanide (**27**) - in vitro/ in vivo biotransformation



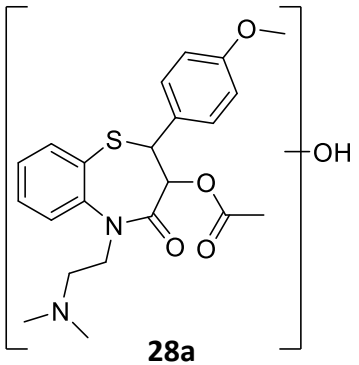
27 **27d**

https://go.drugbank.com/drugs/DB08792

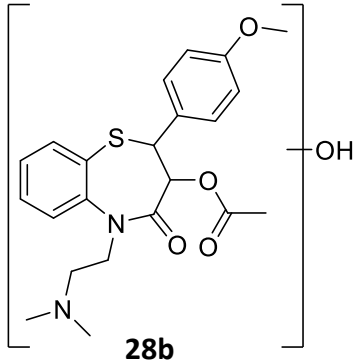
Diltiazem (**28**) - **Biomimetic transformation**



28
tR: 5.67
m/z: 415 (HPLC-MS)
m/z: (HRMS)

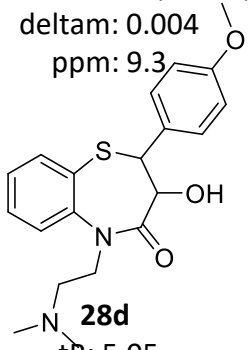


28a
tR: 4.45
m/z: 431 (HPLC-MS)
m/z: 431.1681(HRMS)
deltam: 0.004
ppm: 9.3

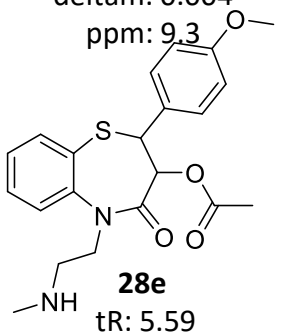


28b
tR: 4.62
m/z: 431 (HPLC-MS)
m/z: 431.1681(HRMS)
deltam: 0.004
ppm: 9.3

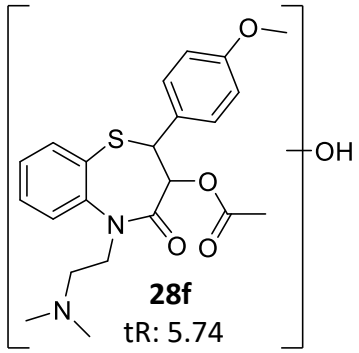
28c
tR: 5.30
m/z: 459 (HPLC-MS)
m/z: (HRMS)



28d
tR: 5.05
m/z: 373 (HPLC-MS)
m/z: 373.1591 (K add is)(HRMS)
deltam: 0.0005



28e
tR: 5.59
m/z: 401 (HPLC-MS)
m/z: 401.1540(HRMS)
deltam: 0.0005

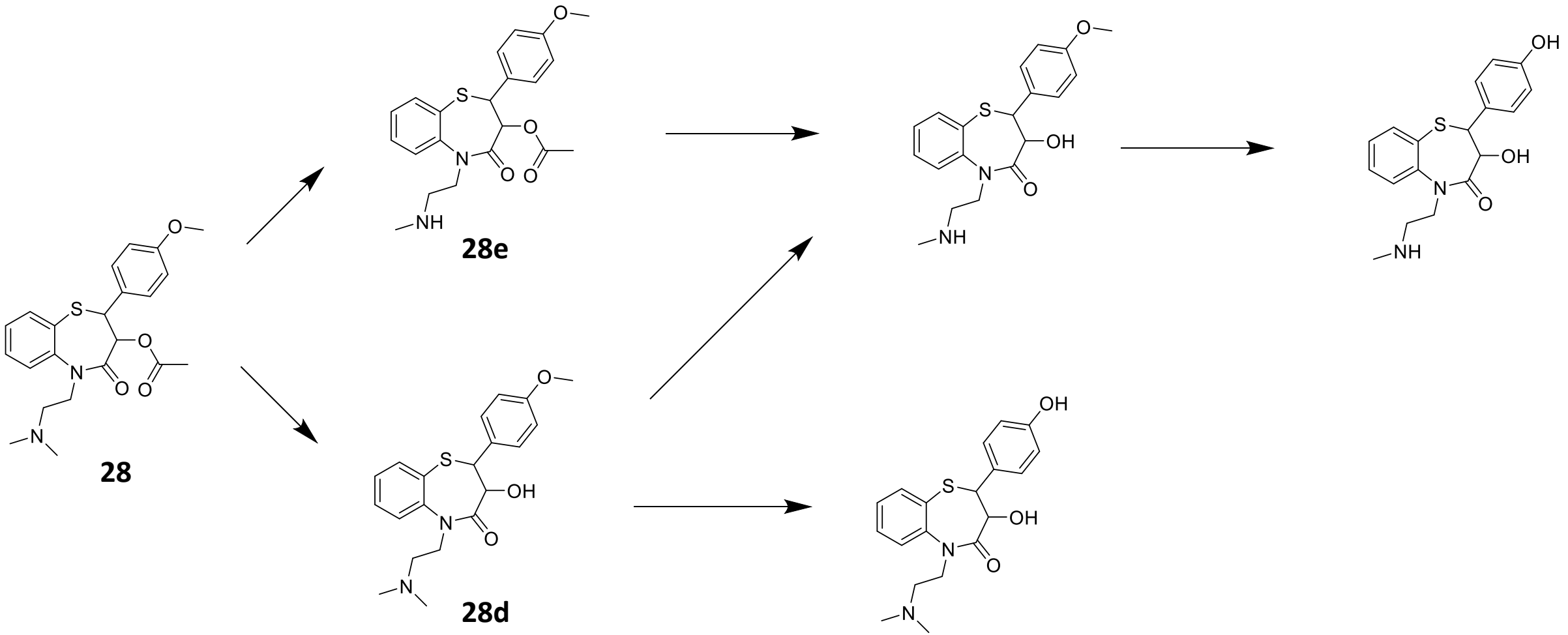


28f
tR: 5.74
m/z: 431 (HPLC-MS)
m/z: 431.1644(HRMS)
deltam: 0.0003

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	18.4	59.1	64.3	57.5	66.3	48.2
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
28a#	4.45	+16	0	0	0	0	**64.9**	12.4	0	0
28b	4.62	+16	0	0	0	0	13.9	0	0	0
28c#	5.30	+44	0	0	0	0	0	0	**49.1**	0
28d*	5.05	-42	0	0	**36.6**	**71.9**	0	0	0	66.9
28e*#	5.59	-14	0	0	0	0	0	**49.7**	28.5	0
28f	5.74	+16	0	0	0	0	0	6.4	17.1	0

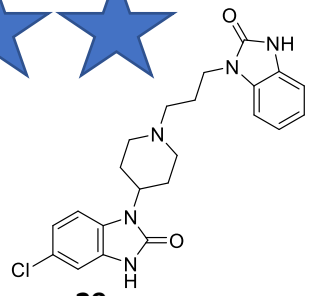
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
Non biomimetic metabolite

Diltiazem (**28**) - in vitro/ in vivo biotransformation

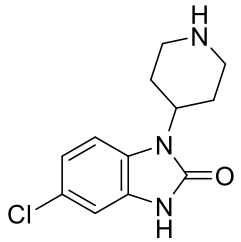


https://www.jstage.jst.go.jp/article/bpb1978/7/1/7_1_24/_article/-char/ja/

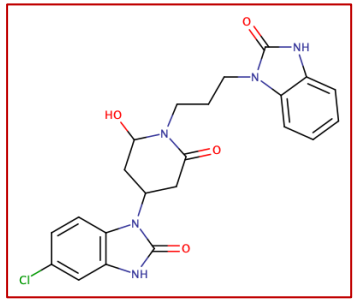
Domperidone (**29**) - **Biomimetic transformation (I)**



29
tR: 4.95
m/z: 426 (HPLC-MS)
m/z: (HRMS)

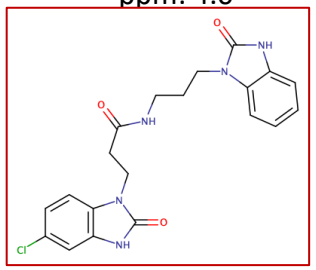


29a
tR: 3.85
m/z: 252 (HPLC-MS)
m/z: 252.0914(HRMS)
deltam: 0.0010
ppm: 4.0

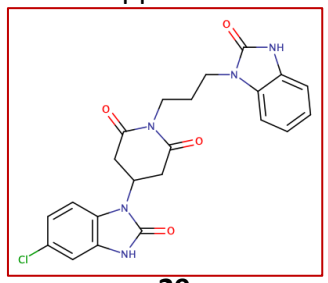


29b
tR: 4.24
m/z: 456 (HPLC-MS)
m/z: 456.1457(HRMS)
deltam: 0.0018
ppm: 3.9

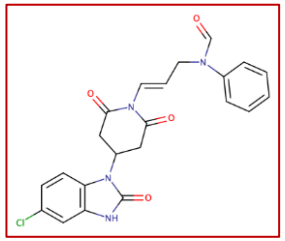
29c
tR: 5.15
m/z: 420 (HPLC-MS)
m/z: (HRMS)



29d
tR: 5.25
m/z: 414 (HPLC-MS)
m/z: 414.1328(HRMS)
deltam: -0.0005



29e
tR: 5.95
m/z: 454 (HPLC-MS)
m/z: 454.0818(HRMS)
deltam: -0.0464

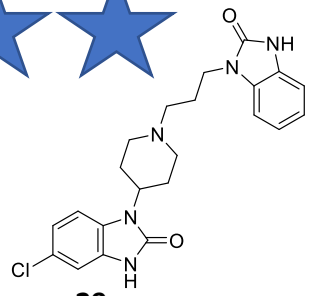


29f
tR: 6.32
m/z: 439 (HPLC-MS)
m/z: (HRMS)

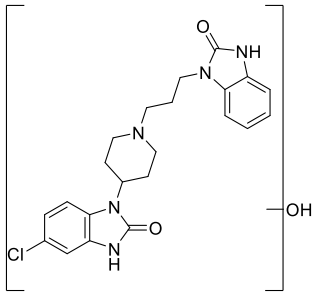
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	97	90.5	44.4	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
29a*#	3.85	-174	0	0	0	0	**23.7**	**30.8**	**8.53**	0
29b#	4.24	+30	0	0	0	0	**27.4**	0	0	0
29c#	5.15	-6	0	0	0	0	0	0	**27.9**	0
29d	5.25	-12	0	0	0	0	6.4	0	0	0
29e	5.95	+28	0	0	0	0	8.5	22.0	0	0
29f	6.32	+13	0	0	0	0	0	0	5.4	0
29g	6.57	NI	0	0	0	0	8.0	0	0	0
29h	7.22	+60	0	0	0	0	10.5	0	0	0
29i*	7.67	+16	0	0	0	0	**8.9**	0	0	0

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Domperidone (**29**) - **Biomimetic transformation (II)**



29
tR: 4.95
m/z: 426 (HPLC-MS)
m/z: (HRMS)



29g
tR: 6.57
m/z: - (HPLC-MS)
m/z: (HRMS)

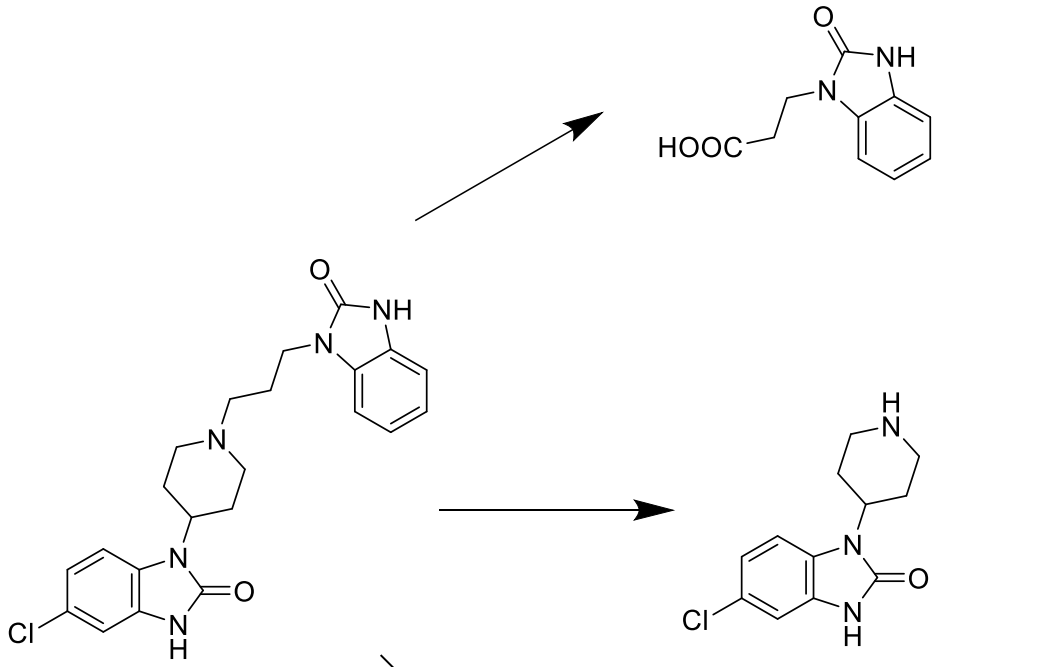
29h
tR: 7.22
m/z: 486 (HPLC-MS)
m/z: 486.1567(HRMS)

29i
tR: 7.67
m/z: 442 (HPLC-MS)
m/z: 442.1392(HRMS)
deltam: -0.0254
ppm: -57.4

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	97	90.5	44.4	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
29a*#	3.85	-174	0	0	0	0	**23.7**	**30.8**	**8.53**	0
29b#	4.24	+30	0	0	0	0	**27.4**	0	0	0
29c#	5.15	-6	0	0	0	0	0	0	**27.9**	0
29d	5.25	-12	0	0	0	0	6.4	0	0	0
29e	5.95	+28	0	0	0	0	8.5	22.0	0	0
29f	6.32	+13	0	0	0	0	0	0	5.4	0
29g	6.57	NI	0	0	0	0	8.0	0	0	0
29h	7.22	+60	0	0	0	0	10.5	0	0	0
29i*	7.67	+16	0	0	0	0	**8.9**	0	0	0

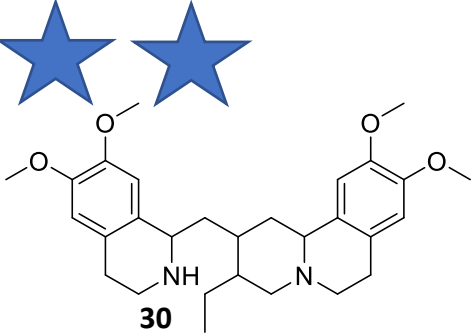
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Domperidone (**29**) - **in vitro/ in vivo biotransformation**

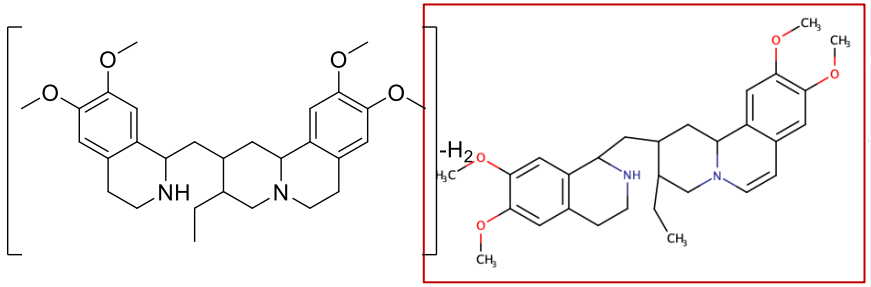


https://link.springer.com/article/10.1007/BF03189515

Emetine (**30**) - **Biomimetic transformation (I)**



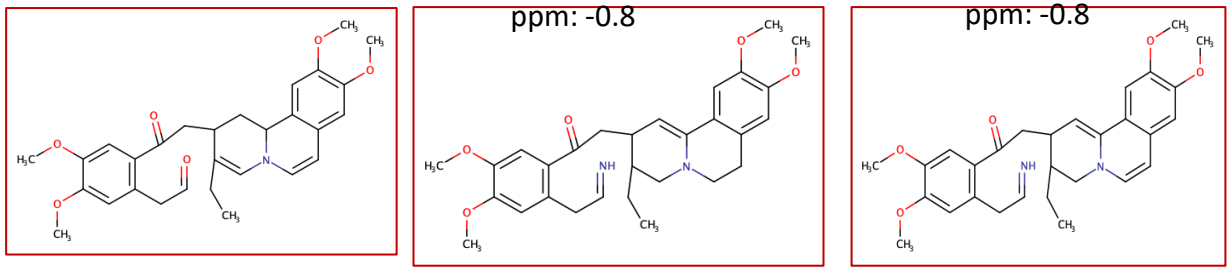
30
tR: 3.42
m/z: 481 (HPLC-MS)
m/z: (HRMS)



30a
tR: 2.80
m/z: 192 (HPLC-MS)
m/z: 192.0696(HRMS)

30b
tR: 3.37
m/z: 479 (HPLC-MS)
m/z: 479.2906(HRMS)
deltam: -0.0004
ppm: -0.8

30c
tR: 3.60
m/z: 475/**479** (HPLC-MS)
m/z: 479.2906(HRMS)
deltam: -0.0004
ppm: -0.8



30d
tR: 3.70
m/z: 492 (HPLC-MS)
m/z: 492.2524(HRMS)
deltam: 0.0138
ppm: 28.0

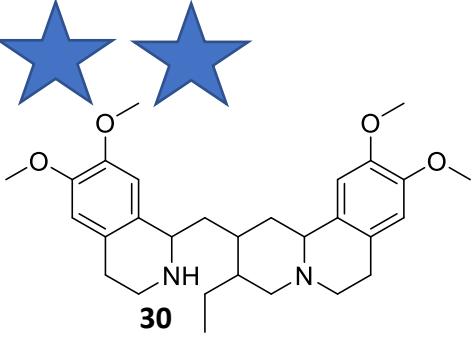
30e
tR: 5.24
m/z: 493 (HPLC-MS)
m/z: 493.2679(HRMS)
deltam: -0.0023
ppm: -4.7

30f
tR: 5.30
m/z: 491 (HPLC-MS)
m/z: 491.2537(HRMS)
deltam: -0.0009
ppm: -1.8

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	76.2	36.8	14.7
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
30a	2.80	-289	0	0	0	0	3.2	8.4	0	0
30b#	3.37	-2	0	0	0	0	**74.2**	0	2.9	0
30c#	3.60	-6/-2	0	0	0	0	4.7	**27.0**	0	0
30d#	3.70	+11	0	0	0	0	2.9	16.8	**31.1**	0
30e	5.24	+12	0	0	0	0	0	0.9	8.4	5.1
30f	5.30	+10	0	0	0	0	0	0	0	5.7
30g	6.59	+10	0	0	0	0	0	0	8.7	0
30h	6.57	-8	0	0	0	0	1.5	9.4	2.4	0

#Major biomimetic metabolite

Emetine (**30**) - **Biomimetic transformation (II)**

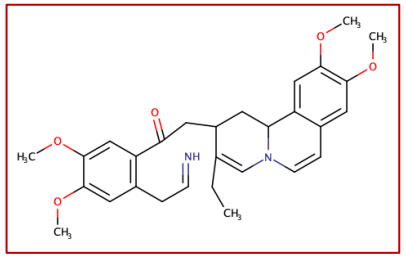


30

tR: 3.42

m/z: 481 (HPLC-MS)

m/z: (HRMS)



30g

tR: 6.59

m/z: 491 (HPLC-MS)

m/z: 491.2488(HRMS)

deltam: -0.0058

ppm: -11.8

30h

tR: 6.57

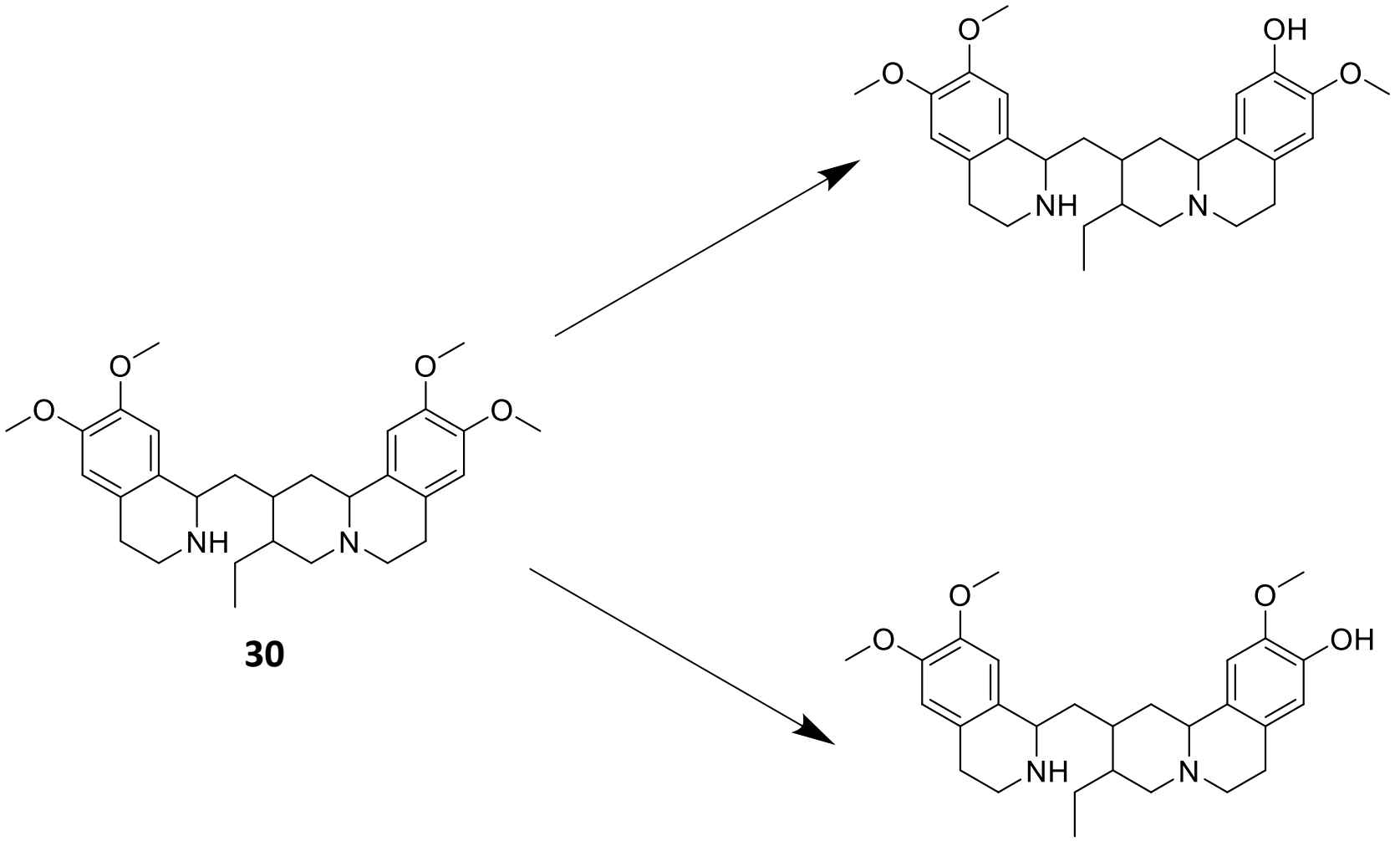
m/z: 473 (HPLC-MS)

m/z: 473.2431(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	76.2	36.8	14.7
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
30a	2.80	-289	0	0	0	0	3.2	8.4	0	0
30b#	3.37	-2	0	0	0	0	**74.2**	0	2.9	0
30c#	3.60	-6/-2	0	0	0	0	4.7	**27.0**	0	0
30d#	3.70	+11	0	0	0	0	2.9	16.8	**31.1**	0
30e	5.24	+12	0	0	0	0	0	0.9	8.4	5.1
30f	5.30	+10	0	0	0	0	0	0	0	5.7
30g	6.59	+10	0	0	0	0	0	0	8.7	0
30h	6.57	-8	0	0	0	0	1.5	9.4	2.4	0

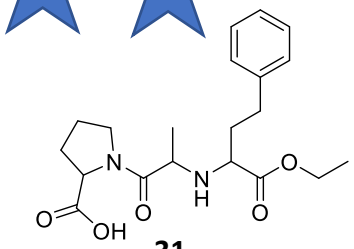
#Major biomimetic metabolite

Emetine (**30**) - in vitro/ in vivo biotransformation

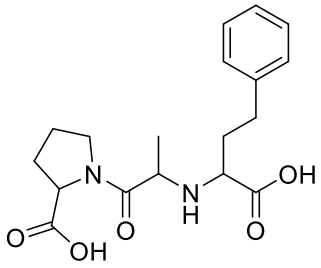


https://www.jstage.jst.go.jp/article/bpb/24/6/24_6_678/_pdf/-char/ja

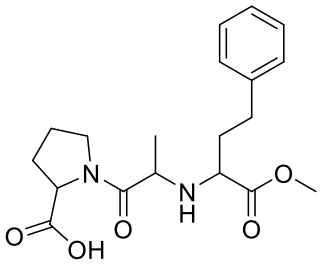
Enalapril (**31**) - **Biomimetic transformation**



31
tR: 5.52
m/z: 377 (HPLC-MS)
m/z: (HRMS)



31a
tR: 4.74
m/z: 349 (HPLC-MS)
m/z: 349.1687(HRMS)
deltam: -0.0076
ppm: -21.8



31b
tR: 5.00
m/z: 363 (HPLC-MS)
m/z: 363.1882(HRMS)
deltam: -0.0038
ppm: -10.5

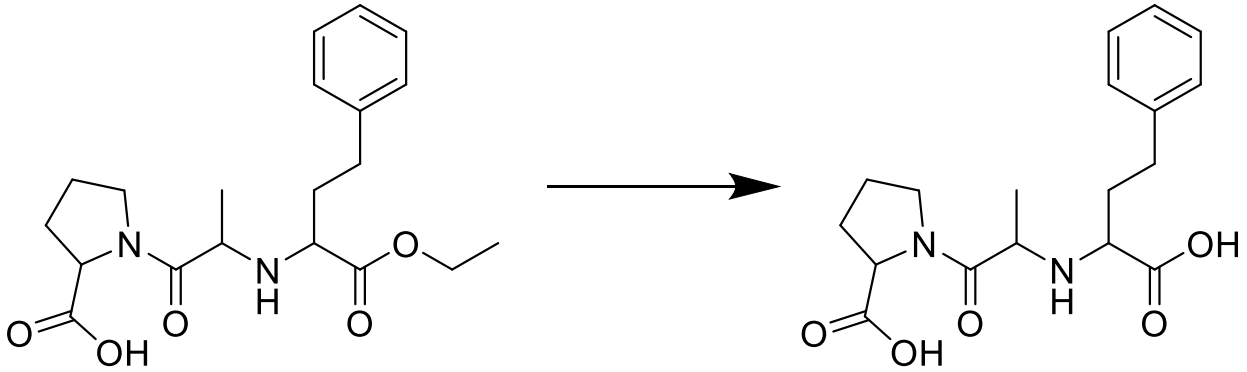
Et - Me exchange (MeOH cosolvent!)

HRMS(31b)-HRMS(31a): 14.0195
mCH2: 14.0157
deltam: 0.0038

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	90.6	0	0	0	85.4
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
31a*	4.74	-28	0	0	0	**11.3**	0	0	0	14.0
31b	5.00	-14	0	0	0	**79.8**	0	0	0	71.2

***in vivo/in vitro metabolite formed by biotransformation**
Non biomimetic metabolite

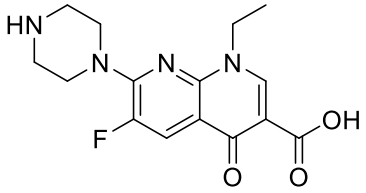
Enalapril (**31**) - in vitro/ in vivo biotransformation



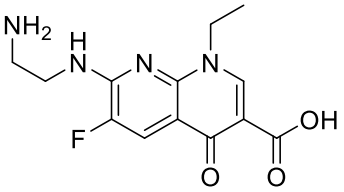
31 **31a**

https://www.tandfonline.com/doi/abs/10.3109/03602538308991383

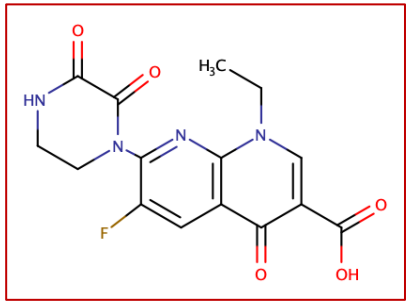
Enoxacin (**32**) - **Biomimetic transformation**



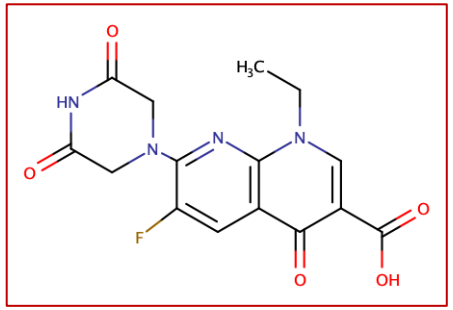
32
tR: 3.69
m/z: 321 (HPLC-MS)
m/z: (HRMS)



32a
tR: 3.52
m/z: 295 (HPLC-MS)
m/z: 317.1030
Na addukt(HRMS)
deltam: 0.0004
ppm: 1.3



or



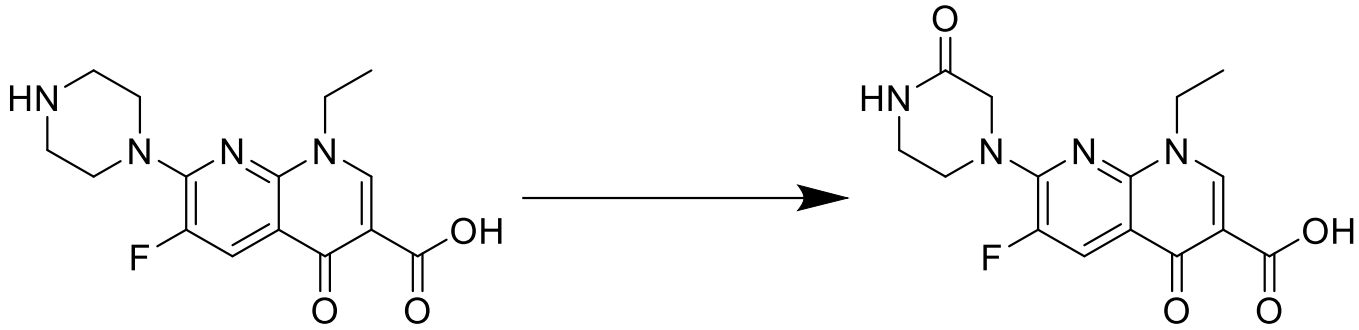
32b
tR: 3.85
m/z: 349 (HPLC-MS)
m/z: 348.9908(HRMS)
deltam: -0.1040
ppm: -298.0

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	0	10.0	75.2	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
32a#	3.52	-26	0	0	0	0	0	**15.1**	**10.5**	0
32b	3.85	+28	0	0	0	0	0	5.0	0	0

#Major biomimetic metabolite

Enoxacin (**32**) - in vitro/ in vivo biotransformation

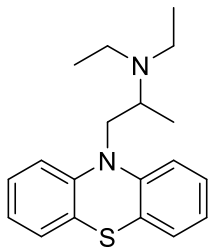
CYP450 inhibition



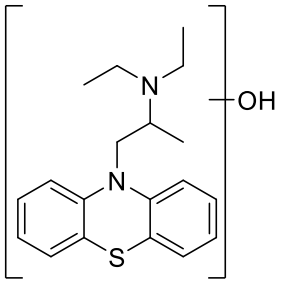
32

https://link.springer.com/article/10.2165/00003495-199651010-00009

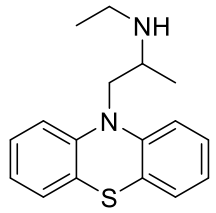
Ethopropazine/Profenamine (**33**) - **Biomimetic transformation (I)**



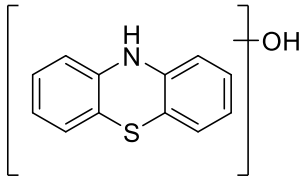
33
tR: 6.17
m/z: 313 (HPLC-MS)
m/z: (HRMS)



33a
tR: 4.77
m/z: 329 (HPLC-MS)
m/z: 329.1714(HRMS)
deltam: 0.0026
ppm: 7.9



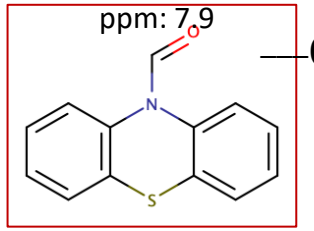
33b
tR: 5.90
m/z: 285 (HPLC-MS)
m/z: 285.1458(HRMS)
deltam: 0.0033
ppm: 11.6



regioisomers

33c
tR: 6.27
m/z: **216**/199
(HPLC-MS)
m/z: 216.0491/
199.0464 (HRMS)
deltam: 0.0008
ppm: 3.7

33d
tR: 6.62
m/z: **216**
(HPLC-MS)
m/z: 216.0491
(HRMS)
deltam: 0.0008
ppm: 3.7



33e
tR: 6.37
m/z: 244 (HPLC-MS)
m/z: 244.0443(HRMS)
deltam: 0.0011

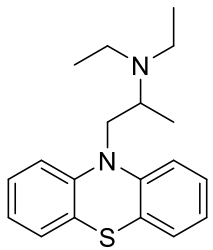
33f
tR: 7.09
m/z: 198 (HPLC-MS)
m/z: 198.0393(HRMS)

33g
tR: 9.59
m/z: 209 (HPLC-MS)
m/z: 209.0508(HRMS)

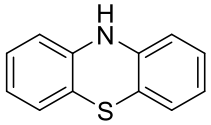
			Non biomimetic				Biomimetic			
Conversion (%)			0	60.5	0	0	100	100	0	23.8
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
33a#	4.77	+16	0	0	0	0	**72.7**	0	2.5	10.8
33b	5.90	-28	0	0	0	0	0	0	0	8.5
33c#	6.27	-97/ -114	0	**19.5**	0	0	6.4	**43.9**	0	8.9
33d#	6.62	-97	0	0	**2.4**	0	0	0	**82.6**	0
33e	6.37	-69	0	0	0	0	9.1	6.3	0	0
33f	7.09	-115	0	0	0	0	4.8	3.4	0	0
33g	9.59	-104	0	**5.2**	0	0	0	14.8	0	0
33h	9.95	+9	0	0	0	0	0	0	10.0	0
33i	10.53	-114	0	**26.3**	**13.1**	0	0	0	0	0

#Major biomimetic metabolite
Non biomimetic metabolite

Ethopropazine/Profenamine (**33**) - **Biomimetic transformation (II)**



33
tR: 6.17
m/z: 313 (HPLC-MS)
m/z: (HRMS)



33h
tR: 9.95
m/z: 322 (HPLC-MS)
m/z: (HRMS)

33i
tR: 10.53
m/z: 199 (HPLC-MS)
m/z: 199.0491(HRMS)
deltam: 0.002
ppm: 10.0

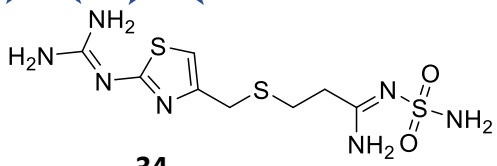
			Non biomimetic				Biomimetic			
Conversion (%)			0	60.5	0	0	100	100	0	23.8
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
33a[#]	4.77	+16	0	0	0	0	**72.7**	0	2.5	10.8
33b	5.90	-28	0	0	0	0	0	0	0	8.5
33c[#]	6.27	-97/ -114	0	**19.5**	0	0	6.4	**43.9**	0	8.9
33d[#]	6.62	-97	0	0	**2.4**	0	0	0	**82.6**	0
33e	6.37	-69	0	0	0	0	9.1	6.3	0	0
33f	7.09	-115	0	0	0	0	4.8	3.4	0	0
33g	9.59	-104	0	**5.2**	0	0	0	14.8	0	0
33h	9.95	+9	0	0	0	0	0	0	10.0	0
33i	10.53	-114	0	**26.3**	**13.1**	0	0	0	0	0

[#]Major biomimetic metabolite
Non biomimetic metabolite

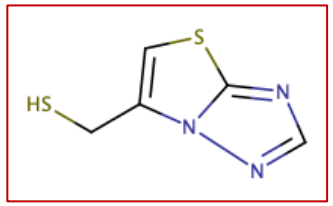
Ethopropazine/Profenamine (**33**) - **in vitro/ in vivo biotransformation**

PK data is not available

Famotidine (**34**) - **Biomimetic transformation (I)**



34
tR: 2.24
m/z: 338 (HPLC-MS)
m/z: (HRMS)

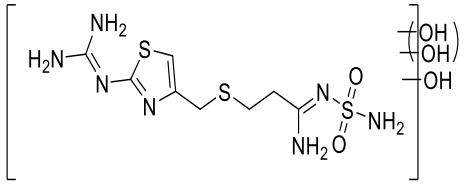


34a
tR: 1.25
m/z: - (HPLC-MS)
m/z: (HRMS)

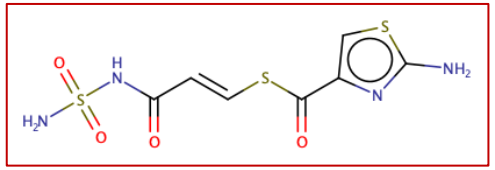
34b
tR: 1.35
m/z: 171 (HPLC-MS)
m/z: 171.0358(HRMS)
deltam: 0.0438
ppm: 256.1

34c
tR: 1.45
m/z: 171 (HPLC-MS)
m/z: 171.0336(HRMS)
deltam: 0.0416
ppm: 243.2

34d
tR: 1.47
m/z: 279 (HPLC-MS)
m/z: (HRMS)

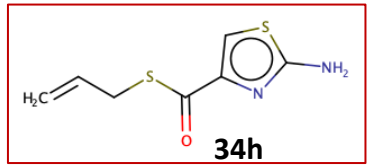


34e
tR: 1.65
m/z: 386/354 (HPLC-MS)
m/z: 386.0770/
354.0488 (HRMS)
deltam: 0.0395/0.0011
ppm: 102.3/3.1



34f
tR: 1.79
m/z: 309 (HPLC-MS)
m/z: (HRMS)

34g
tR: 2.49
m/z: 360 (HPLC-MS)
m/z: (HRMS)

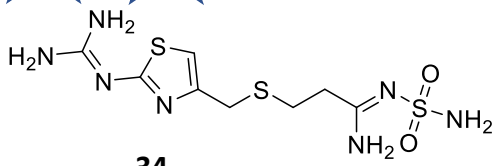


34h
tR: 2.62
m/z: 201 (HPLC-MS)
m/z: 201.0468(HRMS)
deltam: 0.0312
ppm: 155.2

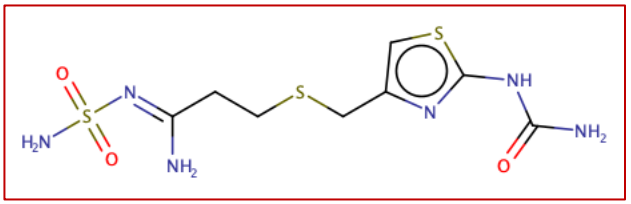
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	100	55.5	100	100	100	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
34a	1.25	NI	0	0	0	0	25.3	20.7	0	0
34b#	1.35	-167	0	0	**2.7**	0	**56.4**	0	0	0
34c#	1.45	-167	0	0	**3.0**	0	0	**36.2**	0	4.3
34d	1.47	-59	0	0	0	0	0	0	10.0	0
34e	1.65	+48/ +16	0	0	**37.3**	0	0	17.0	0	0
34f#	1.79	-29	0	0	0	0	0	0	**33.6**	0
34g	2.49	+22	0	0	0	**8.7**	0	0	0	0
34h	2.62	-137	0	0	0	0	6.4	0	0	0

#Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Famotidine (**34**) - **Biomimetic transformation (II)**



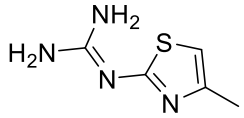
34
tR: 2.24
m/z: 338 (HPLC-MS)
m/z: (HRMS)



34i
tR: 2.80
m/z: 339/260 (HPLC-MS)
m/z: 339.0832/
260.0665(HRMS)
deltam: 0.0464
ppm: 136.8

34j
tR: 2.88
m/z: 350 (HPLC-MS)
m/z: 350.0505(HRMS)

34k
tR: 2.99
m/z: - (HPLC-MS)
m/z: (HRMS)



34l
tR: 3.25
m/z: 156 (HPLC-MS)
m/z: 156.0382(HRMS)
deltam: -0.0088
ppm: -56.4

34m
tR: 3.95
m/z: 275/227 (HPLC-MS)
m/z: (HRMS)

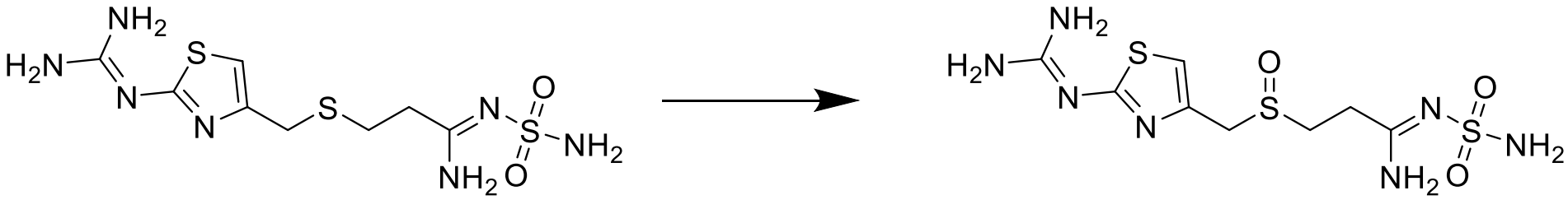
34n
tR: 4.27
m/z: 382 (HPLC-MS)
m/z: 382.3030(HRMS)

34o
tR: 4.74
m/z: 340 (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	100	55.5	100	100	100	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
34i	2.80	+1/ -78	**11.2**	0	0	0	11.8	0	0	0
34j#	2.88	+12	0	0	0	**4.4**	0	0	0	**81.2**
34k	2.99	NI	0	0	0	0	0	5.7	0	0
34l	3.25	-182	0	0	0	**47.2**	0	0	0	13.0
34m	3.95	-63/ -111	**3.0**	0	0	0	0	0	0	0
34n	4.27	+44	0	0	0	0	0	19.2	0	0
34o	4.74	+2	**17.6**	0	0	0	0	0	0	0

#Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

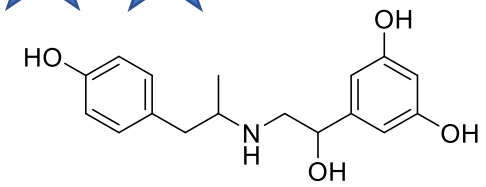
Famotidine (**34**) - in vitro/ in vivo biotransformation



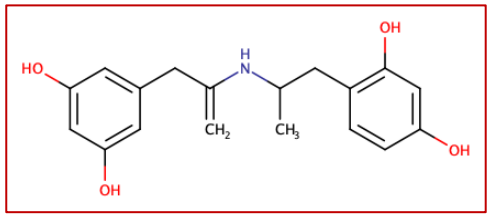
34

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/019462s039lbl.pdf

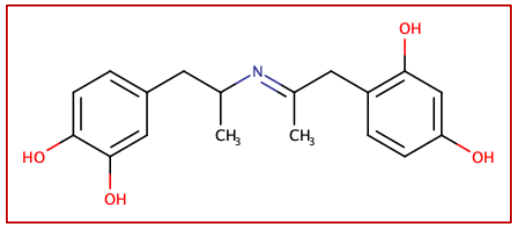
Fenoterol (**35**) - **Biomimetic transformation**



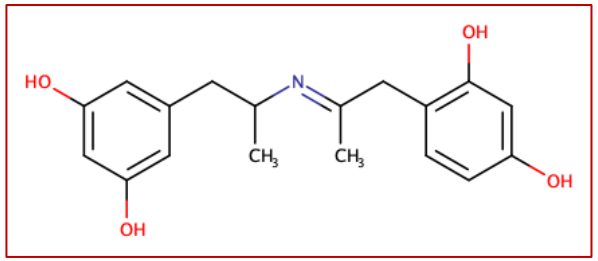
35
tR: 3.07
m/z: 304 (HPLC-MS)
m/z: (HRMS)



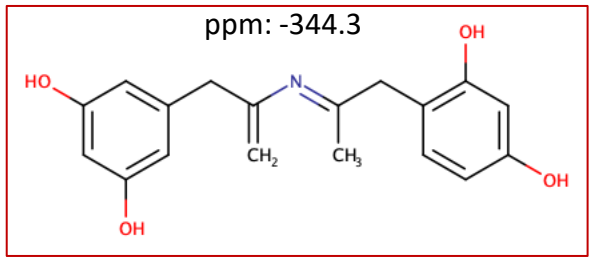
or



35b
tR: 3.35
m/z: 316 (HPLC-MS)
m/z: 316.0461(HRMS)
deltam: -0.1088
ppm: -344.3



35a
tR: 3.27
m/z: 316 (HPLC-MS)
m/z: 316.0461(HRMS)
deltam: -0.1088
ppm: -344.3



35c
tR: 3.60
m/z: 314 (HPLC-MS)
m/z: 314.1399(HRMS)
deltam: 0.0007
ppm: 2.2

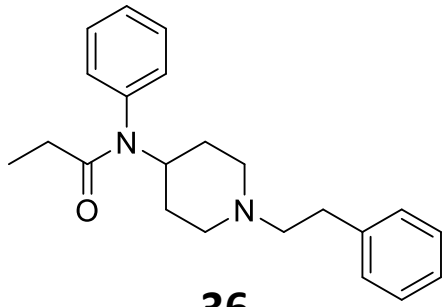
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	100	100	100	100	100	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
35a	3.27	+12	0	0	60.2	52.9	0	0	44.8	47.1
35b	3.35	+12	0	0	39.8	47.1	0	0	35.6	44.3
35c[#]	3.60	+10	0	0	0	0	0	100	19.6	8.6

[#]Major biomimetic metabolite
Non biomimetic metabolite

Fenoterol (**35**) - **in vitro/ in vivo biotransformation**

Hepatic ?

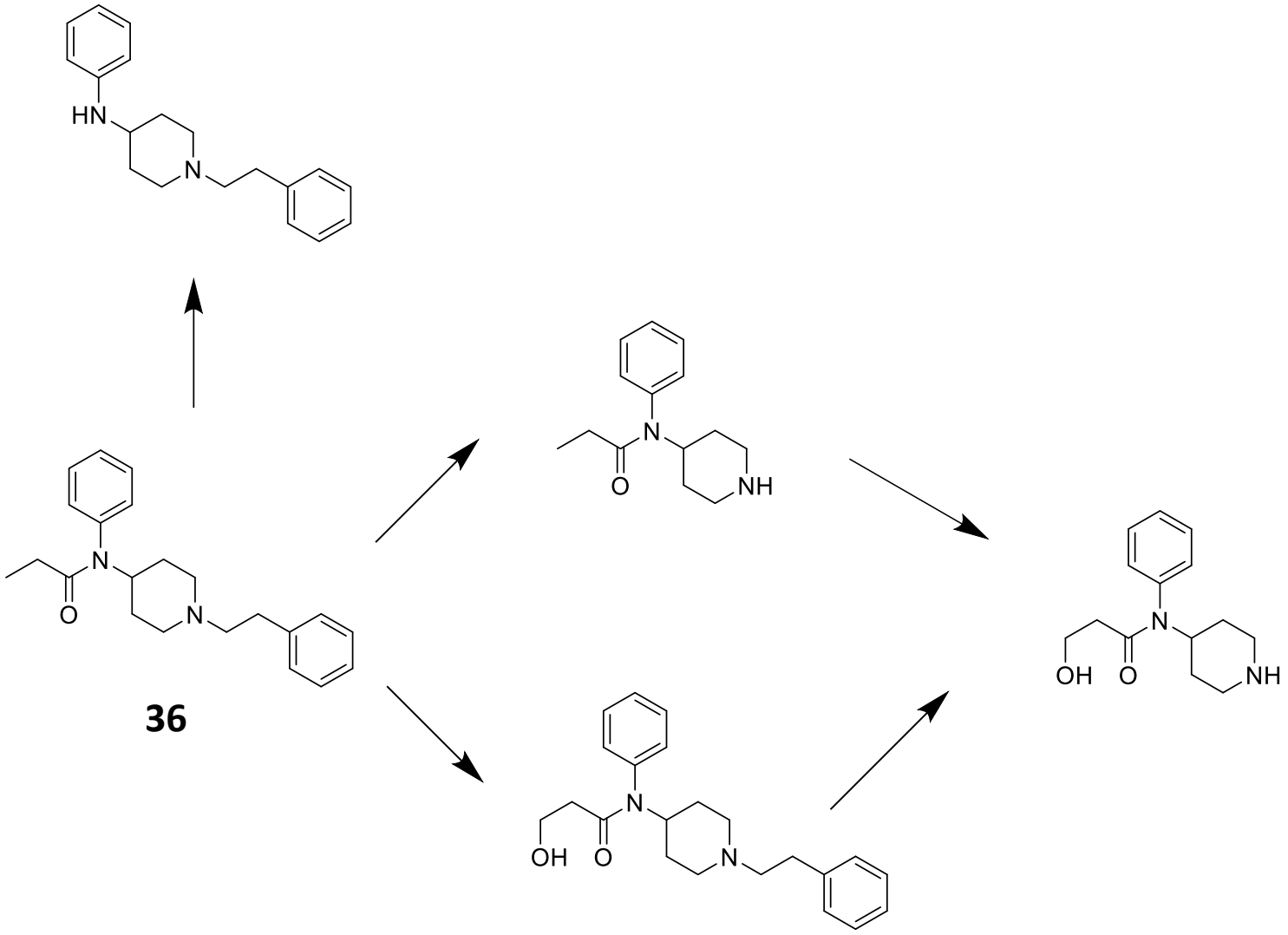
Fentanyl (**36**) - **Biomimetic transformation**



36

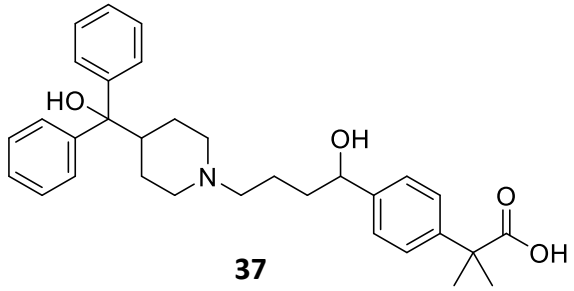
NO Biomimetic transformation

Fentanyl (**36**) - in vitro/ in vivo biotransformation

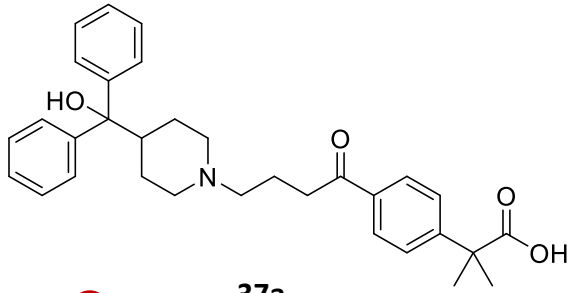


DePriest AZ, Puet BL, Holt AC, Roberts A, Cone EJ: Metabolism and Disposition of Prescription Opioids: A Review. Forensic Sci Rev. 2015 Jul;27(2):115-45.

Fexofenadine (**37**) - **Biomimetic transformation**



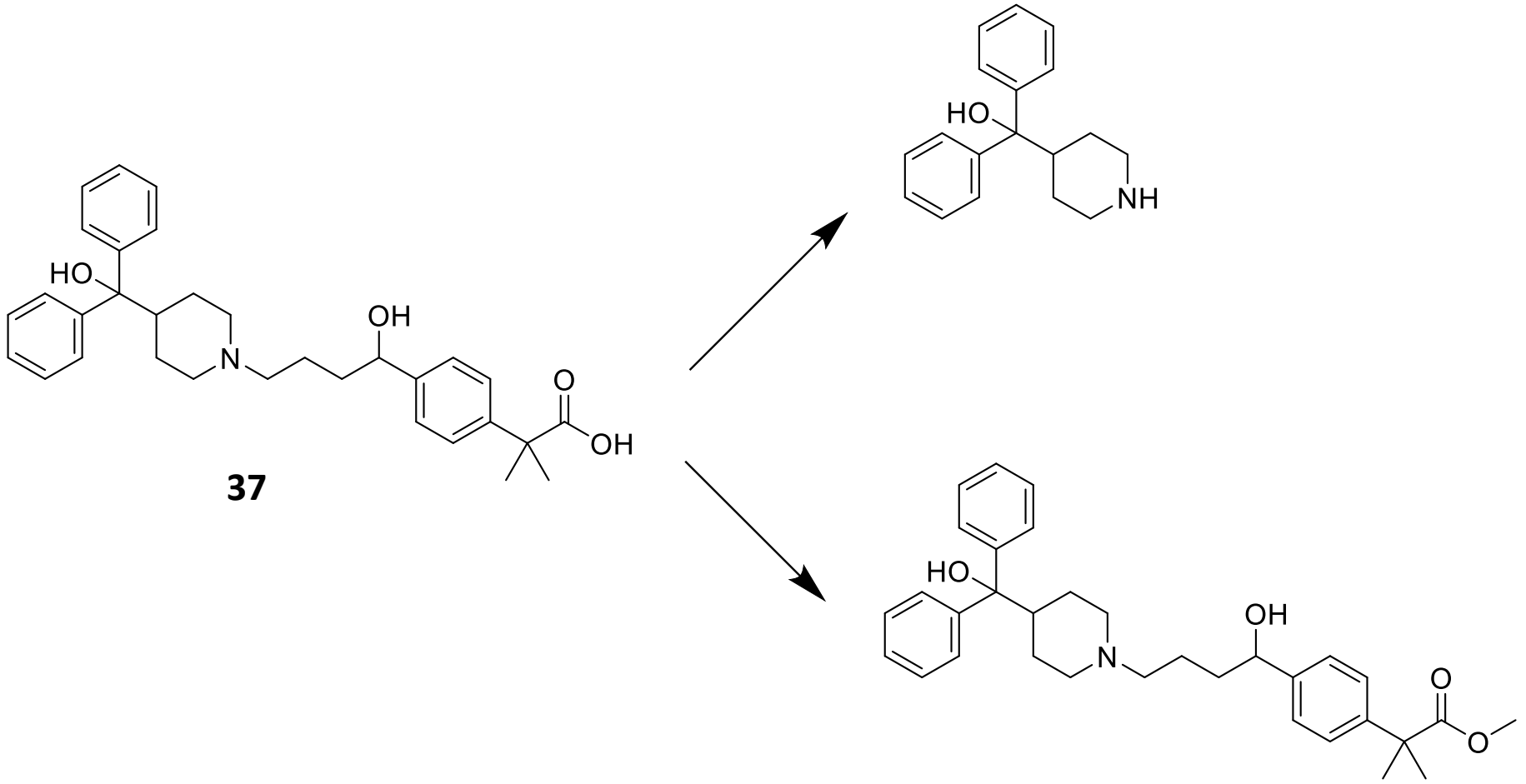
37
tR: 6.18
m/z: 502 (HPLC-MS)
m/z: (HRMS)



37a
tR: 6.52
m/z: 500 (HPLC-MS)
m/z: 500.2798(HRMS)
deltam: -0.0003
ppm: -0.6

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	21.5	27.8	27.1	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
37a	6.52	-2	0	0	0	0	**51.8**	35.7	39.3	0

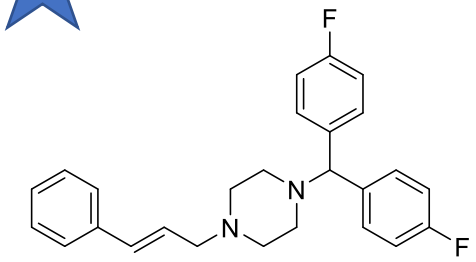
Fexofenadine (**37**) - in vitro/ in vivo biotransformation



37

https://pdf.hres.ca/dpd_pm/00053954.PDF

Flunarizine (**38**) - **Biomimetic transformation**



38
tR: 7.10
m/z: 405 (HPLC-MS)
m/z: (HRMS)

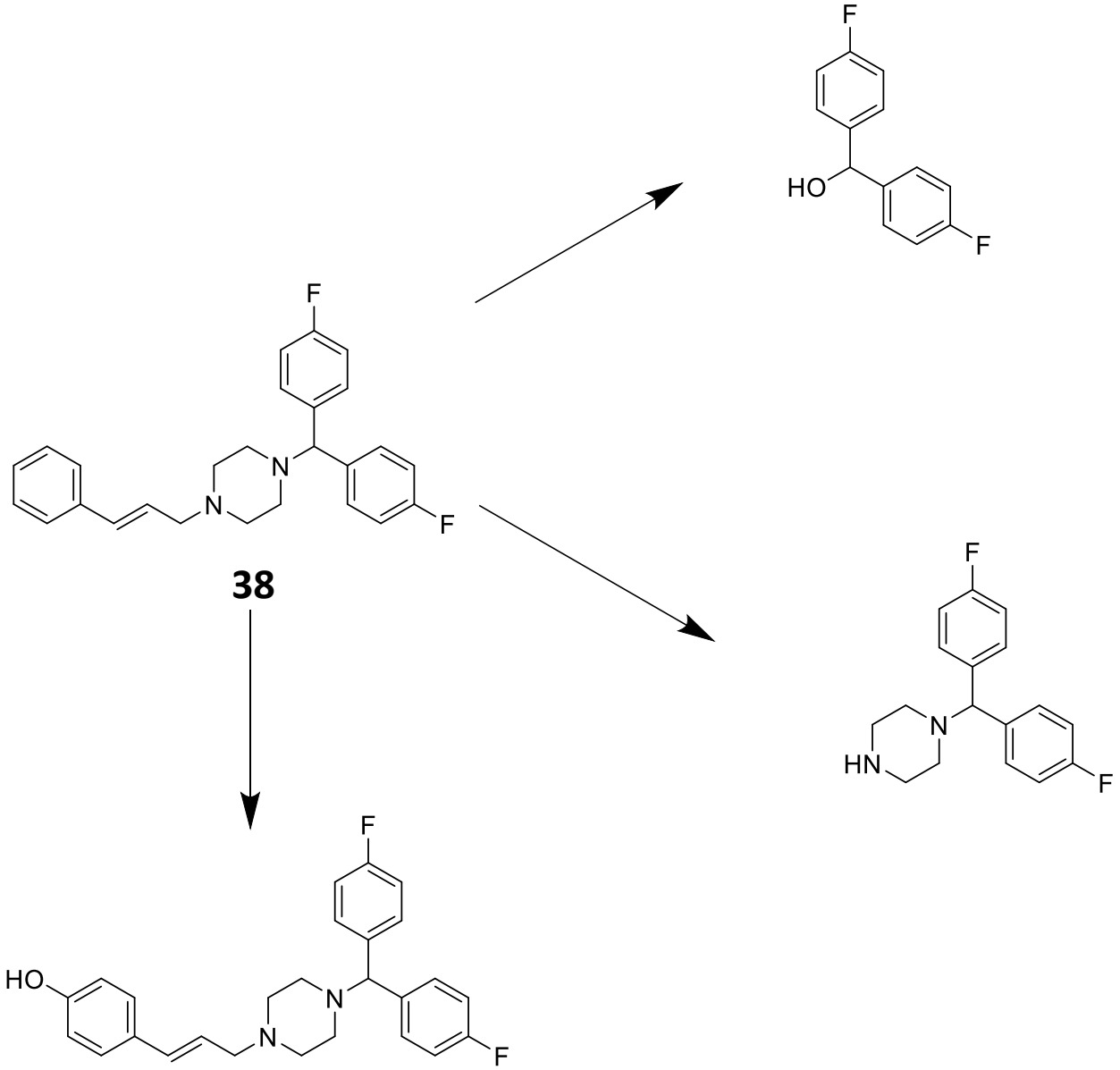
Újra mérni negatív ionmódban

38a
tR: 7.90
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	0	70.7	33.3	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
38a	7.90	NI	0	0	0	0	0	**37.1**	9.7	0

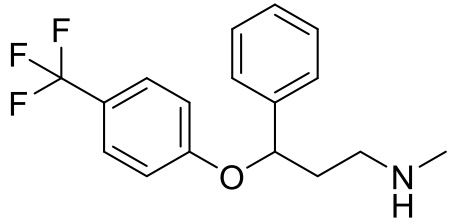
NI: Non-ionizable in positive mode of ESI

Flunarizine (**38**) - in vitro/ in vivo biotransformation



https://www.sciencedirect.com/science/article/pii/S0006291X83717614?via%3Dihub

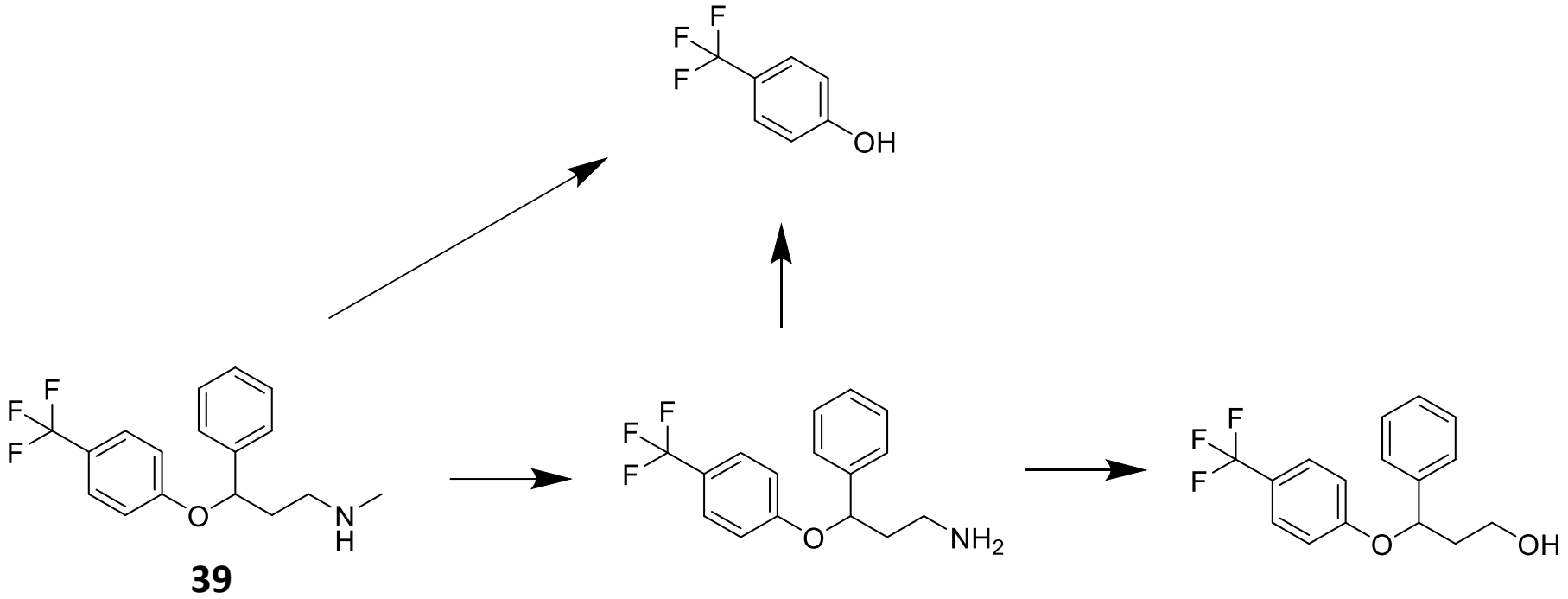
Fluoxetine (**39**) - **Biomimetic transformation**



39

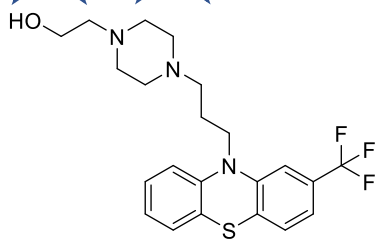
NO Biomimetic transformation

Fluoxetine (**39**) - in vitro/ in vivo biotransformation



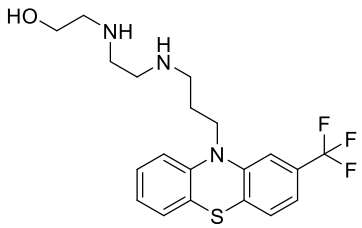
https://dmd.aspetjournals.org/content/28/10/1187

Fluphenazine (**40**) - **Biomimetic transformation (I)**



40
tR: 6.30
m/z: 438 (HPLC-MS)
m/z: (HRMS)

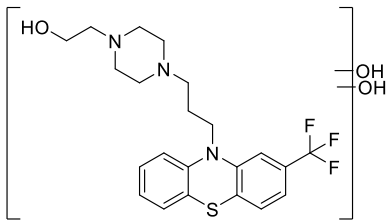
Valahol kell bele egy telítettlenség



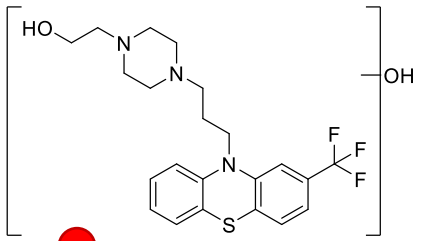
40a
tR: 4.00
m/z: 428 (HPLC-MS)
m/z: 428.1620(HRMS)

40b
tR: 4.24
m/z: 444 (HPLC-MS)
m/z: 444.1568(HRMS)

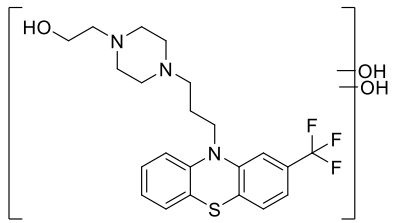
40c
tR: 4.57
m/z: 410 (HPLC-MS)
m/z: 410.1519(HRMS)
deltam: 0.0005
ppm: 1.2



40d
tR: 4.77
m/z: 470 (HPLC-MS)
m/z: 470.1725(HRMS)
deltam: 0.0000



40e
tR: 4.89
m/z: 454 (HPLC-MS)
m/z: 454.1786(HRMS)
deltam: 0.0010

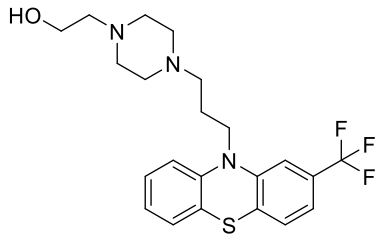


40f
tR: 5.47
m/z: 470 (HPLC-MS)
m/z: 470.1725(HRMS)
deltam: 0.0000

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	69.9	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
40a	4.00	-10	0	0	0	0	13.0	0	0	0
40b	4.24	+6	0	0	0	0	9.2	0	0	0
40c	4.57	-28	0	0	0	0	7.0	2.8	0	0
40d	4.77	+32	0	0	0	0	3.5	40.6	0	0
40e*#	4.89	+16	0	0	0	0	**49.1**	**49.4**	**22.3**	0
40f	5.47	+32	0	0	0	0	17.6	0	0	0
40g	6.42	+2	0	0	0	0	0	0	7.0	0
40h	9.09	-237	0	0	0	0	0	0	15.2	0

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Fluphenazine (**40**) - **Biomimetic transformation (II)**



40
tR: 6.30
m/z: 438 (HPLC-MS)
m/z: (HRMS)

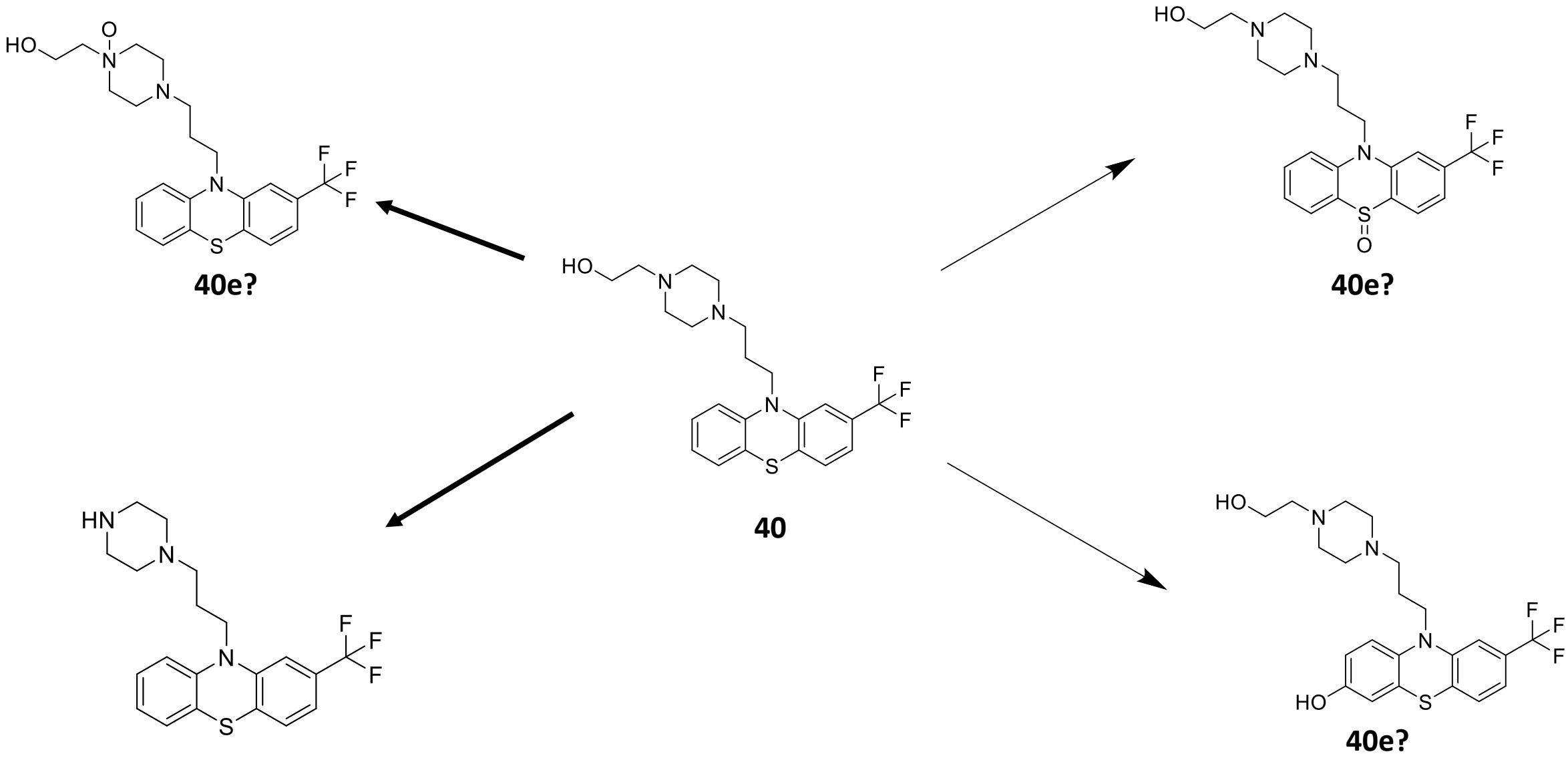
40g
tR: 6.42
m/z: 440 (HPLC-MS)
m/z: (HRMS)

40h
tR: 9.09
m/z: 201 (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	69.9	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
40a	4.00	-10	0	0	0	0	13.0	0	0	0
40b	4.24	+6	0	0	0	0	9.2	0	0	0
40c	4.57	-28	0	0	0	0	7.0	2.8	0	0
40d	4.77	+32	0	0	0	0	3.5	40.6	0	0
40e*#	4.89	+16	0	0	0	0	**49.1**	**49.4**	**22.3**	0
40f	5.47	+32	0	0	0	0	17.6	0	0	0
40g	6.42	+2	0	0	0	0	0	0	7.0	0
40h	9.09	-237	0	0	0	0	0	0	15.2	0

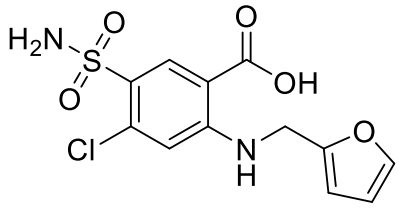
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Fluphenazine (**40**) - **in vitro/ in vivo biotransformation**



https://academic.oup.com/jpp/article-abstract/28/12/869/6196534?redirectedFrom=fulltext&login=true
https://www.sciencedirect.com/science/article/pii/0006295274904213

Furosemide (**41**) - **Biomimetic transformation**



41
tR: 7.10
m/z: 331 (HPLC-MS)
m/z: (HRMS)

Negatív ionmódban újra mérni?

41a
tR: 4.59
m/z: - (HPLC-MS)
m/z: (HRMS)

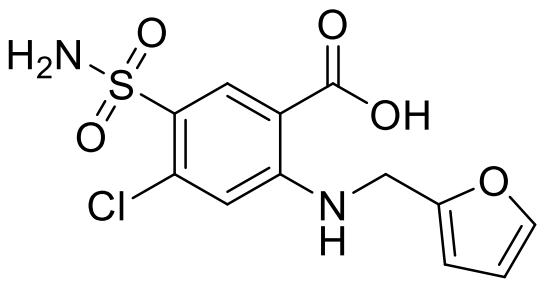
41b
tR: 5.00
m/z: - (HPLC-MS)
m/z: (HRMS)

(-) HRMS csúcs 215.0046, 248.9775

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	55.6	55.6	67.7	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			●	●	●	●	●	●	●	●
41a	4.59	NI	0	0	0	0	20.1	21.3	4.5	0
41b	5.00	NI	0	0	0	0	33.6	31.5	8.6	0

NI: Non-ionizable in positive mode of ESI

Furosemide (**41**) - **in vitro/ in vivo biotransformation**



41

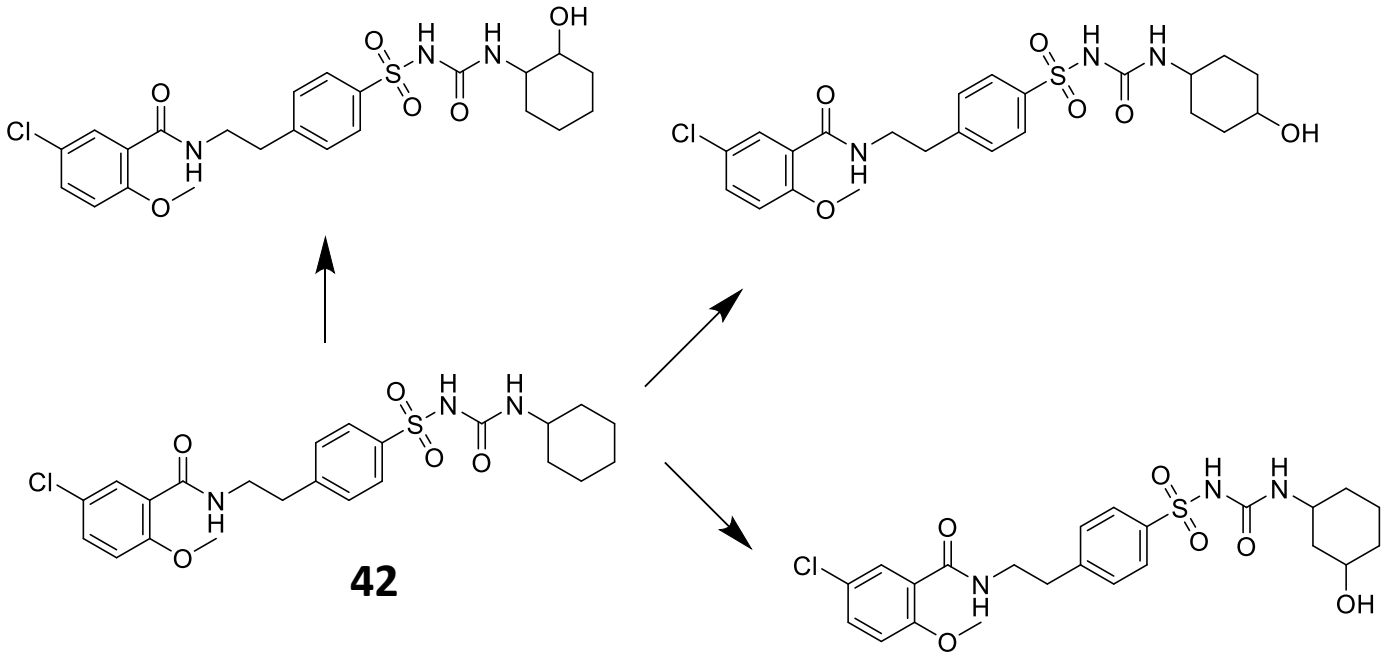
→ Furosemide glucuronide

https://link.springer.com/article/10.2165/00003088-199018050-00004

Glybenclamide (**42**) - **Biomimetic transformation**

NO biomimetic transzformation

Glybenclamide (**42**) - **in vitro/ in vivo biotransformation**

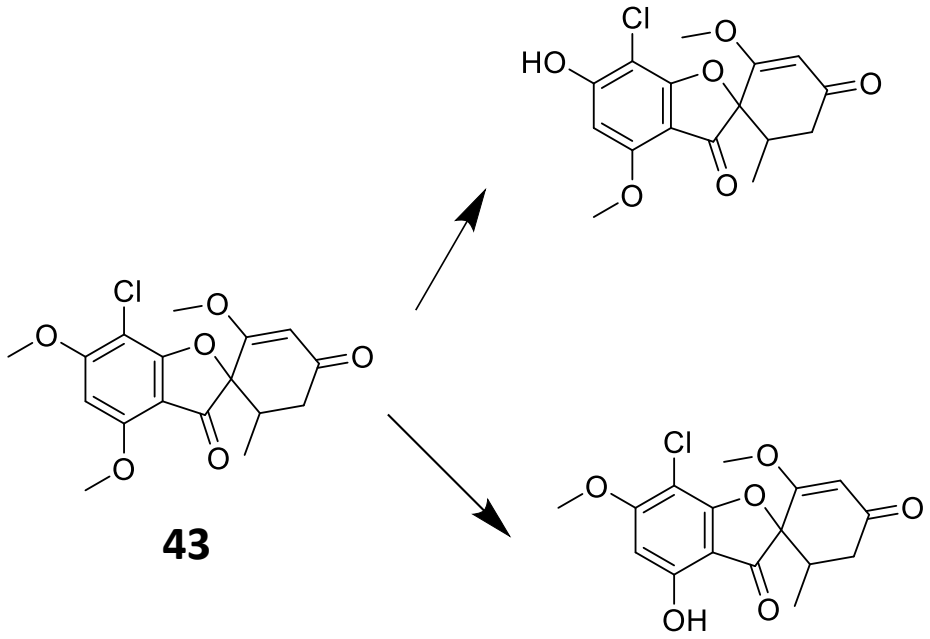


https://www.sciencedirect.com/science/article/pii/S0006295206005363?via%3Dihub

Griseofulvine (**43**) - **Biomimetic transformation**

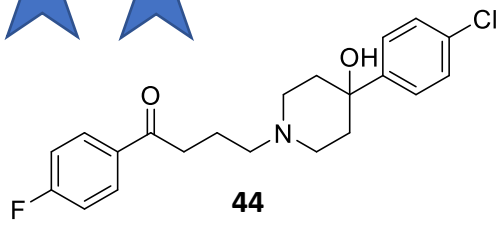
NO biomimetic transformation

Griseofulvine (**43**) - **in vitro/ in vivo biotransformation**



https://www.tandfonline.com/doi/abs/10.3109/03602537508993749

Haloperidol (**44**) - **Biomimetic transformation**



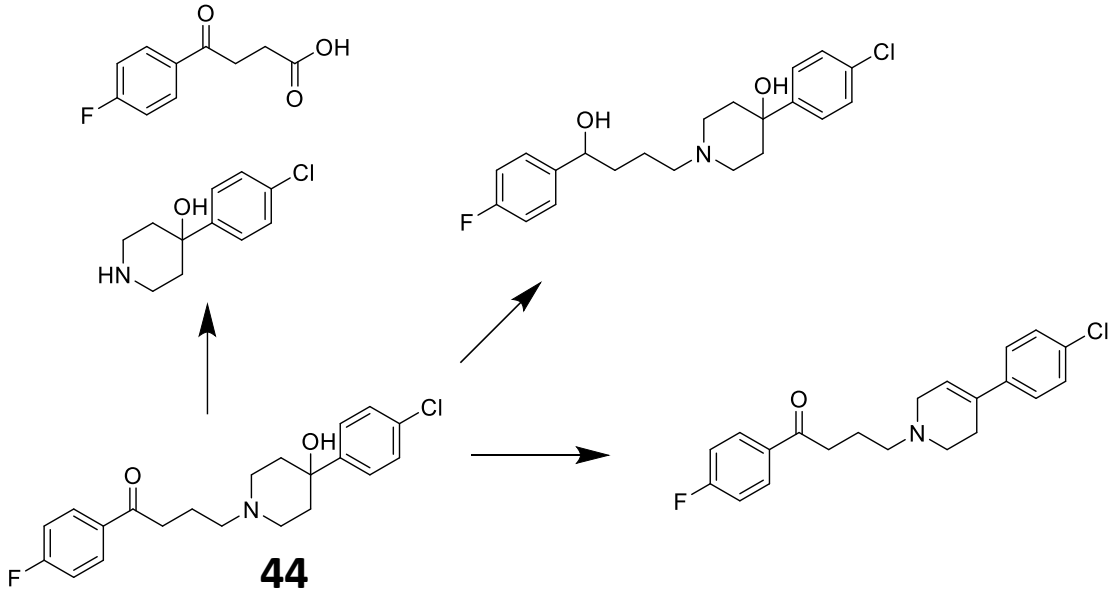
44
tR: 5.68
m/z: 376 (HPLC-MS)
m/z: (HRMS)

Cl-OH csere
-4H –re nézve a deltam-et

44a
tR: 6.07
m/z: 354 (HPLC-MS)
m/z: 354.1066(HRMS)
deltam:-0.0439
ppm: -124.0

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	0	30.6	32.2	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
44a	6.07	-22	0	0	0	0	0	24.0	22.6	0

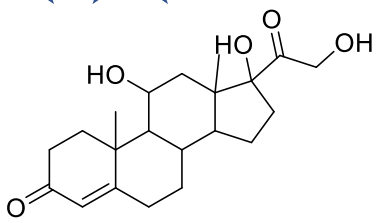
Haloperidol (**44**) - **in vitro/ in vivo biotransformation**



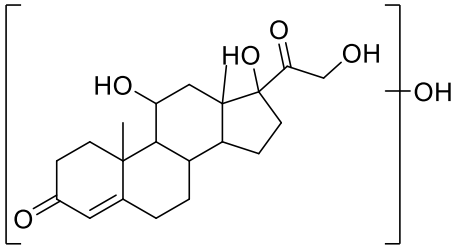
44

https://link.springer.com/article/10.2165/00003088-199937060-00001

Hydrocortisone (**45**) - **Biomimetic transformation**



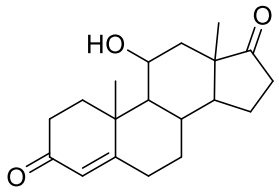
45
tR: 6.64
m/z: 363 (HPLC-MS)
m/z: (HRMS)



45a
tR: 6.50
m/z: - (HPLC-MS)
m/z: (HRMS)

45b
tR: 6.55
m/z: - (HPLC-MS)
m/z: (HRMS)

45c
tR: 6.60
m/z: 379 (HPLC-MS)
m/z: 379.2196(HRMS)
deltam: 0.0075
ppm: 19.8



45d
tR: 6.97
m/z: 349 (HPLC-MS)
m/z: 348.8906(HRMS)

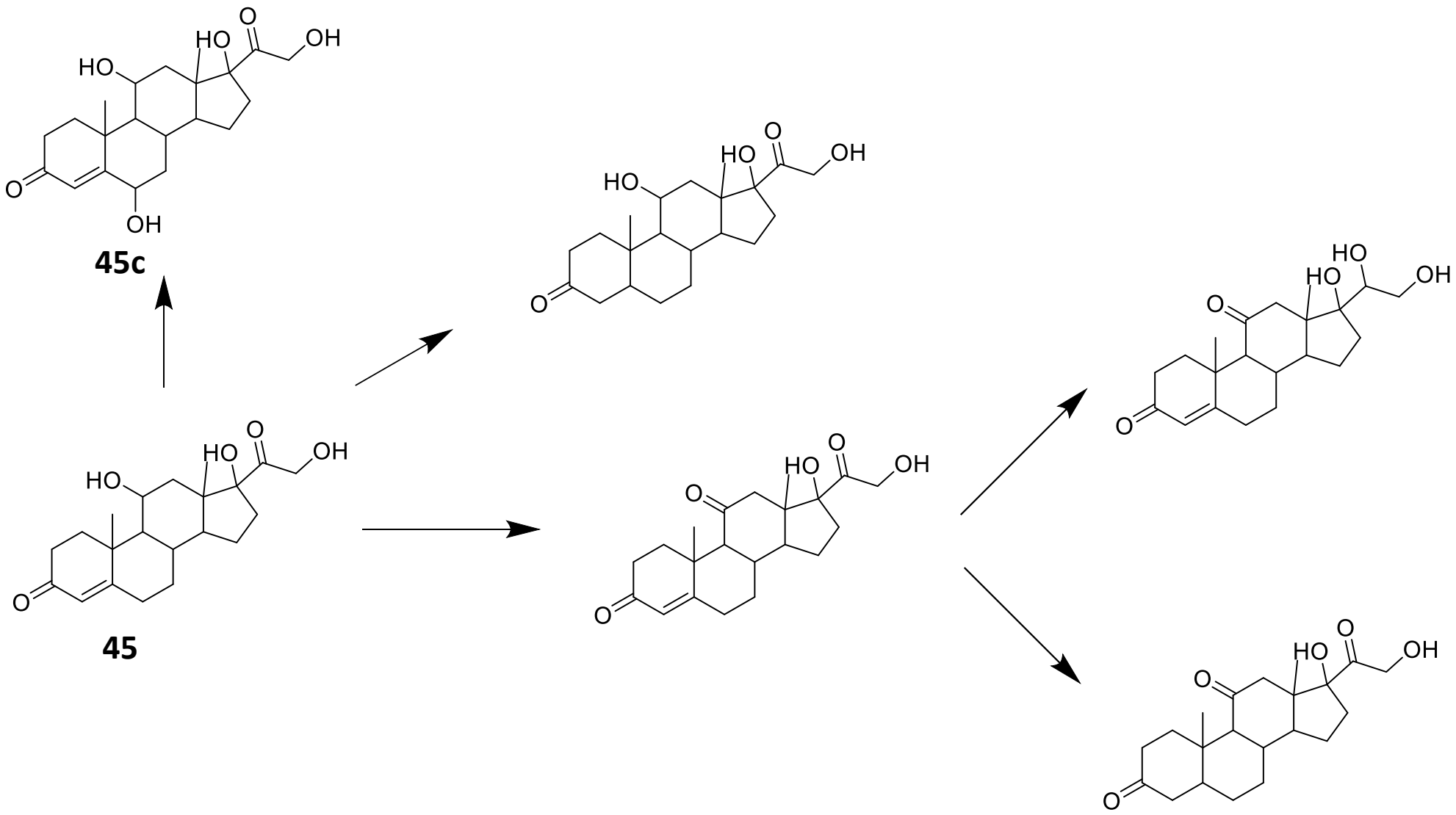
45e
tR: 7.66
m/z: 213 (HPLC-MS)
m/z: 212.8528(HRMS)

45f
tR: 7.82
m/z: 303 (HPLC-MS)
m/z: 303.1109(HRMS)
deltam: -0.0851
ppm: -280.8

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	97.6	0	0	23.7	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
45a	6.50	NI	0	0	0	0	0	0	0	6.6
45b#	6.55	NI	0	0	0	0	0	0	0	**43.7**
45c*	6.60	+16	0	0	0	0	0	0	0	**29.1**
45d	6.97	-14	0	0	0	**86.4**	0	0	**48.0**	10.4
45e	7.66	-150	0	0	0	0	0	0	16.1	0
45f	7.82	-60	0	0	0	3.2	0	0	0	5.82

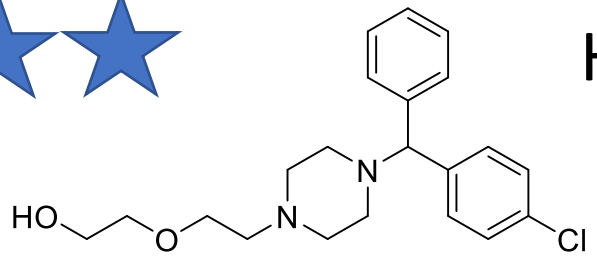
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Hydrocortisone (**45**) - **in vitro/ in vivo biotransformation**

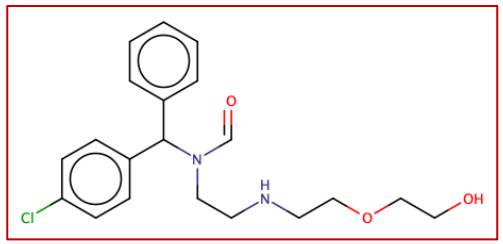


https://doi.org/10.1124/dmd.115.063495

Hydroxyzine (**46**) - **Biomimetic transformation**



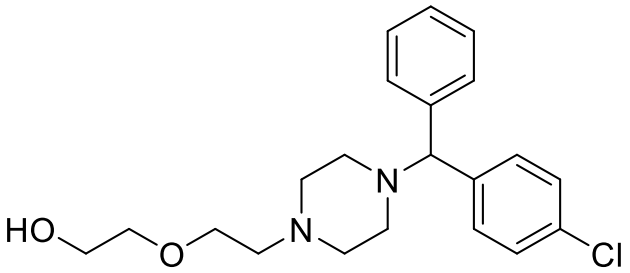
46
tR: 6.07
m/z: 375 (HPLC-MS)
m/z: 375.1844(HRMS)



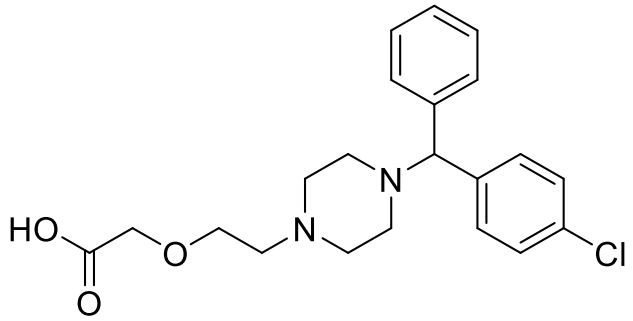
46a
tR: 5.12
m/z: 377 (HPLC-MS)
m/z: 377.1807(HRMS)
deltam: 0.0175
ppm: 46.4

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	0	8.5	16.5	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
46a	5.12	+2	0	0	0	0	0	3.2	0	0

Hydroxyzine (**46**) - **in vitro/ in vivo biotransformation**

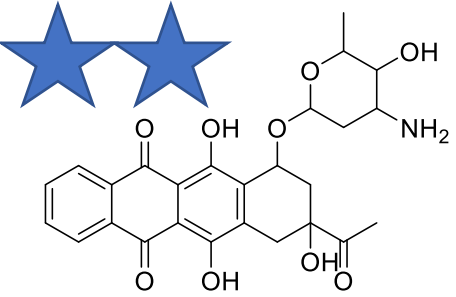


46

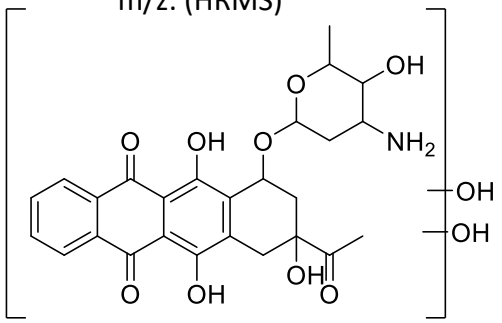


https://www.tandfonline.com/doi/full/10.1517/17425255.2013.759209

Idarubicin (**47**) - **Biomimetic transformation**

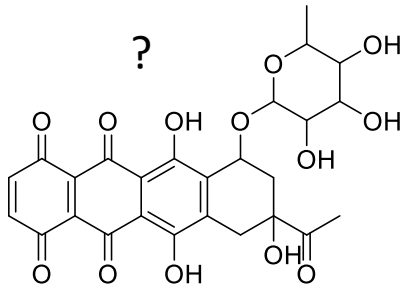


47
tR: 5.80
m/z: 498 (HPLC-MS)
m/z: (HRMS)



47a
tR: 3.80
m/z: 530 (HPLC-MS)
m/z: 530.1664(HRMS)
deltam: 0.0002
ppm: 0.4

47b
tR: 4.04
m/z: 379 (HPLC-MS)
m/z: (HRMS)



47c
tR: 4.62
m/z: 545 (HPLC-MS)
m/z: 545.1863(HRMS)
deltam: 0.0568
ppm: 104.2
ha értelmes a szerkezet

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	100	100	100	58.2	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
47a	3.80	+32	0	0	0	0	22.9	0	0	0
47b	4.04	-119	0	0	0	0	15.4	0	0	0
47c	4.62	+47	0	0	0	0	17.1	34.4	0	11.3
47d	4.72	+47	0	0	0	0	23.5	30.6	0	0
47e	5.82	+38	0	0	0	0	0	8.2	0	0
47f	6.17	-151	0	0	5.6	0	18.1	12.2	7.9	6.8
47g	7.10	NI	0	0	0	0	0	11.0	0	0

NI: Non-ionizable in positive mode of ESI

47d
tR: 4.72
m/z: 545 (HPLC-MS)
m/z: 545.1863(HRMS)

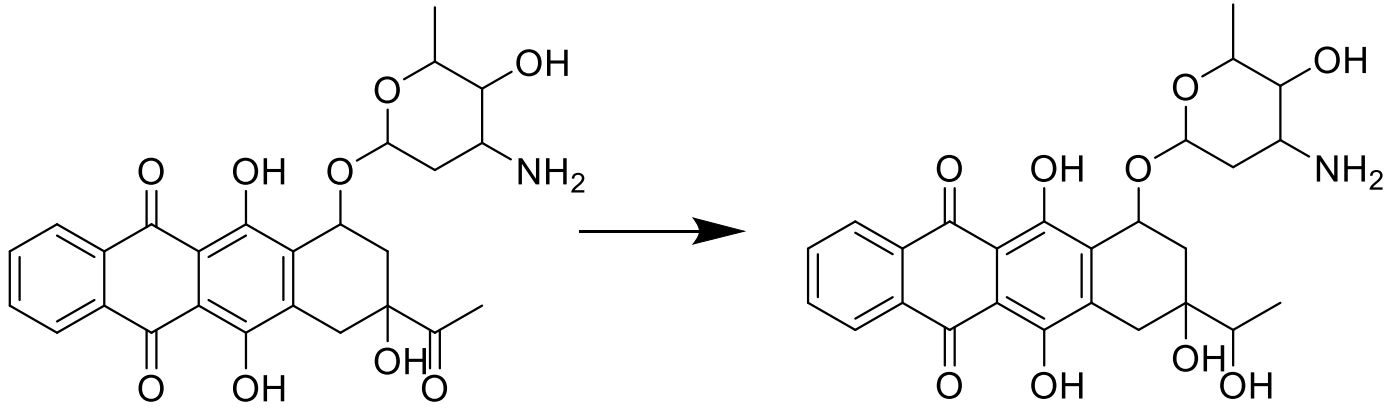
47e
tR: 5.82
m/z: 536 (HPLC-MS)
m/z: 536.1585 v 536.4741 (HRMS)

47f
tR: 6.17
m/z: 347 (HPLC-MS)
m/z: 347.0610(HRMS)

47g
tR: 6.17
m/z: - (HPLC-MS)
m/z: (HRMS)

(+) HRMS 463.1008
nagyobb csúcs

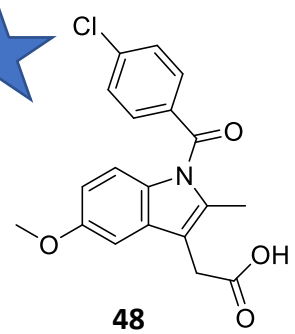
Idarubicin (**47**) - in vitro/ in vivo biotransformation



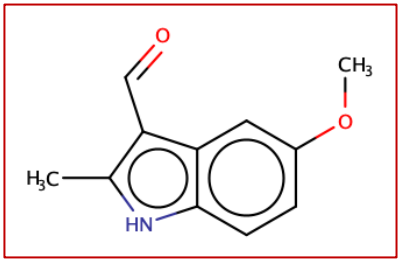
47

https://link.springer.com/article/10.2165/00003088-199324040-00002

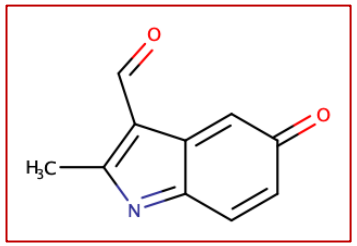
Indomethacin (**48**) - **Biomimetic transformation (I)**



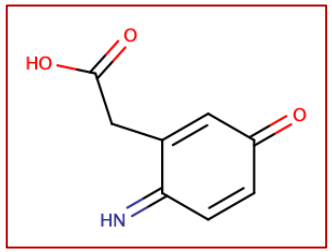
48
tR: 9.09
m/z: 358 (HPLC-MS)
m/z: (HRMS)



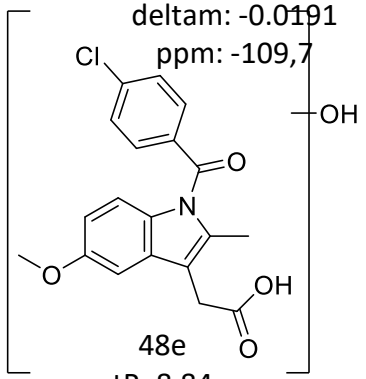
48a
tR: 6.35
m/z: 190 (HPLC-MS)
m/z: 190.0519(HRMS)
deltam: -0.0349
ppm: -183.6



48b
tR: 6.52
m/z: 174 (HPLC-MS)
m/z: 174.0364(HRMS)
deltam: -0.0191
ppm: -109,7



48c
tR: 6.80
m/z: 166 (HPLC-MS)
m/z: 165.9394(HRMS)
deltam:-0.1110
ppm: -668,9



48e
tR: 8.84
m/z: 374 (HPLC-MS)
m/z: 374.0782(HRMS)
deltam:-0.0013
ppm: -3,5

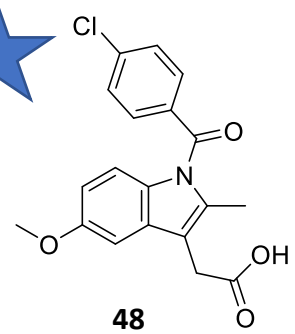
48d
tR: 8.09
m/z: - (HPLC-MS)
m/z: (HRMS)

48f
tR: 9.67
m/z: 415 (HPLC-MS)
m/z: 415.0409(HRMS)

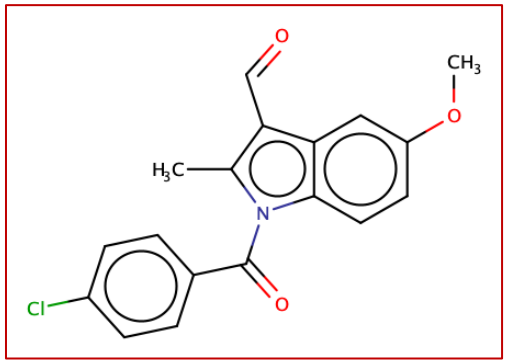
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	68.6	100	100	51.7	61.0	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
48a	6.35	-168	0	0	0	0	0	7	17.9	0
48b	6.52	-184	0	0	**31.3**	**47.1**	0	0	9.4	14.9
49c	6.80	-192	0	0	0	0	0	0	0	25.9
48d	8.09	NI	0	0	0	**52.9**	0	0	0	48.7
48e	8.84	16	0	0	0	0	10.0	0	0	0
48f	9.67	57	0	0	0	0	0.7	5.2	0	3.9
48g	9.74	NI	0	0	0	0	0	6.8	0	0
48h	9.85	NI	0	0	**28.9**	0	0	0	27.5	1.8
48i[#]	10.87	-30	0	0	0	0	**89.4**	**34.3**	0	0

[#]Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Indomethacin (**48**) - **Biomimetic transformation (II)**



48
tR: 9.09
m/z: 358 (HPLC-MS)
m/z: (HRMS)



48g
tR: 9.74
m/z: - (HPLC-MS)
m/z: (HRMS)

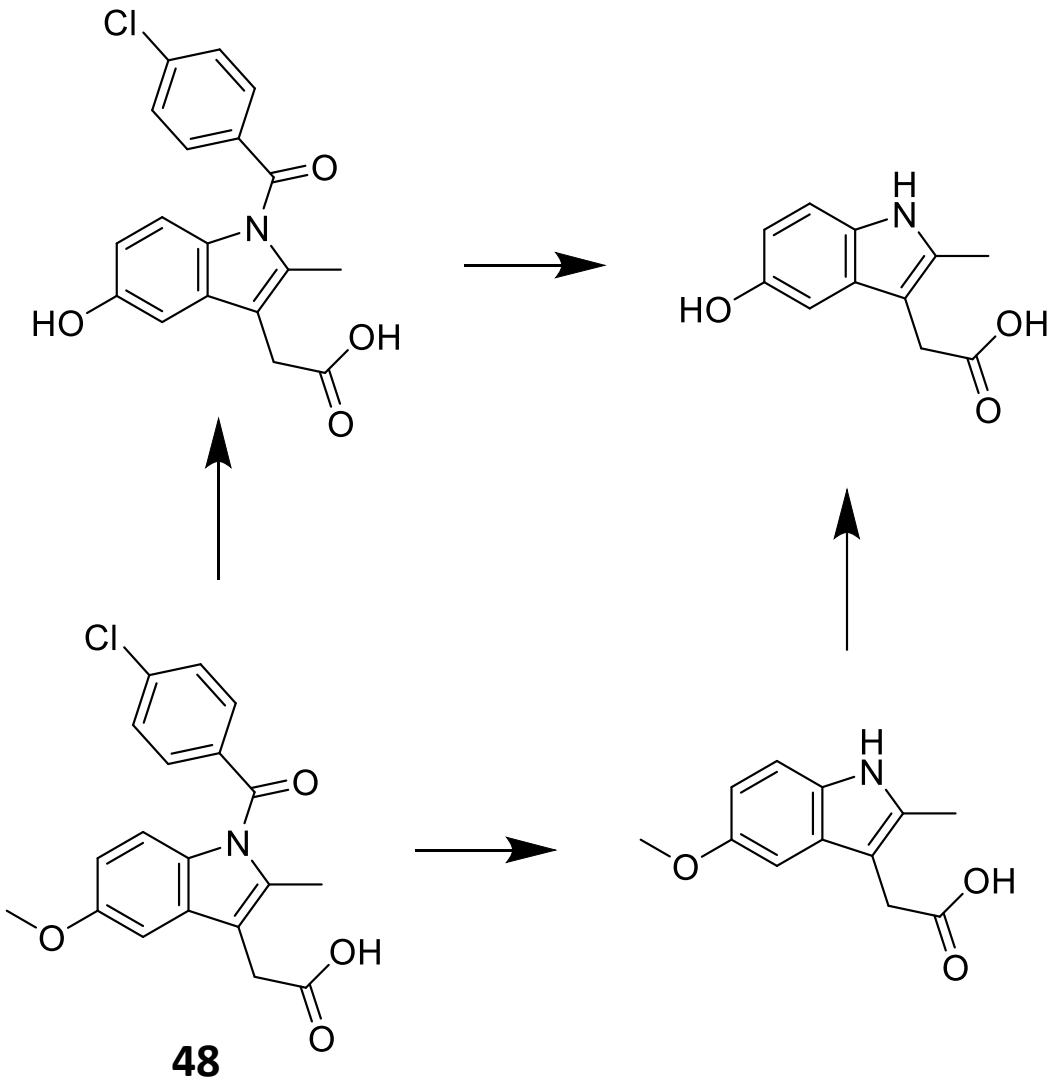
48h
tR: 9.85
m/z: - (HPLC-MS)
m/z: (HRMS)

48i
tR: 10.87
m/z: 328 (HPLC-MS)
m/z: 328.0725(HRMS)
deltam: -0.0015
ppm: -4.6

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	68.6	100	100	51.7	61.0	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
48a	6.35	-168	0	0	0	0	0	7	17.9	0
48b	6.52	-184	0	0	**31.3**	**47.1**	0	0	9.4	14.9
49c	6.80	-192	0	0	0	0	0	0	0	25.9
48d	8.09	**NI**	0	0	0	**52.9**	0	0	0	48.7
48e	8.84	16	0	0	0	0	10.0	0	0	0
48f	9.67	57	0	0	0	0	0.7	5.2	0	3.9
48g	9.74	**NI**	0	0	0	0	0	6.8	0	0
48h	9.85	**NI**	0	0	**28.9**	0	0	0	27.5	1.8
48i[#]	10.87	-30	0	0	0	0	**89.4**	**34.3**	0	0

[#]Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

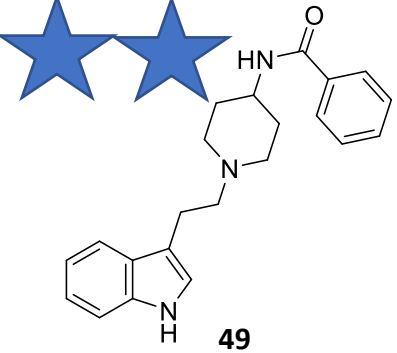
Indomethacin (**48**) - in vitro/ in vivo biotransformation



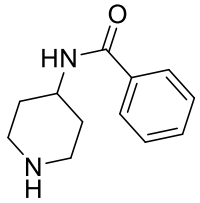
48

https://onlinelibrary.wiley.com/doi/10.1111/j.1755-3768.2012.02520.x

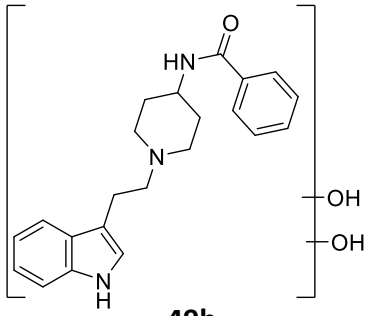
Indoramin (**49**) - **Biomimetic transformation**



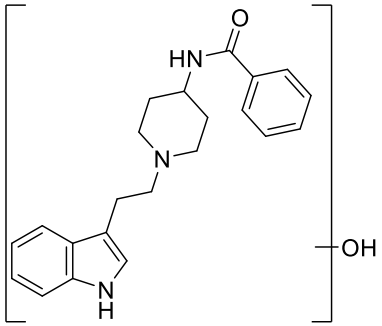
49
tR: 5.05
m/z: 348 (HPLC-MS)
m/z: (HRMS)



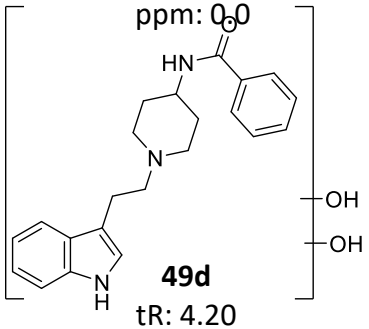
49a
tR: 2.74
m/z: 205 (HPLC-MS)
m/z: 205.1341(HRMS)
deltam: 0.0000
ppm: 0.0



49b
tR: 3.92
m/z: 380 (HPLC-MS)
m/z: 380.1975(HRMS)
deltam:0.0001
ppm: 0.3



49c
tR: 4.14
m/z: 364 (HPLC-MS)
m/z: 364.2022(HRMS)
deltam: -0.0003
ppm: -0.8



49d
tR: 4.20
m/z: 380 (HPLC-MS)
m/z: 380.1975(HRMS)
deltam:0.0001
ppm: 0.3

49e
tR: 4.43
m/z: 340 (HPLC-MS)
m/z: 340.3422(HRMS)

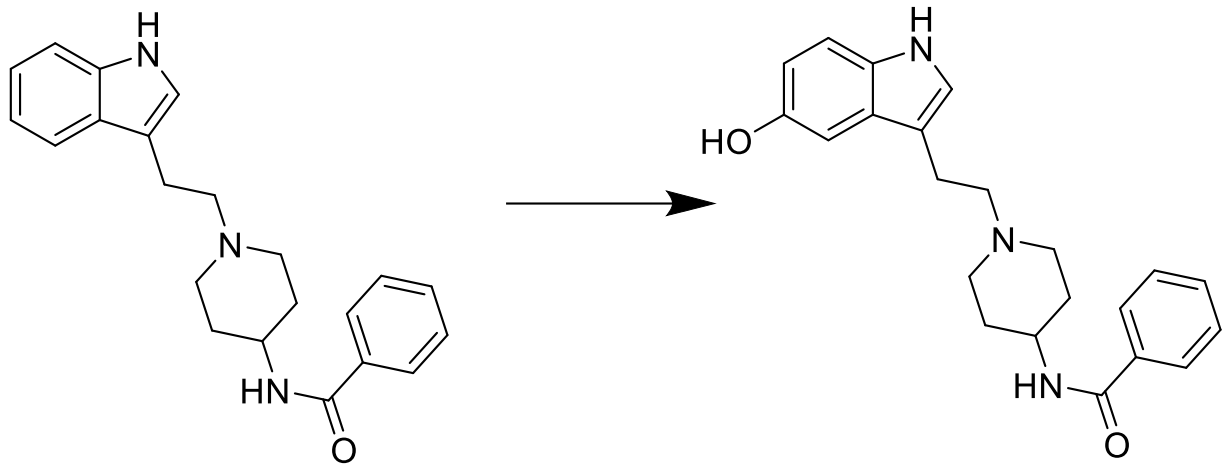
49f
tR: 5.22
m/z: - (HPLC-MS)
m/z: (HRMS)

49g
tR: 5.65
m/z: 452 (HPLC-MS)
m/z: 452.2544(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	97.4	61
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
49a#	2.74	-143	0	0	0	0	26.0	54.6	0	18.3
49b	3.92	32	0	0	0	0	10.8	0	0	7.6
49c*	4.14	16	0	0	0	0	0	43.0	7.3	0
49d#	4.20	32	0	0	0	0	20.3	0	87	0
49e	4.43	-8	0	0	0	0	7.8	2.8	0	8.6
49f	5.22	NI	0	0	0	0	17.4	0	0	0
49g	5.65	104	0	0	0	0	8.3	0	0	0

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Indoramin (**49**) - **in vitro/ in vivo biotransformation**



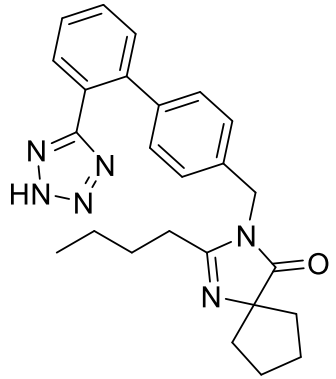
49 **49c**

Szervezetben emellet glükuronidként és szulfátként eliminálódik

https://www.tandfonline.com/doi/abs/10.3109/00498259009046634

https://link.springer.com/article/10.1007/BF00542212#citeas

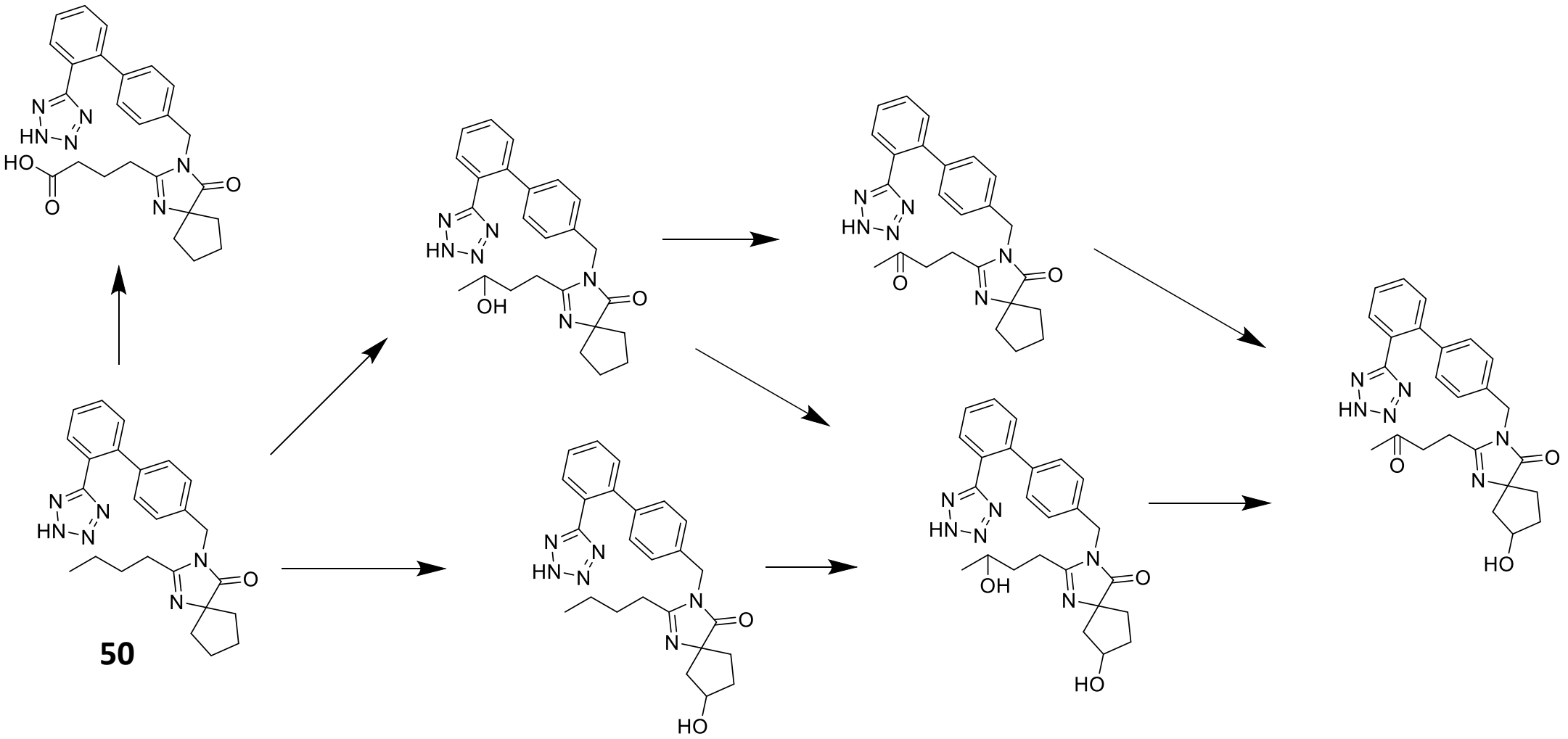
Irbesartan (**50**) - **Biomimetic transformation**



50

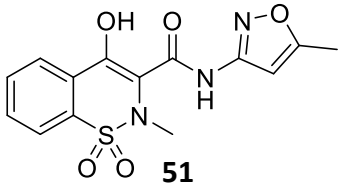
NO biomimetic transformation

Irbesartan (**50**) - in vitro/ in vivo biotransformation



https://dmd.aspetjournals.org/content/26/5/408.short

Isoxicam (**51**) - **Biomimetic transformation**



51
tR: 9.05
m/z: 336 (HPLC-MS)
m/z: (HRMS)

51a
tR: 2.50
m/z: 154 (HPLC-MS)
m/z:
154.0694(HRMS)

51b
tR: 3.60
m/z: 362 (HPLC-MS)
m/z: (HRMS)

51c
tR: 5.12
m/z: 567 (HPLC-MS)
m/z: 567.0587(HRMS)

51d
tR: 5.72
m/z: - (HPLC-MS)
m/z: (HRMS)

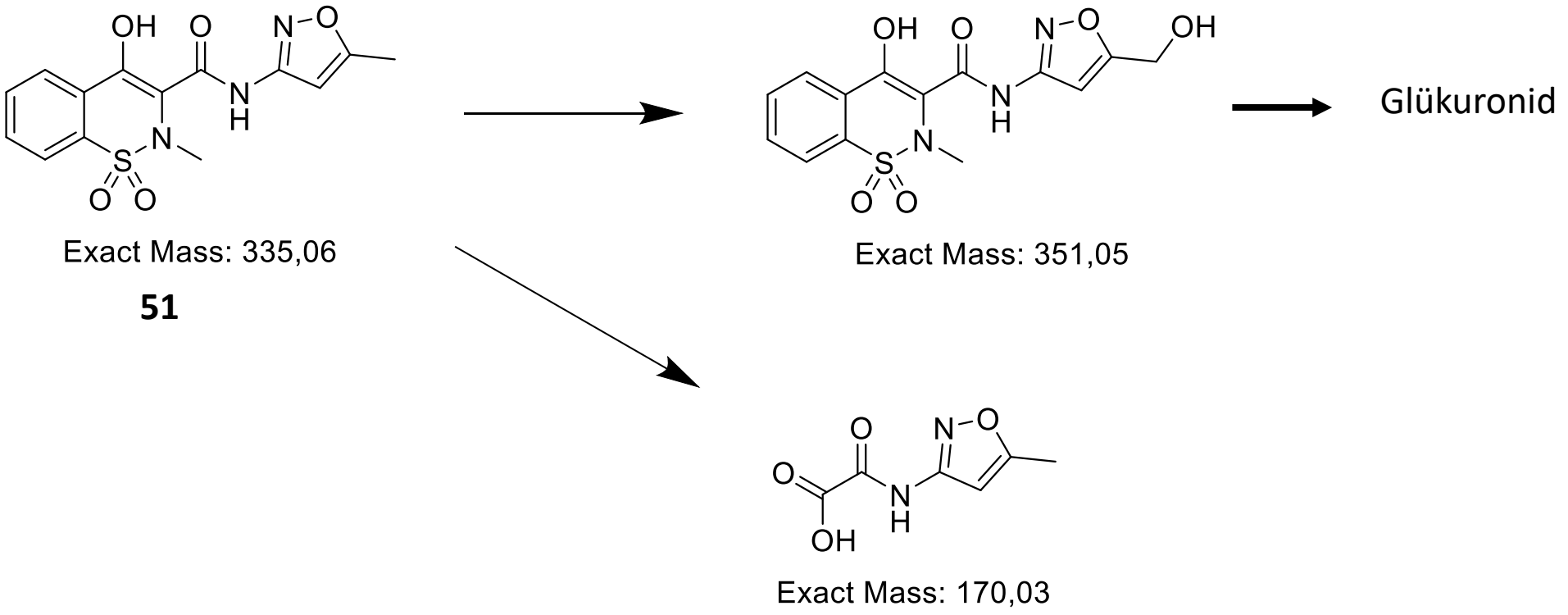
51e
tR: 6.79
m/z: - (HPLC-MS)
m/z: (HRMS)

51f
tR: 8.42
m/z: 334 (HPLC-MS)
m/z: 334.0498(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	70.4	100	36.1	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
51a	2.50	-182	**57.8**	**47.9**	0	**44.8**	55.2	59.7	49.6	46.9
51b	3.60	26	**8.3**	0	0	0	0	0	0	0
51c	5.12	231	0	0	0	0	10.7	11.8	0	0
51d	5.72	NI	0	0	0	0	5.7	5.3	0	0
51e	6.79	NI	0	0	0	0	0	2.8	9.2	0
51f#	8.42	-2	0	0	0	0	7.2	**15.3**	0	0

#Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

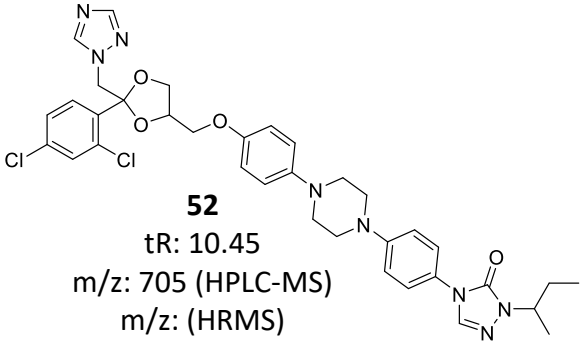
Isoxicam (**51**) - in vitro/ in vivo biotransformation



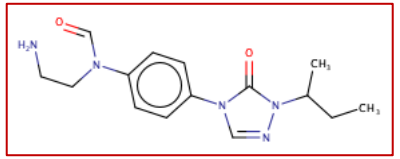
https://www.tandfonline.com/doi/abs/10.3109/03602538909029942?journalCode=idmr20

https://onlinelibrary.wiley.com/doi/abs/10.1002/9781118541203.xen521

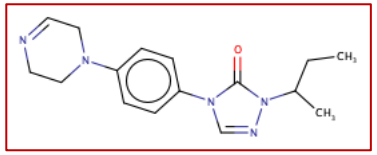
Itraconazole (**52**) - **Biomimetic transformation**



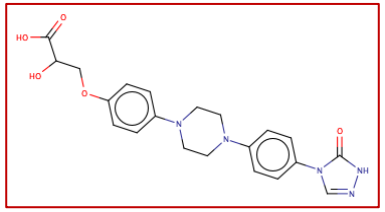
52
tR: 10.45
m/z: 705 (HPLC-MS)
m/z: (HRMS)



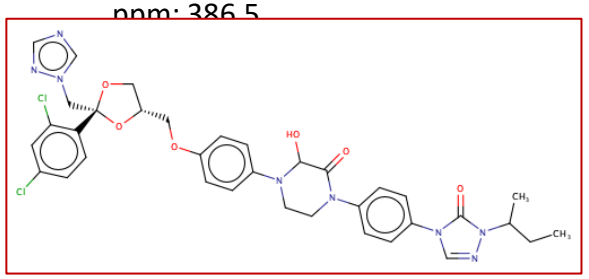
52a
tR: 3.84
m/z: 304 (HPLC-MS)
m/z: 304.295(HRMS)
deltam: 0.1176
ppm: 386.5



52b
tR: 3.95
m/z: 300 (HPLC-MS)
m/z: (HRMS)



52c
tR: 6.20
m/z: 426 (HPLC-MS)
m/z: (HRMS)

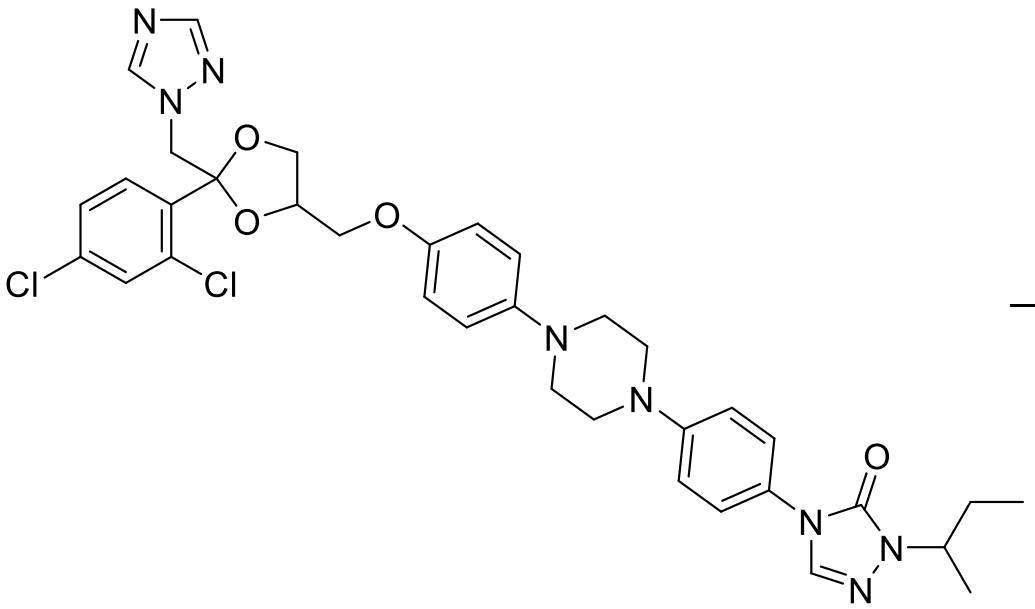


52d
tR: 9.55
m/z: 735 (HPLC-MS)
m/z: 735.198(HRMS)
deltam: -0.0233
ppm: -31.7

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	73.2	?	7.2
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
52a#	3.84	-401	0	0	0	0	**60.0**	0	0	0
52b	3.95	-405	0	0	0	0	29.1	0	0	0
52c#	6.20	-379	0	0	0	0	0	0	**10.4**	0
52d#	9.55	+30	0	0	0	0	0	3.7	0	**12.1**

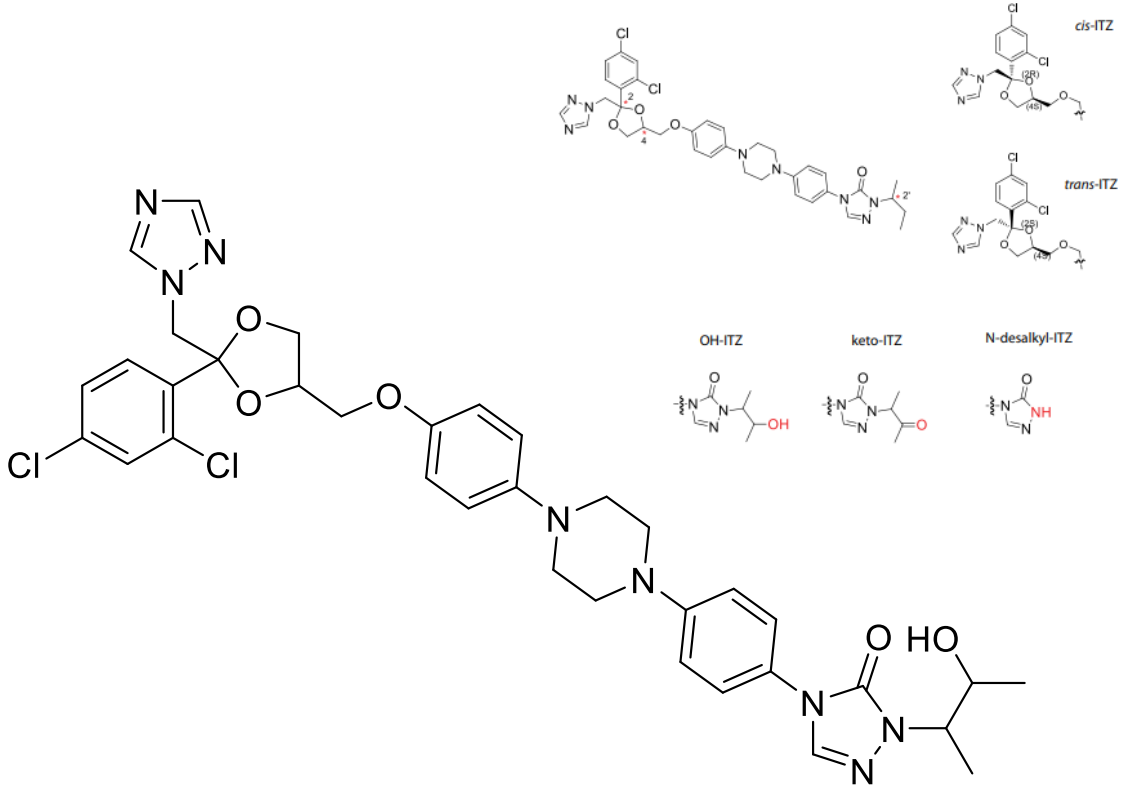
#Major biomimetic metabolite

Itraconazole (**52**) - in vitro/ in vivo biotransformation

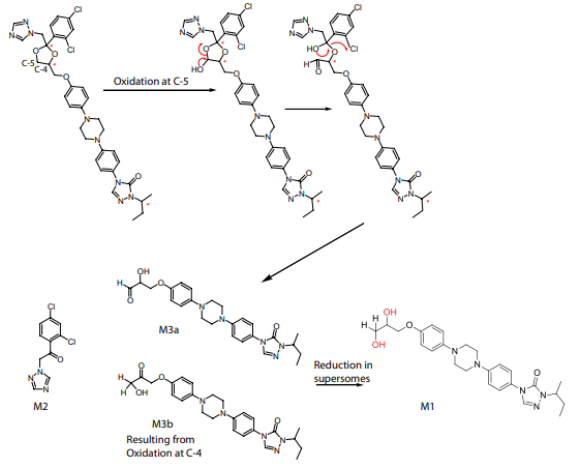


Exact Mass: 704,24

52



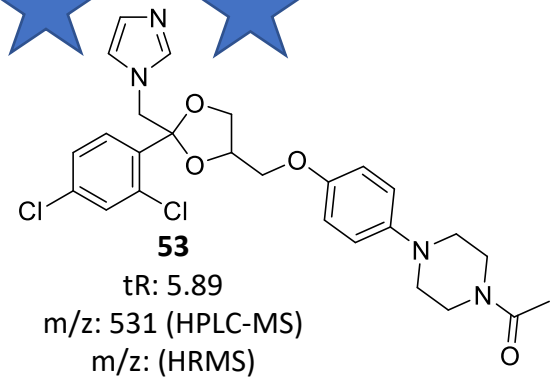
Exact Mass: 720,23



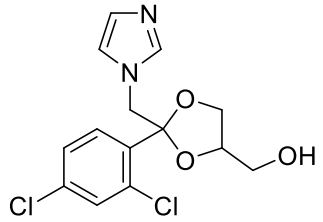
https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1439-0507.1989.tb02296.x

https://dmd.aspetjournals.org/content/40/3/426.short

Ketoconazole (**53**) - **Biomimetic transformation**

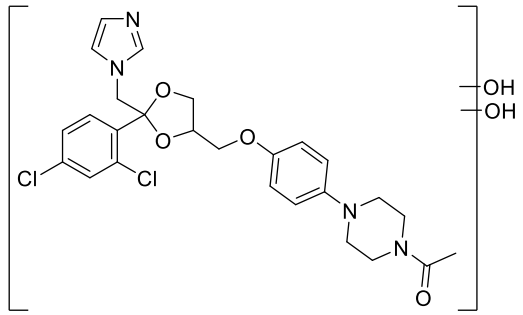


53
tR: 5.89
m/z: 531 (HPLC-MS)
m/z: (HRMS)

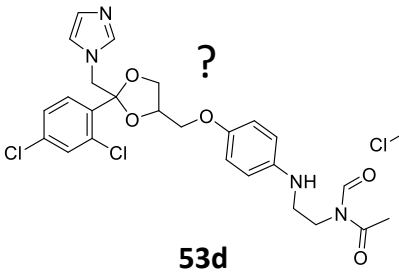


53a
tR: 4.54
m/z: 340 (HPLC-MS)
m/z: (HRMS)

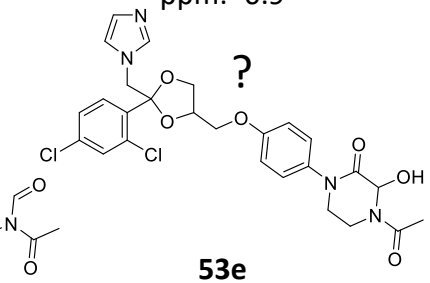
53b
tR: 4.77
m/z: 329 (HPLC-MS)
m/z: 329.0457(HRMS)
deltam: -0.0003
ppm: -0.9



53c
tR: 4.93
m/z: 563 (HPLC-MS)
m/z: (HRMS)



53d
tR: 5.67
m/z: 533 (HPLC-MS)
m/z: 533.1325(HRMS)
deltam: -0.0034
ppm: -6.4



53e
tR: 6.14
m/z: 561 (HPLC-MS)
m/z: 561.1255(HRMS)
deltam: -0.0053
ppm: -9.4

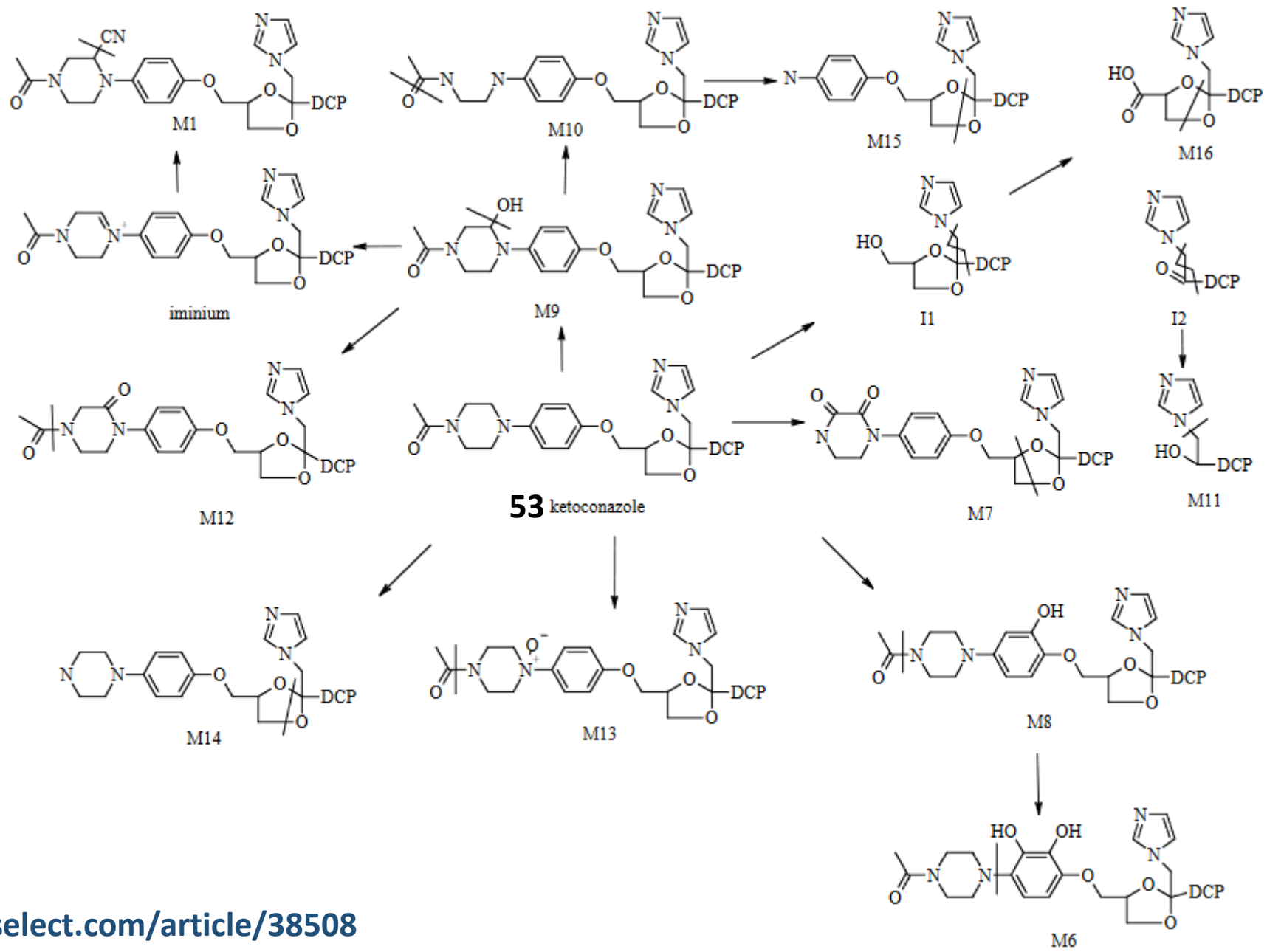
53f
tR: 6.80
m/z: 450 (HPLC-MS)
m/z: 450.0690(HRMS)

53g
tR: 7.37
m/z: 509 (HPLC-MS)
m/z: 509.1239(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	45.5	29.7
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
53a	4.54	-191	0	0	0	0	6.5	0	0	0
53b	4.77	-212	0	0	0	0	5.6	9.8	0	0
53c	4.93	32	0	0	0	0	0	9.1	0	0
53d	5.67	2	0	0	0	0	23.4	15.5	25.1	0
53e[#]	6.14	30	0	0	0	0	**41.5**	**31**	**74.9**	0
53f	6.80	-91	0	0	0	0	9.5	0	0	22.2
53g	7.37	-22	0	0	0	0	13.5	2.1	0	0

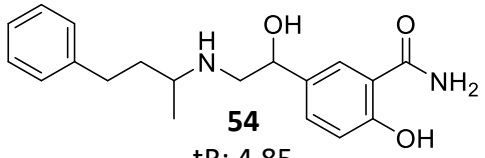
[#]**Major biomimetic metabolite**

Ketoconazole (**53**) - **in vitro/ in vivo biotransformation**

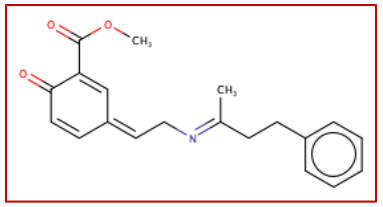


http://www.eurekaselect.com/article/38508

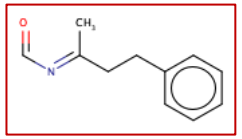
Labetalol (**54**) - **Biomimetic transformation**



54
tR: 4.85
m/z: 329 (HPLC-MS)
m/z: (HRMS)



54b
tR: 5.67
m/z: 324 (HPLC-MS)
m/z: 324.1248(HRMS)
deltam: -0.0352
ppm: -108,6



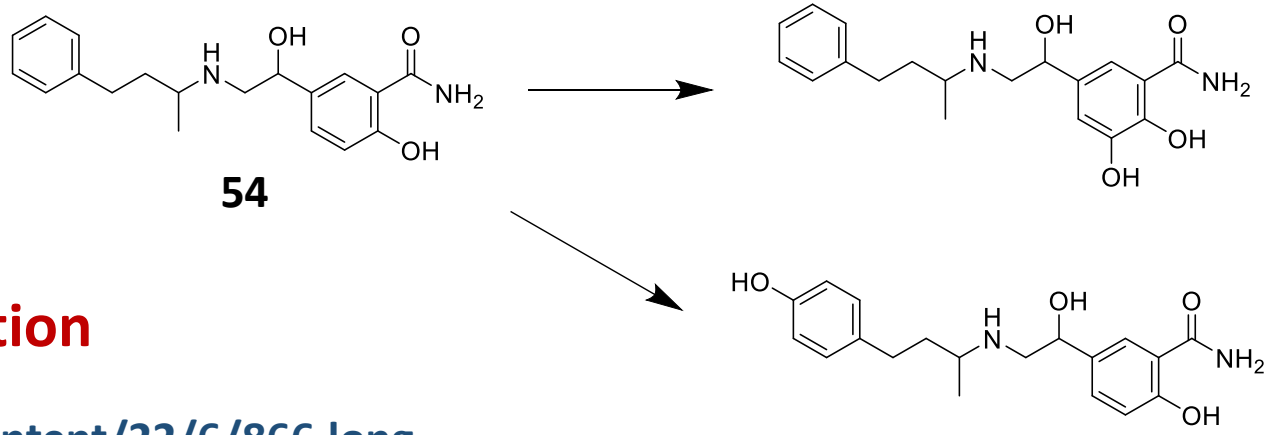
54c
tR: 7.99
m/z: 176 (HPLC-MS)
m/z: 176.0487(HRMS)
deltam: -0.0588
ppm: -334.0

54a
tR: 5.25
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	74.5	83.4	64.5	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
54a[#]	5.25	NI	0	0	0	0	0	**75.3**	**83.2**	0
54b	5.67	-5	0	0	0	0	20.7	0	0	0
54c	7.99	-153	0	0	0	0	20.4	0	0	0

[#]**Major biomimetic metabolite**
NI: Non-ionizable in positive mode of ESI

Labetalol (**54**) - **in vitro/ in vivo biotransformation**

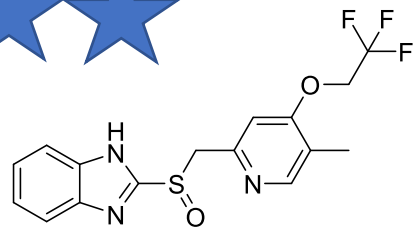


54

Mainly glucuronidation

https://dmd.aspetjournals.org/content/22/6/866.long

Lansoprazole (**55**) - **Biomimetic transformation**



55
tR: 6.02
m/z: 370 (HPLC-MS)
m/z: (HRMS)

55a
tR: 4.25
m/z: 298 (HPLC-MS)
m/z: 298.1199(HRMS)

55b
tR: 4.32
m/z: 286 (HPLC-MS)
m/z: 286.1021(HRMS)

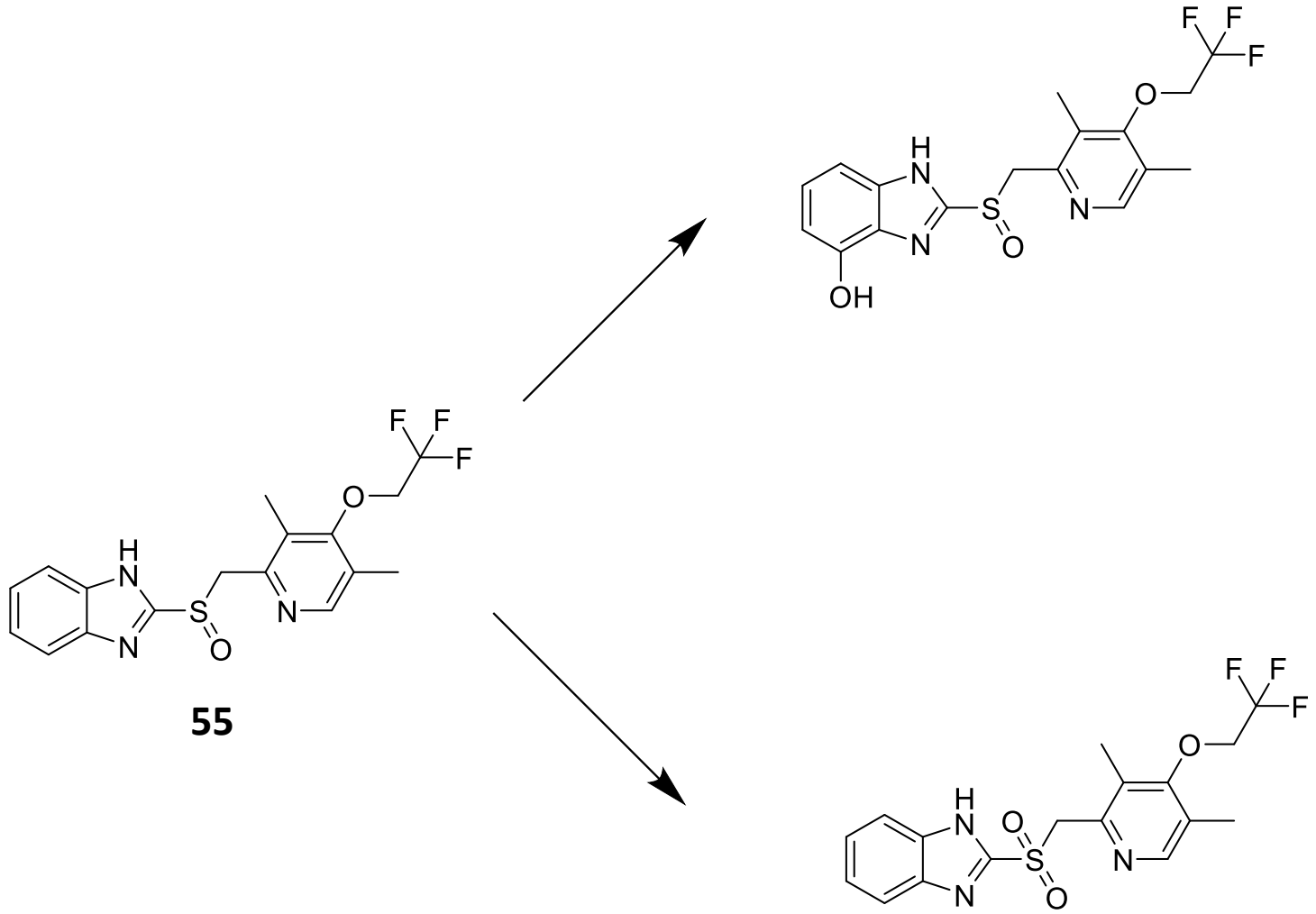
55c
tR: 4.65
m/z: 322 (HPLC-MS)
m/z: 322.1171(HRMS)

55d
tR: 6.17
m/z: 284 (HPLC-MS)
m/z: 284.1032(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			71.5	87.6	0	0	78.4	96.4	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
55a	4.25	-72	**11.1**	**13.9**	0	0	22.8	14.5	0	0
55b	4.32	-84	10.5	0	0	0	0	0	0	0
55c	4.65	-48	6.3	0	0	0	15.4	0	0	0
55d	6.17	-86	**14.4**	**78.7**	0	0	32.9	81.7	0	0

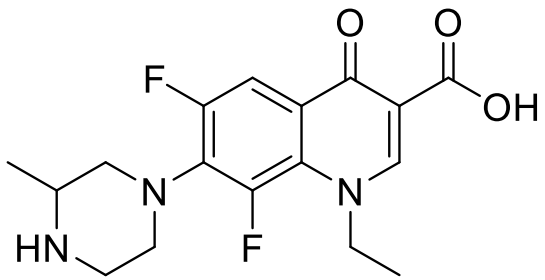
Non biomimetic metabolite

Lansoprazole (**55**) - in vitro/ in vivo biotransformation



https://www.jnmjournal.org/journal/view.html?doi=10.5056/jnm.2013.19.1.25

Lomefloxacin (**56**) - **Biomimetic transformation**



56

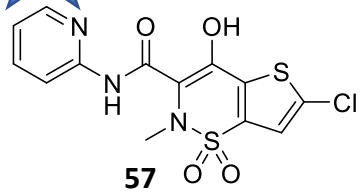
NO biomimetic transformation

Lomefloxacin (**56**) **- in vitro/ in vivo biotransformation**

Mainly glucuronidation

https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/20013s015lbl.pdf

Lornoxicam (**57**) - **Biomimetic transformation (I)**



57
tR: 7.59
m/z: 372 (HPLC-MS)
m/z: (HRMS)

57a
tR: 2.52
m/z: 154 (HPLC-MS)
m/z: 154.0708(HRMS)

57b
tR: 3.00
m/z: 154 (HPLC-MS)
m/z: 154.0823(HRMS)

57c
tR: 4.00
m/z: - (HPLC-MS)
m/z: (HRMS)

57d
tR: 4.70
m/z: 340 (HPLC-MS)
m/z: 340.3670(HRMS)

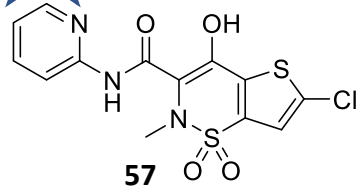
57e
tR: 5.07
m/z: 181 (HPLC-MS)
m/z: 181.0137(HRMS)

57f
tR: 7.92
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	1.5	0	0	100	100	56.5	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
57a	2.52	-218	52.2	52	54.7	51.2	51.9	51.7	60.6	54.4
57b	3.00	-218	0	0	0	0	0	5.7	0	0
57c	4.00	NI	0	0	8.7	0	0	0	15.2	0
57d	4.70	-32	0	0	0	0	7.9	1.6	0	0
57e	5.07	-191	0	0	0	0	10.7	13.3	0	0
57f	7.92	NI	0	0	0	0	4.5	8.1	0	0
57g	8.28	NI	0	0	0	0	6.0	6.4	0	0
57h	8.42	NI	0	0	0	0	7.1	6.4	0	0
57i	8.44	-161	0	0	0	0	0	0	5.2	0

Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Lornoxicam (**57**) - **Biomimetic transformation (II)**



57
tR: 7.59
m/z: 372 (HPLC-MS)
m/z: (HRMS)

57g
tR: 8.28
m/z: - (HPLC-MS)
m/z: (HRMS)

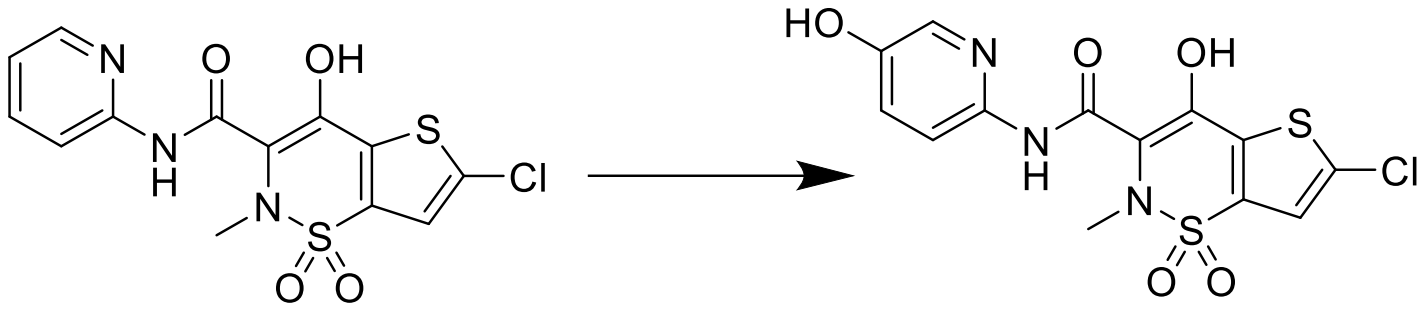
57h
tR: 8.42
m/z: - (HPLC-MS)
m/z: (HRMS)

57i
tR: 8.44
m/z: 211 (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	1.5	0	0	100	100	56.5	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
57a	2.52	-218	52.2	52	54.7	51.2	51.9	51.7	60.6	54.4
57b	3.00	-218	0	0	0	0	0	5.7	0	0
57c	4.00	NI	0	0	8.7	0	0	0	15.2	0
57d	4.70	-32	0	0	0	0	7.9	1.6	0	0
57e	5.07	-191	0	0	0	0	10.7	13.3	0	0
57f	7.92	NI	0	0	0	0	4.5	8.1	0	0
57g	8.28	NI	0	0	0	0	6.0	6.4	0	0
57h	8.42	NI	0	0	0	0	7.1	6.4	0	0
57i	8.44	-161	0	0	0	0	0	0	5.2	0

Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Lornoxicam (**57**) - in vitro/ in vivo biotransformation



57

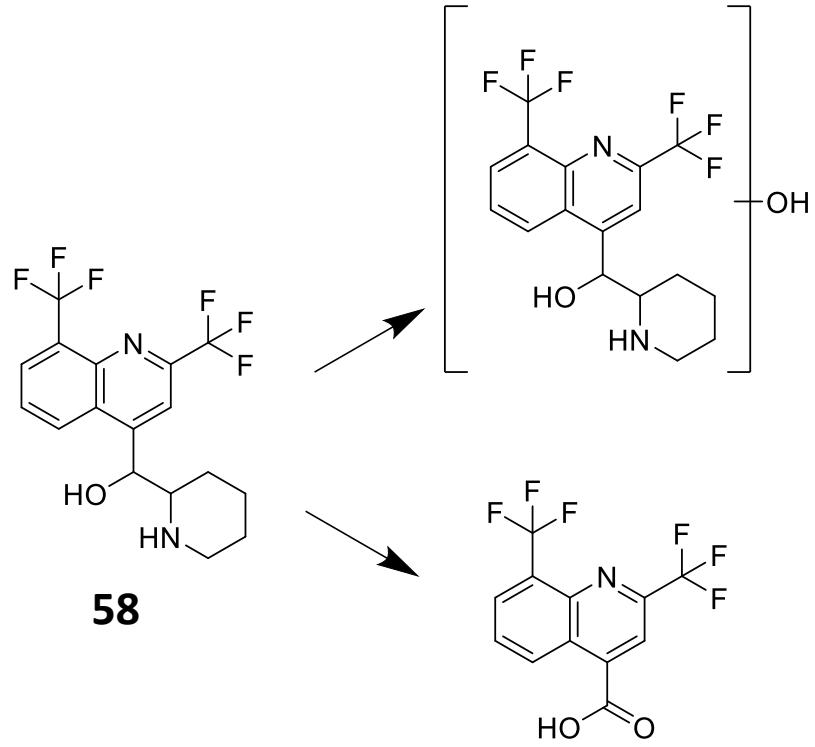
+2 polar, structurally unidentified metabolites

https://link.springer.com/article/10.2165/00003088-199834060-00001

Mefloquine (**58**) - **Biomimetic transformation**

NO biomimetic transformation

Mefloquine (**58**) **-** in vitro/ in vivo biotransformation

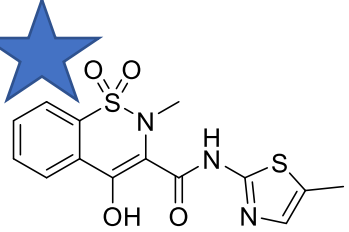


58

Instable

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/019591s026s028lbl.pdf

Meloxicam (**59**) - **Biomimetic transformation**



59
tR: 9.25
m/z: 351 (HPLC-MS)
m/z: (HRMS)

59a
tR: 5.84
m/z: 201 (HPLC-MS)
m/z: 201.0462(HRMS)

59b
tR: 5.97
m/z: 173 (HPLC-MS)
m/z: 173.0438(HRMS)

59c
tR: 6.10
m/z: 173 (HPLC-MS)
m/z: 173.0438(HRMS)

59d
tR: 6.67
m/z: 199 (HPLC-MS)
m/z: 199.0601(HRMS)

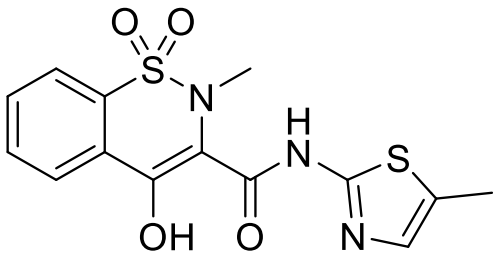
59e
tR: 6.85
m/z: - (HPLC-MS)
m/z: (HRMS)

59f
tR: 8.69
m/z: 210 (HPLC-MS)
m/z: 420.0099(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	57.4	100	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
59a	5.84	-150	0	0	0	0	15.8	12.3	0	0
59b	5.97	-178	0	0	0	0	0	7.0	0	0
59c	6.10	-178	0	0	0	0	0	12.4	0	0
59d	6.67	-152	0	0	0	0	0	25.5	0	0
59e	6.85	NI	0	0	0	0	25.5	12.7	0	0
59f[#]	8.69	-141	0	0	0	0	**58.6**	**27.2**	0	0

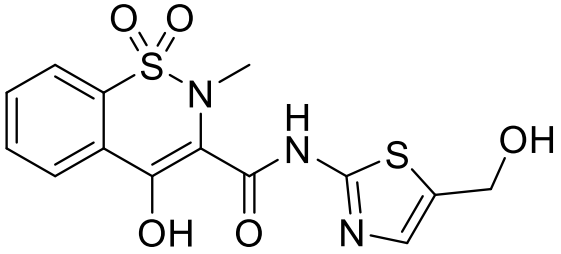
[#]Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Meloxicam (**59**) - in vitro/ in vivo biotransformation

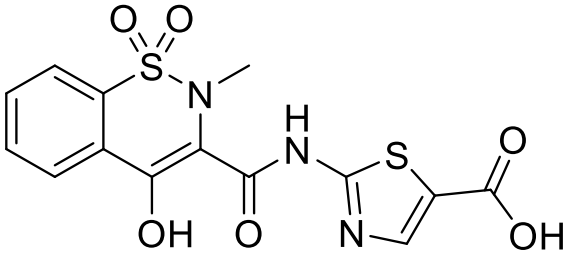


Molecular Weight: 351,40

59



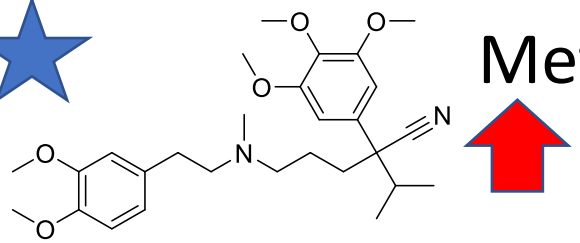
Molecular Weight: 367,39



Molecular Weight: 381,38

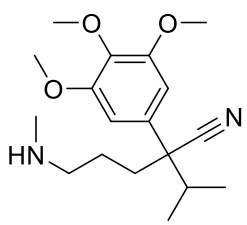
https://www.tandfonline.com/doi/abs/10.1080/004982598239704

Methoxyverapamil/Gallopamil (**60**) - **Biomimetic transformation**



60
tR: 6.15
m/z: 485 (HPLC-MS)
m/z: (HRMS)

?



60a
tR: 2.95
m/z: 165 (HPLC-MS)
m/z: 165.0901(HRMS)

60b
tR: 4.39
m/z: 193 (HPLC-MS)
m/z: 193.1096(HRMS)

60c
tR: 5.20
m/z: 321 (HPLC-MS)
m/z: 321.2179(HRMS)
deltam: 0.0001
ppm: 0.3

?

Valahol demetileződik

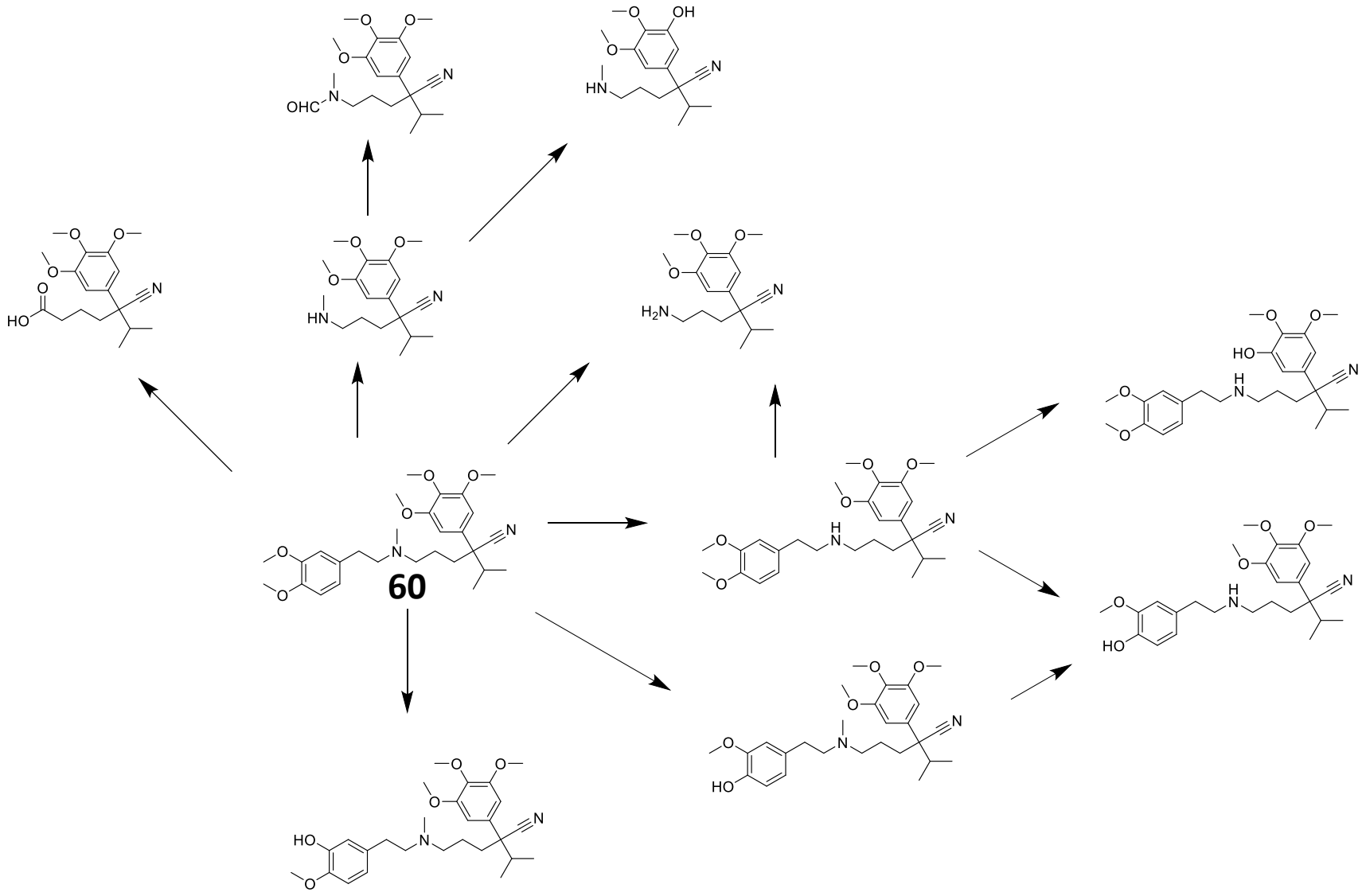
60d
tR: 6.14
m/z: 471 (HPLC-MS)
m/z: 471.2845(HRMS)
deltam: -0.0014
ppm: -3.0

60e
tR: 6.49
m/z: 379 (HPLC-MS)
m/z: (HRMS)

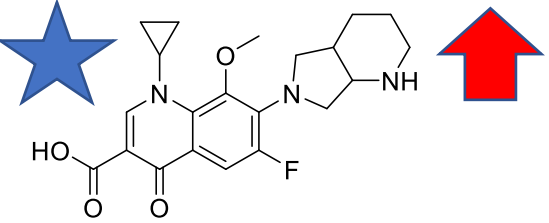
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	100	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
60a	2.95	-320	0	0	0	0	1.9	22.7	0	0
60b	4.39	-292	0	0	0	0	6.6	0	0	0
60c	5.20	-164	0	0	0	0	23.5	12.5	3.9	0
60d#	6.14	-14	0	0	0	0	2.6	**63.1**	8.4	0
60e#	6.49	-106	0	0	0	0	**43.6**	0	0	0

#Major biomimetic metabolite

Methoxyverapamil/Gallopamil (**60**) - in vitro/ in vivo biotransformation



https://link.springer.com/book/10.1007/978-3-642-93678-4?noAccess=true



Moxifloxacin (**61**) - **Biomimetic transformation**

61
tR: 4.54
m/z: 402 (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	28.4	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
61a	3.63	-193	0	0	0	0	13	0	0	0
61b	4.09	-175	0	0	0	0	7.6	0	0	0
61c#	6.68	-109	0	0	0	0	**57.5**	**8.7**	0	0
61d	7.02	-62	0	0	0	0	6.8	0	0	0

#Major biomimetic metabolite

61a
tR: 3.63
m/z: 209 (HPLC-MS)
m/z: (HRMS)

61b
tR: 4.09
m/z: 227 (HPLC-MS)
m/z: (HRMS)

61c
tR: 6.68
m/z: 293 (HPLC-MS)
m/z: 293.0936(HRMS)

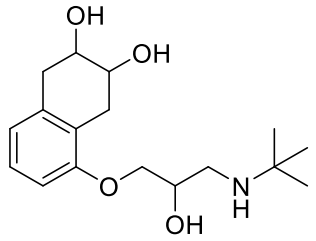
Moxifloxacin (**61**) - **in vitro/ in vivo biotransformation**

The cytochrome P450 system is not involved in metabolism.

61d
tR: 7.02
m/z: 340 (HPLC-MS)
m/z: 340.0833(HRMS)

https://journals.prous.com/journals/servlet/xmlxsl/pk_journals.xml_summary_pr?p_JournalId=4&p_RefId=570201&p_IsPs=N

Nadolol/Solgol (**62**) - **Biomimetic transformation**



62

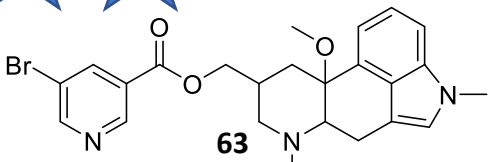
NO biomimetic transformation

Nadolol/Solgol (**62**) - **in vitro/ in vivo biotransformation**

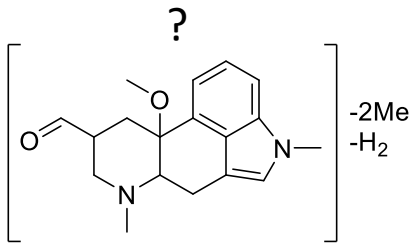
Nadolol is not metabolized in the liver and excreted mainly in the urine.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/018063s063lbl.pdf

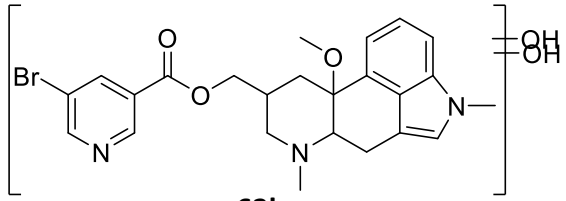
Nicergoline (**63**) - **Biomimetic transformation (I)**



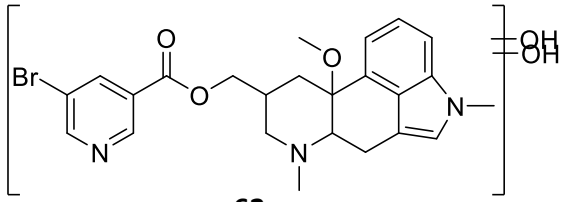
63
tR: 5.99
m/z: 484 (HPLC-MS)
m/z: (HRMS)



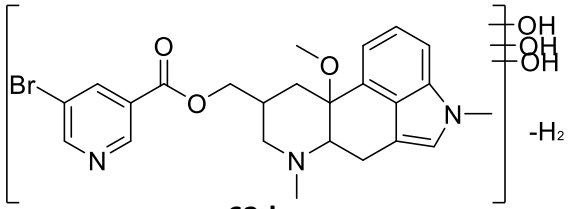
63a
tR: 4.40
m/z: 269 (HPLC-MS)
m/z: 269.1646(HRMS)
deltam: 0.0356
ppm: 132.3



63b
tR: 4.75
m/z: 516 (HPLC-MS)
m/z: 516.3032(HRMS)
deltam: 0.1898
ppm: 367.6



63c
tR: 5.04
m/z: 516 (HPLC-MS)
m/z: 516.3032(HRMS)
deltam: 0.1898
ppm: 367.6

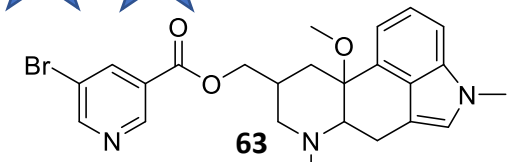


63d
tR: 5.32
m/z: 530 (HPLC-MS)
m/z: 530.3042(HRMS)
deltam: 0.2115
ppm: 398.8

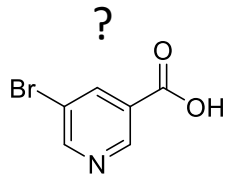
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	100	68.8	100	61.2	100	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
63a	4.40	-215	0	0	69.7	68.9	0	0	63.7	66.5
63b[#]	4.75	32	0	0	0	0	32.8	7.5	0	0
63c	5.04	32	0	0	0	0	14.2	0	0	0
63d	5.32	46	0	0	0	0	6.6	0	0	0
63e	6.45	104	0	0	0	31.1	13.9	0	0	33.5
63f	6.57	104	0	0	0	0	19.7	0	0	0
63g	6.59	-282	0	0	6.6	0	0	9.9	6.2	0
63h	8.05	-268	0	0	23.0	0	0	0	24.5	0
63i	8.29	14	0	0	0	0	6.5	0	0	0

[#]Major biomimetic metabolite
Non biomimetic metabolite

Nicergoline (**63**) - **Biomimetic transformation (II)**



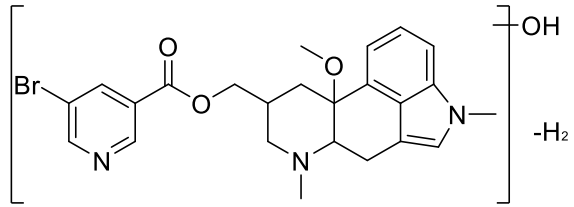
63
tR: 5.99
m/z: 484 (HPLC-MS)
m/z: (HRMS)



63e
tR: 6.45
m/z: 588 (HPLC-MS)
m/z: 588.2511(HRMS)

63f
tR: 6.57
m/z: 588 (HPLC-MS)
m/z: 588.2511(HRMS)

63g
tR: 6.59
m/z: 202 (HPLC-MS)
m/z: 201.9504(HRMS)
deltam: 0.0001
ppm: 0.5



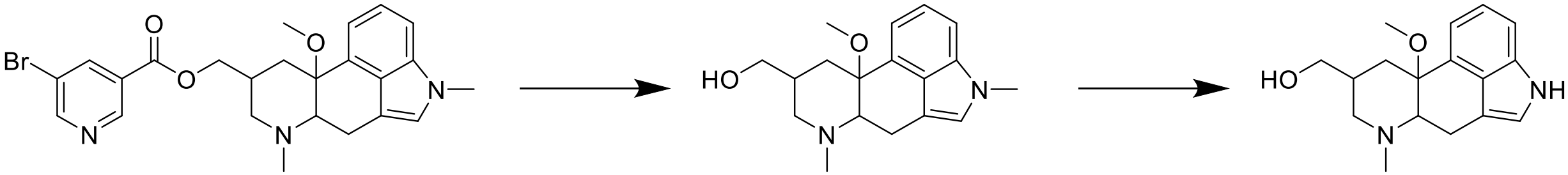
63h
tR: 8.05
m/z: 216 (HPLC-MS)
m/z: (HRMS)

63i
tR: 8.25
m/z: 498 (HPLC-MS)
m/z: 498.2857(HRMS)
deltam: 0.1829
ppm: 367.1

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	100	68.8	100	61.2	100	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
63a	4.40	-215	0	0	69.7	68.9	0	0	63.7	66.5
63b#	4.75	32	0	0	0	0	32.8	7.5	0	0
63c	5.04	32	0	0	0	0	14.2	0	0	0
63d	5.32	46	0	0	0	0	6.6	0	0	0
63e	6.45	104	0	0	0	31.1	13.9	0	0	33.5
63f	6.57	104	0	0	0	0	19.7	0	0	0
63g	6.59	-282	0	0	6.6	0	0	9.9	6.2	0
63h	8.05	-268	0	0	23.0	0	0	0	24.5	0
63i	8.29	14	0	0	0	0	6.5	0	0	0

#Major biomimetic metabolite
Non biomimetic metabolite

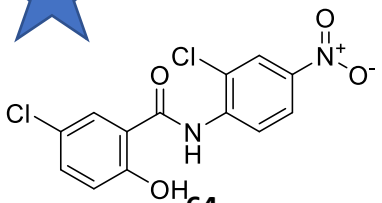
Nicergoline (**63**) - in vitro/ in vivo biotransformation



63

https://www.sciencedirect.com/science/article/pii/0006295272900366

Niclosamide (**64**) - **Biomimetic transformation**



64

tR: 11.53
m/z: - (HPLC-MS)
m/z: (HRMS)

Negatív ionmód?!

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	69.4	98.5	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
64a[#]	8.77	NI	0	0	0	0	22.2	**73.7**	0	0
64b	12.10	NI	0	0	0	0	13.6	26.3	0	0

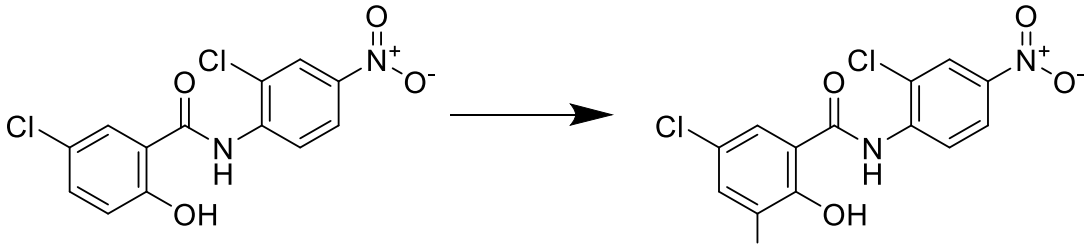
[#]**Major biomimetic metabolite**
NI: Non-ionizable in positive mode of ESI

HRMS 217.1051
303.1101

64a
🔴 tR: 8.77
m/z: - (HPLC-MS)
🟡 m/z: (HRMS)

64b
🔴 tR: 12.10
m/z: - (HPLC-MS)
🟡 m/z: (HRMS)

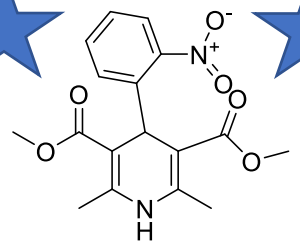
Niclosamide (**64**) - **in vitro/ in vivo biotransformation**



64

https://www.tandfonline.com/doi/full/10.3109/00498254.2015.1047812

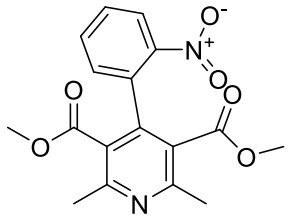
Nifedipine (**65**) - **Biomimetic transformation**



65
tR: 8.70
m/z: 347 (HPLC-MS)
m/z: (HRMS)

65a
tR: 7.25
m/z: 283 (HPLC-MS)
m/z: (HRMS)

65b
tR: 7.90
m/z: 299 (HPLC-MS)
m/z: (HRMS)

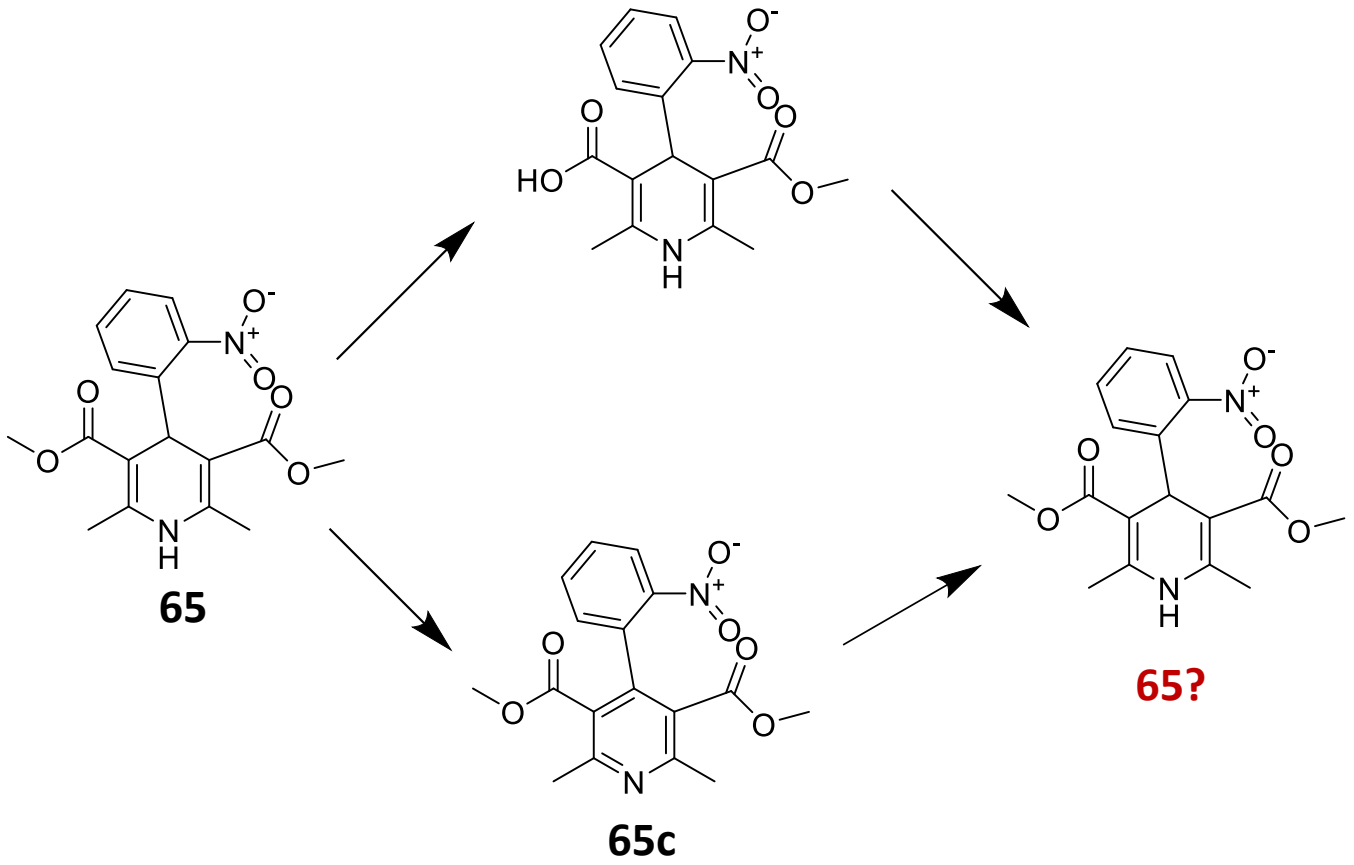


65c
tR: 8.55
m/z: 345 (HPLC-MS)
m/z: 345.1083(HRMS)
deltam: -0.0004
ppm: -1.2

			Non biomimetic				Biomimetic			
Conversion (%)			36.8	55.7	100	43.5	100	100	100	55.5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
65a	7.25	-64	0	0	0	0	0	0	11.8	0
65b#	7.90	-48	0	0	0	**29.9**	0	0	52.1	22.5
65c*#	8.55	-2	**5.5**	**10.6**	**4.1**	**10.6**	**100**	**91.8**	**31.6**	6.9

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
Non biomimetic metabolite

Nifedipine (**65**) - in vitro/ in vivo biotransformation

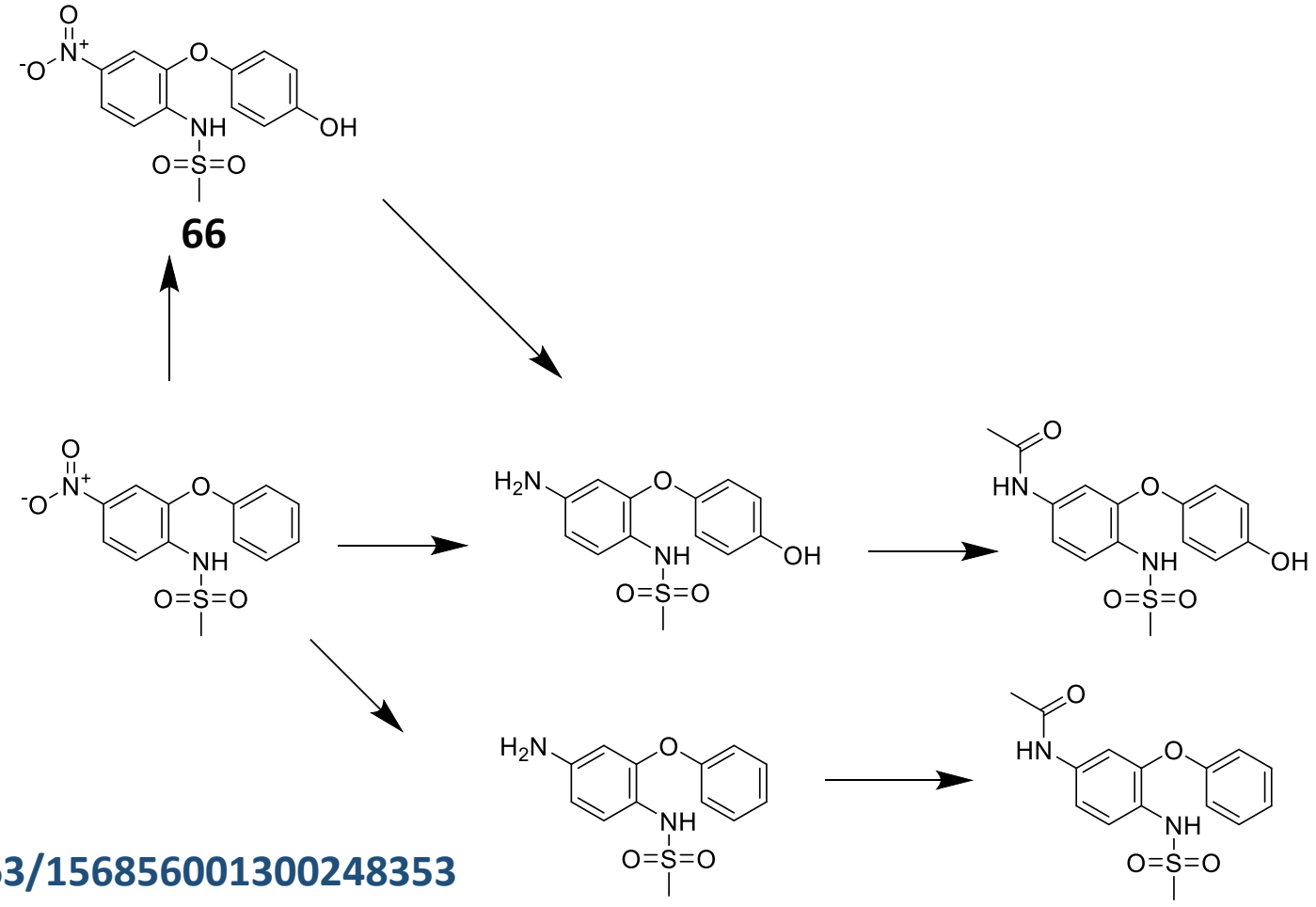


https://www.ahajournals.org/doi/10.1161/01.HYP.5.4_Pt_2.II18

Nimesulide (**66**) - **Biomimetic transformation**

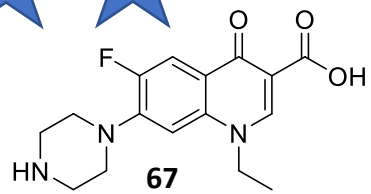
NO biomimetic transformation

Nimesulide (**66**) - **in vitro/ in vivo biotransformation**

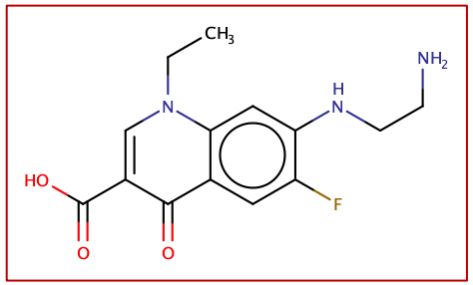


https://link.springer.com/article/10.1163/156856001300248353

Norfloxacin (**67**) - **Biomimetic transformation**



67
tR: 3.72
m/z: 320 (HPLC-MS)
m/z: (HRMS)

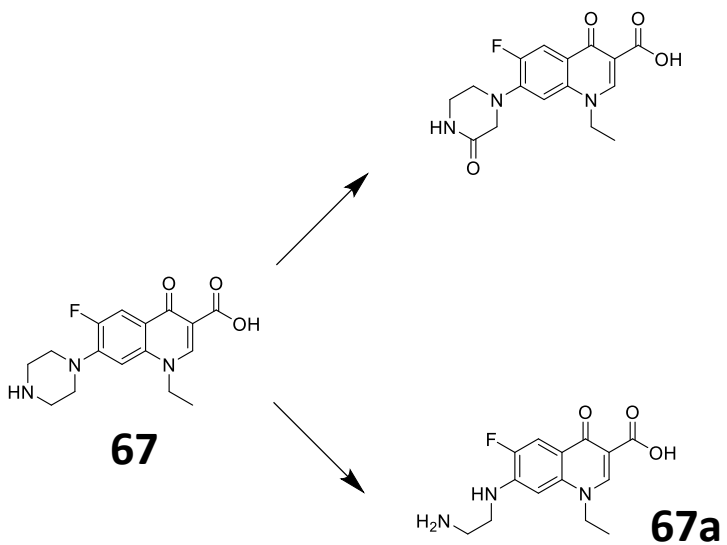


67a
tR: 3.47
m/z: 294 (HPLC-MS)
m/z: 294.1471(HRMS)
deltam: 0.0217
ppm: 73.8

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	9	38.2	0	5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
67a*	3.47	-26	0	0	0	0	0	**13.3**	0	**5.8**

***in vivo/in vitro metabolite formed by biotransformation**

Norfloxacin (**67**) - **in vitro/ in vivo biotransformation**

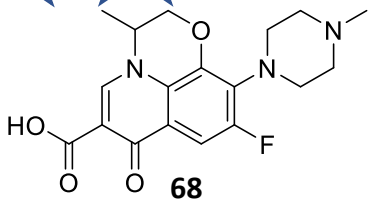


67

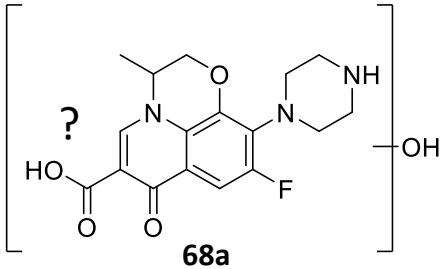
67a

https://www.sciencedirect.com/science/article/abs/pii/S0099542808605407

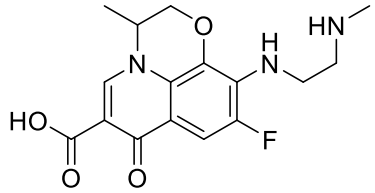
Ofloxacin (**68**) - **Biomimetic transformation**



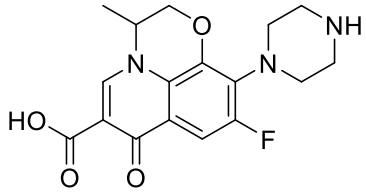
68
tR: 3.72
m/z: 362 (HPLC-MS)
m/z: (HRMS)



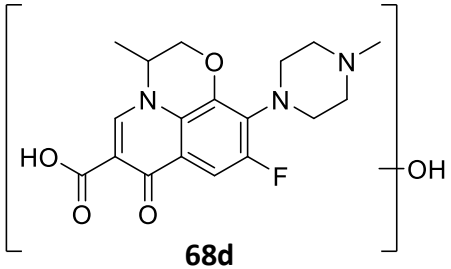
68a
tR: 4.40
m/z: 364 (HPLC-MS)
m/z: 364.1305(HRMS)
deltam: -0.0004
ppm: -1.1



68b
tR: 3.60
m/z: 336 (HPLC-MS)
m/z: 336.1358(HRMS)
deltam: -0.0002
ppm: -0.6



68c
tR: 3.72
m/z: 348 (HPLC-MS)
m/z: 348.1357(HRMS)
deltam: -0.0003
ppm: -0.7

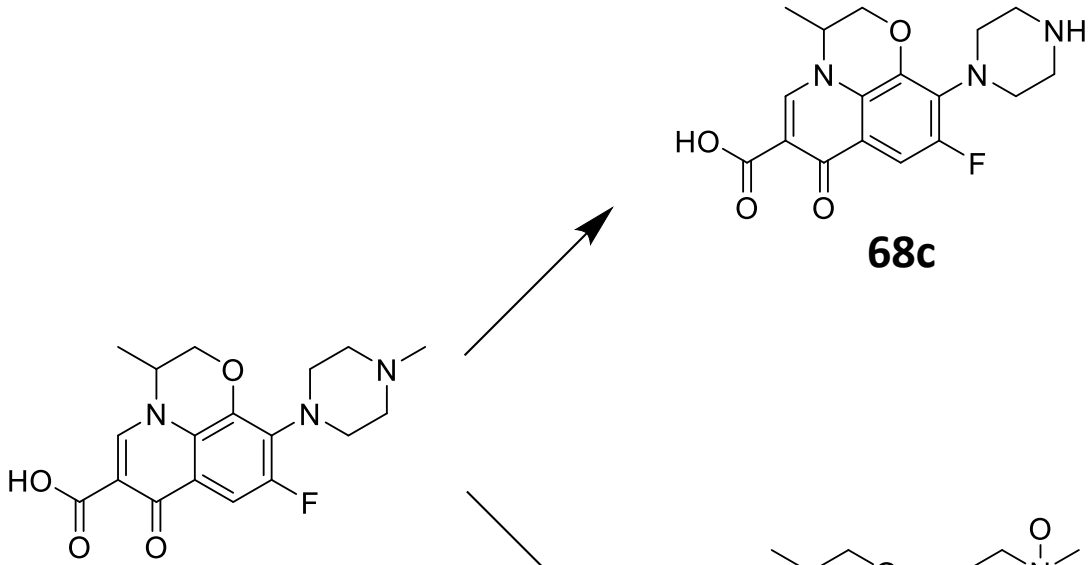


68d
tR: 4.05
m/z: 378 (HPLC-MS)
m/z: 378.1707(HRMS)
deltam: 0.0242
ppm: 64.0

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	28.9	16.5	0	71.4
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
68a	3.40	2	0	0	0	0	0	27.1	0	0
68b#	3.60	-26	0	0	0	0	**5.4**	0	0	0
68c*#	3.72	-14	0	0	0	0	0	**62.4**	0	0
68d*	4.05	16	0	0	0	0	0	**10.5**	0	0

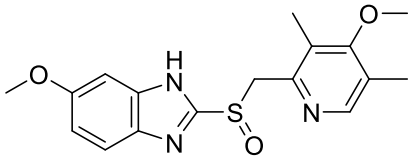
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Ofloxacin (**68**) - in vitro/ in vivo biotransformation



https://dmd.aspetjournals.org/content/18/6/1103

Omeprazole (**69**) - **Biomimetic transformation (I)**



69
tR: 5.12
m/z: 346 (HPLC-MS)
m/z: (HRMS)

69a
tR: 2.87
m/z: 320 (HPLC-MS)
m/z: 320.1379(HRMS)

69b
tR: 4.10
m/z: 182 (HPLC-MS)
m/z: 182.0800(HRMS)

69c
tR: 4.34
m/z: 298 (HPLC-MS)
m/z: 298.1541(HRMS)

69d
tR: 4.90
m/z: 342 (HPLC-MS)
m/z: (HRMS)

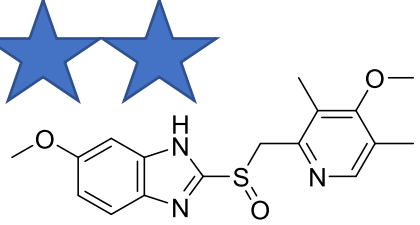
69e
tR: 5.05
m/z: 330 (HPLC-MS)
m/z: 330.0619(HRMS)

69f
tR: 6.00
m/z: 196 (HPLC-MS)
m/z: 195.9559(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			100	100	0	13.3	53.4	100	0	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
69a	2.87	-26	0	**12.4**	0	0	0	0	0	0
69b	4.10	-164	0	0	0	0	23.2	0	0	0
69c	4.34	-48	**8.4**	**4.0**	0	0	34.8	9.4	1.7	0
69d#	4.90	-4	0	0	0	0	0	0	**5.5**	**9.8**
69e	5.05	-16	**51.4**	0	0	0	0	0	0	0
69f#	6.00	-150	0	0	0	0	**31.4**	0	1.4	0
69g	6.57	-103	0	0	0	0	10.7	0	0	0
69h#	6.65	-18	**29.1**	**8.4**	0	0	0	**42.7**	0	0
69i	10.1	-34	11	0	0	0	0	0	0	0

#Major biomimetic metabolite
Non biomimetic metabolite

Omeprazole (**69**) - **Biomimetic transformation (II)**



69
tR: 5.12
m/z: 346 (HPLC-MS)
m/z: (HRMS)

69g
tR: 6.57
m/z: 243 (HPLC-MS)
m/z: 242.9962(HRMS)

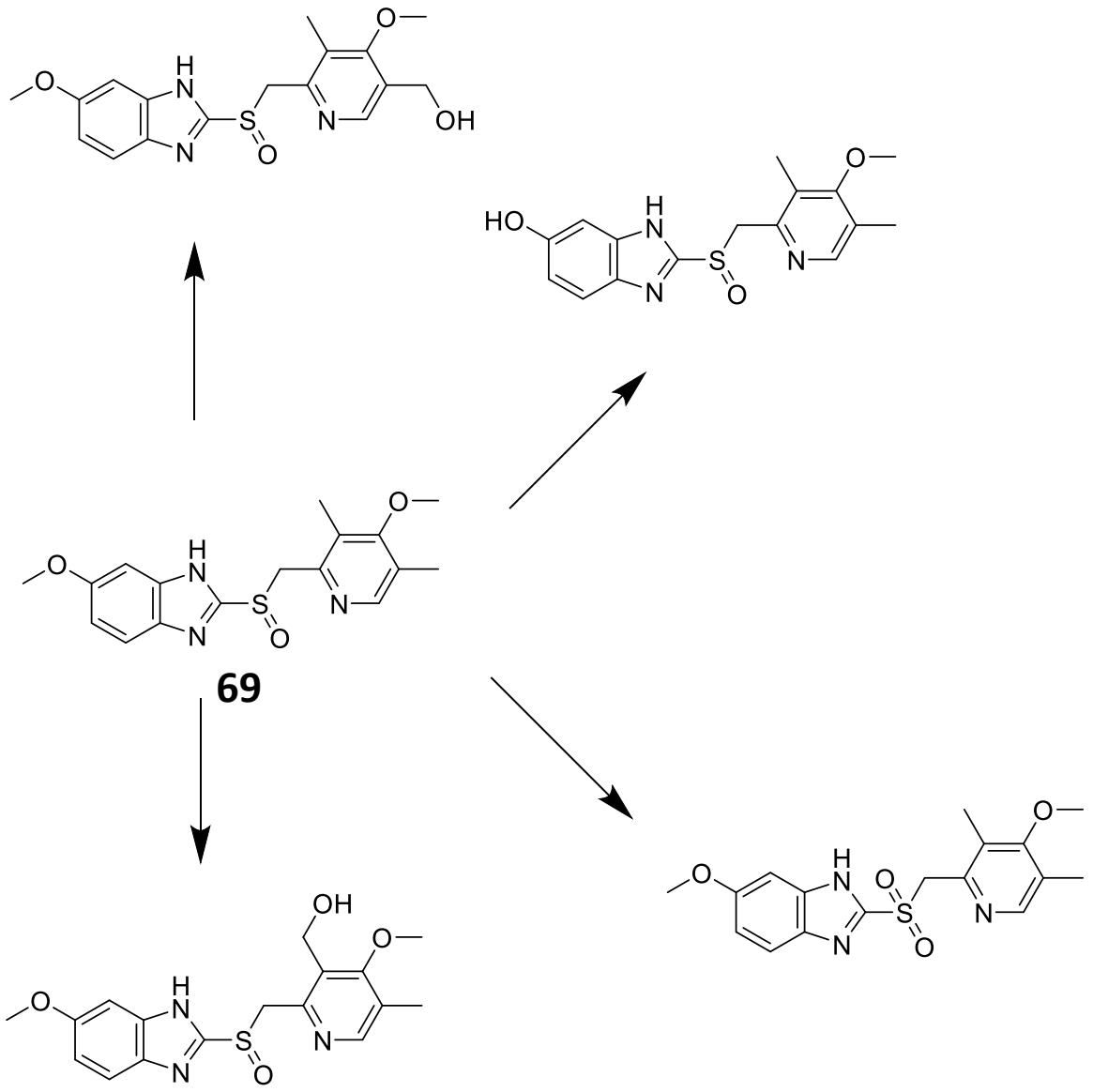
69h
tR: 6.65
m/z: 328 (HPLC-MS)
m/z: 328.1293(HRMS)

69i
tR: 10.1
m/z: 312 (HPLC-MS)
m/z: 312.1285(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			100	100	0	13.3	53.4	100	0	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
69a	2.87	-26	0	**12.4**	0	0	0	0	0	0
69b	4.10	-164	0	0	0	0	23.2	0	0	0
69c	4.34	-48	**8.4**	**4.0**	0	0	34.8	9.4	1.7	0
69d#	4.90	-4	0	0	0	0	0	0	**5.5**	**9.8**
69e	5.05	-16	**51.4**	0	0	0	0	0	0	0
69f#	6.00	-150	0	0	0	0	**31.4**	0	1.4	0
69g	6.57	-103	0	0	0	0	10.7	0	0	0
69h#	6.65	-18	**29.1**	**8.4**	0	0	0	**42.7**	0	0
69i	10.1	-34	11	0	0	0	0	0	0	0

#Major biomimetic metabolite
Non biomimetic metabolite

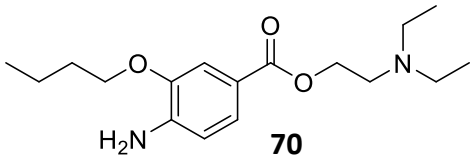
Omeprazole (**69**) - in vitro/ in vivo biotransformation



69

http://www.eurekaselect.com/article/14943

Oxybuprocaine/Benoxinate (**70**) - **Biomimetic transformation (I)**



70
tR: 5.37
m/z: 309 (HPLC-MS)
m/z: (HRMS)

70a
tR: 4.54
m/z: 360 (HPLC-MS)
m/z: 360.2015(HRMS)

70b
tR: 4.67
m/z: 198 (HPLC-MS)
m/z: 198.0173(HRMS)

70c
tR: 5.09
m/z: 192 (HPLC-MS)
m/z: 191.9965(HRMS)

70d
tR: 5.25
m/z: 374 (HPLC-MS)
m/z: 374.2173(HRMS)

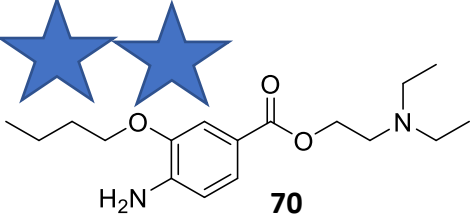
70e
tR: 5.75
m/z: 196 (HPLC-MS)
m/z: 195.9555(HRMS)

70f
tR: 6.20
m/z: 339 (HPLC-MS)
m/z: 339.1909(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			36.2	35.2	94.7	29.6	100	100	95.5	96
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
70a	4.54	50	0	0	0	0	27.2	0	0	0
70b	4.67	-111	0	0	0	0	0	26.2	0	0
70c#	5.09	-117	**5.7**	0	0	0	0	**43.4**	0	24.3
70d	5.25	65	0	0	0	0	31.3	0	0	0
70e	5.75	-113	0	0	0	0	0	30.5	0	0
70f#	6.20	30	0	0	0	0	**41.5**	0	0	0
70g	7.89	-58	0	0	0	0	0	0	14.3	20.5
70h#	9.60	-85	0	0	**95.6**	0	0	0	82.4	**44.3**

#Major biomimetic metabolite
Non biomimetic metabolite

Oxybuprocaine/Benoxinate (**70**) - **Biomimetic transformation (II)**



70
tR: 5.37
m/z: 309 (HPLC-MS)
m/z: (HRMS)

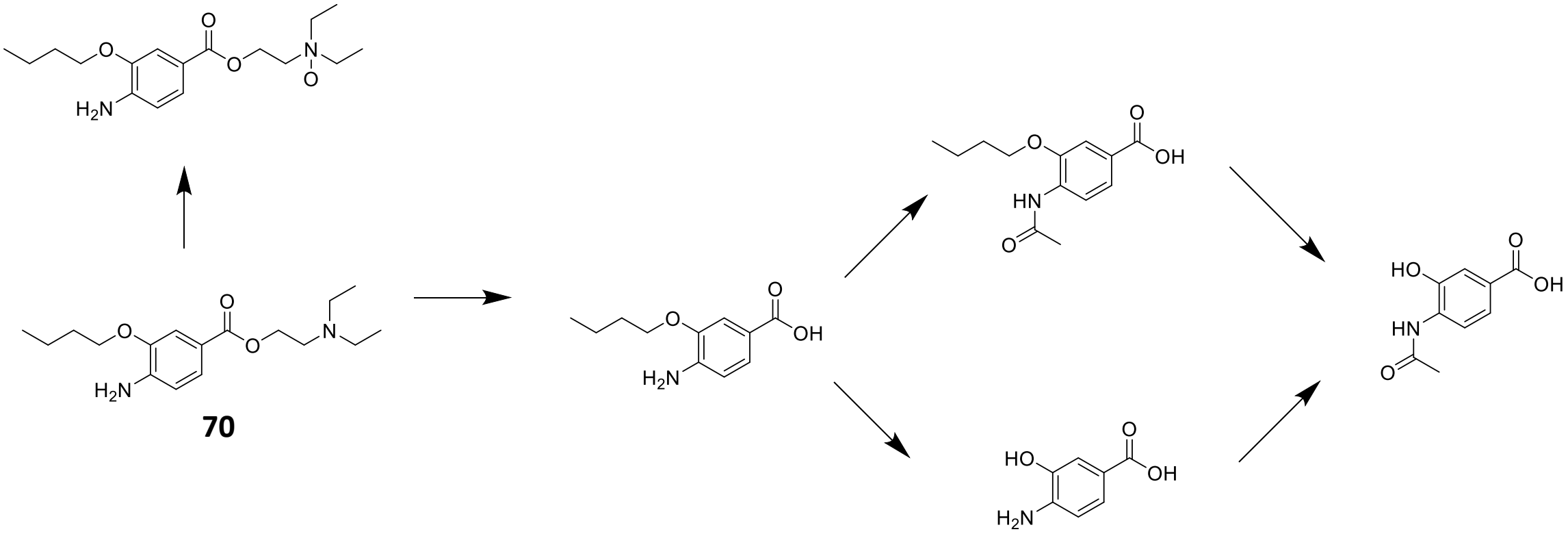
70g
tR: 7.89
m/z: 251 (HPLC-MS)
m/z: 250.8103(HRMS)

70h
tR: 9.60
m/z: 224 (HPLC-MS)
m/z: 224.1277(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			36.2	35.2	94.7	29.6	100	100	95.5	96
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
70a	4.54	50	0	0	0	0	27.2	0	0	0
70b	4.67	-111	0	0	0	0	0	26.2	0	0
70c[#]	5.09	-117	**5.7**	0	0	0	0	**43.4**	0	24.3
70d	5.25	65	0	0	0	0	31.3	0	0	0
70e	5.75	-113	0	0	0	0	0	30.5	0	0
70f[#]	6.20	30	0	0	0	0	**41.5**	0	0	0
70g	7.89	-58	0	0	0	0	0	0	14.3	20.5
70h[#]	9.60	-85	0	0	**95.6**	0	0	0	82.4	**44.3**

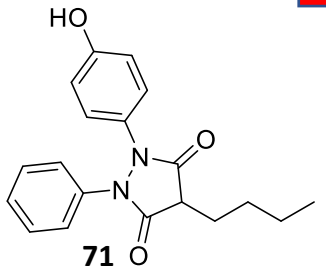
[#]Major biomimetic metabolite
Non biomimetic metabolite

Oxybuprocaine/Benoxinate (**70**) - in vitro/ in vivo biotransformation



https://www.sciencedirect.com/science/article/abs/pii/S0022354915473927

Oxyphenbutazone (**71**) - **Biomimetic transformation**



71
tR: 8.64
m/z: 325 (HPLC-MS)
m/z: (HRMS)

Negatív ionmódban újramérni?

71a
tR: 5.02
m/z: - (HPLC-MS)
m/z: (HRMS)

71b
tR: 5.22
m/z: - (HPLC-MS)
m/z: (HRMS)

71c
tR: 7.79
m/z: - (HPLC-MS)
m/z: (HRMS)

71d
tR: 8.72
m/z: - (HPLC-MS)
m/z: (HRMS)

71e
tR: 9.10
m/z: - (HPLC-MS)
m/z: (HRMS)

71f
tR: 9.74
m/z: - (HPLC-MS)
m/z: (HRMS)

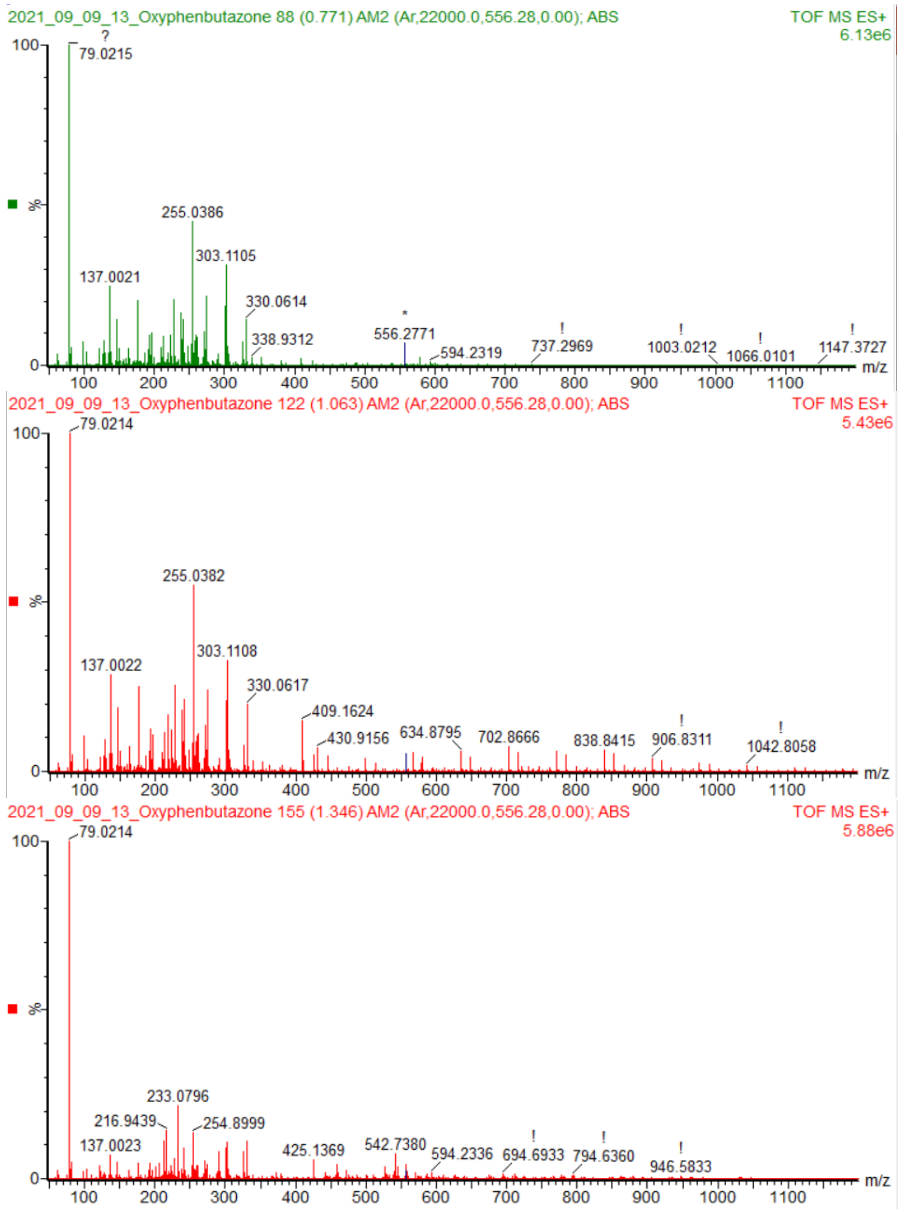
71g
tR: 9.90
m/z: - (HPLC-MS)
m/z: (HRMS)

71h
tR: 10.03
m/z: - (HPLC-MS)
m/z: (HRMS)

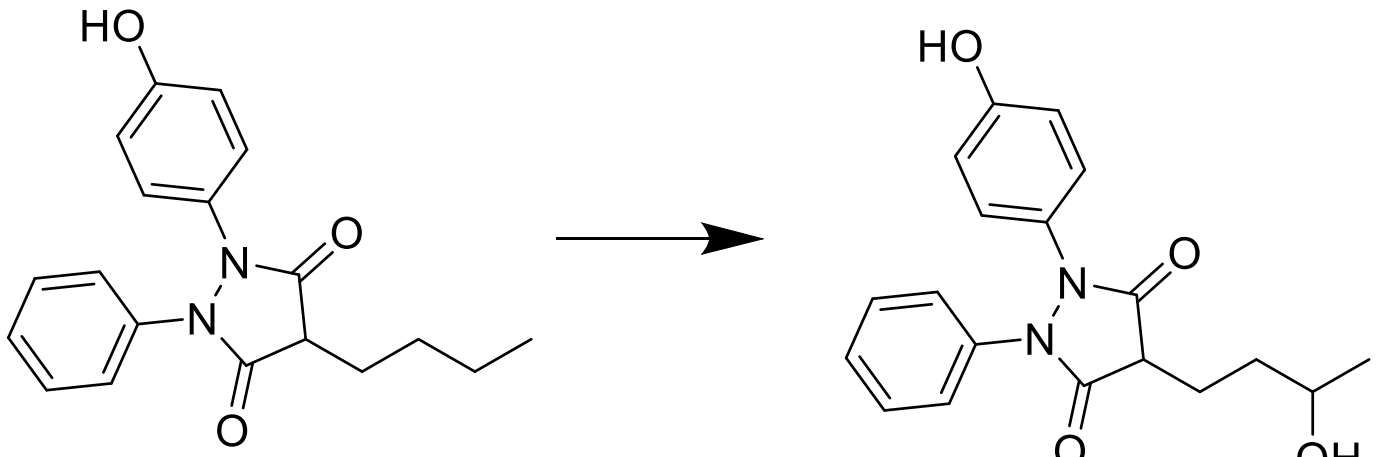
			Non biomimetic				Biomimetic			
Conversion (%)			0?	0?	0?	0?	100	100	100	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
71a	5.02	NI	0	0	37.0	31.8	?	0	34.9	16.4
71b	5.22	NI	5.9	0	8.5	0	?	0	0	15.0
71c	7.79	NI	68.3	71.2	0	0	?	0	0	0
71d	8.72	NI	10.7	14.4	6.8	9.74	?	0	0	7.7
71e	9.10	NI	12.0	14.4	18.3	18.9	?	0	19.2	17.6
71f[#]	9.74	NI	0	0	6.8	5.4	?	100	20.6	14.9
71g	9.90	NI	0	0	0	6.61	?	0	0	8.5
71h	10.03	NI	0	0	22.7	23.6	?	0	18.9	19.9

[#]Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Oxyphenbutazone (**71**) - **Biomimetic transformation**



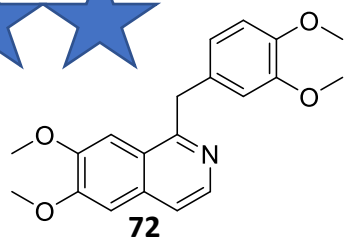
Oxyphenbutazone (**71**) - in vitro/ in vivo biotransformation



71

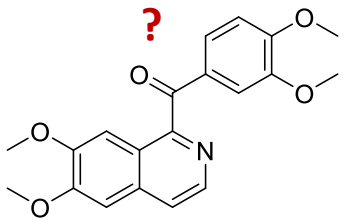
https://link.springer.com/article/10.2165/00003088-197803050-00003

Papaverine (**72**) - **Biomimetic transformation**



72

tR: 4.74
m/z: 340 (HPLC-MS)
m/z: (HRMS)

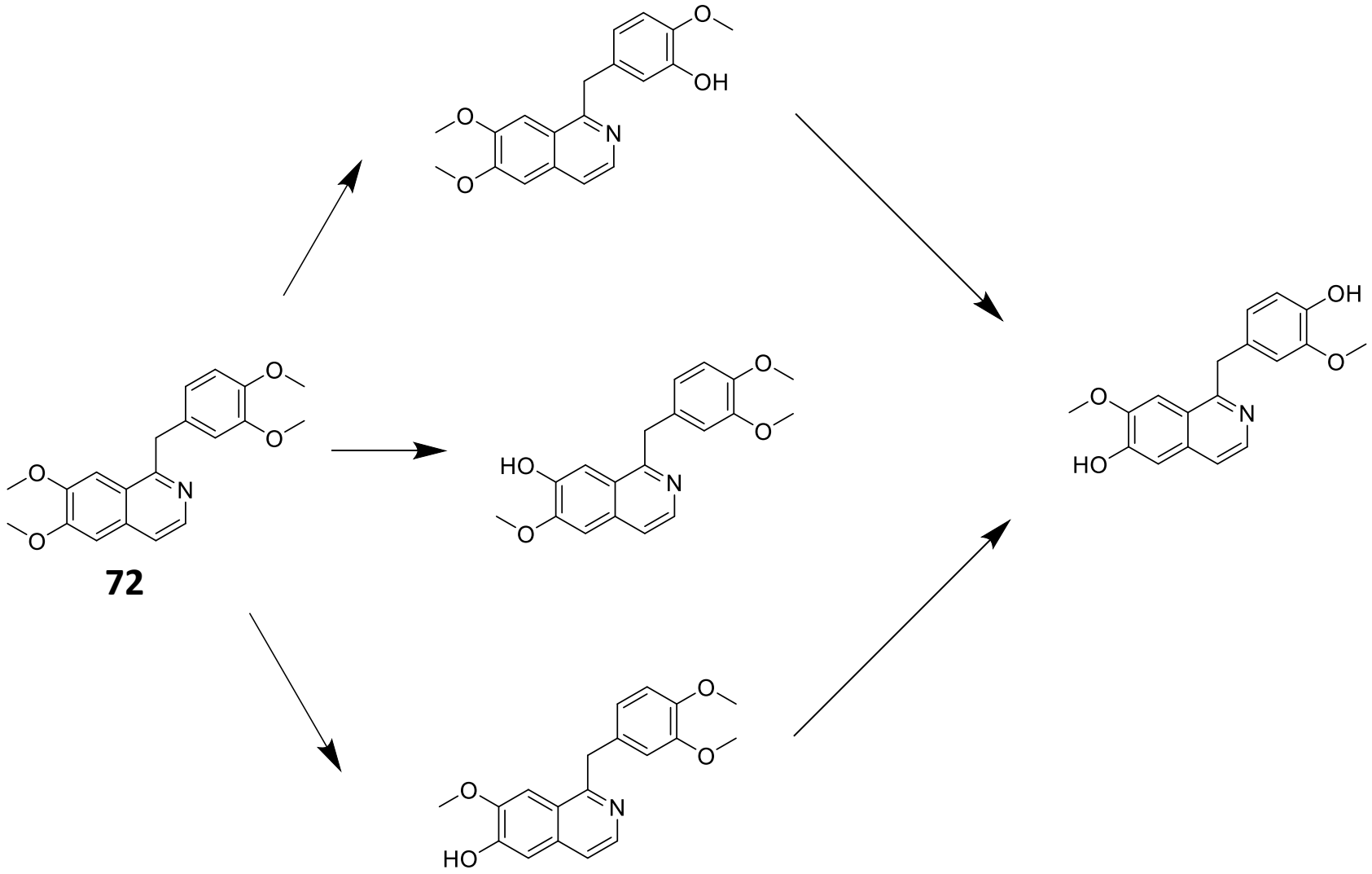


72a

tR: 4.94
m/z: 352 (HPLC-MS)
m/z: 352.1187(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	15.3	0	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
72a	4.94	12	0	0	0	0	**4.7**	0	0	0

Papaverine (**72**) - in vitro/ in vivo biotransformation

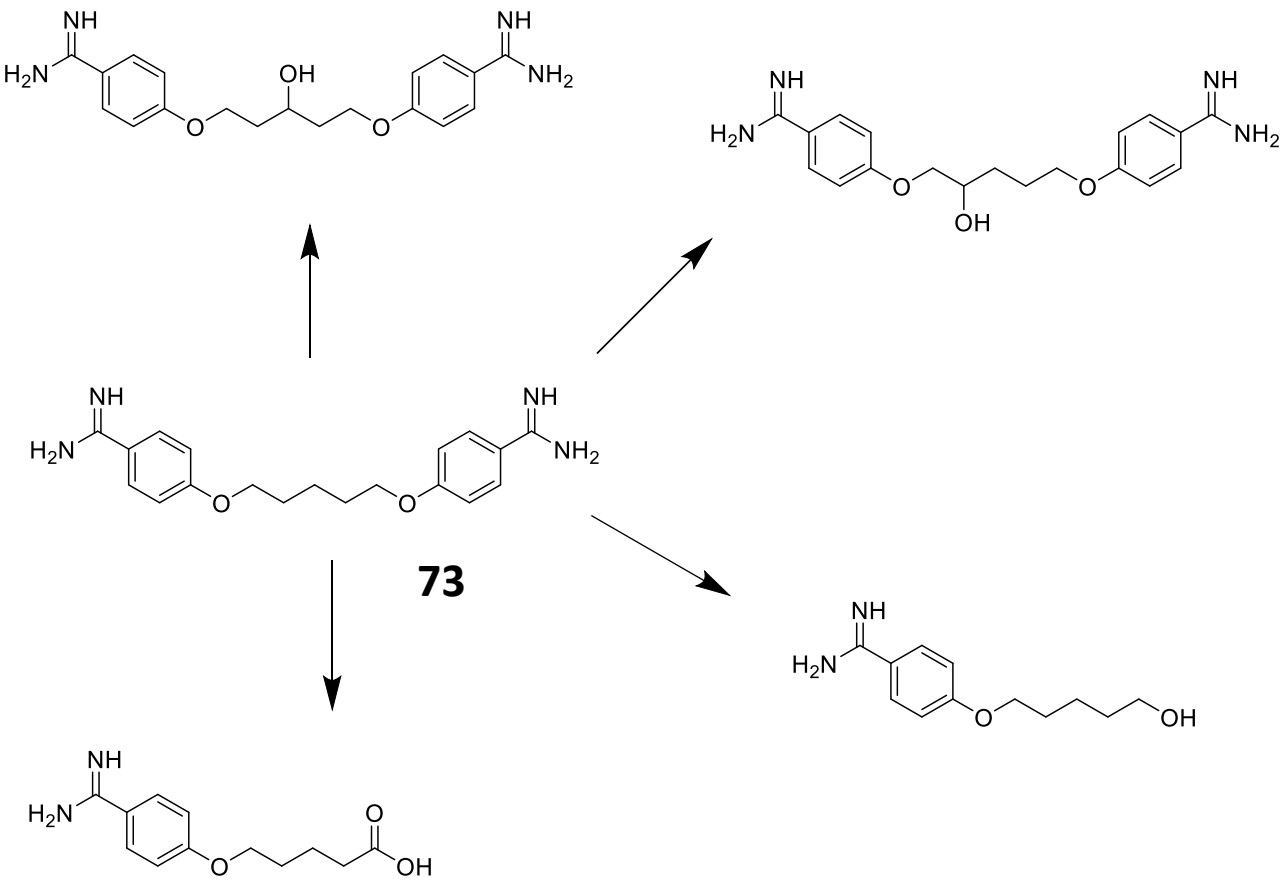


https://www.tandfonline.com/doi/abs/10.3109/00498257509056111

Pentamidine (**73**) - **Biomimetic transformation**

NO biomimetic transformation

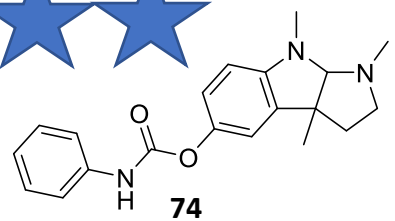
Pentamidine (**73**) - **in vitro/ in vivo biotransformation**



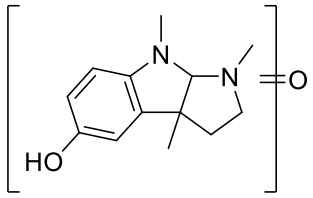
RAT

https://www.sciencedirect.com/science/article/pii/S0378434796002885?via%3Dihub

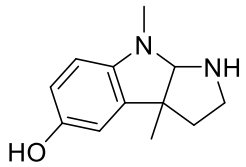
Phenserine (**74**) - **Biomimetic transformation**



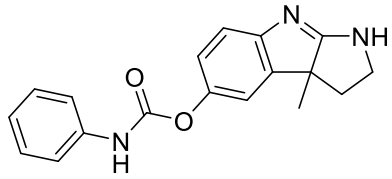
74
tR: 5.39
m/z: 338 (HPLC-MS)
m/z: (HRMS)



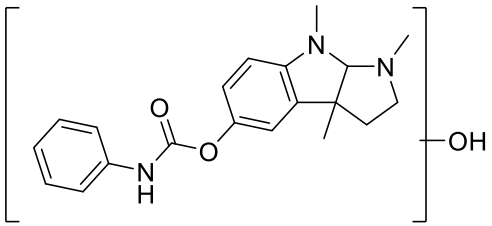
74a
tR: 2.87
m/z: 233 (HPLC-MS)
m/z: 233.1274(HRMS)
deltam: -0.0016
ppm: -6.9



74b
tR: 3.59
m/z: 205 (HPLC-MS)
m/z: (HRMS)



74c
tR: 4.47
m/z: 308 (HPLC-MS)
m/z: 308.1763(HRMS)
deltam: 0.0364
ppm: 118.1



74d
tR: 5.09
m/z: 354 (HPLC-MS)
m/z: 354.1818(HRMS)
deltam: 0.0000
ppm: 0.0

Negatív ionmódban?

74e
tR: 7.17
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			5.4	0	0	0	100	100	24.1	18.2
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
74a	2.87	-105	0	0	0	0	0	11.7	0	0
74b	3.59	-133	**14.3**	0	0	0	0	0	0	0
74c	4.47	-30	0	0	0	0	7.3	0	0	0
74d	5.09	16	0	0	0	0	40	5.8	0	0
74e[#]	7.17	NI	0	0	0	0	**52.7**	**82.5**	**38.8**	**12.4**

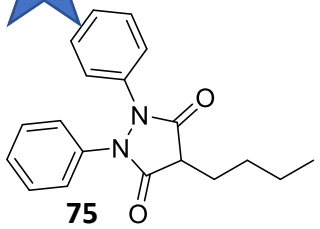
[#]**Major biomimetic metabolite**
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Phenserine (**74**) - in vitro/ in vivo biotransformation

No Data

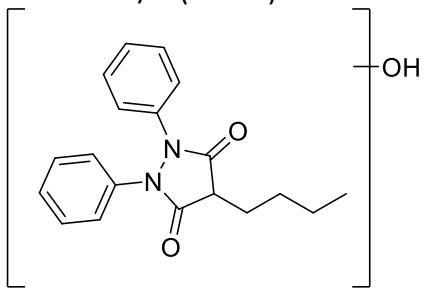
Phenylbutazone (**75**) - **Biomimetic transformation**

Összehasonlítani az oxyphenbutazonnal (71)!



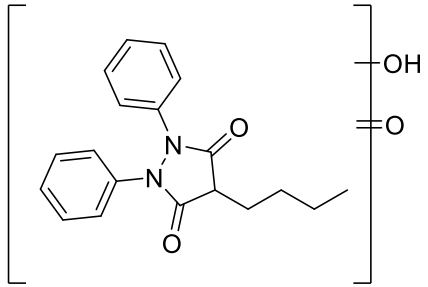
75

tR: 10.25
m/z: 309 (HPLC-MS)
m/z: (HRMS)



75a

tR: 9.29
m/z: 325 (HPLC-MS)
m/z: 325.1562(HRMS)
deltam: 0.0010
ppm: 3.1

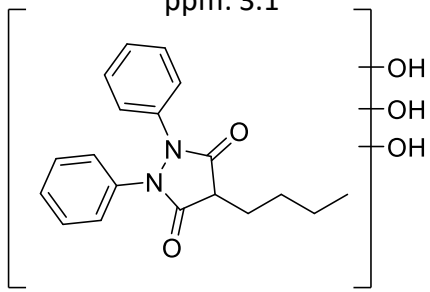


75b

tR: 9.37
m/z: 339 (HPLC-MS)
m/z: 338.9313(HRMS)
deltam: -0.2032
ppm: -599.5

75c

tR: 9.65
m/z: 363 (HPLC-MS)
m/z: 363.1147(HRMS)



75d

tR: 10.20
m/z: 357 (HPLC-MS)
m/z: 715.2930(HRMS)
deltam: -0.0049
ppm: -6.9

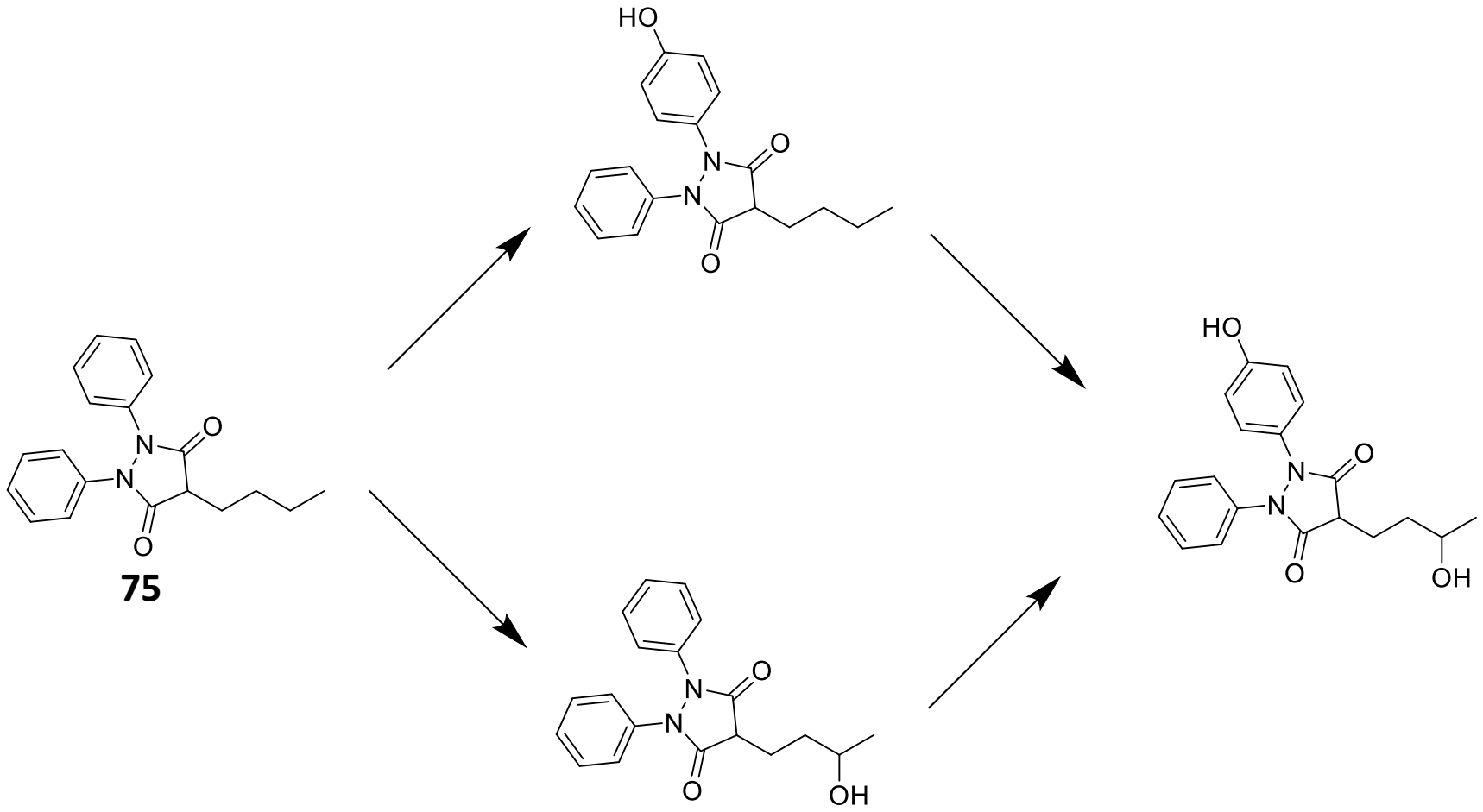
75e

tR: 10.37
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	64.6	0	0	98.6	90.1	100	89.4
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
75a#	9.29	16	**25.5**	0	0	0	**100**	**57.4**	0	0
75b	9.37	30	**35.8**	0	0	0	0	0	0	0
75c#	9.65	54	**8.2**	0	0	0	0	0	0	**86.7**
75d	10.2	48	0	**100**	0	0	0	40	0	0
75e	10.37	**NI**	0	0	**100**	0	0	0	100	3.5

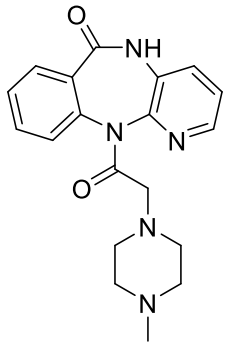
#Major biomimetic metabolite
Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Phenylbutazone (**75**) - in vitro/ in vivo biotransformation



https://www.sciencedirect.com/science/article/abs/pii/S0022354915441851?via%3Dihub

Pirenzepine (**76**) - **Biomimetic transformation**



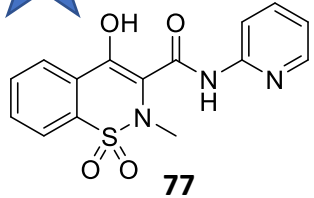
76

NO biomimetic transformation

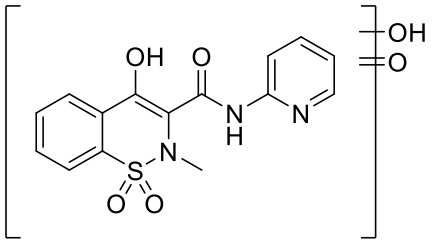
Pirenzepine (**76**) **- in vitro/ in vivo biotransformation**

No Data

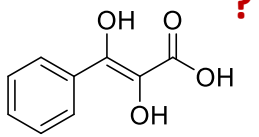
Piroxicam (**77**) - **Biomimetic transformation**



77
tR: 8.117
m/z: 332 (HPLC-MS)
m/z: (HRMS)



77b
tR: 4.95
m/z: 362 (HPLC-MS)
m/z: (HRMS)



Exact Mass: 180.04

77c
tR: 5.34
m/z: 181 (HPLC-MS)
m/z: 181.0124(HRMS)
deltam: -0.0376
ppm: -207.7

77a
tR: 3.05
m/z: 162 (HPLC-MS)
m/z: 162.0153(HRMS)

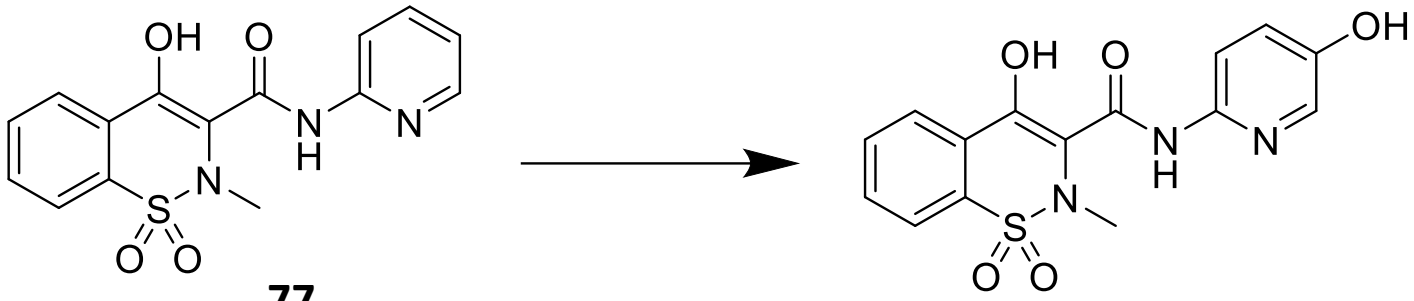
77d
tR: 6.94
m/z: 330 (HPLC-MS)
m/z: 330.0599(HRMS)

77e
tR: 7.24
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non biomimetic				0Biomimetic			
Conversion (%)			0	0	0	0	100	100	8.7	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
77a	3.05	-170	0	0	0	0	0	32.4	0	0
77b	4.95	30	0	0	0	0	16.9	2.7	0	0
77c[#]	5.34	-151	0	0	0	0	**53.6**	**31.8**	0	0
77d	6.94	-2	0	0	0	0	6.1	5.8	0	0
77e	7.24	NI	0	0	0	0	20.6	19.7	0	0

[#]Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Piroxicam (**77**) - in vitro/ in vivo biotransformation



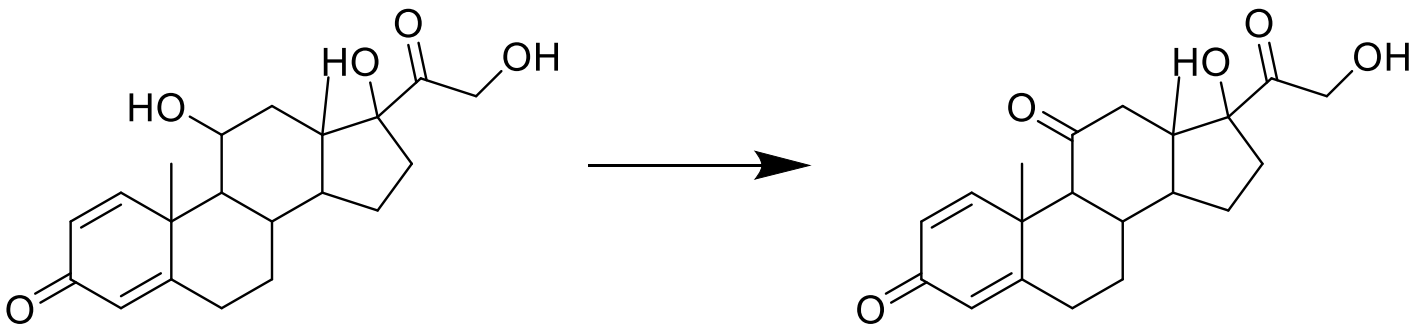
77

https://www.sciencedirect.com/science/article/abs/pii/S0099542808604220

Prednisolone (**78**) - **Biomimetic transformation**

NO biomimetic transformation

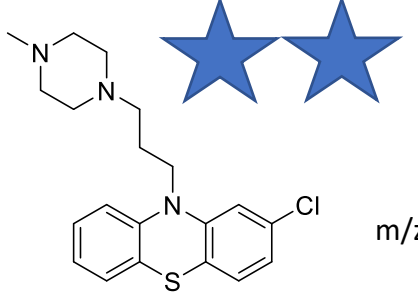
Prednisolone (**78**) - **in vitro/ in vivo biotransformation**



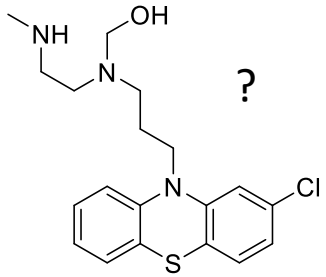
78

https://onlinelibrary.wiley.com/doi/abs/10.1002/bdd.2510150208

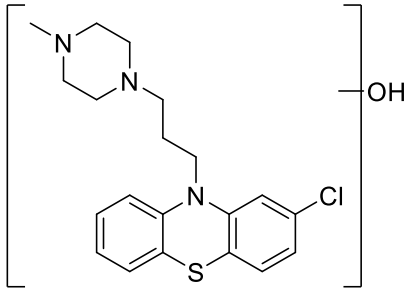
Prochlorperazine (**79**) - **Biomimetic transformation**



79
tR: 6.17
m/z: 374 (HPLC-MS)
m/z: (HRMS)

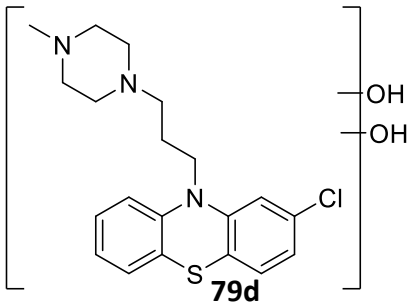


79a
tR: 4.43
m/z: 378 (HPLC-MS)
m/z: 378.1425(HRMS)
deltam: 0.0016
ppm: 4.2

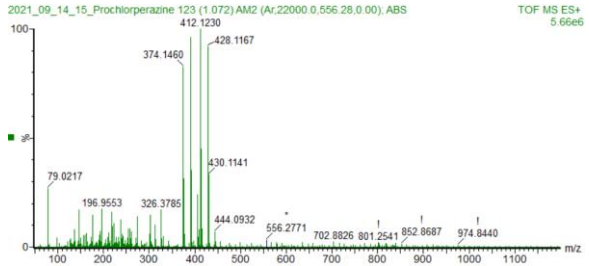


79b
tR: 4.50
m/z: 390 (HPLC-MS)
m/z: 390.1420(HRMS)
deltam: 0.0013
ppm: 3.3

79c
tR: 4.70
m/z: 341 (HPLC-MS)
m/z: (HRMS)



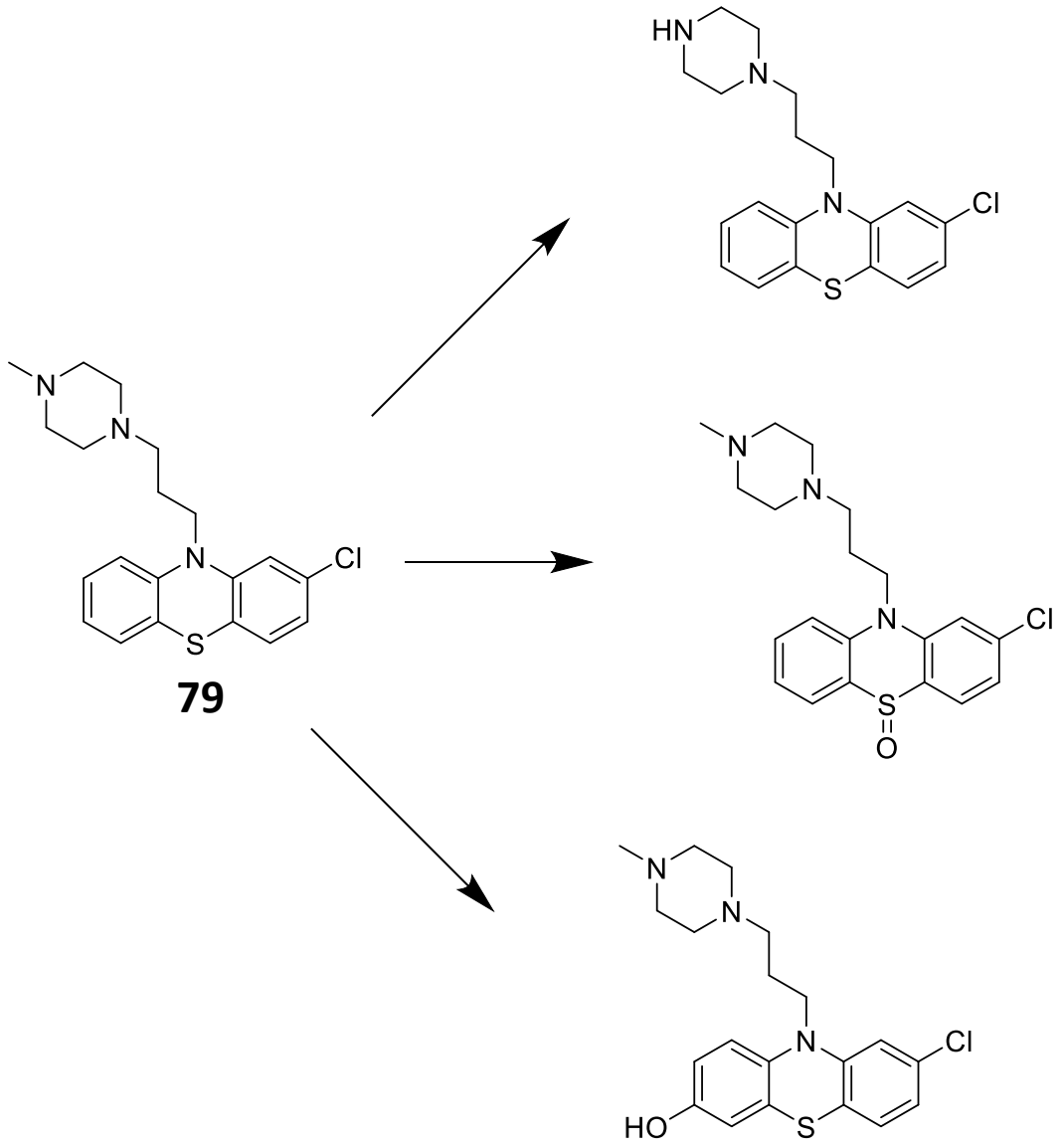
79d
tR: 5.05
m/z: 406 (HPLC-MS)
m/z: 406.1356(HRMS)
deltam: 0.0000
ppm: 0.0



			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	49	5.9
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
79a	4.43	5	0	0	0	0	0	5.4	0	0
79b#	4.50	17	0	0	0	0	**56.0**	19.5	3.3	**21.2**
79c#	4.70	-33	0	0	0	0	7.9	**65.3**	**47.7**	0
79d	5.05	33	0	0	0	0	29.7	0	0	0

#Major biomimetic metabolite

Prochlorperazine (**79**) - **in vitro/ in vivo biotransformation**

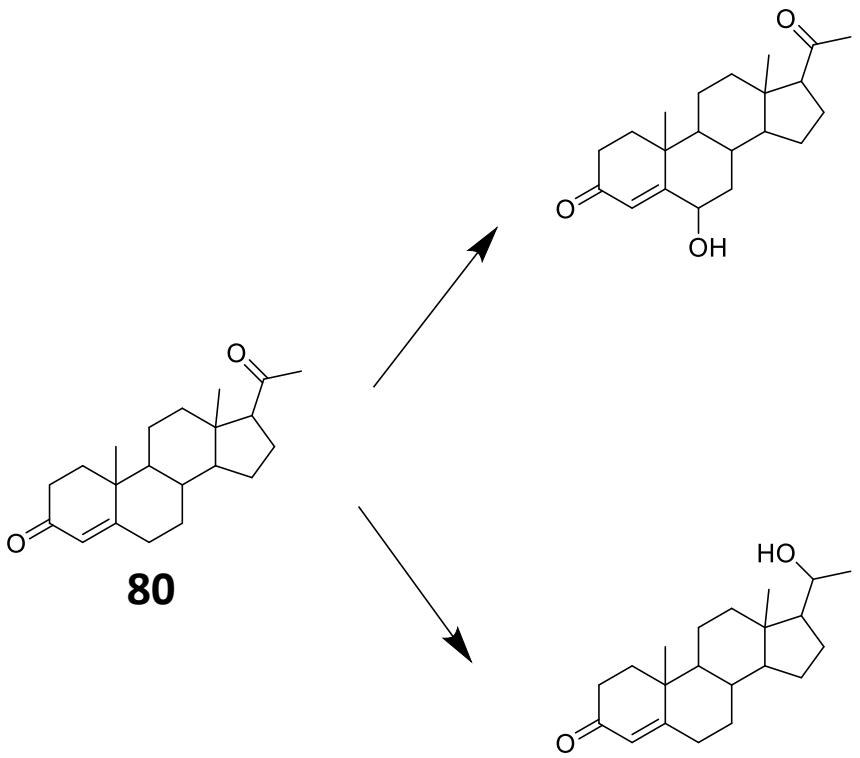


https://journals.sagepub.com/doi/10.1177/0004563217731432

Progesterone – (**80**) - **Biomimetic transformation**

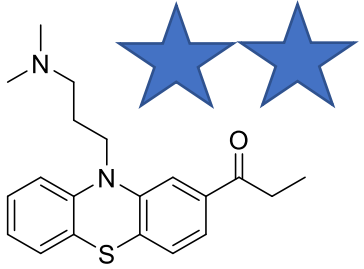
NO biomimetic transformation

Progesterone – (**80**) - **in vitro/ in vivo biotransformation**

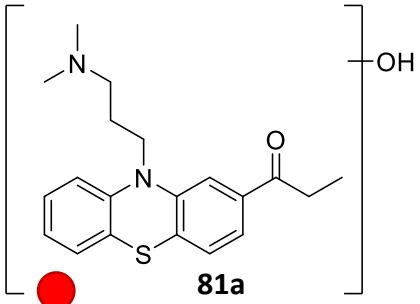


https://www.bmj.com/content/280/6217/825.abstract

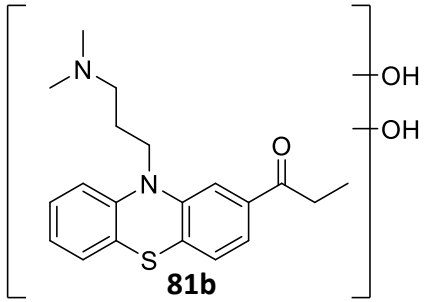
Propionylpromazine (**81**) - **Biomimetic transformation**



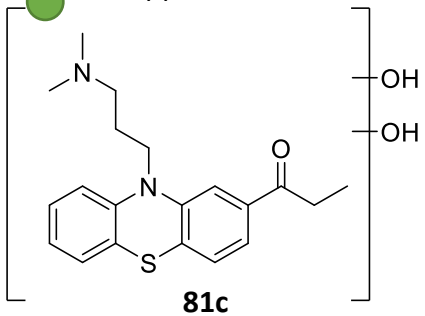
81
tR: 6.14
m/z: 341 (HPLC-MS)
m/z: (HRMS)



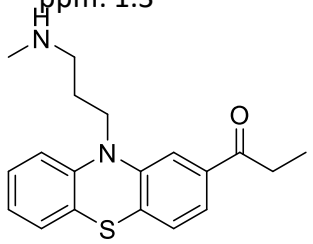
81a
tR: 4.87
m/z: 357(HPLC-MS)
m/z: 357.1680(HRMS)
deltam: 0.0043
ppm: 12.0



81b
tR: 4.95
m/z: 373(HPLC-MS)
m/z: 373.1591(HRMS)
(Na addukt is látszik 395.1407)
deltam: 0.0005
ppm: 1.3



81c
tR: 5.27
m/z: 373(HPLC-MS)
m/z: 373.1597(HRMS)
deltam: 0.0011

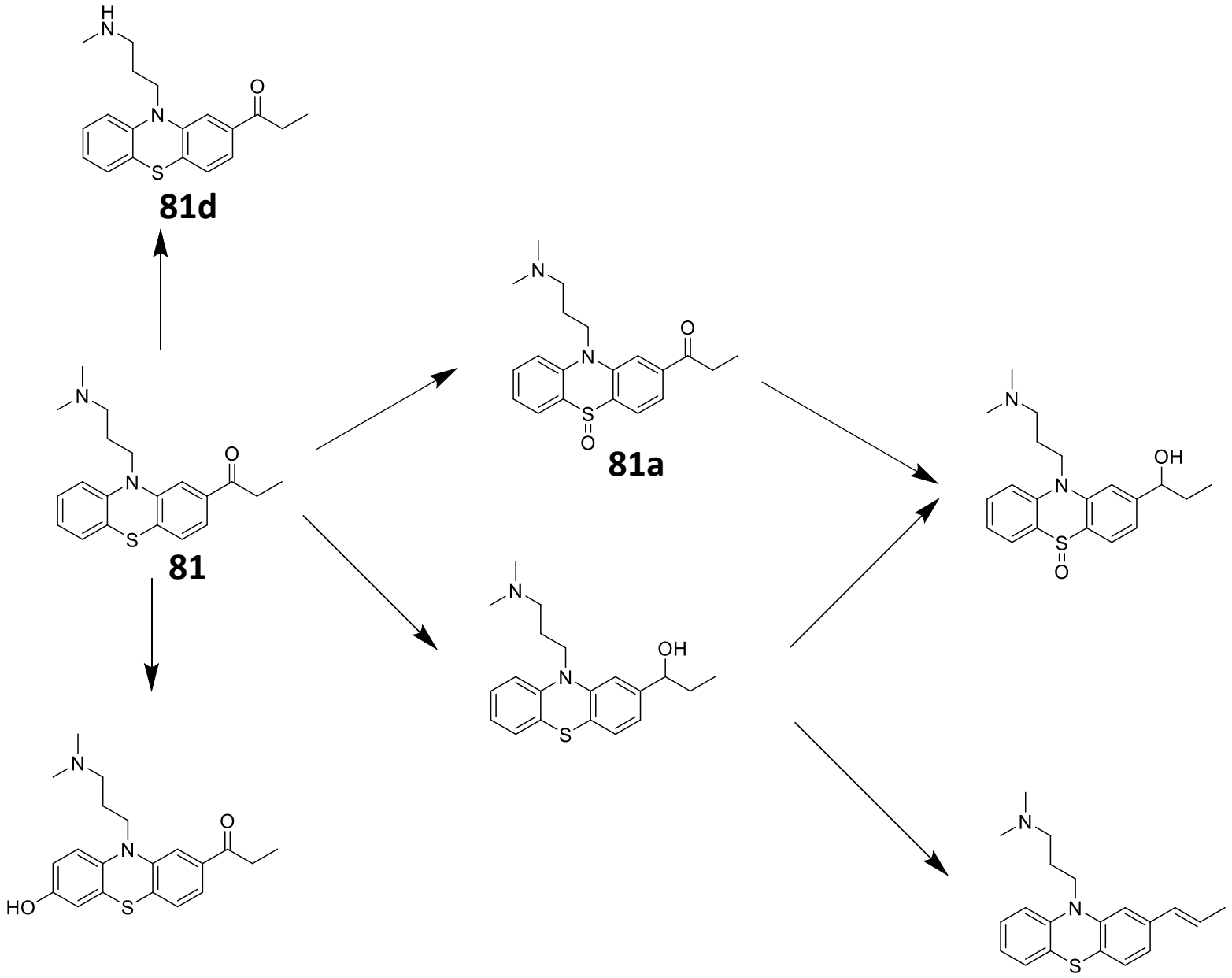


81d
tR: 6.09
m/z: 327(HPLC-MS)
m/z: 327.1548(HRMS)
deltam: 0.0017

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	4.4	16.3
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
81a*#	4.87	16	0	0	0	0	**79.4**	**56.5**	**24.5**	**4.7**
81b	4.95	32	0	0	0	0	0	43.5	0	0
81c	5.27	32	0	0	0	0	20.6	0	0	0
81d*	6.09	-14	0	0	0	0	0	0	**9.5**	**6.1**

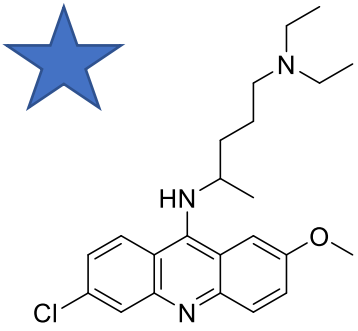
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Propionylpromazine (**81**) - in vitro/ in vivo biotransformation

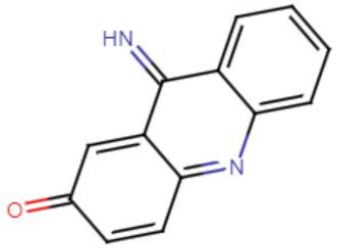


https://www.sciencedirect.com/science/article/pii/S0378434700829096

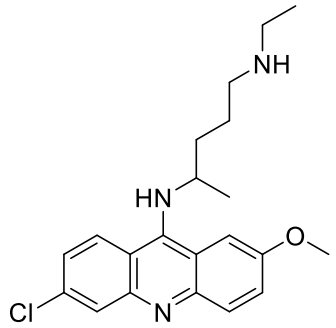
Quinacrine (**82**) - **Biomimetic transformation (I)**



82
tR: 3.90
m/z: 400 (HPLC-MS)
m/z: (HRMS)

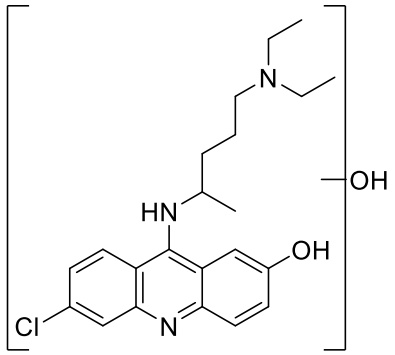


82b
tR: 3.69
m/z: 209 (HPLC-MS)
m/z: 209.0128(HRMS)
deltam: -0.0587
ppm:-280.8



82c
tR: 3.80
m/z: 372 (HPLC-MS)
m/z: 372.1839(HRMS)
deltam: -0.003
ppm: -0.8

82a
tR: 3.57
m/z: 209 (HPLC-MS)
m/z: 209.0128(HRMS)
deltam: -0.0587
ppm:-280.8



82f
tR: 4.10
m/z: 402 (HPLC-MS)
m/z: 402.1768(HRMS)
deltam: -0.0180
ppm: -44.8

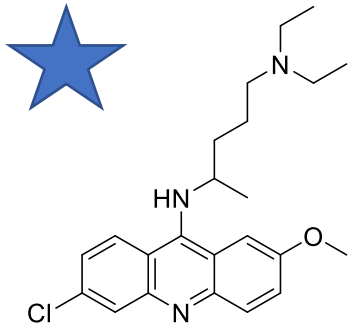
82d
tR: 3.82
m/z: 216 (HPLC-MS)
m/z: 216.0460(HRMS)

82e
tR: 4.04
m/z: 215 (HPLC-MS)
m/z: 215.0942(HRMS)

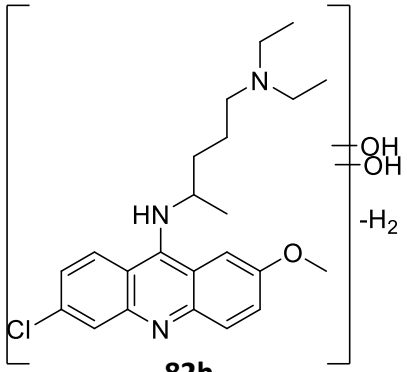
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	85.4	100	58.8	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
82a	3.57	-191	0	0	0	0	7.1	0	0	0
82b	3.69	-191	0	0	0	0	19.5	11.1	0	0
82c#	3.8	-28	0	0	0	0	0	0	**27.6**	10.7
82d#	3.82	-184	0	0	0	0	**36.7**	6.8	0	0
82e#	4.04	-185	0	0	0	0	0	**20.3**	0	0
82f#	4.10	2	0	0	0	0	0	**23.5**	0	0
82g	4.29	-79	0	0	0	0	8.9	0	0	0
82h	4.32	30	0	0	0	0	0	10	0	0
82i	4.75	-60	0	0	0	0	4.9	9.5	0	0
82j	5.24	-199	0	0	0	0	8.7	0	0	0
82k	5.47	0	0	0	0	0	7.0	0	0	0
82l	7.37	-126	0	**10.8**	0	**4.9**	0	11.3	26.5	5.3
82m	8.3	-141	NI	0	0	0	4	7.4	0	0
82n	8.5	-140	11.7	**9.9**	0	**8.2**	0	0	29.6	12.8

#Major biomimetic metabolite, Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Quinacrine (**82**) - **Biomimetic transformation (II)**

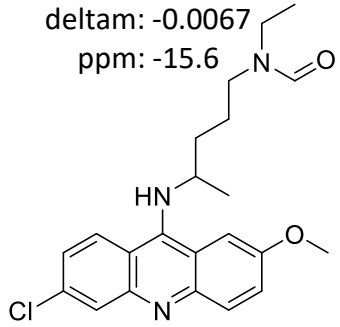


82
tR: 3.90
m/z: 400 (HPLC-MS)
m/z: (HRMS)



82h
tR: 4.32
m/z: 430 (HPLC-MS)
m/z: 430.1830(HRMS)
deltam: -0.0067
ppm: -15.6

82g
tR: 4.29
m/z: 321 (HPLC-MS)
m/z: 321.0724(HRMS)



82k
tR: 5.47
m/z: 400 (HPLC-MS)
m/z: 400.1984(HRMS)
deltam: 0.0192
ppm: 48.0

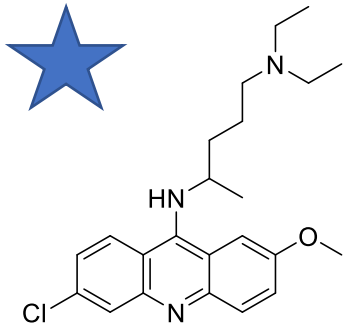
82i
tR: 4.75
m/z: 340 (HPLC-MS)
m/z: (HRMS)

82j
tR: 5.24
m/z: 201 (HPLC-MS)
m/z: 201.0430(HRMS)

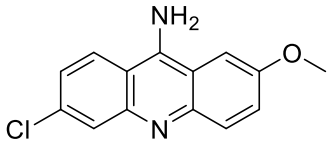
			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	85.4	100	58.8	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
82a	3.57	-191	0	0	0	0	7.1	0	0	0
82b	3.69	-191	0	0	0	0	19.5	11.1	0	0
82c#	3.8	-28	0	0	0	0	0	0	**27.6**	10.7
82d#	3.82	-184	0	0	0	0	**36.7**	6.8	0	0
82e#	4.04	-185	0	0	0	0	0	**20.3**	0	0
82f#	4.10	2	0	0	0	0	0	**23.5**	0	0
82g	4.29	-79	0	0	0	0	8.9	0	0	0
82h	4.32	30	0	0	0	0	0	10	0	0
82i	4.75	-60	0	0	0	0	4.9	9.5	0	0
82j	5.24	-199	0	0	0	0	8.7	0	0	0
82k	5.47	0	0	0	0	0	7.0	0	0	0
82l	7.37	-126	0	**10.8**	0	**4.9**	0	11.3	26.5	5.3
82m	8.3	-141	NI	0	0	0	4	7.4	0	0
82n	8.5	-140	11.7	**9.9**	0	**8.2**	0	0	29.6	12.8

#Major biomimetic metabolite, Non biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

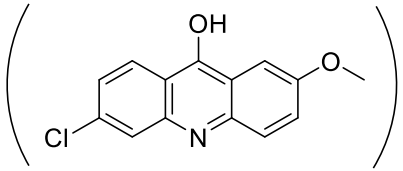
Quinacrine (**82**) - **Biomimetic transformation (III)**



82
tR: 3.90
m/z: 400 (HPLC-MS)
m/z: (HRMS)



82m
tR: 8.30
m/z: 259 (HPLC-MS)
m/z: 259.0609(HRMS)
deltam: -0.0029
ppm: -11.2



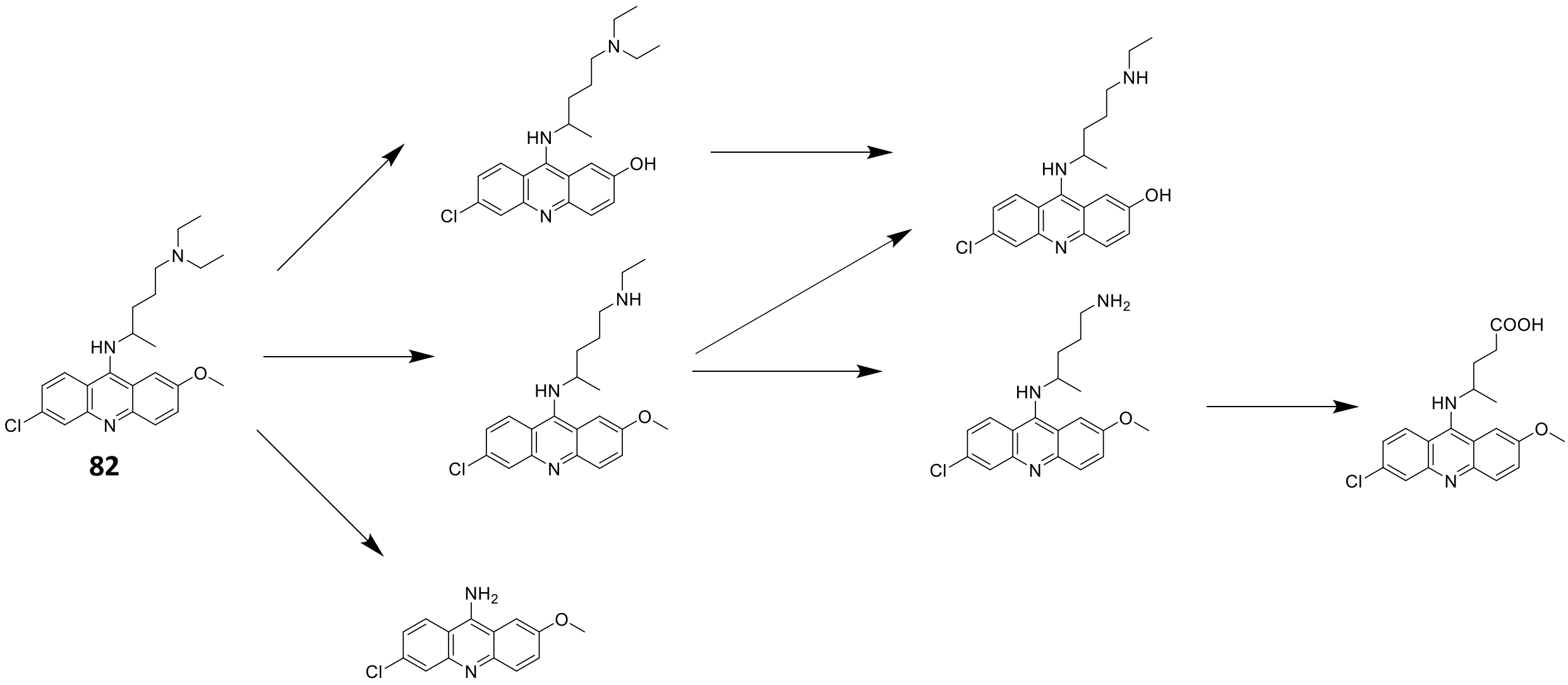
82n
tR: 8.50
m/z: 260 (HPLC-MS)
m/z: 260.0661(HRMS)
deltam: 0.0183
ppm: 70.4

82l
tR: 7.37
m/z: 284 (HPLC-MS)
m/z: 284.3330(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	85.4	100	58.8	100
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
82a	3.57	-191	0	0	0	0	7.1	0	0	0
82b	3.69	-191	0	0	0	0	19.5	11.1	0	0
82c[#]	3.8	-28	0	0	0	0	0	0	**27.6**	10.7
82d[#]	3.82	-184	0	0	0	0	**36.7**	6.8	0	0
82e[#]	4.04	-185	0	0	0	0	0	**20.3**	0	0
82f[#]	4.10	2	0	0	0	0	0	**23.5**	0	0
82g	4.29	-79	0	0	0	0	8.9	0	0	0
82h	4.32	30	0	0	0	0	0	10	0	0
82i	4.75	-60	0	0	0	0	4.9	9.5	0	0
82j	5.24	-199	0	0	0	0	8.7	0	0	0
82k	5.47	0	0	0	0	0	7.0	0	0	0
82l	7.37	-126	0	**10.8**	0	**4.9**	0	11.3	26.5	5.3
82m	8.3	-141	**NI**	0	0	0	4	7.4	0	0
82n	8.5	-140	11.7	**9.9**	0	**8.2**	0	0	29.6	12.8

[#]**Major biomimetic metabolite, Non biomimetic metabolite**
NI: Non-ionizable in positive mode of ESI

Quinacrine (**82**) - in vitro/ in vivo biotransformation

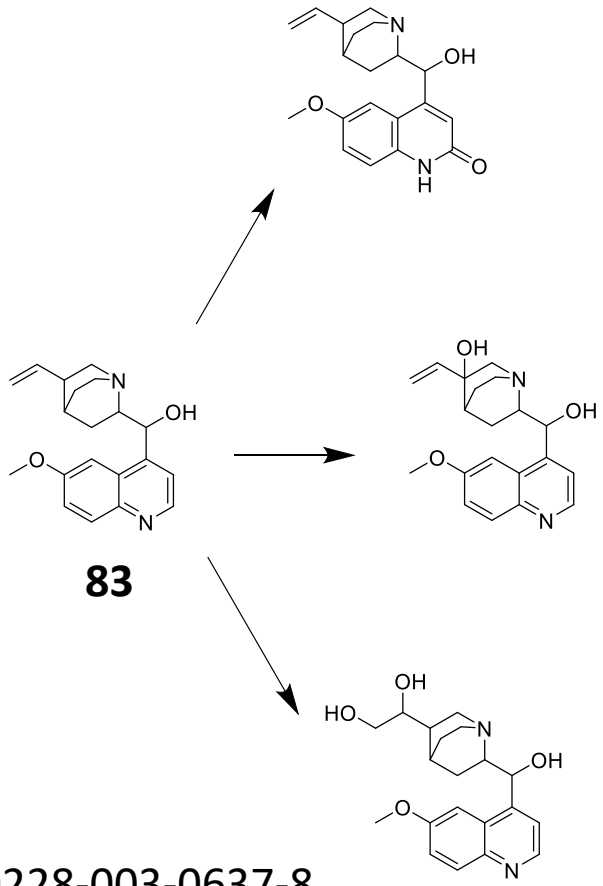


https://dmd.aspetjournals.org/content/34/7/1136.short

Quinine (**83**) - **Biomimetic transformation**

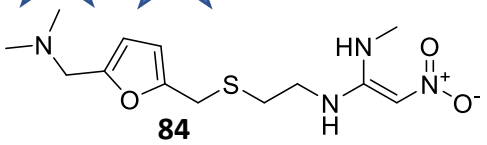
NO biomimetic transformation

Quinine (**83**) - **in vitro/ in vivo biotransformation**

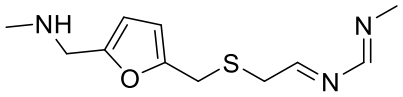


https://link.springer.com/article/10.1007/s00228-003-0637-8

Ranitidine (**84**) - **Biomimetic transformation**



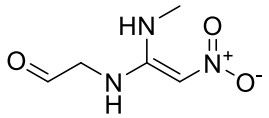
84
tR: 2.40
m/z: 315 (HPLC-MS)
m/z: (HRMS)



?

84a
tR: 1.05
m/z: 180 (HPLC-MS)
m/z: 180.3604(HRMS)

84b
tR: 1.27
m/z: 240 (HPLC-MS)
m/z: 239.9590(HRMS)
deltam: -0.1581
ppm: -658.9

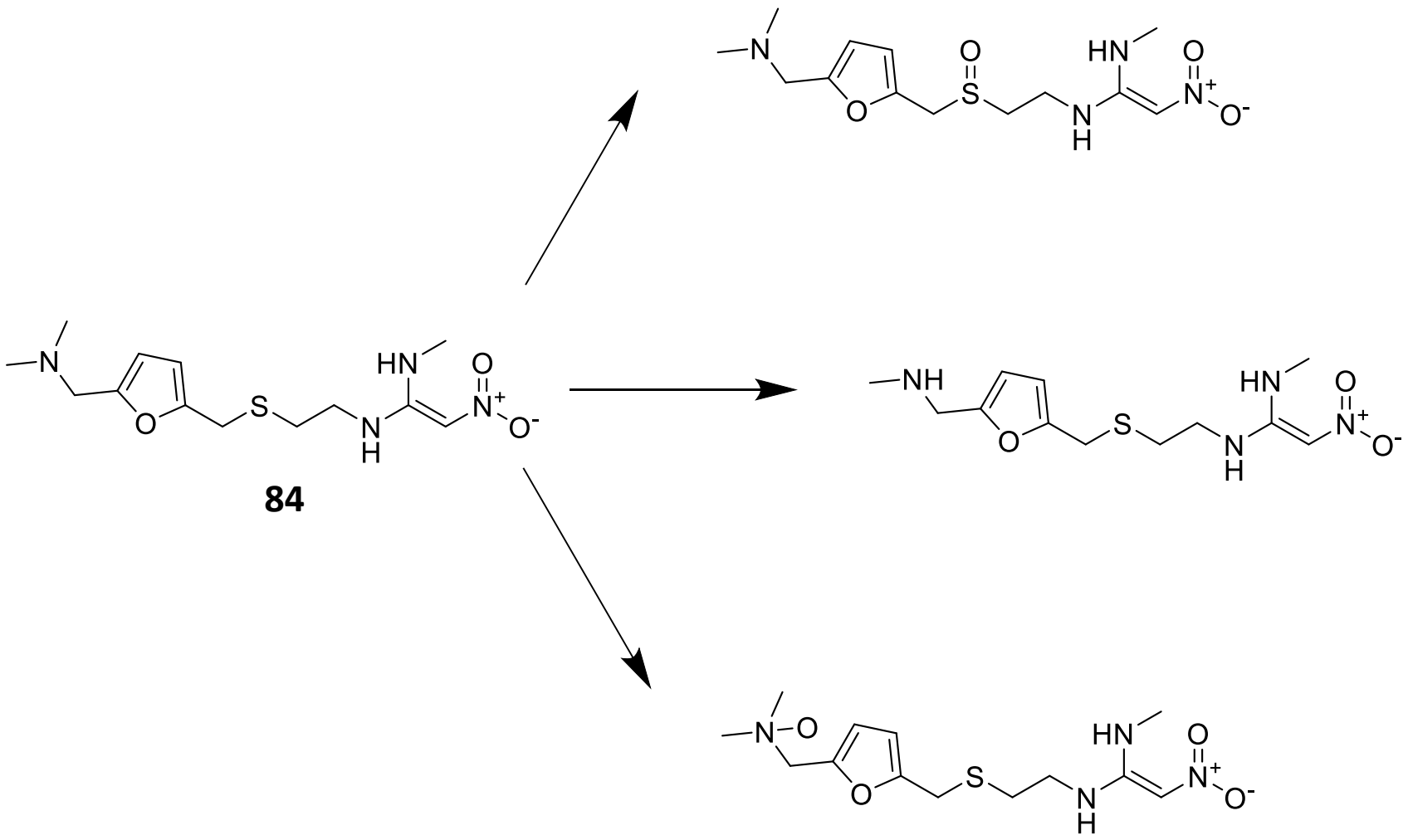


84c
tR: 1.37
m/z: 160 (HPLC-MS)
m/z: 160.0554(HRMS)
deltam: -0.0168
ppm: -105.0

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	33.4	92.6	100	60.6	36.7	92.5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
84a[#]	1.05	-135	0	0	0	0	**87.9**	**13.7**	0	0
84b	1.27	-75	0	**1.1**	**11.2**	**5.9**	12.1	14.4	5.9	6.3
84c	1.37	-155	**2.4**	**1.5**	**10.1**	**1.6**	0	0	5.4	1.2

[#]Major biomimetic metabolite
Non biomimetic metabolite

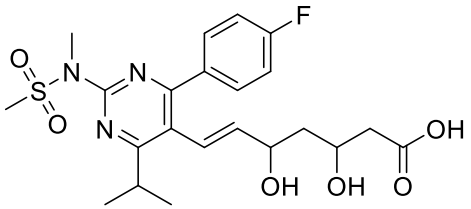
Ranitidine (**84**) - in vitro/ in vivo biotransformation



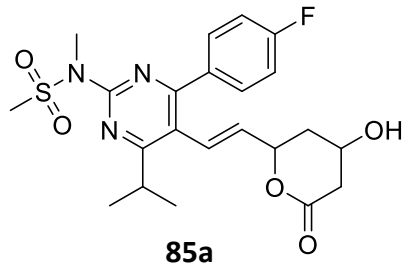
84

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/019090s053,019593s042lbl.pdf

Rosuvastatin (**85**) - **Biomimetic transformation**



85
tR: 8.17
m/z: 482 (HPLC-MS)
m/z: (HRMS)

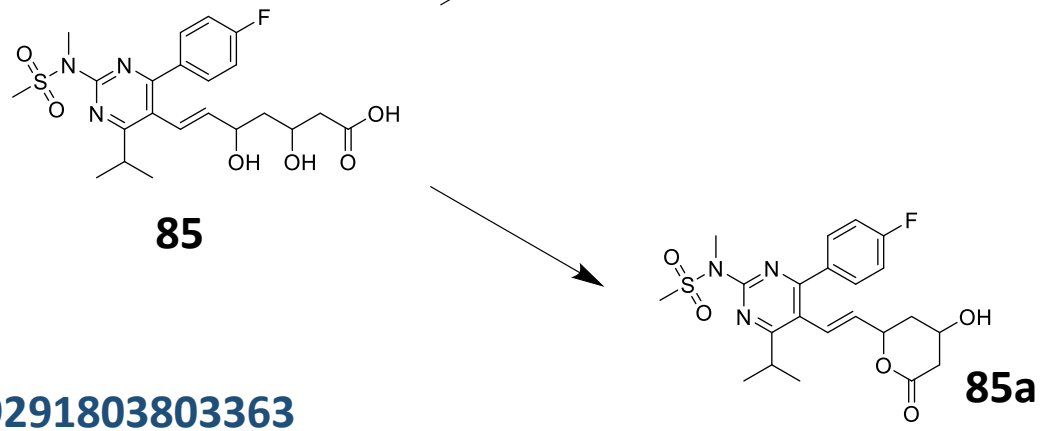


85a
tR: 9.00
m/z: 464 (HPLC-MS)
m/z: 464.1652(HRMS)
deltam: -0.0003
ppm: -0.6

			Non biomimetic				Biomimetic			
Conversion (%)			7.5	0	0	0	21.1	0	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
85a*	9.00	-18	5.3	0	0	0	5.1	0	0	0

***in vivo/in vitro metabolite formed by biotransformation**
Non biomimetic metabolite

Rosuvastatin (**85**) - **in vitro/ in vivo biotransformation**

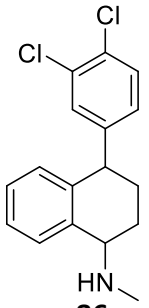


85

85a

https://www.sciencedirect.com/science/article/pii/S0149291803803363

Sertraline (**86**) - **Biomimetic transformation**

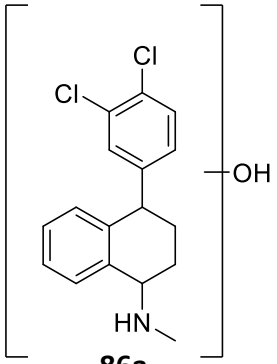


86

tR: 6.34

m/z: 306 (HPLC-MS)

m/z: (HRMS)



86a

tR: 5.35

m/z: 322 (HPLC-MS)

m/z: 322.0714(HRMS)

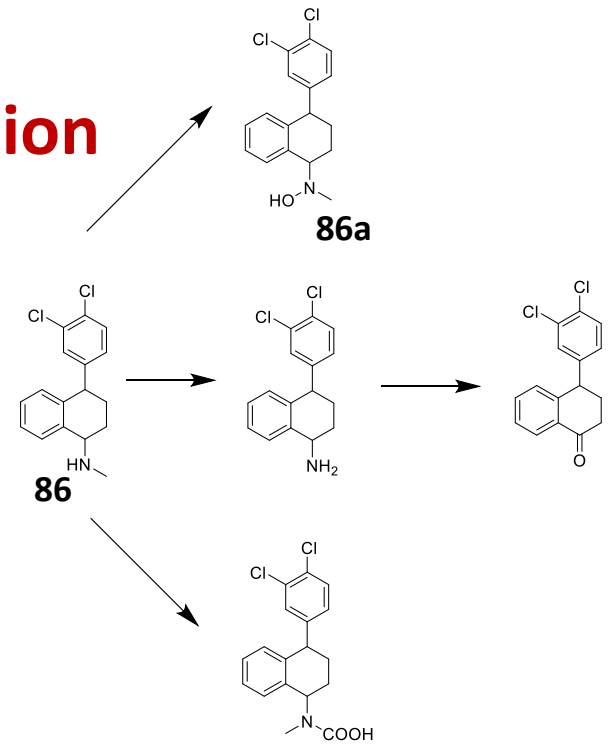
deltam: -0.0051

ppm: -15.8

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	34.4	0	0	16.8
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
86a*	5.35	16	0	0	0	0	**22.2**	0	0	0

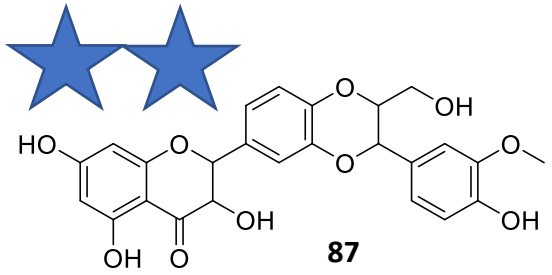
***in vivo/in vitro metabolite formed by biotransformation**

Sertraline (**86**) –
in vitro/ in vivo biotransformation

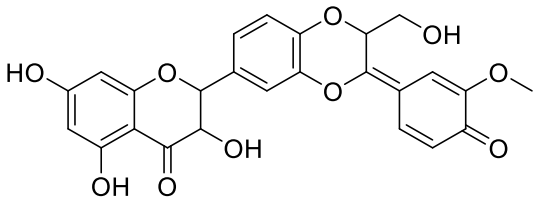


Referencia?!

Silibinin (**87**) - **Biomimetic transformation**



87
tR: 8.32
m/z: 483 (HPLC-MS)
m/z: (HRMS)



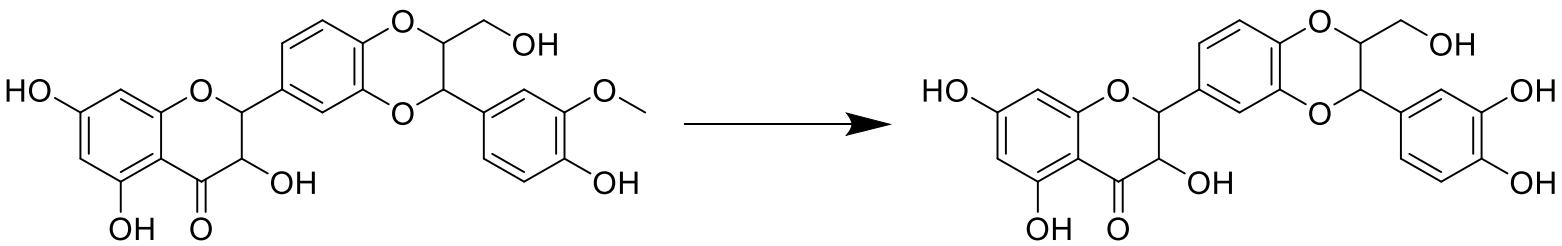
87a
tR: 7.2
m/z: 481 (HPLC-MS)
m/z: 481.3020(HRMS)
deltam: 0.1886
ppm: 391.8

87b
tR: 7.97
m/z: 341 (HPLC-MS)
m/z: 339.1934(-HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	67.5	100	88.2	38.6	84.4
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
87a	7.2	-2	**91**	**95.9**	**98.1**	**91.3**	0	0	91.5	94.8
87b	7.97	-142	0	0	0	0	0	0	0	5.2

Non biomimetic metabolite

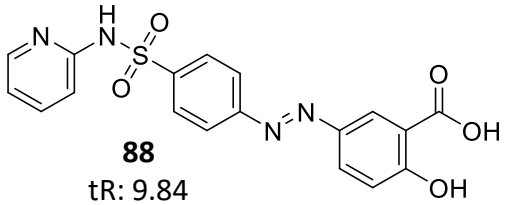
Silibinin (**87**) - **in vitro/ in vivo biotransformation**



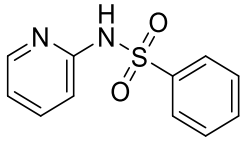
87

Referencia?!

Sulfasalazine (**88**) - **Biomimetic transformation**



88
tR: 9.84
m/z: 399 (HPLC-MS)
m/z: 399.0753(HRMS)



88a
tR: 3.9
m/z: 207 (HPLC-MS)
m/z: 206.9961(HRMS)

88b
tR: 5.72
m/z: 235 (HPLC-MS)
m/z: 235.0634(HRMS)
deltam: 0.0093
ppm: 39.6

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	0	65	9.9	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
88a	3.9	-192	**4.5**	0	0	**19.8**	0	0	0	25.5
88b[#]	5.72	-164	0	0	0	0	3.6	**23.4**	0	0

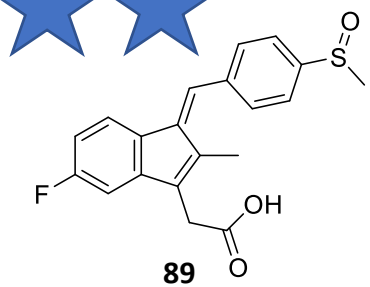
[#]**Major biomimetic metabolite**
Non biomimetic metabolite

Sulfasalazine (**88**) - **in vitro/ in vivo biotransformation**

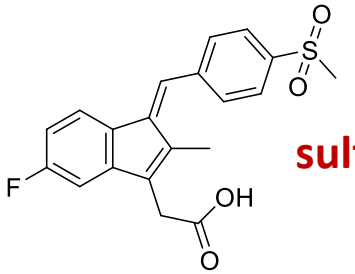
Colon microbiome

https://www.sciencedirect.com/science/article/abs/pii/0016508579902774

Sulindac (**89**) - **Biomimetic transformation**



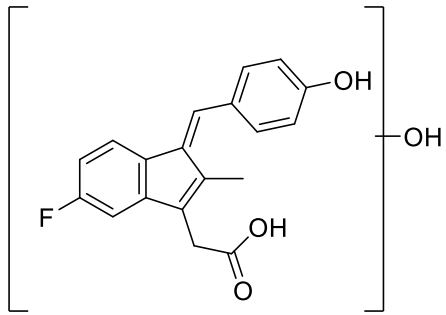
89
tR: 7.94
m/z: 357 (HPLC-MS)
m/z: (HRMS)



sulfone

89a
tR: 6.2
m/z: 391 (HPLC-MS)
m/z: 391.1090(HRMS)

89b
tR: 6.85
m/z: 373 (HPLC-MS)
m/z: 373.0895(HRMS)
deltam: -0.0015
ppm: -4.0

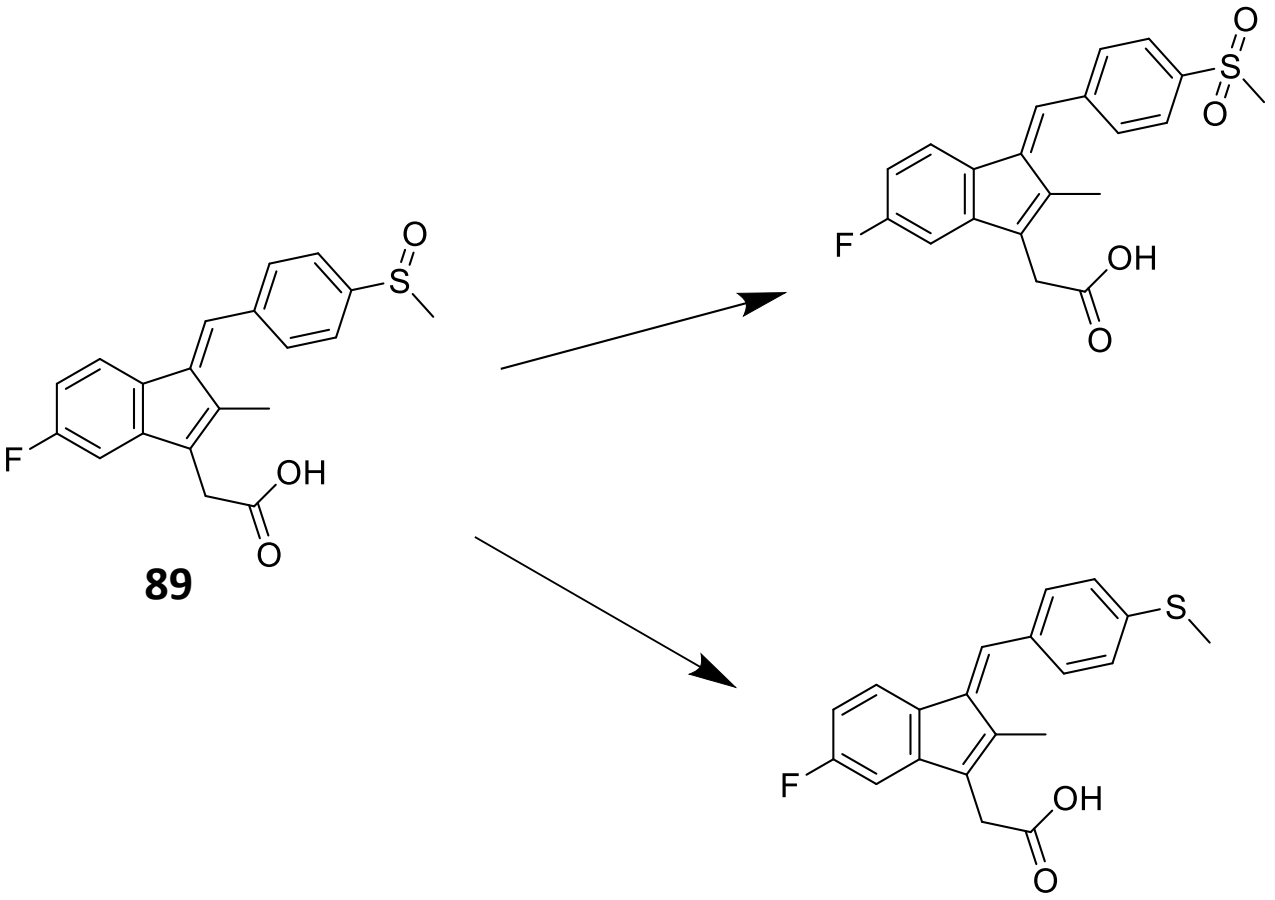


89c
tR: 8.77
m/z: 327 (HPLC-MS)
m/z: 327.3813(HRMS)
deltam: 0.2780
ppm: 849.2

			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	41.8	72	21.8	28.4
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
89a#	6.20	34	0	0	0	0	0	0	0	**24.6**
89b#	6.85	16	0	0	0	0	**13.4**	27.7	0	0
89c	8.77	-30	0	0	0	0	0	22.7	0	0

#Major biomimetic metabolite

Sulindac (**89**) - **in vitro/ in vivo biotransformation**

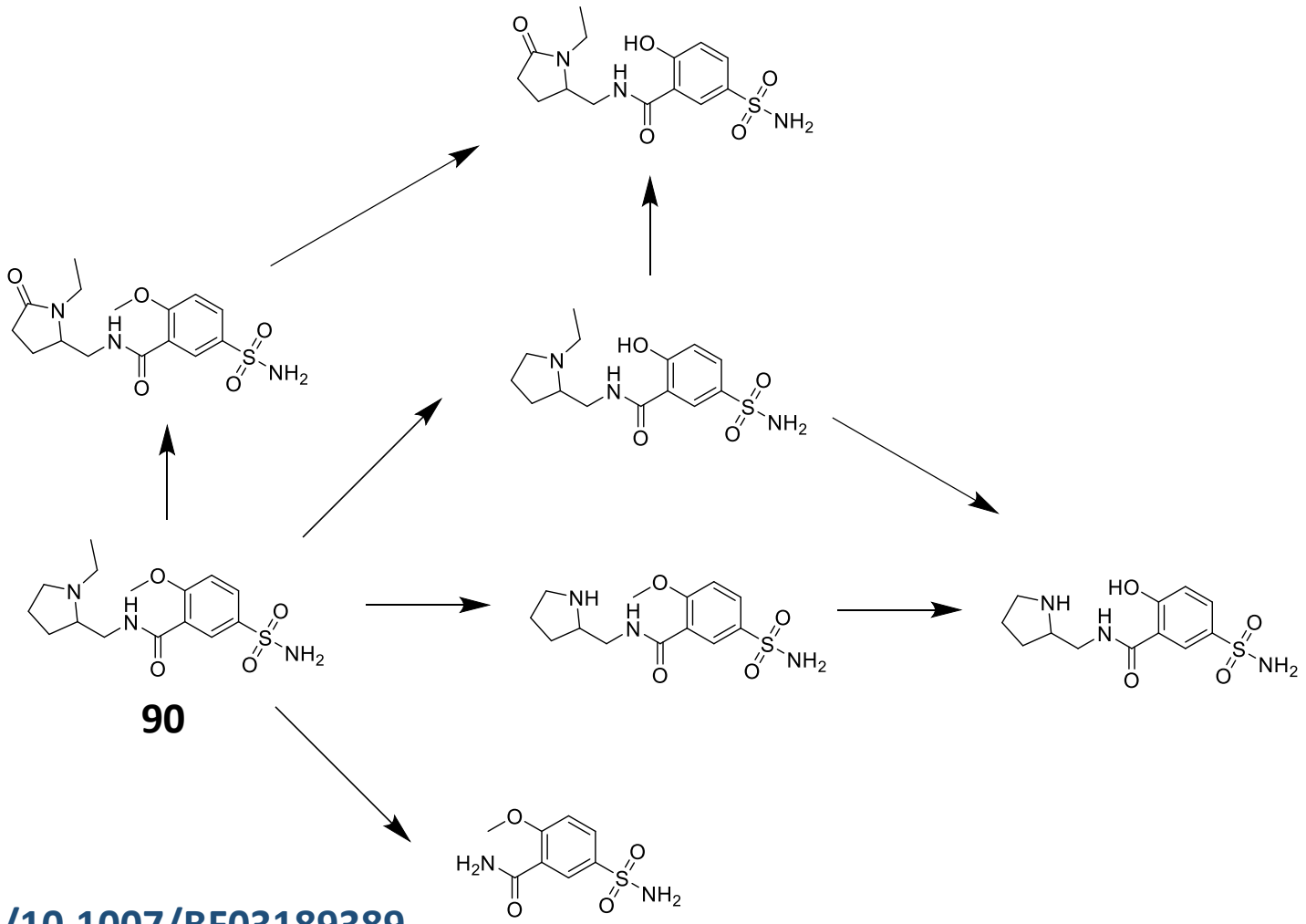


https://ascpt.onlinelibrary.wiley.com/doi/abs/10.1038/clpt.1985.192

Sulpiride (**90**) - **Biomimetic transformation**

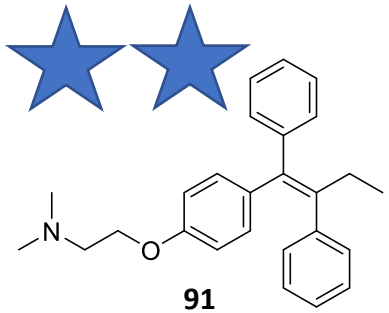
NO biomimetic transformation

Sulpiride (**90**) - **in vitro/ in vivo biotransformation**

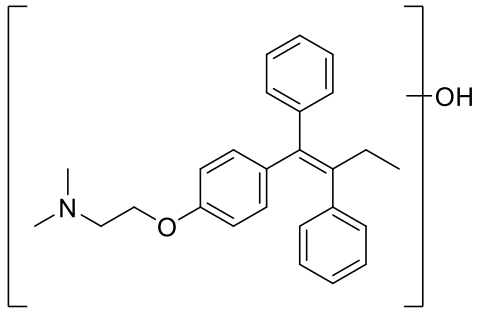


https://link.springer.com/article/10.1007/BF03189389

Tamoxifen (**91**) - **Biomimetic transformation**

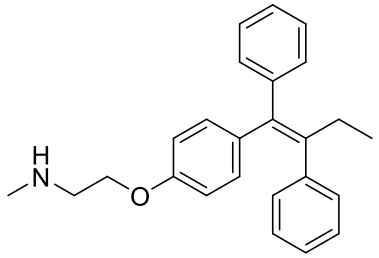


91
tR:
m/z: 372 (HPLC-MS)
m/z: (HRMS)



91a
tR: 7.29
m/z: 388 (HPLC-MS)
m/z: 388.2267(HRMS)
deltam: -0.0010
ppm: -2.6

N-oxide or OH?

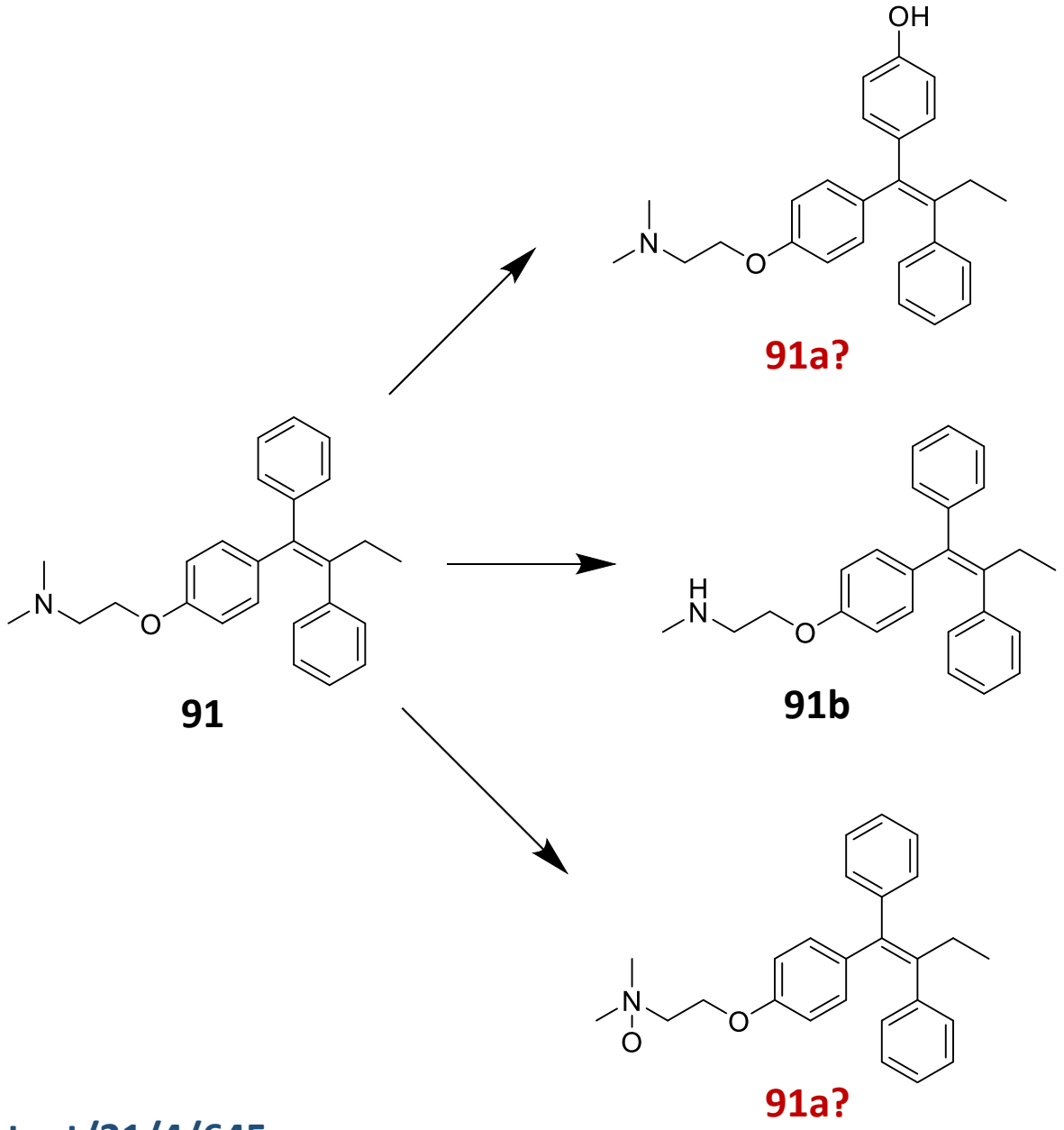


91b
tR: 7.69
m/z: 358 (HPLC-MS)
m/z: 358.2162(HRMS)
deltam: -0.0009
ppm: -2.5

			Non Biomimetic				Biomimetic			
Conversion (%)			0	1.1	0	0	59.2	91	11.7	43.1
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
91a*	7.29	16	0	0	0	0	**9.2**	0	0	0
91b*#	7.69	-14	0	**4.1**	0	0	**38**	**85**	**5.2**	**15.6**

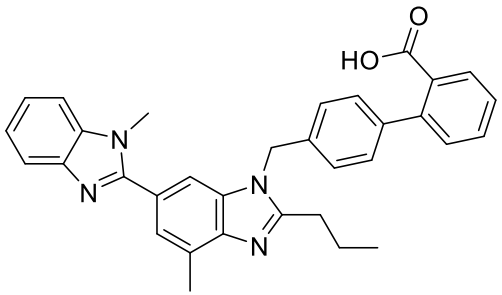
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
Non biomimetic metabolite

Tamoxifen (**91**) - **in vitro/ in vivo biotransformation**



https://dmd.aspetjournals.org/content/21/4/645

Telmisartan (**92**) - **Biomimetic transformation**



92

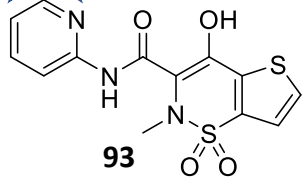
NO biomimetic transformation

Telmisartan (**92**) - **in vitro/ in vivo biotransformation**

Only a glucuronide metabolite, CYP450 is not involved in the metabolism

https://accp1.onlinelibrary.wiley.com/doi/abs/10.1177/00912700004001202

Tenoxicam (**93**) - **Biomimetic transformation**



93
tR: 6.15
m/z: 338 (HPLC-MS)
m/z: (HRMS)

93a
tR: 3.74
m/z: - (HPLC-MS)
m/z: (HRMS)

93b
tR: 3.99
m/z: 171 (HPLC-MS)
m/z: (HRMS)

93c
tR: 4.67
m/z: 340 (HPLC-MS)
m/z: (HRMS)

93d
tR: 5.05
m/z: 181 (HPLC-MS)
m/z: (HRMS)

93e
tR: 6.54
m/z: 227 (HPLC-MS)
m/z: (HRMS)

93f
tR: 6.7
m/z: - (HPLC-MS)
m/z: (HRMS)

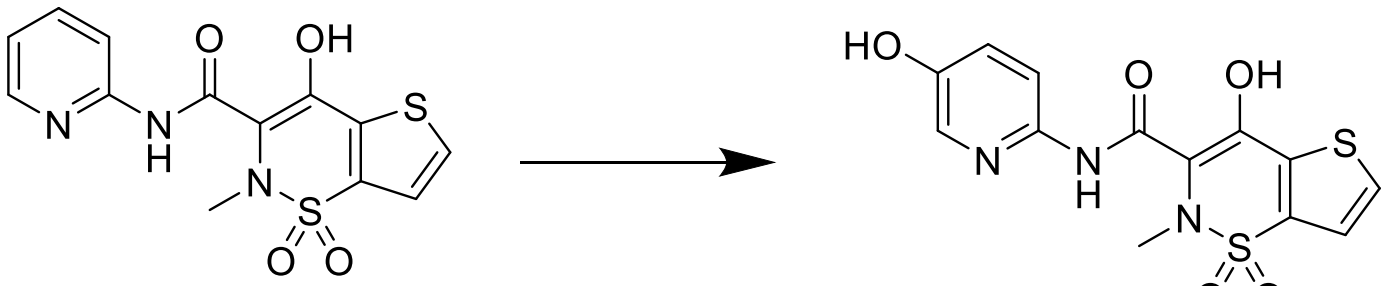
93g
tR: 7.4
m/z: - (HPLC-MS)
m/z: (HRMS)

			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	20.7	69.7
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
93a	3.74	NI	0	0	0	0	7.5	24.5	0	0
93b#	3.99	-167	0	0	0	0	0	0	0	**43.0**
93c	4.67	2	0	0	0	0	17.8	5.3	0	1.2
93d	5.05	-157	0	0	0	0	14.0	12	0	0
93e	6.54	-111	0	0	0	0	11.1	0	0	18.4
93f#	6.70	NI	0	0	0	0	**47.0**	**28.4**	0	5.4
93g#	7.40	NI	0	0	0	0	0	0	**15.2**	5.4

#Major biomimetic metabolite

NI: Non-ionizable in positive mode of ESI

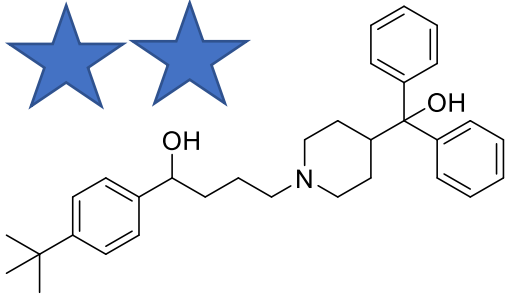
Tenoxicam (**93**) - **in vitro/ in vivo biotransformation**



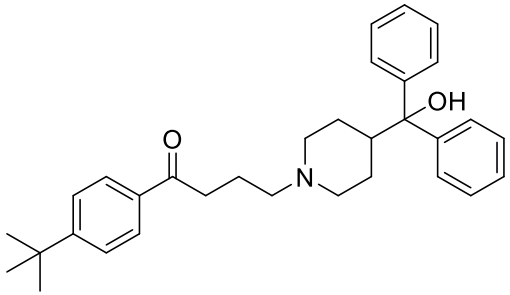
93

https://link.springer.com/article/10.2165/00003088-199426010-00003

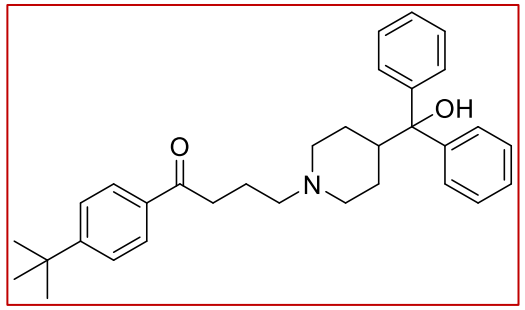
Terfenadine (**94**) - **Biomimetic transformation**



94
tR: **?**
m/z: 472 (HPLC-MS)
m/z: (HRMS)



94a
tR: 7.54
m/z: 470 (HPLC-MS)
m/z: 470.3067(HRMS)
deltam: 0.0008
ppm: 1.7

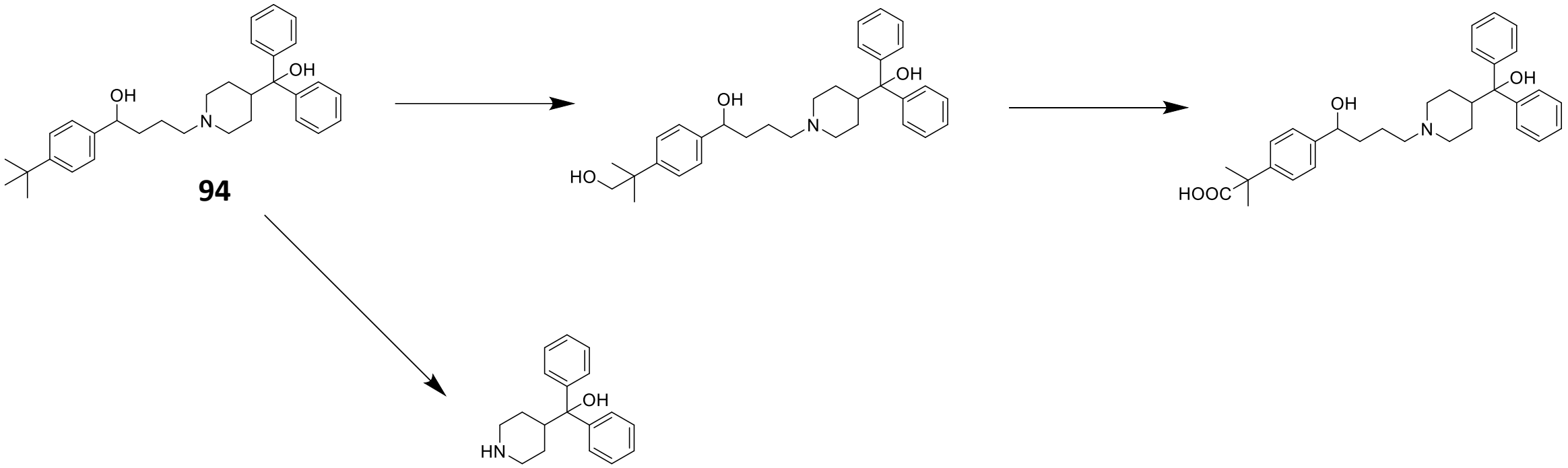


94b
tR: 7.64
m/z: 470 (HPLC-MS)
m/z: 470.3067(HRMS)
deltam: 0.0008
ppm: 1.7

			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	68.3	61.4	0	26.5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
94a	7.54	-2	0	0	0	0	0	0	0	22.2
94b#	7.64	-2	0	0	0	0	**68.0**	**60.8**	0	**30.1**

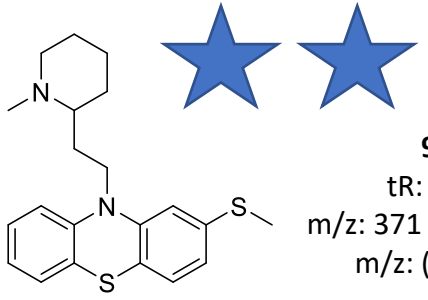
#Major biomimetic metabolite

Terfenadine (**94**) - **in vitro/ in vivo biotransformation**



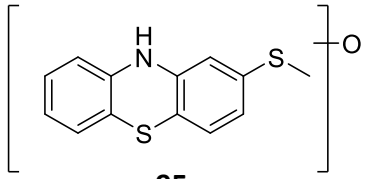
https://www.sciencedirect.com/science/article/pii/S0378434700000426

Thioridazine (**95**) - **Biomimetic transformation**

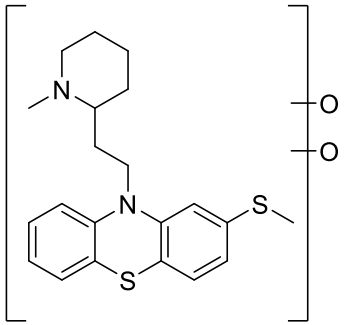


95
tR: 6.74
m/z: 371 (HPLC-MS)
m/z: (HRMS)

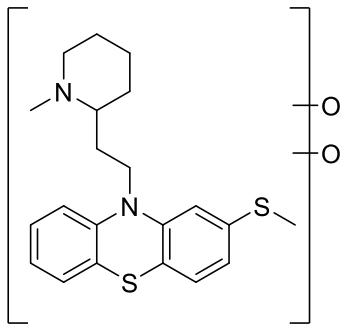
S-oxide
S-sulfoxide



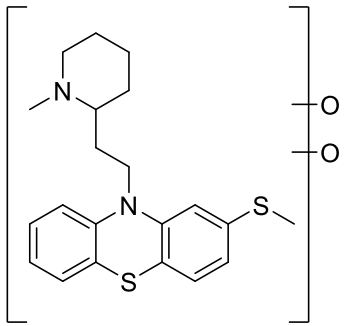
95g
tR: 7.32
m/z: 262 (HPLC-MS)
m/z: (HRMS)



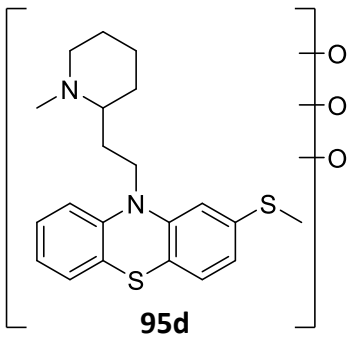
95a
tR: 3.87
m/z: 403 (HPLC-MS)
m/z: 403.1547(HRMS)
deltam: 0.0033
ppm: 8.2



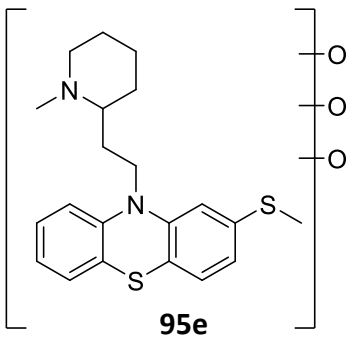
95b
tR: 3.97
m/z: 403 (HPLC-MS)
m/z: 403.1547(HRMS)
deltam: 0.0033
ppm: 8.2



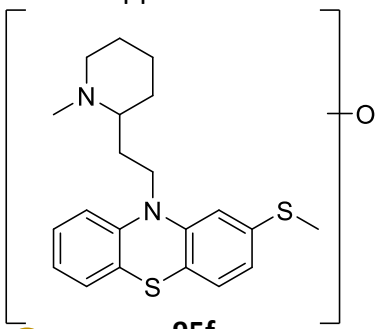
95c
tR: 4.05
m/z: 403 (HPLC-MS)
m/z: 403.1547(HRMS)
deltam: 0.0033
ppm: 8.2



95d
tR: 4.17
m/z: 419 (HPLC-MS)
m/z: 419.1469(HRMS)
deltam: 0.0006
ppm: 1.4



95e
tR: 4.39
m/z: 419 (HPLC-MS)
m/z: 419.1469(HRMS)
deltam: 0.0006
ppm: 1.4

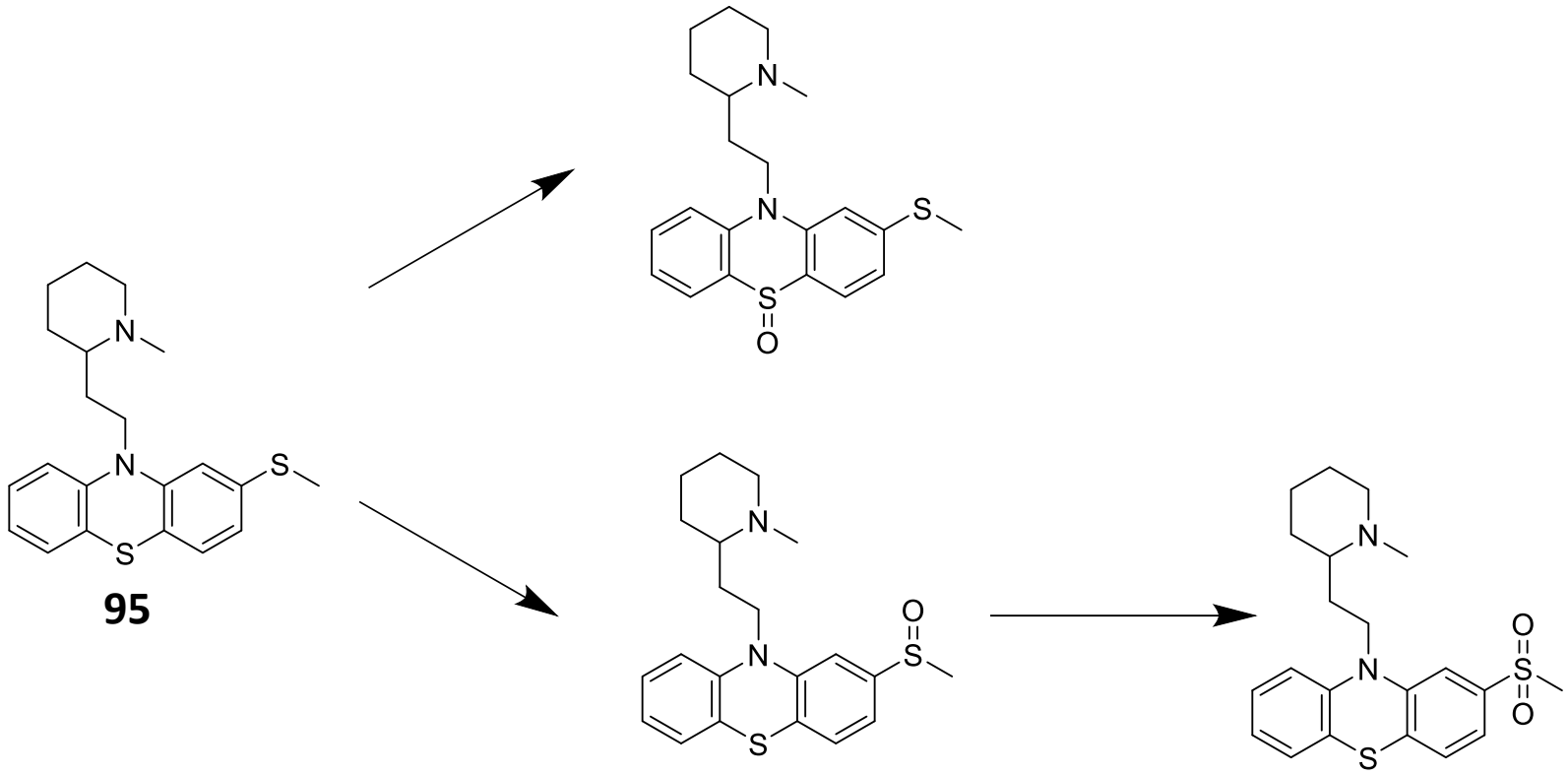


95f
tR: 5.20
m/z: 387 (HPLC-MS)
m/z: 387.1569(HRMS)
deltam:
ppm: 0.0004

			Non Biomimetic				Biomimetic			
Conversion (%)			0	9.8	7.2	0	100	100	21.4	60.1
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
95a	3.87	32	0	0	0	0	21.5	10.3	0	0
95b#	3.97	32	0	0	0	0	**34.5**	19.5	0	22.5
95c	4.05	32	0	0	0	0	8.5	5.0	0	0
95d	4.17	48	0	0	0	0	22.7	0	0	0
95e	4.39	48	0	0	0	0	8.2	0	0	0
95f#	5.20	16	0	**5.4**	**2.5**	0	0	**58.6**	**42.4**	**40.6**
95g	7.32	-109	0	0	0	0	0	0	0	7.7

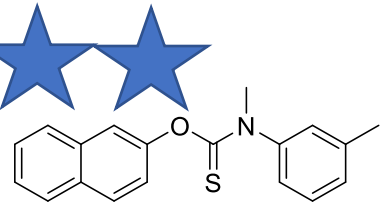
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
Non biomimetic metabolite

Thioridazine (**95**) - **in vitro/ in vivo biotransformation**

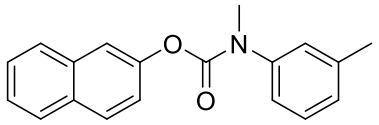


https://www.ingentaconnect.com/content/ben/pri/2011/00000006/00000002/art00005

Tolnaftate (**96**) - **Biomimetic transformation**



96
tR: 11.92
m/z: 308 (HPLC-MS)
m/z: (HRMS)



96a
tR: 7.29
m/z: 191 (HPLC-MS)
m/z: 191.0060(HRMS)

96b
tR: 11.07
m/z: - (HPLC-MS)
m/z: (HRMS)

96c
tR: 11.39
m/z: 292 (HPLC-MS)
m/z: 292.1334(HRMS)
deltam: -0.0004
ppm: -1.4

			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	71.1	0	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
96a	7.29	-117	0	0	0	0	7.5	0	0	0
96b	11.07	NI	0	0	0	0	11.4	0	0	0
96c#	11.39	-16	0	0	0	0	**51.0**	0	0	0

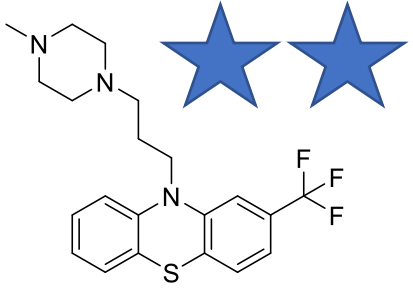
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Tolnaftate (**96**) - **in vitro/ in vivo biotransformation**

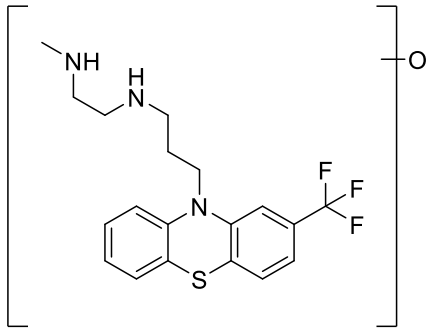
Not metabolized in the human body

https://www.sciencedirect.com/science/article/abs/pii/S0099542808606127

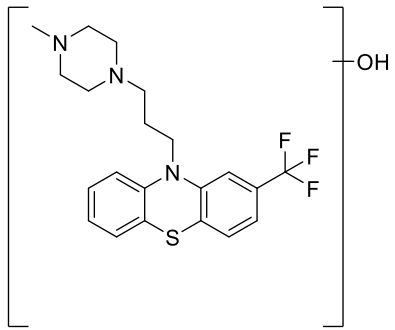
Trifluoperazine (**97**) - **Biomimetic transformation**



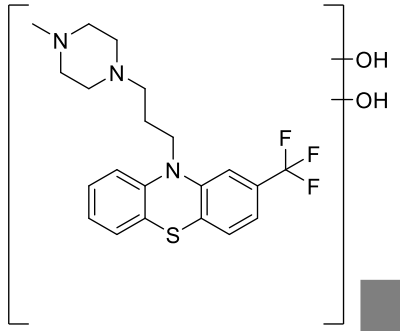
97
tR: 6.60
m/z: 408 (HPLC-MS)
m/z: (HRMS)



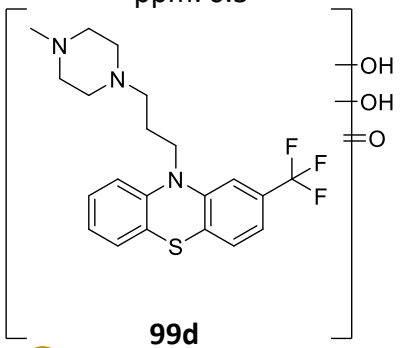
97a
tR: 4.02
m/z: 398 (HPLC-MS)
m/z: 398.1516(HRMS)
deltam: 0.0002
ppm: 0.5



97b
tR: 5.00
m/z: 424 (HPLC-MS)
m/z: 424.1691(HRMS)
deltam: -0.0021
ppm: -5.0



99c
tR: 5.60
m/z: 440 (HPLC-MS)
m/z: 440.1621(HRMS)
deltam: -0.0001
ppm: -0.2

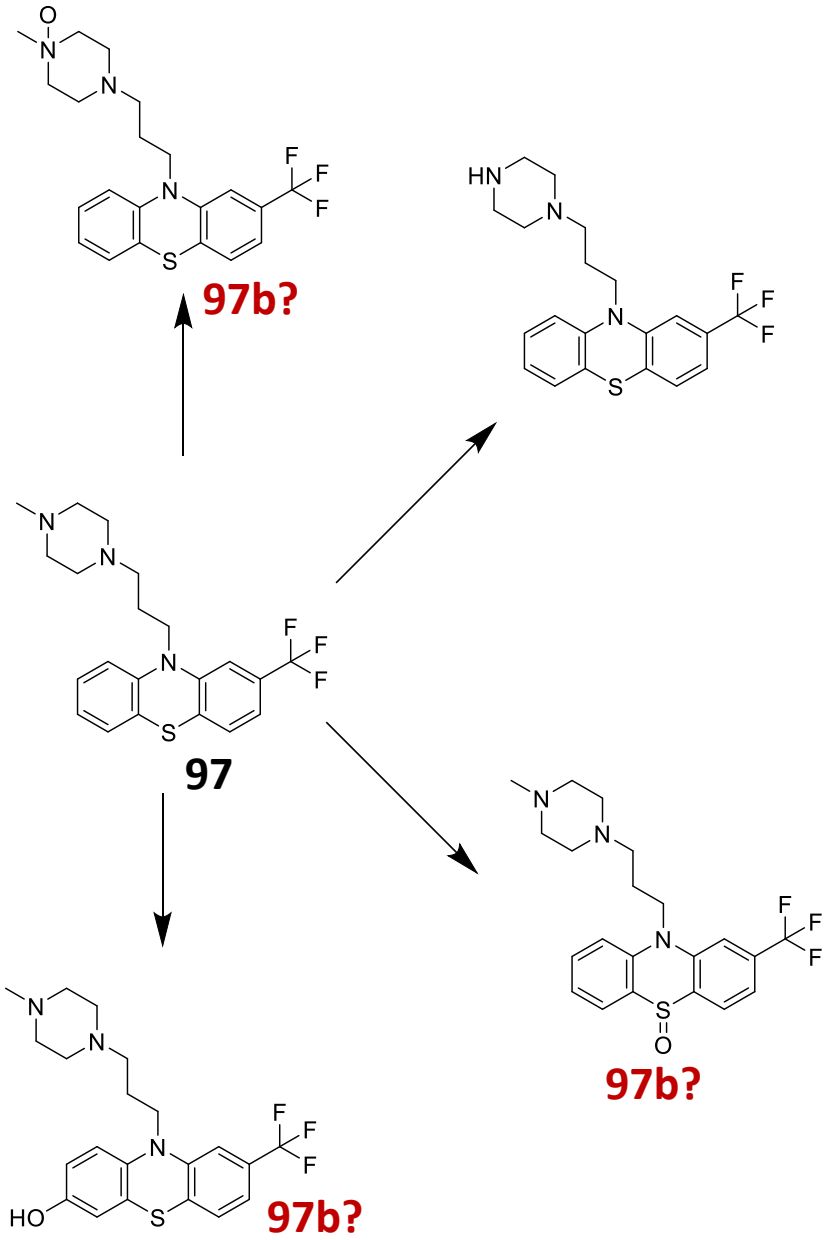


99d
tR: 7.25
m/z: 454 (HPLC-MS)
m/z: 476.1233(HRMS)(Na addukt)
deltam: 0.0001
ppm: 0.2

			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	100	100	68.9	56.0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
97a	4.02	-10	0	0	0	0	8.3	0	0	0
97b*#	5.0	16	0	0	0	0	**68.1**	0	**31.1**	**45.2**
97c	5.60	32	0	0	0	0	14.1	0	0	0
97d#	7.25	46	0	0	0	0	0	**100**	0	0

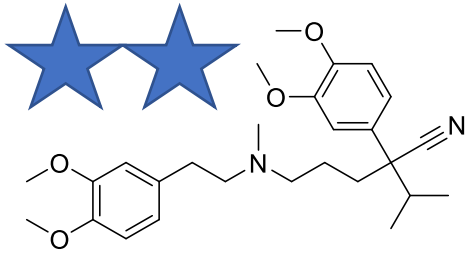
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite

Trifluoperazine (**97**) - **in vitro/ in vivo biotransformation**



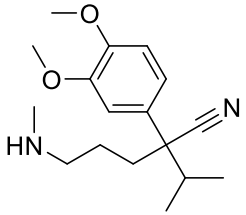
https://www.sciencedirect.com/science/article/pii/0006295274904213

Verapamil (**98**) - **Biomimetic transformation**



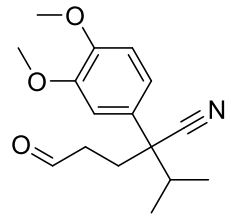
98
tR: 6.09
m/z: 455 (HPLC-MS)
m/z: (HRMS)

Hiányoznak metabolitok!

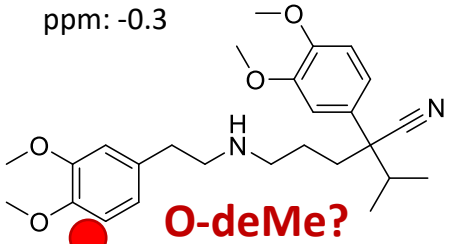


98a
tR: 5.01
m/z: 291 (HPLC-MS)
m/z: 291.2072(HRMS)
deltam: -0.0001
ppm: -0.3

98
tR:
m/z: (HPLC-MS)
m/z: (HRMS)

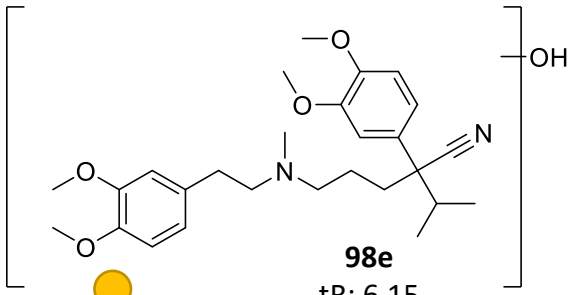


98c
tR: 5.72
m/z: 275 (HPLC-MS)
m/z: 274.9745(HRMS)
deltam: -0.1776
ppm:-645.9



O-deMe?

98d
tR: 5.99
m/z: 441 (HPLC-MS)
m/z: 441.2744(HRMS)
deltam: -0.0009
ppm: -2.0

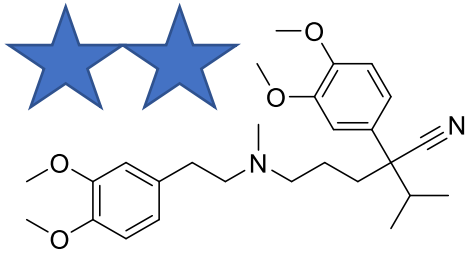


98e
tR: 6.15
m/z: 471 (HPLC-MS)
m/z: 493.2606(HRMS) Na addukt
deltam: -0.0072
ppm: -14.6

			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	85.3	100	68.1	74.5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
98a*	5.01	-164	0	0	0	0	**14.1**	**4.2**	**2.5**	**5.8**
98b	5.64	NI	0	0	0	0	0	0	7.9	0
98c	5.72	-180	0	0	0	0	0	0	0	11.3
98d*#	5.99	-14	0	0	0	0	**21.9**	**22.6**	**16.8**	**17.4**
98e	6.15	16	0	0	0	0	0	6.5	0	6.4
98f	6.47	-247	0	0	0	0	25.1	6.4	0	0
98g	6.70	105	0	0	0	0	12.3	4.3	0	0
98h	6.79	191	0	0	0	0	8.4	0	0	0
98i	7.29	NI	0	0	0	0	0	0	5.5	0
98j	8.10	-122	0	0	0	0	0	2.9	0	11.4
98k	8.20	-121	0	0	0	0	0	0	0	11.8
98l#	9.37	14	0	0	0	0	0	**49.2**	0	0

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Verapamil (**98**) - **Biomimetic transformation**



98
tR: 6.09
m/z: 455 (HPLC-MS)
m/z: (HRMS)

98f
tR: 6.47
m/z: 208 (HPLC-MS)
m/z: (HRMS)

98g
tR:
m/z: 560 (HPLC-MS)
m/z: (HRMS)

98h
tR:
m/z: 646 (HPLC-MS)
m/z: (HRMS)

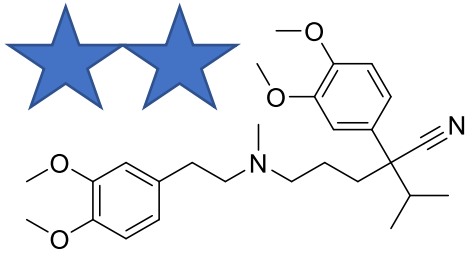
98i
tR:
m/z: - (HPLC-MS)
m/z: (HRMS)

98j
tR:
m/z: 333 (HPLC-MS)
m/z: (HRMS)

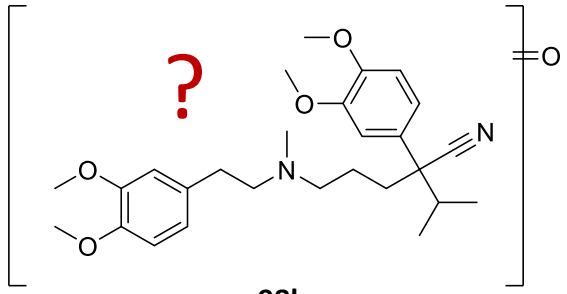
			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	85.3	100	68.1	74.5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
98a*	5.01	-164	0	0	0	0	**14.1**	**4.2**	**2.5**	**5.8**
98b	5.64	NI	0	0	0	0	0	0	7.9	0
98c	5.72	-180	0	0	0	0	0	0	0	11.3
98d*#	5.99	-14	0	0	0	0	**21.9**	**22.6**	**16.8**	**17.4**
98e	6.15	16	0	0	0	0	0	6.5	0	6.4
98f	6.47	-247	0	0	0	0	25.1	6.4	0	0
98g	6.70	105	0	0	0	0	12.3	4.3	0	0
98h	6.79	191	0	0	0	0	8.4	0	0	0
98i	7.29	NI	0	0	0	0	0	0	5.5	0
98j	8.10	-122	0	0	0	0	0	2.9	0	11.4
98k	8.20	-121	0	0	0	0	0	0	0	11.8
98l#	9.37	14	0	0	0	0	0	**49.2**	0	0

***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Verapamil (**98**) - **Biomimetic transformation**



98
tR: 6.09
m/z: 455 (HPLC-MS)
m/z: (HRMS)



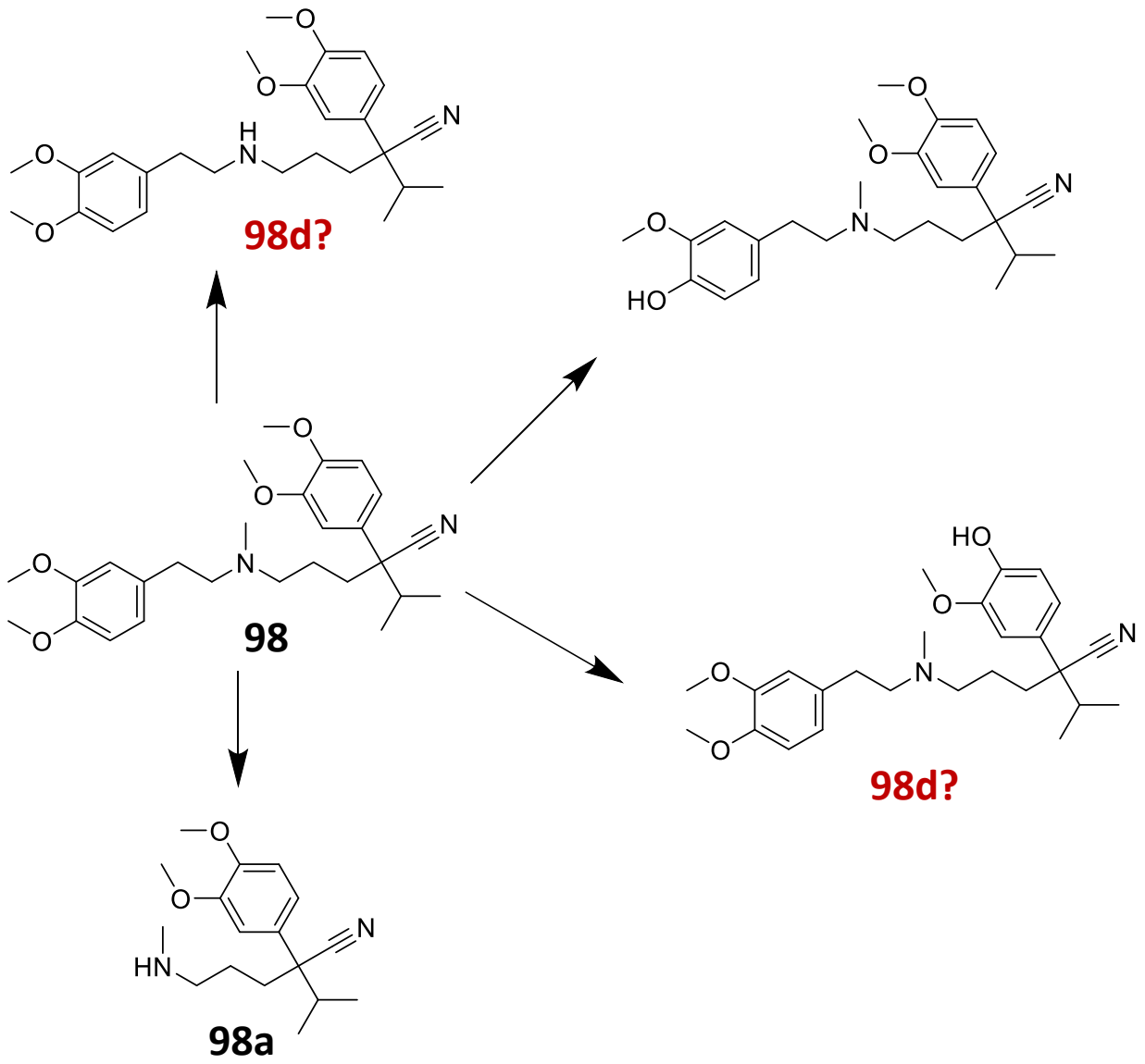
98l
tR: 9.37
m/z: 469 (HPLC-MS)
m/z: 469.2709 és Na addukt is látszik(HRMS)
deltam: 0.0007
ppm: 1.5

98k
tR:
m/z: 334 (HPLC-MS)
m/z: (HRMS)

			Non Biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	85.3	100	68.1	74.5
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
98a*	5.01	-164	0	0	0	0	**14.1**	**4.2**	**2.5**	**5.8**
98b	5.64	NI	0	0	0	0	0	0	7.9	0
98c	5.72	-180	0	0	0	0	0	0	0	11.3
98d*#	5.99	-14	0	0	0	0	**21.9**	**22.6**	**16.8**	**17.4**
98e	6.15	16	0	0	0	0	0	6.5	0	6.4
98f	6.47	-247	0	0	0	0	25.1	6.4	0	0
98g	6.70	105	0	0	0	0	12.3	4.3	0	0
98h	6.79	191	0	0	0	0	8.4	0	0	0
98i	7.29	NI	0	0	0	0	0	0	5.5	0
98j	8.10	-122	0	0	0	0	0	2.9	0	11.4
98k	8.20	-121	0	0	0	0	0	0	0	11.8
98l#	9.37	14	0	0	0	0	0	**49.2**	0	0

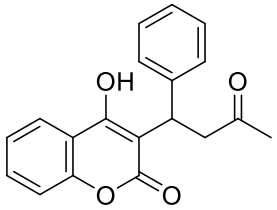
***in vivo/in vitro metabolite formed by biotransformation**
#Major biomimetic metabolite
NI: Non-ionizable in positive mode of ESI

Verapamil (**98**) - **in vitro/ in vivo biotransformation**



https://link.springer.com/article/10.1007/BF00169164

Warfarin (**99**) - **Biomimetic transformation**



99
tR: 9.24
m/z: 309 (HPLC-MS)
m/z: (HRMS)

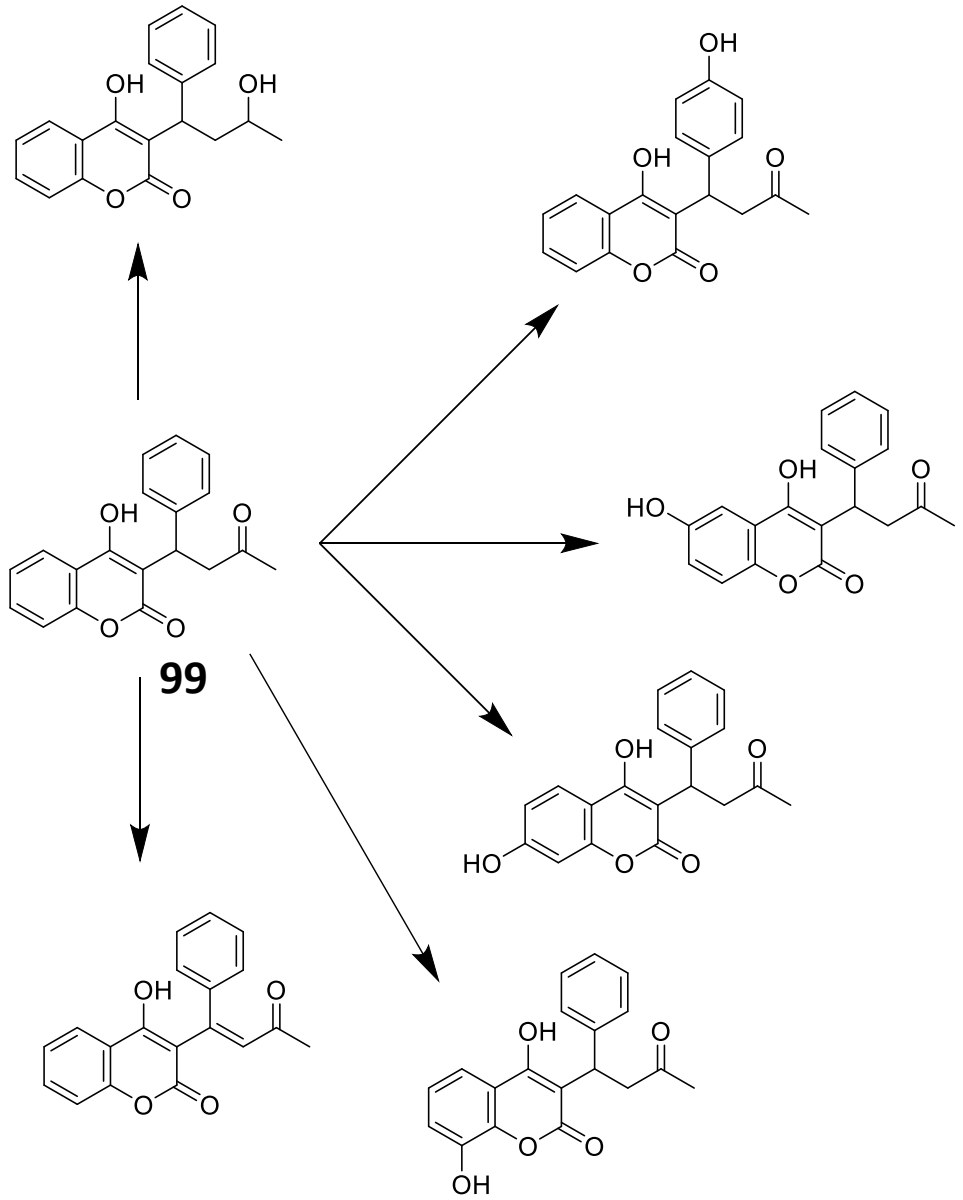
99a
tR: 8.37
m/z: 279 (HPLC-MS)
m/z: 279.0586(HRMS)

99b
tR: 11.07
m/z: 414 (HPLC-MS)
m/z: 414.4296(HRMS)

			Non biomimetic				Biomimetic			
Conversion (%)			0	0	0	0	68.8	100	0	0
	Retention time (min)	Δm	pH 2.7	pH 4.5	pH 6.5	pH 7.4	pH 2.7	pH 4.5	pH 6.5	pH 7.4
			🔴	🟡	🟣	🔵	🔴	🟡	🟣	🔵
99a	8.37	-30	0	0	0	0	0	24.5	0	0
99b#	11.05	105	0	0	0	0	**66.2**	**56.2**	0	0

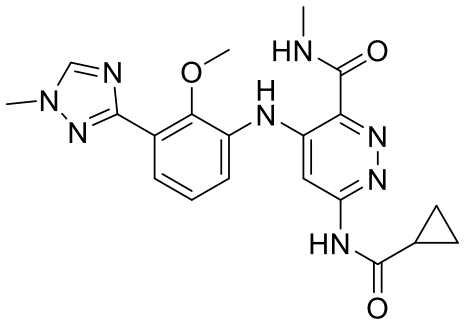
#Major biomimetic metabolite

Warfarin (**99**) - **in vitro/ in vivo biotransformation**



https://link.springer.com/article/10.2165/00003088-200544120-00003

Deucravacitinib (**100**) - **Biomimetic transformation**



100

NO biomimetic transformation

Deucravacitinib (**100**) - **in vitro/ in vivo biotransformation**

No data