# **Supporting Information**

# Synthesis of fused tetrahydropyrido[2,3-c]coumarin derivatives as potential inhibitors for dopamine d3 receptors, catalyzed by hydrated ferric sulfate

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## **Experimental General**

Melting points were recorded on a Büchi melting point apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer 281 IR spectrophotometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Varian 400 spectrometer by using TMS as internal reference; chemical shifts ( $\delta$  scale) are reported in parts per million (ppm). Elemental analyses were carried out using Perkin-Elmer 2400 Series II CHNS/O analyzer at the Department of Chemistry, Indian Institute of Technology Guwahati. Column chromatographic separations were performed using Merck silica gel (60-120 mesh).

## **Crystallographic Description**

Crystal data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated MoK $\alpha$  radiation ( $\lambda = 0.71073$  Å) at 296 K. Cell parameters were retrieved using SMART software and refined with SAINT on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS. The structure was solved by direct methods implemented in SHELX-97 program and refined by full-matrix least-squares methods on F2. All non-hydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. Compound **4c** empirical formula C<sub>21</sub>H<sub>18</sub>ClNO<sub>3</sub>, colorless crystal, formula wt 367.81, Triclinic, P-1, a = 9.4104(10) Å, b = 9.6627(9) Å, c = 10.6311(10) Å, V = 866.08(15) Å<sup>3</sup>, Z = 2, F (0 0 0) = 384, GOF(S) = 1.004. Final indices R<sub>obs</sub> = 0.0384, wR<sub>obs</sub> = 0.0815 with I > 2r(I); R<sub>all</sub> = 0.0504, wR<sub>all</sub> = 0.0865 for all data. Compound **5o** empirical formula C<sub>18</sub>H<sub>15</sub>NO<sub>4</sub>, colorless crystal, formula wt 309.31, Monoclinic, P 21/c, a = 11.8099(5) Å, b = 9.7399(5) Å, c = 12.7370(6) Å, V = 1461.83(12) Å<sup>3</sup>, Z = 4, F (0 0 0) = 648, GOF(S) = 1.031. Final indices R<sub>obs</sub> = 0.0503, wR<sub>obs</sub> = 0.1131 with I > 2r(I); R<sub>all</sub> = 0.0920, wR<sub>all</sub> = 0.1292 for all data.

	Compound 4c (trans	Compound 50 (cis CCDC
	CCDC811857)	838311)
Identification code	Cl-AC-DHP	Fur-AC-DHP
Empirical formula	$C_{21}H_{18}CINO_3$	$C_{18}H_{15}NO_{4}$
Formula weight	367.81	309.31
Temperature	296(2) K	296(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	Triclinic	Monoclinic
Space group	P-1	'P 21/c'
Unit cell dimensions		
a	9.4104(10) Å	11.8099(5) Å
b	9.6627(9) Å	9.7399(5) Å

Table S1. Crystal data and structure refinement for **4c** and **5o**. For atomic coordinates and equivalent isotropic displacement parameters and bond angles, please check the CIF.

с	10.6311(10) Å	12.7370(6) Å
α	78.191(5)	90.00°
β	66.629(6)°	93.828°(2)
γ	89.263(5)°	90.00°
Volume	866.08(15) Å <sup>3</sup>	1461.83(12) Å <sup>3</sup>
Ζ	2	4
Density (calculated)	$1.410 \text{ g/cm}^3$	$1.405 \text{ g/cm}^3$
Absorption coefficient	0.242 mm <sup>-1</sup>	0.100 mm <sup>-1</sup>
F(000)	384	648
Theta range for data collection	2.14 to 28.34°	1.73 to 34.04°
Index ranges	-11 <=h<=11, -11<=k<=12, - 12<=l<=14	-18<=h<=18, -13<=k<=13, -18<=l<=19
Reflections collected	6806	22111
Independent reflections	$4322 R_{int} = 0.0415$	$5974 R_{int} = 0.0273$
Completeness to θ°	98.4% ( $\theta = 28.34^{\circ}$ )	97.8% ( $\theta = 34.04^{\circ}$ )
Refinement method	Full-matrix least-squares on F2	Full-matrix least-squares on F2
Data / restraints / parameters	4322 / 0 / 240	5448 / 0 / 212
Goodness-of-fit on F2	1.004	1.031
Final R indices [>2sigma(I)]	$R_{obs} = 0.0384, wR_{obs} = 0.0815$	$R_{obs} = 0.0503, WR_{obs} = 0.1131$
R indices (all data)	$R_{all} = 0.0504, wR_{all} = 0.0865$	$R_{all} = 0.0920, wR_{all} = 0.1292$
Largest diff. peak and hole	0.216 and -0.210e.Å <sup>-3</sup>	0.173 and -0.210e.Å <sup>-3</sup>

Table SI2. Docking analysis of the synthesized compounds on chain A of human dopamine D3 receptor
(PDB Id: 3PBL)

Product	Score	Substituents, n	Conformations in the largest cluster [out of 100]	H-bond interactions	Pi interactions	Hydrophobic contact residues
5r	-10.56	$Me(C_{4'}), NO_2(C_{10}), n=2$	100	S192	F345	V86
5g	-10.46	OMe( $C_{4^{\circ}}$ ), OMe( $C_{3^{\circ}}$ ), H( $C_{10}$ ), n=2	100	-	F345	V86, L89, V111, I183
5d	-9.94	Br(C <sub>4'</sub> ), H( C <sub>10</sub> ), n=2	100	-	F345	V86, V111, I183
5c	-9.73	Cl(C <sub>4'</sub> ), H( C <sub>10</sub> ), n=2	100	-	F345	V86, V111, I183
5b	-9.6	$Me(C_{1'}), H(C_{10}), n=2$	100	-	F345	V86, V111, I183
5f	-9.54	OMe( $C_{4^{\circ}}$ ), H( $C_{10}$ ), n=2	100	-	F345	V86, L89, V111, I183
5m	-9.51	Br ( $C_{4'}$ ), H( $C_{10}$ ), n=1	100	-	F345	V86, V111
51	-9.28	Cl (C <sub>4</sub> <sup>,</sup> ), H( C <sub>10</sub> ), n=1	100	-	F345	V86, V111, F345
4f	-9.26	OMe( $C_{4^{\prime}}$ ), H( $C_{10}$ ), n=2	100	Y365	-	V86, L89, F106, V107, T369
5p	-9.24	$Cl(C_{4^{\circ}}), Br(C_{10}), n=2$	100	-	F345	V107, I183, F345
<b>5</b> a	-9.11	$H(C_{4^{\cdot}}), H(C_{10}), n=2$	100	-	F345	V86, L89, V111, I183
5e	-9.10	$F(C_{4'}), H(C_{10}), n=2$	100	-	F345	V86, V111, I183
5n	-9.09	$MeO(C_{4'}), H(C_{10}), n=1$	100	-	F345	V86, V111, I183
5k	-8.92	$H(C_{4'}), H(C_{10}), n=1$	100	-	F345	V111, C114, F346
<b>5</b> s	-8.80	Cl, (C <sub>4</sub> ·), MeO ( C <sub>10</sub> ), n=2	100	-	F345	V86, V107, I183, F345
50	-8.39	Furfuryl (C <sub>4</sub> ), H( C <sub>10</sub> ), n=1	100	I183	-	V111, C114, S196
5h	-8.36	Furfuryl( $C_4$ ), H( $C_{10}$ ), n=2	100	-	F345	I183
5q	-8.11	Furfuryl(C <sub>4</sub> ), Br ( C <sub>10</sub> ), n=2	100	-	F345	V107, I183
4g	-8.10	OMe( $C_{4^{\circ}}$ ), OMe( $C_{3^{\circ}}$ ), H( $C_{10}$ ), n=2	100	D110	F345	I183, F345, H349, T369
4s	-8.01	Cl, $(C_{4'})$ , MeO ( $C_{10}$ ), n=2	100	Y365	-	V86, L89, F106, V107, T369
4d	-7.99	$Br(C_{4'}), H(C_{10}), n=2$	100	Y365	-	V86, L89, F106, V107, T369

40	7.08	Furfuryl ( $C_4$ ), H( $C_{10}$ ),	100	V365		V86, L89, F106,
	-7.90	n=1	100	1303	-	V107, T369
412	-7.94	$H(C_n)$ $H(C_n)$ n=1	100	D110	F345	I183, F345,
ТК	-7.94	$\Pi(C_4), \Pi(C_{10}), \Pi^{-1}$	100	DIIO	1 545	H349
4h	-7.91	Furfuryl( $C_4$ ), H( $C_{10}$ ),	100	¥365	F345	S182, F345,
	-7.91	n=2	100	1505	1010	T369, F345
4b	-7 89	$Me(C_{42}) H(C_{10}) n=2$	100	¥365	_	V86, L89, F106,
			100			V107, T369
4c	-7.86	$Cl(C_{4'})$ , H( $C_{10}$ ), n=2	100	Y365	-	V86, L89, F106,
			100			V107, T369
						S182, W342,
41	-7.64	$Cl(C_{4'}), H(C_{10}), n=1$	100	D110	F345	F345, T369,
						F345
4p	-7.32	$Cl(C_{4'}), Br(C_{10}), n=2$	100	Y365	-	V86, T369
4a	-7 30	Furfuryl( $C_4$ ), Br ( $C_{10}$ ),	100	D110	F345	I183 F345
тч	7.50	n=2	100	DIII	1010	1105, 1515
4m	-7.28	Br (C <sub>4</sub> <sup>,</sup> ), H( C <sub>10</sub> ), n=1	100	D110	F345	L89, F345
40	-7.27	$Cl(C_{4^{\prime}}), H(C_{10}), n=2$	100	V365	_	V86, L89, F106,
70	1.21		100	1505		V107, T369
46	-7.12	$F(C_{12})$ $H(C_{10})$ n=2	100	¥365	_	V86, L89, F106,
	7.12	1 (04), 11(010), 11 2	100	1000		V107, T369
4a	-7.04	$H(C_{42}) H(C_{10}) n=2$	72	D110	F345	S182, F345,
	,	m(04), m(010), m =	, <u> </u>	2110	10.0	H349, T369
						L89, S182,
4r	-6.95	$Me(C_{4'}), NO_2(C_{10}), n=2$	100	D110	F345	W342, F345,
						T369
4n	-6.40	MeO(C <sub>4'</sub> ), $H(C_{10})$ , n=1	85	D110	F345	L89, F345
ETQ*	-8.207	compute_AutoDock41_score.py				

# <sup>1</sup>HNMR Spectra of Compound( 4a)



# <sup>13</sup> CNMR of Compound (4a)



# <sup>1</sup>HNMR Spectra of Compound( 5a)



## <sup>13</sup> CNMR of Compound (5a)



## HRMS of Compound (a)



## <sup>1</sup>HNMR Spectra of Compound(4b)



## 13 CNMR of Compound (4b)



## <sup>1</sup>HNMR Spectra of Compound( 5b)



## 13 CNMR of Compound (5b)



## HRMS of Compound (b)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (c)

## <sup>1</sup>HNMR Spectra of Compound( 4c)



#### 13 CNMR of Compound (4c)



## <sup>1</sup>HNMR Spectra of Compound( 5c)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (d)

## <sup>1</sup>HNMR Spectra of Compound( 4d)



## 13 CNMR of Compound (4d)



## <sup>1</sup>HNMR Spectra of Compound( 5d)



<sup>13</sup>CNMR of Compound (5d)



## HRMS of Compound (d)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (e)

## <sup>1</sup>HNMR Spectra of Compound (4e)



## <sup>13</sup>CNMR of Compound (4e)



## <sup>1</sup>HNMR Spectra of Compound( 5e)



## HRMS of Compound (e)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (f)

## <sup>1</sup>HNMR Spectra of Compound (4f)



## <sup>13</sup>CNMR of Compound (4f)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (g)

## <sup>1</sup>HNMR Spectra of Compound( 4g)



## <sup>13</sup>CNMR of Compound (4g)




Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (h)

#### <sup>1</sup>HNMR Spectra of Compound(4h)



## <sup>13</sup>CNMR of Compound (4h)



### HRMS of Compound (h)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (i)

### <sup>1</sup>HNMR Spectra of Compound( 4i)



## <sup>13</sup>CNMR of Compound (4i)



### <sup>1</sup>HNMR Spectra of Compound( 5i)



## HRMS of Compound (i)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (j)

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<sup>1</sup>HNMR Spectra of Compound( 4j)



## HRMS of Compound (j)





**Expansion** <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (k)

### <sup>1</sup>HNMR Spectra of Compound( 4k)



## <sup>13</sup>CNMR of Compound (4k)



### <sup>1</sup>HNMR Spectra of Compound( 5k)



# <sup>13</sup>CNMR of Compound (5k)



### <sup>1</sup>HNMR Spectra of Compound( 4l)



<sup>13</sup>CNMR of Compound (41)



<sup>1</sup>HNMR Spectra of Compound( 5l)



## HRMS of Compound (I)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (m)

### <sup>1</sup>HNMR Spectra of Compound(4m)



## <sup>13</sup>CNMR of Compound (4m)



### <sup>1</sup>HNMR Spectra of Compound( 5m)



<sup>13</sup>CNMR of Compound (5m)







#### <sup>1</sup>HNMR Spectra of Compound( 4n)



## <sup>13</sup>CNMR of Compound (4n)



#### <sup>1</sup>HNMR Spectra of Compound( 40)



<sup>13</sup>CNMR of Compound (40)

Ur-AC-DHF-13C   xp1 \$2pul   SAMPLE SPECIA   ate Apr-16 2011 temp n   olvent COCI3 gain   no exp spin   ile exp spin   ACQUISITION hst   sw 25125.6   pw90 alfa   np 60270   fb 13800 il   bs 10 in   dl 1.000 dp   nt 5003 hs   ct 2570   PROCESS PROCESS   TRANSNITTER Ib   tn Cl3 fn   sfrq 106.554   DISPLA tof   tof 1538.3 sp   tww \$.300 rfl   pw \$.300 rfl   tof 1536.3 sp   tof 1536.3 sp   tww \$.300 rfl   dpi 42 sc   dpi 42 sc   dpi 42 sc   dsse tb	L ot used ot used 0 used 0 used 0 used 18.600 20.000 n y ING 2.80 55536 Y -353.9 20436.7 9274.4 7764.9 -38.1 -378.8 259 4	0 NH 40 0			
156.682	152.848	71.550	60.150	38	

<sup>1</sup>HNMR Spectra of Compound( 50)



## <sup>13</sup>CNMR of Compound (50)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (p)

#### <sup>1</sup>HNMR Spectra of Compound( 4p)



## <sup>13</sup>CNMR of Compound (4p)


<sup>1</sup>HNMR Spectra of Compound (p)

ple Name ′ol	Cl_Br_AC_DHP -1	Position InjPosition	Vial 1	Instrument Name SampleType	Instrument 1 Sample	User Name IRM Calibration Status	All Ions Missed
Filename	Cl_Br_AC_DHP.d	ACQ Method		Comment		Acquired Time	8/10/2011 11:43:12 AM
							<u>.</u>
x10 1 Ba	ckground +Es	St Scan (0.250-0	0.427 min, 12 scan	s) Frag=175.0V	CI_Br_AC_DHF	P.d	
1.825-		446.0204	44	48.0185			
1.8-							
1.775-		+					
1.75-							
1,725-							
1.7-							
1.675-							
1.65							
1.625-							
1 575							
1.575							
1.525							
1.5-							1
1.475							
1.45							
1.425							
1.4 -							
1.375-							
1.35-							
1.325-							
1.3-							
1.2/5							
1 225							
1.2							
1.175							
1.15							
1.125							
1.1-							
1.075							
1.05-		,	447.0211	44	9.0199 45	0.0153 451.0153	
	445 445.	5 446 446.	5 447 447.5 Counts (%	448 448.5 ) vs. Mass-to-C	449 449.5 4 harge (m/z)	450 450.5 451 4	151.5 452
					<b>.</b> ,	5	

## <sup>1</sup>HNMR Spectra of Compound( 4q)



# <sup>13</sup>CNMR of Compound (4q)



## <sup>1</sup>HNMR Spectra of Compound( 5q)



## <sup>1</sup>HNMR Spectra of Compound( 4r)



# <sup>13</sup>CNMR of Compound (4r)

SAMPLE SPECIAL   date Jun 30 2011 temp not used   file CO13 gain not used   file CO13 gain not used   file exp spin not used   file exp spin not used   ACQUISITION bst 6.868   sw 25125.6 pw99 18.600   at 1.195 alfa 20.000   np 60276 FLAGS fb   fb 13800 11 n n   di 1.086 dp y nn   ct 3005 hs nn nn   ct 3005 hs ns 2.08   tn Ch38.3 Sp -450.6 1.99   tof 158.3 Sp -450.6 1.99   ctn ff 3271.3 9.200   pur </th <th></th> <th></th> <th>O<sub>2</sub>N</th> <th>NH 4r</th> <th>Me</th> <th></th> <th></th>			O <sub>2</sub> N	NH 4r	Me		
			77.543				
157.,755	145.046 165.046 165.051 165.161 165.161 165.161 165.161 165.161 165.161	121.034		4 4 9	36.226	23.363	
200 180 160	140	129 100		60 <sup>.</sup>	40	20	ppm

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## HRMS Spectra of Compound (r)





Expansion <sup>1</sup>HNMR spectra for determining the trans : cis ratio for Compound (s)

<sup>1</sup>HNMR Spectra of Compound( 4s)



<sup>13</sup>CNMR of Compound (4s)



## HRMS Spectra of Compound (s)

