Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Selective Recognition of Neurotransmitters in Aqueous Solution by Hydroxyphenyl Aza-Scorpiand Ligands.

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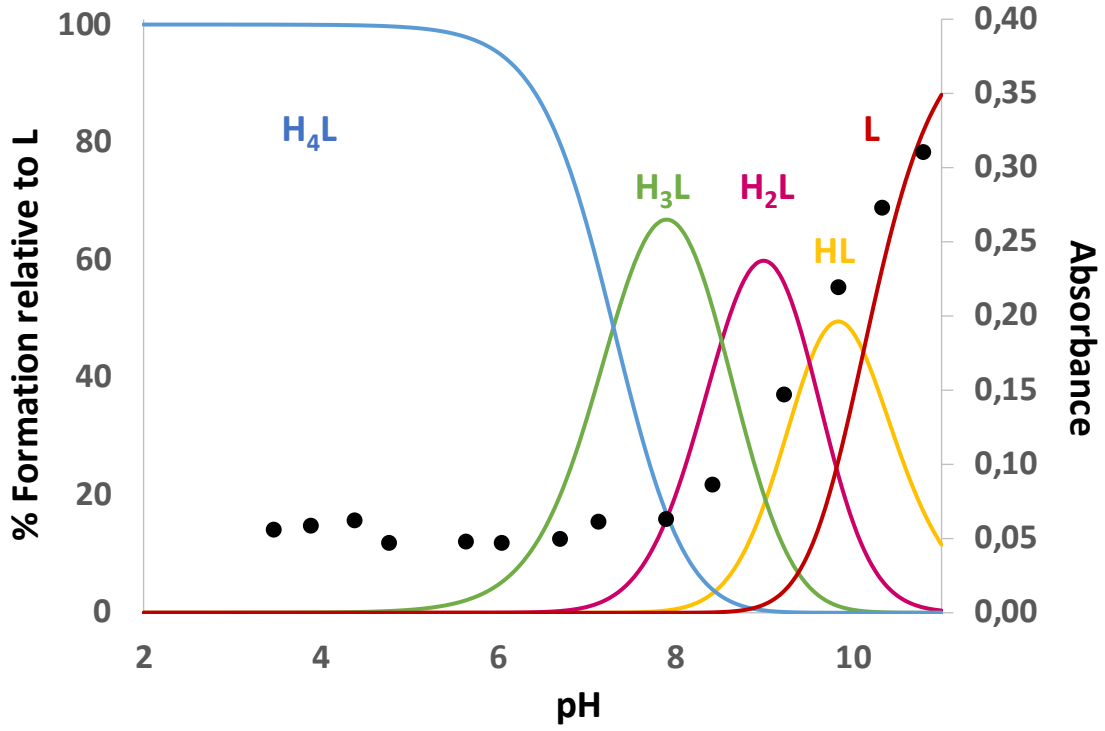

Figure S2. Distribution diagram for **L3** overlapped to UV-VIS data for 293 nm. Determined in 0.15 mol·dm^{-3} NaCl at 298.1 ± 0.1 K with [**L3**] = 10^{-4} mol·dm^{-3}

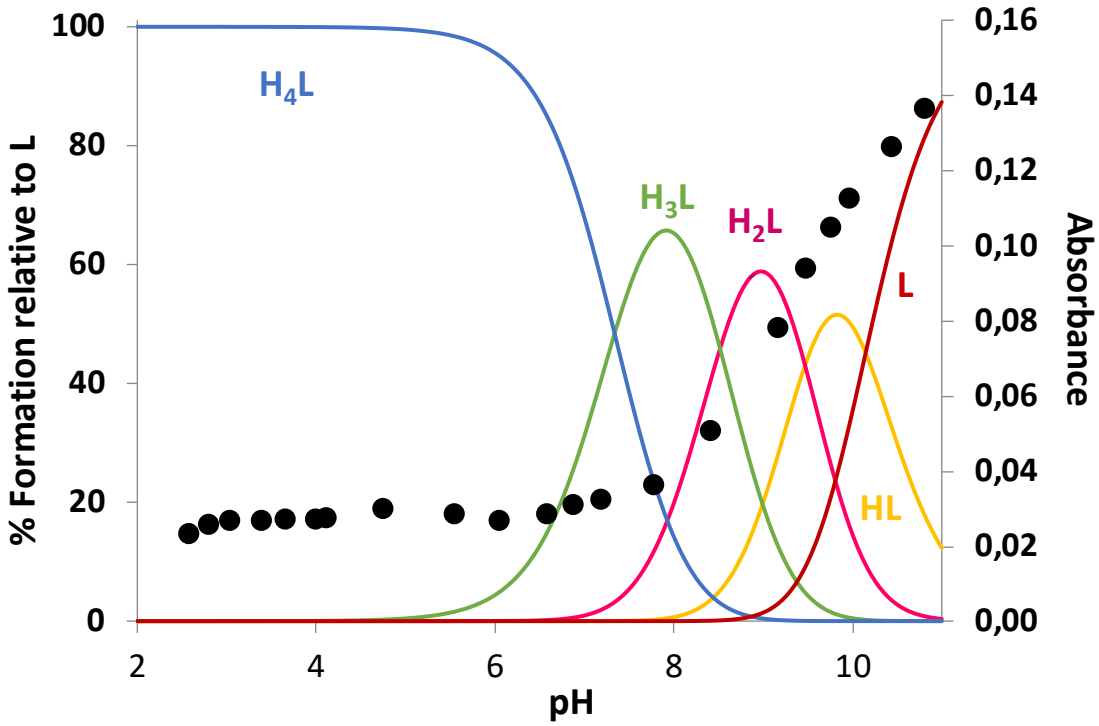

Figure S3. Variation of the ^{1}H NMR spectra of **L1** with pD.

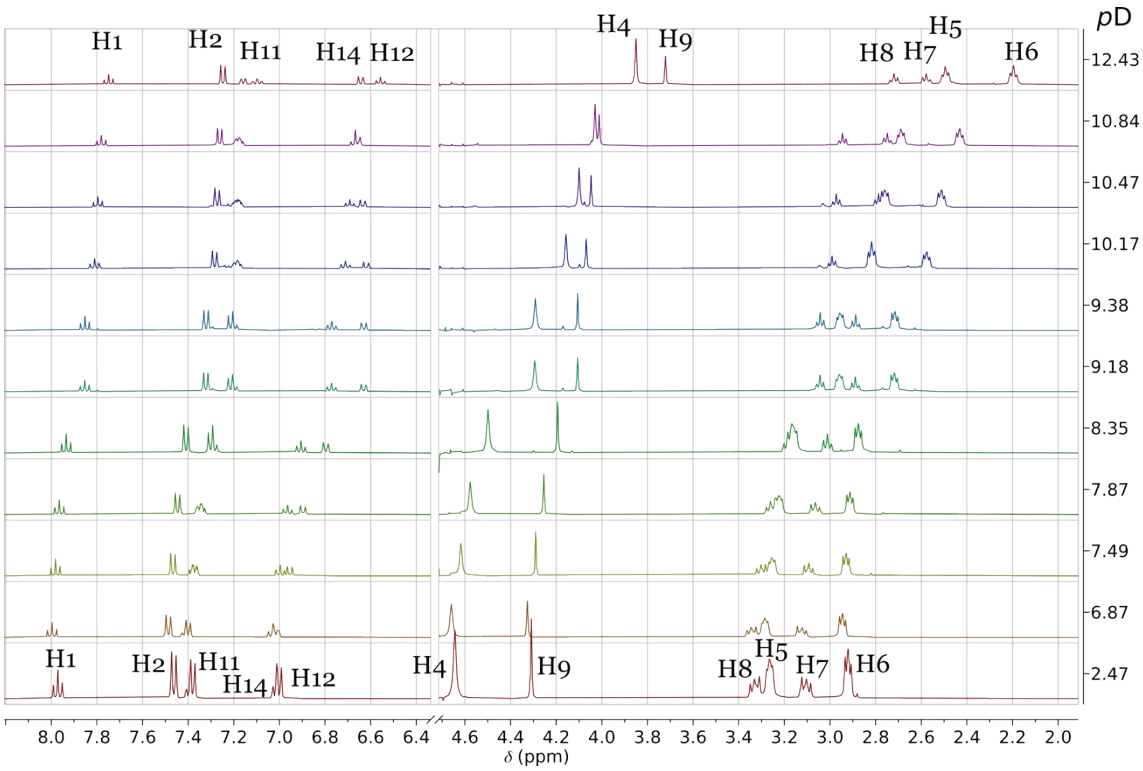

Figure S4. Variation of the ^{13}C NMR spectra of **L1** with pD.

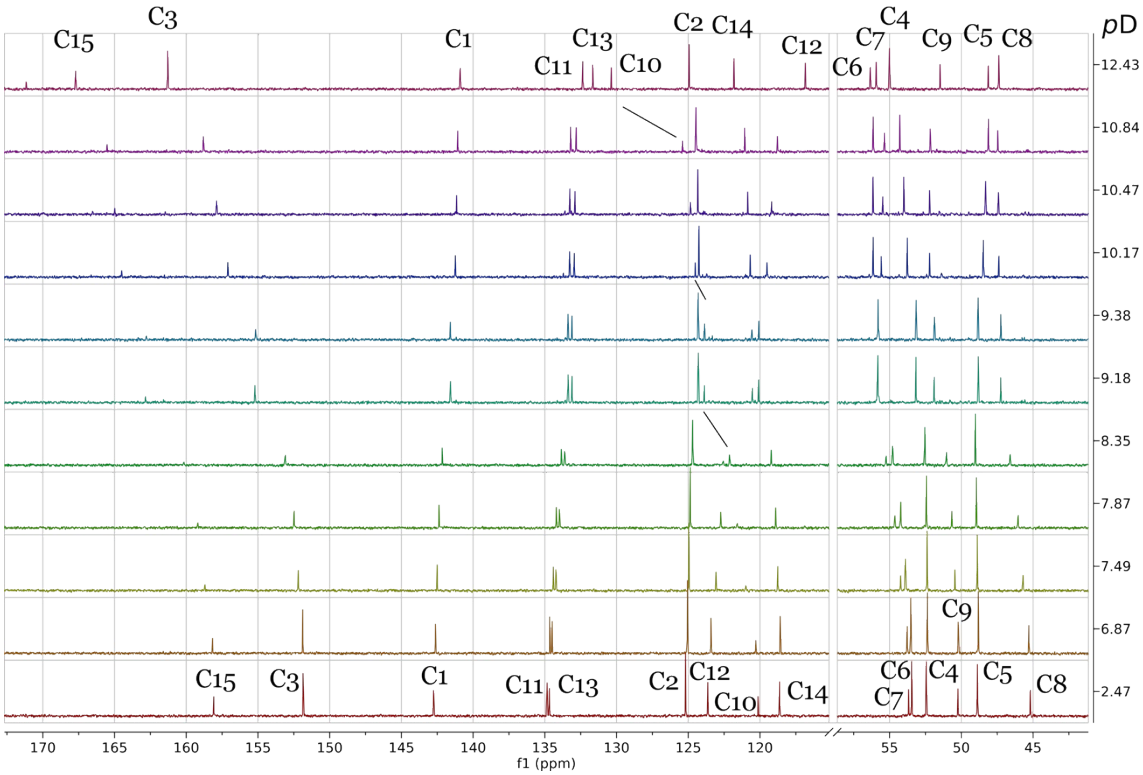

Table S1. Stepwise protonation constants for **L3** determined at 298.1 K in 0.15 mol·dm^{-3} NaCl

The analysis of different UV−Vis data sets centered on the phenolate band by HypSpec program,[i] allows to calculate a pK value of de 9.53 (2), 8.40 (3) y 7.20 (4) for **L3**. These values are in agreement with the results obtained by the potentiometric measurements.

Reaction[a]	**UV-Visible**	**EMF**
H+ L ⇌ HL	-	10.153(9)
H + HL ⇌ H_2L	9.53 (2)	9.473(9)
H + H_2L ⇌ H_3L	8.40 (3)	8.516(8)
H + H_3L ⇌ H_4L	7.20 (4)	7.341(9)

(a) Charges omitted. (b) Values in parenthesis are standard deviations in the last significant figure.

Table S2. Stepwise stability constants for the formation of dopamine complexes with **L1** – **L4** in 0.15 mol·dm^{-3} NaCl at 298.1 K

Reaction	L1	L2	L3	L4
AH + L ⇌ AHL[a]	–	–	3.39 (6)	–
HA + HL ⇌ AH_2L	3.37 (8)[b]	3.63 (6)	4.07 (4)	3.25 (5)
H_2A + L ⇌ AH_2L	–	–	3.82 (4)	–
H_2A + HL ⇌ AH_3L	3.76 (2)	3.54 (3)	3.77 (4)	3.03 (3)
H_2A + H_2L ⇌ AH_4L	4.13 (3)	3.60 (6)	4.18 (4)	3.44 (4)
H_3A + HL ⇌ AH_4L	–	–	4.10 (4)	–
H_3A + H_2L ⇌ AH_5L	3.98 (3)	3.78 (4)	3.87 (4)	3.32 (3)
H_3A + H_3L ⇌ AH_6L	4.01 (3)	3.62 (4)	3.85 (4)	3.33(3)
H_3A + H_4L ⇌ AH_7L	3.95 (7)	3.51 (5)	–	–

(a) Charges omitted. b) Values in parenthesis are standard deviations in the last significant figure.

Table S3. Stepwise stability constants for the formation of serotonin complexes with **L1** – **L5** in 0.15 mol·dm^{-3} NaCl at 298.1 K

Reaction	L1	L2	L3	L4	L5
HL + HA ⇌ H_2LA[a]	4.14 (2)[b]	3.22(3)	3.74 (2)	2.97(3)	2.89(2)
HL + H_2A ⇌ H_3LA	4.23 (1)	3.00(3)	3.57 (2)	2.73(2)	2.87(2)
H_2L + H_2A ⇌ H_4LA	4.60 (1)	2.72(4)	3.61 (2)	2.95(2)	2.77(1)
H_3L + H_2A ⇌ H_5LA	4.93 (2)	2.32(7)	3.53 (3)	3.21(2)	2.76(1)
H_4L + H_2A ⇌ H_6LA	5.11 (3)		3.48 (2)	–	–

(a) Charges omitted. b) Values in parenthesis are standard deviations in the last significant figure.

Table S4. Stepwise stability constants for the formation of tyramine complexes with **L1** – **L5** in 0.15 mol·dm^{-3} NaCl at 298.1 K

Reaction	L1	L2	L3	L4	L5
HL + A ⇌ HLA	–	–		2.93(8)	–
HL + HA ⇌ H_2LA[a]	3.13(3)[b]	3.68(2)	3.31(2)	3.18(3)	–
H_2L + HA ⇌ H_3LA	-	3.73(2)	-	-	
HL + H_2A ⇌ H_3LA	3.67(2)	-	3.61(2)	3.35(4)	–
H_2L + H_2A ⇌ H_4LA	3.49(2)	3.83(2)	3.54(2)	3.35(3)	–
H_3L + H_2A ⇌ H_5LA	3.59(3)	3.84(2)	3.50(2)	3.38(4)	–
H_4L + H_2A ⇌ H_6LA	3.64(5)	3.88(2)	3.59(3)		–

(a) Charges omitted. b) Values in parenthesis are standard deviations in the last significant figure.

Table S5. Thermodynamic data for ligands and neurotransmitters protonation and for the formation of **L1** complexes with serotonin determined at 298.1 K in 0.15 mol·dm^{-3} NaCl.

Reaction[a]	log$K$[b]	$\Delta G°$ (kJ/mol)[b]	$\Delta H°$ (kJ/mol)[c]	$T\Delta S°$ (kJ/mol)[d]
L5				
L + H ⇌ HL	10.338(9)[e]	-58.99(5)	-44.3(1)	14.7(1)
HL + H ⇌ H_2L	9.395(9)	-53.60(5)	-51.9(1)	1.7(1)
H_2L + H ⇌ H_3L	8.23(1)	-46.96(6)	-46.1(1)	0.9(1)
L4				
L + H ⇌ HL	10.006(4)	-57.09(2)	-40.4(2)	16.7(2)
HL + H ⇌ H_2L	8.746(3)	-49.90(2)	-48.4(2)	1.5(2)
H_2L + H ⇌ H_3L	7.368(4)	-42.04(2)	-46.6(2)	-4.6(2)
L3				
L + H ⇌ HL	10.153(9)	-57.93(5)	-37.6(1)	20.3(2)
HL + H ⇌ H_2L	9.473(9)	-54.05(5)	-37.5(1)	16.6(2)
H_2L + H ⇌ H_3L	8.516(8)	-48.59(5)	-43.0(1)	5.6(2)
H_3L + H ⇌ H_4L	7.341(9)	-41.89(5)	-46.1(1)	-4.2(2)
L2				
L + H ⇌ HL	10.13(2)	-57.8(1)	-36.7(1)	21.1(2)
HL + H ⇌ H_2L	9.50(1)	-54.20(6)	-36.0(1)	18.2(2)
H_2L + H ⇌ H_3L	8.52(2)	-48.6(1)	-44.5(1)	4.1(2)
H_3L + H ⇌ H_4L	7.30(2)	-41.7(1)	-45.0(1)	-3.3(2)
L1				
L + H ⇌ HL	9.93(1)	-56.66(6)	-39.02(5)	17.6(1)
HL + H ⇌ H_2L	9.11(1)	-51.98(6)	-40.6(1)	11.4(2)
H_2L + H ⇌ H_3L	7.92(1)	-45.19(6)	-43.1(1)	2.1(2)
H_3L + H ⇌ H_4L	6.76(1)	-38.57(6)	-38.5(1)	0.1(2)
Tyramine				
T + H ⇌ HT	10.399(2)	-59.33(1)	-45.9(2)	13.4(2)

$HT + H \rightleftharpoons H_2T$	9.333(2)	-52.25(1)	-33.5(2)	18.8(2)
Serotonin				
$S + H \rightleftharpoons HS$	10.765(4)	-61.42(2)	-41.6(2)	19.0(2)
$HS + H \rightleftharpoons H_2S$	9.931(3)	-56.66(2)	-44.0(2)	12.7(2)
L5 + Serotonin				
$HS + HL \rightleftharpoons HS(HL)$	2.89(2)	-16.5(1)	16.1(7)	32.6(8)
$H_2S + HL \rightleftharpoons H_2S(HL)$	2.87(2)	-16.4(1)	23.1(7)	39.5(8)
$H_2S + H_2L \rightleftharpoons H_2S(H_2L)$	2.77(1)	-15.80(6)	27.6(8)	43.4(9)
$H_2S + H_3L \rightleftharpoons H_2S(H_3L)$	2.76(1)	-15.75(6)	26.5(8)	42.3(9)
L4 + Tyramine				
$HT + L \rightleftharpoons HT(L)$	2.93(8)	-16.7(5)	20.5(4)	37.2(9)
$HT + HL \rightleftharpoons HT(HL)$	3.18(3)	-18.1(2)	18.9(4)	37.0(6)
$H_2T + HL \rightleftharpoons H_2T(HL)$	3.35(4)	-19.1(2)	15.0(4)	34.1(6)
$H_2T + H_2L \rightleftharpoons H_2T(H_2L)$	3.35(3)	-19.1(2)	16.1(4)	35.2(6)
$H_2T + H_3L \rightleftharpoons H_2T(H_3L)$	3.38(4)	-19.3(2)	15.1(4)	34.4(6)
L4 + Serotonin				
$HS + HL \rightleftharpoons HS(HL)$	2.97(3)	-16.9(2)	12.5(4)	29.4(6)
$H_2S + HL \rightleftharpoons H_2S(HL)$	2.73(2)	-15.6(1)	10.0(4)	25.6(5)
$H_2S + H_2L \rightleftharpoons H_2S(H_2L)$	2.95(2)	-16.8(1)	9.7(4)	26.5(5)
$H_2S + H_3L \rightleftharpoons H_2S(H_3L)$	3.21(2)	-18.3(1)	7.0 (4)	25.3(5)
L3 + Tyramine				
$HT + HL \rightleftharpoons HT(HL)$	3.31(2)	-18.9(1)	10.2(4)	29.1(5)
$H_2T + HL \rightleftharpoons H_2T(HL)$	3.61(2)	-20.6(1)	10.8(4)	31.4(5)
$H_2T + H_2L \rightleftharpoons H_2T(H_2L)$	3.54(2)	-20.2(1)	10.3(4)	30.5(5)
$H_2T + H_3L \rightleftharpoons H_2T(H_3L)$	3.50(2)	-20.0(1)	12.9(3)	32.9(4)
$H_2T + H_4L \rightleftharpoons H_2T(H_4L)$	3.59(3)	-20.5(2)	13.9(3)	34.4(5)
L3 + Serotonin				

$HS + HL \rightleftharpoons HS(HL)$	3.74(2)	-21.3(1)	22.0(5)	43.3(6)
$H_2S + HL \rightleftharpoons H_2S(HL)$	3.57(2)	-20.4(1)	21.1(5)	41.5(6)
$H_2S + H_2L \rightleftharpoons H_2S(H_2L)$	3.61(2)	-20.6(1)	16.3(5)	37.1(6)
$H_2S + H_3L \rightleftharpoons H_2S(H_3L)$	3.53(3)	-20.1(2)	16.1(5)	36.2(7)
$H_2S + H_4L \rightleftharpoons H_2S(H_4L)$	3.48(2)	-19.9(1)	17.2(5)	37.1(6)
L2 + Tyramine				
$HT + HL \rightleftharpoons HT(HL)$	3.68(2)	-21.0(1)	10.0(6)	31.0(7)
$HT + H_2L \rightleftharpoons HT(H_2L)$	3.73(2)	-21.3(1)	10.7(7)	32.0(8)
$H_2T + H_2L \rightleftharpoons H_2T(H_2L)$	3.83(2)	-21.9(1)	7.5(7)	29.4(8)
$H_2T + H_3L \rightleftharpoons H_2T(H_3L)$	3.84(2)	-21.9(1)	7.7(7)	29.6(8)
$H_2T + H_4L \rightleftharpoons H_2T(H_4L)$	3.88(2)	-22.1(1)	6.9 (7)	29.0(8)
L2 + Serotonin				
$HS + HL \rightleftharpoons HS(HL)$	3.22(3)	-18.4(2)	14.4(5)	32.8(7)
$H_2S + HL \rightleftharpoons H_2S(HL)$	3.00(3)	-17.1(2)	13.4(5)	30.5(7)
$H_2S + H_2L \rightleftharpoons H_2S(H_2L)$	2.72(4)	-15.5(2)	5.8(4)	21.3(6)
$H_2S + H_3L \rightleftharpoons H_2S(H_3L)$	2.32(7)	-13.2(4)	6.1(4)	19.3(6)
L1 + Tyramine				
$HT + HL \rightleftharpoons HT(HL)$	3.13(4)	-17.9(2)	16.7(5)	34.6(7)
$H_2T + HL \rightleftharpoons H_2T(HL)$	3.67(2)	-20.9(1)	15.7(4)	36.6(5)
$H_2T + H_2L \rightleftharpoons H_2T(H_2L)$	3.49(2)	-19.9(1)	19.5(5)	39.4(6)
$H_2T + H_3L \rightleftharpoons H_2T(H_3L)$	3.60(3)	-20.5(2)	19.0(4)	39.5(6)
$H_2T + H_4L \rightleftharpoons H_2T(H_4L)$	3.64(5)	-20.8(3)	17.4(5)	38.2(8)
L1 + Serotonin				
$HS + HL \rightleftharpoons HS(HL)$	4.14(2)	-23.6(1)	20.9(4)	44.5(5)
$H_2S + HL \rightleftharpoons H_2S(HL)$	4.23(1)	-24.14(6)	18.5(4)	42.6(5)
$H_2S + H_2L \rightleftharpoons H_2S(H_2L)$	4.60(2)	-26.2(1)	16.0(4)	42.2(5)
$H_2S + H_3L \rightleftharpoons H_2S(H_3L)$	4.94(2)	-28.2(1)	14.6(4)	42.8(5)

$H_2S + H_4L \rightleftharpoons H_2S(H_4L)$	5.14(3)	-29.3(2)	7.9(4)	37.2(6)

(a) Charges omitted. (b) Obtained by means of potentiometric measurements. (c) Obtained by means of ITC. (d) Obtained from $\Delta G° = \Delta H° - T\Delta S°$. (e) Values in parenthesis are standard deviations in the last significant figure.

[i] P. Gans, A. Sabatini and A. Vacca, Determination of equilibrium constants from spectrophometric data obtained from solutions of known pH: The program pHab. *Annali di Chimica*, 1999, **89**, 45-49