Supplementary Material (ESI) for New Journal of Chemistry

SUPPLEMENTARY INFORMATION FOR

Ring-chain tautomerism and protolytic quilibria of 3-hydroxy-3-phosphonoisobenzofuranone studied by ^{1}H, ^{13}C, and ^{31}P NMR-controlled titrations

Sven Augner,[a] Jan Kehler,[b] Zoltán Szakács,[a,c] Eli Breuer,[b]* and Gerhard Hägele[a*]

[a]Inorganic Chemistry and Structural Chemistry, Heinrich-Heine-University Düsseldorf. Universitätsstrasse 1, D-40225-Düsseldorf, Germany. Phone +49-211-81-13166. Fax +49-211-81-11854. Email: haegele@uni-duesseldorf.de

[b]Department of Medicinal Chemistry and Natural Products, School of Pharmacy, The Hebrew University of Jerusalem, P.O.B. 12065, Jerusalem 91120, Israel. Phone +972-2-675-8704, Fax +972-2-675-8934. Email: eli.breuer@huji.ac.il

[c]Laboratory for Speciation, Drug and Trace Analysis, Institute of Chemistry, Eötvös Loránd University, Pázmány Péter sétány 1/A, H-1117 Budapest, Hungary. Email: szakacsz@chem.elte.hu

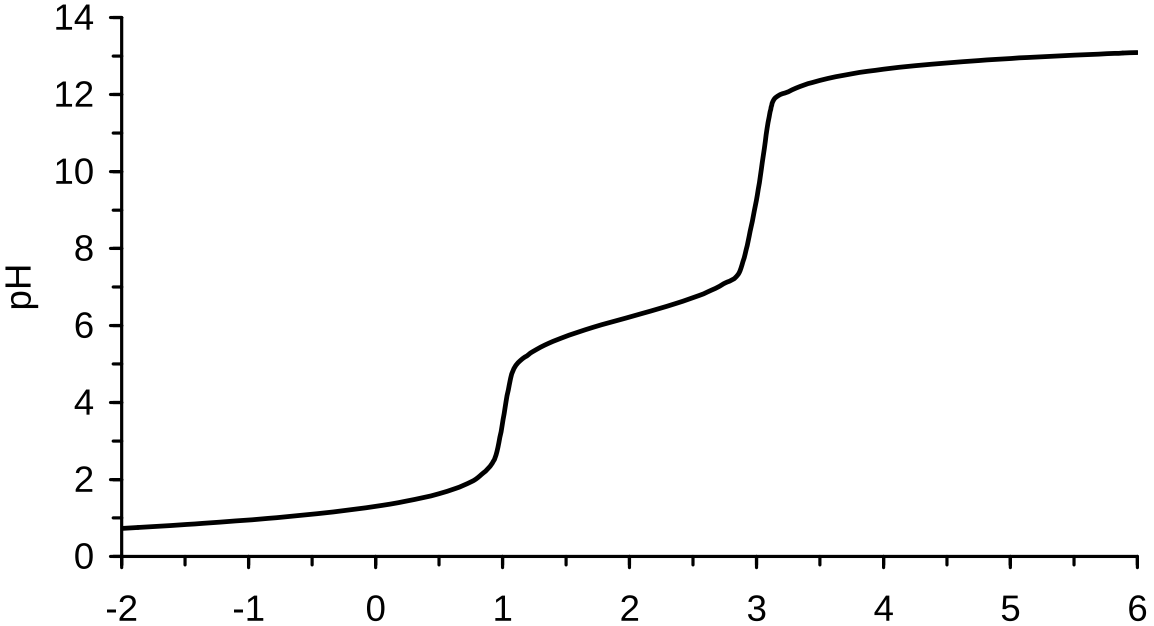

Fig. S1. Potentiometric pH,τ-titration curve of 3-hydroxy-3-phosphonoisobenzofuranone **6** with TMAOH at 1 M ionic strength (TMACl)

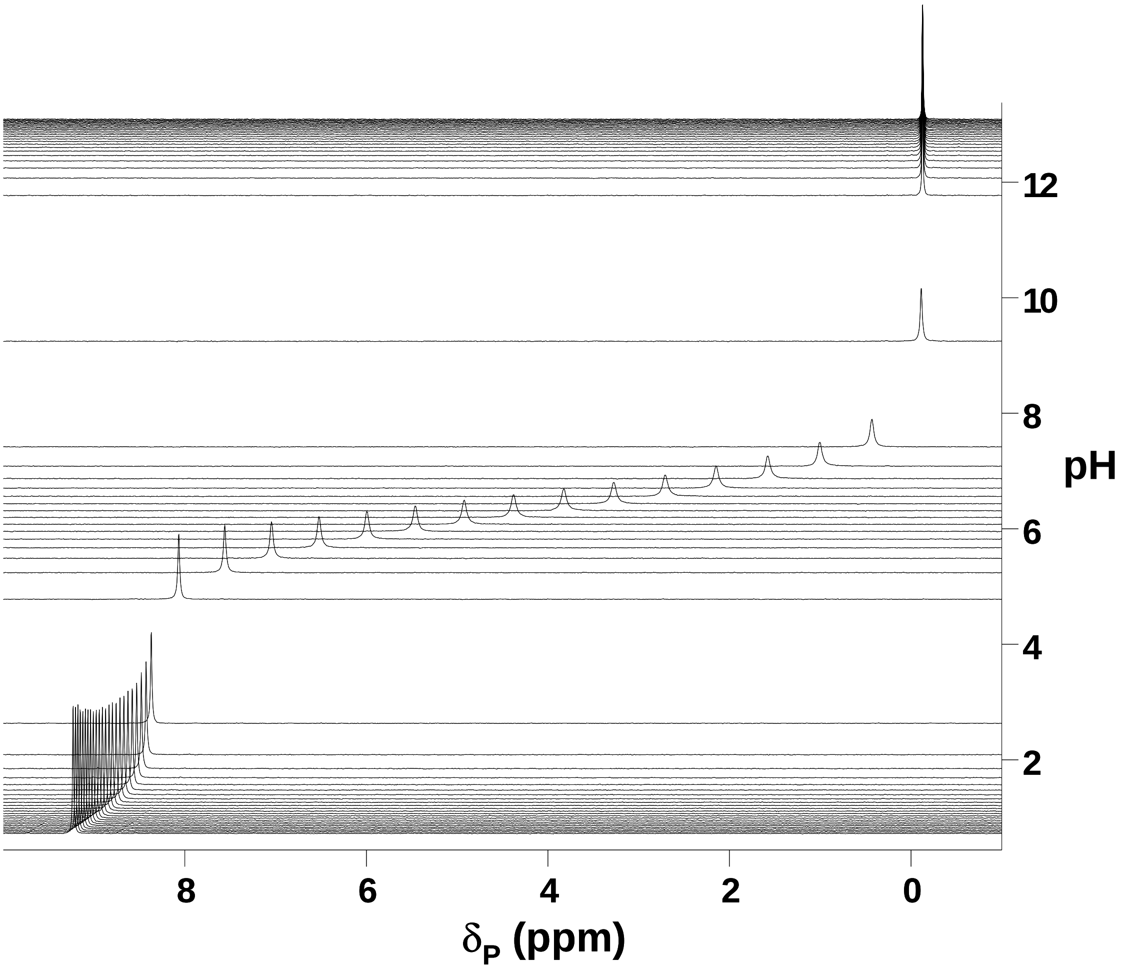

Fig. S2. 202 MHz $^{31}P\{^{1}H\}$ NMR-controlled titration of **6** with 1 M TMAOH. Stacked pH,δ-plot

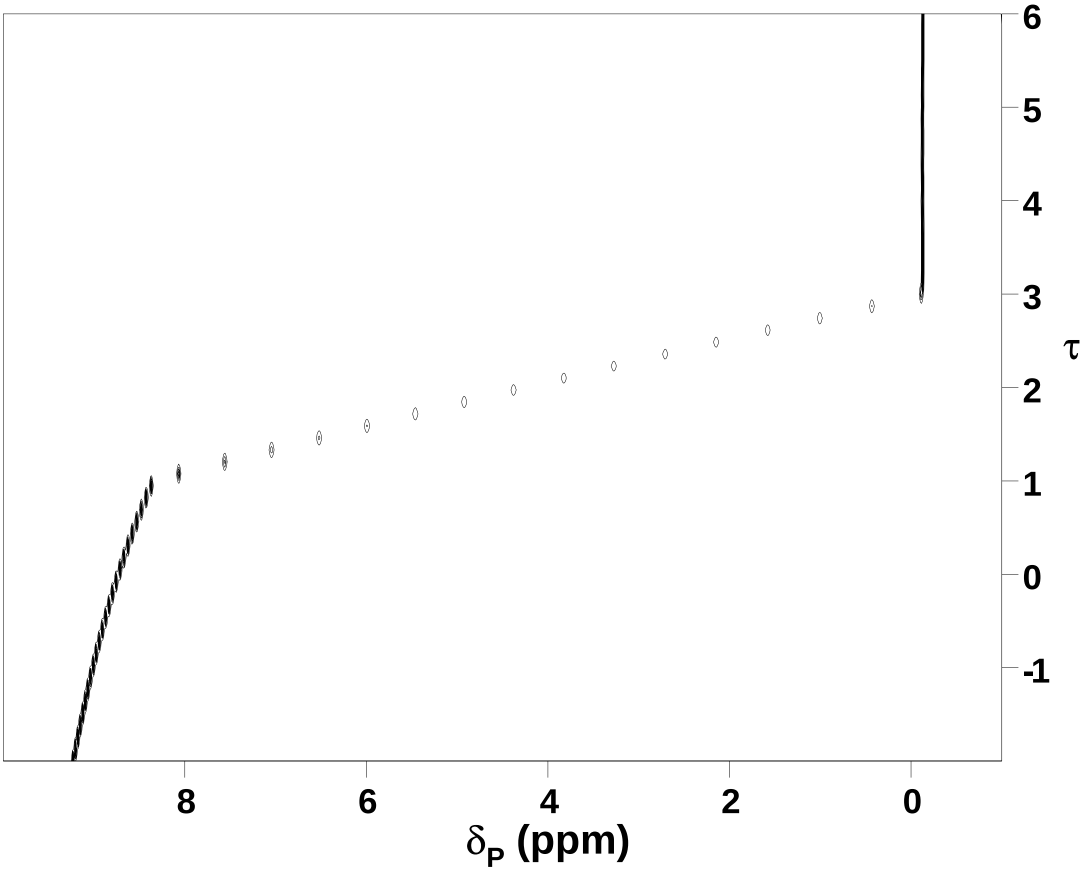

Fig. S3. 202 MHz $^{31}P\{^1H\}$ NMR-controlled titration of **6** with 1 M TMAOH. Contour τ,δ-plot

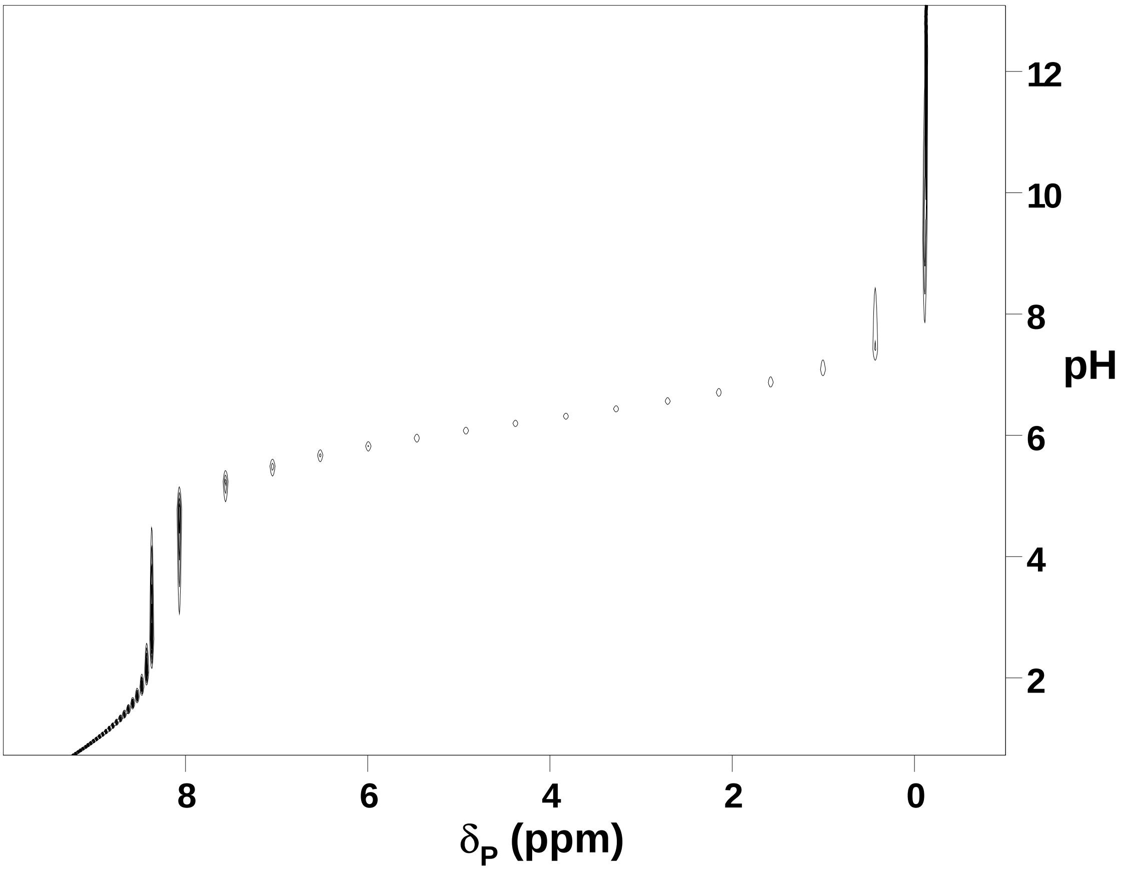

Fig. S4. 202 MHz $^{31}P\{^{1}H\}$ NMR-controlled titration of **6** with 1 M TMAOH. Contour pH,δ-plot.

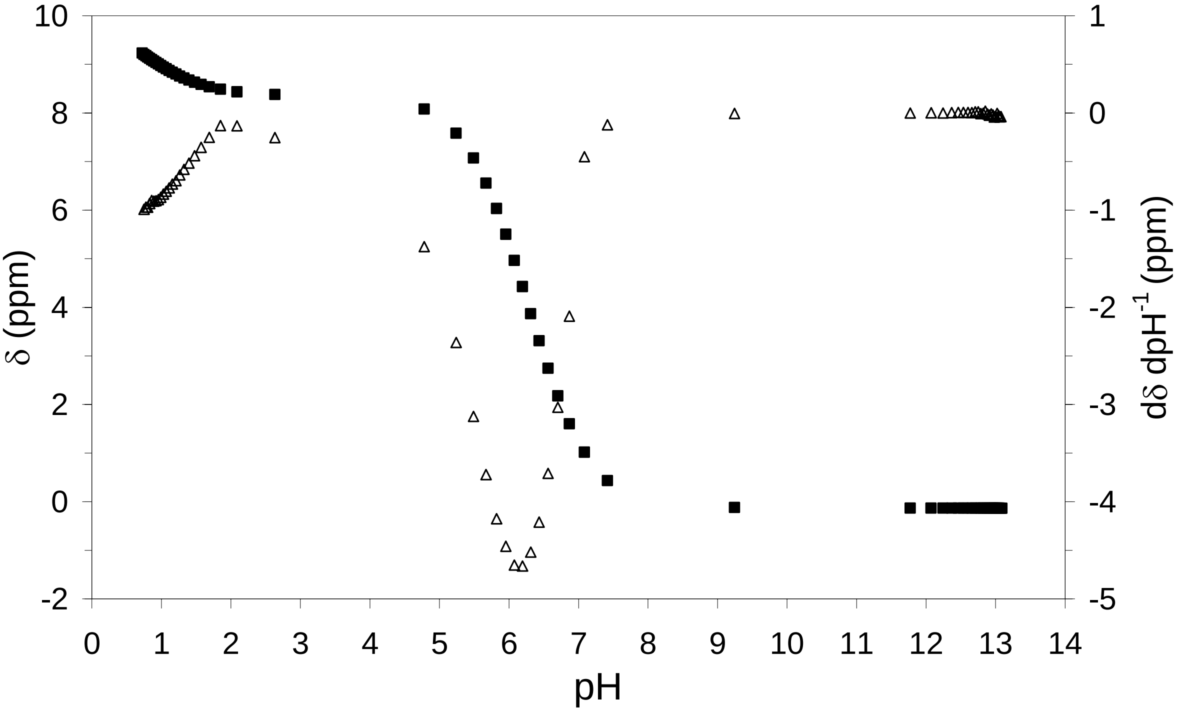

Fig. S5. δ_P (square) and $d\delta_P$ dpH^{-1} (triangle) vs. pH from the 202 MHz ^{31}P{^{1}H} NMR titration of **6**.

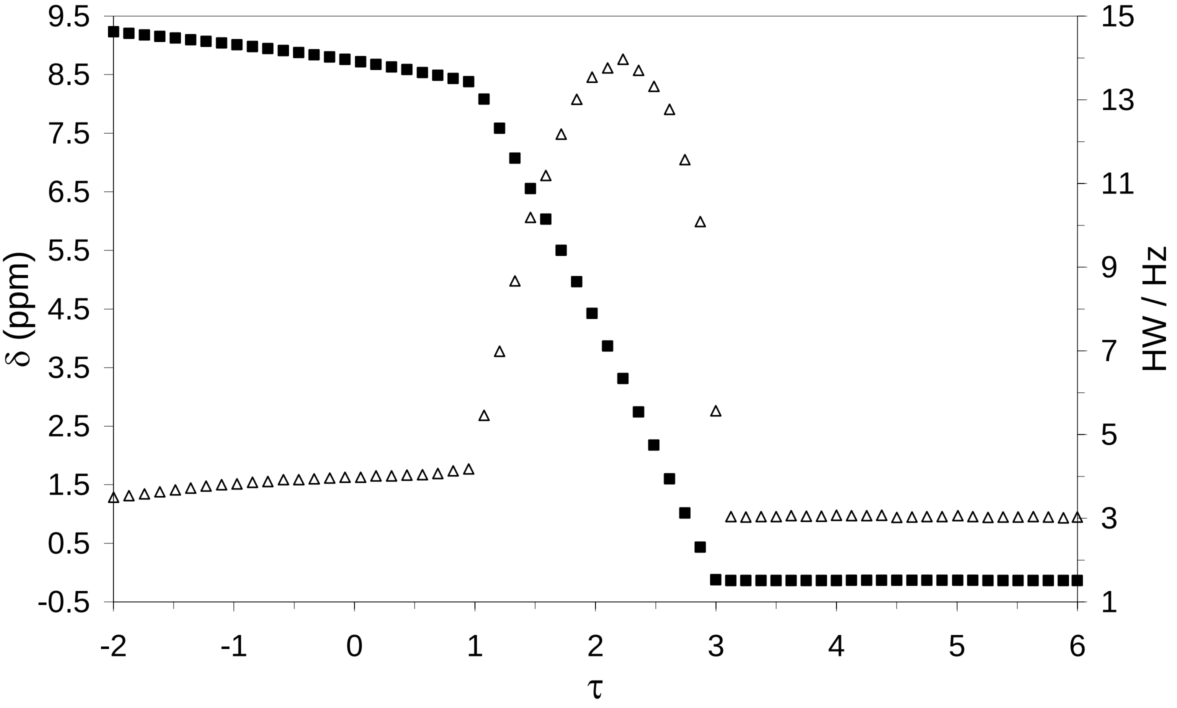

Fig. S6. δ_P (square) and ^{31}P spectral half-width HW (triangle) vs. degree of titration τ from the 202 MHz ^{31}P{^{1}H} NMR titration of **6**

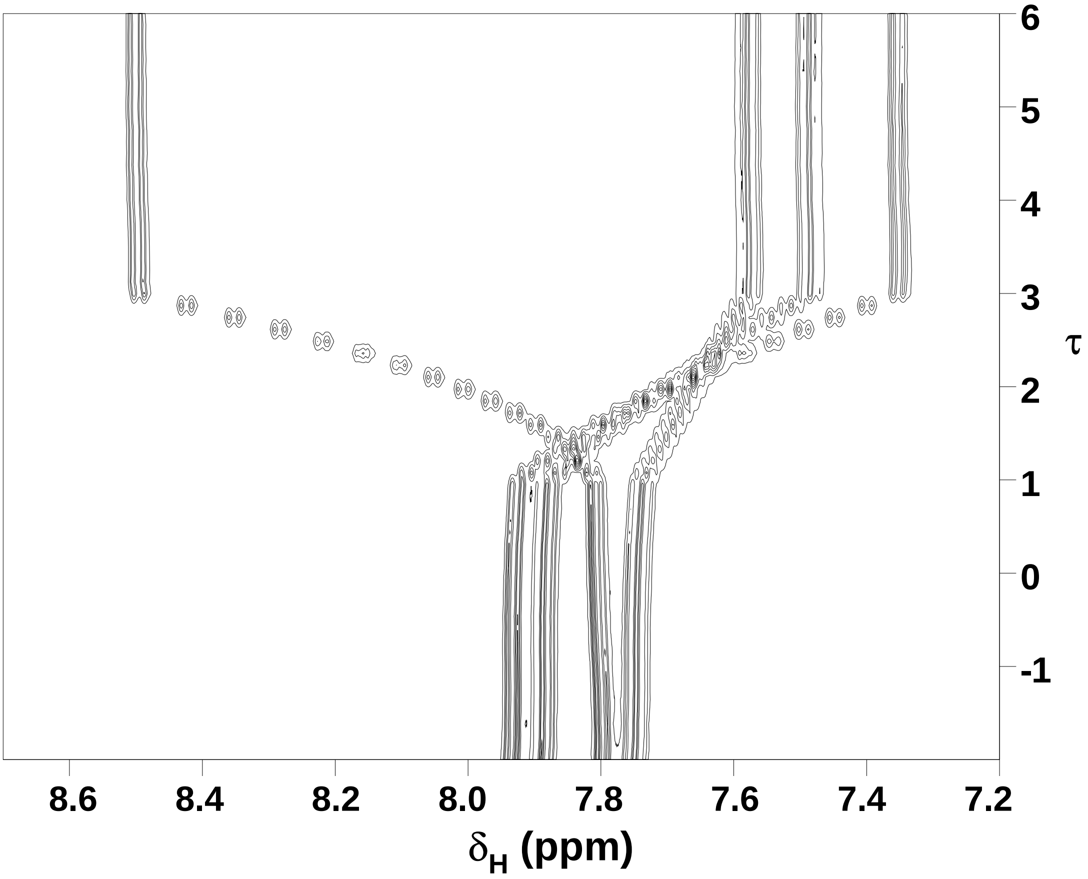

Fig. S7. 500 MHz ^{1}H NMR-controlled titration of **6** with 1 M TMAOH. Contour τ,δ-plot

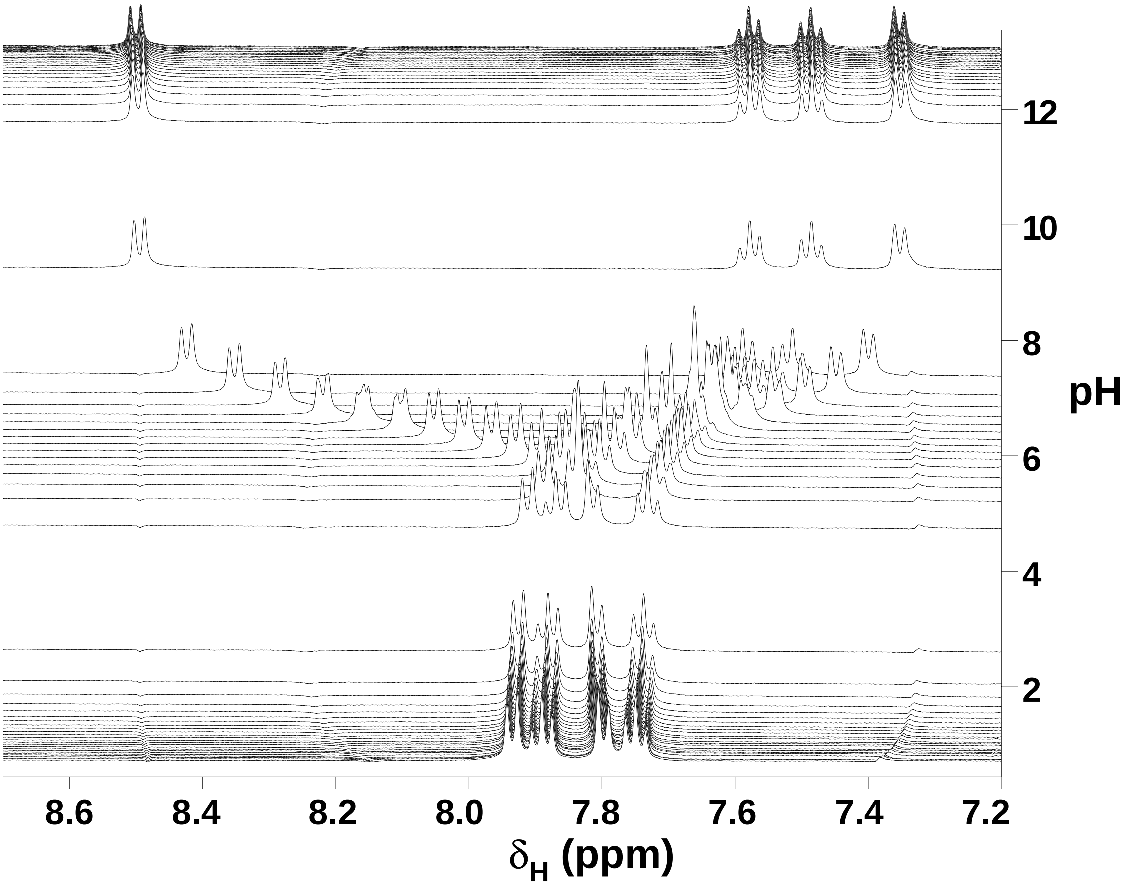

Fig. S8. 500 MHz ^{1}H NMR-controlled titration of **6** with 1 M TMAOH. Stacked pH,δ-plot

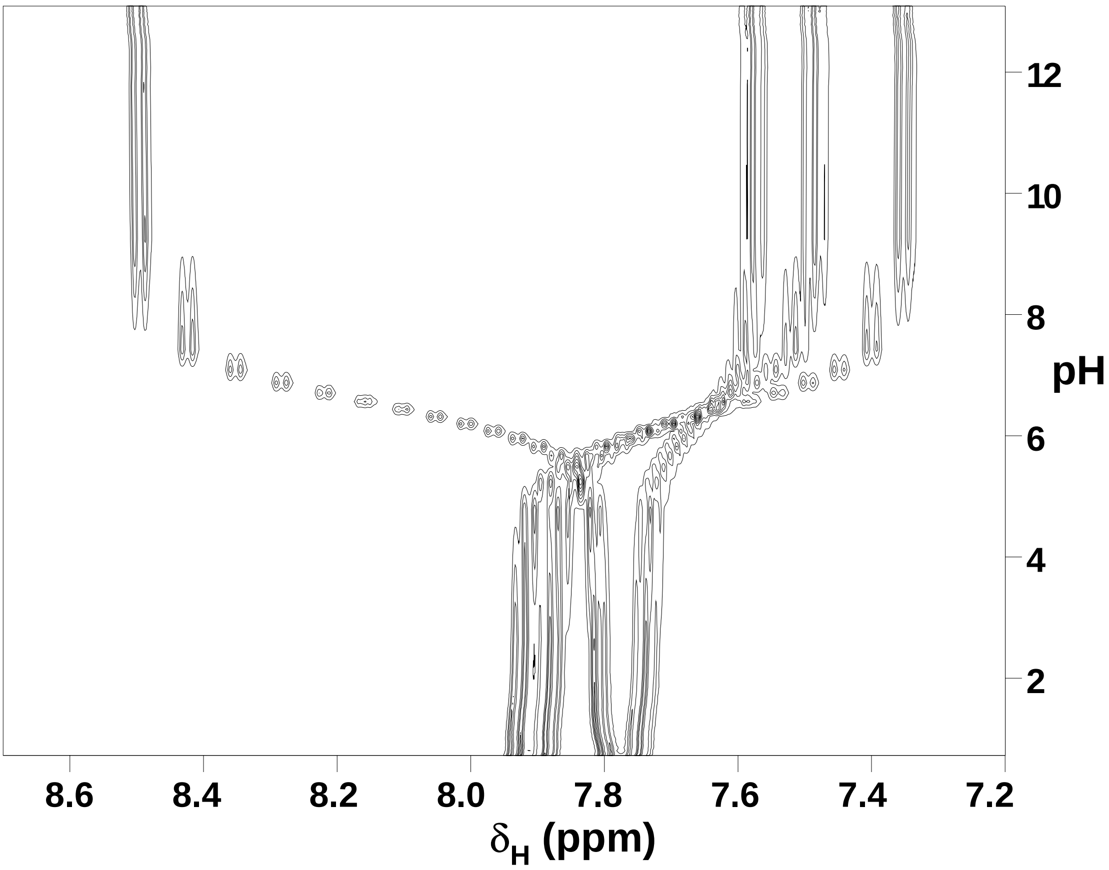

Fig. S9. 500 MHz ^{1}H NMR-controlled titration of **6** with 1 M TMAOH. Contour pH,δ-plot

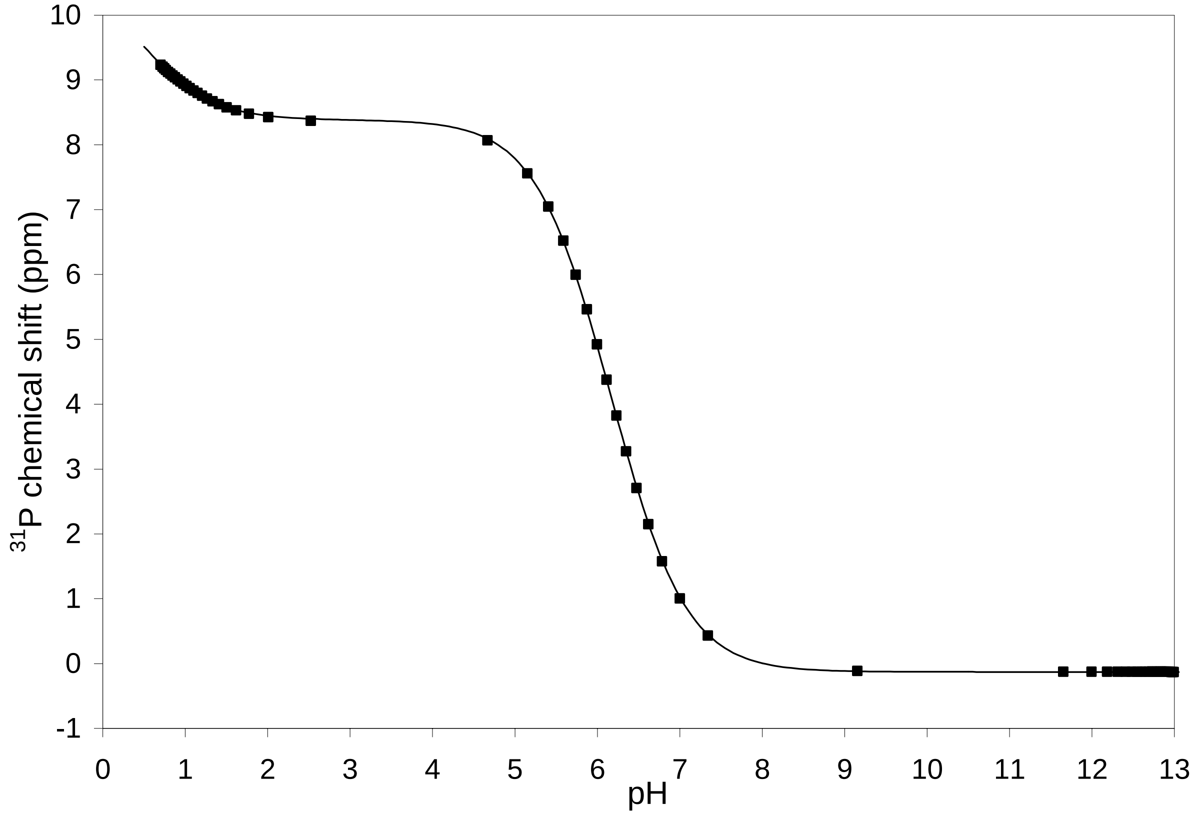

Fig. S10. 202 MHz ^{31}P{^{1}H} NMR-controlled titration curve of **6** vs. TMAOH at 1 M ionic strength (TMACl), fitted by the OPIUM software

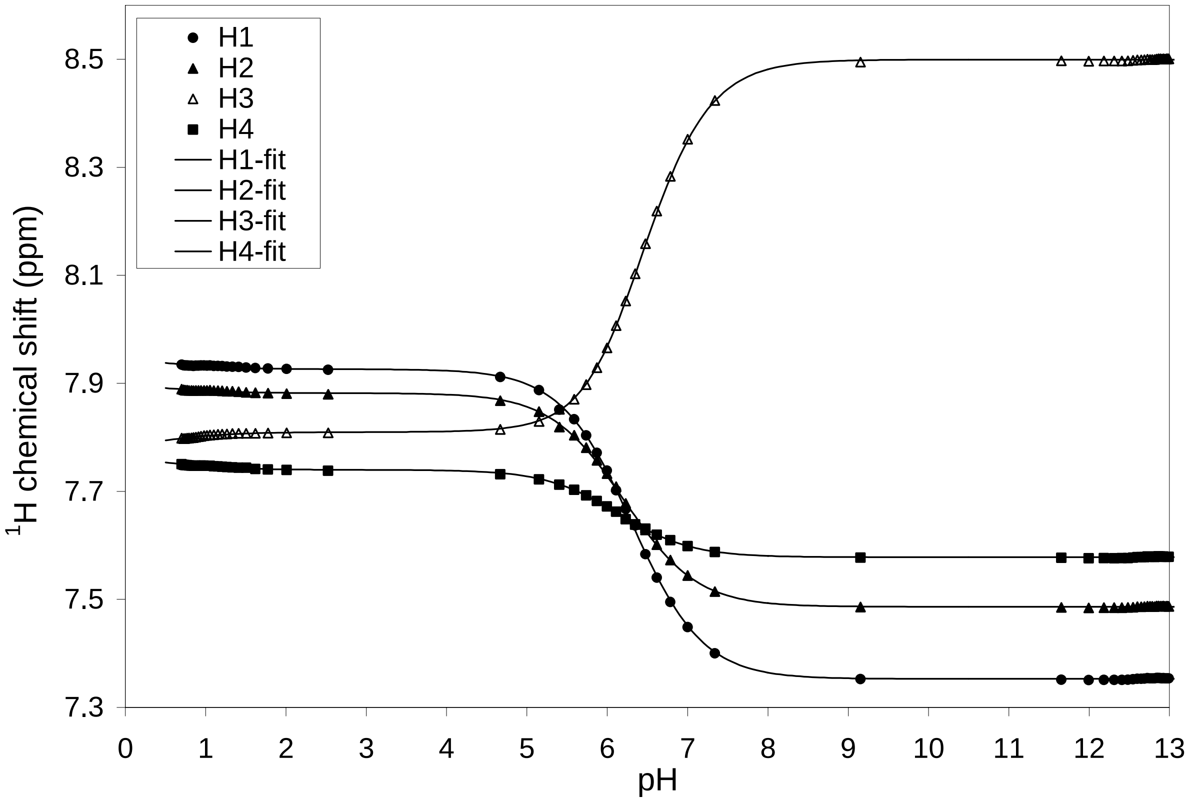

Fig. S11. 500 MHz ^{1}H NMR-controlled titration curves of **6** vs. TMAOH at 1 M ionic strength (TMACl), fitted by the OPIUM software

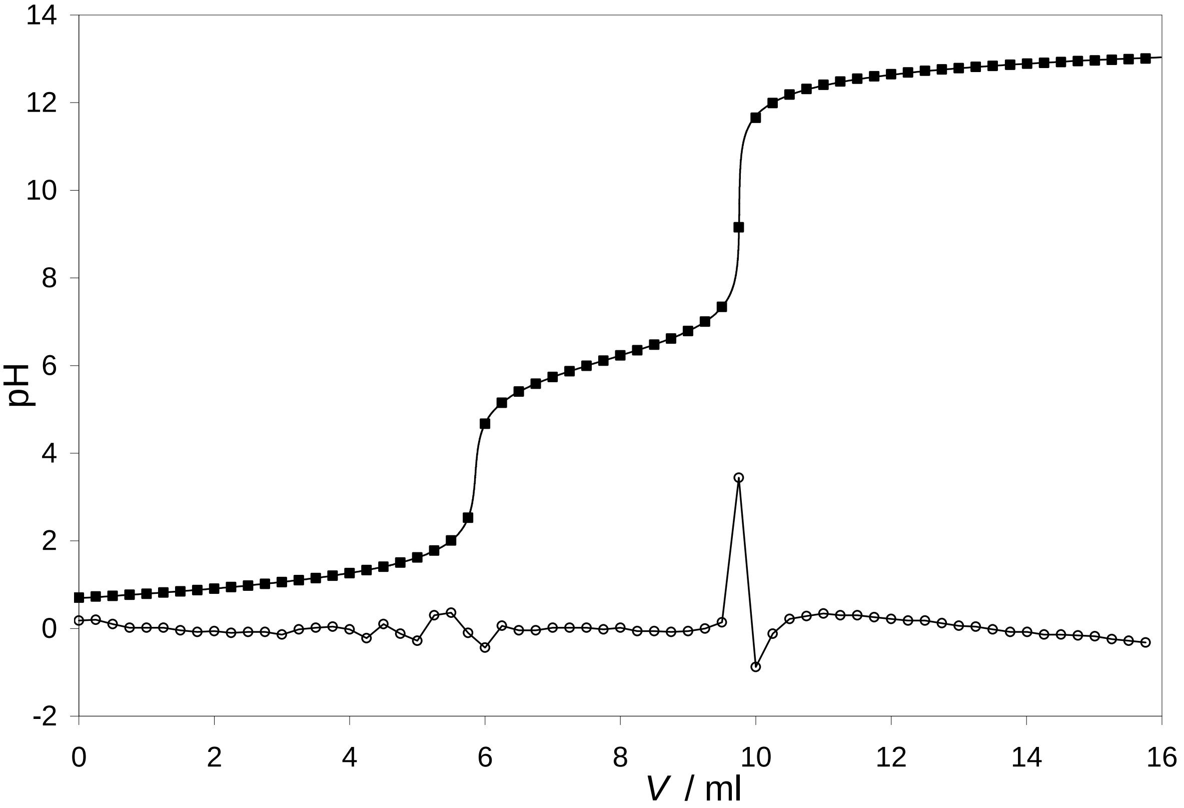

Fig. S12. Potentiometric titration curve, fitted by the OPIUM software from the 202 MHz $^{31}P\{^{1}H\}$ NMR-controlled titration of **6** with TMAOH. The lower trace represents the (observed-calculated) residuals, plotted by using a magnification factor of 20.

Table S1. ^{1}H and ^{13}C chemical shift gradients, Δ = δ(in KOD) – δ(in D_2O) (ppm) of **6-8**, measured in D_2O and KOD solutions

	D_2O / KOD			**D_2O / KOD**
	Gradient Δ			Gradient Δ
H_1	- 0.5628		**C_{VI}**	+ 0.894
H_2	- 0.3867		**C_{III}**	- 7.912
H_3	+ 0.6447		**C_{VII}**	+ 7.549
H_4	- 0.1529		**C_{IV}**	+ 1.015
			C_I	+7.767
			C_{II}	-6.701
			C_V	+9.059
			C_{VIII}	+111.993

Table S2. 500 MHz ^{1}H NMR parameters of 3-hydroxy-3-phosphonoisobenzofuranone (**6**): a) 0.2510 M in D_2O; b) 0.1010 M in 1 M KOD. Chemical shifts δ_H (ppm), resonance frequencies ν_H (Hz), coupling constants $^nJ_{HH}$ (Hz) and spectral half widths HW (Hz)

[c] n.i. = not iterated

Solvent		**D_2O**[a]		**KOD**[b]	
Species		**$H_3L < H_2L^-$**		**L^{3-}**	
δ_i	**Type**	**Data**	**Error**	**Data**	**Error**
1	δ_H	7.9242		7.3540	
2	δ_H	7.8654		7.4832	
3	δ_H	7.7967		8.4423	
4	δ_H	7.7242		7.5717	
5	δ_P	9.398		-0.6386	
ν_i	**Type**	**Data**	**Error**	**Data**	**Error**
1	ν_H	3963.1894	± 0.0009	3677.9346	± 0.0010
2	ν_H	3933.7422	± 0.0008	3742.5942	± 0.0006
3	ν_H	3899.3410	± 0.0009	4222.2400	± 0.0007
4	ν_H	3863.0805	± 0.0009	3786.8131	± 0.0006
5	ν_P	1902.8221	n. i.[c]	-129.2945	n. i.
J_{ik}	**Type**	**Data**	**Error**	**Data**	**Error**
12	$^4J_{HH}$	1.0387	± 0.0010	1.2611	± 0.0009
13	$^5J_{HH}$	0.8136	± 0.0041	0.5820	± 0.0007
14	$^3J_{HH}$	7.7308	± 0.0012	7.6065	± 0.0013
15	$^5J_{PH}$	0.7308	± 0.0035	1.2932	± 0.0022
23	$^3J_{HH}$	7.7421	± 0.0012	7.8928	± 0.0009
24	$^3J_{HH}$	7.4592	± 0.0013	7.4479	± 0.0012
25	$^5J_{PH}$	0.2137	± 0.0048	0.3392	± 0.0021
34	$^4J_{HH}$	0.8480	± 0.0080	1.2202	± 0.0006
35	$^4J_{PH}$	1.0800	± 0.0054	0.2183	± 0.0021
45	$^6J_{PH}$	0.9908	± 0.0086	0.3228	± 0.0017
Half width	**Type**	**Data**	**Error**	**Data**	**Error**
1	HW_H	0.7976	± 0.0020	0.7688	± 0.0018
2	HW_H	0.8057	± 0.0024	0.6953	± 0.0018
3	HW_H	0.8300	± 0.0028	0.6377	± 0.0017
4	HW_H	0.8409	± 0.0020	0.7174	± 0.0014
5	HW_P	3.0630	n. i.	2.0550	n. i.

Table S3. Chemical shifts δ_C (ppm) monitored for six selected titration states of **6**. a) aromatic carbons C_{III}, C_{IV}, C_{VI}, C_{VII} connected to protons; b) aromatic carbons C_{II}, C_V not connected to protons. c) C_I COOH / COO$^-$; d) C_{VIII} COH / CO. n.o. = not observed. br = broad lines. vbr = very broad lines. Only a few coupling constants (Hz) were resolved: $^1J_{PC}$ of C_{VIII} : 199.7 ($\tau = 0$), 197.2 ($\tau = 0.5$), 160.1 ($\tau = 3$); $^2J_{PC}$ of C_{II} : 4.7 ($\tau = 0$), 4.5 ($\tau = 3$); $^3J_{PC}$ of C_V : 47.4 ($\tau = 3$).

τ	**0**	**0.5**	**1**	**1.5**	**2**	**3**
	Chemical shifts δ_C					
C_I	173.91	174.21	174.62	175.66 br	178.25	181.82
C_{II}	148.70	149.30	149.52 br	148.56 vbr	144.75 br	142.16
C_{III}	138.32	138.20	137.91 br	136.92 vbr	134.29 br	130.39
C_{IV}	134.05	133.83	133.65	133.59	134.03	135.02
C_V	128.37	128.38	128.78 br	129-132 vbr	135.01 br	137.40
C_{VI}	128.23	128.12	128.07	128.14 br	128.50	129.14
C_{VII}	126.60	126.58	126.74 br	127.58 vbr	130.17 br	134.16
C_{VIII}	107.10	107.84	n.o.	n.o.	n.o.	219.43