New Journal of Chemistry

Electronic Supplementary Information

Selective recognition of biogenic amine hydrochlorides by heteroditopic dihomooxacalix[4]arenes

Giuseppe Gattuso,[a] Anna Notti,[a] Melchiorre F. Parisi,*[a] Ilenia Pisagatti,[a] Paula Maria Marcos,*[b] José Rosário Ascenso,[c] Giovanna Brancatelli[d] and Silvano Geremia[d]

[a] *Dipartimento di Scienze Chimiche, Università di Messina, Viale F. Stagno d'Alcontres 31, 98166 Messina, Italy. Fax: 39 090 393895; Tel: 39 090 6765170; E-mail: mparisi@unime.it*

[b] *Centro de Ciências Moleculares e Materiais, Faculdade de Ciências da Universidade de Lisboa, Edifício C8, 1749-016 Lisboa, Portugal, and Faculdade de Farmácia da Universidade de Lisboa, Av. Prof. Gama Pinto, 1649-003 Lisboa, Portugal, Fax: 351) 21-7500979; E-mail: pmmarcos@fc.ul.pt*

[c] *Centro de Química Estrutural, Instituto Superior Técnico, Av. Rovisco Pais, 1049-001 Lisboa, Portugal*

[d] *Centro di Eccellenza in Biocristallografia, Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, Via L. Giorgieri 1, 34127 Trieste, Italy*

Contents

Table S1 Crystal data and structure refinement for **1**.

	1
Formula	$2(C_{75}H_{102}N_4O_7)$, 0.6 (CH_3OH)
Formula weight (Da)	2359.72
T (K)	100(2)
λ (Å)	0.700
Crystal system	Triclinic
Space group	*P -1*
Unit cell dimensions (Å, °)	a = 15.65(1), α = 70.56(3) b = 17.82(1), β = 86.08(3) c = 26.44(2), γ = 87.57(4)
V (Å^3)	6934(8)
Z	2
ϱ_{calc} (g/mm^3)	1.132
μ (mm^{-1})	0.043
F(000)	2565.6
Resolution (Å)	24.89 – 1.00
Reflections collected	26784
Independent reflections	13719
Data / restraints / parameters	13714 / 158 / 1490
R_1, wR_2 [I>2σ(I)]	0.1288, 0.3366
R_1, wR_2 (all data)	0.1594, 0.3641
GooF	1.054
CCDC code number	1009330

Crystal structure determination of 1.

1. Treatment of the disorder

The single crystal analyzed was very small and consequently synchrotron radiation was mandatory to obtain a dataset suitable to solve the structure. Furthermore the structure is affected by severe disorder and the data resolution is limited to 1 Å. A detailed description of the disorder modelization is provided below. In the asymmetric unit of **1** two crystallographically independent oxacalixarene molecules were found. In the first oxacalixarene molecule the oxygen atom of one carbonyl group was found to be disordered over two positions (O1oa/O1pb), refined at 0.4/0.6 of partial occupancy. Similarly, the following atoms were refined as they were seen to be disordered over two positions: a methylene carbon atom of one of the two butyloxy substituents at the lower rim (C2la/C2lb, refined at 0.75/0.25 of partial occupancy); three methylene carbon atoms of a (*N′*-phenylureido)butyloxy substituent (C3ha,C3ia,C3la/C3hb,C3ib,C3lb, refined at 0.4/0.6 of partial occupancy); three methylene carbon atoms of the second butyloxy substituent (C4ia,C4la,C4ma/C4ib,C4lb,C4mb, refined at 0.55/0.45 of partial occupancy); three *p-tert*-butyl groups at the upper rim, refined at 0.6/0.4, 0.5/0.5, 0.75/0.25 of partial occupancy; and one methylene carbon atom of the $CH_2{-}O{-}CH_2$ bridging group (C3za/C3zb, refined at 0.4/0.6 of partial occupancy). In the second oxacalixarene molecule the two ureido moieties were also found to be disordered over two positions (O5ga-N5na/O5gb-N5nb and C7ha-C7wa/C7hb-C7wb, refined at 0.5/0.5 and 0.6/0.4 of partial occupancy, respectively). Other atoms seen to be disordered over two positions were: three methylene carbon atoms of one of the lower rim butyloxy substituents (C6ha,C6ia,C6la/C6hb,C6ib,C6lb, refined at 0.6/0.4 of partial occupancy); four carbon atoms of the second butyloxy substituent (C8ha-C8ma/C8hb-C8mb) were divided in two orientations refined at 0.6/0.4 of partial occupancy; one *p-tert*-butyl group, refined at 0.45/0.55 of partial occupancy; one methylene carbon atom of the $CH_2{-}O{-}CH_2$ bridging group (C8zc/C8zd, refined at 0.55/0.45 of partial occupancy). All the atoms belonging to the disordered moieties were refined isotropically, as their contribution to the scattering was rather limited and affected by disorder. Because of severe disorder, in some cases restraints on bond lengths and angles (DFIX, DANG) and thermal parameters (SIMU) were introduced.

2. Structure description.

The asymmetric unit of the centrosymmetric triclinic crystal contains two crystallographically independent molecules (**I** and **II**) and a methanol solvent molecule (Fig. 2 in the main text). In both cases, the macrocycle adopts a *cone*-in conformation, where the *p-tert*-butyl groups of the D rings lean toward the cavity, with the corresponding butyloxy groups directed away from it (more

noticeably in **I**, see Fig. S1). The dihedral angles formed by the D ring mean plane and the dihomooxacalixarene mean plane, defined by the methylene bridging groups are 64.2(2) and 73.7(2)° in **I** and **II**, respectively (Table S2). Thus, the Ar-CH_2OCH_2-Ar bridging moiety shows a different conformation in the two receptors, with torsion angles of 75(1) and 62.6(7)° for **I** and **II**, respectively. In **I**, the CH_2OCH_2 bridging fragment is hydrogen bonded to a methanol molecule (O···O 2.82(2) Å). The ureido groups at the lower rim of each receptor are involved in an intramolecular double hydrogen bond NH···O, a recurring recognition motif in *N*,*N*′-disubstituted ureas[1] (see Table S3 for N···O distances). The orientation of the NHCONH ureido moiety is different in the two molecules, being almost parallel in **I** and orthogonally oriented in **II** (Fig. 2). Indeed, one of the NH urea donor groups in **I** interacts with a methanol molecule through a weak hydrogen bond and as a result the one-dimensional chain, consisting of bifurcated NH···O hydrogen bonds between urea NH donors and the C=O acceptors, is disrupted (Fig. S2).

Table S2 Dihedral angles ($\theta_{A–B}$) between the aromatic rings and the mean plane of the two dihomooxacalixarene molecules **I** and **II**.

	θ_A (°)	θ_B (°)	θ_C (°)	θ_D (°)
I	133.2(2)	100.8(2)	122.7(3)	64.2(2)
II	137.3(2)	97.4(3)	121.2(2)	73.7(2)

Table S3. Hydrogen bond interactions detected in the crystal structure of **1** [Å].

D−H···A	*d*(D···A)
intramolecular	
I	
N(1n)···O(3p)	2.892(8)
N(1q)···O(3p)	2.843(7)
II	
N(5na)···O(7pa)	3.11(2)
N(5q)···O(7pa)	2.80(1)
N(5q)···O(7pb)	2.95(2)
intermolecular	
N(3n)···O(5p)	2.872(7)
N(3q)···O(5p)	2.905(8)
N(7q)···O(1me)[a]	3.00(2)
N(7na)···O(1pa)[b]	2.55(2)

[a] *-x+1, -y+1, -z+1*; [b] *x, y+1, z*

1) (*a*) L. S. Reddy, S. K. Chandran, S. George, N. J. Babu and A. Nangia, *Cryst. Grow. Des*., 2007, **7**, 2675–2690; (*b*) L. S. Reddy, S. Basavoju, V. R. Vangala and A. Nangia, *Cryst. Grow. Des.*, 2006, **6**, 161–173; (*c*) S. George, A. Nangia, C. K. Lam, T. C. W. Mak and J. F. Nicoud, *Chem. Commun.*, 2004, 1202–1203.

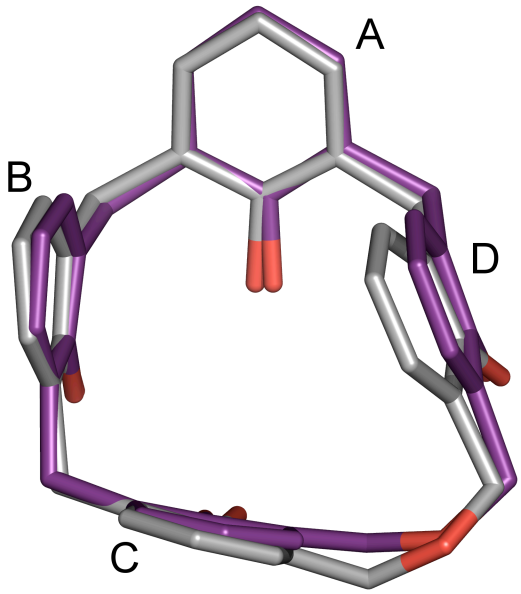

Fig. S1 Top view of the superimposed crystallographic structures of homooxacalix[4]arene **1** (molecules **I** and **II** are depicted in grey and magenta respectively) with the pertinent labelling of the aromatic rings. Although the cavity adopts an overall *cone-in* conformation in both molecules, the orientation of the Ar-CH_2OCH_2-Ar bridging moiety is dissimilar as a result of a different degree of tilting of the D ring (the *tert*-butyl groups at the upper rim as well as the lower rim substituents have been omitted for clarity).

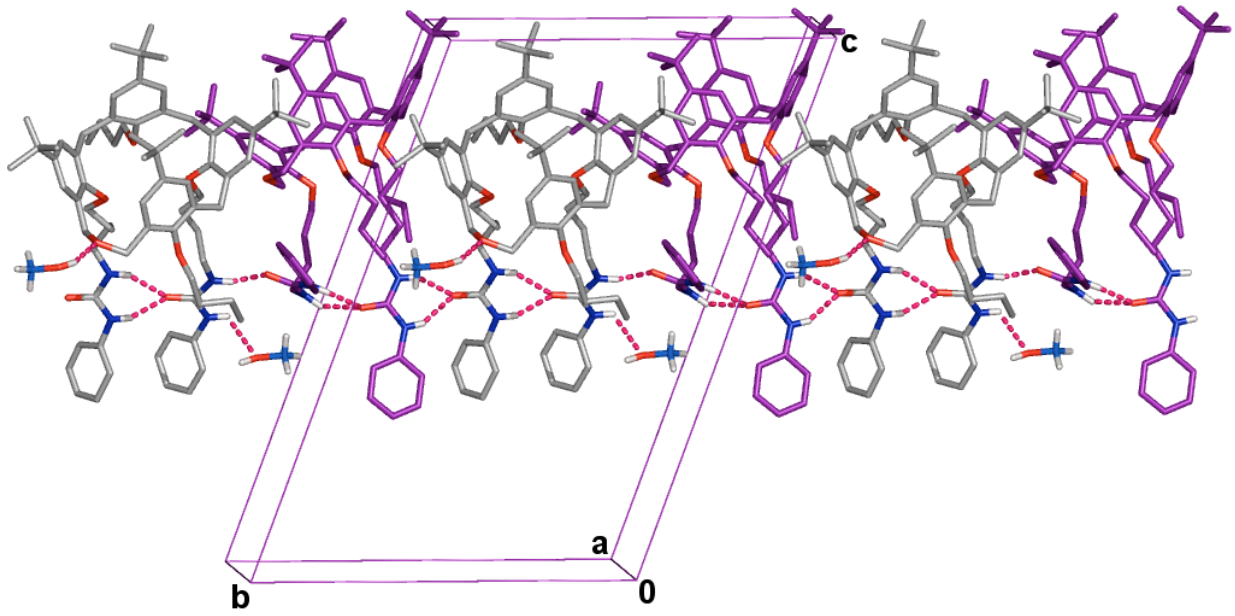

Fig. S2 The receptor molecules **I** and **II** are involved in an α-network, a tape of bifurcated N–H···O hydrogen bonds from NH donors to O acceptor. The one-dimensional chain propagating along the b axis is disrupted by the presence of a methanol solvent molecule, interacting with one ureido NH group as hydrogen bonding acceptor.

Table S4 Chemical shifts (ppm) of the ureido NH resonances of the free receptors **1** and **2** and their ternary complexes with *n*-$BuNH_3^+X^-$ (500 MHz, $CDCl_3$, 298 K, 1.0 mM).

	δ (ppm)			
	N*H*Ph		N*H*CH_2	
1	8.07	7.97	6.28	5.84
n-$BuNH_3^+$⊂**1**⊃Cl^-	9.03	9.01	6.87	6.87
n-$BuNH_3^+$⊂**1**⊃Br^-	8.76	8.69	6.88	6.88
n-$BuNH_3^+$⊂**1**⊃I^-	8.45	8.35	7.07	6.84
2	7.84	7.43	5.86	5.71
n-$BuNH_3^+$⊂**2**⊃Cl^-	8.99	8.95	7.58	–[a]
n-$BuNH_3^+$⊂**2**⊃Br^-	8.73	8.62	–[a]	–[a]
n-$BuNH_3^+$⊂**2**⊃I^-	8.46	8.33	–[a]	–[a]

[a] Not assigned as a result of extensive peak overlapping.

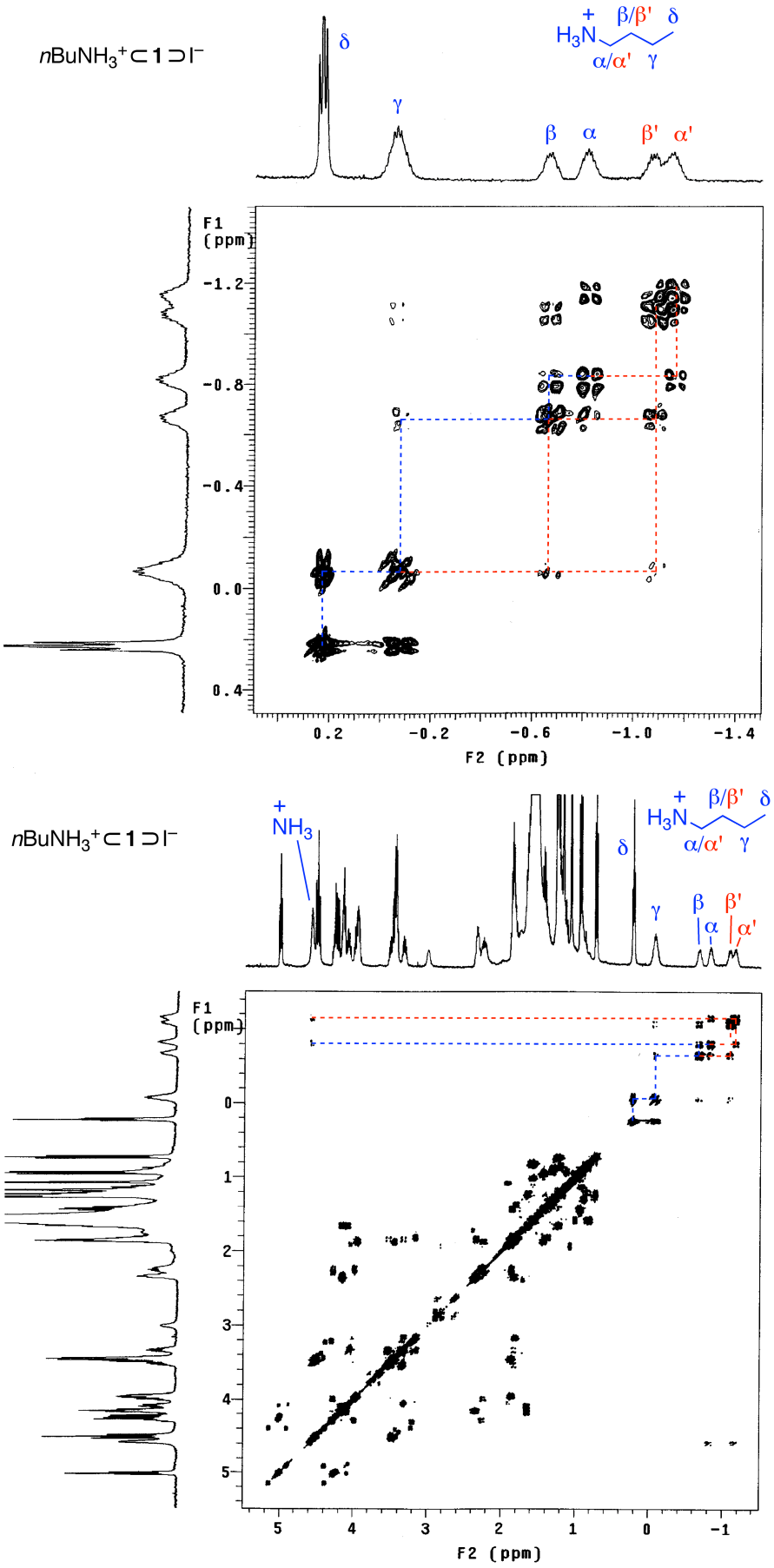

Fig. S3 Sections of the COSY spectrum (500 MHz, $CDCl_3$, 298 K) of [**1**] = [*n*-$BuNH_2$·HI] = 1.0 mM.

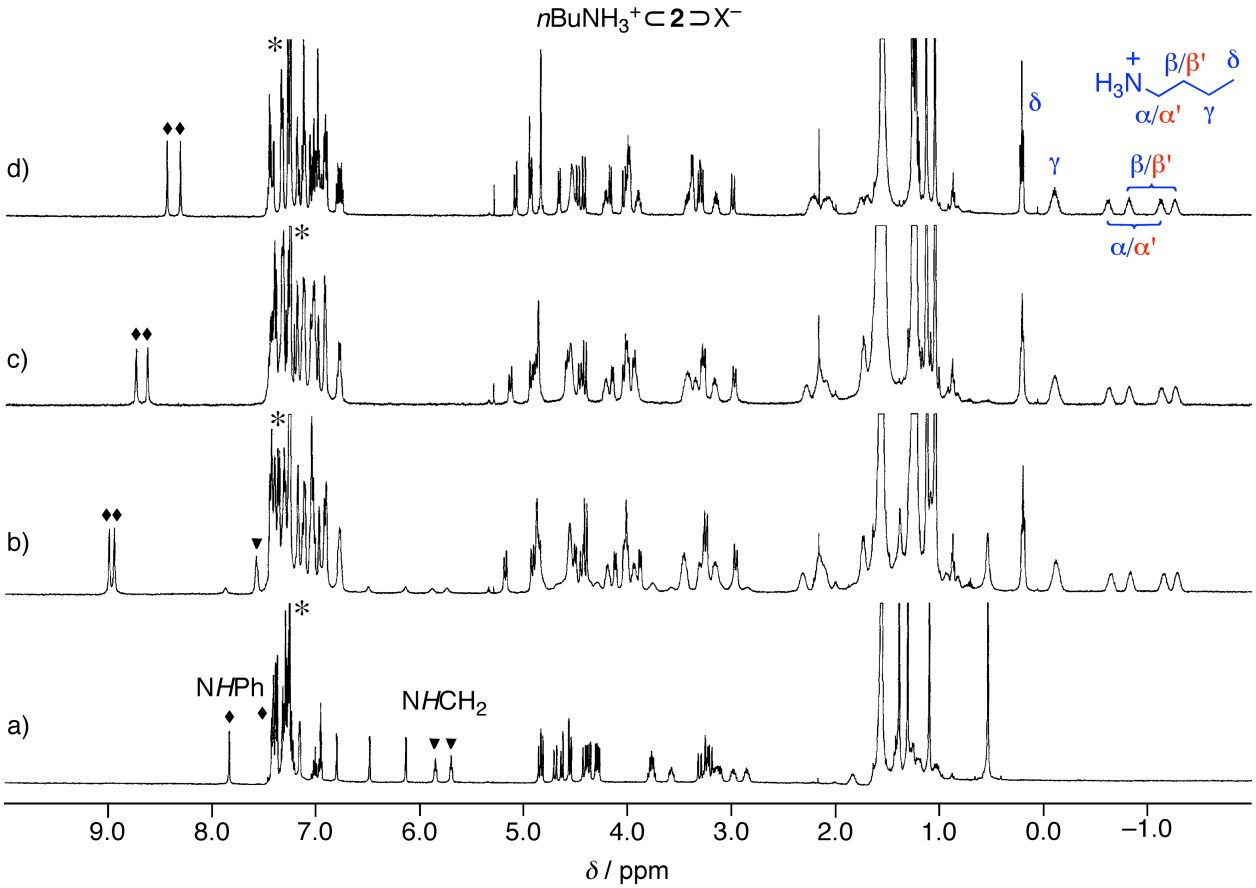

Fig. S4 ^{1}H NMR spectra (500 MHz, $CDCl_3$, 298 K) of: a) [**2**] = 1.0 mM, b) [**2**] = [*n*-$BuNH_2$·HCl] = 1.0 mM, c) [**2**] = [*n*-$BuNH_2$·HBr] = 1.0 mM and d) [**2**] = [*n*-$BuNH_2$·HI] = 1.0 mM. The asterisk indicates the resonance of the residual solvent signals.

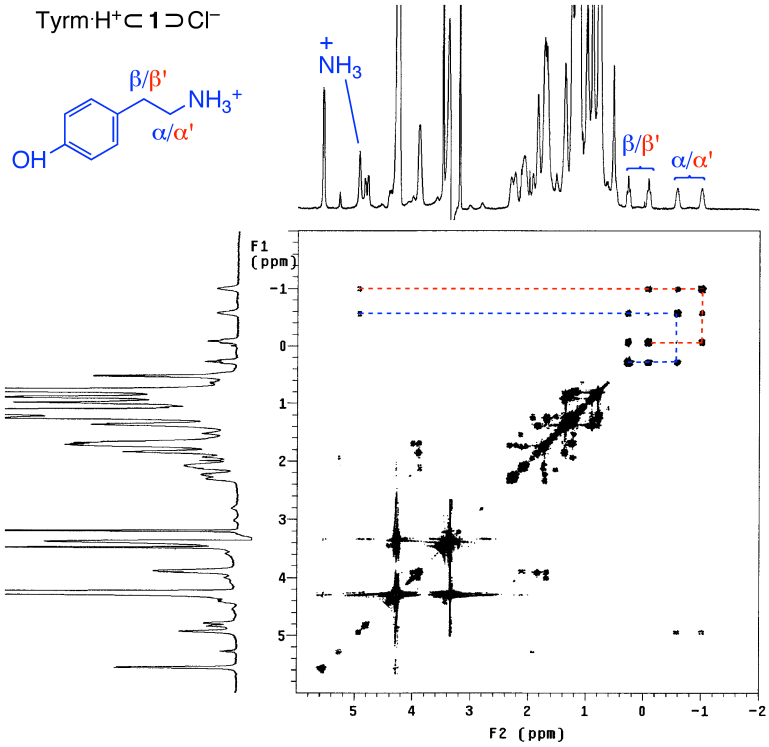

Fig. S5 Section of the COSY spectrum (500 MHz, $CDCl_3$/CH_3OH, 10:1 v/v) of [**1**] = [Tyrm·HCl] = 5.0 mM at 253 K.

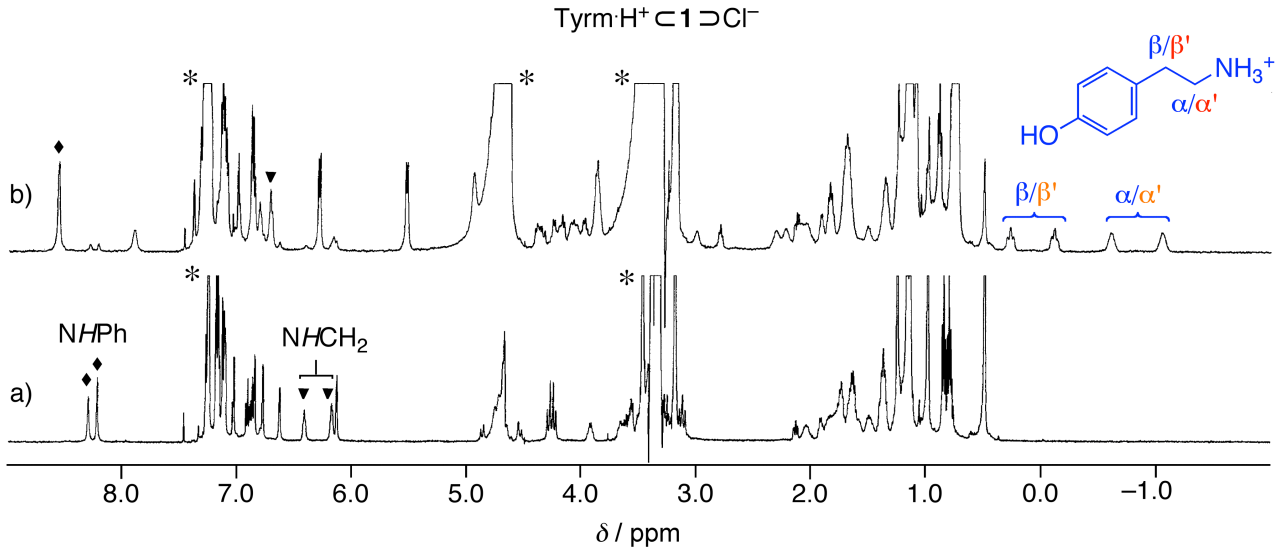

Fig. S6 ^{1}H NMR spectra (500 MHz, $CDCl_3/CH_3OH$ 10:1 v/v) of: a) [**1**] = 1.0 mM at 233 K and b) [**1**] = [Tyrm·HCl] = 1.0 mM at 233 K.

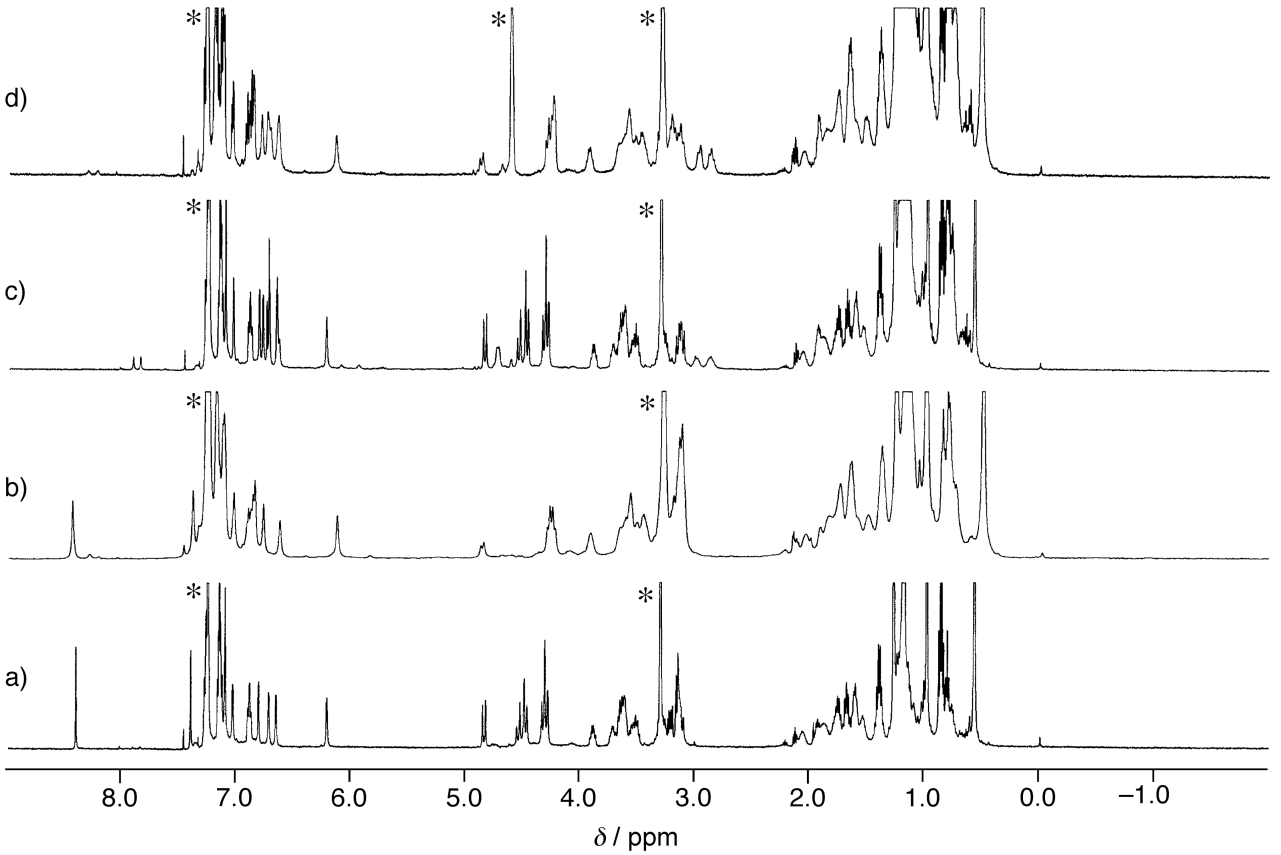

Fig. S7 ^{1}H NMR spectra (500 MHz, $CDCl_3/CD_3OD$ 10:1 v/v) of: a) [**1**] = [Hist·2HCl] = 1.0 mM at 298 K, b) [**1**] = [Hist·2HCl] = 1.0 mM at 233 K, c) [**1**] = [Nore·HCl] = 1.0 mM at 298 K and d) [**1**] = [Nore·HCl] = 1.0 mM at 233 K.