Electronic Supporting Information

for

Nickel(II) complexes of *N*–CH_2CF_3 cyclam derivatives as contrast agents for ^{19}F magnetic resonance imaging

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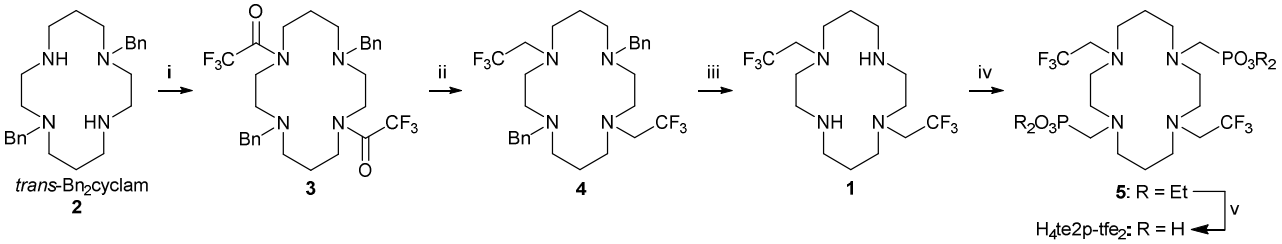
Contents

General experimental conditions

The 1,8-dibenzylcyclam (*trans*-Bn_2cyclam) hydrochloride was prepared by published method.[1] Paraformaldehyde was filtered from aged aqueous solutions of formaldehyde (Lachema) and was dried in a desiccator over conc. H_2SO_4. Cyclam (CheMatech) and other chemicals from commercial sources were used as received. NMR spectra were recorded on the VNMRS300, Varian^{UNITY} *INOVA* 400 or Bruker Avance III 600 spectrometers using 5-mm sample tubes. NMR chemical shifts are given in ppm and coupling constants are reported in Hz. Unless stated otherwise, all NMR spectra were collected at 25 °C. For the ^{1}H and ^{13}C{^{1}H} NMR measurements in D_2O, *t*-BuOH was used as internal standard (δ_H = 1.25, δ_C = 30.29). The pD in D_2O solution was calculated by +0.4 correction to reading of calibrated pH-electrode. For the measurements in $CDCl_3$, TMS was used as internal standard (δ_H = 0.00, δ_C = 0.00). For other solvents used for ^{1}H and ^{13}C NMR measurements, signals of (residual) non/semi-deuterated solvents were used.[2] For ^{31}P NMR measurements, 70 % aq. H_3PO_4 was used as external reference (δ_P = 0.00). For ^{19}F NMR measurements, trifluoracetic acid (TFA, 0.1 M in D_2O, δ_F = –76.55 ppm, external standard), perfluorobenzene (PFB, δ_F = –164.9 ppm) or 2,2,2-trifluoroethanol (TfeOH, δ_F = –77.0 ppm) were used as internal standards. Abbreviations s (singlet), t (triplet), q (quartet), m (multiplet) and b (broad) are used in order to express the signal multiplicities. All ^{13}C NMR spectra were measured using a broad-band ^{1}H decoupling. Longitudinal relaxation times T_1 were measured using inversion recovery sequence with spectrometer offset identical to compound signal and properly calibrated pulse length. Relaxation times T_2* were estimated from signal half-width. The positive or negative ESI-MS spectra were acquired on the Bruker ESQUIRE 3000 spectrometer with ion-trap detection. Thin-layer chromatography (TLC) was performed on TLC aluminium sheets with silica gel 60 F254 (Merck). For the detection, UV, ninhydrin spray (0.5 % in EtOH), dipping of the sheets in 5 % aq. $CuSO_4$ or I_2 vapour exposition were used. Elemental analyses were performed at the Institute of Macromolecular Chemistry (Academy of Sciences of the Czech Republic, Prague). AAS was measured employing spectrometer AAS 3 (Zeiss-Jena) with acetylene-air flame atomization. Throughout the paper, pH means –log[H^+].

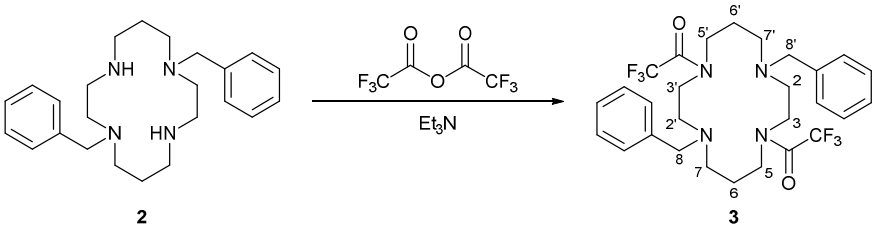
Ligands syntheses

The syntheses of ligands it overviewed in Scheme S1.



Scheme S1 (*i*) trifluoroacetic anhydride (4 eq.), Et_3N (5 eq.), dry $CHCl_3$, room temperature (RT), 3 h; (*ii*) $NaBH_4$ (10 eq.), $BF_3{\cdot}Et_2O$ (10 eq.), dry diglyme, 120 °C, 12 h; (*iii*) 10 % Pd/C, H_2 (balloon), AcOH/EtOH/H_2O (1/5/4, v/v/v), 40 °C, 24 h; (*iv*) neat $P(OEt)_3$, $(CH_2O)_n$, 70 °C, 12 h; (*v*) (1) trimethylsilylbromide (=TMSBr; 20 eq.), dry acetonitrile, RT, 12 h; (2) H_2O excess, RT.

1,8-bis(trifluoroacetyl)-4,11-dibenzyl-1,4,8,11-tetraazacyclotetradecane, 3



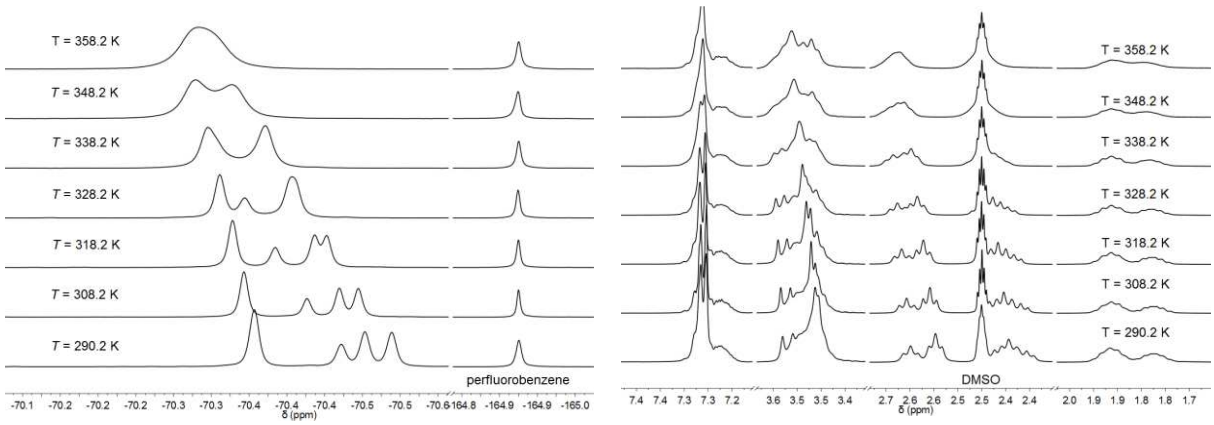
Trans-Bn_2cyclam hydrochloride (**2**·4HCl·4H_2O, 1.00 g, 1.7 mmol) was suspended in 5 % aq. NaOH (75 ml) and extracted three times with $CHCl_3$ (75 ml). The organic phases were unified and dried using anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. Amine free base was dissolved in anhydrous $CHCl_3$ (50 ml) and trifluoroacetic anhydride (930 µl, 6.4 mmol, 4 eq.) and dry triethylamine (1.1 ml, 8.0 mmol, 5 eq.) were added. The mixture was stirred at room temperature for 3 h. Volatiles were evaporated *in vacuo* and product was purified by crystallization from hot EtOH yielding compound **3** as white solid (750 mg, 78 %).

NMR spectra of compound **3** at 25 °C are complicated by a relative rigidity of amide groups which results in three possible conformers. In one of them, the atom with and without apostrophe (below) are not chemically equivalent. Therefore, for each carbon atom, four signals are expected. Some of them are overlaid by random coalescence. However, measurement at elevated temperature up to 80 °C did not lead to better resolution; at this temperature, signals are very broad due to their coalescence. For VT-NMR spectra, see Figure S1.

TLC: R_f = 0.7 (conc. aq. NH_3/EtOH = 1/50).

NMR: ^{1}H (600 MHz; DMSO-d_6): 1.70–1.81 and 1.81–1.92 (2×bm, 4H, H6 and H6'); 2.40, 2.44, 2.47 (3×t, 4H, H7 and H7', $^3J_{HH}$ = 6.0, $^3J_{HH}$ = 6.4, $^3J_{HH}$ =6.4); 2,59 and 2,65 (2×t, 4H, H2 and H2'); 3.46–3.60

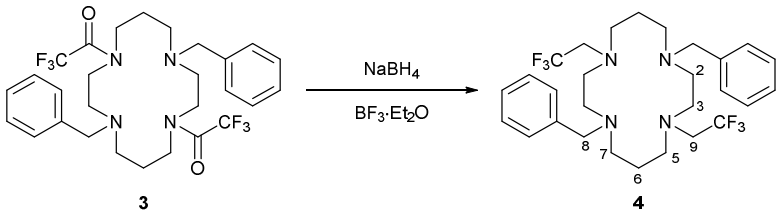
(bm, 12H, H3, H3', H5, H5', H8 and H8'); 6.96–7.72 (bm, 10H, phenyl). ^{13}C (151 MHz; DMSO-d_6): 23.8, 23.9, 25.8 and 26.0 (4×s, C6 and C6'); 45.8, 45.9, 46.2-bs, 46.3, 46.4, 46.9, 47.0 (7×s and bs, C3, C3', C5 and C5'); 50.7, 51.0, 51.2-bs, 51.47, 51.52, 51.7, 52.6 (7×s and bs, C2, C2',C7, C7'); 59.1 59.2, 59.5, 59.6 (4×s, C8 and C8'); 116.3 (q, CF_3, $^1J_{CF}$ = 288); 127.0, 127.1, 128.1, 128.6, 128.8, 129.0 (6×s, phenyl C–H); 138.6-bs, 138.9, 139.0 (bs and 2×s, phenyl q-C); 155.4, 155.5, 155.6 (3×q, C=O and C'=O, $^2J_{FC}$ = 35). ^{19}F (282 MHz; DMSO-d_6): –78.37, –70.45, –70.48, –70.51. ^{19}F (282 MHz; DMSO-d_6; 80 °C): –70.31.
MS(+): 573.3 (calc. 573.3, [**3**+H]$^+$).
Elem. anal.: found C 58.32; H 6.17; N 9.55 (calc. for $C_{28}H_{34}N_4F_6O_2$, M_r = 572.6; C, 58.73; H, 5.99; N, 9.78).



A B

Figure S1 NMR spectra of compound **3** acquired at different temperatures. (A): ^{19}F NMR. (B): ^{1}H NMR.

1,8-bis(2,2,2-trifluoroethyl)-4,11-dibenzyl-1,4,8,11-tetraazacyclotetradecane, 4



3 **4**

In three-necked flask, $NaBH_4$ (4.6 g, 122 mmol, 10 eq.) and **3** (7.0 g, 12.2 mmol) were suspended in anhydrous diglyme (100 ml) under Ar-atmosphere. Then, $BF_3{\cdot}Et_2O$ (14 ml, 122 mmol, 10 eq.) diluted by anhydrous diglyme (100 ml) was added dropwise under gentle stream of argon. B_2H_6 in escaping gas was removed by bubbling through 5 % NaOH in 10 % aq. H_2O_2. The reaction mixture was stirred at 120 °C overnight. After cooling, 12 % aq. HCl (10 ml) was added dropwise. The volatiles were evaporated *in vacuo*. Crude product was dissolved in 5 % aq. NaOH (100 ml) and extracted into $CHCl_3$ (3×100 ml).

Combined organic layers were dried using anhydrous Na_2SO_4 and evaporated and product **4** was crystallized as a white solid from hot $CHCl_3$ (5.1 g, 76 %).

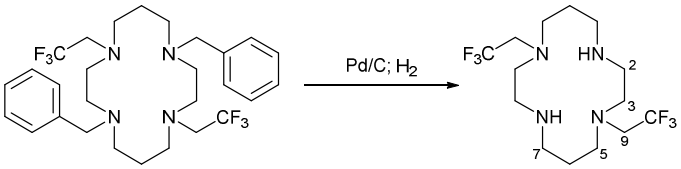
TLC: R_f = 0.8 (MeOH).

NMR: ^{1}H (400 MHz; $CDCl_3$): 1.67 (p, 4H, H6, $^3J_{HH}$ = 6.8); 2.51 (t, 4H, H7, $^3J_{HH}$ = 7.0); 2.57 (t, 4H, H2, $^3J_{HH}$ = 6.2); 2.68 (t, 4H, H5, $^3J_{HH}$ = 6.9); 2.77 (t, 4H, H3, $^3J_{HH}$ = 6.0); 2.92 (q, 4H, H9, $^3J_{HF}$ = 9.6); 3.52 (s, 4H, H8); 7.17–7.41 (bm, 10H, phenyl). ^{13}C (151 MHz; $CDCl_3$; 25): 24.9 (s,C6); 51.2 (bs, C7 and C2); 52.2 (s, C3); 52.5 (s, C5); 55.3 (q, C9, $^2J_{CF}$ = 30); 59.5 (s, C8); 126.1 (q, CF_3, $^1J_{CF}$ = 282); 127.1, 128.3, 129.2, 140.0 (s, phenyl). ^{19}F (282 MHz; $CDCl_3$): –72.5(bs).

MS(+): 545.3 (calc. 545.3, [**4**+H]$^+$).

Elem. anal.: found C 61.50; H 7.15; N 9.98 (calc. for $C_{28}H_{38}N_4F_6$, M_r = 544.6; C, 61.75; H, 7.03; N, 10.29).

1,8-bis(2,2,2-trifluoroethyl)-1,4,8,11-tetraazacyclotetradecane, 1



4 **1**

Compound **4** (4.0 g, 7.4 mmol) was dissolved in AcOH/EtOH/H_2O mixture (1/5/4 v/v, 100 ml) and 10 % Pd/C (200 mg) was added. The flask was evacuated, filled with hydrogen and the mixture was stirred under hydrogen atmosphere (balloon) at 40 °C for 24 h. The catalyst was filtered off, and the filtrate was evaporated to dryness, co-evaporated with 35 % aq. HCl (10 ml) and the residue was triturated with EtOH. Yield 2.4 g (65 %).

TLC: R_f = 0.1 (conc. aq. NH_3/EtOH = 1/50).

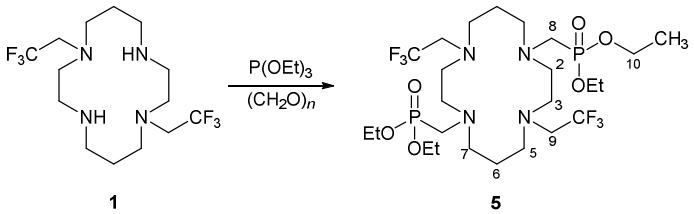
NMR: ^{1}H (600 MHz; D_2O; pD = 3.1): 1.89–2.05 (bm, 4H, H6); 2.92 (bt, 4H, H7, $^3J_{HH}$ = 5.6); 3.08 (bm, 4H, H2); 3.35 (bs, 4H, H3); 3.38 (q–partially overlapped with other signals, 4H, H9, $^3J_{HF}$ = 9.8); 3.41 (t, 4H, H5, $^3J_{HH}$ = 6.4). ^{13}C (151 MHz; D_2O; pD = 3.1): 23.7 (s, C6); 45.7 (s, C3); 47.7 (s, C5); 52.5 (s, C2); 53.5 (s, C7); 53.9 (q, C9, $^2J_{CF}$ = 30); 126.5 (q, CF_3, $^1J_{CF}$ = 282). ^{19}F (282 MHz; D_2O; pD = 3.1): –64.9 (t, $^3J_{HF}$ = 9.4).

MS(+): 365.2 (calc. 365.2, [**1**+H]$^+$).

Elem. anal.: found C 32.64; H 5.91; N 10.56; Cl 28.40 (calc. for **1**·4HCl, M_r = 473.8; C, 32.96; H, 5.93; N, 10.98; Cl, 27.79).

Single crystals of **1**·2HCl·2H$_2$O suitable for X-ray diffraction analysis were prepared by slow evaporation of diluted aqueous solution of **1**·4HCl.

1,8-bis(diethoxyphosphorylmethyl)-4,11-bis(trifluoroethyl)-1,4,8,11-tetraazacyclotetradecane, 5



1 5

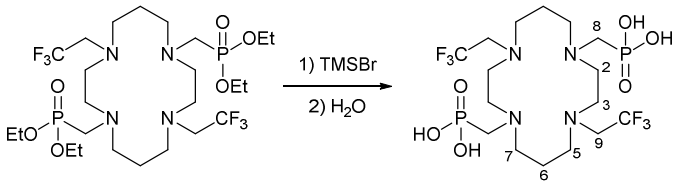
Compound **1**·4HCl (1.00 g, 2.1 mmol) was extracted from 5 % aq. NaOH (50 ml) by $CHCl_3$ (3×50 ml). Organic phases were unified, dried by anhydrous Na_2SO_4 and the solvent was evaporated. Triethyl phosphite (20 ml) and paraformaldehyde (254 mg, 13 mmol, 4 eq.) were added and the mixture in a flask closed by stopper was stirred at 70 °C for 12 h. Unreacted $(CH_2O)_n$ was filtered off and $P(OEt)_3$ was evaporated on rotary evaporator. Crude product was isolated after chromatography on strong cation exchanger (100 ml, H^+-form); impurities were washed off by EtOH (500 ml) and the product was eluted by EtOH/conc. aq. NH_3 = 5/1 mixture (v/v, 250 ml). The crude product was further purified by chromatography (SiO_2, MeOH) affording **5** as a colourless oil.

TLC: R_f = 0.8 (MeOH).

NMR: ^{1}H (300 MHz; MeOH-d_4): 1.29 (d, 12H, CH_3, $^3J_{HH}$ = 7.1); 1.62 (p, 4H, H6, $^3J_{HH}$ = 6.7); 2.72 (bm, 14H, H2, H3, H5, H7); 2.91 (d, 4H, H8, $^2J_{HP}$ = 9.8); 3.14 (q, 4H, H9, $^3J_{HF}$ = 9.9); 4.09 (pseudo-p, 8H, H10, $^3J_{HP} \sim {}^3J_{HH}$ = 7.2). ^{13}C (101 MHz; MeOH-d_4): 16.9 (d, CH_3, , $^4J_{CP}$ = 5.8); 26.0 (s, C6); 51.0 (d, C8, $^1J_{CP}$ = 159); 53.2 (s, C3); 53.6 (s, C5); 53.8 (d, C7, $^2J_{CP}$ = 7); 53.9 (d, C2, $^2J_{CP}$ = 8); 56.2 (q, C9, $^2J_{CF}$ = 30); 63.5 (d, C10, $^2J_{CP}$ = 7); 127.8 (q, CF_3, $^1J_{CF}$ = 281). ^{19}F (282 MHz; MeOH-d_4): –71.0 (t, $^3J_{HF}$ = 9.9). ^{31}P (121 MHz; MeOH-d_4): 27.2 (pseudo-p, $^2J_{HP} \sim {}^3J_{HP}$ = 8.0). ^{31}P{^{1}H} (121 MHz; MeOH-d_4): 27.2 (s).

MS(+): 665.9 (calc. 665.6, [**5**+H]$^+$); 687.9 (calc. 687.3, [**5**+Na]$^+$); 703.9 (calc. 703.3, [**5**+H]$^+$).

1,8-bis(dihydroxyphosphorylmethyl)-4,11-bis(2,2,2-trifluoroethyl)-1,4,8,11-tetraazacyclotetradecane, H_4te2p-tfe$_2$



5 H_4te2p-tfe$_2$

Entire amount of the crude product from the previous reaction was dried by repeated (2×) evaporation with anhydrous MeCN. Dried amine was dissolved in anhydrous MeCN (60 ml) and TMSBr (3.2 ml, 18 mmol, large excess) was added. The reaction mixture was stirred in dark at room temperature overnight. The mixture was evaporated *in vacuo* and the residue was dissolved in MeCN. The solution

was added dropwise to water (25 ml). Mixture was evaporated and the residue was dissolved in MeOH and precipitated by addition of Et_2O. The solid was isolated by centrifugation. The product, H_4te2p-tfe$_2$, was isolated in the zwitterionic form after purification on strong cation exchanger (100 ml, H^+-form). Impurities were removed by water (500 ml) and the product was eluted off by 10 % aq. pyridine. Lyophilization affords 842 mg (74 % based on **5**) of white solid. X-ray quality single crystals of H_4te2p-tfe$_2$·4HBr·0.5H_2O were obtained by slow diffusion of aq. ligand solution which was layered over conc. aq. HBr.

NMR: ^{1}H (300 MHz; D_2O; pD = 6.3): 2.00 (bs, 4H, H6); 2.86 (bs, 4H, H5); 3.12 (s, 4H, H3); 3.17 (d, 4H, H8, $^2J_{HP}$ = 11.3); 3.32 (q, 4H, H9, $^3J_{HF}$ = 9.4); 3.66 (bs, 8H, H2 and H7). ^{13}C (151 MHz; D_2O; pD = 6.3): 23.3 (s, C6); 50.5 (s, C3); 53.0 (d, C8, $^1J_{CP}$ = 127); 53.5 (s, C5); 53.9 (s, C2); 54.2 (q, C9, $^2J_{CF}$ = 31); 55.3 (s, C7); 126.6 (q, CF_3, $^1J_{CF}$ = 282). ^{19}F (376 MHz; D_2O; pD = 6.3): –68.9 (t, $^3J_{HF}$ = 9.3). ^{31}P{^{1}H} (162 MHz; D_2O; pD = 6.3): 6.2 (bs).

MS(–): 550.5 (calc. 551.2, $[M–H]^-$); (+): 552.6 (calc. 553.2, $[M+H]^+$).

Elem. anal.: found C 32.46; H 5.85; N 9.52; P 10.53 (calc. for H_4te2p-tfe$_2$·2H_2O, M_r = 588.4; C, 32.66; H, 6.17; N, 9.52; P 10.53).

Complex syntheses

cis-[Ni(1)(Cl)$_2$]

Ligand hydrochloride (**1**·4HCl, 50 mg, 0.1 mmol) was mixed with Ni(ClO_4)$_2$ (42 mg, 0.11 mmol, 1.1 eq) in 3 ml of water (pH adjusted to 6.9 by diluted aq. NaOH). After ca 1 d at 60 °C, a violet precipitate appeared. The mixture was heated for 6 d at the same temperature to complete the reaction.

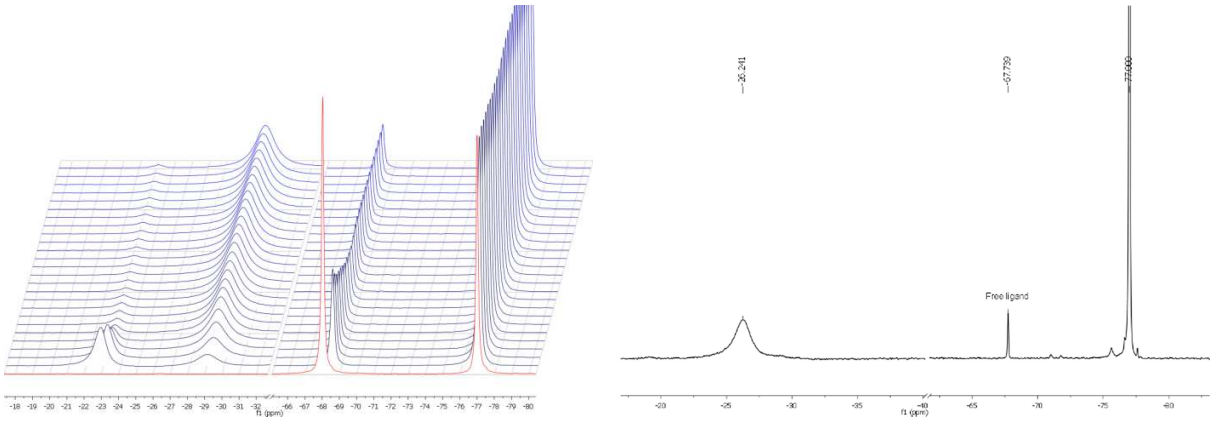
Further heating of the undisturbed reaction mixture (in flame-sealed ampoule) at 105 °C for 7 d yielded light green single crystals of *cis*-[Ni(**1**)Cl_2]. The same compound was obtained also when aqueous solution of *cis*-[Ni(**1**)(H_2O)$_2$](ClO_4)$_2$ (prepared as mentioned below) was layered over 5 % aq. NaCl and the mixture was left at room temperature for 2 d.

cis-[Ni(1)(H_2O)$_2$](ClO_4)$_2$

Ligand as **1**·4HCl (200 mg, 0.42 mmol) was dissolved in 5 % aq. NaOH (25 ml) and the solution was extracted with $CHCl_3$ (3×25 ml). Organic phases were combined and evaporated to dryness. Free base **1** was dissolved in MeOH (5 ml). To this solution, a solution of Ni(ClO_4)$_2$·6H_2O (115 mg, 0.31 mmol, 0.75 eq.) in water (5 ml) was added. The mixture was stirred in an opened vial placed in oil bath heated to 80 °C for 4 d; during this time, the volume was gradually reduced as MeOH evaporated, and some distilled water was added several times to keep volume of the reaction mixture ~3–5 ml. The mixture was

filtered through 0.1-μm syringe filter. Absence of free Ni(II) was proved by negative reaction with 1 % dimethylglyoxime in EtOH. The solution was evaporated *in vacuo* and the residue was dissolved in water (10 ml, final pH ~7.4) and the solution was extracted with $CHCl_3$ (8×10 ml) to remove excess of free ligand (controlled by ^{19}F NMR). The complex was not isolated and its concentration in this stock aq. solution was determined by means of AAS. Any attempts to grow single crystals were unsuccessful.
TLC: decomposition (see below).
NMR: Only extremely broad signals and no signals were found in ^{1}H NMR and ^{13}C NMR spectra, respectively. ^{19}F (282 MHz, D_2O, pD = 7.62, 25 °C): –26.2, T_1 = 1.72(1) ms, T_2^* ≈ 820 μs.
MS(+): 210.8 (calc.211.1 $[Ni(\mathbf{1})]^{2+}$); 420.9 (calc. 421.1 $[Ni(\mathbf{1})-H]^{+}$) ; 456.9 (calc. 456.1 $[Ni(\mathbf{1})Cl]^{+}$); 520.8 (calc. 520.1 $[Ni(\mathbf{1})(ClO_4)]^{+}$).
It should be noticed that the *cis*-$[Ni(\mathbf{1})(H_2O)_2]^{2+}$ complex is easily decomposed (transchelation) in diluted aqueous ammonia, even during TLC with ammonia-containing eluents; it points out to a rather low thermodynamic and kinetic stability in ammonia solutions.

Mechanism of the complex formation was followed by ^{19}F NMR by following procedure. Ligand as **1**·4HCl (100 mg, 0.21 mmol) was dissolved in 5 % aq. NaOH (10 ml) and the solution was extracted by $CHCl_3$ (3×10 ml). Organic phases were combined and evaporated. Compound **1** was dissolved in the DMSO (2 ml) and water (1 ml) was added. Approximate concentration of **1** in stock solution (55 mM) was determined by comparison of ^{19}F-NMR signal integral intensity with that of trifluoroethanol (TfeOH) as a standard. In NMR tube, the stock solution of **1** (200 μl, 11 μmol) was mixed with DMSO-d_6 (300 μl) and TfeOH (1 μl). The mixture was heated to 50 °C and ^{19}F-NMR spectrum was measured. Then, 0.2 M aq. $Ni(ClO_4)_2$ (50 μl, 10 μmol, 0.9 equiv.) was quickly added and the reaction was followed by ^{19}F-NMR over 2 h. The spectra were phase-corrected, and 50 Hz exponential apodization and baseline correction were applied. In the NMR experiment, aq. DMSO was chosen as the solvent keeps reaction mixture fully homogeneous even at the starting point. ^{19}F NMR spectral changes during course of the reaction are shown in Figure S2.



A **B**

Figure S2 (**A**): Time dependence of ^{19}F NMR spectra during Ni(ClO_4)$_2$–**1** complexation in DMSO:water 6.5:1 mixture at 50 °C (blue lines); red line represents spectrum of the free ligand before Ni(ClO_4)$_2$ addition. As an internal standard, trifluoroethanol was used. (B): ^{19}F NMR spectrum of [Ni(**1**)(H_2O)$_2$](ClO_4)$_2$ in water (pH 7.1, 5 mM) with trifluoroethanol as internal standard (δ_F = –77 ppm).

***trans*-[Ni(1)](ClO_4)$_2$**

Solution of *cis*-[Ni(**1**)(H_2O)$_2$](ClO_4)$_2$ (2 ml 0.2 M) was mixed with solution of 18 g $NaClO_4$ in 12 ml water, and the mixture was left for 2 weeks at room temperature. During this period, a red precipitate appeared. The precipitate was isolated by centrifugation.

Single crystals of *trans*-[Ni(**1**)](ClO_4)$_2$ were prepared by analogous procedure: 1 ml of 50 % $NaClO_4$ was layered with 0.2 ml of 0.05 M *cis*-[Ni(**1**)(H_2O)$_2$](ClO_4)$_2$, and the mixture was left undisturbed for 3 weeks.

Isomerization of *trans*-[Ni(**1**)(H_2O)$_2$](ClO_4)$_2$ to *cis*-[Ni(**1**)(H_2O)$_2$](ClO_4)$_2$ was studied by following way: sample of the red *trans*-[Ni(**1**)](ClO_4)$_2$ (15 mg) was dissolved in D_2O (0.5 ml) with 1 µl of trifluoroethanol, and time-evaluation of ^{19}F NMR spectra was measured (Figure S3). Consistent values of half-times for this rearrangement process were calculated from single-exponential fit of time-dependences of both signals intensities: $\tau_{½}$ = 3.6(2) h from decrease of *trans*-[Ni(**1**)(H_2O)$_2$]$^{2+}$ signal and $\tau_{½}$ = 3.4(1) h from increase of *cis*-[Ni(**1**)(H_2O)$_2$]$^{2+}$ signal.

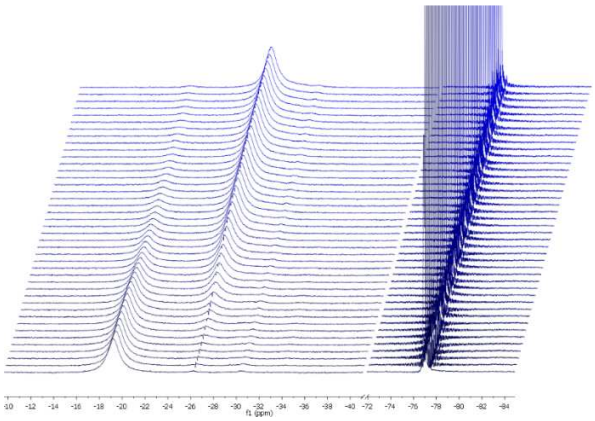


Figure S3 Time dependence of ^{19}F NMR spectra during isomerization of species after dissolution of red *trans*-[Ni(1)]$(ClO_4)_2$ in water at 25 °C. As an internal standard, trifluoroethanol was used.

***cis*-[Ni(1)$(H_2O)_2$]$(OTs)_2$**

To prepare single crystals of *cis*-[Ni(**1**)$(H_2O)_2$]$(OTs)_2$, equimolar amounts of Ni$(TsO)_2$ (47 mg, 0.12 mmol) and free base **1** (freshly prepared from 50 mg, 0.11 mmol of its hydrochloride **1**·4HCl) were mixed in water:MeOH 1:1 mixture (2 ml, native pH 7.5). After short heating at 50 °C, a pink precipitate appeared. The suspension was flame-sealed into ampoule and the mixture was heated at 105 °C for 7 d. During this time, the pink precipitate was transformed to blue bar-like crystals, which were used for X-ray diffraction analysis.

(NH_4){*trans*-[Ni(Hte2p-tfe_2)]}

The ligand H_4te2p-tfe_2·$2H_2O$ (100 mg, 0.16 mmol) was dissolved in water (5 ml) and $NiCl_2$·$6H_2O$ (47 mg, 0.20 mmol, 1.25 eq.) was added. Solution pH was adjusted to 10 by 5 % aq. NH_3 and the mixture was stirred at 75 °C for 24 h. The complex was purified by column chromatography (SiO_2, 6×3 cm) with EtOH/conc. aq. NH_3 5/1 as mobile phase. Fractions containing pure product were combined, evaporated to dryness and the product was crystallised from minimal amount of water with a drop of 5 % aq. NH_3 by diffusion of acetone. Absence of free Ni(II) was proved by negative reaction with 1 % dimethylglyoxime in EtOH.

Yield 87 mg (75 %).

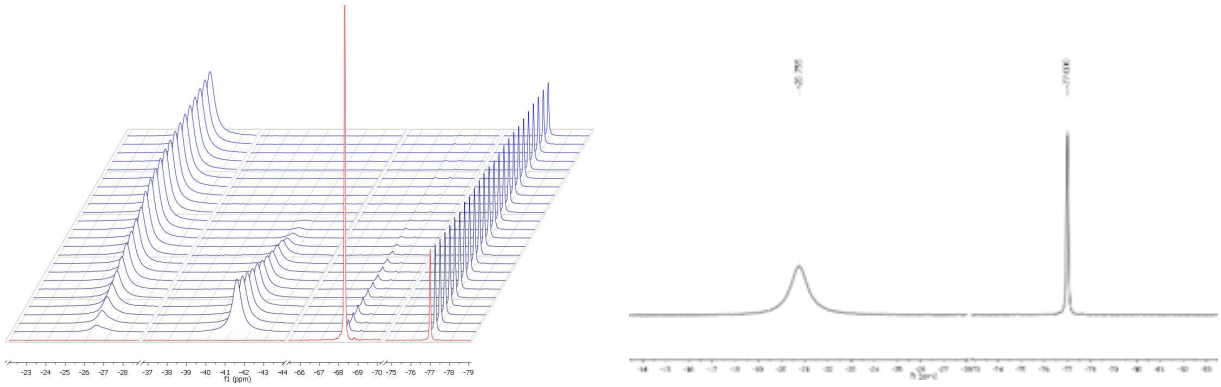
TLC: R_f = 0.5 (EtOH/aq. conc. NH_3 5/1).

NMR: Only extremely broad signals and no signals were found in ^{1}H NMR and ^{13}C/^{31}P NMR spectra, respectively. ^{19}F (282 MHz, D_2O, pD = 6.7, 25 °C): –20.8, T_1 = 2.32(5) ms, T_2* ≈1.3 ms.

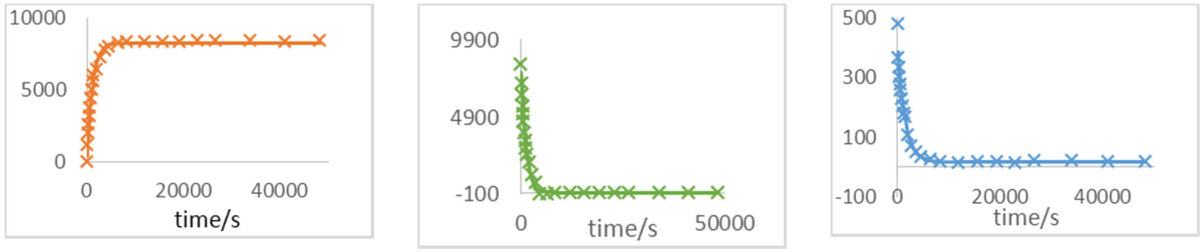
MS(+): 609.7 (calc. 609.1, [Ni{H_3te2p-tfe_2}]$^+$); MS(–): 607.5 (calc. 607.1, [Ni{Hte2p-tfe_2}]$^-$).

Elem. anal.: found C 28.03; H 5.71; N 10.15 (calc. for $(NH_4)\{$*trans*-[Ni(Hte2p-tfe$_2$)]$\}\cdot 3H_2O$, $C_{16}H_{41}F_6N_5NiO_9P_2$, M_r = 681.2; C, 28.17; H, 6.06; N, 10.27).
Single crystals of $(NH_4)\{$*trans*-[Ni(Hte2p-tfe$_2$)]$\}\cdot 3.25H_2O$ were prepared by acetone vapour diffusion into aq. solution of the complex containing slight excess of ammonia.

The following procedure was used to investigate mechanism of the complex formation by ^{19}F NMR. The ligand, H_4te2p-tfe$_2$, in zwitterionic form (10.6 mg, 17.3 µmol) was dissolved in D_2O (0.5 ml) containing 0.1 % *t*-BuOH and trifluoroethanol (TfeOH, 10 µL) was added. Solution pH was adjusted to 10.0 by adding of 5 % aq. NH_3, reaction mixture was heated to 75 °C and ^{19}F NMR spectrum was measured. Then, $NiCl_2\cdot 6H_2O$ (4.7 mg, 19.7 µmol, 1.1 eq) in D_2O (100 µL) was added and the reaction progress was followed by ^{19}F NMR over 13.5 h. The spectra were phase-corrected, and 10 Hz exponential apodization and baseline correction were applied. Time-dependence of integral values of signals at δ_F = –26.4 (*trans*-[Ni(te2p-tfe2)]$^{2-}$), –41.1 (intermediate) and –68.3 ppm (te2p-tfe$_2^{4-}$) was analysed using Matlab[3] using first order kinetic equation: $I(t) = A + B\cdot\exp(-k_{obs}t)$, where $I(t)$ are integral values in time, k_{obs} is the first-order rate constant and A and B are parameters characterising initial and final integral values. The results are shown in Figure S4.



A **B**



trans-[Ni(te2p-tfe$_2$)]$^{2-}$ Intermediate H_4te2p-tfe$_2$

C

Figure S4 (**A**): Time dependence of ^{19}F NMR spectra during Ni(II)–H_4te2p-tfe$_2$ complexation (blue lines); red line represents spectrum of the free ligand before $NiCl_2$ addition. As an internal standard, trifluoroethanol was used (75 °C, diluted aq. ammonia, pH ~10). (**B**): ^{19}F NMR spectrum of *trans*-[Ni(te2p-tfe$_2$)]$^{2-}$ in water (pH 7.4, 22 mM) with trifluoroethanol as internal standard (δ_F = –77 ppm) (**C**): Time dependences of ^{19}F NMR signal integral intensities (×) and fits (solid lines) using general equation $I(t) = A + B\cdot\exp(-k_{obs}t)$, where $I(t)$ are signal integral intensities at time t, k_{obs} is the first-order rate constant and A and B are scale factors characterising initial and final intensities. Values of the rate constants k_{obs} are following: decrease in concentration of the free ligand $^{lig}k_{obs} = 0.71(3)\cdot10^{-3}$ s^{-1}, decrease in concentration of the intermediate $^{int}k_{obs} = 0.85(8)\cdot10^{-3}$ s^{-1}, increase of concentration of the final product $^{cplx}k_{obs} = 0.89(7)\cdot10^{-3}$ s^{-1}.

X-ray diffraction

The selected crystals were mounted on a glass fibre in random orientation and the diffraction data were acquired at 150(1) K (Cryostream Cooler Oxford Cryosystem) using Mo-K_α radiation (λ = 0.71073 Å). The diffraction data were collected employing ApexII CCD diffractometer and analysed using the SAINT V8.27B (Bruker AXS Inc., 2012) program package. The structure was solved by direct methods (SHELXS97)[4] and refined by full-matrix least-squares techniques (SHELXL97)[5]. Absorption correction using Gaussian integration was applied.[6] All non-hydrogen atoms were refined anisotropically. Although hydrogen atoms were found in the electron difference map, they were fixed in original (those bound to nitrogen and oxygen atoms) or theoretical (those belonging to carbon atoms) positions using riding model with U_{eq}(H) = 1.2 U_{eq}(X) to keep a number of refined parameters low.

For compound **4**·2HCl·2H$_2$O, the ligand molecule lies on centre of symmetry, *i.e.* the independent unit consists from one half of formula unit. In the case of H$_4$te2p-tfe$_2$·4HBr·0.5H$_2$O, the independent unit consists from two halves of ligand molecules laying on symmetry centres and four bromide anions. In addition, a number of several low-intensity maxima in electron difference map points to a disordered solvate. It was attributed to 0.5 water molecule and squeezed off using PLATON.[7] The independent unit of *cis*-[Ni(**1**)(H$_2$O)$_2$](TsO)$_2$ is formed by whole molecular formula. For *cis*-[Ni(**1**)Cl$_2$], the molecule possess two-fold symmetry, with one half of the molecule as an independent unit. Electron map difference maxima close to fluorine atoms point to a disorder in trifluoromethyl group. This was best refined as staggered in two positions with fixed relative occupancy 95:5 and with isotropic refinement of atoms in the less-occupied positions. In the case of *trans*-[Ni(**1**)](ClO$_4$)$_2$, one half of centrosymmetric complex molecule and one perchlorate anion forms the independent unit. In the case of (NH$_4$){*trans*-[Ni(Hte2p-tfe$_2$)]}·3.25H$_2$O, the independent unit is formed by whole molecular formula. Water solvate molecules were best refined as disordered in several positions, making in total 3.25 molecules. Selected experimental data are listed in Table S1, and selected geometric parameters are listed in Table S2 and Table S3. Relevant data for the structures have been deposited at the Cambridge Crystallographic Data Centre.

Table S1 Experimental data for the reported crystal structures.

Parameter	**1**·2HCl·2H$_2$O	H$_4$te2p-tfe$_2$·4HBr·0.5H$_2$O	*cis*-[Ni(**1**)(H$_2$O)$_2$](TsO)$_2$	*cis*-[Ni(**1**)Cl$_2$]	*trans*-[Ni(**1**)](ClO$_4$)$_2$	*trans*-(NH$_4$)[Ni(Hte2p-tfe$_2$)]·3.25H$_2$O
Formula	$C_{14}H_{32}Cl_2F_6N_4O_2$	$C_{16}H_{37}Br_4F_6N_4O_{6.5}P_2$	$C_{28}H_{44}F_6N_4NiO_8S_2$	$C_{14}H_{26}Cl_2F_6N_4Ni$	$C_{14}H_{26}Cl_2F_6N_4NiO_8$	$C_{16}H_{39.5}F_6N_5NiO_{9.25}P_2$
M_r	473.34	885.08	801.50	494.00	622.00	684.68
Colour	colourless	colourless	light blue	light blue green	red	light blue
Habit	prism	prism	bar	prism	prism	bar
Crystal system	monoclinic	triclinic	orthorhombic	monoclinic	triclinic	monoclinic
Space group	P2$_1$/*n*	P–1	P*bca*	C2/*c*	P–1	P2$_1$/*n*
a [Å]	9.5863(6)	7.3372(2)	8.7262(3)	22.2787(9)	8.2589(8)	9.4281(4)
b [Å]	9.4059(7)	11.5789(3)	25.5904(15)	6.4382(3)	8.5203(7)	16.7420(7)
c [Å]	11.7418(8)	17.6946(4)	30.9247(18)	16.0685(7)	9.2443(8)	17.0428(6)
α [°]	90	85.446(1)	90	90	71.903(4)	90
β [°]	105.367(2)	88.825(1)	90	122.852(1)	68.416(3)	90.310(1)
γ [°]	90	80.982(1)	90	90	72.718(3)	90
V [Å^3]	1020.88(12)	1479.96(6)	6905.7(6)	1936.19(15)	562.54(9)	2690.09(19)
Z	2	2	8	4	1	4
$D_{calcd.}$ [g cm^{-3}]	1.540	1.986	1.542	1.695	1.836	1.691
μ [mm^{-1}]	0.390	5.625	0.768	1.341	1.200	0.938
Unique refl.	2354	6780	6742	2232	1490	6159
Obsd. refl. [$I > 2\sigma(I)$]	2157	5621	4408	1973	1080	4968
R; *R*' [$I > 2\sigma(I)$]	0.0324; 0.0354	0.0268; 0.0381	0.0563; 0.1029	0.0385; 0.0448	0.0498; 0.0775	0.0322; 0.0476
wR; *wR*' [$I > 2\sigma(I)$]	0.0787; 0.0814	0.0561; 0.0581	0.1060; 0.1212	0.0951; 0.0984	0.1168; 0.1331	0.0735; 0.0803
CCDC	1430241	1430242	1430240	1430237	1430238	1430239

Solid-state structure of 1·2HCl·2H$_2$O

Structure of the $(H_2\mathbf{4})^{2+}$ cation adopts common[8] conformation of diprotonated cyclam derivatives. It is stabilized by intramolecular hydrogen bond between protonated and unprotonated amino group ($d_{N\cdots N}$ = 2.99 and 3.01 Å) as shown in Figure S5. The structure confirms higher basicity of secondary amino groups comparing to tertiary ones.

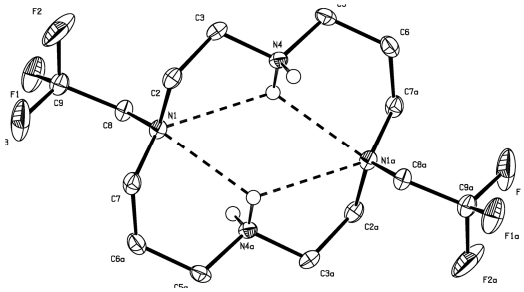
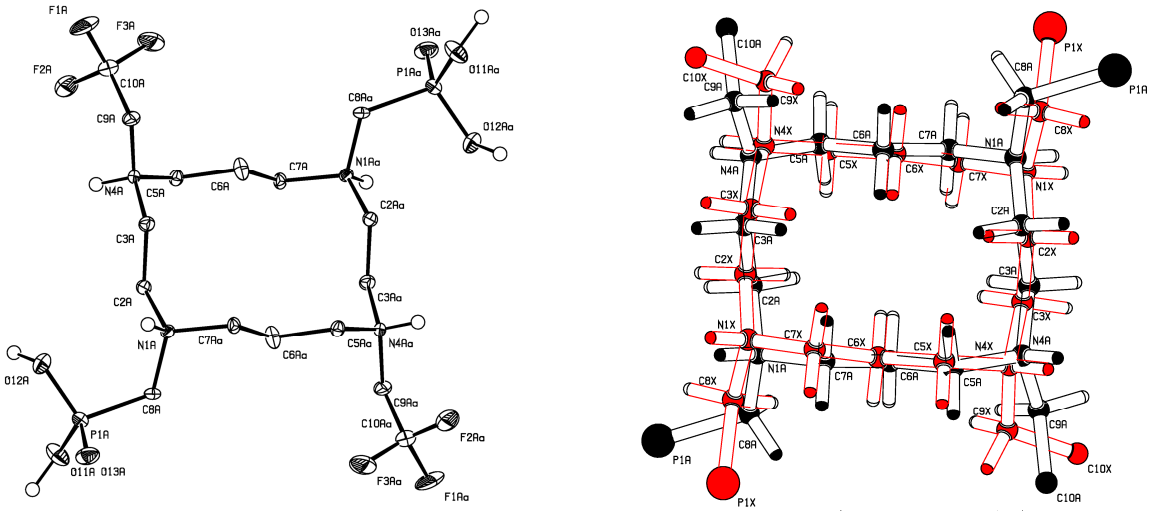


Figure S5 Molecular structure of the $(H_2\mathbf{1})^{2+}$ cation found in the crystal structure of **1**·2HCl·2H$_2$O. Intramolecular hydrogen bonds are dashed. Carbon-bound hydrogen atoms are omitted for clarity.

Solid-state structure of H$_4$te2p-tfe$_2$·4HBr·0.5H$_2$O

Fully protonated ligand molecule, $(H_8\text{te2p-tfe}_2)^{4+}$, found in the crystal structure of H$_4$te2p-tfe$_2$·4HBr·0.5H$_2$O, adopts rectangular conformation (3,4,3,4)-A[8] with nitrogen atoms in the corners (Figure S6A). It is the most frequently observed conformation of the fully protonated polyazamacrocycles.[8] The two independent ligand molecules exhibit almost identical geometric parameters of the macrocycle, but differ in orientation of pendant substituents (Figure S6B).



A **B**

Figure S6 (A): Molecular structure of cation $(H_8\text{te2p-tfe}_2)^{4+}$ found in the crystal structure of H$_4$te2p-tfe$_2$·4HBr·0.5H$_2$O. One of two independent ligand molecules is shown. Carbon-bound hydrogen atoms are omitted for clarity. (B): Overlay of two independent ligand molecules. Only pivot atoms of pendant substituents are shown.

Solid-state structure of *cis*-[Ni(1)Cl_2]

Two-fold symmetric molecule of *cis*-[Ni(**1**)Cl_2] shows slightly distorted octahedral sphere with macrocyclic ligand in *cis*-V configuration, with central Ni(II) on laying slightly "out" of the macrocycle (angle N1-Ni-$N1^{\#}$ = 171°) (Figure S7). Coordination bonds from tertiary amino groups are significantly longer (2.26 Å) comparing to those between the central metal ion and secondary amino groups (2.10 Å).

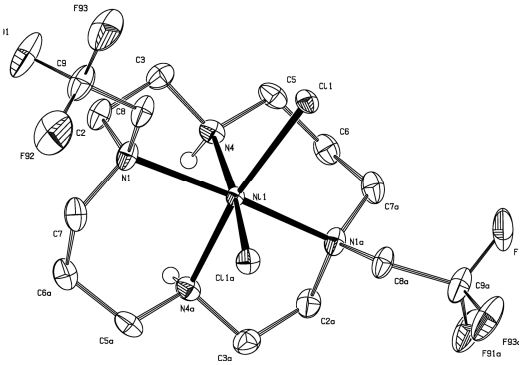


Figure S7 Molecular structure of *cis*-[Ni(**1**)Cl_2] found in its crystal structure. Carbon-bound hydrogen atoms are omitted for clarity.

Selected geometric parameters of Ni(II) coordination spheres found in the solid-state structures

Table S2 Coordination geometry of Ni(II) cation in the prepared complexes.

Parameter	*cis*-[Ni(**1**)(H_2O)$_2$](TsO)$_2$[a]	*cis*-[Ni(**1**)Cl_2][b]	*trans*-[Ni(**1**)](ClO_4)$_2$[c]	(NH_4){*trans*-[Ni(Hte2p-tfe$_2$)]}·3.25H_2O[d]
			Distances (Å)	
Ni–N1	2.217(3)	2.260(2)	1.992(5)	2.108(2)
Ni–N4	2.087(3)	2.100(2)	1.946(5)	2.221(2)
Ni–N8	2.254(3)	2.260(2)[#]	1.992(5)[$]	2.093(2)
Ni–N11	2.072(3)	2.100(2)[#]	1.946(5)[$]	2.229(2)
Ni–X1	2.100(2)	2.419(1)	–	2.063(1)
Ni–X2	2.072(2)	2.419(1)	–	2.102(1)
			Angles (°)	
N1-Ni-N4	83.23(12)	82.09(9)	87.9(2)	85.35(6)
N1-Ni-N8	171.80(11)	171.32(11)[#]	180[$]	178.02(6)
N1-Ni-N11	92.25(11)	91.95(9)[#]	92.1(2)	93.98(6)
N1-Ni-X1	97.53(10)	96.75(6)	–	86.62(6)
N1-Ni-X2	90.09(11)	89.48(6)	–	95.97(6)
N4-Ni-N8	90.67(12)	91.95(9)[#]	92.1(2)[$]	93.77(6)
N4-Ni-N11	96.01(11)	93.59(12)[#]	180[$]	179.24(6)
N4-Ni-X1	92.50(10)	89.67(6)	–	91.02(6)
N4-Ni-X2	172.01(11)	171.06(7)	–	91.37(6)
N8-Ni-N11	82.91(11)	82.09(9)[#]	87.9(2)[$]	86.89(6)
N8-Ni-X1	88.17(10)	89.48(6)[#]	–	91.63(6)
N8-Ni-X2	96.38(11)	96.75(6)[#]	–	85.82(6)
N11-Ni-X1	167.73(12)	171.06(7)[#]	–	88.59(6)
N11-Ni-X2	88.60(11)	89.67(6)[#]	–	89.04(6)
X1-Ni-X2	84.01(9)	88.35(3)	–	176.61(5)

[a]X1 = O1W, X2 = O2W. [b]X1 = Cl1, X2 = Cl1[#]. [#]two-fold symmetry-related atoms: N8 = N1[#], N11 = N4[#], # = –x+2, y, –z+1/2. [c] N8 = N1[$], N11 = N4[$], $ = –x+1, –y+1, –z+1. [d]X1 = O11, X2 = O21.

Table S3 The Ni···F distances found in crystal structures of the studied Ni(II) complexes.

cis-[Ni(**1**)(H_2O)$_2$](TsO)$_2$		*cis*-[Ni(**1**)Cl_2]		*trans*-[Ni(**1**)](ClO_4)$_2$		(NH_4){*trans*-[Ni(Hte2p-tfe$_2$)]·3.25H_2O	
Atoms	Distances (Å)	Atoms	Distances (Å)	Atoms	Distances (Å)	Atoms	Distances (Å)
Ni···F161	5.297	Ni···F91	5.127	Ni···F91	4.872	Ni···F181	5.151
Ni···F162	5.045	Ni···F91A	5.086	Ni···F92	5.033	Ni···F182	5.113
Ni···F163	5.107	Ni···F92	5.032	Ni···F93	4.848	Ni···F183	5.360
Ni···F181	5.325	Ni···F92A	5.237	–	–	Ni···F201	5.126
Ni···F182	5.087	Ni···F93	5.281	–	–	Ni···F202	5.117
Ni···F183	5.114	Ni···F93A	5.105	–	–	Ni···F203	5.458

Potentiometry

Stock solution of $Ni(NO_3)_2$ was prepared by dissolution of recrystallized hydrate in water. The Ni(II) content was determined by titration with Na_2H_2edta standard solution. A standard HCl was prepared by dilution of conc. HCl (purris. grade, Aldrich). A standard NMe_4OH solution was prepared by passing an aq. NMe_4Cl solution through a Dowex 1 column in the OH^--form under argon atmosphere and using CO_2-free deionized water.[9] A carbonate-free NMe_4OH solution (~0.2 M) was standardized against potassium hydrogen phthalate, and the HCl stock solution (~0.03 M) against the NMe_4OH standardized solution. Ligand concentration in the stock solution was calculated from the weighted amount of the solid ligand, and it corresponded well with the value obtained during fitting procedure together with determination of the protonation constants. Water ion product was taken from the literature ($pK_W = 13.81$).[10] The constants with their standard deviations were calculated with the OPIUM program package.[11] The program minimises the criterion of the generalized least squares method using the calibration function $E = E_0 + S\cdot\log[H^+] + j_1\cdot[H^+] + j_2\cdot K_W/[H^+]$ where the additive term E_0 contains the standard potentials of the electrodes used and the contributions of inert ions to the liquid-junction potential, term S corresponds to the Nernstian slope, and the $j_1\cdot[H^+]$ and $j_2\cdot K_W/[H^+] = j_2\cdot[OH^-]$ terms describe contributions of the H^+ and OH^- ions to the liquid-junction potential, respectively. The calibration parameters were determined from titration of the standard HCl with the standard NMe_4OH solutions before and after each titration of ligand or ligand/metal ion mixture to give calibration-titration pairs used for calculations of the constants. Titrations were carried out in a thermostatted vessel at 25.0±0.1 °C, at constant ionic strength $I(NMe_4Cl) = 0.1$ M, using a PHM 240 pH-meter, a 2-ml ABU 900 automatic piston burette and a GK 2401B combined electrode (all Radiometer). The concentration of the ligand was approximately 0.004 M and ligand-to-metal ratio was 1:1. An inert atmosphere was ensured by a constant passage of argon saturated with the water vapours.

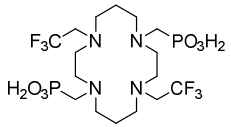
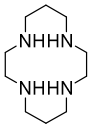
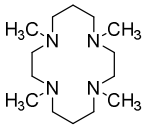
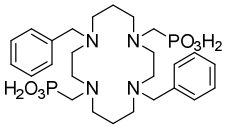
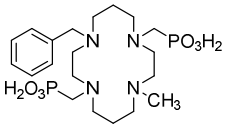
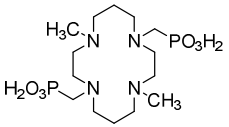
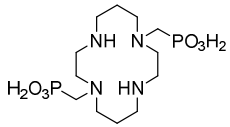
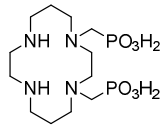
The measurements were taken with HCl excess added to the initial mixture, and the mixtures were titrated with stock NMe_4OH solution. In a study of protonation equilibrium of the free ligand, the systems were studied by conventional titrations in the pH range 1.8–12.0 (~40 data points per titration). The initial volume was ~5 cm^3 and four parallel titrations were carried out. The equilibrium in Ni(II)–H_4te2p-tfe$_2$ system was established slowly and, therefore, out-of-cell technique was used. Each solution as titration data point (~1 cm^3) was prepared separately in an ampoule which was flame-sealed. Two parallel sets of ampoules were equilibrated at 50 °C for 2 weeks. The ampoules were cooled down and left at room temperature for 24 h. The electrode potential at each titration point (ampoule) was determined for each titration set with freshly calibrated electrode. Titrations were done in pH range 2.4–7.0 with ~20 points per each titration set. Calculated overall protonation and stability constants are compiled in Table S4 and their comparison with published data is given in Table S5.

Table S4 Overall protonation ($\log\beta_h$) and stability ($\log\beta_{hlm}$) constants, and consecutive protonation constants of H_4te2p-tfe$_2$ and its *trans* Ni(II) complex (I = 0.1 M NMe_4Cl, 25 °C).

h	$\log\beta_h$	$\log K(H_hL)$	h	l	m	$\log\beta_{hlm}$	$\log K(H_hLM)$
1	10.857(5)	10.86	0	1	1	13.28(6)	–
2	20.956(5)	10.09	1	1	1	19.13(5)	5.85
3	26.557(9)	5.60	2	1	1	23.58(33)	4.4
4	31.289(8)	4.73					

$\beta_h = [H_hL]/\{[H]^h\cdot[L]\}$. $K(H_hL) = [H_hL]/\{[H]\cdot[H_{h-1}L]\}$.
$\beta_{hlm} = [H_hL_lM_m]/\{[H]^h\cdot[L]^l\cdot[M]^m\}$. $K(H_hLM) = [H_hLM]/\{[H]\cdot[H_{h-1}LM]\}$.

Table S5 Comparison of consecutive protonation constants log$K$(H_hL) and stability and protonation constants of Ni(II) complexes of H_4te2p-tfe$_2$ with related ligands.

h	H_4te2p-tfe$_2$	cyclam [12]	tmc [12]	1,8-H_4te2p-Bn$_2$ [13]	1,8-H_4te2p-Bn,Me [13]	1,8-H_4te2p-Me$_2$	1,8-H_4te2p	1,4-H_4te2p [14]
								
				log$K$(H_hL)				
1	10.86 [a]	11.4 [a]	9.36 [a]	10.53 [a]	10.87 [a]	11.47 [a] [13]	–	–
2	10.09 [a]	10.28 [a]	9.02 [a]	10.68 [a]	11.42 [a]	12.17 [a] [13]	26.41 [#] [13]	25.72 [#]
3	5.60 [b]	1.6 [a]	2.54 [a]	7.10 [b]	7.24 [b]	7.20 [b] [13]	6.78 [b] [13]	6.56 [b]
4	4.73 [b]	2.1 [a]	2.25 [a]	6.44 [b]	6.38 [b]	6.33 [b] [13]	5.36 [b] [13]	5.19 [b]
5	–	–	–	–	1.60 [c]	1.52 [c] [13]	1.15 [c] [13]	2.30 [c]
6	–	–	–	–	1.0 [c]	0.85 [c] [13]	–	–
				logK_{NiL}				
	13.28	22.2	8.65	–	–	15.55 [15]	21.99 [16]	21.92
				log$K$(NiH_hL)				
1	5.85 [b]	–	–	–	–	7.27 [b] [15]	7.31 [b] [16]	6.14 [b]
2	4.4 [b]	–	–	–	–	5.1 [b] [15]	4.77 [b] [16]	5.12 [b]

[a]Protonation of macrocycle amino group. [b]Protonation of phosphonate moiety to $–PO_3H^–$. [c]Unresolved simultaneous protonation of ring amino group and hydrogenphosphonate moiety to $–PO_3H_2$. [#]Overall protonation constant for two consecutive steps, log$K$(HL)+log$K$(H_2L).
Constants are defined in following way (charges are omitted for clarity):
$K(H_hL) = [H_hL] / \{[H]\cdot[H_{h-1}L]\}$
$K_{NiL} = [NiL] / \{[Ni]\cdot[L]\}$
$K(NiH_hL) = [NiH_hL] / \{[H]\cdot[NiH_{h-1}L]\}$.

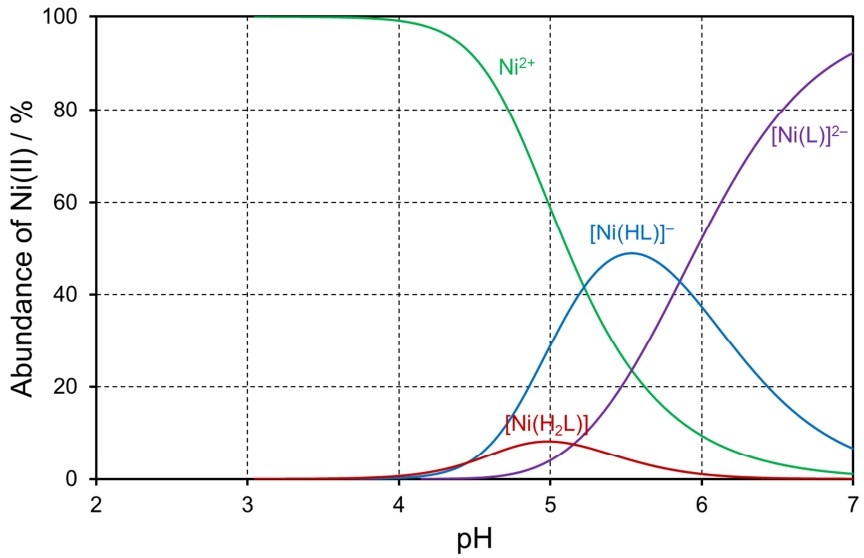


Figure S8 Distribution diagram of the Ni(II)–H_4te2p-tfe_2 system (c_M = c_L = 0.004 M, I = 0.1 NMe_4Cl, "frozen" equilibrium at 50 °C, measured at 25 °C).

Dissociation kinetics studies

Inertness of the *trans*-[Ni($H_n$te2p-tfe_2)]$^{n-2}$ (0.5 mM) and [Ni(**1**)$(H_2O)_2$]$^{2+}$ (0.8 mM) complexes against acid-assisted dissociation was studied in 1 M aq. HCl at 37 and 80 °C using UV spectroscopy at 230 nm. The rate constants were determined by regression analysis using equation for the first-order kinetics, $A_{230}(t) = a + b\cdot\exp(-k_{obs}t)$, where $A_{230}(t)$ is absorbance at 230 nm in a time, k_{obs} is first-order reaction rate constant, and a and b are parameters characterising initial and final absorbance of the sample. The values of k_{obs}, reaction half-life time ($\tau_{½}$) and time for dissociation from 99 % (τ_{99}) are compiled in Table S6.

Table S6: First-order rate constant (k_{obs}), reaction half-life ($\tau_{½}$) and 99 % reaction time (τ_{99}) for HCl-assisted dissociation of studied complexes in 1 M aq. HCl.

Parameter	Complex			
	cis-[Ni(**1**)$(H_2O)_2$]$^{2+}$		*trans*-[Ni($H_n$te2p-tfe_2)]$^{(n-2)}$	
t / °C	37	80	37	80
k_{obs} / $10^{-5}\cdot s^{-1}$	2.442(1)	417(2)	2.005(2)	4.24(1)
$\tau_{½}$ / h	7.883(1)	0.0462(2)	9.60(1)	4.54(1)
τ_{99} / h	52.26(1)	0.306(2)	63.67(7)	30.12(6)

^{19}F NMR/MRI

Aqueous solutions of samples 1) 10 mM *trans*-$(NH_4)_2$[Ni(te2p-tfe$_2$)] 2) 10 mM H_4te2p-tfe$_2$ and 3) 20 mM trifluoroethanol (fluorine concentration was identical in all samples) were filled into separate 1 ml glass vials.

MR Imaging was measured on 4.7-T Bruker MRI scanner equipped with a home-made ^{1}H/^{19}F surface single loop coil (diameter 40 mm), tunable to both 200 (^{1}H) and 188 (^{19}F) MHz.

Base ^{1}H images (200 MHz) were acquired using a T_1-weighted gradient echo sequence with TE = 3.715 ms and TR = 99 ms, FOV = 35×35 mm, matrix 256×256.

^{19}F MR images were obtained using a gradient echo sequence with TE = 1.3 ms and TR = 3 ms optimized for visualization of fast relaxing signals. Slowly relaxing samples were visualized using turbospin echo sequence employing TE = 40 ms and TR = 2000 ms. Field of view (FOV) was 35×35 mm, slice thickness 5 mm, matrix 32×32. The matrix was interpolated to 256×256 to match that of proton images. Acquisition times of ^{19}F MRI experiments were approx. 34 min.

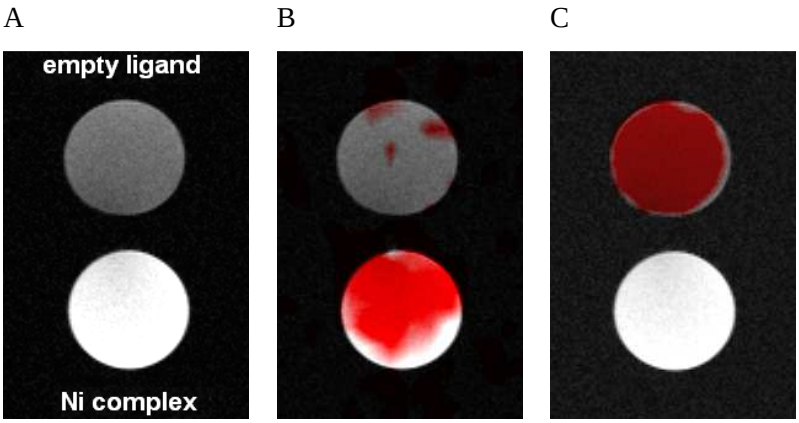


Figure S9 MRI study of phantoms containing free ligand **1** and *cis*-[Ni(**1**)$(H_2O)_2$]$(ClO_4)_2$ complex (c_F = 0.004 M in both samples), B = 4.7 T, 25 °C, home-made ^{1}H/^{19}F surface single loop coil. (**A**): ^{1}H MRI scan, gradient echo sequence, flip angle 30°, TE = 3.7 ms, TR = 100 ms, matrix 256×256. (**B**): Overlay of ^{1}H MRI with ^{19}F MRI; ^{19}F MRI was optimized for the complex; acquired at δ = –26 ppm, gradient echo sequence, TE = 1.3 ms, TR = 3 ms, matrix 32×32 interpolated to 256×256. (**C**): Overlay of ^{1}H MRI with ^{19}F MRI; ^{19}F MRI was optimized for the ligand; acquired at δ = –70 ppm, turbospin echo sequence, TE = 40 ms, TR = 2000 ms, matrix 32×32 interpolated to 256×256.

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