Journal Name

RSCPublishing

ARTICLE

A study of anion binding behaviour of 1,3-*alternate* thiacalix[4]arene–based receptors bearing urea moieties†

Cite this: DOI: 10.1039/xoxxoooooox

Received ooth January 2012,
Accepted ooth January 2012

DOI: 10.1039/xoxxoooooox

www.rsc.org/

Shofiur Rahman,[a,b] Hirotsugu Tomiyasu,[a] Hiroto Kawazoe,[a] Jiang-Lin Zhao,[a] Hang Cong,[c] Xin-Long Ni,[c] Xi Zeng,[c] Mark R. J. Elsegood,[d] Thomas G. Warwick,[d] Simon J. Teat,[e] Carl Redshaw,[f] Paris E. Georghiou[b] and Takehiko Yamato*[a]

Three novel thiacalix[4]arene receptors **4**$_{a\sim c}$ each with a 1,3-*alternate* conformation and possessing two urea moieties linking various phenyl groups substituted with either *para* electron-donating or -withdrawing groups have been synthesized. The binding properties of these receptors were investigated by means of ^{1}H NMR spectroscopy and UV-vis absorption titration experiments using various anions. The structures and complexation energies were also studied by density functional theory (DFT) methods. The results suggested that receptor **4**$_c$, which possesses two *p*-(trifluoromethyl)phenyl ureido moieties, can complex most efficiently in the urea cavity and exhibits high selectivity towards F^- and AcO^- ions.

Introduction

Calix[*n*]arenes[1] have three-dimensional tuneable shapes and are used as molecular building blocks with potentially many applications in supramolecular chemistry. Thiacalix[4]arenes[2,3] are calix[*n*]arenes in which the phenolic groups are bridged by sulfur atoms instead of methylene groups, and have received much recent attention for potential applications in various fields across chemistry, biology and environmental science. Various anions such as F^- (e.g., in dental caries prevention, in inhalation anesthetics and in the treatment of osteoporosis) also play fundamental roles in biological, medicinal, catalysis, and environmental chemistry.[4] The design and synthesis of anion-selective receptors[5] is more difficult than that of cation-selective receptors. This is due to some unique features of anions such as their much larger sizes in comparison with those of cations, and also due to the large variety of geometries available,[6] some anions are spherical (F^-, Cl^-, Br^-, I^-) others are trigonal or Y-shaped (AcO^-) and others are tetrahedral ($H_2PO_4^-$), etc.. Anion recognition using artificially-designed receptors[6] based on calix[*n*]arenes is an important research topic in the area of supramolecular chemistry. Calix[*n*]arene urea derivatives are capable of effectively recognizing and sensing important anions via hydrogen-bonding interactions between the anions and the urea NH protons.[7,8]

Lhoták and co-workers[9] have reported anion receptors based on either upper-rim substituted calix[4]arenes or thiacalix[4]arenes which contain two *p*-nitrophenyl or *p*-tolyl urea moieties.[9a~c,h] These anion receptors exhibited effective recognition abilities towards selected anions in common organic solvents. Recently, Kumar and co-workers reported an anion receptor based on a calix[4]arene in a 1,3-*alternate* conformation and bearing containing two *p*-nitrophenyl-ureido moieties.[10] This compound exhibited strong binding and good selectivity towards Cl^- ion due to strong hydrogen bonding between the Cl^- ion and the N-H protons, both in THF or chloroform solutions. However, investigations concerning the influence on the acidity of the urea protons by either electron–donating or electron–withdrawing groups located on the *p*-position of phenyl groups of urea moieties in analogous thiacalix[4]arenes and the binding of various anions have received scant attension.[11j]

In this article, we report the synthesis of three novel thiacalix[4]arenes receptors **4**$_{a\sim c}$ with a 1,3-*alternate* conformation and possessing two urea moieties linking various

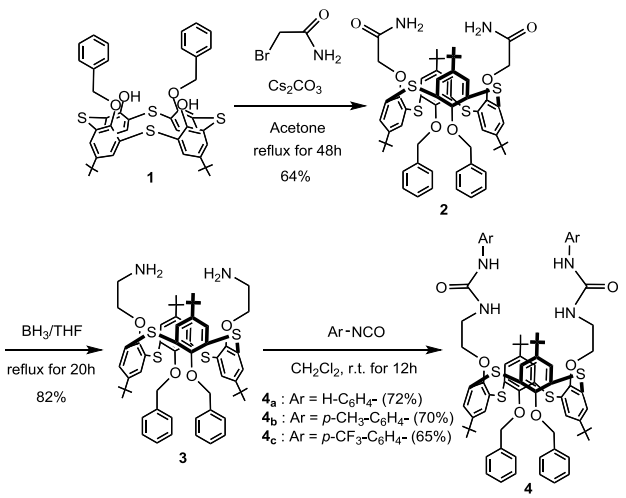
[a]*Department of Applied Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi 1, Saga 840-8502 Japan, E-mail: yamatot@cc.saga-u.ac.jp*
[b]*Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland and Labrador A1B 3X7, Canada*
[c]*Department Key Laboratory of Macrocyclic and Supramolecular Chemistry of Guizhou Province, Guizhou University, Guiyang, Guizhou, 550025, China*
[d]*Chemistry Department, Loughborough University, Loughborough LE11 3TU, UK.*
[e]*ALS, Berkeley Lab, 1 Cyclotron Road, Bereleley, CA 94720, USA*
[f]*Department of Chemistry, The University of Hull, HU6 7RX, UK*
†Electronic Supplementary Information (ESI) available: Details of the ^{1}H/^{13}C NMR spectra, ^{1}H NMR spectroscopic and UV-vis titration experimental data and computational studies. See DOI: 10.1039/b000000x/

phenyl groups bearing either *para* electron-donating or electron-withdrawing groups, together with two benzyl groups at the opposite sides of the thiacalix[4]arene cavity.[11] In our studies, the complexation properties of $\mathbf{4}_{\mathbf{a\sim c}}$ towards F^-, Cl^-, Br^-, I^-, AcO^- and $H_2PO_4^-$ ions were investigated by ^{1}H-NMR spectroscopy (with $\mathbf{4}_{\mathbf{a\sim c}}$) and UV-vis absorption (with $\mathbf{4}_{\mathbf{c}}$) titration experiments. Furthermore, the structures and complexation energies for all complexes of the receptors $\mathbf{4}_{\mathbf{a\sim c}}$ with various anions were also determined by theoretical studies using DFT methods.

Results and discussions

Synthesis

O-Alkylation of 1,3-*alternate*-**1** was conducted using 2 equivalents of bromoacetamide in the presence of 2 equivalents of Cs_2CO_3 according to the reported procedure, and afforded the desired 1,3-*alternate*-**2** in 60 % yield.[12] The amide reduction of 1,3-*alternate*-**2** was carried out with a large excess of BH_3/THF solution, and afforded the desired 1,3-*alternate*-**3** in 65 % yield. The condensation of 1,3-*alternate*-**3** with 2.2 equivalents of the appropriate isocyanate in CH_2Cl_2 furnished the receptors $\mathbf{4}_{\mathbf{a\sim c}}$ in good yields (Scheme 1). The ^{1}H NMR spectrum of receptors $\mathbf{4}_{\mathbf{a\sim c}}$ in $CDCl_3$ exhibits the characteristics of a 1,3-*alternate* conformation such as two singlets (18H each) for the *tert*-butyl protons, two triplets (4H each) for the -OCH_2CH_2- protons, two singlets (4H each) for the aromatic protons and two singlets (2H each) for the four urea NH protons. Moreover, concentration dependence of the ^{1}H NMR chemical shifts of the urea protons in receptor $\mathbf{4}_{\mathbf{c}}$ was not observed (Fig. S11). This (lack of) observation indicates that receptor $\mathbf{4}_{\mathbf{c}}$ has strong intramolecular hydrogen bonds between the two urea groups linking the *p*-(trifluoromethyl)phenyl moieties. The molecular structure of receptor $\mathbf{4}_{\mathbf{a}}$ was also verified by X-ray crystallographic analysis (Fig. 1, S12). Receptor $\mathbf{4}_{\mathbf{a}}$ was recrystallized from a mixture of



Scheme 1 Synthesis of receptors 1,3-*alternate*-$\mathbf{4}_{\mathbf{a\sim c}}$.

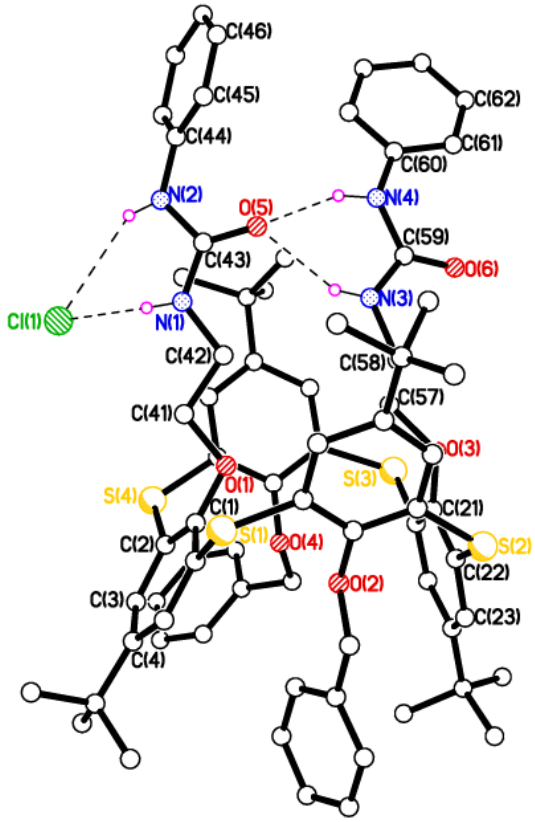


Fig. 1 X–ray crystal structure of receptor $\mathbf{4}_{\mathbf{a}}\cdot Cl^-$. H–bonds shown as dashed lines. One of four similar molecules in the asymmetric unit is shown in two orientations rotated by approx. 90°. H atoms not involved in H-bonding, minor disorder components, and solvent of crystallization are omitted for clarity. Guest used: tetrabutylammonium (TBA) salt.

$CHCl_3$–CH_3CN (3:2, v/v) by slow evaporation. These results indicate that receptor $\mathbf{4}_{\mathbf{a}}$ adopts the 1,3-*alternate* conformation in the solid state. In case of receptor $\mathbf{4}_{\mathbf{a}}$, there are four thiacalixarenes, two Cl^- ions, two tetrabutylammonium ions, one chloroform and two acetonitrile molecules in the asymmetric unit. Interestingly, it was found that the two urea groups approach each other and are oriented in parallel due to the existence of dual intramolecular hydrogen bonding (in the case of receptor $\mathbf{4}_{\mathbf{a}}$, for the molecule shown: N(3)–H(3)···O(5) 2.13(3); N(4)–H(4)···O(5) 2.17(3) Å; for the second molecule: N(1A)–H(1A)···O(6A) 2.15(3), N(2A)–H(2A)···O(6A) 2.20(3) Å; for the third molecule: N(3B)–H(3B)···O(5B) 2.30(3), N(4B)–H(4B)···O(5B) 2.17(2) Å; for the fourth molecule: N(1C)–H(1C)···O(6C) 2.31(3), N(2C)–H(2C)···O(6C) 2.27(3) Å) (Fig. 1, S12). Moreover, in the case of receptor $\mathbf{4}_{\mathbf{a}}$, pairs of calixarene molecules are linked via four H-bonds between two urea NH moieties on each calixarene and Cl^- ion.

Table 1. Association constants[a] of receptors $\mathbf{4}_{a\sim c}$ with anions.[b]

Host	R	Association constant K_a [M^{-1}]					
		F^- Spherical	Cl^- Spherical	Br^- Spherical	I^- Spherical	AcO^- Y-shape	$H_2PO_4^-$ Tetrahedral
$\mathbf{4}_a$	H	6,745±472	2,937 ±206	1,453±102	410±29	6,305±441	2,727±191
$\mathbf{4}_b$	Me	3,550 ±286	1,557±109	734±51	203±14	3,033±212	1,338±94
$\mathbf{4}_c$	CF_3	13,950 ±977	6,590±461	2,920±204	883 ±62	12,878±901	5,790±405

[a] Measured in $CDCl_3$–CD_3CN (10:1, v/v) at 298 K by the ^1H NMR titration method using the chemical-shift change of the NH_a proton (Fig. S13–S49); host concentration was 4.0×10^{-3} M. [b] Guests used: TBA salts.

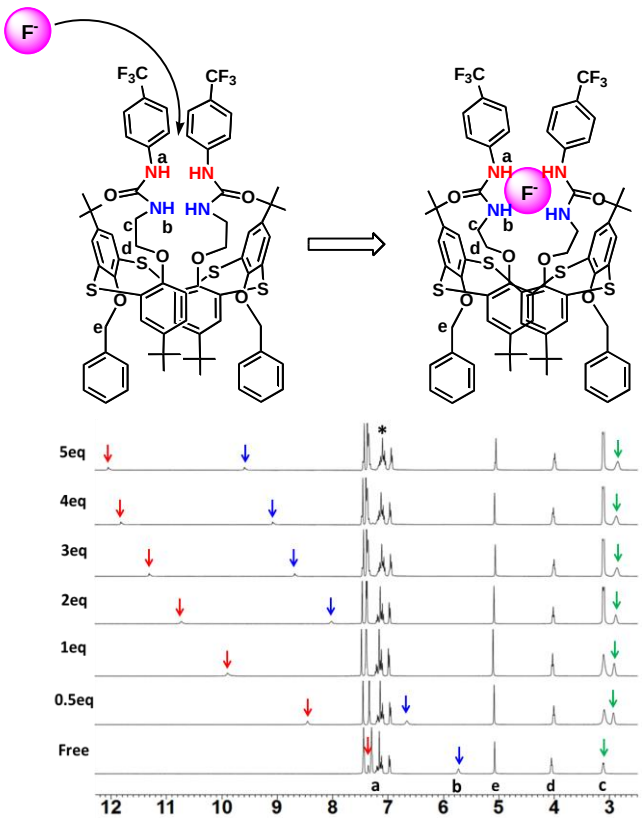


Fig. 2 Binding mode of receptor 4c upon addition of F^- ion at 298 K as TBA salts and partial ^1H NMR spectra of $\mathbf{4}_c$ (4.0×10^{-3} M) in $CDCl_3$–CD_3CN (10:1, v/v) upon addition of F^- ion at 298 K.

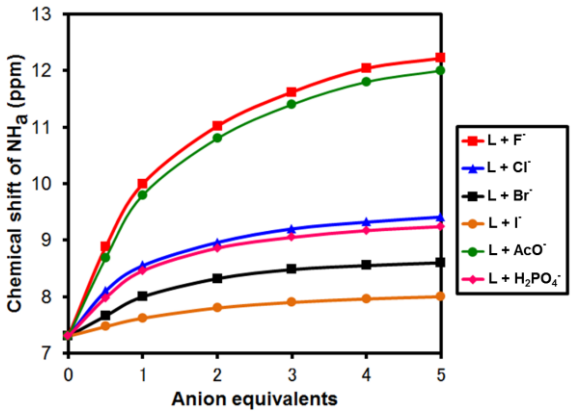


Fig. 3 Titration curves of receptor $\mathbf{4}_c$ with various anions as their TBA salts in $CDCl_3$–CD_3CN (10:1, v/v) at 298 K.

Binding studies

The binding properties of receptors $\mathbf{4}_{a\sim c}$ in the presence of various anions as their tetrabutylammonium (TBA) salts, in $CDCl_3$–CD_3CN (10:1) solution, were investigated by means of ^1H-NMR titration spectroscopic experiments. As shown in Fig. 2, for the complexation of F^- ion with receptor $\mathbf{4}_c$, the signals for the NH_a protons (red) progressively shifted downfield by 4.55 ppm (δ = 7.35 to 11.9 ppm) until five equivalents of F^- ion was added. On the other hand, the signals for the NH_b protons (blue) progressively shifted downfield by 3.88 ppm (δ = 5.72 to 9.60 ppm) until five equivalents of F^- ion were added. These results are strongly suggestive of F^- ion recognition by receptor $\mathbf{4}_c$ via hydrogen–bonding interactions between the F^- ion and the N–H protons. The titration curves shown in Fig. 2, 3 (for $\mathbf{4}_c$) and Fig. S13–S49 show that further addition of various anions to the solution of each receptors $\mathbf{4}_{a\sim c}$ in $CDCl_3$ solution, resulted in clear downfield shifts of the ^1H NMR signals of the NH_a protons. All of the results obtained clearly suggest that anion recognition by the receptors is via hydrogen-bonding interactions between the anion and the NH protons. In particular, as shown in Fig. 2, receptor $\mathbf{4}_c$ exhibited the highest selectivity amongst all of the anions tested, toward F^- and AcO^- ions. K_a values for receptors $\mathbf{4}_{a\sim c}$ and the anions tested were determined by ^1H NMR spectroscopic titration experiments.[13a] (Table 1). These results suggest that the K_a values are influenced by the electron-donating or electron-withdrawing groups located at the *p*-position of the phenyl

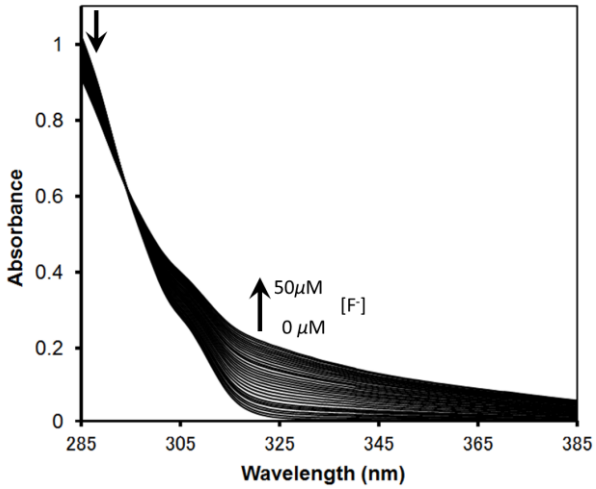


Fig. 4 UV–vis absorption spectra of receptor $\mathbf{4_c}$ (2.5 μM) upon the addition of F^- (0–50 μM) at 298 K as a TBA salt in CH_2Cl_2.

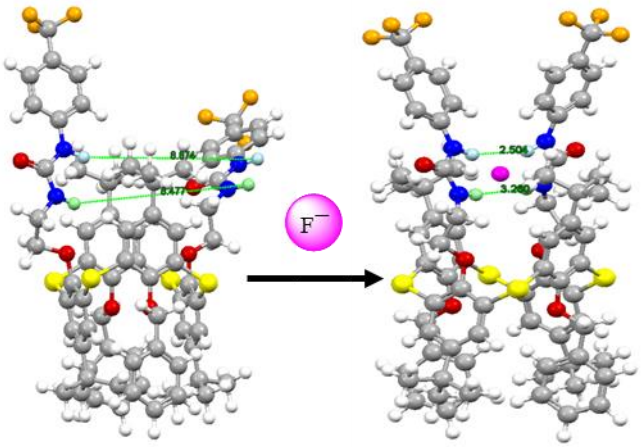


Fig. 5 Geometry-optimized (ball-and-stick) structures of: *Left*: $\mathbf{4_c}$; *Right*: 1;1 complex of $\mathbf{4_c}\supset F^-$. Colour code: F^- = magenta; nitrogen = blue; NH_a = light blue; NH_b = light green; sulphur = yellow; CF_3(fluoride) = orange; and oxygen atom = red.

Table 2. Association constants[a] of receptors $\mathbf{4_c}$ with anions.[b]

Anion	F^-	Cl^-	AcO^-	$H_2PO_4^-$
K_a [M^{-1}]	465,405±32,578	9,060±634	418,495±29,519	8,258±578

[a] Measured in CH_2Cl_2 at 298 K by UV–vis titration method (Fig. S50–S58); host concentration was 2.5 μM. [b] Guests used: TBA salts.

ureido moieties. The K_a values for $\mathbf{4_c}$ having the electron-withdrawing CF_3 groups on the phenyl ureido moieties, were greater than those for the other two receptors. The K_a values for $\mathbf{4_b}$ which had the electron-donating CH_3 groups on the ureido phenyl moieties were lower than those for $\mathbf{4_a}$ and $\mathbf{4_b}$. Therefore, the introduction of electron–withdrawing groups at the *p*-position of the phenyl ureido groups appears to increase the acidity of the urea protons, and hence enhance the anion-binding ability through hydrogen-bonding interactions. Furthermore, receptor $\mathbf{4_c}$ had the highest K_a values of all three receptors with each of the anions tested and also had the most effective recognition ability toward F^- and AcO^- ions. Further complexation studies of $\mathbf{4_c}$ with F^-, Cl^-, AcO^- and $H_2PO_4^-$ ions were carried out using UV–vis spectroscopic titration experiments. Receptor $\mathbf{4_c}$ (2.5 μM) exhibits a broad absorption band at 295 nm in its UV–vis absorption spectrum. Upon addition of F^- ion (0–50 μM) to the solution of $\mathbf{4_c}$, Fig. 4 reveals a gradual decrease in the absorption of the band at 288 nm with a simultaneous increase in the absorption at 320 nm and a clear isosbestic point at 295 nm. From the above, it is clear that receptor $\mathbf{4_c}$ bearing the CF_3 groups has the most effective recognition ability toward F^- ions. A Job's plot for the binding between the receptor $\mathbf{4_c}$ and F^- ion reveals a 1:1 stoichiometry (Fig. S52), and the K_a for the complexation[13b] of receptor $\mathbf{4_c}$ with F^- ion was determined to be 465,405 ± 32,578 M^{-1} by the UV–vis titrations in CH_2Cl_2 solution (Fig. S51). These results strongly suggested that F^- ion recognition by receptor $\mathbf{4_c}$ was via a hydrogen-bonding interaction between F^- ion and NH protons, as shown in Fig. 4. The K_a values obtained by similar UV-vis titration experiments of $\mathbf{4_c}$ with the other anions are summarized in Table 2. To further investigate the binding properties of receptors $\mathbf{4_{a\sim c}}$ with the anions tested, a computational study was carried out. The individual structures for all studies in the gas-phase were fully geometry-optimized using Gaussian 09[14] with the B3LYP level of DFT and the 3-21G basis set. Significant changes were observed for the distances between two urea NH moieties on each of the receptors $\mathbf{4_{a\sim c}}$ in their anion complexes. The conformation changes for $\mathbf{4_c}$ upon 1:1 complexation with F^- ion can be seen in Fig. 5 (more precise details for the computation studies for receptors $\mathbf{4_{a\sim c}}$ with the different anions are shown in Fig. S59–S94). Fig. 5 shows the computed structure (*right*) of the 1:1 complex of $\mathbf{4_c}$ with F^- ion. Because of the hydrogen-bonding between the F^- ion and two urea NH protons, distances between two urea NH moieties ($NH_a\cdots NH_{a'}$ and $NH_b\cdots NH_{b'}$) on two *p*-(trifluoromethyl)phenyl ureido moieties decrease from 8.783 to 2.530 (Å) and from 8.379 to 3.251 (Å), respectively. This also strongly supports the experimental evidence obtained for the formation of a 1:1 ($\mathbf{4_c}\supset F^-$) complex. The calculated complexation energies (ΔE kJ mol^{-1}) for receptors $\mathbf{4_{a\sim c}}$ with the anion complexes are shown in Table 3. The trend for the complexation energies for $\mathbf{4_{a\sim c}}$ are in the order: $F^- > AcO^- > H_2PO_4^- > Cl^- > Br^- > I^-$, which is in agreement with the trend observed for the observed complexation data obtained by means of ^1H NMR spectroscopy and UV-vis absorption titration experiments.

Conclusion

In summary, three novel receptors $\mathbf{4_{a\sim c}}$ bearing a thiacalix[4]arene in a 1,3-*alternate* conformation have been synthesized. These receptors possess two ureas moieties linking various aryl groups bearing electron-donating or -withdrawing groups at their *p*-positions, which act as anion-binding sites and two benzyl groups at the opposite side of thiacalix[4]arene cavity. The binding of various anions at the two urea moieties was investigated by using ^1H NMR, UV-vis absorption titration experiments. It was found that receptor $\mathbf{4_c}$ has a much higher

affinity towards all of the selected anions and especially for F^- and AcO^- ions.

Experimental Section

General

All melting points were determined with a Yanagimoto MP-S1 melting point apparatus. ^{1}H-NMR spectra were determined at 300 MHz with a Nippon Denshi JEOL FT-300 NMR spectrometer with TMS as an internal reference; J-values are given in Hz. UV-vis spectra were measured with a Shimadzu 240 spectrophotometer. Mass spectra were obtained on a Nippon Denshi JMS-01SG-2 mass spectrometer at an ionization energy of 70 eV using a direct inlet system through GLC. Elemental analyses were performed by Yanaco MT-5.

Materials

Unless otherwise stated, all other reagents used were purchased from commercial sources and were used without further purification. Compounds **1**,[11d,12] **2**[12] and **3**[12] were prepared following the reported procedures.

Preparations

4_a: To a solution of compound **3** (150 mg, 0.166 mmol) in CH_2Cl_2 (10 mL) was added phenyl isocyanate (44 mg, 0.37 mmol) and the mixture was stirred at room temperature for 24 h under argon. The resulting precipitate was collected by filtration, washed with CH_3OH to give receptor **4_a** as a white solid. Recrystallization from $CHCl_3$–CH_3OH (2:1) gave receptor **4_a** (146 mg, 72 %) as a white solid. M.p. 200–202 °C. IR: υ_{max} (KBr)/cm^{-1}: 3220, 2958, 1683, 1542, 1439, 1214, 1206, 1137, 994, 812 and 760. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (18H, s, *t*Bu × 2), 1.22 (18H, s, *t*Bu × 2), 3.05 (4H, br, *CH*$_2$NH × 2), 4.01 (4H, br, O*CH*$_2$ × 2), 5.08 (4H, s, O*CH*$_2$ × 2), 5.56 (2H, s, N*H* × 2), 6.90–7.22. (20H, m, Phenyl–*H* × 20), 7.09 (4H, s, Ar–*H* × 4), 7.18 (2H, s, N*H* × 2) and 7.41 (4H, s, Ar–*H* × 4) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.9 (CH_3), 31.0 (CH_3), 33.9 ($C(CH_3)_3$), 34.1 ($C(CH_3)_3$), 40.9 (CH_2), 70.8 (OCH_2), 72.0 (OCH_2), 124.6 (ArC), 125.9 (ArC), 126.2 (ArC), 126.3 (ArC), 126.5 (ArC), 126.7 (ArC), 128.0 (ArC), 128.3 (ArC), 128.5 (ArC), 128.6 (ArC), 128.8 (ArC), 129.0 (ArC), 129.1 (ArC), 129.3 (ArC), 130.0 (ArC), 132.0 (ArC), 135.2 (ArC), 142.8 (ArC), 146.1 (ArC) and 155.4 (CO) ppm. FABMS: *m/z*: 1224.50 (M^+). $C_{72}H_{80}N_4O_6S_4$ (1224.50): calcd C 70.55, H 6.58, N 4.57. Found: C 70.52, H 6.57, N 4.58.

4_b: To a solution of compound **3** (150 mg, 0.166 mmol) in CH_2Cl_2 (10 mL) was added *p*–tolyl isocyanate (48 mg, 0.37 mmol) and the mixture was stirred at room temperature for 24 h under argon. The resulting precipitate was collected by filtration, washed with CH_3OH to give receptor **4_b** as a white solid. Recrystallization from $CHCl_3$–CH_3OH (3:1) gave receptor **4_b** (146 mg, 70 %) as white solid. M.p. 203–204 °C. IR: υ_{max} (KBr)/cm^{-1}: 3301, 2946, 1605, 1583, 1426, 1211, 1196, 1123, 1016, 889 and 802. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (18H, s, *t*Bu × 2), 1.22 (18H, s, *t*Bu × 2), 2.29 (6H, s, *CH*$_3$ × 2), 3.06 (4H, br, *CH*$_2$NH × 2), 4.03 (4H, br, O*CH*$_2$ × 2), 5.05 (4H, s, O*CH*$_2$ × 2), 5.50 (2H, br, N*H* × 2), 6.86 (2H, s, N*H* × 2), 6.96–7.18. (18H, m, Phenyl–*H* × 18), 7.10 (4H, s, Ar–*H* × 4) and 7.41 (4H, s, Ar–*H* × 4) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.0 (CH_3), 31.3 (CH_3), 34.3 ($C(CH_3)_3$), 39.4 (CH_2), 70.1 (OCH_2), 71.3 (OCH_2), 119.8 (ArC), 121.9 (ArC), 125.1 (ArC), 125.2 (ArC), 125.4 (ArC), 125.9 (ArC), 126.2 (ArC), 126.5 (ArC), 127.1 (ArC), 127.5 (ArC), 127.8 (ArC), 128.0 (ArC), 128.3 (ArC), 128.5 (ArC), 128.6 (ArC), 128.8 (ArC), 129.0 (ArC), 129.1 (ArC), 129.3 (ArC), 130.0 (ArC), 135.1 (ArC), 136.2 (ArC), 147.8 (ArC), 148.0 (ArC), 149.5 (ArC), 151.9 (ArC), 154.0 (ArC) and 158.4 (CO) ppm. FABMS: *m/z*: $[M+H]^+$ Calcd for $C_{74}H_{85}N_4O_6S_4$ (1253.5352) ; Found 1253.4812.

4_c: To a solution of compound **3** (150 mg, 0.166 mmol) in CH_2Cl_2 (10 mL) was added *p*–(trifluoromethyl)phenyl isocyanate (68 mg, 0.366 mmol) and the mixture was stirred at room temperature for 24 h under argon. The resulting precipitate was collected by filtration, washed with CH_3OH to give receptor **4_c** as a white solid. Recrystallization from $CHCl_3$–CH_3OH (3:2) gave receptor **4_c** (147 mg, 65%) as a white solid. M.p. 210–211 °C. IR: υ_{max} (KBr)/cm^{-1}: 3279, 2923, 1602, 1572, 1538, 1225, 1170, 1091, 1068, 905 and 794. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (18H, s, *t*Bu × 2), 1.19 (18H, s, *t*Bu × 2), 3.12 (4H, br, *CH*$_2$NH × 2), 4.03 (4H, br, O*CH*$_2$ × 2), 5.08 (4H, s, O*CH*$_2$ × 2), 5.75 (2H, s, N*H* × 2), 6.92–7.30. (18H, m, Phenyl–*H* × 18), 7.13 (4H, s, Ar–*H* × 4), 7.33 (2H, s, N*H* × 2) and 7.41 (4H, s, Ar–*H* × 4) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.1 (CH_3), 35.6 ($C(CH_3)_3$), 40.0 (CH_2), 70.1 (OCH_2), 70.9 (OCH_2), 118.1 (ArC), 118.8 (ArC), 122.2 (ArC), 122.4 (ArC), 122.7 (ArC), 122.9 (ArC), 123.0 (ArC), 123.3 (ArC), 123.6 (ArC), 124.0 (ArC), 124.4 (ArC), 124.8 (ArC), 126.1 (ArC), 126.5 (ArC), 126.8 (ArC), 127.3 (ArC), 127.8 (ArC), 128.0 (ArC), 128.7 (ArC), 129.3 (ArC), 129.5 (ArC), 138.2 (ArC), 138.9 (ArC), 149.2 (ArC), 155.2 (ArC) and 160.7 (CO) ppm. FABMS: *m/z*: 1361.4861 $[M+H]^+$. $C_{74}H_{79}F_6N_4O_6S_4$ (1361.4787): calcd C 65.27, H 5.77, N 4.11. Found: C 65.32, H 5.75, N 4.08.

Determination of the association constants

The association constants (K_a) were determined by using ^{1}H NMR spectroscopic titration experiments with a constant concentration of host receptor (4.0×10^{-3} M) and varying the guest concentrations (0–8.0×10^{-3} M). The ^{1}H NMR chemical shifts of the urea protons (NH) signal were used as a probe. The K_a values for the complexes of receptor **$4_{a\sim c}$** were calculated by nonlinear curve-fitting analysis of the observed chemical shifts of the NH protons according to the literature procedure.[13a]

^{1}H NMR titration experiments

A solution of Bu_4NX (X = F, Cl, Br, I, AcO, H_2PO_4) in CD_3CN (4.0×10^{-3} M) was added to a $CDCl_3$ solution of receptor **$4_{a\sim c}$** in an NMR tube. ^{1}H NMR spectra were recorded after addition of

the reactants and the temperature of the NMR probe was kept constant at 27 °C.

Crystallographic analyses of 4_a

Diffraction data were collected on a Bruker APEX 2 CCD diffractometer equipped with graphite-monochromated Mo-Kα radiation at 150(2)K.[15] Data were corrected for Lorentz and polarisation effects and for absorption.[15] The structures were solved by direct methods and refined by full-matrix least-squares methods, on F^2.[16] The asymmetric unit contains four calixarenes two chloride anions, two tetrabutylammonium cations, one chloroform and two acetonitrile molecules of crystallisation. Within each of the four calixarenes there are pairs of N–H···O hydrogen bonds between urea moieties to a single carbonyl O atom. Looking down on the S_4 square-shaped planes of the four unique calixarenes, three are approximately geometrically aligned in parallel while one, containing S(1A), is slightly twisted.

Two *t*Bu groups on calixarenes were modelled as disordered over two sets of positions for the Me groups. See tables for the occupation factors. Two *n*-butyl chains in the cations exhibit some signs of disorder, but this was not modelled. The chloroform molecule was modelled as fully disordered over two sets of positions. There are two molecules of acetonitrile of crystallisation which reside in claixarene clefts on molecules containing S(1) and S(1B).

Pairs of calixarene molecules are linked via four H-bonds between both urea N–H moieties on each calixarene and a chloride ion. *n*-butyl ammonium cations reside close to the chloride anions, due to electrostatic attraction. So, each pair of calixarenes is able to capture one chloride ion. The overall packing type is in layers.

Crystal data for $\mathbf{4_a}$: $C_{144}H_{160}N_8O_{12}S_8 \cdot C_{16}H_{36}N^+ \cdot Cl^- \cdot 0.5(CHCl_3) \cdot C_2H_3N$, M = 2829.91. Triclinic, space group $P^{-}1$, a =15.1315 (5), b = 28.8618 (11), c = 35.9491 (13) Å, V = 15113.8 (9) Å^3. Z = 4, Dc = 1.244 g.cm^{-3}, F(000) = 6044, T = 100 K, μ(Mo-Kα) = 0.226 cm^{-1}, λ(Mo-$K\alpha$) = 0.71073 Å, colourless crystal of size 0.16 × 0.13 × 0.04 mm^3. The total number of reflections measured, to θ_{max} = 25.3°, was 42128 of which 27707 were unique (R_{int} = 0.062); 8953 were 'observed' with $I > 2\sigma(I)$. For the 'observed' data only, R_1 = 0.068; wR_2 = 0.185 for all 42128 reflections and 3705 parameters. Residual electron density within +/– 0.86 eÅ^{-3}.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1062186 for $\mathbf{4_a}$. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: 144-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Supporting information: ^{1}H, ^{13}C NMR & IR spectra of compounds **2**, **3** and $\mathbf{4_{a\sim c}}$.

Acknowledgements

This work was performed under the Cooperative Research Program of "Network Joint Research Center for Materials and Devices (Institute for Materials Chemistry and Engineering, Kyushu University)". We would like to thank the OTEC at Saga University and the International Cooperation Projects of Guizhou Province (No. 20137005) for financial support. CR thanks the EPSRC for a travel grant. The computational work has been assisted by the use of computing resources provided by WestGrid and Compute/Calcul Canada. We thank Dr. Grigory Shamov, Westgrid/U. Manitoba for support.

Notes and references

1 (*a*) C. D. Gutsche, *Calixarenes, An Introduction*, Royal Society of Chemistry: Cambridge, UK, 2008; (*b*) A. Ikeda and S. Shinkai, *Chem. Rev.*, 1997, **97**, 1713–1734; (*c*) D. Coquière, S. Le Gac, U. Darbost, O. Sénèque, I. Jabin and O. Reinaud, *Org. Biomol. Chem.*, 2009, **7**, 2485–2500; (*d*) K. Cottet, P. M. Marcos and P. J Cragg, *Beilstein, J. Org. Chem.* 2012, **8**, 201–226; (*e*) L. Mutihac, J. H. Lee, J. S. Kim and J. Vicens, *Chem. Soc. Rev.*, 2011, **40**, 2777–2796; (*f*) L. Baldini, A. Casnati, F. Sansone and R. Ungaro, Chem. Soc. Rev., 2007, **36**, 254–266; (*g*) J. S. Kim and D. T. Quang, *Chem. Rev.*, 2007, **107**, 3780–3799; (*h*) R. Joseph and C. P. Rao, *Chem. Rev.*, 2011, **111**, 4658–4702; (*i*) C. Capici, Y. Cohen, A. D'Urso, G. Gattuso, A. Notti, A. Pappalardo, S. Pappalardo, M. F. Parisi, R. Purrello, S.Slovak and V. Villari, *Angew. Chem., Int. Ed.*, 2011, **50**, 12162–12167; (*j*) C. Talotta, C. Gaeta1, Z. Qi, C. A. Schalley and P. Neri, *Angew. Chem., Int. Ed.*, 2013, **52**, 7437–7441; (*k*) M.-X. Wang, *Acc. Chem. Res.*, 2012, **45**, 182–195.

2 (*a*) H. Kumagi, M. Hasegawa, S. Miyanari, Y. Sugawa, Y. Sato, T. Hori, S. Ueda, H. Kamiyama and S. Miyano, *Tetrahedron Lett.*, 1997, **38**, 3971–3972.

3 (*a*) P. Lhoták, *Eur. J. Org. Chem.*, 2004, 1675–1692; (*b*) N. Morohashi, F. Narumi, N. Iki, T. Hattori and S. Miyano, *Chem. Rev.*, 2006, **106**, 5291–5316; (*c*) R. Kumar, Y.–O. Lee, V. Bhalla, M. Kumar and J.–S. Kim, *Chem. Soc. Rev.*, 2014, **43**, 4824–4870.

4 (*a*) P. D. Beer and P. A. Gale, *Angew. Chem. Int. Ed.*, **2001**, 40, 486–516; (*b*) T. Nabeshima, T. Saiki and S. Kumitomo, *Org. Lett.*, 2002, **4**, 3207–3209; (*c*) T. Nabeshima, Y. Yoshihira, T. Saiki, S. Akine and E. Horn, *J. Am. Chem. Soc.*, 2003, **125**, 28–29; (*d*) A. Y. Zhukov, T. A. Fink, I. I. Stoikov and I. S. Antipin, *Russ. Chem. Bull., Int. Ed.*, 2009, **58**, 1007–1014; (*e*) K. Mohr, J. Schmitz, R. Schrage, C. Trnkle and U. Holzgrabe, *Angew. Chem. Int. Ed.*, 2013, **52**, 508–516; (*f*) R. Nussinov and C.–J. Tsai, *Cell*, 2013, **153**, 293–305.

5 (*a*) H. Lu, W. Xu, D. Zhang, C. Chen and D. Zhu, *Org. Lett.*, 2005, **7**, 4629–4632; (*b*) F. M. Pfeffer, T. Gunnlaugsson, P. Jensen and P. E. Kruger, *Org. Lett.*, 2005, **7**, 5357–5360; (*c*) L. Fang, W.–H. Chan, Y.–B. He, D. W.–J. Kwong and A. W.–M. Lee, *J. Org. Chem.*, 2005, **70**, 7640–7646; (*d*) T. Gunnlaugsson, P. E. Kruger, P. Jensen, J. Tierney, H. D. Paduka Ali and G. M. Hussey, *J. Org. Chem.*, 2005, **70**, 10875–10878; (*e*) A. Dahan, T. Ashkenazi, V. Kuznetsov, S. Makievski, E. Drug, L. Fadeev, M. Bramson, S. Schokoroy, E. Rozenshine–Kemelmakher and M. Gozin, *J. Org. Chem.*, 2007, **72**, 2289–2296; (*f*) S. Saha, A. Ghosh , P. Mahato , S. Mishra , S. K. Mishra, E. Suresh , S. Das

and A. Das, *Org. Lett.*, 2010, **12**, 3406–3409; (*g*) S. Kondo, M. Nagamine, S. Karasawa, M. Ishihara, M. Unno and Y. Yano, *Tetrahedron*, 2011, **67**, 943–950; (*h*) M. Alešković, N. Basarić, I. Halasz, X. Liang, W. Qin and K. Mlinarić–Majerski, *Tetrahedron*, 2013, **69**, 1725–1734; (*i*) S. Lee, Y. Hua and A. H. Flood, *J. Org. Chem.*, 2014, **79**, 8383–8396; (*j*) Y. Jo, N. Chidalla and D.–G. Cho, *J. Org. Chem.*, 2014, **79**, 9418–9422; (*k*) F. Zapata, A. Caballero, P. Molina, I. Alkorta and J. Elguero, *J. Org. Chem.*, 2014, **79**, 6959–6969.

6 (*a*) J. L. Sessler, P. A. Gale and W. S. Cho, Anion Receptor Chemistry; Royal Society of Chemistry: Cambridge, U.K., 2006; (*b*) P. D. Beer, P.A. Gale, *Angew. Chem., Int. Ed*., 2001, **40**, 486–516.

7 (*a*) J. F. Zhang, Y. Zhou, J. Yoon and J. S. Kim, *Chem. Soc. Rev*., 2011, **40**, 3416–3429; (*b*) C. Lodeiro, J. L. Capelo, J. C. Mejuto, E. Oliveira, H. M. Santos, B. Pedras and C. Nuñez, *Chem. Soc. Rev*., 2010, **39**, 2948–2976; (*c*) L. E. Santos-Figueroa, M. E. Moragues, E. Climent, A. Agostini, R. Martínez-Máñez and F. Sancenón, *Chem. Soc. Rev*., 2013, **42**, 3489–613; (*d*) C. Pérez-Casas and A. K. Yatsimirsky, *J. Org. Chem.*, 2008, ***73*** **(6)**, 2275–2284.

8 (*a*) J. P. Clare, A. Statnikov, V. Lynch, A. L. Sargent and J. W. Sibert, *J. Org. Chem.*, 2009, **74**, 6637–6646; (*b*) Q.–S Lu, L. Dong, J. Zhang, J. Li, L. Jiang, Y. Huang, S. Qin, C.–W. Hu and X.–Q. Yu, *Org. Lett.*, 2009, **11**, 669–672; (*c*) S. Goswami, D. Sen and N. K. Das, *Org. Lett.*, 2010, **12**, 856–859; (*d*) A. Aldrey, C. Núñez, V. García, R. Bastida, C. Lodeiro, A. Macías, *Tetrahedron*, 2010, **66**, 9223–9230; (*e*) P. Dydio, T. Zieliński and J. Jurczak, *Org. Lett.*, 2010, **12**, 1076–1078; (*f*) V. K. Bhardwaj, S. Sharma, N. Singh, M. S. Hundal and G. Hundal, *Supramol. Chem.*, 2011, **23**, 790–800; (*g*) G.–W. Lee, N.–K. Kim and K.–S. Jeong, *Org. Lett.*, 2011, **13**, 3024–3027; (*h*) H. M. Chawla, S. N. Sahu, R. Shrivastava, S. Kumar, *Tetrahedron Lett*., 2012, **53**, 2244–2247; (*i*) S. Goswami, A. Manna, S. Paul, K. Aich, A. K. Das and S. Chakraborty, *Tetrahedron Lett.*, 2013, **54**, 1785–1789; (*j*) K. Pandurangan, J. A. Kitchen and T. Gunnlaugsson, *Tetrahedron Lett.*, 2013, **54**, 2770–2775; (*k*) S. Areti, J. K. Khedkar, R. Chilukula and C. P. Rao, *Tetrahedron Lett*., 2013, **54**, 5629–5634; (*l*) C. Jin, M. Zhang, C. Deng, Y. Guan, J. Gong, D. Zhu, Y. Pan, J. Jiang and L. Wang, *Tetrahedron Lett*., 2013, **54**, 796–801; (*m*) P. M. Marcos, F. A. Teixeira, H. Kooijman, M. A. P. Segurado, J. R. Ascenso, R. J. Bernardino, S. Michel and V. Hubscher–Bruder, *J. Org. Chem*., 2014, **79**, 742–751; (*n*) E. Brunetti, J.–F. Picron, K. Flidrova, G. Bruylants, K. Bartik and I. Jabin, *J. Org. Chem*., 2014, **79**, 6179–6188.

9 (*a*) J. Kroupa, I. Stibor, M. Pojarová, M. Tkadlecová and P. Lhoták, *Tetrahedron*, 2008, **64**, 10075–10079; (*b*) O. Kundrat, H. Dvorakova, I. Cisarova, M. Pojarova and P. Lhoták, *Org. Lett.*, 2009, **11**, 4188–4191; (*c*) O. Kundrat, I. Cisarova, S. Böhm, M. Pojarova and P. Lhoták, *J. Org. Chem.*, 2009, **74**, 4592–4596; (*d*) O. Kundrat, H. Dvorakova, V. Eigner and P. Lhoták, *J. Org. Chem.*, 2010, **75**, 407–411; (*e*) O. Kundrat, J. Kroupa, S. Böhm, J. Budka, V. Eigner and P. Lhoták, *J. Org. Chem.*, 2010, **75**, 8372–8375; (*f*) O. Kundrát, V. Eigner, P. Cuřínová, J. Kroupa and P. Lhoták, *Tetrahedron*, 2011, **67**, 8367–8372; (*g*) O. Kundrat, V. Eigner, H. Dvorakova, and P. Lhoták, *Org. Lett.*, 2011, **13**, 4032–4035; (*h*) P. Slavik, M. Dudic, K. Flidrova, J. Sykora, I. Cisarova, M. Pojarova and P. Lhoták, *Org. Lett.*, 2012, **14**, 3628–3631; (*i*) O. Kundrat, H. Dvorakova, S. Böhm, V. Eigner and P. Lhoták, *J. Org. Chem.*, 2012, **77**, 2272–2278; (*j*) M. Mačková, M. Himl, J. Budka, M. Pojarová, I. Císařová,, V. Eigner, P. Cuřínová, H. Dvořáková and P. Lhoták, *Tetrahedron*, 2013, **69**, 1397–1402; (*k*) J. Lukášek, S. Böhm, H. Dvořáková, V. Eigner and P. Lhoták, *Org. Lett.*, 2014, **16**, 5100–5103.

10 J. N. Babu, V. Bhalla, M. Kumar, R. K. Mahajan and R. K. Puri, *Tetrahedron Lett.*, 2008, **49**, 2772–2775.

11 (*a*) C. Perez-Casas and T. Yamato, *J. Incl. Phenom. Macrocyclic Chem.*, 2005, **53**, 1–8; (*b*) T. Yamato, C. Perez-Casas, H. Yamamoto, M. R. J. Elsegood, S. H. Dale and C. Redshaw, *J. Incl. Phenom. Macrocyclic Chem.*, 2006, **54**, 261–269; (c) C. Perez-Casas, S. Rahman, N. Begum, Z. Xi and T. Yamato, *J. Incl. Phenom. Macrocyclic Chem.*, 2008, **60**, 173–185; (*d*) X.-L. Ni, H. Tomiyasu, T. Shimizu, C. Perez-Casas, X. Zeng, and T. Yamato, *J. Incl. Phenom. Macrocyclic Chem.*, 2010, **68**, 99–108; (*e*) X.–L. Ni, X. Zeng, C. Redshaw and T. Yamato, *J. Org. Chem.*, 2011, **76**, 3358–3370; (*f*) X.-L. Ni, X. Zeng, C. Redshaw and T. Yamato, *Tetrahedron*, 2011, **67**, 3248–3253; (*g*) X.–L. Ni, J. Tahara, S. Rahman, X. Zeng, D. L. Hughes, C. Redshaw and T. Yamato, *Chem. Asian. J.*, 2012, **7**, 519–527; (*h*) X.–L. Ni, H. Cong, A. Yoshizawa, S. Rahman, H. Tomiyasu, U. Rayhan, X. Zeng and T. Yamato, *J. Mol. Struct.*, 2013, **1046**, 110–115; (*i*) H. Tomiyasu, C.–C. Jin, X.–L. Ni, X. Zeng, C. Redshaw, T. Yamato, *Org. Biomol. Chem.*, 2014, **12**, 4917–4923; (*j*) H. Tomiyasu, N. Shigyo, X.–L. Ni, X. Zeng, C. Redshaw and T. Yamato, *Tetrahedron*, 2014, **70**, 7893–7899.

12 C. Perez-Casas, H. Hopfl, A. K. Yatsimirsky, *J. Incl. Phenom. Macrocyclic Chem.*, 2010, **68**, 387–398.

13 (*a*) L. Fielding, *Tetrahedron*, 2000, **56**, 6151-6170; (*b*) H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, 1949, **71**, 2703–2707.

14 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg,; M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, Jr. J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Revision D.01*; Gaussian, Inc., Wallingford CT, 2013.

15 SAINT and APEX 2 (2008) software for CCD diffractometers. Bruker AXS Inc., Madison, USA

16 G. M. Sheldrick, *Acta Crystallogr*., 2008, **A64**, 112–122.

