Synthesis, structure, and complexation properties of tetraamide derivatives of thiacalix[4]arene in different conformations*

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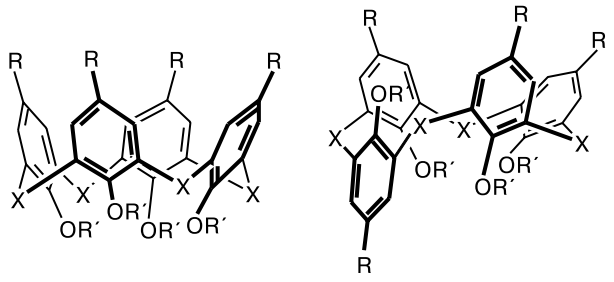
The interaction of *p-tert*-butylthiacalix[4]arene with *N*,*N*-diethylchloroacetamide was studied in the presence of alkali metal carbonates in acetone. Three stereoisomers, *viz.*, cone, partial cone, and 1,3-alternate, of the tetraamide derivative of thiacalixarene substituted at the lower rim were synthesized selectively using the template effect of alkali metal cations, as well as a complex of the 1,3-alternate stereoisomer with potassium chloride. The structures of the compounds synthesized were studied by 2D NMR spectroscopy. A high extraction ability of the compounds toward alkali metal cations was demonstrated.

Key words: thiacalix[4]arenes, amides, template effect, stereoisomerism, extraction, alkali metals, inclusion compounds, X-ray diffraction analysis, NMR spectroscopy.

Calix[4]arenes **1—6** have three-dimensional cage structures with pronounced molecular cavities.[1—3] Due to wide possibilities of modifying the upper and lower rims, they are convenient molecular platforms for the creation of pre-organized structures and supramolecular ensembles. The selective functionalization of the macrocycle by suitable heteroatomic groups provides the construction of a molecular system with several spatially pre-organized binding centers and, hence, with high efficiency and selectivity of binding of different substrates. Additional possibilities for the design of molecular receptors were developed due to existence of several stereoisomers of the calix[4]arene platform: cone, partial cone, and 1,3- and 1,2-alternates.[1]

Recently[4] synthesized thiacalix[4]arene **2** is of great interest due to the appearance of new challenges related to the introduction of the bridging sulfur atoms, which can participate in complexation.[5] In addition, an increase in the sizes of the macrocycle cavity compared to that of calixarene **1** is significant in this respect.[6] Approaches to the synthesis of different stereoisomers of thiacalix[4]arene remain poorly studied. Therefore, in the present work we continued to study the regularities of functionalization of



Compound	X	R	R′
1	CH_2	Bu^t	H
2	S	Bu^t	H
3	S	Bu^t	CH_2CONEt_2
4	CH_2	Bu^t	CH_2CONEt_2
5	S	Bu^t	CH_2COPh
6	S	Bu^t	CH_2CO_2Et

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the lower rim of thiacalix[4]arene by electrophilic agents, which contain moieties capable of efficient coordinating with metal cations. We also studied the complexation of the resulting macrocycles with alkali metal cations. For this purpose, we studied the reaction of *p-tert*-butylthiacalix[4]arene **2** with *N*,*N*-diethylchloroacetamide using the template effect of metal ions, which has been found earlier.[7–9] Alkali metal carbonates M_2CO_3 (M = Na, K, Cs) were used as bases, and the reactions were carried out in boiling acetone.

Results and Discussion

The initial tetra-*tert*-butylthiacalix[4]arene **2** exists in the cone conformation in both crystal and solution due to cooperative cyclic bonding of the phenol groups.[4,10] However, the functionalization of the lower rim of the macrocycle results, in many cases, in a change in its conformation and the formation, as a rule, of a mixture of several stereoisomers, namely, cone, partial cone, and 1,2- and 1,3-alternates.

The functionalization of the phenol groups of thiacalix[4]arene by alkyl halides in acetone or acetonitrile gives the tetrasubstituted products in the 1,3-alternate conformation regardless of the nature of the metal cation.[11,12] Stereoisomers of the thiacalix[4]arene derivatives substituted at the lower rim **5** and **6** were synthesized through the control by alkali metal cations.[7,8] The main condition for the appearance of the template effect of cations in this reaction is the use of alkylating agents that contain groups capable of coordinating with alkali metal cations (C(O)OR, C(O)Alk, C(O)Ar, $C(O)NR_2$, *etc.*). As shown from the reactions of thiacalixarene **2** with ethyl bromoacetate[7] and α-bromoacetophenone,[8] when sodium, potassium, or cesium carbonates are used as bases, the products are mainly formed in the cone, partial cone, or 1,3-alternate conformation, respectively.

In the present work, it seemed of interest to study the effect of the electron-donor properties of groups in the alkylating agents on the selectivity of formation of the stereoisomers and their complexation properties. Therefore, the reaction of thiacalix[4]arene **2** with *N*,*N*-diethylchloroacetamide was studied in the presence of alkali metal carbonates, because the amide group is a stronger donor than an ester or phenylcarbonyl group. In addition, it was principally important to estimate the effect of pre-organization related to the fact that four amide moieties were attached on the thiacalix[4]arene platform.

The study of the reaction of thiacalix[4]arene **2** with *N*,*N*-diethylchloroacetamide showed that the stereochemical result of the reaction depends on the nature of the base used (template effect), as in the case of the reactions with ethyl bromoacetate and α-bromoacetophenone. Tetraamide derivatives **3** in conformations of cone, partial cone, and 1,3-alternate were synthesized in high yields when sodium, potassium, and cesium carbonates, respectively, were used (Table 1). No 1,2-alternate stereoisomer of **3** was formed.

However, unlike the earlier studied reactions with ethyl bromoacetate and α-bromoacetophenone, the reaction mixture using potassium carbonate as a base yielded a complex of the potassium cation with stereoisomer **3** in the 1,3-alternate conformation in 24% yield in addition to the main product, *viz.* compound **3** in the partial cone conformation. When the amount of K_2CO_3 in the reaction mixture was increased, the yield of the partial cone stereoisomer decreased sharply, and the $K^+ \cdot$ **3** complex (1,3-alternate) became the main product (79%). This indicates that the formation of the partial cone stereoisomer is a kinetically controlled process due to a considerable barrier of its transition to the thermodynamically more stable conformer 1,3-alternate. This transition occurs only in a sixfold excess of K_2CO_3 in the reaction mixture over the starting calixarene and only for the tetraamide derivative for which, as has been shown by our extraction studies, the binding constants are higher by several orders of magnitude than those in the case of the tetraester and tetraphenylcarbonyl derivatives. This result agrees with the known data[13] that reported the synthesis of tetraamide **3** in the 1,3-alternate conformation in 41% yield in the presence of a tenfold excess of potassium carbonate.

It should be mentioned that no similar template effect is observed in the reaction of classical calixarene **1** with diethylchloroacetamide. Tetraamide **4** in the cone conformation[14] is formed in the presence of both sodium hydride and potassium carbonate. In the latter case, tetraamide **4** in the 1,3-alternate conformation was isolated[15] as an admixture (5% yield) from the reaction mixture. The use of cesium carbonate as a base gives a mix-

Table 1. Conditions of synthesis and the yields of stereoisomers of macrocycle **3**

Base	Ratio of reactants **2** : $ClCH_2C(O)NEt_2$: M_2CO_3	Yield of stereoisomers **3** (%)			
		Cone	Partial cone	1,3-Alternate	$K^+ \cdot$ 1,3-alternate
Na_2CO_3	1 : 8 : 4	88	—	—	—
K_2CO_3	1 : 8 : 4	—	58	10	24
K_2CO_3	1 : 8 : 6	—	11	—	79
Cs_2CO_3	1 : 8 : 4	—	11	62	—

ture containing of the cone and partial cone conformations.[16]

It is more difficult to determine the macrocycle conformation when the methylene bridges in calix[4]arene **1** are replaced by the sulfur atoms in thiacalix[4]arene **2**. Macrocycle **3** in the cone and 1,3-alternate conformations is symmetric and, hence, the ^{1}H NMR spectra of these conformers are simple and resemble each other in the number and multiplicity of signals: they consist of singlets of aromatic protons and singlets of protons of the methyl and methylene groups. This is also valid for the ^{13}C NMR spectra. The signals can be assigned to conformations by a comparison of the chemical shifts of protons of the methylene groups in the OCH_2CO substituents. In the 1,3-alternate conformation of compound **3**, they are in the shielding field of two adjacent aromatic rings of calixarene, and their signals are shifted upfield than those for the cone conformation. Therefore, isomers **3** with signals of the methylene protons at δ 5.29 and 4.65 were identified as a cone and 1,3-alternate, respectively. The structures of conformers **3** were also determined by analysis of the influence of the anisotropic effects of the aromatic groups on the chemical shifts of protons in the ^{1}H NMR spectra: in the cone conformation the singlet of aromatic protons is observed at δ 7.25, whereas in the 1,3-alternate conformation it is observed at δ 7.51. In addition, compounds **3** were studied by 2D NMR spectroscopy (COSY, HSQC, HMBC, and ROESY methods) with full assignment of atoms. According to the data of these methods (weak cross-peaks 5,5*/3,3* and 7a,b/3,3*, for the atom numbering see Fig. 1), a fast chemical exchange is observed: interconversion C_{2v}—$C_{2v'}$ of the symmetry forms of macrocycle **3** in the cone conformation (Fig. 2).

The ROESY spectra of all conformers synthesized contain negative exchange cross-peaks between protons a and b of the ethyl groups at the nitrogen atom of the amide substituents due to hindered rotation about the C(O)—N bond. To assign the chemical shifts of atoms a and b, we considered the integral intensities of the cross-peaks H(5)/H(7a),H(8a) > H(5)/H(7b),H(8b) in the ROESY spectrum.

The 1,3-alternate conformation is determined due to the positive cross-peaks of the H(3) and H(4b) protons in the ROESY spectrum relative to the opposite H(5), H(7a), H(7b), H(8a), and H(8b) atoms, which are absent in the cone stereoisomer of macrocycle **3**.

The ^{1}H NMR spectrum of the K^+ complex with compound **3** in the 1,3-alternate conformation is a more complicated than the spectra of the cone and 1,3-alternate stereoisomers (the atoms are enumerated in Fig. 1). This spectrum consists of two singlets of the aromatic protons, two singlets of the methylene protons of the OCH_2CO groups, two quartets of the methylene groups at the nitro-

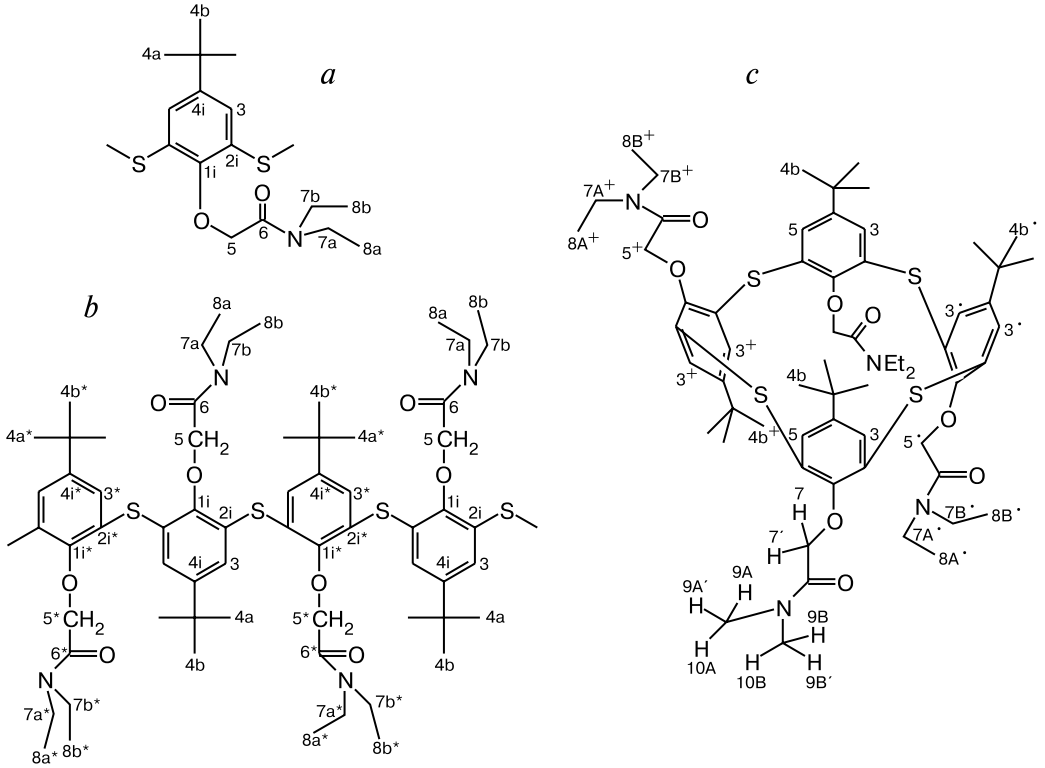


Fig. 1. Numeration of atoms in the conformers of macrocycle **3**: cone and 1,3-alternate (*a*), complex of the 1,3-alternate conformer with potassium chloride (*b*), and partial cone (*c*).

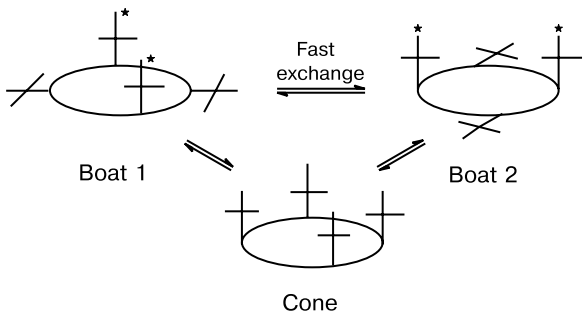
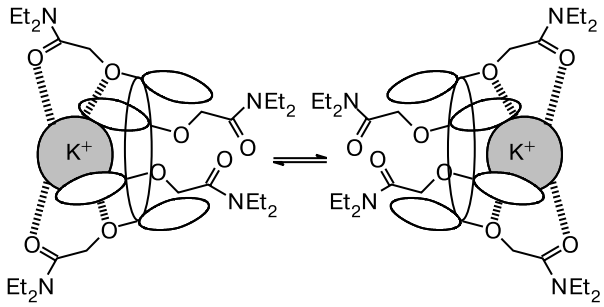


Fig. 2. Interconversion boat 1—cone—boat 2 of macrocycle **3** in solution.

gen atoms, two singlets of the *tert*-butyl protons, and two triplets of the methyl protons of the ethyl groups. The 2D ROESY spectrum of the K^+ complex with compound **3** in the 1,3-alternate conformation has negative exchange cross-peaks of structurally equivalent protons H(3)/H(3*), H(4b)/H(4b*), and H(5)/H(5*).

These cross-peaks of the structurally equivalent protons indicate the mobile equilibrium and slow chemical exchange (Scheme 1) between the *N*,*N*-diethylacetamide groups linked at different sides of the macrocycle. It is evident that the cation exchanges slowly between the ligand moieties of the macrocycle (in the NMR time scale) and, therefore, no averaged pattern is observed in the ^{1}H NMR spectrum. The order of cross-peak intensities in the ROESY spectrum is the following: 4b*/5 > 4b/5*, 3*/5 > 3/5*, 3*/7A,7B > 3/7A*,7B. According to the latter, the full proton assignment was carried out. The formation of the 1 : 1 complex of K^+ with compound **3** in the 1,3-alternate conformation was also confirmed by ESI mass spectrometry (*m*/*z* 1211, $[M + K]^+$) and elemental analysis data.

Scheme 1



The ^{1}H NMR spectrum of compound **3** in the partial cone conformation exhibits signals of protons of three nonequivalent *tert*-butyl groups in a ratio of 2 : 1 : 1 and signals of the aromatic protons and protons of the OCH_2 groups, which appear as two doublets and two singlets. The ROESY spectrum contains many positive cross-peaks,

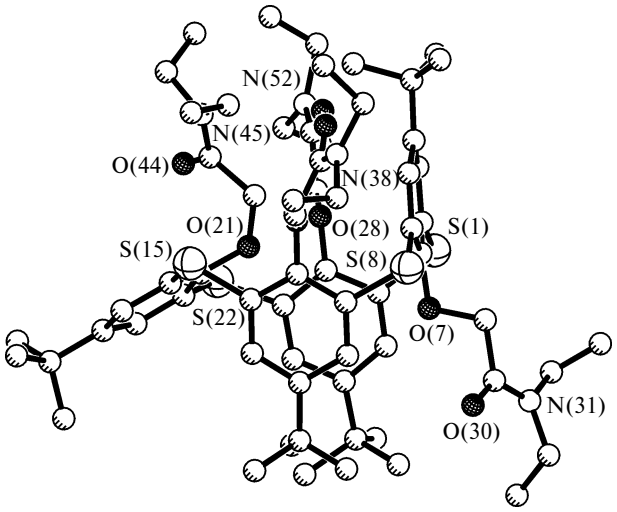


Fig. 3. Crystal structure of macrocycle **3** in the partial cone conformation. Hydrogen atoms are omitted here and in Figs 4 and 5.

which show that the protons of the upper and lower rims are neighbors: $4b^+/5^\bullet$ > $4b^+/7,7'$ (m) ≈ $4b/5^+$; $4b/3^\bullet$ (w) < $4b/3^+$; $7A^+,7B^+/5^\bullet$ (m); $5^+/5$ (s) > > $7,7'/3^+$ (m) > $5^\bullet/3^+$; $4b^+/7A^\bullet$ > $4b^+/7b^\bullet$; $4b/7B^+$; $10B/5^\bullet$; $4b^+/5^\bullet,7,7'$; $4b^+/9B,7A^\bullet,7B^\bullet$; $7D^\bullet/9A$; 9D/5 (the atoms are enumerated in Fig. 1).

The structures of two stereoisomers **3** (partial cone and 1,3-alternate) were confirmed by X-ray diffraction analysis. A calixarene molecule in the partial cone conformation crystallizes in an orthorhombic crystal system without solvate molecules (Fig. 3). The dihedral angles between the opposite phenyl rings are 5.0 and 63.0°. The cavity formed by three phenyl rings and the diethylcarbamoylmethyl substituent is closed by the *tert*-butyl groups and inaccessible, in fact, for solvate molecules. The bulky substituents at the upper and lower rim of the calixarene hinder the molecular packing in crystal, which is indicated by the calculated value of the packing coefficient equal to 63.8%, and also prevent any significant intermolecular interactions, except for two contacts of the C—H...O and S...S types. The former of them occurs between the H(410) proton of the methyl group of the diethylcarbamoylmethyl substituent and the O(44′) atom of the carboxyl group of the same substituent of the adjacent molecules has the parameters *d*(H(410)...O(44′)) 2.44 Å, and the C(41)—H(410)—O(44′) angle is 164°. The symmetry procedure $2 - x$, $1/2 + y$, $1/2 - z$ links calixarene molecules to form an infinite chain along the crystallographic axis 0*y* in crystal. The second interaction (S...S, 3.35 Å) between the S(1) and S(15) atoms of the molecules linked by the symmetry procedure $-1 + x$, y, z organizes the calixarene molecules along the 0*x* axis in such a manner that a two-dimensional layered supramolecular structure is formed in crystal. As a whole, the

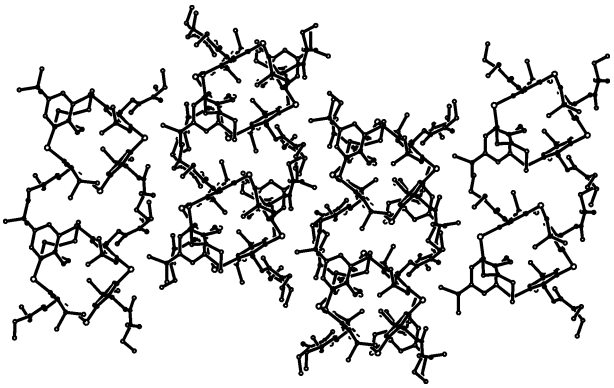


Fig. 4. Molecular packing of macrocycle **3** in the partial cone conformation in crystal. The view along the crystallographic axis 0*z*.

molecular packing in crystal is characterized by similar layers lying in parallel along the crystallographic axis 0*z* (Fig. 4). The calixarene molecules are arranged in the adjacent layers in such a way that regular piles of molecules along the 0*z* axis are formed in crystal. It is interesting that the compound crystallizes in the non-centrosymmetric space group, although its molecule contains no chiral atoms.

Calixarene **3** in the 1,3-alternate conformation also crystallizes without solvate molecules (Fig. 5). An isolated molecule in this conformation has its own symmetry C_2 but looses this symmetry in crystal because, first of all, of different conformations of the diethylcarbamoylmethylene substituents and *tert*-butyl groups. In this case, the conformation of the calixarene cage remains rather symmetric: the dihedral angles between the opposite phenyl rings of calixarene are equal to 1.99° and 0.99°, and

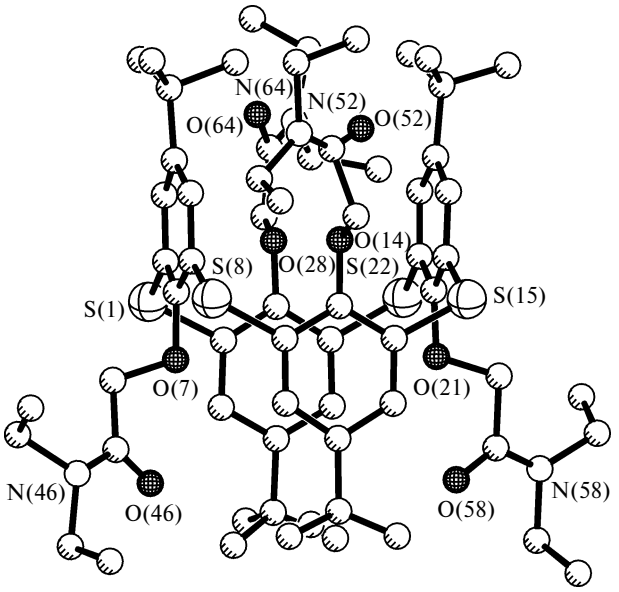


Fig. 5. Crystal structure of macrocycle **3** in the 1,3-alternate conformation.

the molecule is in the general position in the orthorhombic unit cell.

A rather low packing coefficients of the molecules in crystal (61.6%) and the absence of any significant intermolecular interactions can be explained, most likely, by the same factors as those in the partial cone conformation. Molecules of the compound in crystal form layers parallel to the 0*xy* plane, and their mutual arrangement in the layer (Fig. 6, *a*) prevents specific interactions between the sulfur atoms of the adjacent molecules. Moreover, the layers along the 0*z* axis are also shifted relatively to each

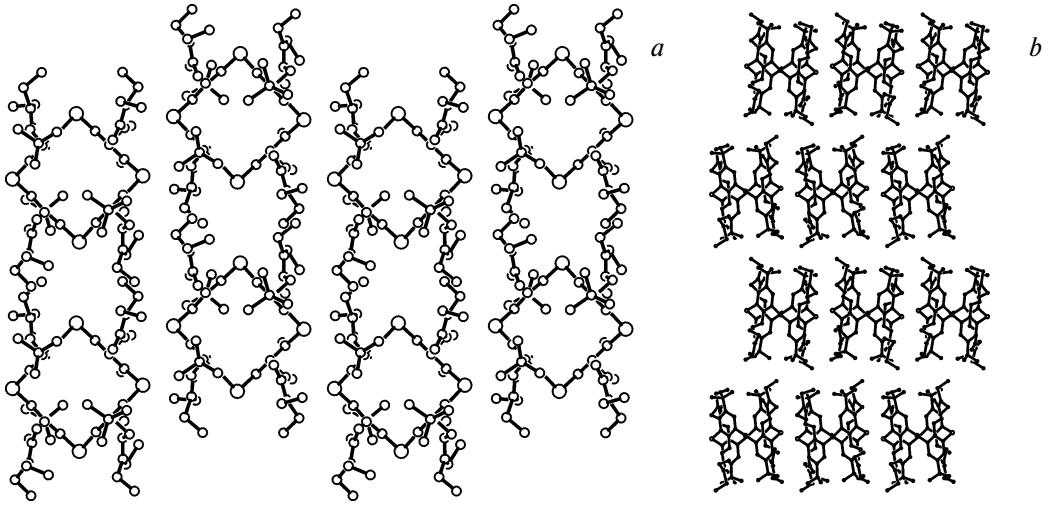


Fig. 6. Molecular packing of macrocycle **3** in the 1,3-alternate conformation in the layer (*a*) and the formation of layers in crystals (*b*). The view along the crystallographic axes 0*z* (*a*) and 0*y* (*b*).

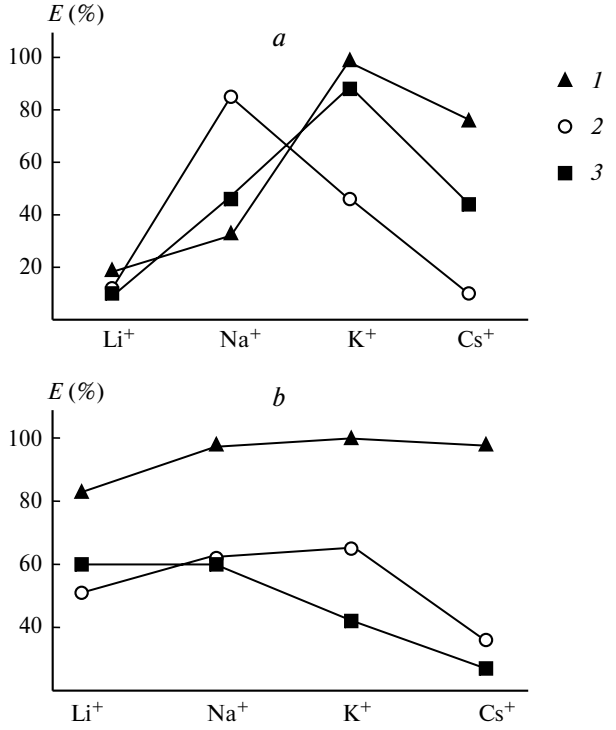


Fig. 7. Degree of extraction (E) by macrocycles **5** (*a*) and **3** (*b*) in the 1,3-alternate (*1*), cone (*2*), and partial cone (*3*) conformations (extraction conditions: $[\mathbf{5}]_0 = 2.5 \cdot 10^{-3}$ mol L^{-1}, $[MOH]_0 = 0.1$ mol L^{-1}, $[HPic]_0 = 2.5 \cdot 10^{-4}$ mol L^{-1} (*a*); $[\mathbf{3}]_0 = 3.5 \cdot 10^{-4}$ mol L^{-1}, $[MOH]_0 = 7.0 \cdot 10^{-5}$ mol L^{-1}, and $[HPic]_0 = 5.0 \cdot 10^{-5}$ mol L^{-1} (*b*)).

other (Fig. 6, *b*) and, therefore, no piles are formed in the structure due to π—π-interactions.

It is known[2,3] that the selectivity of ion binding depends on the macrocycle conformation: the functionalized calixarenes in different conformations (cone, partial cone, and 1,3-alternate) bind metal ions in a different manner. The extraction properties of *p-tert*-butylthiacalix[4]arenes in different conformations tetrasubstituted at the lower rim containing phenylcarbonyl[8] (**5**) and ester[7] (**6**) moieties have been studied previously. Thiacalixarenes **5** and **6** are efficient and selective extragents: in the cone conformation they extract predominantly sodium cations, in the partial cone conformation they extract potassium cations, and the 1,3-alternate is the best extragent for potassium and cesium cations[8] (Fig. 7, *a*).

The extraction of alkali metal ion picrates in a water—CH_2Cl_2 system was studied to estimate the ability of macrocycles **3** to recognize these ions. The conformers of compound **3** are very efficient but not selective extragents: all conformers of compound **3** taken in concentrations used for the extraction of alkali metal cations by compounds **5** and **6** showed the 100% efficiency. To determine the degree of extraction of alkali metal cations by these compounds, we had to decrease considerably the concentrations of the ligand, alkali metal picrate, and base (Fig. 7, *b*).

Evidently, not only the conformation but also the nature of donor groups exert an effect on the extraction ability. A comparison of the degrees of extraction for the conformers of macrocycles **5** and **6**, which were determined under the same conditions,[7,8] shows that conformers **5** demonstrate, as a whole, higher efficiency and selectivity than conformers **6**, *i.e.*, the replacement of the ethoxy group by the phenyl group enhances the efficiency and selectivity of extraction. The introduction of strongly donating amide groups $CH_2C(O)NEt_2$ into the lower rim of thiacalix[4]arene **2** results in considerable changes in the extraction ability. The conformers of macrocycle **3** are much more efficient in extracting alkali metal picrates than the conformers of macrocycle **5**. For macrocycle **3**, alkali metal picrates are almost completely transferred into the organic phase already at an equimolar ratio ion : ligand **3** (see Fig. 7, *a* and *b*). The selectivity of extraction is changed substantially. The strongest extragent of alkali metal picrates is the 1,3-alternate stereoisomer of compound **3**, which is characterized by the very low selectivity in the series of alkali metal cations. As a whole, it should be mentioned that conformers **3** extract alkali metal picrates more efficiently but much less selectively than macrocycles **5** and **6** (Table 2).

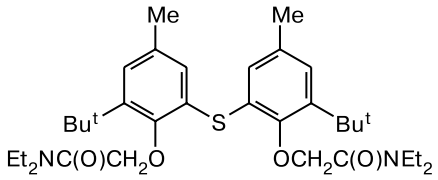
It is remarkable that the Li^+ cation is rather efficiently extracted by all stereoisomers **3**, unlike earlier studied macrocycles **4** and **5**. Macrocycle **3** in the partial cone conformation extracts the lithium cation more efficiently than other alkali metal cations. Taking into account the substantially higher energy of the lithium ion transfer from the aqueous to organic phase in the series of alkali cations, we can speak about the creation of a highly efficient complexing agent for the lithium cation.

A model compound, *viz.*, 3,3′-di-*tert*-butyl-5,5′-dimethyl-2,2′-bis(*N*,*N*-diethylcarbamoylmethoxy)diphenyl sulfide (**7**), was synthesized by the reaction of 2,2′-thiabis(4-methyl-6-*tert*-butyl)phenol with excess diethylbromoacetamide in the presence of K_2CO_3 in acetone for quantitative estimation of the effect of the spatial preorganization of binding centers (due to their fixation on the calixarene platform) on the complexation properties of tetraamides **3**. This compound can be considered as a "half" of macrocycle **3** containing diethylacetamide

Table 2. Degree of extraction of alkali metal cations by stereoisomers **3**

Conformer **3**	Li^+	Na^+	K^+	Cs^+
Cone	0.62	0.78	0.80	0.45
Partial cone	0.67	0.71	0.57	0.33
1,3-Alternate	0.89	0.99	0.94	0.99

groups, which are of ion binding but are not spatially pre-organized (due to rotation about the C—S bonds).



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It turned out that model diamide **7** cannot extract alkali metal picrates into the organic phase. Even when the concentrations of metal picrate in water and the ligand in the organic phase are higher by three and one orders of magnitude, respectively, than the concentration at which thiacalix[4]arene-based tetraamides demonstrate the almost complete extraction of picrates to the organic phase, the degree of extraction by lipophilic diamide **7** is negligible (the initial concentrations of the ligand in the organic phase and metal hydroxide and picrate in the aqueous phase were $[\mathbf{7}]_0 = 2.5 \cdot 10^{-3}$ mol L^{-1}, $[MOH]_0 = 0.1$ mol L^{-1}, and $[HPic]_0 = 2.5 \cdot 10^{-4}$ mol L^{-1}, respectively). In this case, the macrocyclic cooperative effect (more than 10 orders of magnitude) is observed, when the groups, which do manifest or do not weak coordination properties, form an efficient coordinating system on the calix[4]arene platform due to spatial pre-organization.

Thus, we studied the reaction of *N*,*N*-diethylchloroacetamide with thiacalix[4]arene **2** and synthesized selectively, using the template effect of alkali metal cations, three isomers of tetraamide **3** substituted at the lower rim, namely, cone, partial cone, and 1,3-alternate, and also the complex of the 1,3-alternate stereoisomer with potassium chloride. The study of the extraction ability of synthesized macrocycles **3** from the aqueous phase to dichloromethane showed their very high extraction ability with respect to alkali metal cations.

Experimental

Prior to use solvents were purified according to known procedures.[17]

^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 (500.13 (^{1}H) and 125.77 MHz (^{13}C)) and Bruker DRX-300 (300.13 (^{1}H) and 75.475 MHz (^{13}C)) spectrometers, using Me_4Si as internal standard. Signals in the ^{1}H and ^{13}C NMR spectra were exactly assigned using 2D NMR spectroscopy (COSY, ^{1}H/^{13}C HSQC, ^{1}H/^{13}C HMBC, NOESY, and ROESY methods).

IR spectra in the 400—4000 cm^{-1} interval were measured on a Bruker Vector 22 Fourier spectrometer (resolution 1 cm^{-1}, accumulation 64 scans) in KBr pellets. Mass spectra were obtained on a MALDI-TOF Dynamo Finnigan mass spectrometer. 1,8,9-Trihydroxyanthracene or *p*-nitroaniline were used as matrices.

Elemental analysis was carried out on a Perkin—Elmer PE 2400 series 2 CHNS/O analyzer. Melting points of substances were determined on a BOETIUS instrument. Purity of compounds was monitored by TLC on Silufol UV 254 plates and from melting points.

UV spectra were recorded on a Lambda 35 spectrophotometer (Perkin—Elmer).

Thiacalix[4]arene **2** was synthesized according to a known procedure.[4] 2,2′-Thiabis(4-methyl-6-*tert*-butyl)phenol was commercially available (Acros Organics).

Synthesis of stereoisomers of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis[(*N*,*N*-diethylcarbamoyl)methoxy]-2,8,14,20-tetrathiacalixarene (3) (general procedure). A mixture of thiacalix[4]arene **2** (2.08 mmol), *N*,*N*-diethyl-2-chloroacetamide (16.64 mmol), and anhydrous alkali metal carbonate (8.32 mmol) in anhydrous acetone (50 mL) was refluxed under argon for 60 h. The course of the reaction was monitored by TLC. The solvent was removed under reduced pressure adding CH_2Cl_2 (250 mL) and 10% HCl (40 mL). The organic layer was separated, washed with water (3×50 mL), dried with $MgSO_4$, and filtered off. Then the reaction mixture was treated using different methods, which depended on the bases used.

Base Na_2CO_3. After the solvent was removed, acetonitrile (15 mL) was added to the solid residue that formed. The residue was filtered off and washed with pentane (20 mL). Compound **3** in the cone conformation was isolated in a yield of 2.17 g (88%).

Base K_2CO_3. After the solvent was removed, acetonitrile (20 mL) was added to the solid residue. The precipitate was filtered off and washed with acetonitrile, and compound **3** in the 1,3-alternate conformation was isolated in a yield of 0.24 g (10%). Acetonitrile was completely removed from the filtrate, the residue was dissolved in chloroform (8 mL), and pentane was added until a precipitate of the K^+ complex with compound **3** in the 1,3-alternate conformation was formed (0.58 g, 24%). Compound **3** in the partial cone conformation was obtained by column chromatography of the filtrate on silica gel using an EtOH—$CHCl_3$ (1 : 12) mixture as eluent in a yield of 1.41 g (58%) (R_f 0.54).

Base Cs_2CO_3. After the solvent was removed, acetonitrile (20 mL) was added to the solid residue. The precipitate was filtered off and washed with pentane to obtain compound **3** in the 1,3-alternate conformation (1.3 g). The filtrate was subjected to column chromatography on silica gel using an EtOH—$CHCl_3$ (1 : 12) mixture as eluent. Two fractions were isolated: compound **3** in the partial cone conformation (0.28 g, 11%) and an additional amount (0.2 g) of compound **3** in the 1,3-alternate conformation (total yield 62%, R_f 0.125).

Compound 3, cone conformation. M.p. 224—226 °C. Found (%): C, 66.14; H, 8.13; N, 4.50; S, 10.99. $C_{64}H_{92}N_4O_8S_4$. Calculated (%): C, 65.49; H, 7.90; N, 4.77; S, 10.93. IR, ν/cm^{-1}: 2964 (CH), 1662 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.05 (s, 36 H, H(4b)); 1.08 (t, 12 H, H(8b), J = 6.5 Hz); 1.19 (t, 12 H, H(8a), J = 6.4 Hz); 3.33 (q, 8 H, H(7b)); 3.46 (q, 8 H, H(7a)); 5.29 (s, 8 H, H(5)); 7.25 (s, 8 H, H(3)). ^{13}C NMR ($CDCl_3$), δ: 13.04 (C(8b)); 14.41 (C(8a)); 31.15 (C(4b)); 33.98 (C(4a)); 39.70 (C(7b)); 41.10 (C(7a)); 71.47 (C(5)); 128.87 (C(2)); 134.28 (C(3)); 145.45 (C(4)); 157.90 (C(1)); 167.44 (C(6)) (the atoms are enumerated in Fig. 1, *a*). MALDI TOF mass spectrum, *m*/*z*: 1196 $[M + Na]^+$.

Compound 3, partial cone conformation. M.p. 229—231 °C. Found (%): C, 65.70; H, 8.17; N, 4.66; S, 10.89. $C_{64}H_{92}N_4O_8S_4$. Calculated (%): C, 65.49; H, 7.90; N, 4.77; S, 10.93. IR, ν/cm^{-1}: 2965 (CH), 1665 (C=O). ^{1}H NMR ($CDCl_3$), δ: 0.94 (t, 3 H,

H(8B˙)); 0.97 (t, 3 H, H(8A$^+$)); 1.03 (s, 18 H, H(4b)); 1.12 (t, 6 H, H(10B)); 1.13 (t, 6 H, H(10A)); 1.15 (t, 3 H, H(8B$^+$)); 1.16 (t, 3 H, H(8A˙)); 1.26 (s, 9 H, H(4b˙)); 1.38 (s, 9 H, H(4b$^+$)); 3.17 (q, 2 H, H(7B˙)); 3.20 (m, 2 H, H(9A′)); 3.31 (q, 2 H, H(7A˙)); 3.33 (m, 2 H, H(9B′)); 3.36 (m, 2 H, H(7B$^+$)); 3.37 (m, 2 H, H(7A$^+$)); 3.41 (m, 2 H, H(9B)); 3.47 (m, 2 H, H(9A)); 4.69 (d, 2 H, H(7′), J = 13.0 Hz); 4.72 (s, 2 H, H(5$^+$)); 4.96 (d, 2 H, H(7), J = 13.0 Hz); 5.15 (s, 2 H, H(5˙)); 7.02 (d, 2 H, H(3), J = 2.5 Hz); 7.54 (s, 2 H, H(3˙)); 7.57 (d, 2 H, H(5), J = 2.5 Hz); 7.89 (s, 2 H, H(3$^+$)). ^{13}C NMR ($CDCl_3$), δ: 12.81 (C(8B˙)); 13.09 (C(8B$^+$)); 13.16 (C(10B)); 14.15 (C(8A˙)); 14.41 (C(10A)); 14.56 (C(8A$^+$)); 31.07 (C(4b)); 31.24 (C(4b$^+$)); 31.32 (C(4b˙)); 33.94 (C(4a)); 34.01 (C(4a˙)); 34.33 (C(4a$^+$)); 38.80 (C(7b˙)); 40.09 (C(9B)); 40.22 (C(7B$^+$)); 40.67 (C(7A˙)); 41.14 (C(9A)); 41.93 (C(7A$^+$)); 67.35 (C(5˙)); 70.29 (C(5$^+$)); 91.93 (C(7)); 127.02 (C(6)); 127.58 (C(2)); 127.92 (C(2$^+$)); 128.13 (C(2˙)); 133.72 (C(5)); 134.70 (C(3)); 134.91 (C(3˙)); 135.66 (C(3$^+$)); 144.22 (C(4˙)); 145.89 (C(4)); 145.92 (C(4$^+$)); 157.64 (C(1˙)); 157.72 (C(1)); 159.06 (C(1$^+$)); 166.46 (C(6$^+$)); 166.48 (C(8)); 167.83 (C(6˙)) (the atoms are enumerated in Fig. 1, *c*). MALDI TOF mass spectrum, *m/z*: 1196 [M + Na]$^+$, 1211 [M + K]$^+$.

Compound 3, 1,3-alternate conformation. M.p. 300 °C. Found (%): C, 65.67; H, 8.14; N, 4.72; S, 10.93. $C_{64}H_{92}N_4O_8S_4$. Calculated (%): C, 65.49; H, 7.90; N, 4.77; S, 10.93. IR, ν/cm^{-1}: 2963 (CH), 1675 (C=O). ^{1}H NMR ($CDCl_3$), δ: 0.97 (t, 12 H, H(8a)); 1.13 (t, 12 H, H(8b)); 1.23 (s, 36 H, H(4b)); 3.26 (q, 8 H, H(7a)); 3.36 (q, 8 H, H(7b)); 4.65 (s, 8 H, H(5)); 7.51 (s, 8 H, H(3)). ^{13}C NMR ($CDCl_3$), δ: 12.99 (C(8b)); 14.42 (C(8a)); 31.28 (C(4b)); 34.14 (C(4a)); 39.91 (C(7b)); 41.47 (C(7a)); 69.21 (C(5)); 127.70 (C(2)); 132.95 (C(3)); 145.70 (C(4)); 157.55 (C(1)); 166.53 (C(6)) (the atoms are enumerated in Fig. 1, *a*). MALDI TOF mass spectrum, *m/z*: 1196 [M + Na]$^+$, 1211 [M + K]$^+$.

Complex of compound 3 with potassium chloride in the 1,3-alternate conformation. A mixture of compound **2** (7 g, 9.71 mmol), *N*,*N*-diethyl-2-chloroacetamide (11.62 g, 77.6 mmol), and dry K_2CO_3 (8.05 g, 58.26 mmol) in anhydrous acetone (100 mL) was refluxed under argon for 60 h. The course of the reaction was monitored by TLC. After cooling, acetone was removed, CH_2Cl_2 (250 mL) and 10% HCl (60 mL) were added, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×70 mL). The combined organic extracts were washed with water (3×50 mL) and dried with $MgSO_4$, the solvent and excess diethylchloroacetamide were removed under reduced pressure, and CH_2Cl_2 (20 mL) and pentane (80 mL) were added to a residue. The precipitate was filtered off and twice washed with pentane. The complex of compound **3** with potassium chloride in the 1,3-alternate conformation was isolated in a yield of 9.0 g (79%). M.p. 256—260 °C. Found (%): C, 58.10; H, 7.09; Cl, 6.29; N, 4.28; S, 9.43. $C_{64}H_{92}N_4O_8S_4 \cdot KCl \cdot 0.5CHCl_3$. Calculated (%): C, 58.72; H, 7.08; Cl, 6.79; N, 4.28; S, 9.79. ^{1}H NMR ($CDCl_3$), δ: 1.12 (t, 6 H, H(8b)); 1.13 (t, 6 H, H(8a)); 1.14 (t, 6 H, H(8b*)); 1.20 (s, 18 H, H(4b)); 1.22 (s, 18 H, H(4b*)); 1.23 (t, 6 H, H(8a*)); 3.15 (q, 8 H, H(7a), H(7a*)); 3.37 (m, 8 H, H(7b), H(7b*)); 4.76 (s, 4 H, H(5)); 4.85 (s, 4 H, H(5*)); 7.32 (s, 4 H, H(3)); 7.56 (s, 4 H, H(3*)). ^{13}C NMR ($CDCl_3$), δ: 12.99 (C(8b), C(8b*)); 14.04 (C(8a*)); 14.53 (C(8a)); 30.60 (C(4b)); 30.67 (C(4b*)); 34.22 (C(4a)); 34.40 (C(4a*)); 39.81 (C(7b), C(7b*)); 40.57 (C(7a*)); 41.08 (C(7a)); 67.04 (C(5)); 68.65 (C(5*)); 127.42 (C(2*)); 130.39 (C(2)); 131.87 (C(3)); 134.17 (C(3*)); 146.96 (C(4)); 149.04 (C(4*)); 154.00 (C(1*)); 156.93 (C(1)); 165.10 (C(6)); 166.19 (C(6*)) (the atoms are enumerated in Fig. 1, *b*). MALDI TOF mass spectrum, *m/z*: 1211 [M + K]$^+$. ESI mass spectrum, *m/z*: 1211 [M + K]$^+$.

The filtrate was purified by column chromatography on silica gel using an EtOH—$CHCl_3$ (1 : 15) mixture as eluent and yielded compound **3** in the partial cone conformation in a yield of 1.30 g (11%).

3,3′-Di-*tert*-butyl-5,5′-dimethyl-2,2′-bis(*N*,*N*-diethylcarbamoylmethoxy)diphenyl sulfide (7). A mixture of 2,2′-thiabis(4-methyl-6-*tert*-butyl)phenol (2 g, 5.58 mmol), *N*,*N*-diethyl-2-bromoacetamide (3.24 g, 16.7 mmol), and K_2CO_3 (3.08 g, 22.53 mmol) was refluxed for 28 h in anhydrous acetone (60 mL). The course of the reaction was monitored by TLC. After the reaction mixture was cooled, acetone was removed, and 30% HCl (50 mL) and $CHCl_3$ (250 mL) were added to the residue. The organic phase was separated, washed with water (3×50 mL), and dried with $MgSO_4$. The drying agent was filtered off, and chloroform and excess diethylbromoacetamide were removed under reduced pressure. Product **7** was isolated as a colorless oil in a yield of 2.7 g (87%). Found (%): C, 70.24; H, 8.91; N, 4.45; S, 5.30. $C_{34}H_{52}N_2O_4S$. Calculated (%): C, 69.82; H, 8.96; N, 4.78; S, 5.48. IR, ν/cm^{-1}: 1650 (C=O), 2965 (CH). ^{1}H NMR ($CDCl_3$), δ: 1.04, 1.12 (both t, 6 H each, Me, J = 7.1 Hz); 1.40 (s, 18 H, 3 Me); 2.18 (s, 6 H, Me); 3.32, 3.37 (both q, 4 H each, CH_2, J = 7.1 Hz); 4.78 (s, 4 H, OCH_2); 6.73, 7.05 (both d, 2 H each, H arom., J = 7.1 Hz). MALDI TOF mass spectrum, *m/z*: 586 [M + Na]$^+$.

Procedure of extraction studies. Alkali metal picrates were prepared by pouring together aqueous solutions of picric acid and solutions of metal hydroxides, which were pre-titrated with a 0.1 *M* solution of HCl. Aqueous solutions of picrates (4 mL) containing excess metal hydroxide and solutions of the compounds under study in CH_2Cl_2 (4 mL) were stirred for 60 min at ~20 °C and kept for 90 min to separate phases. The initial concentrations of the ligand in the organic phase and metal hydroxide and picrate in the aqueous phase were $[\mathbf{3}]_0 = 3.5 \cdot 10^{-4}$ mol L^{-1}, $[MOH]_0 = 7.0 \cdot 10^{-5}$ mol L^{-1}, and $[HPic]_0 = 5.0 \cdot 10^{-5}$ mol L^{-1}, respectively.

The absorbances of the aqueous phase before and after extraction (A_i and A_0, respectively) were determined at 355 nm. The extraction percentage (E) was calculated by the equation

$$E = [(A_0 - A_i)/A_0] \cdot 100.$$

X-ray diffraction analysis of compound 3 in the partial cone and 1,3-alternate conformations. X-ray diffraction analyses were carried out on an Enraf-Nonius CAD-4 automated four-circle diffractometer at 20 °C using Cu-Kα radiation (λ(Cu-Kα) = 1.54184 Å). The crystals of compound **3** in the partial cone conformation are orthorhombic. At 20 °C a = 10.520(3) Å, b = 23.40(1) Å, c = 26.96(1) Å, V = 6637(5) Å^3, Z = 4, d_{calc} = 1.17 g cm^{-3}, and space group $P2_12_12_1$. The crystals of compound **3** in the 1,3-alternate conformation are also orthorhombic. At 20 °C a = 19.46(2) Å, b = 12.630(5) Å, c = 27.72(1) Å, V = 6813(8) Å^3, Z = 4, d_{calc} = 1.14 g cm^{-3}, and space group $Pna2_1$. The unit cell parameters of intensities of 9419 (partial cone) and 6486 (1,3-alternate) reflections, of which 5559 (partial cone) and 4288 (1,3-alternate) reflections had $I \geq 2\sigma$, were measured at room temperature (graphite mono-

chromator, ω/2θ scan mode, θ ≤ 74.19°). The crystal structures were determined by a direct method using the SIR program,[18] and non-hydrogen atoms were refined in the full-matrix anisotropic approximation for F^2. Then the hydrogen atoms, whose contribution to the structural amplitudes were taken into account with fixed positional and isotropic temperature parameters at the final refinement stages, were revealed from the difference electron density series. The final divergence factors were $R = 0.079$, $R_w = 0.197$ for 5559 observed reflections with $F^2 \geq 2\sigma$ (partial cone); $R = 0.074$, $R_w = 0.189$ for 4288 observed reflections with $F^2 \geq 2\sigma$ (1,3-alternate). All calculations were performed by the WINGX program package.[19] The figures were drawn and intermolecular interactions were calculated using the PLATON program.[20]

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