

1 **Lithium cations in a self-assembled electrostatic nanocapsule†**

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39 **ABSTRACT:**

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41 Cascade self-assembly of small components, without the employment of preformed hosts, yielded a
42 $\{\text{Ni}_{12}\text{Li}_2\}$ nanometric capsule with multiple endo- and exo-guests (water molecules, Li^+ , and Et_3NH^+
43 cations) linked to selective hydrophilic and hydrophobic binding sites of NiIII hexanuclear
44 metallamacrocycles. The synthesis was achieved by using $(\text{Bu}_4\text{N})\text{N}_3$ as a starting reagent instead of the
45 conventional sodium azide to selectively introduce the Li^+ cations.

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47 After the pioneering work of Cram, Lenh, and Pedersen (Nobel prize 1987), the study of the chemistry
48 of non-covalent interactions is consolidated as an important research field that has reached an
49 extraordinary level of complexity. A great deal of interest during the last years has been focused on the
50 3D supramolecular arrangements having cavities, which can encapsulate guest molecules as a mimic of
51 biological entities,¹ recognition and sensing,² or catalysis³ by taking advantage of the unique properties
52 of the inner cavities in comparison with the bulk solution. The employment of preformed organic
53 receptors such as cyclophanes, calixarenes, cyclodextrins among others in the predictable host–guest
54 chemistry has been one of the common strategies to generate bowls or capsules in which the weak
55 interactions (H-bonds, π – π stacking, etc.) play a crucial role.⁴ A different strategy to promote the
56 supramolecular structures has been the use of small units, which can be self-assembled in a one-pot
57 reaction by the incorporation of cations as linkers between organic donors. This methodology has
58 yielded a variety of beautiful metallocages, in which the cations are placed at the vertexes of polygonal
59 or polyhedral architectures⁵ with a positive charge that becomes efficient hosts to encapsulate the
60 anions. More recently, the attention has been focused on more sophisticated multi-guest capsules based
61 on the heterotropic binding of endo- and exosites that promote the cooperative interactions among them
62 or even the allosteric effects.⁶ The carbonate anion exhibits an enormous coordination chemistry as a
63 consequence of its large number of coordination modes (until μ_{10} -CO₃²⁻).⁷ Among them, the
64 interesting μ_6 -CO₃²⁻ mode is prone to generate NiII discrete or decorated hexanuclear metallocycles or
65 metallacrowns containing the μ_6 -CO₃²⁻ templating anion.⁷ Employing the adequate coligands, the
66 resulting cationic or anionic metallamacrocycles can host either the chloride anions or the K⁺ cations as
67 in the case of [Ni₉(μ_6 -CO₃)(OH)₆(hchp)₃(Hchp)₃(O₂CCH₂NMe₃)₉Cl]⁶⁺ (Hchp = 6-chloro-2-
68 pyridonate)^{7a} or the azido containing [Ni₆(μ_6 -CO₃)($\mu_{1,1}$ -N₃)₆(OAc)₃(dpkMeCN–H)₃]²⁻
69 (dpkMeCN–H = the cyanomethylated ligand derived from dipyridylketone), respectively.^{7b}
70 Following these premises, we have used different small pieces with or without O-donors and different
71 polarities to assemble a new metallamacrocycle containing the gem-diol (py₂C(O)(OH)⁻), derived from
72 the hydrolysis of the dipyridylketone (dpk),⁸ azido, and pyrazole (Hpz) co-ligands. The one-pot
73 reaction in the presence of lithium cations generated a nanometric supramolecular assembly of
74 approximate dimensions (1.9 × 1.6 × 1.6 nm³). The resulting system was one capsule with a tetradeca
75 metallic core and two different endo-guests along with the unusual presence of exo-guests, related to the
76 hexanuclear carbonato/dpk family^{7b,d} having the formula (Et₃NH)₂{Li(H₂O)}₂[Ni₆((μ_6 -
77 CO₃)(N₃)₆(pz)₃(py₂C(O)(OH))₃)]₂ (1). However, it was quite surprising that in spite of the high
78 entropic cost, up to 44 small components self-assembled to yield a capsule of the nanometric size, which
79 contains two lithium cations stabilized, for the very first time, only by the action of the electrostatic
80 effects.
81 The azido source is far to be innocent, and recently, Stamatatos et al.⁹ pointed out the characterization of
82 unprecedented topologies and nuclearities by the successful employment of Me₃SiN₃ to avoid the
83 problems arising from the poor solubility of sodium azide in organic solutions.¹⁰ In the present case, the

84 key of the syntheses was the employment of tetrabutylammonium azide salt as a starting reagent
85 profiting two key properties: very high solubility in common organic solvents and the control of metallic
86 cations present in the reaction media.

87 Complex 1 contains two $[\text{Ni}_6(\mu_6\text{-CO}_3)(\text{N}_3)_6(\text{pz})_3\{\text{py}2\text{C}(\text{O})(\text{OH})\}_3]^{2-}$ metallacycles, which consist of
88 a hexagonal arrangement of the NiII cations held together by one $\mu_6\text{-CO}_3^{2-}$ ligand placed in the center
89 of the ring. In addition to this bridge, the NiII cations were alternatively linked by one end-on azido and
90 one pyrazole bridges or one end-on azido and one O-donor from one dipyridyl-diol, as indicated by the
91 structure in Fig. 1 (lateral view). The octahedral NiN_4O_2 environment was equal for all the NiII cations
92 (two N-azide, one N-pz, one N-pyridyl, one O- $\text{py}2\text{C}(\text{O})(\text{OH})^-$, and one O-carbonate). Three $\mu_{1,1}\text{-N}_3$
93 and the three pyrazolate ligands were placed below the main Ni_6 plane, whereas the other three $\mu_{1,1}\text{-N}_3$
94 and the three $\text{py}2\text{C}(\text{O})(\text{OH})^-$ ligands were placed above this main plane. As a consequence of this
95 arrangement, all the O-donors and the anionic charges from the $\text{py}2\text{C}(\text{O})(\text{OH})^-$ ligands were placed in
96 the same side of the molecule, generating a hydrophilic cavity in one side of the ring, whereas the
97 pyrazole rings form a hydrophobic cavity on the other side, resulting in a double-bowl with opposite
98 binding properties, as demonstrated by the structure in Fig. 1 (top view). The dianionic centrosymmetric
99 $\{\text{Ni}_{12}\text{Li}_2\}$ complex was then formed by two hexanuclear NiII metallacycles, two LiI cations, two water
100 molecules, and two $\text{exo-Et}_3\text{NH}^+$ counter cations that fulfill the charge balance (see Fig. 2).

101 The distance between the mean Ni_6 planes was 8.195 Å, and the lithium cations were placed quasi
102 equidistant among them (4.116 and 4.069 Å). Each lithium ion was placed in a tetrahedral LiO_4
103 coordination environment, formed by the two water molecules and two protonated R-OH groups
104 provided by two $\text{py}2\text{C}(\text{O})(\text{OH})^-$ ligands with large $\text{Li}\cdots\text{O}$ distances.

105 The Ni_6 rings are the main building block that promotes a large variety of supramolecular cascade
106 interactions, which finally yields in the $(\text{Et}_3\text{NH})_2\{\text{Li}(\text{H}_2\text{O})\}_2[\text{Ni}_6((\mu_6\text{-CO}_3)(\text{N}_3)_6(\text{pz})_3$
107 $(\text{py}2\text{C}(\text{O})(\text{OH})_3)]_2$ system. Each metallamacrocycle was a template containing one carbonate anion
108 that allowed the quasiregular hexagonal arrangement of the NiII cations. The different polarity of the
109 starting ligands (pyrazole and $\text{py}2\text{C}(\text{O})(\text{OH})^-$) and its distribution generated two surfaces with different
110 characteristics. On the one hand, the hydrophilic side of the ring (containing all the deprotonated O-
111 donors and the alcoxyl arms of the $\text{py}2\text{C}(\text{O})(\text{OH})^-$ ligands) linked one water molecule by means of two
112 H-bonds with two deprotonated RO-groups, where the $\text{O}_{10}\cdots\text{O}_3$ and $\text{O}_{10}\cdots\text{O}_3$ distances were 2.998(3)
113 and 2.796(7) Å, respectively. The hydrophilic sides of two metallamacrocycles were linked by weak H-
114 bonds between these water molecules and one of the alcoxyl arms of the other moiety of the capsule
115 ($\text{O}_{10}\cdots\text{O}_{2'}$, 2.991(9) Å), by means of a weak direct contact between the two alcoxyl arms ($\text{O}_{2'}\cdots\text{O}_{6'}$,
116 3.155(7) Å). This anionic oxophilic cavity thus becomes the preferred site to host the two lithium
117 cations, which by means of electrostatic interactions contribute to stabilize the capsule (see top structure
118 in Fig. 3).

119 On the other hand, the hydrophobic sides of the rings host the triethylammonium cations that were
120 linked by means of three weak H bonds ($\text{C-H}\cdots\text{N}$), with the azido bridging N-donors (N13, N19, and

121 N25), and the three CH $\cdots\pi$ interactions were established by one of the H-atoms of the –CH₂– group and
122 the π system of the pyrazole rings, (see the middle structure in Fig. 3). These kinds of interactions,
123 favored by the presence of electronegative heteroatoms and/or the charges on the ring, are equally
124 important than H-bonds or π – π stacking when stabilizing the supramolecular arrangements.¹¹
125 As a result, the complete neutral capsule was determined by the two hydrophilic sides of the two
126 metallamacrocycles, with four endo guests and the hydrophobic ends that link the two exo guests (see
127 the down structure in Fig. 3).

128 One of the most striking features of complex 1 was related to the coordination of the lithium cations that
129 show four Li \cdots O distances in the sharp 2.713–2.835 Å range. Further analysis of the structures reported
130 in the CCDC database showed that the Li–O distances could be extremely variable as a function of the
131 properties of the O-donors and the coordination number. For the tetrahedral LiO₄ environment, the most
132 usual distances were comprised between 1.9–2.0 Å (1500 entries), and only a few tetrahedral units
133 involving four alcoxyl or phenoxyl O-donors (only 20 entries) exhibited four larger distances comprised
134 between 2.0–2.1 Å. The Li–O distances in the range of 2.3–2.65 Å were limited to high coordination
135 numbers and poor donor atoms (crown ethers) like those found in the [Li(12Cr₄)₂]⁺ sandwich
136 compounds (148 entries). In absolute terms, the coordination environment of the lithium cations in
137 complex 1 shows the largest Li \cdots O distances reported till now, and it is so unusual that a BSV
138 calculation yielded a value of 0.1. In fact, the lithium cations were placed inside a negatively charged
139 electrostatic cavity, which was able to include them in a practically perfect ionic interaction. The μ _{1,1}-
140 N₃ bridges typically induce ferromagnetic interactions between the Ni^{II} cations, even in double or triple
141 bridges mixed with other ligands.¹⁰ The magnetic study was not the target of this work but to provide
142 information to the reader, has been mentioned in the ESI.† In conclusion, we reported a synthetic
143 strategy for fabricating host–guest supramolecular structures that opens new perspectives in the active
144 field of azido-cluster chemistry, controlling the introduction of alkaline cations in the reaction media.
145 The reported compound is a rare example of a cascade of supramolecular interactions (template, H-
146 bonds, CH- π , and electrostatic) that allows the stabilization of a nanocapsule with multiple endo- and
147 exo-guests. The endo-lithium cations provide a unique example of two lithium cations inside an
148 electrostatic box. A complete series of supramolecular arrangements from capsules to bowls based on
149 the same hexanuclear metallamacrocycle and also acting as a metallacrown depending on the cation
150 size, cation charge, and exo-counter cation will be published in the future paper.

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152 **ACKNOWLEDGEMENTS**

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192 **Legends to figures**

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194 **Figure.1** Top, frontal, and lateral view of the template {Ni₆} ring showing the hexagonal arrangement
195 of the Ni^{II} cations and the two hydrophobic and hydrophilic sides of the metallamacrocycle. The
196 pyrazole rings are highlighted in orange and the phenyl rings from the gem-diol form of dpk ligand in
197 grey. Bottom, labelled core of the {Ni₆} ring..

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199 **Figure.2** Molecular view of complex 1.(top). Color key: Ni, green; Li, orange; N, navy; O, red; C, grey.

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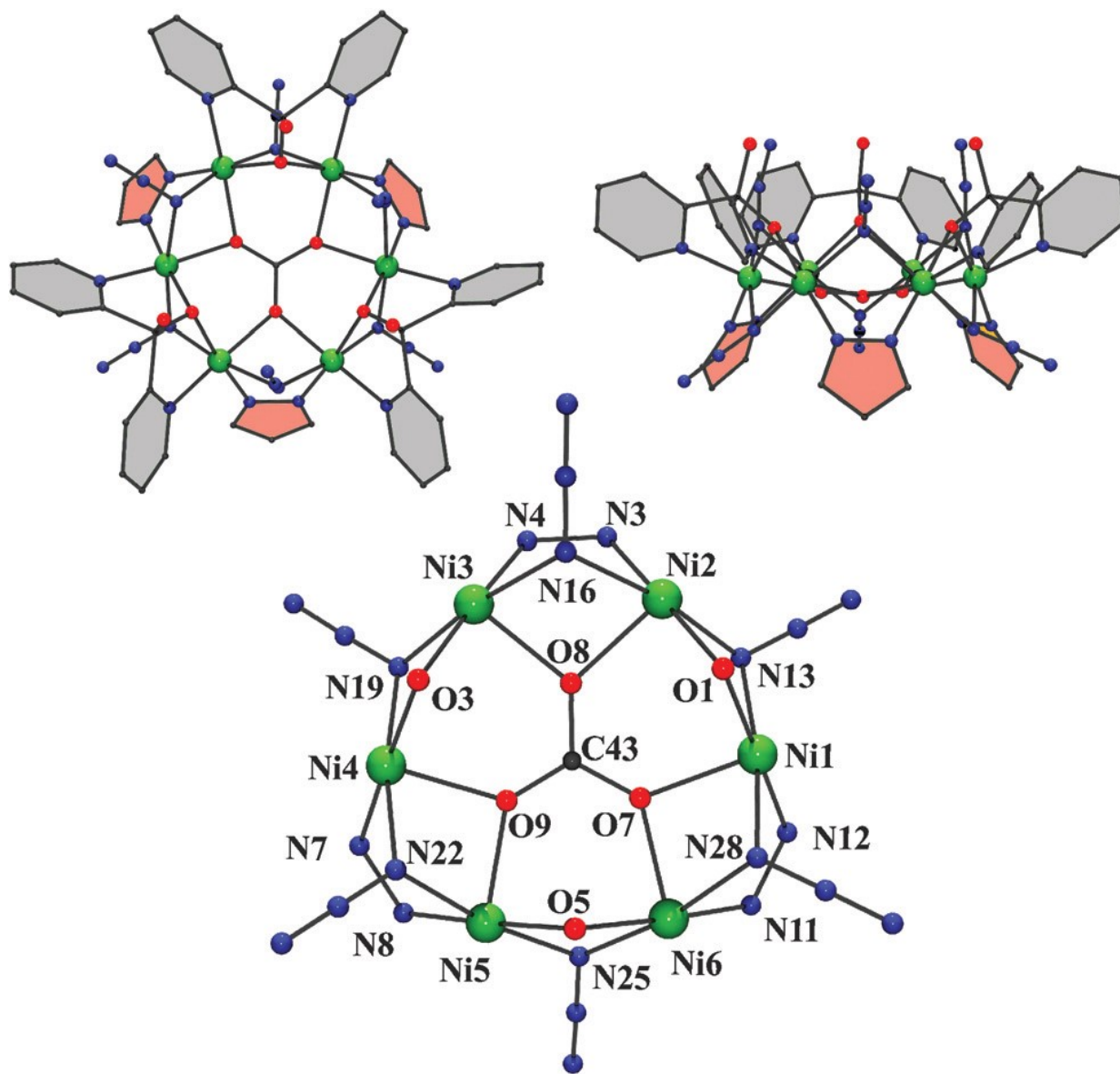
201 **Figure.3.** The supramolecular interactions present in compound 1: top, weak H-bonds and Li⁺
202 electrostatic interactions between the two Ni₆ metallacycles; middle, CH \cdots π interactions between the
203 Et₃NH⁺ cations and the anionic metallamacrocycles. Bottom, resulting multicomponent capsule, (C-
204 atoms from the metallamacrocycles, brown; C-atoms from the Et₃NH⁺ cation, pink).

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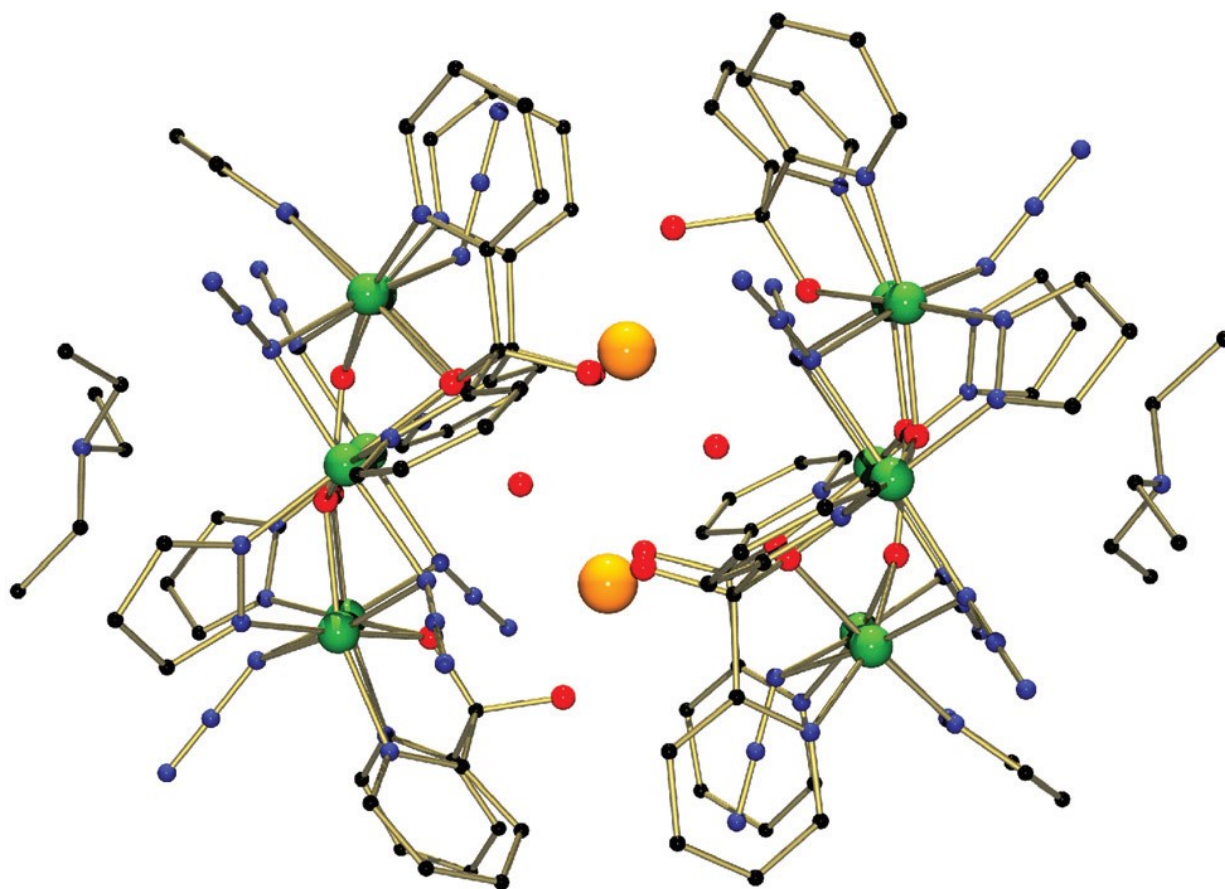
FIGURE 1



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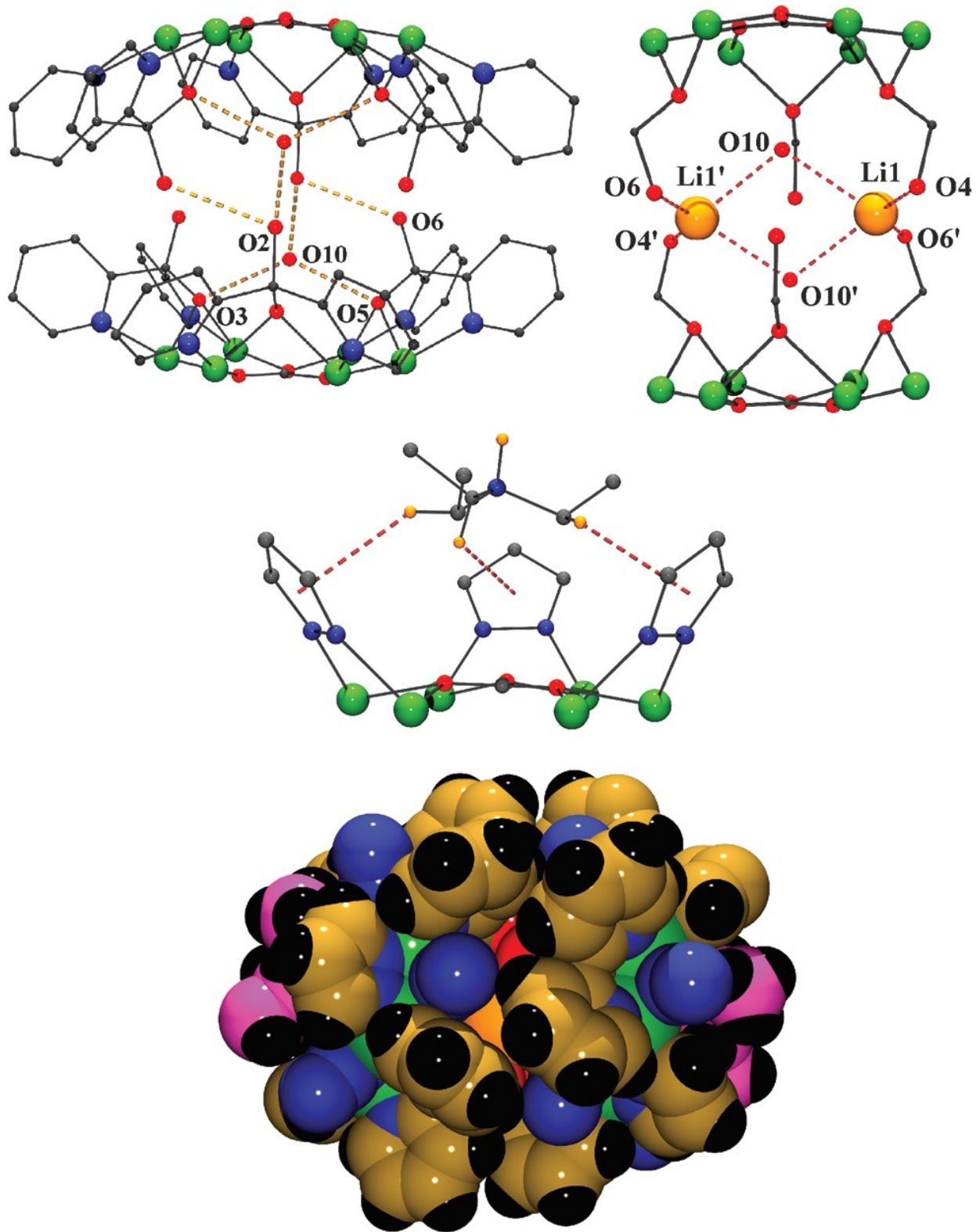
FIGURE 2



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FIGURE 3



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