Organic LETTERS

Letter

pubs.acs.org/OrgLett

New "Pyrene Box" Cages for Adaptive Guest Conformations

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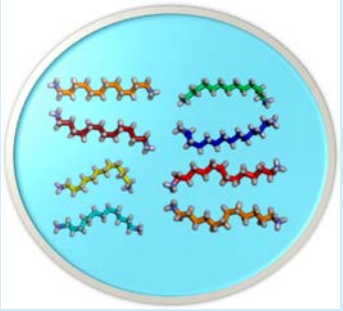
Supporting Information

ABSTRACT: The possibility of controlling the compression extent and the coiling shape of the 1,12-diammoniumdodecane guest is shown by changing the dimensions of the internal space of the host guanidinium 1,3,5,8 pyrene-tetrasulfonate $\mathbf{PTS^{4-}}$ crystalline capsules by using guanidinium ($\mathbf{G^+}$), amino-guanidinium ($\mathbf{AG^+}$), and diaminoguanidinium ($\mathbf{A_2G^+}$) cations.



Lipid-binding proteins encapsulate hydrocarbon chains by using weak hydrophobic and anchoring electrostatic or H-bonding interactions.[1−4] Similar phenomena have been observed with the artificial systems.[5−7] The compression of *n*-alkanes inside artificial H-bonded capsules in water has been extensively described by Rebek Jr. et al.[5] and Gibb et al.[6] Lehn et al. reported the first linear elongated structures of 1,ω-diammonium-alkanes recognized by bitopic macrocyclic cylinders.[7a,b] As in biological systems, the constitutional flexibility of the alkyl chains, inducing synergetic interactions between the host−guest components, can in some cases be reinforced by supplementary strong interactions.[5−7] Dynamic selection of alkane can be adaptively obtained on guest encapsulation.[6] Variable *bridge*, *loop*, and *tail* conformations of 1,12-diammonium-dodecane confined inside the lamellar space of montmorillonite have been proposed.[7c]

Our previous experience in the confinement of compressed alkanes at the molecular level, both in aqueous solution and in solid state, concerns the use of a crystalline pyrene box self-assembled from available commercial materials: the 1,3,5,8 pyrene-tetrasulfonate anions, $\mathbf{PTS^{4-}}$, the guanidinium cations, $\mathbf{G^+}$, and 1,ω-diammonium-alkanes (Figure 1).[8] The 1,ω-diammonium-alkanes are anchored via their ammonium tethering groups, interacting via H-bonding and ionic interactions with the sulfonate groups of $\mathbf{PTS^{4-}}$ anions. This mechanism is responsible for squeezing progressively longer springs inside a fixed chemical space. To our surprise, we observed that adaptive encapsulation occurs and both highly compressed and noncompressed chains are equally favored.[8a]

Strategy

We previously observed that the variable relative spatial disposition of the $\mathbf{PTS^{4-}}$ platforms within the crystal, related to the presence or the absence of the $\mathbf{G^+}$ cations, induces a different dimensional disposition of the sulfonate anchoring points used for the 1,ω-diammonium-alkane binding.[8a,b] This

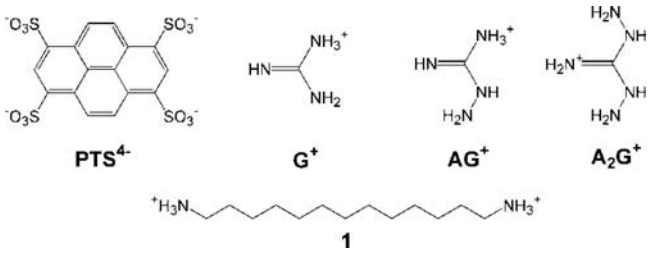


Figure 1. Crystalline "pyrene boxes" are self-assembled from available commercial materials: the 1,3,5,8 pyrene-tetrasulfonate anions, $\mathbf{PTS^{4-}}$, the guanidinium ($\mathbf{G^+}$), aminoguanidinium ($\mathbf{AG^+}$), and diaminoguanidinium ($\mathbf{A_2G^+}$) cations, and 1,12-diammonium-dodecane, **1**.

behavior, together with the conformational versatility of alkane chains, leads us to consider controlling the molecular conformation of the alkane guest by designing and changing the shape and size of the encapsulating space. Generally speaking, it should be possible to control the compression extent and the coiling shape of the alkane guest, by changing the internal space of the host. One possibility is to move from initial crystalline **PTSG** pyrene box[8] toward novel **PTSAG** and $\mathbf{PTSA_2G}$ cages, where aminoguanidinium ($\mathbf{AG^+}$) and diaminoguanidinium ($\mathbf{A_2G^+}$) cations may be used instead of $\mathbf{G^+}$. This change in capsule design would completely modify the relative spatial disposition of the components and its interior and, consequently, the conformation of the encapsulated alkyl chain. This is not simply a matter of size of used cations, but it also brings important conformational changes of the dimensions of the interior chemical space, due to their ability to act simultaneously as H-bond donors and acceptors.[9,10]

Received: March 17, 2015
Published: April 20, 2015

DOI: 10.1021/acs.orglett.5b00779
Org. Lett. 2015, 17, 2178−2181

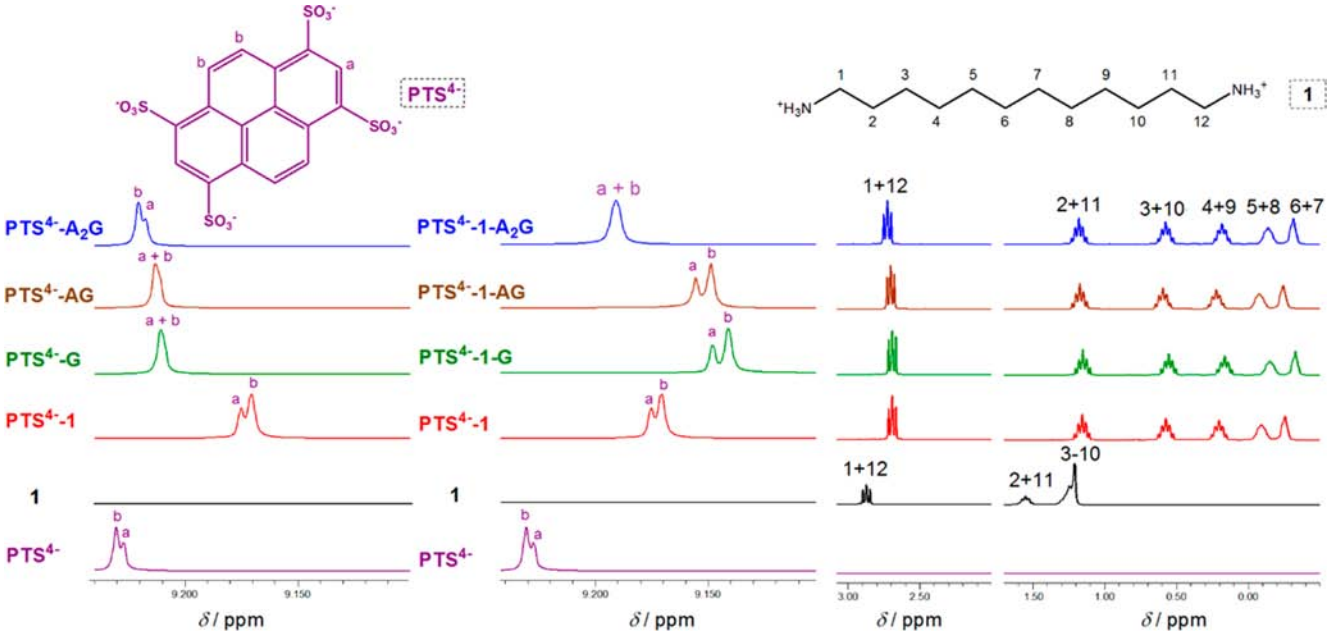


Figure 2. ^{1}H NMR spectra in D_2O at 25 °C: (a) the aromatic region for $\mathbf{PTS}^{4-}$, **1**, $\mathbf{PTS}\{\mathbf{1}\}_2$, **PTSG**, **PTSAG**, and $\mathbf{PTSA_2G}$ and (b) the aromatic and the aliphatic region for $\mathbf{PTS}^{4-}$, **1**, $\mathbf{PTS}\{\mathbf{1}\}_2$, **PTSG**{**1**}, **PTSAG**{$\mathbf{1}_2$}, and $\mathbf{PTSA_2G}\{\mathbf{1}\}$ capsules.

NMR Studies in Aqueous Solution

The host−guest proxy interactions between model guest 1,12-diammonium-dodecane, **1**, and $\mathbf{PTS}^{4-}$ can be detected in aqueous solution.[8] The preorganization of **PTSG**, **PTSAG**, and $\mathbf{PTSA_2G}$ capsules is confirmed by the upfield shifts (0.01−0.02 ppm) of the H_a and H_b protons of $\mathbf{PTS}^{4-}$ when compared with the spectra of $\mathbf{PTS}^{4-}$ recorded in the absence of guanidinium cations: $\mathbf{G}^+$, $\mathbf{AG}^+$, and $\mathbf{A_2G}^+$ (Figure 1a). The upfield shifts increase in the order $\mathbf{A_2G}^+ < \mathbf{AG}^+ = \mathbf{G}^+$ with a more important effect on the central H_a protons relative to the external H_b protons of $\mathbf{PTS}^{4-}$. This correlates well with the specific close proximity packing of the $\mathbf{PTS}^{4-}$ anions observed in the crystal structures. The relative slipping of the $\mathbf{PTS}^{4-}$ anions is dependent on the H-bonding imposed by the guanidinium cations in agreement with the observed upfield shifts of the H_a and H_b protons of $\mathbf{PTS}^{4-}$. Interestingly, we observed increased upfield shifts (0.05−0.06 ppm) of the H_a and H_b protons of $\mathbf{PTS}^{4-}$ in the presence of only 1,12-diammonium-dodecane **1** when compared with the spectra recorded for the **PTSG**, **PTSAG**, and $\mathbf{PTSA_2G}$ capsules (Figure 2a). This means that, when protonated, 1,12-diamino-dodecane **1** is H-bonded to $\mathbf{PTS}^{4-}$ anions, a preorganized capsule $\mathbf{PTS}\{\mathbf{1}\}_2$ is formed in aqueous solution positioning the $\mathbf{PTS}^{4-}$ anions in close proximity, interacting with 1,12-diammonium-dodecane **1** via hydrophobic interactions. The addition of guanidinium $\mathbf{G}^+$ and $\mathbf{AG}^+$ cations to an aqueous solution of $\mathbf{PTS}\{\mathbf{1}\}_2$ results in the amplification of the upfield shifts (0.08−0.09 pm) of H_a and H_b protons of $\mathbf{PTS}^{4-}$ confirming the stabilization of host−guest complexes **PTSG**{**1**} and **PTSAG**{**1**} (Figure 2b). The downfield shifts (0.014 ppm) of H_a and H_b protons of $\mathbf{PTS}^{4-}$ induced by the addition of $\mathbf{A_2G}^+$ cations confirm the stabilization of more slipped superstructures with less superposed $\mathbf{PTS}^{4-}$ in the structure of $\mathbf{PTSA_2G}\{\mathbf{1}\}$ (Figure 2b). The formation of $\mathbf{PTS}\{\mathbf{1}\}$, **PTSG**{**1**}, **PTSAG**{**1**}, and $\mathbf{PTSA_2G}\{\mathbf{1}\}$ complexes is confirmed by the upfield shifts of the protons of encapsulated **1** when compared with the spectra of **1** recorded in the absence of the capsule components (Figure 2b). In all cases the prevalent interaction observed is the ion-pairing between $\mathbf{PTS}^{4-}$ and the 1,12-diammonium-dodecane **1** resulting in a shielding of the methylene groups signals situated in the middle of the chain by about 1.5 ppm. The upfield shifts observed for $\mathbf{PTS}\{\mathbf{1}\}$ (1.46 ppm) are slightly amplified by the presence of $\mathbf{G}^+$, $\mathbf{AG}^+$, and $\mathbf{A_2G}^+$ cations (1.5−1.53 ppm), as shown by the chemical shift values of central H_5−H_8 proton peaks, due to the supplementary stabilization of the **PTSG** and $\mathbf{PTSA_2G}$ capsules, in which the motion of alkane chains is largely restricted. The signal corresponding to the methylene groups in the 1- and 12-terminal positions of the alkyl chain remains practically unchanged for all $\mathbf{PTS}\{\mathbf{1}\}$, **PTSG**{**1**}, **PTSAG**{$\mathbf{1}_2$}, and $\mathbf{PTSA_2G}\{\mathbf{1}\}$ species (Figure 2b). This is in good agreement with the crystal structures presented below, where the middle of the chain is shielded by the pyrene rings and the terminal atoms are close to the edge, almost out of the capsules, tethered both to sulfonate moieties and to water molecules. The broad H_5−H_8 proton signals, showing −C−H/π (PTS) interactions, are reminiscent of important dynamic behavior of alkane chains during the ion-pairing process. This is also consistent with the dynamic variable coiled conformations observed in the X-ray crystal structures presented below where the alkyl chains adopt adaptive folded conformations within the confined space.

X-ray Single Crystal Structures

Previous crystallographic analysis showed high compression of 1,12-diammonium-dodecane **1** within the **PTSG** host.[8a,b] From these previous studies we know that $\mathbf{PTS}^{4-}$ anions and two of the $\mathbf{G}^+$ cations are strongly interacting in the crystal via H-bonding ($d_{O\cdots H-N}$ of 2.00 Å) and charge interactions. This network is reinforced by two bridging water molecules, which are simultaneously H-bonded to $\mathbf{G}^+$ ($d_{O\cdots H-N}$ of 2.00 Å) and to $\mathbf{PTS}^{4-}$($d_{S\cdots H-O}$ of 1.98 Å), playing a significant role in the stabilization of the pyrene box. The presence of $\mathbf{G}^+$ cations induces a slightly slipped relative position of the $\mathbf{PTS}^{4-}$ in the pyrene box, **PTSG**{**1**} in which **1** forms two anchoring H-bonds ($d_{N\cdots O}$ of 1.93 Å) with two sulfonate moieties of two different $\mathbf{PTS}^{4-}$ platforms, themselves nonbonded to $\mathbf{G}^+$ cations.

DOI: 10.1021/acs.orglett.5b00779
Org. Lett. 2015, 17, 2178−2181

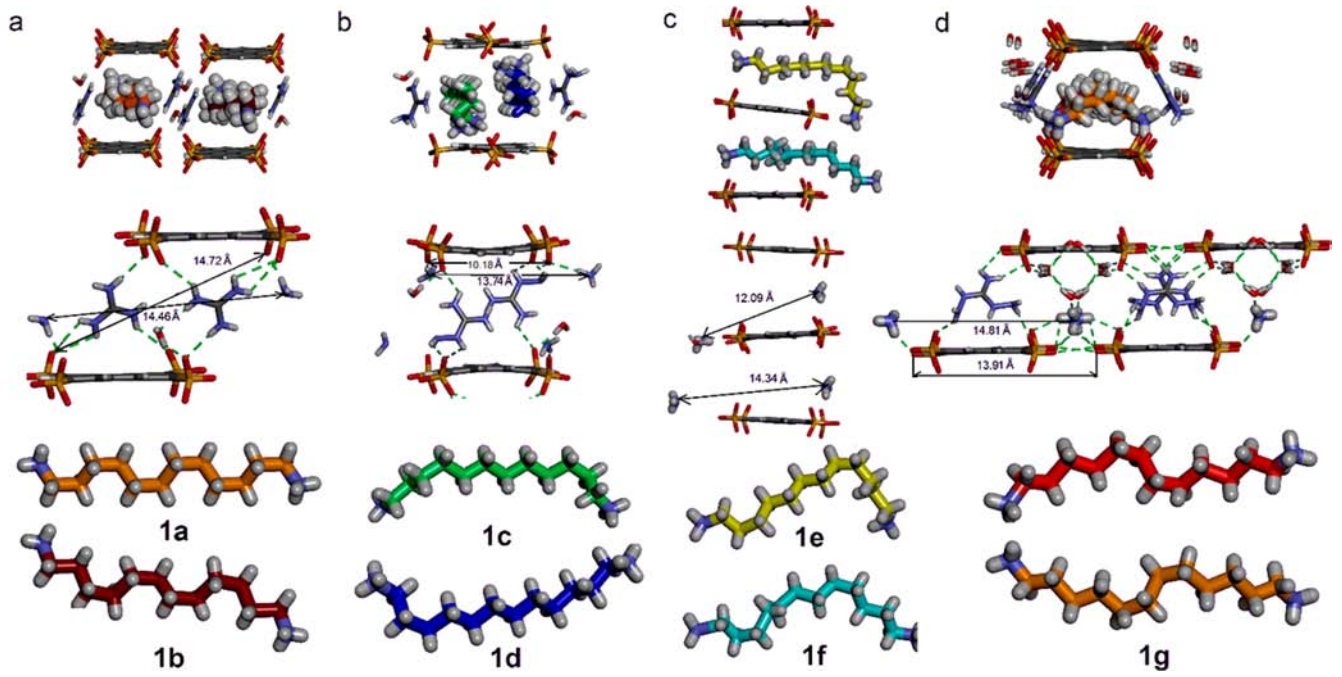


Figure 3. X-ray structures of (a) **PTSG**, (b) **PTSAG**, (c) **PTS**, and (d) **PTSA$_2$G** systems: (top) side view of the inclusion complexes; (middle) side view of the H-bonded matrices highlighting the distances between two sulfonate binding groups and the distance between the ammonium groups of encapsulate **1**; (bottom) encapsulated conformers **1a**−**g** present inside the **PTSG**, **PTSAG**, **PTS**, and **PTSA$_2$G** boxes. The identical conformers **1g** present the different orientations within capsules **PTSAG** and **PTSA$_2$G**, respectively.

The N_1−N_{12} distance is 14.46 Å, corresponding with a 13% compression with respect to the length (16.53 Å) of fully extended **1**. A deeper crystallographic analysis of the electron density maps allowed us to identify two coexisting confined conformers **1a** and **1b** in a 2:1 ratio, with conformer **1a** and **1b** having, respectively, six and four gauche conformations in the middle of the chain (Figure 3a).

The natural development of this work is related to the designing of novel pyrene boxes. Very interesting, in the **PTSAG{1$_2$}** "AG−pyrene box", the **AG**$^+$ cations are integrated into the network via the guanidinium ($d_{O\cdots H-N}$ of 2.52 Å) and the amino ($d_{O\cdots H-N}$ of 2.16 Å) moieties, acting as H-bond donors for the sulfonate groups. Two bridging water molecules, simultaneously H-bonded to amino moiety of **AG**$^+$ ($d_{O\cdots H-N}$ of 2.24 Å) and to **PTS**$^{4-}$ ($d_{S\cdots H-O}$ of 1.96 Å), play a significant role in stabilization of the AG−pyrene box. This novel H-bonded network induces a "face to face" relative arrangement of the **PTS**$^{4-}$ platforms into the crystalline AG−pyrene box, so that the average distance between the sulfonate groups is drastically reduced to 10.18 Å. Despite 1,12-diammonium-dodecane **1** being much longer than this distance, it is H-bonded to two diagonally disposed sulfonate groups on the same **PTS**$^{4-}$ platform (Figure 3b). More remarkable, two confined molecules of **1** with different conformations are filling the space between the two **PTS**$^{4-}$ platforms of the AG−pyrene box. Both conformers have two gauche conformations unsymmetrically positioned along the alkyl chain, between C3−C4 and C10−C11, and between C2−C3 and C10−C11, respectively. The N_1−N_ω distance in the case of **1c** is 13.74 Å, corresponding to a 17% compression of the extended linear length of **1**, while conformer **1d** is slightly more elongated at 14.36 Å, corresponding to a 13.4% compression.

The same relative "face to face disposition" arrangement of the **PTS**$^{4-}$ platforms in a novel free guanidinium−"pseudo-pyrene box" **PTS{1}** is actually obtained by crystallizing a 1:2 mixture of **1**/**PTS**$^{4-}$ so that the average distance between the two planes of the sulfonate groups is drastically reduced with respect to the crystalline AG−pyrene box (Figure 3c). In this structure the 1,12-diammonium-dodecane chain **1** which is too long to fit the new constraints and encapsulation environment, exists as two different confined molecules with slightly different conformations filling the space between the two **PTS**$^{4-}$ platforms of the AG−pyrene box. The conformers **1e** and **1f** have two gauche conformations unsymmetrically and differently positioned along the alkyl chain, between C2−C3 and C8−C9, and between C2−C3 and C7−C8, respectively. The N_1−N_{12} distance in the case of **1e** H-bonded to two diagonally disposed sulfonate groups on the two parallel **PTS**$^{4-}$ platforms, is 12.09 Å, corresponding to a 17% compression of the extended linear length of **1**, while conformer **1f** immobilized at the interface between two **PTS**$^{4-}$ platforms is slightly more elongated at 14.34 Å, similar to **1d**.

Another incremental change to **A$_2$G**$^+$ cation leads to another relative slipped position of the **PTS**$^{4-}$ platforms in the new structurally different **PTSA$_2$G{1}** AG−pyrene box, with the N_1−N_ω distance of 14.81 Å, corresponding to a 11% compression of the linear extended chain. This value is very similar to that observed for the **PTSG{1}** box. In **PTSA$_2$G{1}**, 1,12-diammonium-dodecane **1** is H-bonded to two diagonally disposed sulfonate groups on the same **PTS**$^{4-}$ platform. One confined molecule of **1g** with two gauche conformations between C5−C6 and C7−C8, symmetrically positioned in the middle of the alkyl chain. In the **PTSA$_2$G{1}**, the **A$_2$G**$^+$ cations are integrated into the network via guanidinium ($d_{O\cdots H-N}$ of 2.84 Å) and amino ($d_{O\cdots H-N}$ of 2.14 and 2.28 Å) moieties acting as H-bond donors for the sulfonate groups (Figure 3d). The **A$_2$G**$^+$ cations are dimensionally fitting in the space between the sulfonate groups of **PTS**$^{4-}$ and present an unsymmetrical H-bonding of the amino groups to the **PTS**$^{4-}$. Importantly, four bridging water molecules, which are simultaneously H-bonded to ammonium moiety of **1** ($d_{O\cdots H-N}$ of 1.86 Å) and to **PTS**$^{4-}$

DOI: 10.1021/acs.orglett.5b00779
Org. Lett. 2015, 17, 2178−2181

($d_{S\cdots H-O}$ of 1.94 Å), play a critical role in binding of **1** in the A_2G−pyrene box. As a result, 1,12-diammonium-dodecane **1** is practically immobilized at the interface between two PTS^{4-} platforms.

Taking into account our previous results on the initial **PTSG** pyrene box, all the data presented here demonstrate that the 1,12-diammoniumdodecane **1** could be adaptively incorporated/encapsulated into novel **PTS**, **PTSAG**, and $PTSA_2G$ pyrene boxes. Its binding is subjected to the specific adaptation of the long alkyl chain to the available dimensionally different confining space.[1−4] The compression under confinement results in an adaptive decrease of the overall length of the natural uncompressed all-trans "zigzag"-type 1,12-diammonium-dodecane **1**. The sulfonate binding sites of the pyrene box hosts presented here may be positioned at different distances, while the 1,12-diammonium-dodecane **1** may bind on the same or different PTS^{4-} platforms. Thus, by designing the interior space of the host, one can control the conformation of the encapsulated guest alkane. The variable degrees of compression observed in the X-ray single-crystal structures represent static snapshots of the dynamic conformational processes occurring when of alkane chains are encapsulated within and reduced space.

On a more general note, molecular encapsulation of flexible alkane chains is a complex process in which dynamic exchanges between several constitutionally different confined conformers may be observed. The structures are sufficiently stable to allow a conventional structure determination by X-ray diffraction. The adaptive chemistry of alkane chains offers interesting perspectives on understanding their chemical behaviors of dynamically interacting guests in a small space, relevant for many biological occurrences.[11−13]

■ ASSOCIATED CONTENT

Supporting Information

Supplementary NMR and X-ray diffraction details. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was conducted within the framework of DYNANO, PITN-GA-2011-289033 (www.dynano.eu), ANR DYNAMULTIREC, and ANR-10-LABX-05-01 "LABEX Chemisyst" (to D.D.) awarded by "Pole Balard" Montpellier.

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DOI: 10.1021/acs.orglett.5b00779
Org. Lett. 2015, 17, 2178−2181