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Synthesis and characterization of a cyclotriveratrylene-capped azaphosphatrane

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ABSTRACT

A cyclotriveratrylene (CTV)-capped azaphosphatrane **4**, which contains an endohedral proton within the cavity of the azaphosphatrane, was synthesized in high yield and then characterized. The endohedral proton of **4** was highly sheltered from strongly basic conditions by the CTV-capped structure.

The chemistry of atranes that contain five-membered tricyclic frameworks has attracted considerable interest in recent years.[1] Most studies on aza-atranes including tripodal ligands such as tris(amidoethyl)amine (tren anion) $[(RNCH_2CH_2)_3N]^{3-}$ have focused on coordination of main group atoms such as phosphorus, antimony, and bismuth. Azaphosphatranes are precursors of pro-azaphosphatranes (also known as Verkade's bases) and are very useful in a number of important organic transformations (Fig. 1).[2] Azastibatranes and azabismatranes have been proposed as potential precursors for metal-organic chemical vapor deposition of thin films of bismuth- or antimony-containing materials, respectively.[3] Despite kinetically-stabilized aza-atranes being important to construct a wide variety of these compounds, very few attempts have been studied to stabilize the central atom of aza-atranes.

We recently reported novel hemicryptophane **3**, which is composed of a cyclotriveratrylene (CTV) moiety and a tren ligand connected by a rigid spacer.[4] The small covalent molecule encapsulates the central aza-atrane structure and can be used as a new kind of protective group for aza-atranes. Recently, Raytchev et al. reported the first synthesis of an encaged Verkade's base and evaluated the thermodynamic and kinetic consequences.[5]

The precursor **2** was slightly longer than hemicryptophane **3** and was neutralized with potassium *t*-butoxide (*t*-BuOK) in THF; the observed pK_a was similar to that of deprotonated **1a**. In this Letter, we report the synthesis and characterization of a CTV-capped azaphosphatrane. The unusual reactivity of the endohedral proton within the cavity of the molecule is used to clarify the relationship between the size and reactivity of the hemicryptophane.

Scheme 1 depicts the synthetic route to CTV-capped azaphosphatrane **4**. Hemicryptophane **3** was synthesized by our previously reported procedure.[6] The reaction of **3** with bis(dimethylamino)chlorophosphine in chloroform solution under a nitrogen atmosphere produced **4** in 87% yield. Azaphosphatrane **4** can be safely stored at room temperature as a solid under an inert atmosphere. The structure of **4** was confirmed by HR-MS, and ^1H, ^{13}C, and ^{31}P NMR spectroscopy.[7]

The ^1H NMR profiles of **3** and **4** showed that they possess a C_3-symmetric conformation in DMSO-d_6 solution (Scheme 1 and Fig. 2). The ^{31}P NMR chemical shift at −34.39 ppm for **4** was upfield compared to that for **1a**.[8] The large coupling constant of 485 Hz indicates H–P bond formation. The existence of covalent N_{eq}–P bonds in **4** was suggested by the observation of P–N_{eq}–CH_2 coupling (4.7 Hz) and P–N_{eq}–benzyl-CH_2 coupling (6.1 Hz).[9] The signals from the alkyl protons of tren in **4** (i and j) were shifted downfield compared to those of **3**. These results confirm the formation of an azaphosphatrane structure. Note that the two benzyl protons (f) split into two average signals at 2.70 and 3.56 ppm and remained unchanged even at 373 K, indicating that the conformation of the benzyl unit is highly restricted on the NMR timescale.

DFT gas-phase structure optimization and frequency calculations were performed at the B3LYP/6-31G level of theory.[10] A polarization function ($\zeta_d = 0.34$) was added to the P atom to give

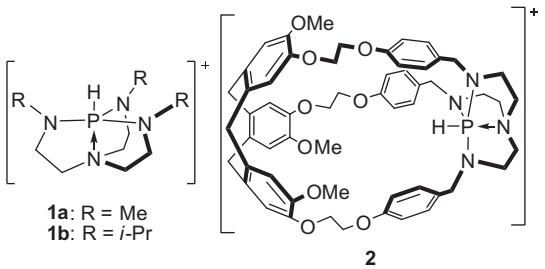

Figure 1. Structures of azaphosphatrane **1** and Raytchev's azaphosphatrane **2**.

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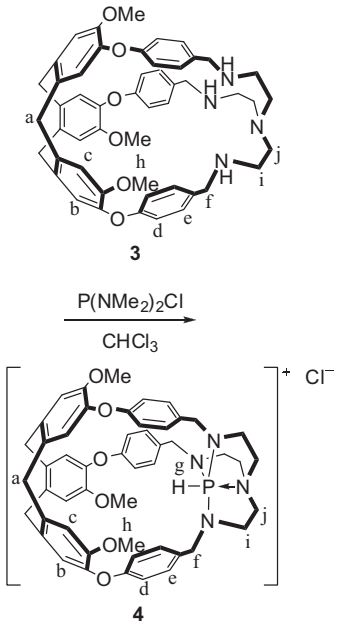

Scheme 1. Synthesis of CTV-capped azaphosphatrane **4**.

a better description of the penta coordination. The optimized structure of cation **4** is shown in Figure 3. The CTV-capped structure forms a folded helical structure because of stabilization caused by CH-π interactions between the phenyl ring spacers. This structure is supported experimentally by the upfield shift of the phenyl protons (d and e) of **4** in its ^{1}H NMR spectrum (Scheme 1 and Fig. 2). The P–N_{ax} bond length (2.18 Å) is slightly elongated compared to that in the known crystal structure of **1a** (1.98 Å).[11] However, the theoretically determined ^{31}P chemical shift (δ −33.2 ppm) agrees well with experimental results.

The reaction of **1a** with excess *t*-BuOK (pK_a = 32)[12] or sodium hexamethyldisilazide (NaHMDS; pK_a = 26)[13] in dry DMSO-d_6 solution at ambient temperature simultaneously produced deprotonated **1a** in 69% yield and deuterated **1a** in 31% yield. However, **4** remained unchanged under harsh neutralization conditions in an excess of *t*-BuOK, NaHMDS, or deprotonated **1a** in dry DMSO-d_6 or THF-d_8 solutions at 343 K after 24 h.[14] Moreover, the base sodium methylsulfinylmethylide (NaDMSO; pK_a = 35),[13] which is smaller than the 23-membered entrance of the cavity, was also unable to neutralize **4** at 343 K after 24 h. Sterically hindered **1b** was neutralized immediately in these harsh conditions. These results indicate that the CTV-capped structure protects the endohedral proton of azaphosphatrane significantly and that its reactivity is closely connected to the size of the CTV-capped structure.

Novel CTV-capped azaphosphatrane **4** was obtained in high yield. The reactivity of the endohedral proton of **4** was suppressed as a result of protection by the CTV-capped structure. This novel protecting group is applicable to the synthesis of other unstable aza-atrane structures; research focused on this is in progress.

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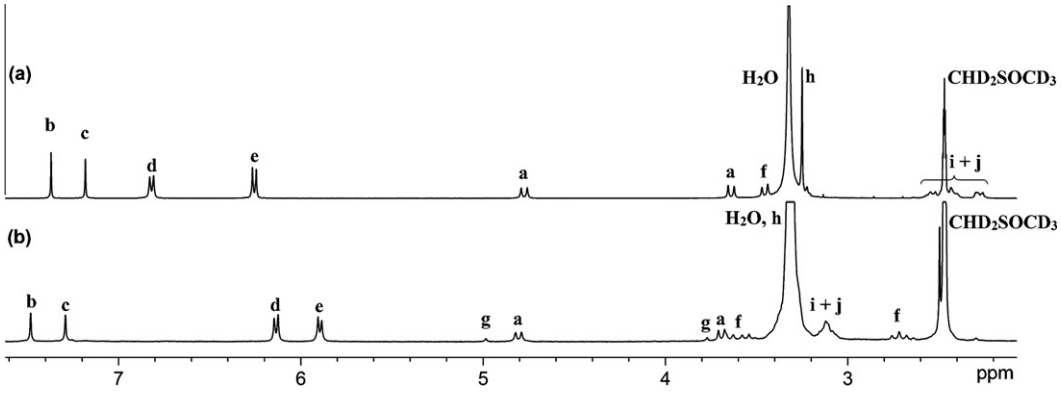

Figure 2. ^{1}H NMR spectra (400 MHz, DMSO-d_6, 298 K) of: (a) **3**, and (b) **4**.

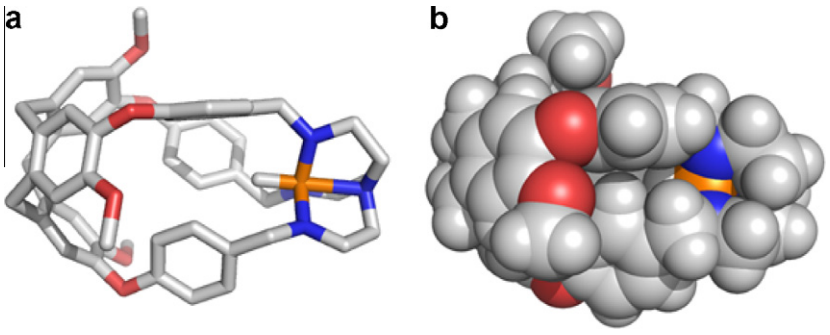

Figure 3. (a) Optimized structure of cation **4**; hydrogen atoms were omitted for clarity. (b) Space filling model of cation **4**.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.05.127.

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6. A solution of hemicryptophane **3** (50 mg, 62 μmol) and bis(dimethylamino)chlorophosphine (14 μL, 96 μmol) in chloroform (2.7 mL) was stirred at 0 °C for 30 min under a nitrogen atmosphere and allowed to warm to ambient temperature for 48 h. The reaction mixture was added dropwise to diethyl ether. The precipitate was filtered to give 49.6 mg (87%) of **4** as a white solid.
7. Mp >280 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 2.70 (dd, 3H, J_{PH} = 32.4 Hz, J_{HH} = 16.0 Hz), 3.11–3.21 (m, 12H), 3.37 (s, 9H), 3.56 (dd, 3H, J_{PH} = 31.2 Hz, J_{HH} = 16.0 Hz), 3.48 (d, 3H, J_{HH} = 13.3 Hz), 4.41 (d, 1H, J_{PH} = 485 Hz), 4.84 (d, 3H, J_{HH} = 12.9 Hz), 5.93 (d, 6H, J_{HH} = 8.7 Hz), 6.17 (d, 6H, J_{HH} = 8.7 Hz), 7.34 (s, 3H), 7.53 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 33.8, 42.4, 46.1 (d, J_{PC} = 5.7 Hz), 50.1 (d, J_{PC} = 9.5 Hz), 55.2, 114.1, 115.3, 127.8, 129.4, 131.2, 133.0, 138.8, 141.7, 149.6, 158.3; ^{31}P NMR (DMSO-d_6, 243 MHz) δ −34.39 ppm; IR (KBr) 3422, 2935, 2733, 2360, 1608, 1504, 1207 cm^{-1}; HR-MS (ESI–TOF) Calcd for $C_{51}H_{52}N_4O_6P_1$: 847.3624 $[M]^+$. Found: 847.3600 $[M]^+$.
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14. *General neutralization procedure for* ***4***. A solution of **4** (4.8 mg, 5.4 μmol) and base (27 μmol) in dry DMSO-d_6 (0.60 mL) was allowed to stand at 373 K for 24 h. The progress of the reaction was observed by ^{1}H and ^{31}P NMR analysis.