Bicyclo[10.10.10]dotriacontanes: the Largest Bicyclo[*n*.*n*.*n*]alkane Ever Known

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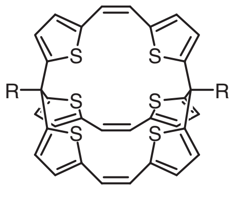
Bicyclo[10.10.10]dotriacontanes, the largest bicyclo[*n*.*n*.*n*]alkanes ever known, have been first synthesized by Raney nickel reduction of trithienylmethanophanes consisiting of two tris(2-thienyl)methanes and three etheno bridges. X-ray crystallographic analysis of a crystalline derivative confirmed the structure, though disorder of included hexane molecules lowered the accuracy.

Bicyclo[*n*.*n*.*n*]alkane with long methylene chains would be the simplest type of alkane-cage molecule. It would be conceptually of interest whether such alkane-cage molecules can act, if at all, as host molecules for atoms or small molecules. The largest member so far known has been bicyclo[8.8.8]hexacosane[1] whose cavity is yet too small to be called a cage molecule.

We have recently reported the synthesis of novel cage molecules, trithienylmethanophanes[2] **1a**, **1b**, which are composed of two tris(2-thienyl)methanes and three etheno bridges, by the McMurry coupling of tris(5-formyl-2-thienyl)methanes.[3,4] In view of the synthetic equivalency of thiophene with *n*-butane through Raney nickel reduction,[5–7] compounds **1** would be ideal precursors for hitherto unknown bicyclo[10.10.10]dotriacontanes (**2**). Here we wish to report the synthesis of **2b**–**2d**, the largest members of bicyclo[*n*.*n*.*n*]alkane ever known.



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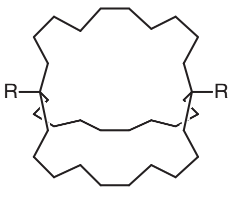

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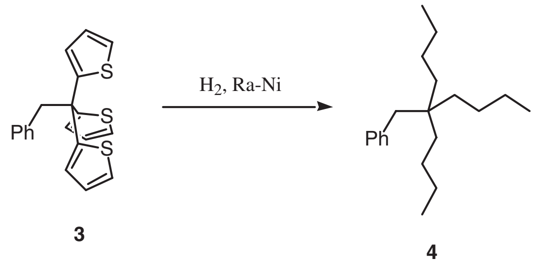
a: R = H
b: R = CH_2Ph
c: R = $CH_2C_6H_3$-3,5-$(OCH_3)_2$
d: R = $CH_2C_6H_3$-3,5-$(OH)_2$

At first, we studied the Raney nickel reduction of 1-phenyl-2,2,2-tris(2-thienyl)ethane **3**, a nearly half part of **1b**, to optimize the reaction conditions, because the availability of the cage compounds **1** is rather poor. The phenyl group in **3** was expected to serve as a probe for UV-detection in the thin layer chromatography (Scheme 1). Hydrodesulfurization of **3** was examined under various conditions, i.e., temperature, reaction time, activity of Raney nickel, and pressure of hydrogen. Although the expected hydrocarbon **4** was sometimes obtained fairly cleanly at reflux temperatures of solvents in air, the reproducibility was poor. The crude products mostly exhibited small signals of olefinic protons even with use of a large excess amount of the reducing agents. It was found, however, that compound **3** is reduced cleanly to **4** using an excess amount of Raney nickel W7 under medium pressure (0.3 MPa) of hydrogen in ethanol–benzene at 85 °C for 5 h.



Scheme 1.

Reduction of **1b** under the successful conditions for **3** gave **2b**[8] as colorless viscous oil in 82% yield (Scheme 2). The EI mass spectrum of **2b** shows strong fragment peaks assignable to $[(M - CH_2Ph)^+$; 100%] and $[(M - 2 \times CH_2Ph)^+$; 40%]. The rather simple ^1H and ^{13}C NMR spectra agree with the D_{3h} symmetric structure of **2b**, in particular, the latter spectrum exhibiting only four aromatic carbon and seven aliphatic carbon signals.

$$\mathbf{1b} \xrightarrow[82\%]{\text{i)}} \mathbf{2b}$$

$$\mathbf{1c} \xrightarrow[99\%]{\text{i)}} \mathbf{2c} \xrightarrow[93\%]{\text{ii)}} \mathbf{2d}$$

i) 50 equiv. (w/w) Raney Nickel W7, 0.3 MPa H_2, EtOH–benzene, 85 °C, 5 h, ii) excess BBr_3, CH_2Cl_2, –30 °C then rt 1 h.

Scheme 2.

To obtain the structural information in more detail, X-ray analysis of **2** was desirable. However, **2b** has remained oily upon attempted crystallizations. We expected that introduction of intermolecular hydrogen bonds should make **2** more crystalline and designed compound **2d** that has 3,5-dihydroxyphenyl groups in place of phenyl groups of **2b**. The precursor **1c**[9] was prepared in similar way for **1b**. Raney nickel reduction of **1c**, followed by passing through a short alumina column to eliminate the metal and then chromatography on silica gel, afforded **2c**[10] in 99% yield as colorless oil. Demethylation of **2c** with boron tribromide in dichloromethane gave **2d**[10] in 93% yield (Scheme 2). As expected, compound **2d** was obtained as colorless solid and its careful recrystallization from hexane–ethyl acetate furnished single crystals.

Figure 1 shows an ORTEP drawing of **2d**.[11] The crystal contains one hexane molecule in a unit-cell, not in the cavity of **2d**, in highly disordered manner, thus preventing discussions on the detailed structure. Nevertheless, the ORTEP drawing confirms the bicyclo[10.10.10]dotoriacontane structure of **2d**. Figure 2

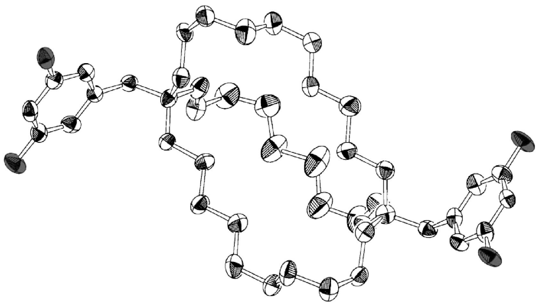


Figure 1. ORTEP drawing of **2d**. Hydrogen atoms and the disordered hexane molecule are omitted for clarity.

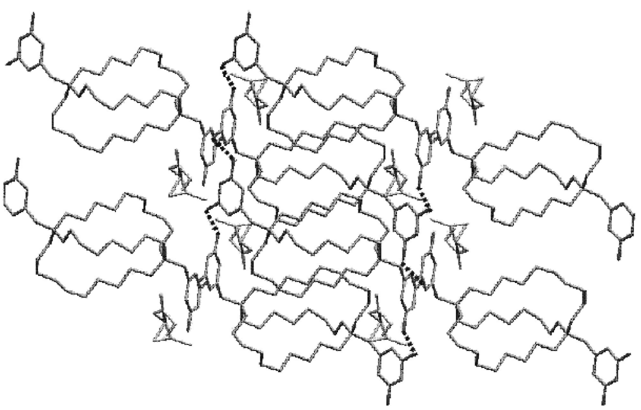


Figure 2. Crystal packing of **2d** viewed along *b* axis. Dashed lines indicate hydrogen bond.

shows the crystal packing where supramolecular networks through hydrogen-bondings between 3,5-dihydoroxylphenyl groups are seen.

The cavity of **2d** is estimated to be approximately 5.0 × 1.4 × 1.4 Å in size, which is not so large, and there has been observed little sign of inclusion of small molecules such as benzene, naphthalene and their derivatives in the cavity as far as ^{1}H NMR spectral monitoring are concerned. For obtaining confirmative conclusion on the host-ability of bicyclo[*n.n.n*]alkanes, synthesis and examinations with the bicycloalkanes with longer alkyl chains might be necessary.

In conclusion, we have synthesized the first bicyclo[10.10.10]dotoriacontane derivatives by Raney nickel hydrodesulfurization of the precursor trithienylmethanophanes. In view of possible trilithiation or aromatic electrophilic substitution of tris(2-thienyl)methanes, such as **3**, at 5-postions of the thienyl groups, the present trithienylmethanophane-Raney nickel reduction method would lead to a variety of large bicylo[*n.n.n*]alkanes and related compounds. The synthesis of those compounds are under way.

References and Notes

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2 IUPAC naming for the parent compound: 33,34,35,36,37,38-hexathiaoctacyclo[$10.10.10.1^{2,5}.1^{8,11}.1^{13,16}.1^{19,22}.1^{23,26}.1^{29,32}$]dotriaconta-2,4,6,8,10,13,15,17,19,21,23,25,27,29,31-pentadecaene.

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8 **2b**; colorless viscous oil, MS (EI) m/z (relative int.) 626 (6%, M^+), 535 (100%, $[M - CH_2Ph]^+$), 444 (40%, $[M - 2 \times CH_2Ph]^+$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.99–7.17 (m, 10H), 2.43 (s, 4H), 0.76–1.43 (m, 60H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 139.45, 130.36, 127.53, 125.48, 42.72, 38.83, 35.77, 29.25, 28.14, 27.52, 21.85; IR (neat) ν 2926s, 2853s, 1493w, 1460m, 1382w, 1262w, 1095w, 802w, 701m, 483w cm^{-1}.

9 **1c**; yellow crystals; mp 308 °C (decomp.); MS (FAB) m/z 897 ($[M + H]^+$), 745 ($[M - C_6H_3(OMe)_2]^+$), 594 ($[M - 2 \times C_6H_3(OMe)_2]^+$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.73 (d, $J = 3.7$ Hz, 6H), 6.71 (d, $J = 3.7$ Hz, 6H), 6.49 (s, 6H), 6.28 (t, $J = 2.2$ Hz, 2H), 6.12 (d, $J = 2.2$ Hz, 4H), 3.74 (s, 4H), 3.59 (s, 12H).

10 **2c**; colorless viscous oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 6.29 (t, $J = 2.1$ Hz, 2H), 6.25 (d, $J = 2.1$ Hz, 4H), 3.74 (s, 12H), 2.43 (s, 4H), 0.76–1.29 (m, 60H); **2d**; colorless prisms; mp 177.4–177.9 °C; MS (FAB) m/z 692 ($[M + H]^+$), 568 ($[M - C_6H_3(OH)_2]^+$); ^{1}H NMR (270 MHz, acetone-d_6) δ 7.98 (s, 4H), 6.20 (t, $J = 2.1$ Hz, 2H), 6.15 (d, $J = 2.1$ Hz, 4H), 2.38 (s, 4H), 0.86–1.34 (m, 60H); ^{13}C NMR (67.8 MHz, acetone-d_6) δ 158.42, 141.90, 109.67, 100.92, 60.39, 43.27, 39.30, 36.52, 28.69, 28.07, 22.39.

11 Crystallographic data for **2d**·*n*-hexane; $C_{52}H_{88}O_4$, $M =$ 770.21, triclinic, $P\bar{1}$ (no. 2), $a = 10.774(4)$, $b = 14.267(7)$, $c = 16.825(8)$, $\alpha = 109.95$, $\beta = 95.15(1)$, $\gamma = 91.61(2)$, $V = 2416(1)$ Å^3, $Z = 2$, $D_{calc} = 1.069$ gcm^{-3}, 24283 reflections measured, 10834 unique ($R_{int} = 0.139$) used in refinement, $R = 0.151[I > 2\sigma(I)]$, $wR = 0.461$, GOF = 1.03.

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