Synthesis of novel cage molecules bicapped with tris(2-thienyl)methanes

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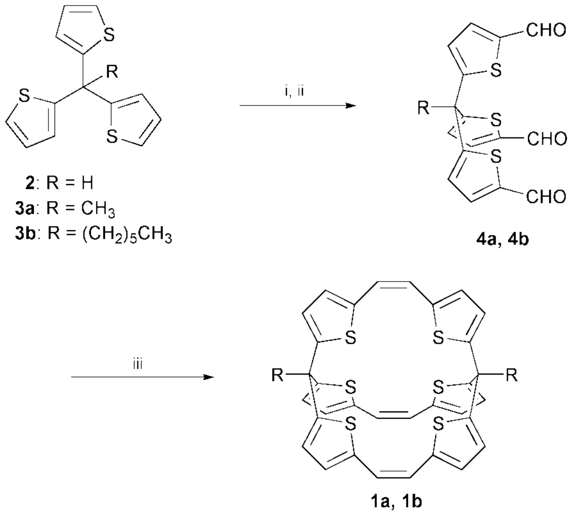
Received (in Cambridge, UK) 7th December 2000, Accepted 8th February 2001
First published as an Advance Article on the web 27th February 2001

The McMurry coupling of tris(5-formyl-2-thienyl)methanes affords novel cage molecules which are bicapped with tris(2-thienyl)methanes and where all the sulfur atoms of thienyl groups direct inward.

Cage molecules have been attracting increasing attention from the viewpoint of host–guest or supramolecular chemistry.[1] There are a number of types in the basic skeleton of cage molecules and one of such families is that of cage molecules bicapped with triphenylmethanes (triphenylmethanophanes).[2] Here we report on the first synthesis of cage molecules bicapped with tris(2-thienyl)methanes **1a** and **1b** (trithienylmethanophanes) where the thiophenes are bridged with etheno groups and the sulfur atoms are direct inward forming a three dimensional cavity. Related three or two dimensional sulfur-rich and unsaturated cyclophanes, macrobicyclic tetrathiafulvalene-bridged cage molecules or sulfur bridged annulenes have been reported.[3,4] Differing from triphenylmethanophanes, the thienyl groups in trithienylmethanophanes act as either π-electron donors, as aryl groups or electron-pair donors due to the sulfur atoms.

For the synthesis of **1a** and **1b** we chose tris(2-thienyl) methane **2** as the starting material because it has a number of favorable features such as easy lithiation–alkylation at the central methyl carbon (Cα-alkylation)[5] and possible metalation and functionalization at C5 of the thienyl groups in the Cα-alkylation products. It has been reported that treatment of **2** with BuLi–TMEDA in THF followed by addition of alkyl halides selectively yielded Cα-alkylation products.[5] In our case, however, C5-alkylation appreciably competed against Cα-alkylation under similar conditions and the separation of both the products was difficult. We have found that treatment of **2** with BuLi (1.2 equiv.) in THF in the presence of an excess amount (1.5 equiv.) of diisopropylamine (−70 °C then rt) followed by addition of alkyl halides provides a simpler procedure as well as excellent selectivity for Cα-alkylation with primary alkyl halides (Scheme 1).†[6]



Scheme 1 i, 5.0 eq. BuLi–THF, 0 °C, 2 h; ii, excess DMF (**4a**: 64%; **4b**: 83%); iii, TiCl$_4$, Zn, CuI–DME, rt, overnight → reflux, 24 h (**1a**: 8%; **1b**: 7%).

Treatment of 1,1,1-tris(2-thienyl)ethane **3a**, thus obtained by methylation with methyl iodide, with five equivalents of BuLi in THF and subsequent addition of excess DMF afforded, after chromatographic purification on silica gel, trialdehyde **4a**‡ in 64% yield from **2**. Similarly hexyl compound **4b**‡ was obtained in 83% yield from **2** *via* **3b**. The McMurry coupling[7,8] of **4a** with low valent titanium in DME gave the trithienylmethanophane **1a**‡ in 5–8% yield as a sole, readily isolable, yellow crystalline substance. Trialdehyde **4b** also gave **1b**‡ in 7% yield. Although **1a** and **1b** are stable at solid state and in neutral solution, they slowly decomposed in CHCl$_3$–CF$_3$COOH (9 : 1 v/v) at rt when the effect of acid or encapsulation of proton in the cavity was examined by means of NMR spectroscopy.

^{1}H and ^{13}C NMR spectra show a high symmetry of **1a** and **1b** exhibiting only three proton-signals and six carbon-signals besides the signals of the alkyl groups. The vicinal coupling constants obtained from the ^{13}C satellite signals of the olefin protons of **1a** (δ 6.45, $J^{13}{}_{\text{C-H}}$ = 161.6 Hz, $J_{\text{H-H}}$ = 11.7 Hz) and **1b** (δ 6.50, $J^{13}{}_{\text{C-H}}$ = 161.4 Hz, $J_{\text{H-H}}$ = 11.9 Hz) indicate the *cis* configuration of the three etheno bridges. The UV-vis absorptions (325, 270 nm) are at slightly longer wavelengths than those of *cis*-1,2-bis(2-thienyl)ethene (322, 250 nm).[9] Inter-

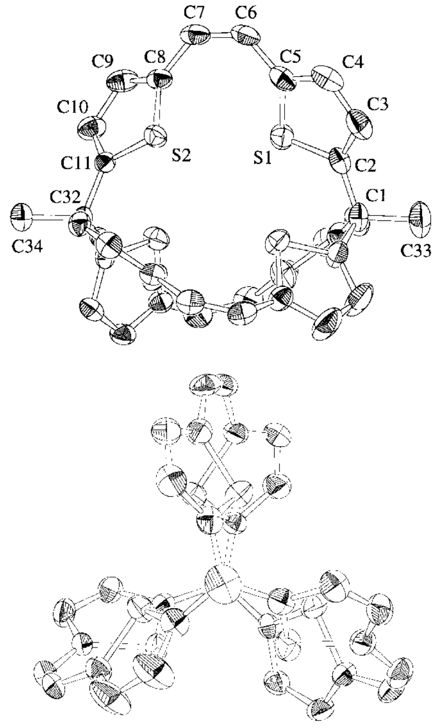


Fig. 1 ORTEP drawing (30% thermal ellipsoids) of the cage molecule **1a** (upper: side view; lower: viewed along the C_3 axis). Selected bond lengths (Å) and angles (°): C1–C2 1.523(5), C2–C3 1.369(5), C3–C4 1.403(5), C4–C5 1.369(5), C5–C6 1.444 (5), C6–C7 1.330(5), S1–C2 1.712(4), S1–C5 1.715(4), C2–C1–C33 110.2(3), C5–C6–C7 130.5(3), C6–C7–C8 130.3(3), C11–C32–C34 109.7(3).

DOI: 10.1039/b009811f

estingly, the mass spectra of the trithienylmethanophanes, in particular the EI spectrum of **1b**, suggest fair stability of dealkylated monocation and dication showing strong peaks at *m/z* 679 ($[M - \text{hexyl}]^+$, 100%) and 297 ($[M - 2 \times \text{hexyl}]^{2+}$, 38%). Upon cyclic votammetry, **1b** shows an irreversible oxidation peak at +1.12 V (*vs.* Ag/Ag$^+$, in 0.1 M $Bu_4N^+ClO_4^-$/CH_3CN, ferrocene/ferrocene$^+$ = 0.33 V).

Recrystallization of **1a** from benzene–hexane afforded a single crystal suitable for X-ray structure analysis.§ The X-ray results establish the cage structure (Fig. 1) and reveal several structural features of **1a**. First, all the three etheno bridges have *cis* configuration, as ^{1}H NMR spectrum suggests, with considerably widened bond angles (av. 131.0°). Second, all the sulfur atoms of the six thienyl groups direct inward. Third, the molecule thus has a three dimensional cavity, though rather small, surrounded with six sulfur atoms, the cavity-size being about 0.7 Å in diameter. The cavity might encapsulate a Cu(II) ion. In a preliminary experiment, treatment of **1a** with $Cu(ClO_4)_2 \cdot n$AcOH in toluene–nitromethane precipitated dark green powder which was sparingly soluble in organic solvents.

In conclusion, the McMurry coupling of tris(5-formyl-2-thienyl)methanes affords novel cage molecules bicapped with tris(2-thienyl)methanes. The host–guest chemistry of **1a** and **1b**, further synthetic utility of trialdehyde **4**, and the synthesis of the cage cations suggested by the mass spectra are in progress. In addition, reductive desulfurization of trithienylmethanophanes **1** would form novel three dimensional hydrocarbons having a bicyclo[10.10.10]dotriacontane skeleton, and such attempts are also ongoing.

This work was supported by a Grant-in-Aids for Scientific Research of Priority Area (No. 10146102) from the Ministry of Education, Science, Sports and Culture, Japan.

Notes and references

† Diisopropylamine mediates rapid equilibrium between Cα-lithio-species (thermodynamically more stable and hence less reactive) and C5-lithio-species (less stable and much more reactive) in nearly exclusive favor for the former which gives Cα-alkylation products with non-bulky, reactive alkyl halides. It is also important to add alkyl halides above 0 °C so as to keep the reactivity of the Cα anion high enough. The crude product from this procedure was used for the next step.

‡ *Selected physical and spectroscopic data* for **4a**: yellow powder; mp 134.5–136.0 °C; MS (EI) *m/z* (rel intensity) 360 ($[M]^+$, 42), 345 ($[M - CH_3]^+$, 100), 331 ($[M - CHO]^+$, 47); δ_H(270 MHz, $CDCl_3$): 9.88 (s, 3H), 7.65 (d, J = 3.8 Hz, 3H), 6.99 (d, J = 3.8 Hz, 3H), 2.39 (s, 3H); δ_C(67.8 MHz, $CDCl_3$): 182.80, 160.52, 143.27, 135.76, 127.60, 47.96, 32.83; **4b**: yellow oil; δ_H(270 MHz, $CDCl_3$) 9.87 (s, 3H), 7.65 (d, J = 3.8 Hz, 3H), 7.10 (d, J = 3.8 Hz, 3H), 2.62 (m, 2H), 1.24–1.42 (m, 8H), 0.87 (m, 3H); **1a**: yellow plates; mp > 270 °C (decomp.); MS (FAB) *m/z* = 624 (M^+), 609 ($[M - CH_3]^+$); δ_H(270 MHz, $CDCl_3$) 6.86 (d, J = 3.6 Hz, 6H), 6.80 (d, J = 3.6 Hz, 6H), 6.45 (s, 6H), 2.25 (s, 6H); δ_C(67.8 MHz, $CDCl_3$) 153.96, 136.98, 128.99, 123.87, 122.55, 45.77, 29.35; UV-vis (CH_2Cl_2) λ_{max} nm 325 (log ε = 4.23), 288 sh, 270 (4.62); **1b**: yellow powder; mp 209.5–211.5; MS (EI) *m/z* (rel intensity) 764 ($[M]^+$, 36%), 679 ($[M - C_6H_{13}]^+$, 100), 594 ($[M - 2\,C_6H_{13}]^+$, 42), 297 ($[M - 2\,C_6H_{13}]^{2+}$, 38); NMR; ^{1}H δ_H(270 MHz, $CDCl_3$) 6.88 (d, J = 3.7 Hz, 6H), 6.78 (d, J = 3.7 Hz, 6H), 6.50 (s, 6H), 2.49 (m, 4H), 1.25–1.49 (m, 16H), 0.87 (m, 6H); δ_C(67.8 MHz, $CDCl_3$) 153.35, 137.14, 127.92, 124.52, 123.47, 50.63, 41.06, 31.85, 29.88, 25.22, 22.80, 14.25; UV-vis (CH_2Cl_2) λ_{max} nm 315 sh, 290 sh, 268 (log ε = 4.58).

§ *Crystal data* for **1a**: $C_{34}H_{24}S_6$, M = 624.94, triclinic, space group $P\bar{1}$ (no. 2), a = 10.596(3), b = 15.960(2), c = 9.860(1) Å, α = 92.75(1), β = 106.40(2), γ = 88.74(2)°, U = 1597.8(5) Å^3, Z = 2, D_c = 1.374 M gm^{-3}, μ = 0.455 mm^{-1}, $F(000)$ = 684. 8871 reflections measured, 8867 unique (R_{int} = 0.037) used in refinement. $R1$ = 0.040 (3859 data, $I > 2\sigma(I)$), wR = 0.113 (all data).

CCDC 156652. See http://www.rsc.org/suppdata/cc/b0/b009981f/ for crystallographic files in .cif format.

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