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Synthesis of tetramers of 1,3-adamantane derivatives

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Abstract—Novel tetramers of 1,3-adamantane and 5,7-dibutyl-1,3-adamantane were synthesized by the coupling reaction of 3-bromo-1,1′-biadamantane or 3-bromo-5,5′,7,7′-tetrabutyl-1,1′-biadamantane with sodium in *n*-octane or with magnesium in diethyl ether. Although the former 1,3-adamantane tetramer showed poor solubility in organic solvents, the latter tetrameric 5,7-dibutyl-1,3-adamantane was readily soluble in THF, chloroform and benzene and was successfully characterized by NMR, IR, SEC and elemental analyses.

Adamantane (tricyclo[3.3.1.1^{3,7}]decane) is a highly symmetrical (T_d symmetry) cage compound and shows good chemical and thermal stability, and various functional groups can be introduced on the tertiary bridgehead carbon under suitable reaction conditions.[1,2] Interestingly, adamantane can be thought of as a large carbon atom because of the tetrahedral location of four methine carbons and the direction of four bridgehead C–H bonds. Therefore, 1,1′-biadamantane (**1**) can be considered as a large analog of ethane, and higher oligo(1,3-adamantane)s having flexible cage–cage bonding corresponding to propane, butane, pentane and so on. It also should be pointed out that the structure of the diamond involves the framework of oligo(1,3-adamantane)s in its lattice, since adamantane can be recognized as the repeating unit of the diamond, as shown in Fig. 1. To the best of our knowledge, although the dimeric adamantane **1** was synthesized long ago via the Wurtz coupling reaction of 1-bromoadamantane,[1] no higher oligomers have been obtained. In this communication, we report the first successful synthesis of tetrameric 1,3-adamantane showing good solubility in organic solvents by introducing flexible butyl substituents on the framework.

The synthesis of 1,3-adamantane tetramer is depicted in Scheme 1. The bromination of **1** with Br_2 in CCl_4 afforded a mixture of 3-bromo-1,1′-biadamantane (**2**)[3] and 3,3′-dibromo-1,1′-biadamantane (**3**).[1,4] Column chromatography (silica gel, hexane/CH_2Cl_2 = 9/1, v/v) of the reaction mixture gave **2** in 58% and **3** in 40% yield. The isolated monobromide **2** was subsequently reacted with sodium in *n*-octane under reflux conditions to form a proposed tetramer of adamantane **4**, via the bridgehead coupling reaction. An off-white solid was obtained in good yield after the usual workup of the reaction mixture. By assuming the complete removal of bromine from **2**, the yield of product was almost quantitative. After Soxhlet extraction with THF, the reduced dimer **1** was recovered in 42% yield from the product as a soluble fraction. The residue of white powder

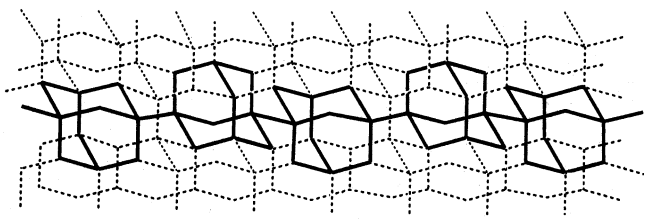
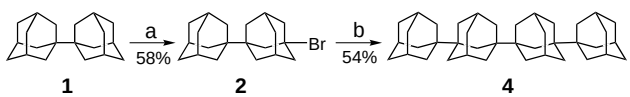


Figure 1. Structure of poly(1,3-adamantane) in diamond lattice.



Scheme 1. *Reagents and conditions*: (a) Br_2, CCl_4, 30°C, 72 h; (b) Na, *n*-octane, reflux, 12 h.

Keywords: 5,7-dibutyl-1,3-adamantane tetramer; coupling reaction; bridgehead carbon; 3-bromo-5,5′,7,7′-tetrabutyl-1,1′-biadamantane; solubility.

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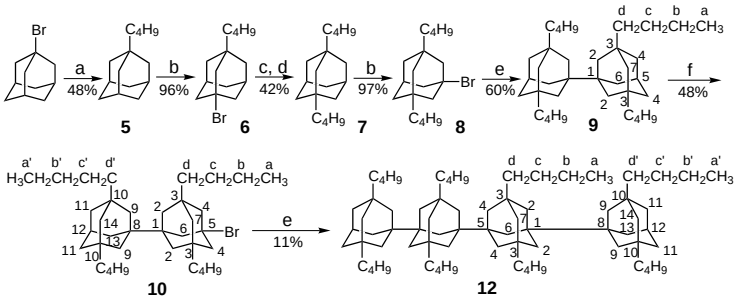

Scheme 2. *Reagents and conditions*: (a) C_4H_9MgBr, CH_2Cl_2, reflux, 12 h; (b) Br_2, 105°C, 5 h; (c) silver triflate, 2,2-dimethylbutane, 0°C, 3 h; (d) C_4H_9MgBr, Et_2O, rt, 12 h; (e) Mg, Et_2O, reflux, 48 h; (f) Br_2, CCl_4, 30°C, 72 h.

(~54%), which was unfortunately insoluble in any organic solvents, could be identified as **4** by the IR spectroscopy and the elemental analysis.[5] However, the poor solubility of **4** precluded its complete characterization by NMR spectroscopy and size exclusion chromatography (SEC) measurement.

We then introduced two butyl substituents into the adamantane repeating unit to increase the solubility of the oligomeric products, and a series of oligo(5,7-dibutyl-1,3-adamantane)s was synthesized as shown in Scheme 2. The introduction of a butyl substituent on the bridgehead carbon of the adamantyl skeleton was achieved in 48% yield by the reaction of 1-bromoadamantane and butylmagnesium bromide in dichloromethane as previously reported.[6] The resulting 1-butyladamantane (**5**) was brominated with Br_2 to afford 1-bromo-3-butyladamantane (**6**) in 96% yield. After treating **6** with silver triflate in 2,2-dimethylbutane,[7] butylmagnesium bromide in diethyl ether was added to the reaction mixture to give 1,3-dibutyladamantane (**7**) in 42% yield. The reaction of **7** with Br_2 gave 1-bromo-3,5-dibutyladamantane (**8**) in 97% yield. The magnesium-mediated coupling reaction of **8** in diethyl ether[8] and the following recrystallization provided a symmetrical dimer, 3,3′,5,5′-tetrabutyl-1,1′-biadamantane (**9**) in 60% yield. The bromination of **9** with Br_2 under diluted conditions in CCl_4 and column chromatography (silica gel, hexane) afforded a monobromide (**10**) in 48% yield along with a dibromide (**11**)[4] in 43% yield. The resulting monobromide **10** was then allowed to react with magnesium in diethyl ether under reflux condition to give a tetramer of dibutyladamantane **12**. It is suggested from the NMR and SEC analyses that the coupling reaction smoothly proceeded and the bromide was completely consumed to give a mixture of the reduced dimer **9** and the tetramer **12**. The tetramer, soluble in benzene, chloroform and THF, was successfully obtained in 11% yield after repeated recrystallization from diethyl ether, and the isolation of **12** was confirmed by SEC, ^1H and ^{13}C NMR and IR spectroscopies, and elemental analysis.[5] The ^1H NMR analysis clarified that **12** possessed two methine protons at both terminal adamantane units. Consistent with the presence of a plane of symmetry in **12**, its ^{13}C NMR spectrum consists of fourteen sp^3 resonances derived from 1,3-adamantyl skeleton. This is further confirmed by the 2D NMR spectroscopy of **12**. It should be noted that all four sp^3 carbon signals attributed to the butyl group were split into two signals showing the same intensities. This is probably due to the small difference in the chemical shifts of the butyl substituents on either the inner or outer adamantane framework of the tetramer. Thus, we have succeeded in the synthesis of a thermally-stable[9] tetrameric 1,3-adamantane derivative bearing solubility-enhancing butyl groups. Unfortunately, crystals suitable for an X-ray analysis of **12** have not yet been obtained. The resulting 5,7-dibutyl-1,3-adamantane tetramer **12** possesses two terminal methine carbons capable of further chemical modifications (bromination and coupling reaction) and opens up a synthetic pathway to novel higher oligomers having well-defined nano-architecture.

Acknowledgements

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4. The reaction of dibromides **3** or **11** with sodium gave polymeric products containing 1,3-adamantyl repeating units. The results of polymerization will be published elsewhere.
5. Selected data for **2**: off-white solid, mp 147–148°C, ^1H NMR ($CDCl_3$, 300 MHz): 1.53–1.70 (m, 18H), 1.98 (bs, 3H), 2.16–2.33 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz): 29.0, 32.9, 33.5, 35.47, 35.51, 36.7, 37.5, 42.8, 47.7, 49.3, 69.6 (C-Br); IR (KBr) 824 (C-Br), 1029, 1300, 1345, 1448, 2848, 2901, 2929 cm^{-1}. For **4**: off-white solid, mp >370°C (decomposed), IR (KBr) 1310, 1346, 1353, 1448, 2851, 2901, 2931 cm^{-1}. Anal calcd for $C_{40}H_{58}$ (538.9): C, 89.15; H, 10.85; found: C, 89.16; H, 10.83. For **9**: off-white solid, mp 73–74°C, ^1H NMR ($CDCl_3$, 300 MHz): 0.90 (t, 12H, $CH_3CH_2CH_2CH_2$, $J=7$ Hz), 0.96–1.27 (m, 44H), 1.41 (bs, 4H), 2.04 (bs, 2H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.3 (Ca), 23.9 (Cb), 25.0 (Cc), 29.8 (C5), 33.5 (C3), 34.9 (C6), 37.9 (C1), 40.6 (C2), 42.0 (C4), 44.8 (Cd), 47.2 (C7); IR

(KBr) 1320, 1466, 2836, 2893, 2926, 2952 cm^{-1}. For **10**: colorless liquid, ^1H NMR ($CDCl_3$, 300 MHz): 0.91 (t, 12H, CH_3, $J=7$ Hz), 0.96–1.28 (m, 40H), 1.42 (bs, 2H), 1.95 (m, 4H), 2.06 (bs, 3H, CH); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.24 and 14.32 (Ca,a′), 23.7 and 23.8 (Cb,b′), 24.98 and 25.05 (Cc,c′), 29.7 (C12), 33.6 (C10) 35.1 (C13), 38.17 (C3), 38.25 (C8), 39.0 (C2), 40.7 (C9), 41.8 (C11), 43.2 (C1), 43.6 (Cd), 44.6 (Cd′), 45.3 (C7), 47.0 (C14), 47.1 (C6), 53.5 (C4), 70.2 (C5); IR (neat) 735, 839 (C-Br), 1174, 1321, 1348, 1450, 2845, 2896, 2928 cm^{-1}. For **12**: off-white solid, mp 206–207°C, ^1H NMR ($CDCl_3$, 300 MHz): 0.88–0.94 (2t, 24H, CH_3, $J=7$ Hz), 0.98–1.30 (m, 88H), 1.44 (s, 8H), 2.06 (bs, 2H, terminal CH); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.20 and 14.22 (Ca,a′), 23.9 and 24.0 (Cb,b′), 25.1 and 25.2 (Cc,c′), 30.0 (C12), 33.1 (C6), 33.7 and 34.0 (C3 and C10), 35.3 (C13), 38.41 and 38.44 (C1 and C5), 38.7 (C8), 40.3 (C4), 40.7 (C2), 41.1 (C9), 42.0 (C11), 44.7 and 45.1 (Cd,d′), 46.7 (C7), 47.2 (C14); IR (KBr) 1341, 1446, 1483, 2856, 2897, 2926, 2952 cm^{-1}. Anal calcd for $C_{72}H_{122}$ (987.8): C, 87.55; H, 12.45; found: C, 87.83; H, 12.17.

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