all-trans-1,2,3,4,5,6-Hexaisopropylcyclohexane: An All-Axial Hexaalkyl Cyclohexane

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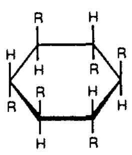
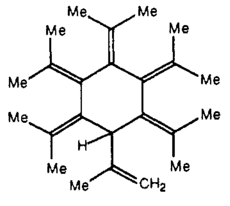
One of the central principles of the conformational analysis of substituted cyclohexane rings is that in the chair conformation, alkyl substituents prefer equatorial over axial positions.[1] This preference is normally rationalized in terms of repulsive interactions present in the axial conformation between the alkyl substituent and the axial hydrogens at the 3 and 5 positions of the cyclohexane ring. In general, the bulkier the alkyl group, the larger the preference for the equatorial position.[2] It should be noted that although the conformational preferences are commonly analyzed in terms of enthalpic contributions, the entropy term is by no means negligible. It was recently shown that for isopropylcyclohexane, there is a large entropic contribution to the free energy difference (2.2 cal K^{-1} mol^{-1}).[3] For polyalkyl-substituted compounds, it is generally assumed that the preferred conformation is such that as many groups as possible will adopt equatorial positions, and this expectation is normally borne out by the experiments. For example, in *all-trans*-1,2,3,4,5,6-hexaethylcyclohexane the six ethyl groups are located at equatorial positions.[4] Only in special cases, such as alkylidene-2-alkylcyclohexane systems, is there a tendency of the alkyl substituent to occupy the axial position.[5] To the best of our knowledge, no polyalkyl cyclohexane has ever been reported in which all the alkyl groups prefer axial over equatorial positions. In this communication we report a first example of a molecule that displays such a novel conformational behavior: *all-trans*-1,2,3,4,5,6-hexaisopropylcyclohexane (**1**).[6,7]



R = i-Pr

1



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In order to synthesize the desired compound, we reasoned that it will be desirable to build the skeleton in as few synthetic steps as possible. Catalytic reduction of a known isomer of dodecamethyl[6]radialene[8] (**2**) seemed an attractive possibility, since it was reported that hydrogenation of **2** (Pd/EtOH–cyclohexane–acetic acid) yielded a mixture of the dihydro and tetrahydro products,[8b] and it seemed likely to us that under more drastic conditions, all the double bonds would be reduced. We therefore prepared **2** by the one-step procedure of Iyoda et al.[8a] and submitted it to catalytic reduction.

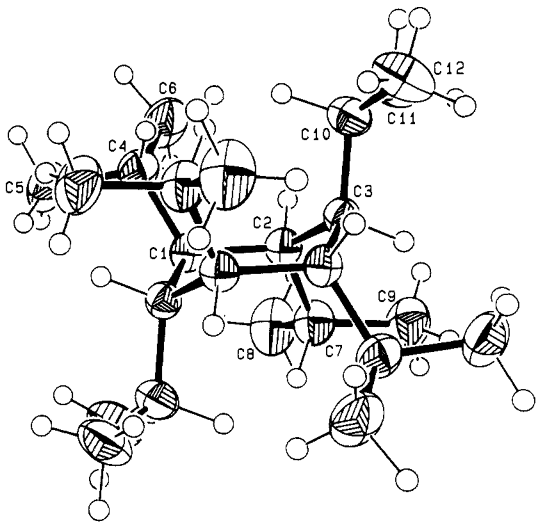

Figure 1. Side view and numbering scheme of *all-trans*-1,2,3,4,5,6-hexaisopropylcyclohexane (**1**).

Table I. Selected Experimental (X-ray) and Calculated (Molecular Mechanics) Structural Parameters of **1**[a]

parameter	exptl	calcd
C1–C2	1.553 (5)	1.550
C4–C5	1.526 (7)	1.540
C4–C6	1.531 (5)	1.550
C2–C1–C4	116.0 (3)	117.2
C1–C2–C3	114.2 (4)	113.4
C2–C3–C10	112.0 (3)	113.2
C1–C4–C5	111.6 (3)	112.7
C1–C4–C6	114.2 (4)	114.6
C5–C4–C6	106.8 (4)	105.2
C1–C2–C3–C1′	46.5	49.2
C3′–C1–C3–C2	−46.7	−49.2
C4–C1–C2–C7	−140.1	−138.4
C1–C2–C3–C10	−87.1	−86.6
C4–C1–C2–C3	85.3	85.6

[a] Bond lengths in Å, bond and dihedral angles in deg. Tagged and untagged atoms (e.g. C1 and C1′) are related by inversion.

Hydrogenation of **2** under drastic conditions (Rh/alumina and Pd/C, 950 psi H_2, 130 °C) yielded **1**. Both the ^1H and ^{13}C NMR displayed an extremely simple NMR spectrum, indicating a highly symmetric structure.[9] A single crystal of **1** was grown by slow evaporation of a solution of **1** in MeOH/ether. The X-ray structure of **1** was solved in the space group $P\bar{1}$ with one molecule in the unit cell. Figure 1 shows a side view of the crystal structure of the molecule. Selected structural parameters are collected in Table I, together with values calculated by molecular mechanics (see below). A complete list of positional parameters, bond lengths, and angles is deposited as supplementary material (Tables S1–S3). As seen in the figure, **1** exists in a somewhat flattened chair conformation of approximate S_6 symmetry in which the six isopropyl groups are located at axial positions. The conformation of the isopropyl groups is such that the isopropyl methine hydrogens are all directed toward the center of the cyclohexane ring.

In order to estimate the energy difference between the all-axial and all-equatorial conformation we resorted to molecular mechanics calculations. For that purpose we used the MM2 implementation of the program BIGSTRN-3.[10,11] In addition to the crystallographic axial conformation, four equatorial conformations were considered. These conformations had homodirectional, "gear meshed" isopropyl groups (cf. A in Figure 2), "gear clashed"

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[5] For a review of the so called "allylic strain" see: Johnson, F. *Chem. Rev.* **1968**, 375.

[6] Only a few hexasubstituted cyclohexanes are known. See: Farina, M.; Grassi, M.; Di Silvestro, G. *J. Am. Chem. Soc.* **1985**, *107*, 5100 and references therein.

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[8] (a) Iyoda, M.; Tanaka, S.; Otani, H.; Nose, M.; Oda, M. *J. Am. Chem. Soc.* **1988**, *110*, 8494. (b) Iyoda, M.; Tanaka, S.; Nose, M.; Oda, M. *J. Chem. Soc., Chem. Commun.* **1983**, 1058.

[9] ^1H NMR ($CDCl_3$, room temperature, 200.13 MHz) δ 0.91 (d, J = 6 Hz, 36 H), 1.45 (d, J = 10.1 Hz, 6 H), 1.57 (m, 6 H). ^{13}C NMR ($CDCl_3$, room temperature, 50.32 MHz) δ 23.47, 31.46, 41.29.

[10] BIGSTRN-3: Nachbar, R. B., Jr.; Mislow, K. QCPE No. 514. Nachbar, R. B., Jr.; Mislow, K. *QCPE Bulletin* **1986**, *6*, 96.

[11] Input geometries were based on standard bonds and angles. Geometry optimization was carried out with the full-matrix Newton–Raphson method.

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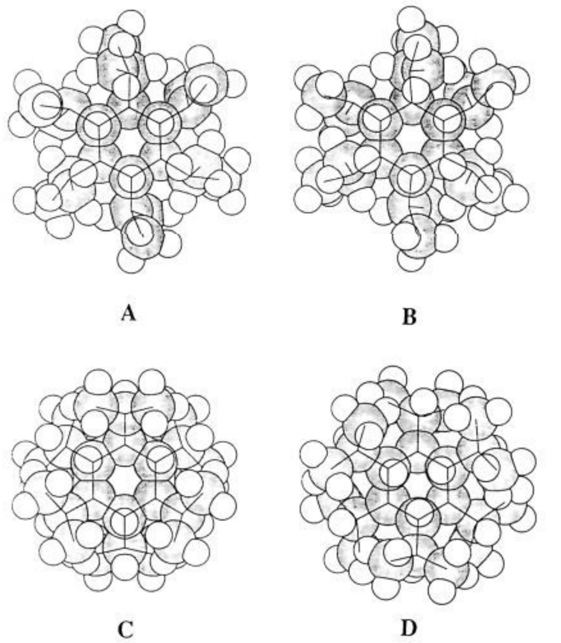

Figure 2. Space-filling models of the calculated equatorial conformations of **1**. Atom balls are drawn with 33% of the atomic radius. All conformations are viewed along the normal to the mean cyclohexane plane. The carbon skeleton is overlayed on the space-filling models for clarity.

groups (B), and syn-periplanar (C) and anti-periplanar (D) arrangements of the two $CHCHMe_2$ methine hydrogens. The minimized conformations had S_6, D_3, D_{3d}, and S_6 symmetries and were calculated to lie 13.9, 17.1, 51.2, and 58.1 kcal mol^{-1} above the axial conformation. The calculations indicate that the all-axial conformation of S_6 symmetry indeed corresponds to the minimum energy conformation. In general, there is excellent agreement between calculated and experimental structural parameters of **1** (Table I). The calculated energy difference between the gear meshed (A) and gear clashed (B) equatorial conformations of **1** (3.2 kcal mol^{-1}) is appreciably lower than for hexaisopropylbenzene (31.9 kcal mol^{-1}).[12]

What is the reason for the relative destabilization of the equatorial conformation? It seems likely that the unavoidable torsional and/or steric strain present at any equatorial disposition of the isopropyl group is responsible of the equatorial → axial stability reversal. Even in the low-energy equatorial conformation A, one of the methyls of each isopropyl group is nearly eclipsed ($\phi = 20.2°$) with the axial cyclohexane methine proton. Work is under way to see whether the axial $\rightleftharpoons$ equatorial conformational reversal could be present in other cyclohexane systems.

Acknowledgment. We thank Dr. James H. Geiger for helpful discussions and Dr Shmuel Cohen for the crystal structure determination. This research was supported by a grant from the United States–Israel Binational Science Foundation (BSF), to whom we are grateful. The Fritz Haber Research Center at the Hebrew University is supported by the Minerva Gesellschaft für die Forschung, mbH, Munich, Federal Republic of Germany.

Registry No. 1, 124358-20-9; **2**, 88919-68-0.

Supplementary Material Available: Crystallographic data for **1** and tables of final positional parameters, bond lengths, bond angles, and thermal parameters (3 pages). Ordering information is given on any current masthead page.

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[12] The gear meshed conformation resembles the lowest energy conformation (all geared) of hexaisopropylbenzene. Arnett, E. M.; Bollinger, J. M. *J. Am. Chem. Soc.* **1964**, *86*, 4729. Hopff, H.; Gati, A. *Helv. Chim. Acta* **1965**, *48*, 509. Siegel, J.; Gutierrez, A.; Schweizer, W. B.; Ermer, O.; Mislow, K. *J. Am. Chem. Soc.* **1986**, *108*, 1569.

Generation and Trapping of the Diphenylhydrazido(2−) Complex $Cp_2Zr(N_2Ph_2)$. Insertion of Internal Alkynes into a Metal−Nitrogen Bond, Leading to 2,3-Diazametallacyclopentenes

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Despite the large number of early-metal complexes containing metal–nitrogen or metal–oxygen bonds, insertion of olefins or alkynes into these bonds is rare.[1,2] In fact, this process is not well documented for transition-metal amide complexes in general. Insertion of nonpolar carbon–carbon bonds into early-metal nitrogen bonds represents an especially challenging problem because of their high (81–95 kcal/mol)[3] bond energy.

We have been seeking to prepare strained systems containing nitrogen bonded to zirconium, in the hope that they will exhibit enhanced Zr–N reactivity toward simple organic compounds and lead to reactions that involve the formation of new carbon–nitrogen bonds (the few known complexes with strained Zr–O and Zr–N bonds also contain Zr–C bonds, and insertion occurs into the latter preferentially[4]). We now report our first observation of M–N bond insertion, in the generation of the (η^2-1,2-diphenylhydrazido(2−))zirconocene complex $Cp_2Zr(N_2Ph_2)$ (**2**). This species has not been isolated, but can be trapped by coordination with various dative ligands. Significantly, the complex undergoes insertion of alkynes into one of the Zr–N bonds, leading to the formation of diazametallacyclopentenes.

The chemistry we have observed is summarized in Scheme I. The (η^2-hydrazido)methylzirconium complex **1** was prepared in 83% yield by treatment of $Cp_2Zr(Me)(Cl)$[5] with the monopotassium salt of 1,2-diphenylhydrazine in toluene. Our first evidence for the generation of **2** was obtained by thermolysis of this material in THF at 65 °C for 2.5 days, which provides $Cp_2Zr(N_2Ph_2)(THF)$ (**3**) in 80% yield. Complex **3** can be prepared independently (60–80% yield) by addition of 1-lithio-1,2-diphenylhydrazine to $[Cp_2Zr(H)(Cl)]_n$ in THF, but it is obtained most efficiently (90–95% yield) by the addition of Cp_2ZrCl_2 in THF to a slurry of the 1,2-dithio-1,2-diphenylhydrazide[6a] in ether at room temperature.[6b]

The coordinatively unsaturated intermediate **2** is most conveniently generated by dissociation of THF from adduct **3**. Thus, treatment of **3** with pyridine or trimethylphosphine led to complexes **4** and **5** in 72% and 83% isolated yields, respectively. Crystals of the pyridine complex **4** suitable for an X-ray diffraction study were grown from a 50/50 mixture of toluene and hexane

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