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PERMETHYLCYCLOHEXANE[1)]

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Summary: Permethylcyclohexane 2 has been synthesized and investigated by dynamic NMR spectroscopy. An unexpectedly low barrier ($\Delta G^{\ddagger}_{333}$ = 70.0 kJ/mol) of its chair-to-chair interconversion was found.

In connexion with the reported high barrier ($\Delta G^{\ddagger}_{333}$ = 72.4 kJ/mol) of the chair-to-chair interconversion of all-*cis*-1,2,3,4,5,6-hexamethylcyclohexane 1[2)], apparently due to large nonbonding interactions in the planar part of the transition state 1*[3)], we became interested in the synthesis and dynamics of the so far unknown permethylcyclohexane 2, where such interactions could be expected to be even more pronounced (see 2*). We report here on the synthesis of this highly crowded cyclohexane and on an unexpectedly low barrier ($\Delta G^{\ddagger}_{333}$ = 70.0 kJ/mol) of its chair-to-chair interconversion.

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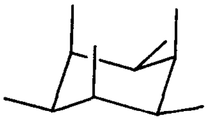

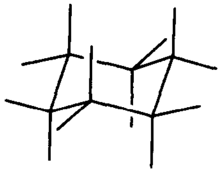

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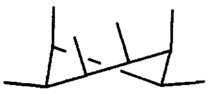
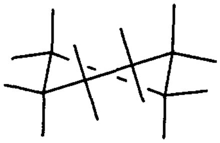
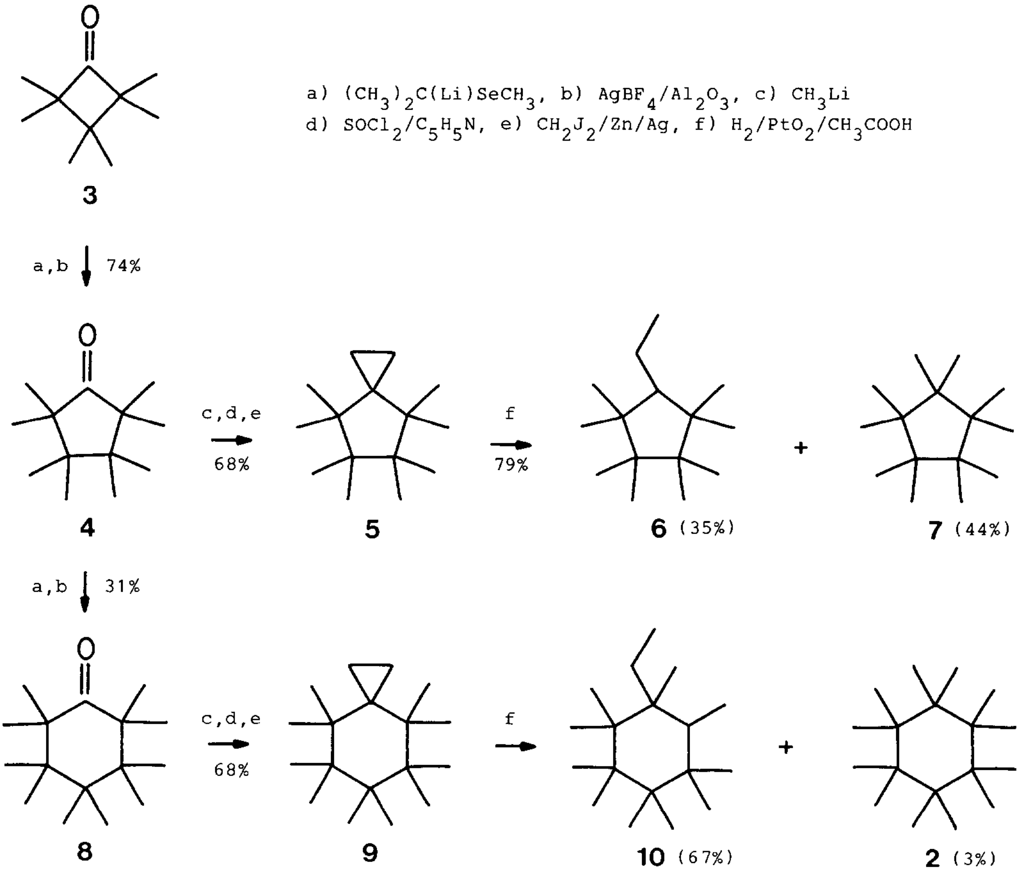




2*

The synthesis of permethylcyclohexane 2 was achieved as follows: according to a general procedure developed by Krief[4)], hexamethylcyclobutanone 3[5)] was first homologized to octamethylcyclopentanone 4 (mp. 191-193°C, 74% yield)[6)] and decamethylcyclohexanone 8 (mp. 245-250°C, 31% yield)[6)] by reaction of the appropriate ketone with 2-lithio-2-selenopropane [1.5 equiv., 0.5 hr, -78°C (3) and 1.0 equiv., 6 hr, -30°C (4)] in ether/pentane and subsequent rearrangement of the resulting ß-hydroxyselenide with silvertetrafluoroborate/alumina (2.0/8.0 equiv., 2 hr, 0°C and 1 hr, 25°C) in tetrachloromethane.

Octamethylcyclopentanone 4 was then used in a search for optimum conditions for the conversion of 8 to 2: addition of methyllithium (2.0 equiv., 1 hr, 60°C) in ether, treatment with thionylchloride (2.0 equiv., 0.5 hr, 0°C) in pyridine and cyclopropanation of the resulting olefin with a large excess of diiodomethane/zinc/silver[7] (5.0 equiv., 3 hr, 60°C) yielded the spirane 5 (mp. 95-105°C, 68% yield)[6], which was then hydrogenated over platinum dioxide (1.0 equiv., 1.1 atm H_2, 16 hr, 50°C)[8] in acetic acid to yield the expected[9] permethylcyclopentane 7 (mp. 86-90°C, 44% yield)[6] and 1-ethyl-2,2,3,3,4,4,5,5-octamethylcyclopentane 6 (mp. 76-82°C, 35% yield)[6].


a) $(CH_3)_2C(Li)SeCH_3$, b) $AgBF_4/Al_2O_3$, c) CH_3Li
d) $SOCl_2/C_5H_5N$, e) $CH_2J_2/Zn/Ag$, f) $H_2/PtO_2/CH_3COOH$

Turning to the synthesis of 2, we found the reaction sequence leading to 5 equally effective in the production of 9 (mp. > 300°C, 68% yield)[6], but unexpectedly the hydrogenation over platinum dioxide (2 equiv., 1.1 atm. H_2, 120 hr, 50°C)[8] in acetic acid now yielded largely the rearranged 1-ethyl-1,2,3,3,4,4,-5,5,6,6-decamethylcyclohexane 10 (mp. 185-192°C, 67% yield)[6] and only minor amounts of the desired permethylcyclohexane 2 (mp.> 295°C, 3% yield)[6]. Both 2 and 10 were separated from starting material and several as yet unidentified products by preparative glpc[10]. While the gross structure of 10 could be resolved by connectivity studies[11], no evidence is available as to the relative stereochemistry of the substituents at C-1 and C-2.

On the contrary, both structure and conformation of the title compound 2 could be unequivocally established by NMR: the high resolution ^{1}H NMR (200 MHz, CF_2Cl_2, acetone-d_6, $-10^{\circ}C$) showed 1:1 quartets at δ = 1.07 and 1.30 ppm ($^4J_{HH}$ = 0.68 Hz), the ^{13}C NMR (50.3 MHz, C_6D_6, $+22^{\circ}C$) three lines at δ = 25.14 (C_{ax})[12], 27.40 (C_{eq})[12] and 44.18 ppm (C_{quart}), thus proving that 2 exists in solution at ambient temperature in a fixed chair conformation of D_{3d} symmetry. In order to determine the inversion barrier, we have studied the temperature dependence of the ^{1}H NMR spectrum at 79.6 MHz in 1,1,2,2-tetrachloroethane-d_2. The resonance lines of the methyl groups here appeared as 1:1 singlets at δ = 0.95 and 1.16 ppm with $\Delta\nu$ = 16.4 Hz (1.5°C) and coalesced at +60.0 ± 0.5°C. Insertion of these data into the Eyring relation affords $\Delta G^{\ddagger}_{333}$ = 70.0 ± 1.0 kJ/mol and hence an inversion barrier nearly identical with the barrier for 1 ($\Delta G^{\ddagger}_{333}$ = 72.4 kJ/mol)[2].

It is thus obvious, that the additional six methyl groups in 2 have raised the energy of the ground and transition state to nearly an equal extent. In a tentative explanation of this unusual result, we refer to the ground state geometry of 1, as determined by X ray diffraction (see fig.1)[13]: a total of three 1,3-diaxial interactions here have been diminished by simply displacing the methyl groups outwards and the corresponding hydrogen atoms inwards with respect of the ring. Normal dihedral angles throughout the ring (53°) demonstrate that these displacements are energetically more favourable than a flattening of the ring.

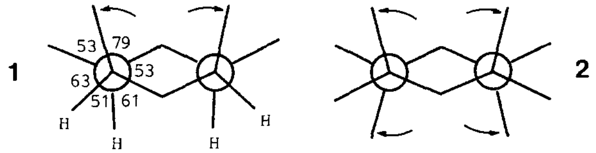


Fig.1: Ground state geometry of 1[13] and supposed ground state geometry of 2 in Newman projection

Clearly, this situation can no longer be valid for 2 (see fig.1). A total of six 1,3-diaxial interactions should now cause an outward displacement of all methyl groups and a simultaneous flattening of the ring. We feel that the resulting steric compression towards the ring plane along with six additional 1,2-diequatorial interactions not present in 1 could well account for the complete compensation of the increase in the transition state energy observed, but for a deeper understanding of the conformational properties of 2, a recent computational force field study[14] should be consulted.

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References and notes

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3) For a detailed analysis using a modified MM2 force field see: C.Jaime and E.Osawa, Tetrahedron 39, 2769 (1983).

4) D.Labar and A.Krief, J.Chem.Soc.Chem.Commun. 1982, 564; D.Labar, J.L.Laboureur and A.Krief, Tetrahedron Lett. 1982, 983.

5) 5 has been obtained on a large scale through exhaustive methylation of the readily available 2,2,3,3-tetramethylcyclobutanone [D.A.Bak and W.T.Brady, J. Org. Chem. 44, 107 (1979)] according to a procedure described by A.A.Millard and M.W.Rathke [J. Org. Chem. 43, 1834 (1978)]. Other methods for the preparation of 5 are available: H.Bestian and D.Günther, Angew. Chem. 75, 841 (1963); M.Braun, R.Dammann and D.Seebach, Chem. Ber. 108, 2368 (1975).

6) All new compounds gave correct elemental analyses and/or high resolution mass spectral data. IR, Raman (2), ^{1}H NMR, ^{13}C NMR and mass spectral data are in accord with the structures given. ^{13}C NMR data ($CDCl_3$, unless otherwise stated) are as follows: 2 (C_6D_6): 25.14, 27.40, 44.18; 4: 23.74, 24.64, 44.07, 50.58, 229.29; 5: 6.97, 24.39, 26.19, 37.46, 43.43, 47.73; 6: 15.37, 19.70, 22.01, 23.60, 24.59, 29.53, 44.68, 47.57, 59.97; 7: 25.95, 47.95; 8: 24.40, 25.76, 26.61, 43.72, 44.95, 52.47, 221.45; 9: 2.46, 12.91, 22.73, 23.84, 25.21, 25.33, 27.14, 27.91, 29.20, 41.35, 43.28, 44.51; 10: 10.74, 12.78, 21.58, 21.76, 22.86, 24.10, 24.48, 24.71, 25.10, 25.09, 27.01, 29.77, 40.79, 42.79, 43.10, 43.19, 43.95, 44.84.

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8) The reaction conditions are essentially the same as described by C.W.Woodworth, V.Buss and P.v.R.Schleyer (J. Chem. Soc. Chem. Commun. 1968, 569) for the hydrogenation of cyclopropanoadamantane.

9) For selectivity studies in the hydrogenation of substituted cyclopropanes see: C.Gröger, H.Musso and I.Rossnagel, Chem. Ber. 113, 3621 (1980).

10) 2m x 1/4" all-glass system, 15% DC 550 on chromosorb W AW/DMCS 60/80 mesh, 220°C; rel. retention times: 0.62, 0.69, 0.75, 0.85 (18%, unidentified products), 0.93 (67%, 10), 1.00 (12%, 9) and 1.17 (3%, 2).

11) ^{1}H NMR double resonance measurements revealed the existence of an ethyl group and of a methyl group bound to quaternary and tertiary carbon atoms respectively. The decision between the 1,2-arrangement indicated in the scheme and a possible 1,3-arrangement was then made by carbon-carbon connectivity studies using INADEQUATE techniques [R.Richarz, W.Ammann and T.Wirthlin, J. Magn. Reson. 45, 270 (1981)].

12) Compare the assign ments given for methylcyclohexane [F.A.L.Anet, C.H.Bradly and G.W.Buchanan, J. Am. Chem. Soc. 93, 258 (1971)] and 1,1-dimethylcyclohexane [D.K.Dalling, D.M.Grant and L.F.Johnson, ibid. 93, 3678 (19719].

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14) O.Ermer, private communication; P.M.Ivanov, E.Osawa and O.Ermer, to be published.

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