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SYNTHESIS AND REARRANGEMENT OF SOME 4,5-DISUBSTITUTED HOMOCUBYL DERIVATIVES

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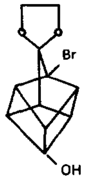
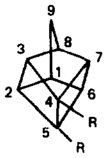
A recent report by Zwanenburg and Klunder[1] concerning the synthesis and reactions of the bridgehead substituted homocubyl alcohol derivative, 1, prompts us to report our efforts to prepare some reactively functionalized 4,5-disubstituted homocubyl derivatives, 2. These compounds were desired for a study of their chemical, pyrolytic, and transition metal-catalyzed rearrangements. Additionally, the unique 4,5-functionalization was considered essential for activation of the central bond for subsequent transformation into derivatives containing the unknown tetracyclo$[4.3.0.0^{3,9},0^{4,7}]$ skeleton for a study of the chemical and spectral interaction of substituents in the 2 and 5 positions.[2]



1



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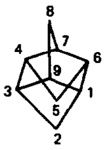
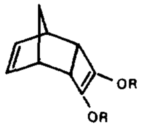


3

In view of the successful preparation of some homocubyl derivatives via internal photochemical cycloaddition,[4] it was decided to examine the photochemical behavior of 3,4-bis-trimethylsiloxytricylco$[4.2.1.0^{2,5}]$non-3-ene, 4, and its homologs 5 and 6.[5] The use of the bis-trimethylsiloxylated olefins as starting materials was suggested by their strong ultraviolet absorption[6] and the anticipated subsequent facile hydrolytic removal of the protecting groups.



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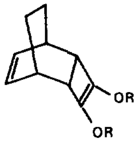

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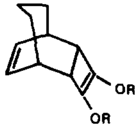
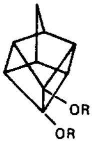


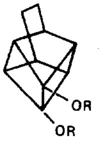
6

R=$(CH_3)_3Si$

Irradiation of a degassed 0.15M solution of 4 (35°, 2537 Å) in cyclohexane resulted in the rapid disappearance of the characteristic infrared absorption at 1710 cm^{-1} of the starting material and the production of a single volatile product (80-85%) of very similar GLPC retention time. On the basis of analytical and spectral data supported by chemical transformation, the structure of the product (MW 294) was assigned as 4,5-bis-trimethylsiloxypentacyclo $[4.3.0.0^{2,5}.0^{3,8}.0^{4,7}]$nonane, 7a. Consistently, no infrared absorption was observed above 3000 cm^{-1}, a fact consistent with that reported for a number of cubyl and homocubyl derivatives.[7a] The infrared spectrum showed strong bands at 2980, 1355, 1305, 1255, 930, 905, 875, and 840 cm^{-1}. The NMR spectrum (100 MHz) reflected the high molecular symmetry and showed only three singlets at τ (CCl_4) 6.85 (s, 6H, 1/2 wd 2.3 Hz), 8.22 (s, 2H, 1/2 wd 2.7 Hz), and 9.75 (s, 18H). Apparently the bridgehead methine protons show an accidental equivalence. No unreactive solvent was found that separated the methine signals into their components although the base of the low field absorption was significantly broadened and assumed some fine structure in pyridine.



7a R=$(CH_3)_3Si$
7b R=H
7c R=Ac

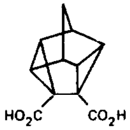


8

R=$(CH_3)_3Si$

9

R=$(CH_3)_3Si$



10

Since previous reports of the direct photochemical generation of homocubyl derivatives via intramolecular cycloaddition have depended on photosensitization,[4] the irradiation of 4 (3000 Å) was examined in acetone solvent. Surprisingly, 7a was not detected in the irradiation mixture and the consumption of starting material was accompanied by the formation of higher boiling products and polymer. The caged product was stable under the irradiation conditions.

Attempts to extend the scope of this reaction to the homologous derivatives 5 and 6 were of limited success. When 5 was irradiated under similar conditions, the consumption of starting material was accompanied by the formation of large amounts of non-volatile products and polymer. A small quantity (ca. 5%) of a volatile product was isolated which had spectral properties consistent with the desired structure, 8. This material (MW 306) had NMR absorptions at τ (CCl_4) 7.17 - 7.55 (m, 6H), 8.70 (m, 4H 1/2 wd 4 Hz), and 9.8 (s, 18H). The IR spectrum of 8 showed no absorption above 3000 cm^{-1} and had strong bands at 2950, 2920, 1355, 1340, 1290, 1250, 900, 860, and 830 cm^{-1}.

Irradiation of 6, failed to produce any isolable isomeric products and resulted in the rapid consumption of starting material. As with 4, the use of acetone as the solvent for irradiation of 5 and 6 did not produce the desired transformation. The failure of 5 and 6 to undergo cycloaddition in high yield in contrast to 4 may result from a combination of the progressively increasing distance between the reactive centers in the higher homologs coupled with the greater reactivity of the more strained norbornene double bond of 4.

When the photoproduct, 7a, was heated in the absence of solvent to 245° for 2 hr, it was converted into a new product. After this time, only 15-18% of the starting material remained. The infrared spectrum of the thermal rearrangement product (MW 294) showed absorptions at 3050, 2960, 1380, 1255, 1185, 965, 890, and 840 cm^{-1}. The high frequency carbon-hydrogen stretch at 3050 cm^{-1} considered in conjunction with the absence of vinyl protons in the NMR spectrum implied the presence of a cyclopropane ring.[7] The NMR spectrum was again that of a symmetrical compound with absorbances at τ (CCl$_4$) 7.43 (m, 2H), 7.84 (t, J=3Hz, 4H), 8.58 (m, 2H, 1/2 wd 3Hz), and 9.78 (s, 18H). The actual splitting patterns of the ring protons were very similar to those reported by Wenkert and coworkers for the photoacid 10.[7a] This spectral data is consistent with the structure 9.

Further support for this structural assignment is derived from the silver (I) catalyzed rearrangement of 7a. Catalytic amounts of silver tetrafluoroborate in chloroform transformed 7a rapidly to a product identical in every respect with the thermal rearrangement product 9. The presence of bulky oxygenated substituents directly attached to the strained ring junction apparently does not alter the reaction pathway from that predicted.[8] The facile thermal rearrangement of 7a is curious in light of the reported stability of a number of homocubyl derivatives.[9] The relationship of this thermal lability to substituent type and position is under investigation with some other substituted homocubyl derivatives.

Treatment of 7a with dry methanol at room temperature (3 hr) resulted in the complete consumption of starting material. The white solid thus obtained (mp 104-8°) in 80% yield was identified as the desired 4,5-dihydroxypentacyclo[4.3.0.0^{2,5},0^{3,8},0^{4,7}]nonane, 7b, by its spectral data. Direct ion source injection yielded a molecular ion at m/e 150. The IR spectrum of 7b (nujol) showed a strong and broad hydroxyl stretch centered at 3245 cm^{-1} and additional strong absorptions at 2980, 2960, 2940, 2910, 2840, 1320, 1290, 1215, 1220, and 820 cm^{-1}. When the spectrum of 7b in a KBr pellet was recorded, a weak carbonyl absorption appeared at 1770 cm^{-1} implying partial decomposition during pressing. The diol was readily soluble in polar solvents such as acetone, methanol, pyridine, and DMSO without decomposition. The NMR spectrum of 7b showed absorptions at τ (DMSO d_6) 4.67 (br s, 2H), 7.08 (sharp singlet superimposed on a broad base, 6H), and 8.40 (s, 2H, 1/2 wd 3Hz). The low field protons readily exchanged in D_2O. When 7b was treated with trimethylsilyl chloride and pyridine at room temperature 7a was regenerated, precluding skeletal rearrangement during alcoholysis. In a similar manner the diol 7b yielded the diacetate derivative 7c upon treatment with acetyl chloride. The NMR spectrum of 7c showed characteristic absorbances at τ (CCl_4) 6.60 (m, 2H), 6.78 (m, 2H), 7.05 (s, 6H), and 8.28 (m, 2H, 1/2 wd 3Hz). The IR spectrum showed the expected bands at 1740 and 1280 cm^{-1}. Interestingly, 7c could be produced in high yield directly from 7a upon treatment with acetyl chloride and boron trifluoride etherate.

Work on the chemistry of these polycyclic derivatives is proceeding.

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