Protoadamantene as a Synthetic Precursor to 2,4-Diaxial Adamantane Derivatives

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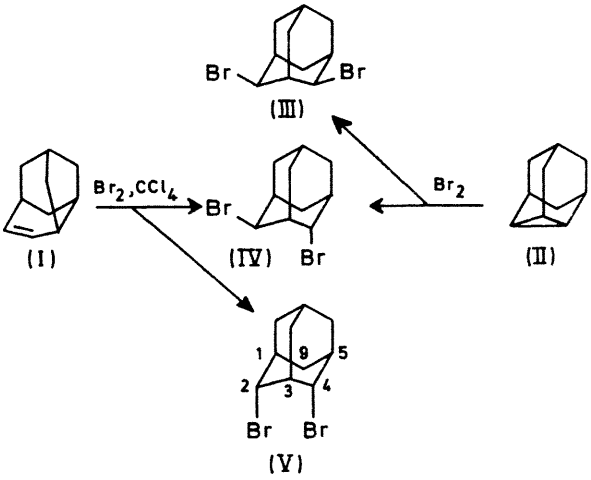
Summary 2,4-*Diaxial*-dibromoadamantane (V) and 2,4-*diaxial*-dihydroxyadamantane (VII) are obtained by bromination of protoadamantene (I) and by treatment of protoadamantene epoxide (VI) with aqueous acid, respectively.

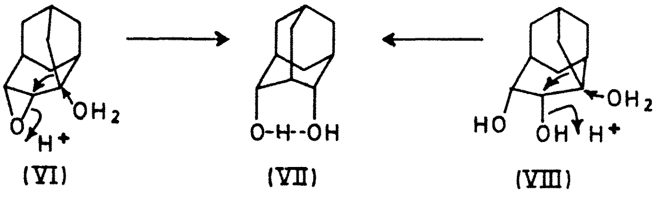
PROTOADAMANTENE (I)[1-3] complements 2,4-dehydroadamantane (II)[4] as a precursor for the preparation of 2,4-difunctionally substituted adamantane derivatives. Furthermore, (I) tends to give rise to *diaxial* products, which may be difficult to obtain otherwise.



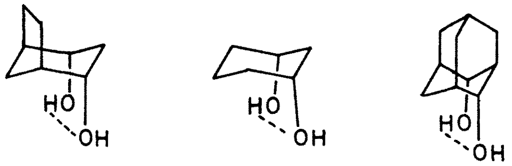
2,4-Dehydroadamantane (II) reacts with bromine to give a mixture of 2,4-*diequatorial*-dibromoadamantane (III) m.p. 115—117°, and the *axial–equatorial* isomer (IV) m.p. 120—122°.[4] The bromination of (I)† in CCl_4 also gives some (IV), but the major product (2 : 1 ratio) is the formerly unknown 2,4-*diaxial*-dibromoadamantane (V), m.p. 171·8—173·0°. (V) can easily be separated from (IV) by column chromatography on silica gel. The structure of (V) was determined chemically by reduction with tri-n-butyltin hydride to give a mixture of adamantane and 2-bromoadamantane.

The n.m.r. spectrum of (V) is of some interest, since it has already been predicted on the basis of expected chemical shift additivities.[5] The observed spectrum corresponds well with that calculated; almost all of the observed chemical shifts are within 0·1 p.p.m. of the predicted values. However, the chemical shifts of the bridgehead protons adjacent to the bromine atoms as well as the 9-*equatorial* hydrogen are observed to be somewhat further downfield than predicted; these shifts amount to 0·17 p.p.m. for 1-H and 5-H, 0·27 p.p.m. for 3-H, and 0·25 p.p.m. for 9-*eq*-H.

m-Chloroperbenzoic acid reacts in CH_2Cl_2 with (I)† to give a 6 : 1 ratio (g.l.c.) of *exo*- (VI) and *endo*-epoxides. This mixture, m.p. 237·5—239·0°, reacted with acid in aqueous acetone solution to give 2,4-*diaxial*-dihydroxyadamantane (VII), m.p. 305—310° dec., rather cleanly. As the mechanism shown below indicates, the *diaxial* diol (VII) would be expected to arise from concerted rearrangement of the *exo*-epoxide (VI). Reduction of protoadamantene epoxide with $LiAlH_4$ gave 4-*exo*-protoadamantanol[6] as the main product, thus confirming the *exo*-stereochemistry assigned the major epoxide component.



Diol (VII) was identical with the major product of $LiAlH_4$ reduction of 4-*axial*-hydroxy-2-adamantanone.[7] Confirming the preliminary report,[7] (VII) gave a single C*H*OH triplet (*J* 2·8 Hz) at δ 4·05 in its n.m.r. spectrum; the i.r. spectrum of (VII) in high dilution in CCl_4 showed free and hydrogen-bonded peaks at 3616 and 3530 cm⁻¹, respectively.‡ Diol (VII) also resulted by treatment of 4-*exo*-5-*exo*-dihydroxyprotoadamantane (VIII) with 25% aqueous sulphuric acid at 100° for 1·5 h. Compound (VIII), m.p. 212—216°, was the product of the reaction of (I)† with OsO_4 in ether, followed by reduction with $NaHSO_3$ in 50% aqueous pyridine solution.



The magnitude of the intramolecular hydrogen-bond spectral shift of diol (VII), 86 cm⁻¹, is revealing concerning the detailed conformation of six-membered rings. It is now well established that cyclohexane is somewhat flattened[8] with the consequence that axial groups are bent outwards, away from the central "axis" of the molecule.[8] In adamantane, such flattening of any one cyclohexane

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† The protoadamantene (I) used in this work was prepared following ref. 2.
‡ I.r. spectrum determined by T. Gorrie.

ring is opposed by structural constraints, and nearly tetrahedral geometry around each carbon atom results.[9] Axial groups in adamantane cannot bend outward nearly as easily as in cyclohexane. This is demonstrated by the larger $\Delta\nu$ for (VII), 86 cm^{-1}, than for cyclohexane-1,3-*cis*-diol, 75 cm^{-1}.[10] In the former compound, the hydroxy-groups are closer together. The addition of an ethylene bridge to cyclohexane has the opposite effect and flattens the six-membered ring even further.[11,12] This "inverse reflex effect" is nicely illustrated by diol (IX), whose $\Delta\nu$ is only 39 cm^{-1}.[12]

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