Chemistry of 4-Protoadamantyl Derivatives[1]

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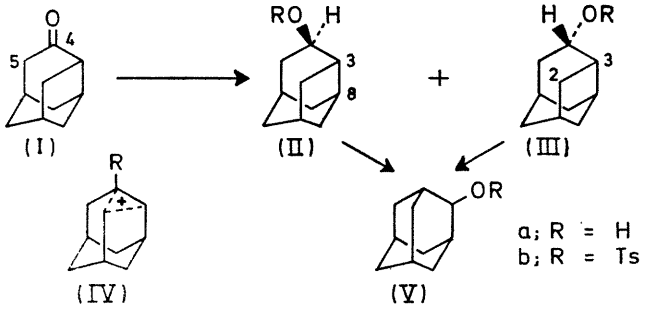
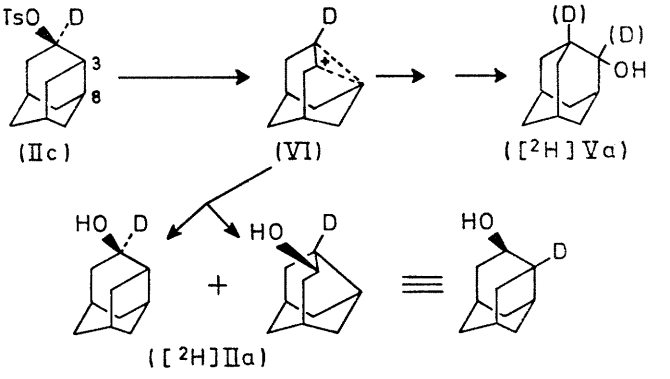
Summary 4-Protoadamantanone (I) is converted into epimeric secondary and tertiary alcohols; 4-*exo*-protoadamantyl derivatives react rapidly to give 2-adamantyl products while 4-*endo*-protoadamantyl derivatives react more slowly and tend to undergo a degenerate rearrangement before giving ultimately 2-adamantyl products.

CARBONIUM ion reactions of 2-adamantyl derivatives give[2,3] small amounts of skeletally isomerized tricyclo[4,3,1,$0^{3,8}$]-dec-4-yl ("4-protoadamantyl")[4] products. Cation-stabilizing 1-substituents facilitate this rearrangement. Nitrous acid deamination of 2-aminoadamantan-1-ol[5] gives a 92% yield of 4-protoadamantanone (I),[2,6] m.p. 208—210°. This ketone, which exchanges only the two 5-hydrogens for deuterium in basic heavy water, is reduced by $LiAlH_4$ to a 2:1 mixture of 4-*endo*-protoadamantanol (IIa), m.p. 214—216°, and its 4-*exo*-isomer (IIIa) m.p. 204—206°. These alcohols can be separated by column chromatography on silica gel (benzene + 2% ether). The less polar 4-*exo*-protoadamantanol (IIIa) proves to be identical with the alcohol obtained from 2-adamantyl derivatives by rearrangement.[2,3] A bridged ion (IV; R = H) may be involved in this process, but it would be expected to be highly unsymmetrical.[7] The stereochemical assignments of (IIa) and (IIIa), consistent with their chemical behaviour, were confirmed by analysis of their n.m.r. spectra. The C*H*OH proton of (IIa), but not of (IIIa), shows a large coupling constant to one of the hydrogens at C-5, a feature expected from examination of Dreiding models.



As would be expected, it is often easy to convert the strained protoadamantyl system back into adamantyl products. Protoadamantane[2,4] very readily gives adamantane with $AlBr_3$ in CS_2 at 25°; no intermediates are detectable by g.l.c. In concentrated sulphuric acid at 125°, 4-protoadamantanone (I) rearranges to adamantanone in 27% yield. This protoadamantyl → adamantyl skeletal rearrangement is especially easy for 4-*exo*-protoadamantyl derivatives [(III) *etc.*] which have the favourable anti-periplanar relationship between the leaving group and the C-2–C-3 bond. In aqueous sulphuric acid, (IIIa) is converted to 2-adamantanol (Va) much more rapidly than is the *endo*-isomer (IIa). While (IIa) can easily be converted into its tosylate by the usual pyridine method, (IIIa) gives only rearranged product (Vb) under these conditions. We have not yet been able to prepare (IIIb) by any method. A rough relative reactivity estimate (60% acetone, 25°) using (Vb), (IIb), and the 3,5-dinitrobenzoate of (III) gave, respectively, $1:22{\cdot}5:3{\cdot}6 \times 10^5$ (corrected for the use of different leaving groups).

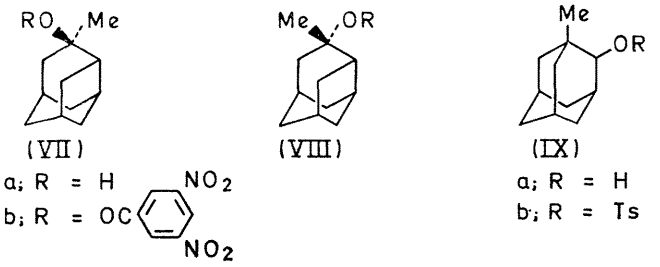
In the 4-*endo*-protoadamantyl derivatives (II), the C-3–C-8 bond bears the anti-periplanar relationship to the leaving group. Migration of this bond leads to a degenerate rearrangement which we have been able to demonstrate by deuterium labelling experiments. Solvolysis of 4-*endo*-[4-^{2}H]protoadamantyl tosylate (IIc) in 60% acetone for 6 half-lives gave a 1:4 mixture of 4-*endo*-protoadamantanol ([^{2}H] IIa) and 2-adamantanol ([^{2}H] Va); integration of the C*H*OH signal *in both products* indicated just 0·5 *proton* to be present (within experimental error). Migration of the C-3–C-8 and the resultant deuterium scrambling are rapid and precede "leakage" from the possible bridged ion intermediate (VI) to (IV; R = H) and the 2-adamantyl products ([^{2}H] Va).



In contrast, solvolysis of 4-*exo*-[4-^{2}H]protoadamantyl 3,5-dinitrobenzoate in 60% acetone yields *unscrambled* products which show C*H*OR n.m.r. integration for 1·0 proton: [1-^{2}H]adamantanol and 2-[1-^{2}H]adamantyl 3,5-dinitrobenzoate, the latter formed by ion-pair return.

Methyl Grignard reagent gives with 4-protoadamantanone (I) a 1:2 mixture of 4-methyl-4-*endo*-protoadamantanol (VIIa) and the *exo*-epimer (VIIIb). Treatment of this mixture in acetone–water solution with a trace of HCl yields the thermodynamically more stable isomer, 1-methyl-2-adamantanol (IXa), almost quantitatively. Compound (VIIIa) was assigned the *exo* configuration because its 3,5-dinitrobenzoate (VIIIb) solvolyses in 60% acetone at 50° ten times faster than (VIIb). In this solvent at 75°, (VIIb), (VIIIb) and 1-methyl-2-adamantyl tosylate (IXb) give essentially the same mixture of products by kinetic control: 60—70% (IXa), 24—33% (VIIIa), and 2—7% olefins; (VIIa) was not detectable. This result, which is to be compared with the formation of only 0·5% 4-*exo*-protoadamantyl products on buffered acetolysis of 2-adamantyl tosylate (Vb),[2,3] suggests that bridged ion (IV) is more important and more nearly symmetrical when R = Me

than when R = H! The methyl group also facilitates "leakage" from the *endo*-series intermediate (VI). In (IV; R = Me) the methyl substituent counterbalances electronically the unfavourable strain introduced by partial bond migration; bridged ion (IV; R = Me) is more stable as the result. In support, it is found that 1-methyl-2-adamantyl tosylate (IXb) solvolyses at 25° in 60% acetone 24 times faster than 2-adamantyl tosylate (Vb).



After submission of this communication, two reports on protoadamantane chemistry have appeared.[8]

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