The 4-Protoadamantyl → 2-Adamantyl Rearrangement; Chirality of the 2-Adamantyl Cation

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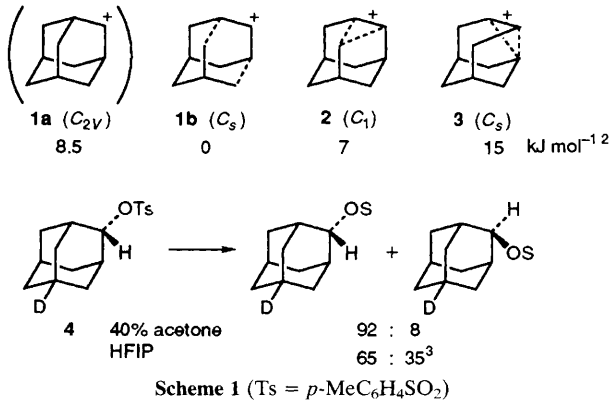
Homochiral *exo*- and *endo*-[4-^{2}H]-4-protoadamantyl substrates have been found to rearrange with the formation of enantiomerically pure [1-^{2}H]-2-adamantanol; the data indicate that bridged and open 2-adamantyl cations interconvert slowly, in contrast to analogous 4-protoadamantyl cations.

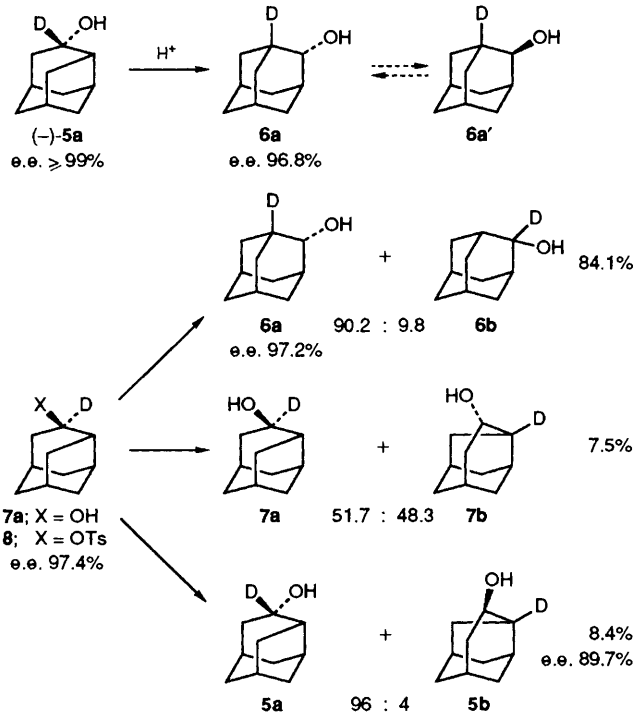
Much experimental and computational effort has been directed to the 4-protoadamantyl → 2-adamantyl rearrangement, an important step in the synthesis of adamantoid hydrocarbons.[1] *Ab initio* studies by Dutler *et al.* place the bridged ions **2** (C_1) and **3** (C_s) 7 and 15 kJ mol^{-1}, respectively, above the open ion **1b** (C_s).[2] The 'classical' structure **1a** (C_{2v}) is found to be a transition state whose distortion toward **1b** can be interpreted in terms of enhanced hyperconjugation (Scheme 1). Predominant, albeit incomplete, retention of configuration in solvolyses of labelled 2-adamantyl sulfonates (*e.g.* **4**) supports the intervention of **1b**, or of mixtures of **1b** and **2**.[3,4] We utilized optically active [4-^{2}H]-4-protoadamantyl substrates to characterize the reactivity of **2** and **3** in solution. In addition to mechanistic insight, we have gained access to homochiral [1-^{2}H]-2-adamantanols (**6a** and **6a'**).†

† The vibrational circular dichroism of these compounds is currently under investigation (T. B. Freedman).

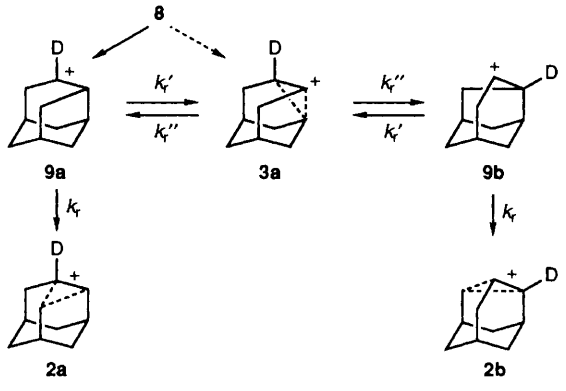
4-Protoadamantanone was reduced with $LiAlD_4$ to give **5a** and **7a**.[5] Each alcohol was resolved by HPLC of the



Scheme 1 (Ts = *p*-$MeC_6H_4SO_2$)



Scheme 2 (e.e. = enantiomeric excess)



Scheme 3

corresponding camphanoate. The configurations of (−)-**5a** and (−)-**7a** were correlated by way of (+)-4-protoadamantanone; the absolute configuration of (−)-**5** is known to be (4*S*).[6] Enantiomeric purities were determined by GC on a cyclodextrin phase.[7] Acid-catalysed rearrangement of **5a** in aqueous-organic solvents (*e.g.* 1.75 mol dm^{-3} $HClO_4$ in 60% dioxane, 60 °C, 2.5 h) afforded **6a** with virtually complete retention of enantiomeric purity, as shown by ^2H NMR in the presence of the chiral shift reagent Eu(hfc)$_3$ (Scheme 2); Eu(hfc)$_3$ = tris(heptafluoropropylhydroxymethylenecamphorato)europium(III). The reaction conditions are thought to minimize stereochemical control by the counter-ion[8] and do not cause significant racemization of **6a** (12.5% racemization of **6a** was observed with 1.75 mol dm^{-3} $HClO_4$ in 60% dioxane, 85 °C, 24 h).

Our data indicate that the conversion of **5a** into **6a** is mediated by the bridged carbocation **2a**. The formation of **2a** from **5a** is likely to proceed with participation of C-2 (k_Δ).[5] In order to see whether anchimeric assistance is essential to stereoselectivity, we turned to *endo*-4-protoadamantyl substrates. Acid-catalysed rearrangement of **7a** was not practical. Rather vigorous conditions were required which led to partial racemization of **6a**. Therefore, we resorted to solvolysis of the tosylate **8** (60% acetone, 2,6-lutidine, 75 °C, 1 h).[5] The enantiomeric purity of **8** was fully retained in the major product **6a**. Scrambling of the deuterium label in *endo*-4-protoadmantanol **7** was nearly complete whereas *exo*-4-protoadamantanol **5** and 2-admantanol **6** were formed with deuterium distributions of 24:1 and 9.2:1, respectively (Scheme 2).

Obviously, **3a** cannot be the (only) ion arising from **8**; anchimeric assistance (k_Δ) makes at best a minor contribution. As the major reaction path, we suggest unassisted ionization of **8** (k_c) with formation of the 4-protoadamantyl cation **9a** whose rearrangement (k_r, k_r') is fast relative to nucleophilic capture (k_{H_2O}) (Scheme 3). While **5b** must originate from **9b**, solvolytic displacement (k_s) at **8** is thought to be the major source of **5a**. The bridged ion **3a**, on the other hand, undergoes rearrangement (k_r'') and substitution (→ **7a**, **b**) at similar rates. The distribution of products indicates that **9a** is only 3.4 ± 1 kJ mol^{-1} above **3a** in energy.‡

In summary, we have shown that the 4-protoadamantyl cation is but marginally stabilized by bridging (**3** *vs.* **9**). Both **3** and **9** rearrange to give the chiral 2-adamantyl cation **2**. Interconversion of **2** with the achiral 2-adamantyl cation **1** does not occur in solvolyses of 4-protoadamantyl substrates.§. The astounding kinetic stability of **2** is not anticipated by current theory.[2]

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‡ In terms of Scheme 3, the product ratio **6a**/(**6b** + **7a** + **7b** + **5b**) = 4.74 equals k_r/k_r'. For **3a**, k_r''/k_{H_2O} is given by (**5b** + **6b**)/(**7a** + **7b**) = 1.13. The ratio **6b**/**5b** = 25 provides an upper limit for k_r/k_{H_2O}, disregarding *endo* substitution of **9b**. As the lower limit we take k_r/k_{H_2O} = 12.5, assuming equal amounts of *exo*- and *endo*-substitution. Provided that k_{H_2O} for **3** and **9** is the same (diffusion control), we get k_r/k_r'' = 11–22, k_r'/k_r'' = K = 2.3–4.6, and ΔG (**9**)–ΔG (**3**) = 2.4–4.4 kJ mol^{-1} (at 348 K).

§ It appears that **1** and **2** are formed competitively (k_c, k_Δ) in solvolyses of 2-adamantyl substrates (*e.g.* **4**).