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SYNTHESES OF 1,2-DISUBSTITUTED ADAMANTANES[1]

Ashraf N. Abdel-Sayed and Ludwig Bauer*
Department of Medicinal Chemistry
University of Illinois at Chicago
P.O. Box 6998, Chicago, Illinois, 60680, U.S.A.

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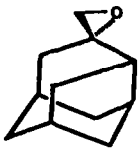
Abstract: Electrophilically-catalyzed reactions of 4-exo- and 4-endo-epoxymethyleneprotoadamantane (1) and of 4-protoadamantanone (2) provided a variety of 1,2-disubstituted adamantanes. Reactions of 1 with Lewis acids such as aluminum chloride, bromide and iodide at -78 °C afforded 2-chloro-, 2-bromo-, and 2-iodo-1-(hydroxymethyl)adamantanes in excellent yields. An interesting fluoride ion transfer took place when 1 was reacted with boron trifluoride to form 2-fluoro-1-(hydroxymethyl)adamantane. The reaction of 1 with benzene in the presence of aluminum bromide produced 1-(hydroxymethyl)-2-phenyladamantane in 70% yield. From the acid-catalyzed addition and rearrangement of 2 with hydrohalic acids there were obtained excellent yields of 2-halo-1-adamantanols and 1,2-dihaloadamantanes. 2-Halo-1-adamantanols served as starting materials for the synthesis of twelve additional 1,2-dihaloadamantanes. The boron trifluoride catalyzed reaction of 2 with acetic anhydride furnished 1,2-diacetoxyadamantane in 84% yield. Mechanisms for these various reactions are discussed.

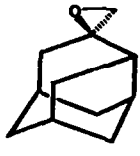
In contrast to many facile substitutions at bridgehead carbons of adamantanes, direct substitutions on bridge carbons seldom take place. To synthesize 1,2-disubstituted adamantanes, circuitous routes needed to be invented. Syntheses of 1,2-disubstituted adamantanes relied on some free radical reactions,[2-5] or cyclizations of suitable bicyclic precursors.[6-10] Later, protoadamantane-adamantane rearrangements proved to be very useful in the synthesis of 1,2-disubstituted adamantanes.[11-22] This paper reports new and versatile syntheses of a number of 1,2-disubstituted adamantanes (Table I) from epoxides 1 and from 4-protoadamantanone (2).

Syntheses and stereochemistry of epoxides 1

Syntheses of 1 are readily accomplished by reacting 4-protoadamantanone (2) with either dimethylsulfonium or dimethyloxosulfonium methylide.[17,18] Chakrabarti and coworkers,[17] using the sulfonium ylide, obtained a mixture of the exo and endo isomer in the ratio of 3:2. Upon repeating Farcasiu's experiment[18] using dimethyloxosulfonium methylide, we found that the product consisted almost exclusively of the exo isomer of 1 (exo:endo being 15:1). The ratio of the exo and endo isomer of 1 was determined by capillary column gas chromatography/mass spectrometry (GC/MS) which clearly showed two peaks but with identical mass spectra. The structures of these isomers were established through the chemical shifts of their oxirane methylene protons in the 360 MHz ^{1}H NMR spectrum.[17]

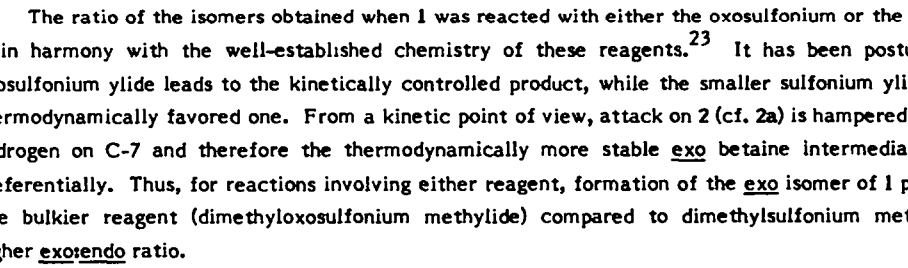


1, exo



1, endo

The ratio of the isomers obtained when 1 was reacted with either the oxosulfonium or the sulfonium ylide is in harmony with the well-established chemistry of these reagents.[23] It has been postulated that the oxosulfonium ylide leads to the kinetically controlled product, while the smaller sulfonium ylide provides the thermodynamically favored one. From a kinetic point of view, attack on 2 (cf. 2a) is hampered by the flagpole hydrogen on C-7 and therefore the thermodynamically more stable exo betaine intermediate 3 is formed preferentially. Thus, for reactions involving either reagent, formation of the exo isomer of 1 predominates.[26] The bulkier reagent (dimethyloxosulfonium methylide) compared to dimethylsulfonium methylide, gave a higher exo:endo ratio.



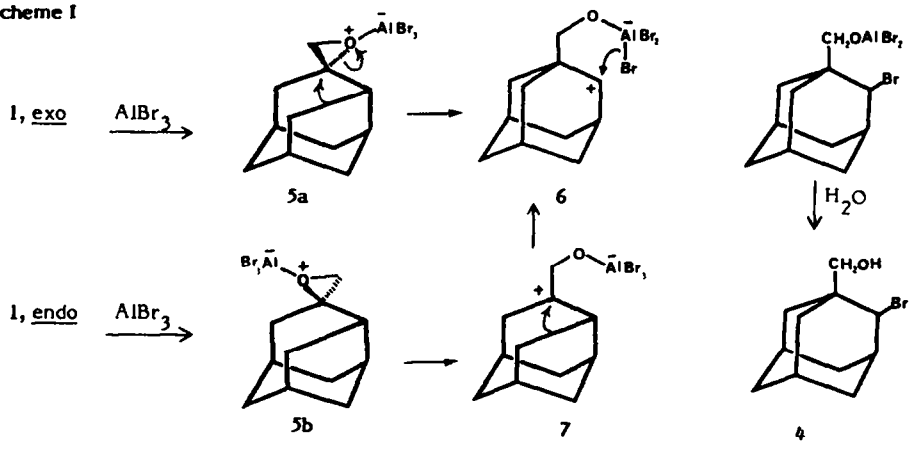
2 2a 3 1, exo isomer

Electrophilically-catalyzed ring openings and rearrangements of 1

We describe highly efficient methods of rearranging 1 to a number of 1-(hydroxymethyl) 2-substituted adamantanes by Lewis acids under extremely mild conditions. Under electrophilic catalysis, both isomers of 1 ring open with concomitant rearrangement to the more stable adamantane skeleton.[17,18] The overall reaction represents an important approach to the synthesis of a variety of 2-substituted 1-(hydroxymethyl)adamantanes. Chakrabarti[17] reacted 1 with 40% hydrogen bromide in acetic acid to obtain 2-bromo-1-(hydroxymethyl)adamantane (4) in 30% yield. Upon reexamining this reaction, it became apparent that 4 was just one component in a complex mixture of products (GC/MS).

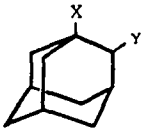
A greatly improved method consisted of treating 1 with aluminum bromide in dichloromethane at -78 °C to furnish 4 in 82% yield. The mechanism for such a transformation would commence with the coordination of the Lewis acid with 1. Ring opening of the oxonium ion of the exo isomer of 1 and subsequent rearrangement to the 2-adamantyl cation (6) can occur in a concerted manner (cf. 5a) since the migrating C-C bond is antiperiplanar to the leaving group. This σ-participation is characteristic for reactions of 4-exo-protoadamantyl derivatives.[14,19,24,27,28] The intermediate 6 is structurally perfect for nucleophilic attack at C-2 by one of the bromines via a 6-membered cyclic transition state to form 4 (**Scheme I**).

Scheme I



The corresponding endo oxonium cation, 5b, can cleave to provide the 4-protoadamantyl carbonium ion (7) which readily rearranges to the more stable 2-adamantyl cation (6), the precursor for 4.

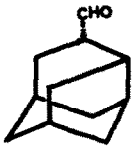
Table I. 1,2-Disubstituted Adamantanes Synthesized from 1 and 2



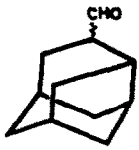
Compd	X	Y	Compd	X	Y	Compd	X	Y
4	CH_2OH	Br	19	AcO	AcO	29	F	Br
8	CH_2OH	Cl	20	AcO	AcO	30	F	I
10	CH_2OH	I	21	OH	Cl	31	Cl	Br
11	CH_2OH	F	22	Cl	Cl	32	Cl	I
12	CH_2OH	Ph	23	OH	Br	33	Br	Cl
13	CO_2H	Cl	24	Br	Br	34	Br	I
14	CO_2H	Br	25	OAc	Br	35	OAc	Cl
15	CO_2H	I	26	OH	I	36	OAc	I
16	CO_2H	Ph	27	I	I	37	I	Cl
17	CO_2H	F	28	F	Cl	38	I	Br

where Ac = $COCH_3$

In view of the success of the reaction of 1 with aluminum bromide, reactions with other Lewis acids were investigated. The reaction of 1 with aluminum chloride, zinc chloride or ferric chloride in various solvents (e.g., dichloromethane, ether, carbon disulfide, hexane) provided the chloro alcohol, 8. The best yield (84%) was realized when the reaction was conducted in dichloromethane using aluminum chloride. With the other two Lewis acids, a significant amount of aldehydes 9 was also produced. The rearrangement of 1 to 9 by Lewis acids has been reported.[17] In similar reactions of 1 with either AlI_3 or SnI_4, the iodo alcohol 10 was obtained. Aluminum iodide in carbon disulfide gave the best yield of 10 (79%) without detectable amounts of 9.



9, exo



9, endo

We explored the synthesis of the 2-fluoro derivative by a similar reaction. The epoxides 1 had been reported to rearrange to 9 after being treated with boron trifluoride in benzene (2 min, 25 °C).[17] In spite of the low nucleophilicity of fluoride ion, interestingly enough, we obtained the fluoro alcohol (11), when 1 was reacted with boron trifluoride in dichloromethane at -78 °C. Such a fluoride ion transfer during reactions of epoxides with boron trifluoride had only been reported recently.[29]

Friedel-Crafts reaction of 1

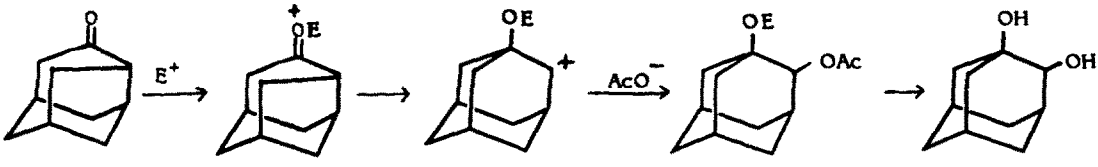
We were interested in utilizing 1 directly in the synthesis of 1-(hydroxymethyl)-2-aryladamantanes. However, a Friedel-Craft reaction of 1 with benzene in the presence of one equivalent of aluminum bromide yielded only the bromo alcohol 4. This was not surprising since intramolecular attack by bromide ion would be expected to be faster than attack by the less nucleophilic benzene at the carbocationic center of 6. In the presence of more than one equivalent of the Lewis acid, the intermediate bromo alcohol 4 underwent a Friedel-Crafts reaction to produce 12. This reaction constitutes a convenient one-pot synthesis of 12 from 1. The alcohol 12 could also be obtained by an independent Friedel-Crafts reactions of either 4 or 8 with benzene. When the chloro alcohol 8 was reacted with benzene in the presence of aluminum bromide, it was found that halogen exchange first took place on 8 to form 4 (GC/MS) and subsequently 4 was converted to 12 by a Friedel-Crafts reaction.

2-Substituted 1-adamantanecarboxylic acids

Syntheses of a number of 2-substituted 1-adamantanecarboxylic acids via rather lengthy routes from 4-homoadamantanone have been reported.[7,8] Having synthesized a number of 2-substituted 1-(hydroxymethyl)-adamantanes in 2 steps from 4-protoadamantanone, the corresponding acids became readily available by oxidation. 2-Chloro- (13), 2-bromo- (14), 2-iodo- (15), 2-phenyl- (16), and the hitherto unknown, 2-fluoro-1-adamantanecarboxylic acid (17) were prepared by this method.

Electrophilic additions involving the rearrangement of 4-protoadamantanone (2)

A number of 1,2-disubstituted adamantanes were synthesized by the electrophilically-catalyzed addition-rearrangements of 4-protoadamantanone (2). For example, the boron-trifluoride catalyzed addition of acetic anhydride to 2 afforded the diacetate (19) in 84% yield. Electrophilic species in the medium (e.g. BF_3 or CH_3CO^+) designated by E^+, can generate the oxonium ion, 18. Rearrangement of 18 to the 2-adamantyl cation (18a) and subsequent neutralization leads to 18b. The 1-acetoxy group would be in place in the final product if CH_3CO^+ is the initiating electrophile, E^+. Alternatively, acetylation of 18b as a last step would produce 19.

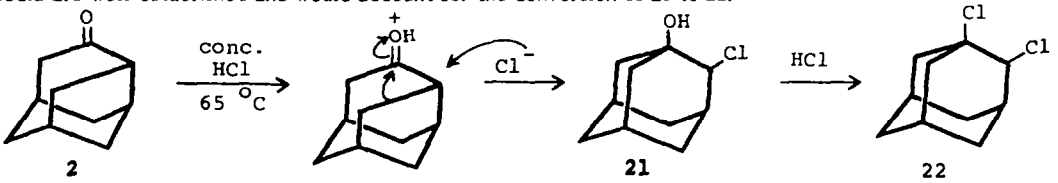


2 18 18a 18b, E = H 19, E = Ac 20

Transesterification of 19 in methanol containing potassium carbonate gave 1,2-adamantanediol (20). The diol (20) could not be obtained by direct hydration of 4-protoadamantanone (2) in aqueous acids (e.g., 50%

sulfuric acid, reflux, 2 days). The starting material was recovered quantitatively. This is not surprising since the diol (**20**) is known to rearrange to 4-protoadamantanone (**2**) upon exposure to acids.[24]

The reaction of 4-protoadamantanone (**2**) with concentrated hydrochloric acid at 65 °C afforded a mixture of 2-chloro-1-adamantanol (**21**) and 1,2-dichloroadamantane (**22**). The reaction was accelerated by the addition of anhydrous zinc chloride. The protonated ketone **18** (E = H) rearranges and picks up chloride ion to furnish **21**. 1,2-Dichloroadamantane (**22**) was formed apparently from 2-chloro-1-adamantanol (**21**) since longer reaction times converted **2** completely to **22**. Displacements of alcohols at bridgehead carbons in electrophilic media are well-established and would account for the conversion of **21** to **22**.[30a]



2 **21** **22**

A cognate reaction of 4-protoadamantanone (**2**) with 48% hydrobromic acid gave a mixture of 2-bromo-1-adamantanol (**23**) and 1,2-dibromoadamantane (**24**). When 48% hydrobromic acid was replaced by 30% hydrogen bromide in acetic acid there was also obtained 2-bromo-1-adamantyl acetate (**25**) in addition to **23** and **24**. Presumably, in the presence of a large excess of acetic acid, the bromo alcohol **23** was acetylated to give **25**. 2-Iodo-1-adamantanol (**26**) and 1,2-diiodoadamantane (**27**) were prepared during the reaction of 4-protoadamantanone (**2**) with hydrogen iodide (generated from potassium iodide and phosphoric acid).

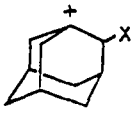
Synthesis of 1,2-dihaloadamantanes

The availability of so many precursors suggested the synthesis of a number of mixed 1,2-dihaloadamantanes in view of their interesting NMR spectral parameters.[40] 2-Chloro-, 2-bromo- and 2-iodo-1-adamantanols (**21**, **23** and **26**) served as starting materials for the preparation of a number of "mixed" 1,2-dihaloadamantanes. Thus, 1-fluoro-2-haloadamantanes (**28**, **29**, and **30**) were isolated in excellent yields by reacting the corresponding alcohols with diethylaminosulfur trifluoride (DAST). Also **23** and **26** were treated with thionyl chloride to form 2-bromo-1-chloro- and 1-chloro-2-iodoadamantanes, **31** and **32**, respectively.

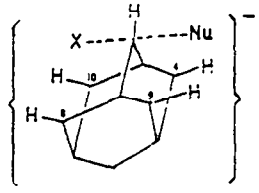
1-Bromo-2-chloro- and 1-bromo-2-iodoadamantanes (**33** and **34**, respectively) were obtained from the corresponding alcohols (**21** and **26**) upon reaction with 30% hydrogen bromide in acetic acid. Acetates **35** and **36** were isolated as by-products. These esters were converted to the starting alcohols by potassium carbonate in methanol. Reaction with 48% hydrobromic acid (instead of 30% hydrogen bromide in acetic acid) required elevated temperatures and surprisingly some substitution took place at C-2 also. For example, 2-chloro-1-adamantanol (**21**) afforded 1-bromo-2-chloroadamantane (**33**) contaminated with approximately 10% of 1,2-dibromoadamantane (**24**). Separation of these products by fractional crystallization, sublimation, or chromatography, proved futile.

The same problem was encountered during attempts to prepare 1-iodo-2-chloro- and 1-iodo-2-bromoadamantanes (**37** and **38**, respectively) from the corresponding alcohols and hydrogen iodide. The desired mixed dihalo products were always contaminated by 1,2-diiodoadamantane (**27**). It is of course of interest to note that the 2-chloro and 2-bromo groups were displaced by iodide ion in this protic medium. Thus, for the preparation of **37** and **38**, alternate approaches were sought.

Reactivities of the two halogens in 1,2-dihaloadamantanes toward nucleophilic displacement are quite different. Nucleophilic displacements at C-1 and C-2 of adamantanes proceed with different mechanisms and have been the subject of many studies.[30] The bridgehead halogen is substituted by an S_N1 mechanism with the formation of the intermediate 2-halo-1-adamantylcarbonium ion (**39**). Such a carbonium ion (**39**) is expected to be destabilized due to the electron-withdrawing effect of the neighboring halo group at C-2.



39



40

Bridgehead halogens in 1,2-dihaloadamantanes tend to be inert towards nucleophilic displacement. Indeed, 1,2-dibromoadamantane failed to undergo either acetolysis (reflux in acetic acid for 7 days), or hydrolysis (aqueous DMSO or DMF at 150 °C for 7 days). But, the other halogen at C-2 can undergo S_N2 displacements, but very slowly. The transition state for such reactions tend to be impeded by the presence of the four axial hydrogens at C-4, C-9, C-8, and C-10 (cf. **40**). Furthermore, the electron-withdrawing effect of the halo groups at C-1 further reduces the reactivity of the 2-halo group. In fact, we prepared 2-chloro-1-iodo- and 2-bromo-1-iodoadamantanes (**37** and **38**, respectively) by the nucleophilic displacement of the iodo group at C-2 in 1,2-diiodoadamantane (**27**) by the reaction with either potassium chloride or potassium bromide in HMPA at 150 °C. No displacement took place at C-1.[31]

Conclusions

We demonstrated the usefulness of protoadamantane-adamantane rearrangements in the synthesis of 1,2-disubstituted adamantanes. Efficient methods for the rearrangement of epoxides **1** were developed and enabled us to synthesize a number of 2-substituted 1-(hydroxymethyl)adamantanes. These alcohols were readily oxidized to the corresponding carboxylic acids. We have investigated also the rearrangements of 4-protoadamantanone to provide 2-substituted 1-adamantanols. Syntheses of twelve 1,2-dihaloadamantanes with different combinations and permutations of fluoro, chloro, bromo, and iodo groups at C-1 and C-2 are also reported.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover apparatus and are uncorrected. Microanalyses were performed by Microtech Laboratories, Skokie, Illinois. ^1H and ^{13}C NMR spectra were recorded on a Nicolet NIC-360 NB spectrometer operating at 361.1 MHz for ^1H and 90.8 MHz for ^{13}C. Chemical shifts are reported in parts per million (δ) downfield from internal $(CH_3)_4Si$. Mass spectra and GC/MS analyses were performed on a Varian MAT 112S or on a Finnigan MAT 4510 spectrometer using either DB-1 30 m x 0.32 mm i.d. or a DB-5 30 m x 0.25 mm i.d. fused silica capillary columns and He as carrier gas. In general, the reported ions are those with m/z above 40 and with relative intensities greater than 5% of the base peak, unless otherwise deemed important.

Gas chromatographic (GC) analyses were carried out on a Varian Aerograph 2740 instrument using 3% SE-30 on 100/120 mesh Veraport in a 30 5 ft. x 1/8 in. column with temperature programming from 150 to 250 °C at a rate of 10 °C/min. The majority of the reactions reported here were monitored periodically by GC analysis. Flash chromatography[32] used silica gel 40 μm particle size (J.T. Baker).

All solvents and reagents were used as purchased, unless otherwise specified. Dimethyl sulfoxide was dried by vacuum distillation (∿1 Torr) from CaH_2 at temperatures not exceeding 90 °C. Benzene was dried azeotropically. "Petroleum ether" refers to that fraction bp 30-60 °C. "Brine" refers to a saturated aqueous salt solution. The statement that solvents were removed "in vacuo" implies that a rotary flash evaporator was utilized, usually connected to a water pump (∿20-30 Torr). Distillation of the last traces of solvents sometimes required high-vacuum (< 1 Torr).

4-Exo- and 4-endo-epoxymethyleneprotoadamantane (1)

Method A: The reaction between 4-protoadamantanone (**2**)[33,34] and trimethylsulfonium iodide was carried out as described by Chakrabarti et al.[17] except that NaH was used instead of t-BuOK. The product was a waxy solid (94%); mp 60-64 °C, (lit.[17] mp 62-64 °C); GC/MS (DB-1 column, isothermal, 110 °C) indicated the presence of the two epimers (exo:endo ratio, 3:2), R_t, 5.16 and 5.53 min. Both isomers showed this MS: m/z (rel intensity) 164 (14, M^+), 135 (11), 134 (45), 122 (14), 121 (15), 119 (10), 105 (11), 93 (32), 92 (100), 91 (49), 79 (46), 78 (18), 77 (33), 67 (16), 65 (13); ^1H NMR ($CDCl_3$) δ 2.72 (narrow AB q approaching a singlet, CH_2O, endo isomer), 2.65, and 2.51 (AB q, J = 4.65 Hz, CH_2O, exo isomer), 1.4-2.4 (a series of complex multiplets, 14 H); ^{13}C NMR ($CDCl_3$) of the exo isomer: δ 60.51 (C-4), 50.93 (CH_2O), 42.65 (C-3), 41.54 (C-9), 39.21 (C-10), 38.37 (C-5), 36.01 (C-1), 35.63 (C-2), 34.35 (C-8), 33.20 (C-7), 28.21 (C-6); of the endo isomer: δ 60.44 (C-4), 57.62 (CH_2O), 43.02 (C-3), 41.54 (C-9), 39.46 (C-10), 36.86 (C-5), 35.78 (C-1), 35.56 (C-2), 35.37 (C-8), 33.43 (C-7), 29.40 (C-6). Assignments of ^{13}C signals were accomplished by means of 2-D INADEQUATE experiments.[35-37]

These epoxides (**1**) were not very stable at room temperature and tended to rearrange to 4-(endo- and exo)protoadamantanecarbaldehyde[17] which were detected by the appearance of two ^1H NMR signals at 9.77

and 9.86 ppm (s, CHO, exo and endo in $CDCl_3$). The epoxides (1) are very sensitive to acids. It was advantageous to remove traces of HCl in $CDCl_3$ by storing this solvent over anhydrous K_2CO_3.

Method B: The same procedure was followed as described in **Method A** but trimethyloxosulfonium iodide[18] was used instead of trimethylsulfonium iodide. The epoxides were obtained in 92% yield; GC/MS and 360 MHz ^1H NMR indicated that the exo isomer was formed predominantly (exo:endo ratio, 15:1).

The mixture of epoxides (1) prepared by method B was used in all subsequent reactions of 1.

2-Halo-1-(hydroxymethyl)adamantanes. General procedure

A solution of the epoxides (1) (32.3 mmol) in the specified solvent (5 mL) was injected gradually through a rubber septum into a stirred solution of the Lewis acid (32.3 mmol) in the same solvent (250 mL) at -78 °C (under N_2). The mixture was stirred at -78 °C (4 h), was allowed to warm gradually to room temperature (1 h) and was then poured carefully into ice-water (100 mL). The aqueous layer was extracted with dichloromethane (2 x 100 mL) and the combined organic phases were washed with water, then brine, dried ($MgSO_4$), and evaporated, in vacuo. Flash chromatography of the residue using stepwise elution with 10-20% ether in petroleum ether, followed by recrystallization from hexane furnished pure halo alcohols.

2-Chloro-1-(hydroxymethyl)adamantane (8): was obtained in 84% yield from 1 and $AlCl_3$ in dichloromethane; mp (hexane) 153-154 °C; GC, R_t = 2.4 min; ^1H NMR ($CDCl_3$) δ 4.38 (m, 1H, H-2), 3.58 and 3.19 (dd, 2H, J_{gem} = 11.2 Hz, CH_2O), 1.61 (s, 1H, OH), 2.20-2.13 (m, 2H), 1.96-1.93 (m, 2H), 1.22 (m, 1H), 1.89-1.57 (a series of complex multiplets, 8H); MS, m/z (rel intensity) 184 (9), 182 (27, M^+-H_2O), 171 (31), 169 (100, M^+-CH_2OH), 164 (72, M^+-Cl), 135 (13), 133 (56), 105 (26), 93 (19), 91 (65), 79 (48), 77 (27), 67 (24), 65 (13). Anal. Calcd for $C_{11}H_{17}ClO$: C, 65.83; H, 8.54; Cl, 17.66. Found: C, 66.14; H, 8.65; Cl. 17.38.

2-Bromo-1-(hydroxymethyl)adamantane (4): was produced (82%) by reacting 1 with $AlBr_3$ in dichloromethane; mp (hexane) 136-137 °C; lit.[17] mp 138 °C; GC, R_t = 3.1 min; ^1H NMR ($CDCl_3$) δ 4.65 (m, 1H, H-2), 3.51 and 3.18 (dd, 2H, J_{gem} = 11.1 Hz, CH_2O), 1.93 (s, 1H, OH), 2.29-2.26 (m, 2H), 1.28 (m, 1H), 2.01-1.63 (a series of complex multiplets, 10H); MS, m/z (rel intensity) 246 (0.4) and 244 (0.4, M^+), 215 and 213 (2, M^+-CH_2OH), 166 (13), 165 (100, M^+-Br), 147 (63), 133 (19), 119 (32), 105 (34), 93 (17), 91 (67), 79 (39), 77 (21), 67 (26).

2-Iodo-1-(hydroxymethyl)adamantane (10): A solution of AlI_3 in carbon disulfide was allowed to react with 1 as described in the "General procedure". In the workup, however, the organic extract was washed with 5% $NaHSO_3$ solution before the final wash with brine. The iodo alcohol (10) was obtained in 79% yield; mp (hexane) 102-103 °C; GC, R_t = 3.7 min; ^1H NMR ($CDCl_3$) δ 4.88 (m, 1H, H-2), 3.35 and 3.20 (dd, 2H, J_{gem} = 11.2 Hz, CH_2O), 1.95 (s, 1H, OH), 2.36 (m, 2H), 1.33 (m, 1H), 2.05-1.71 (a series of complex multiplets, 10H); MS, m/z (rel intensity) 261 (0.7, M^+-CH_2OH), 165 (100, M^+-I), 147 (73), 119 (57), 105 (53), 95 (14), 93 (39), 92 (27), 91 (99), 81 (36), 79 (79), 77 (37), 67 (57). Anal. Calcd for $C_{11}H_{17}IO$: C, 45.22; H, 5.86; I, 43.44. Found: C, 44.92; H, 5.86; I, 43.75.

1-Hydroxymethyl-2-fluoroadamantane (11): The epoxides (1, 600 mg, 3.6 mmol) were reacted with BF_3 etherate (0.49 mL, 3.96 mmol) in dichloromethane (30 mL), as described in the "General procedure". The products were separated by flash chromatography. The first fractions were eluted by 5% ether in petroleum ether and contained a waxy solid (206 mg) identified by ^1H NMR as a mixture of exo and endo 4-protoadamantanecarboxaldehyde[17]. Further elution with 10-20% ether in petroleum ether afforded the fluoro alcohol (11) (260 mg, 40%); mp (hexane) 150-151 °C; ^1H NMR ($CDCl_3$) δ 4.66 (m, H-2, 1H, J_{FH} = 51.4 Hz), 3.50 and 3.28 (dd, 2H, CH_2O, J_{gem} = 11.0 Hz), 2.22 (s, 1H, OH), 2.18 (m, 1H), 2.01-1.85 (m, 5H), 1.75-1.53 (m, 6H), 1.31 (m, 1H); MS, m/z (rel intensity) 184 (1, M^+), 166 (13, M^+-H_2O), 164 (30, M^+-HF), 154 (15), 153 (100, M^+-CH_2OH), 133 (17), 111 (11), 93 (12), 91 (17), 79 (26), 67 (12). Anal. Calcd for $C_{11}H_{17}FO$: C, 71.71; H, 9.29; F, 10.31. Found: C, 71.36; H, 9.37; F, 9.73.

1-(Hydroxymethyl)-2-phenyladamantane (12)

Method A: A solution of 1 (2.0 g, 12.2 mmol) in carbon disulfide (10 mL) was injected into a solution of $AlBr_3$ (6.53 g, 24.4 mmol) in the same solvent (100 mL), cooled to -78 °C (N_2). The mixture was stirred at -78 °C for 4 h and was then allowed to warm to 0 °C for 1 h. Dry benzene (10 mL) was added and stirring continued at 0 °C for 3 h. The reaction was monitored by GC and was quenched as soon as it was complete. Unnecessarily long reaction times should be avoided as these may lead to intractable mixtures. The reaction mixture was poured into ice-water (200 mL) and was extracted with $CHCl_3$ (3 x 150 mL). The organic phase was washed with water, then with brine, dried ($MgSO_4$) and solvents were evaporated, in vacuo. Flash chromatography of the residue using 5-10% ethyl acetate in petroleum ether as an eluent produced 12 initially

an oil which slowly solidified to a waxy solid (1.9 g, 70%); mp 60-63 °C; GC, R_t = 6.0 min; ^{1}H NMR ($CDCl_3$) δ 7.18-7.45 (m, 5H, Ph), 3.18 and 3.06 (AB q, 2H, CH_2O, J_{AB} = 11.1 Hz), 2.94 (m, 1H, H-2), 2.20-2.09 (m, 5H), 1.93-1.85 (m, 4H), 1.80-1.76 (m, 2H), 1.61-1.59 (m, 2H), 1.42 (m, 1H); MS, m/z (rel intensity) 242 (16, M^+), 224 (36, M^+-H_2O), 211 (100, M^+-CH_2OH), 129 (30), 117 (20), 115 (14), 91 (94), 79 (35), 67 (18). Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.01; H, 9.26.

Method B: To a cooled (10 °C) solution of either **4** or **8** (7.35 mmol) in dry benzene (150 mL) was added $AlBr_3$ (2.53 g, 9.51 mmol). The mixture was stirred for 2-4 h at 10 °C and was monitored by GC. The workup procedure was as described above. The yield of **12** was 1.5-1.7 g (85-94%).

Reactions of 4-protoadamantanone with hydrohalic acids

A. With hydrochloric acid: A mixture of 4-protoadamantanone (7.5 g, 0.05 mol), conc. HCl (200 mL), and $ZnCl_2$ (13.6 g, 0.1 mol) was stirred at 65 °C for 8 h[38]. The mixture was then cooled, diluted with water (400 mL) and extracted with $CHCl_3$ (3 x 200 mL). The extract was washed with a saturated solution of $NaHCO_3$, then with water, dried ($MgSO_4$), and evaporated, in vacuo. Flash chromatography in petroleum ether eluted 1,2-dichloroadamantane (**22**, 2.89 g, 28%); mp 186-187 °C, (lit.[12,13] mp 178-180, 183-185 °C); GC, R_t = 1.7 min.

Further elution with a gradient of ether in petroleum ether (5-50%) afforded 2-chloro-1-adamantanol (**21**, 5.58 g, 60%); mp (hexane) 235-236 °C (sealed tube); GC, R_t = 1.3 min; ^{1}H NMR ($CDCl_3$) δ 4.23 (br s, 1H, H-2), 2.71 (s, 1H, OH), 2.29 (m, 1H), 2.07-2.14 (m, 4H), 1.94 (m, 1H), 1.84-1.75 (m, 3H), 1.67-1.61 (m, 2H), 1.53 (m, 1H), 1.46 (m, 1H); MS, m/z (rel intensity) 188 (8), 186 (25, M^+), 151 (4, M^+-Cl), 129 (5), 128 (5), 109 (3), 95 (100, M^+-Cl-C_4H_9), 79 (16), 77 (10), 67 (9), 53 (10). Anal. Calcd for $C_{10}H_{15}ClO$: C, 64.34; H, 8.09; Cl, 18.99. Found: C, 64.08; H, 8.04; Cl, 18.97.

B. With hydrobromic acid: 4-Protoadamantanone (3.0 g, 0.02 mol), was stirred with 30% HBr in acetic acid (12.4 mL) at 80-90 °C for 18 h[38]. The mixture was cooled, diluted with water (100 mL) and extracted with $CHCl_3$ (3 x 200 mL). The extract was washed with a saturated solution of $NaHCO_3$, then with water, dried ($MgSO_4$), and evaporated, in vacuo. Using flash chromatography, 1,2-dibromoadamantane (**24**, 1.38 g, 23%) was obtained by elution with petroleum ether; mp 123-124 °C, lit.[12] mp 121-123 °C[12]; GC, R_t = 2.8 min.

Further elution with 5% ether in petroleum ether furnished 2-bromo-1-adamantyl acetate (**25**) (1.09 g, 19%) as colorless oil; GC, R_t = 2.6 min; ^{1}H NMR ($CDCl_3$) δ 5.35 (br s, 1H, H-2), 2.68 (m, 1H), 2.36 (br s, 1H), 2.31-2.26 (m, 2H), 2.17 (m, 1H), 2.13-2.10 (m, 2H), 2.00 (s, 3H, CH_3CO), 1.85 (m, 2H), 1.74 (m, 1H), 1.69 (m, 2H), 1.56 (m, 1H); MS, m/z (rel intensity) 274 (3), 272 (3, M^+), 214 (80), 212 (85, M^+-AcOH), 193 (36, M^+-Br), 172, (13), 170 (12), 151 (74), 133 (71), 107 (7), 105 (9), 95 (36), 91 (67), 27 (79), 67 (18), 55 (15), 43 (100), 41 (29). The acetate was hydrolyzed to 2-bromo-1-adamantanol (**23**) by refluxing with 1% solution of K_2CO_3 in methanol.

Continued elution with a 5-30% gradient of ether in petroleum ether produced 2-bromo-1-adamantanol (**23**, 1.38 g, 31%); mp (hexane) 188-189 °C; GC, R_t = 1.6 min; ^{1}H NMR ($CDCl_3$) δ 4.50 (br s, 1H, H-2), 2.48 (s, 1H, OH), 2.38 (m, 1H), 2.20-2.17 (m, 3H), 2.09-2.04 (m, 2H), 1.87-1.79 m, 3H), 1.68-1.64 (m, 2H), 1.55-1.53 (m, 2H); MS, m/z (rel intensity) 232 (1), 230 (1, M^+), 151 (100, M^+-Br), 133 (5), 107 (7), 95 (87, M^+-Br-C_4H_9), 93 (12), 91 (15), 81 (10), 79 (12), 77 (10), 67 (10), 53 (6). Anal. Calcd for $C_{10}H_{15}BrO$: C, 51.96; H, 6.54; Br, 34.57. Found: C, 51.84; H, 6.37; Br, 34.27.

C. With hydriodic acid: A mixture of 4-protoadamantanone (3.0 g, 0.02 mol), KI (6.0 g), 85% H_3PO_4 (75 mL), was stirred at 65-85 °C for 24 h (under N_2).[38] The mixture was cooled, diluted with water (100 mL) and extracted with $CHCl_3$ (3 x 200 mL). The $CHCl_3$ extract was washed with a saturated solution of $NaHSO_3$, $NaHCO_3$ solution, and then water and was dried ($MgSO_4$). 1,2-Diiodoadamantane (**27**, 3.31 g, 43%) was eluted by petroleum ether (flash chromatography), mp 107-108 °C, lit.[16,39] mp 105-108, 106-108 °C; GC, R_t = 4.8 min.

Further elution with a gradient of ether in petroleum ether (5-30%) yielded 2-iodo-1-adamantanol (**26**, 2.58 g, 47%); mp (hexane) 111-112 °C; GC, R_t = 2.4 min; ^{1}H NMR ($CDCl_3$) δ 4.75 (br s, 1H, H-2), 2.40 (m, 1H), 2.31 (s, 1H, OH), 2.24 (m, 1H), 2.16-2.13 (m, 3H), 2.06 (m, 1H), 1.87-1.85 (m, 2H), 1.76 (m, 1H), 1.69-1.56 (m, 4H); MS, m/z (rel intensity) 278 (0.4, M^+), 151 (100, M^+-I), 133 (10), 107 (19), 95 (26, M^+-I-C_4H_9), 93 (18), 91 (43), 81 (31), 79 (25), 67 (27), 55 (24). Anal. Calcd for $C_{10}H_{15}IO$: C, 43.15; H, 5.44; I, 45.63. Found: C, 42.87; H, 5.43; I, 45.79.

1,2-Diacetoxyadamantane (19)

Into a stirred mixture of 4-protoadamantanone (3.0 g, 0.02 mol) and acetic anhydride (65 mL), was injected BF_3 etherate (1 mL) (N_2 atmosphere). Stirring was continued at room temperature for 6 h. The mixture was shaken with ice-water (500 mL) when the diacetate crystallized out. The product was filtered, washed thoroughly with water and dried in a vacuum dessicator over NaOH and $CaCl_2$. Low-temperature recrystallization from petroleum ether furnished the pure product (4.28 g, 84%); mp 83-85 °C, GC, R_t = 3.1 min; ^{1}H NMR ($CDCl_3$) δ 5.41 (m, 1H), 2.30 (m, 2H), 2.21-2.11 (m, 5H), 2.09 (s, 3H, CH_3), 1.94 (m, 1H), 1.93 (s, 3H, CH_3), 1.80-1.73 (m, 2H), 1.67 (m, 2H), 1.47 (m, 1H); MS, m/z (rel intensity) 192 (33, M^+-AcOH), 174 (2), 150 (94), 135 (3), 121 (9), 108 (17), 107 (10), 95 (18), 93 (7), 91 (8), 79 (14), 68 (8), 55 (6), 43 (100, $COCH_3^+$). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.70; H, 7.97.

Upon refluxing 1,2-diacetoxyadamantane with a 1% solution of K_2CO_3 in methanol (0.5 h), there was isolated 1,2-adamantanediol (96%); mp 327-330 °C, lit.[12,13] mp 326-330, 328-330 °C.

2-Substituted 1-adamantanecarboxylic acids. General procedure

To a stirred solution of the corresponding 2-substituted 1-(hydroxymethyl)adamantane (0.543 mmol) in acetone (3 mL), was added 0.5 mL of Jones reagent. (A 50 mL stock solution of this reagent consists of 13.4 g of CrO_3 and 11 mL of concentrated H_2SO_4 in H_2O.) After the mixture was stirred for 2.5 h, methanol (0.5 mL) was added to destroy excess oxidizing agent. The mixture was diluted with water and extracted with $CHCl_3$ (3 x 75 mL). The organic layer was extracted by 10% NaOH solution (2 x 50 mL), then with water (50 mL). The combined aqueous extract was acidified with dilute HCl, and extracted again with $CHCl_3$ (3 x 100 mL). The $CHCl_3$ extract was washed with brine, dried ($MgSO_4$) and evaporated, in vacuo. The residue was recrystallized either from hexane or aqueous ethanol to furnish the pure acids.

2-Fluoro-1-adamantanecarboxylic acid (17): yield, 92%; mp 158-159 °C; ^{1}H NMR ($CDCl_3$) δ 11.27 (br s, 1H, COOH), 4.99 (dd, 1H, H-2, $^2J_{HF}$ = 49.8 Hz, J_{HH} = 3.8 Hz), 2.25-2.22 (m, 2H), 2.01-1.96 (m, 3H), 1.91-1.86 (m, 4H), 1.75-1.71 (m, 3H), 1.54 (m, 1H); mass spectrum, m/z (rel intensity) 198 (3, M^+), 179 (21, M^+-F), 178 (3, M^+-HF), 153 (100, M^+-COOH), 134 (31), 133 (22), 79 (28), 77 (12), 67 (13), 65 (6), 55 (11). Anal. Calcd for $C_{11}H_{15}FO_2$: C, 66.65; H, 7.62; F, 9.58. Found: C, 66.63; H, 7.75; F, 9.14.

2-Chloro-1-adamantanecarboxylic acid (13): yield, 96%; mp 168-169 °C, lit.[7] mp 157-159 °C.

2-Bromo-1-adamantanecarboxylic acid (14): yield, 89%; mp 161-162 °C, lit.[7,17] mp 160, 160-161 °C.

2-Iodo-1-adamantanecarboxylic acid (15): yield, 93%; mp 195-196 °C, lit.[8] mp 195.5-196 °C.

2-Phenyl-1-adamantanecarboxylic acid (16): yield, 86%; mp 166-167 °C, lit.[8] mp 167-168 °C.

2-Substituted 1-fluoroadamantanes. General procedure

To a cooled solution (-78 °C) of $(C_2H_5)_2NSF_3$ (2.2 mmol) in dichloromethane (50 mL), under N_2 atmosphere, was added a solution of the respective 2-substituted 1-adamantanol (2 mmol) in dichloromethane (10 mL). The mixture was allowed to warm gradually to room temperature. After 30 min, water (200 mL) was added and the organic layer was separated. The extract was washed with a saturated solution of $NaHCO_3$, then with brine, dried ($MgSO_4$), and solvents were evaporated, in vacuo. The product was purified by either vacuum sublimation or flash chromatography using 1% ether in petroleum ether as an eluent.

2-Chloro-1-fluoroadamantane (28): yield, 90%; mp 225-226 °C; ^{1}H NMR ($CDCl_3$) δ 4.28 (m, 1H), 2.42 (m, 1H), 2.34 (m, 1H), 2.23 (m, 1H), 2.19-2.15 (m, 2H), 2.07 (m, 1H), 1.91 (m, 1H), 1.84 (m, 1H), 1.74 (m, 1H), 1.68-1.65 (m, 3H), 1.48 (m, 1H); MS, m/z (rel intensity) 190 (3), 188 (9, M^+), 153 (13, M^+-Cl), 152 (100, M^+-HCl), 137 (7), 133 (4), 111 (13), 110 (36), 109 (17), 97 (83), 95 (6), 93 (16), 92 (29), 91 (25), 79 (24), 77 (17), 67 (12), 56 (14), 55 (6). Anal. Calcd for $C_{10}H_{14}ClF$: C, 63.66; H, 7.48; Cl, 18.79; F, 10.07. Found: C, 63.47; H, 7.57; Cl, 18.62; F, 10.11.

2-Bromo-1-fluoroadamantane (29): yield, 93%; mp 175-176 °C; ^{1}H NMR ($CDCl_3$) δ 4.46 (m, 1H), 2.47 (m,1H), 2.41 (m, 1H), 2.25-2.14 (m, 4H), 1.94 (m, 1H), 1.85 (m, 1H), 1.78 (m, 1H), 1.70-1.64 (m, 3H), 1.53 (m, 1H); MS, m/z (rel intensity) 234 (3), 232 (3, M^+), 153 (100, M^+-Br), 133 (11), 111 (5), 109 (4), 97 (11), 91 (16), 79 (7), 77 (5), 67 (10), 55 (4). Anal. Calcd for $C_{10}H_{14}BrF$: C, 51.52; H, 6.05; Br, 34.28; F, 8.15. Found: C, 51.63; H, 6.04; Br, 34.33; F, 7.87.

1-Fluoro-2-iodoadamantane (30): yield, 81%; mp 47-49 °C; ^{1}H NMR ($CDCl_3$) δ 4.65 (m, 1H), 2.46-2.44 (m, 2H), 2.30-2.28 (m, 2H), 2.17 (m, 2H), 2.01 (m, 1H), 1.85 (m, 1H), 1.79 (m, 1H), 1.71-1.64 (m, 4H); MS, m/z (rel intensity) 280 (7, M^+), 153 (100, M^+-I), 133 (12), 111 (5), 109 (3), 97 (10), 91 (19), 79 (7), 77 (5), 67 (10), 55 (5). Anal. Calcd for $C_{10}H_{14}FI$: C, 43.20; H, 5.04; I, 45.30; F, 6.78. Found: C, 42.73; H, 5.01; I, 46.12; F, 6.71.

1-Chloro-2-haloadamantanes. General procedure

To a solution of the respective 2-halo-1-adamantanol (1.0 mmol) in $CHCl_3$ (10 mL), was added $SOCl_2$ (0.36 mL). The mixture was stirred at room temperature for 24 h then refluxed for 2 h. The solvents and excess $SOCl_2$ were evaporated, in vacuo. The crude product was subjected to flash chromatography using petroleum ether as an eluent to give the pure product.

2-Bromo-1-chloroadamantane (31): yield, 64%; mp 155-156 °C; ^{1}H NMR ($CDCl_3$) δ 4.59 (m, 1H), 2.36 (m, 1H), 2.45-2.43 (m, 2H), 2.33 (m, 1H), 2.45 (m, 1H), 2.15 (m, 1H), 2.09 (m, 1H), 1.92-1.87 (m, 3H), 1.71 (m, 2H), 1.56 (m, 1H); MS, m/z (rel intensity) 252 (0.5), 250 (3.4), 248 (2.9) (M^+), 215 (3), 213 (3), (M^+-Cl), 171 (30), 169 (100), (M^+-Br), 133 (77), 115 (5), 113 (7), 105 (21), 93 (12), 91 (87), 79 (28), 77 (30), 67 (19), 65 (20), 55 (14). Anal. Calcd for $C_{10}H_{14}BrCl$: C, 48.12; H, 5.65; Br, 32.02; Cl, 14.21. Found: C, 47.90; H, 5.63; Br, 31.84; Cl, 14.11.

1-Chloro-2-iodoadamantane (32): yield 69%, mp 69-70 °C; GC, R_t = 2.9 min; ^{1}H NMR ($CDCl_3$) δ 4.86 (m, 1H), 2.61-2.55 (m, 2H), 2.46 (m, 1H), 2.40 (m, 1H), 2.30 (m, 1H), 2.20 (m, 1H), 2.07 (m, 1H), 1.96-1.92 (m, 2H), 1.81 (m, 1H), 1.73 (m, 2H), 1.65 (m, 1H); MS, m/z (rel intensity) 298 (1), 296 (3, M^+), 261 (2, M^+-Cl), 171 (26), 169 (83, M^+-I), 133 (89), 127 (6), 115 (6), 113 (8), 105 (27), 93 (15), 91 (100), 81 (10), 79 (31), 77 (34), 67 (24), 65 (19), 55 (17). Anal. Calcd for $C_{10}H_{14}ClI$: C, 40.50; H, 4.72; Cl, 11.95; I, 42.79. Found: C, 40.27; H, 4.66; Cl, 11.31; I, 43.33.

Reaction of 2-halo-1-adamantanols with HBr. General procedure

The respective 2-halo-1-adamantanol (3.0 mmol) was stirred with 30% HBr in acetic acid (20 mL) at room temperature for 4 h. The mixture was poured into ice-water (100 mL) and extracted with $CHCl_3$ (3 x 200 mL). The $CHCl_3$ extract was washed with saturated solution of $NaHCO_3$, then with brine, dried ($MgSO_4$), and solvents were evaporated, in vacuo. Flash chromatography of the residue separated pure products.

1-Bromo-2-chloroadamantane (33) and 2-chloro-1-adamantyl acetate (35) were obtained from 2-chloro-1-adamantanol (21), as described above. Using petroleum ether as an eluent, 1-bromo-2-chloroadamantane (33), (448 mg, 60%) was obtained (60%); mp 152-153 °C; GC, R_t = 2.6 min; ^{1}H NMR ($CDCl_3$) δ 4.46 (m, 1H, H-2), 2.78 (m, 1H), 2.59 (m, 1H), 2.41-2.37 (m, 2H), 2.29 (m, 1H), 2.11 (m, 1H), 2.06-2.04 (m, 2H), 1.94 (m, 1H), 1.84 (m, 1H), 1.76-1.74 (m, 2H), 1.56 (m, 1H); MS, m/z (rel intensity) 172 (3), 170 (10, M^+-Br), 171 (34), 169 (100, M^+-HBr), 133 (52), 105 (24), 93 (10), 91 (51), 79 (30), 77 (20), 67 (13), 65 (14), 55 (13). Anal. Calcd for $C_{10}H_{14}BrCl$: C, 48.12; H, 5.65; Br, 32.02; Cl, 14.21. Found: C, 48.38; H, 5.72; Br, 31.85; Cl, 14.29.

Further elution with 5% ethyl acetate in petroleum ether furnished 2-chloro-1-adamantyl acetate (35, 205 mg, 29%) as a colorless liquid; GC, R_t = 2.5 min; ^{1}H NMR ($CDCl_3$) δ 5.14 (m, 1H, H-2), 2.60 (m, 1H), 2.29-2.28 (m, 2H), 2.18-2.07 (m, 4H), 2.00 (s, 3H, CH_3), 1.82 (m, 2H), 1.74 (m, 1H), 1.68 (m, 2H), 1.49 (m, 1H); MS, m/z (rel intensity) 228 (1, M^+), 171 (5), 170 (35), 169 (16), 168 (100, M^+-AcOH), 133 (54), 128 (13), 126 (33), 95 (62), 91 (58), 79 (28), 77 (15), 67 (14), 55 (10), 43 (57, CH_3CO^+). Hydrolysis of this acetate regenerated 2-chloro-1-adamantanol.

When 48% HBr was used instead of 30% HBr in acetic acid, the mixture had to be heated to 80 °C to complete the reaction. The desired product, 1-bromo-2-chloroadamantane, was contaminated with about 10% of 1,2-dibromoadamantane. Repeated recrystallizations, sublimations, or chromatography on silica gel failed to yield an analytically-pure product.

1-Bromo-2-iodoadamantane (34) and 2-iodo-1-adamantyl acetate (36) were obtained from the reaction of 2-iodo-1-adamantanol (1.0 g, 3.6 mmol) with HBr, as described above. Flash chromatography of the crude product, using petroleum ether, eluted 1-bromo-2-iodoadamantane (0.83 g, 67%); mp 94-95 °C, lit.[39] mp 91-92 °C; GC, R_t = 3.8 min.

Further elution with 5% ether in petroleum ether yielded 2-iodo-1-adamantyl acetate (264 mg, 22%) as a colorless liquid which slowly crystallized; mp 43-44 °C; GC, R_t = 3.5 min; ^{1}H NMR ($CDCl_3$) δ 5.55 (m, 1H), 2.76 (m, 1H), 2.41 (m, 1H), 2.32-2.30 (m, 2H), 2.21-2.18 (m, 2H), 2.09 (m, 1H), 2.02 (s, 3H, CH_3), 1.94 (m, 1H), 1.83-1.77 (m, 2H), 1.71 (m, 2H), 1.66 (m, 1H); MS, m/z (rel intensity) 320 (0.4, M^+), 261 (1, M^+-AcO), 260 (1, M^+-AcOH), 192 (54, M^+-I), 152 (25), 151 (100), 133 (29), 109 (10), 107 (23), 105 (15), 95 (29), 93 (24), 91 (66), 81 (22), 79 (30), 77 (19), 67 (27), 55 (19), 53 (11), 43 (93, CH_3CO^+). Anal. Calcd for $C_{12}H_{17}IO_2$: C, 45.01; H, 5.35; I, 39.64. Found: C, 45.24; H, 5.39; I, 39.66.

2-Halo-1-iodoadamantanes. General procedure

A mixture of 1,2-diiodoadamantane (300 mg, 0.77 mmol), either dry KBr or KCl (70 mmol) in HMPA (10

mL) was stirred at 140-160 °C for 7 days. The mixture was cooled, diluted with water (100 mL) and extracted with hexane (3 x 75 mL). The extract was washed with brine, dried ($MgSO_4$), and the solvent was evaporated, in vacuo. The crude product was purified by flash chromatography using petroleum ether as the eluting solvent.

2-Chloro-1-iodoadamantane (37): yield, 70%; mp 43-44 °C; GC, R_t = 3.2 min; ^1H NMR ($CDCl_3$) δ 4.59 (m, 1H), 2.98-2.89 (m, 2H), 2.72 (m, 1H), 2.38-2.36 (m, 3H), 2.02 (m, 1H), 1.92-1.80 (m, 5H), 1.65 (m, 1H); MS, m/z (rel intensity) 298 (0.3), 296 (1, M^+), 261 (0.5, M^+-Br), 171 (32), 169 (100, M^+-I), 133 (65), 127 (8), 105 (28), 93 (12), 91 (72), 79 (41), 77 (24), 67 (18), 65 (14), 55 (15), 53 (13). Anal. Calcd for $C_{10}H_{14}ClI$: C, 40.50; H, 4.76; Cl, 11.95; I, 42.79. Found: C, 40.56; H, 4.76; Cl, 11.65; I, 42.87.

2-Bromo-1-iodoadamantane (38): yield, 79%, mp 77-78 °C; GC, R_t = 3.8 min; ^1H NMR ($CDCl_3$) δ 4.81 (m, 1H), 3.03-2.99 (m, 2H), 2.78 (m, 1H), 2.46-2.42 (m, 3H), 2.04 (m, 1H), 1.94-1.88 (m, 3H), 1.84-1.82 (m, 2H), 1.71 (m, 1H); MS, m/z (rel intensity) 342 (1), 340 (1, M^+), 261 (7, M^+-Br), 215 (79), 213 (82), M^+-I), 133 (100), 105 (37), 93 (18), 91 (94), 79 (46), 77 (29), 67 (23), 65 (21), 55 (22), 53 (16). Anal. Calcd for $C_{10}H_{14}BrI$: C, 35.02; H, 4.14; Br, 23.39; I, 37.29. Found: C, 35.08; H, 4.11; Br, 23.39; I, 37.29.

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