Face Selection in the Reduction of p,p'-Disubstituted 5,7-Diphenyl-2-adamantanones and Hydrolysis of the Corresponding 2-Adamantyl Tosylates†

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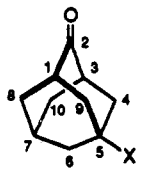
The reduction of 5,7-diphenyl-2-adamantanone with sodium borohydride in 2-propanol is affected by the introduction of a *p*-nitro substituent in one of the rings: the *E*-alcohol is obtained in small but easily measurable excess of 1.30:1. Conversely, the introduction of a *p*-amino group leads to an excess of *Z*-isomer by roughly the same factor (1.28). When both substituents are present, they evidently cooperate to produce a ratio of 1.64. The tosylates of the alcohols were prepared and their solvolysis rates measured in 3% aqueous hexafluoro-2-propanol and compared with those of the parent and *p*-substituted 5-phenyl-2-adamantyl tosylates. Additivity of substituent effects was again observed, but the *p*-aminophenyl group in these reactions was deactivating compared to phenyl, presumably due to H-bonding and/or protonation of the amino group in the acidic medium.

5-Substituted 2-adamantanones **1** and their derivatives have served as probes in studies of the electronic factor involved in face selection in addition and elimination processes.[1] The adamantane skeleton offers the dual advantages of two faces that are sterically virtually identical and of a rigidity that banishes conformational uncertainty. The reactions studied so far have included



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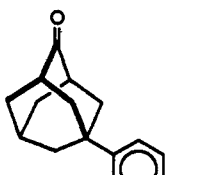

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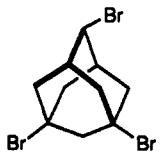

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examples of nucleophilic addition to the carbonyl group, electrophilic addition to related olefins, the capture of carbocations, radicals and carbenes, metal complexation, and a host of pericyclic processes such as thermal cycloadditions, photocycloaddition, and sigmatropic shifts; the 5-substituents have included both electron-donating and -withdrawing groups.[2] We have to date been able to fit all of our data with the general rule that the reagent preferentially attacks that face which places it in a position antiperiplanar to the more electron-rich vicinal bond(s). Similar findings have been reported by Halterman[3] and Mehta.[4] The rationale behind this rule is Winstein's σ participation[5] in the case of cations and Cieplak's transition state hyperconjugation[6] in the addition to double bonds. We have argued[1,7] that these two concepts are basically the same and that they underlie all addition and elimination stereochemistry unencumbered by steric complications. Reservations have been expressed, however, for example, by Houk,[8] Frenking,[9] and Coxon.[10]

The present study was undertaken for two reasons. One of these was that in our original study,[1] we had sought to demonstrate the electronic nature of the remote substituent effect on face selection by modifying the 5-phenyl group with various substituents. This meant that all of reactions the substituted phenyl groups were basically being compared with the hydrogen at C_7 and only indirectly with each other. This circumstance led to an overestimate of the effect, as pointed out by Adcock;[11] the originally reported value of $\Delta\rho$ for the sodium borohydride reduction of 2-adamantanone, −0.39, was revised to −0.245 in a reinvestigation[12] which also hinted at a variable nature of one of the key substituents, namely the amino group. A direct comparison of substituted and unsubstituted phenyl groups would clearly have avoided this problem. The second reason was our longstanding interest in the question how far (i.e., through how many bonds) substituent effects can be transmitted and still be observable. This interest has been whetted by reports of spectroscopic evidence[13] of long-range interactions between remote donor and acceptor groups and of chemical effects such as electron transfer[14] and solvolysis[15] as well. Throughout this paper the substituent positions should be read as in structure **1**. This is done to avoid confusion although the resulting nomenclature is not always correct (thus, 2,5,7-tribromoadamantane (**3**) is really the 1,3,6-isomer, etc.).

Synthesis

For compounds **4**-(X, Y), **3** seemed clearly the ideal starting material since it can be obtained[16] by bromination

† Based in part on the Ph.D. thesis of I. H. Song.

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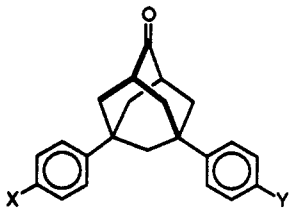
of the easily available tricyclo[5.2.1.$0^{2,6}$]decane, and byproducts 1,2,3,5,6,7-hexabromonaphthalene[17] and 1,5,7-tribromoadamantane[18] are relatively easily removed; after

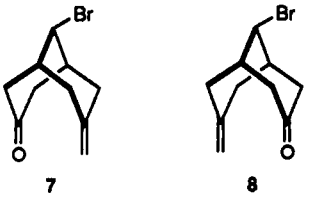


4-(X, Y)

several trials, we were able consistently to get up to 30% of pure **3**. Our hope was that the more labile tertiary bromines should be replaceable by phenyl groups under Friedel–Crafts conditions that would leave the secondary bromine untouched. Conditions were soon found to convert 1-bromoadamantane into 1-phenyladamantane that were too mild for 2-bromoadamantane (BF_3·Et_2O). However, **3** was unreactive under these same conditions, even with a 100-fold excess of the catalyst. The stronger Lewis acid aluminum bromide led to instant conversion into 2,5,7-triphenyladamantane (**5**) even at 5 °C. Stannic chloride led to the slow exchange of one and then both of the tertiary bromines by chlorines, as could readily be demonstrated by means of mass spectra. Stannic and zinc bromide were ineffective as catalysts altogether.

With the easy availability of **5** we conceived of a plan to prepare the benzylic α-hydroperoxide and then to decompose it to 4-$(H)_2$ and phenol; this process is analogous to the commercial production of acetone and phenol from cumene, via its hydroperoxide. The oxidation of **5** with dry oxygen, using AIBN as initiator and chlorobenzene as solvent did indeed succeed in producing a peroxide capable of oxidizing iodide; however, its decomposition with sulfuric acid gave many products but no ketones were among them. Another plan involved the known[16] hydrolysis of **3** in low yield to the corresponding trihydroxy compound, followed by oxidation to 5,7-dihydroxy-2-adamantanone (**6**). We were able to improve the first step to quantitative and obtain **6** in 70% yield overall. However, under conditions that readily convert 5-hydroxy-2-adamantanone into the 5-phenyl ketone (BF_3·OEt_2 in refluxing benzene), **6** did not react. Its low solubility was the problem. Since 5,7-dibromo-2-adamantanone has been reported[19] to be formed from the highly inaccessible 2,2,5,7-tetrabromoadamantane by reaction with silver salts, we tried similar reactions with **3**. Silver trifluoroacetate did not react; silver perchlorate led to Grob fragmentation to give the readily separated enones **7** and **8**.

At this point it seemed clear that the secondary bromine would continue to defeat us, and that an analog of **3** was needed carrying a different group at C_2. Direct 5,7-dibromination of adamantanone does not occur;[20] but the corresponding dibromination of 2-adamantanecarboxylic acid is known.[21] The dibromo acid was readily converted



7 **8**

in 77% yield to the diphenyl analog **9**, which was further transformed into 4-(H, H) as shown in Scheme 1.

In a prelude to synthetic studies leading to the *p*- and *p,p'*-substituted derivatives of 4-$(H)_2$, we briefly restudied the nitration of **2**-H. In our earlier work,[1] we had encountered only **2**-NO_2, but Adcock reported[11] that two unspecified isomers also form, in yields of 8 and 17%. Standard nitration with HNO_3–H_2SO_4 at −30 °C apparently gave only the para isomer; at somewhat higher temperatures, the *o,p*-dinitrophenyl ketone also forms, and at room temperature after 2 h, it is the only product.

When the low-temperature reaction was tried with 4-$(H)_2$, however, only 4-$(NO_2)_2$ was obtained. Since Halterman had succeeded in carrying out the mononitration of 2,2'-diphenylcyclopentanone, we tried to use his procedures[3] to prepare 4-(H, NO_2), but this led to difficult-to-separate mixtures of 4-$(H)_2$, 4-$(NO_2)_2$, and 4-(H, NO_2). Various small modifications led to a way of eliminating the dinitro compound and hence to the formation of a simpler and more readily separable mixture. Catalytic or zinc dust reduction of the mononitro compound, gave 4-(H, NH_2). Selective reduction of the dinitro ketone to give 4-(NH_2, NO_2) proved to be the most difficult. Idoux' method of selectively reducing polynitrated aromatics[22] with ammonium polysulfide failed to affect 4-$(NO_2)_2$ at all. Zinc dust in acetic acid gave only 4-$(NH_2)_2$, even in the early stages of the reaction; we assume that the mono-reduced compound forms a salt in the acidic medium which is rapidly reduced further. After many trials, we eventually succeeded in obtaining small amounts of 4-(NH_2, NO_2) by means of a catalytic reduction procedure (Figure 1).

All three of the unsymmetrical ketones **4** were reduced to mixtures of the epimeric alcohols; these mixtures were either separated and converted into the tosylates, or tosylated first and then separated as discussed further below.

Reductions

We followed our usual approach, namely, first to determine the optimal conditions for the reaction, next, to measure the ratio of isomers in the crude mixture and then to isolate the pure isomers, and finally, to determine their configurations. In all cases, borohydride reduction in 2-propanol proceeds essentially quantitatively. With 4-(H, NO_2), the ^1H NMR spectrum of the product mixture did not show any peaks readily ascribed to the two expected epimers; however, upon carefully controlled addition of a solution of the shift reagent Eu(fod)$_3$, the doublets attributable to the axial methylene protons "underneath" the hydroxy groups were shifted strongly to lower field, out of the multiplet usually observed at about 2 ppm and into the clear region between 5 and 7 ppm. Integration of these baseline-separated doublets gave a product ratio of 1.30. After chromatographic separation of the isomers,

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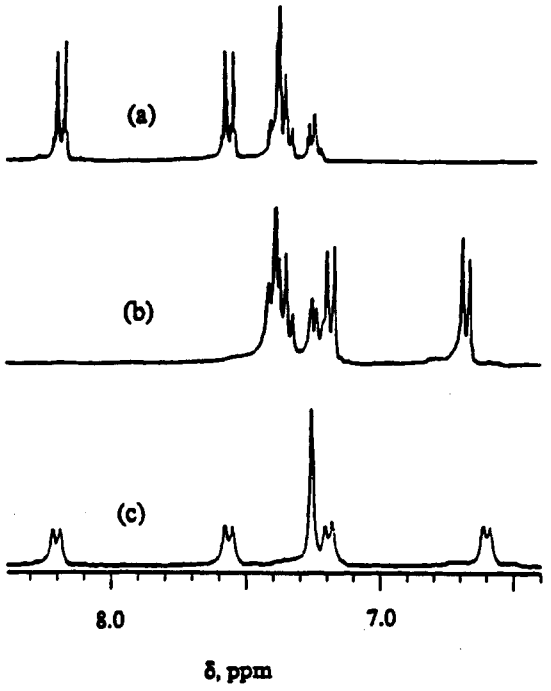
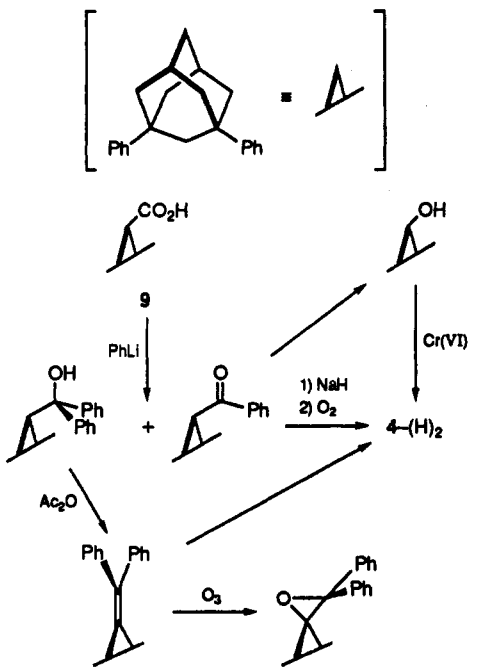


Figure 1. The aromatic region of the ^1H NMR spectra of (a) 4-(H, NO_2), (b) 4-(H, NH_2), and (c) 4-(NH_2, NO_2), in $CDCl_3$.

Scheme 1



the same shift reagent readily allowed us to assign the configurations, based on the response of the aromatic protons. In the *Z*-isomer, the nitrophenyl protons ortho to the adamantyl skeleton are clearly shifted the most strongly; in the *E*-isomer, this attribute applies to the phenyl protons ortho to the bridgehead carbon (see Figure 2). Finally, to determine which isomer had been the major one in the crude mixture, we compared the peaks used for the integration with those seen in the same positions with an artificial mixture in which the *Z*-isomer was dominant. This clearly confirmed that the *E*-isomer was the major one in the original reaction product (Figure 3).

In the case of 4-(H, NH_2), we could not operate in the same way since the amino group, as expected, competes

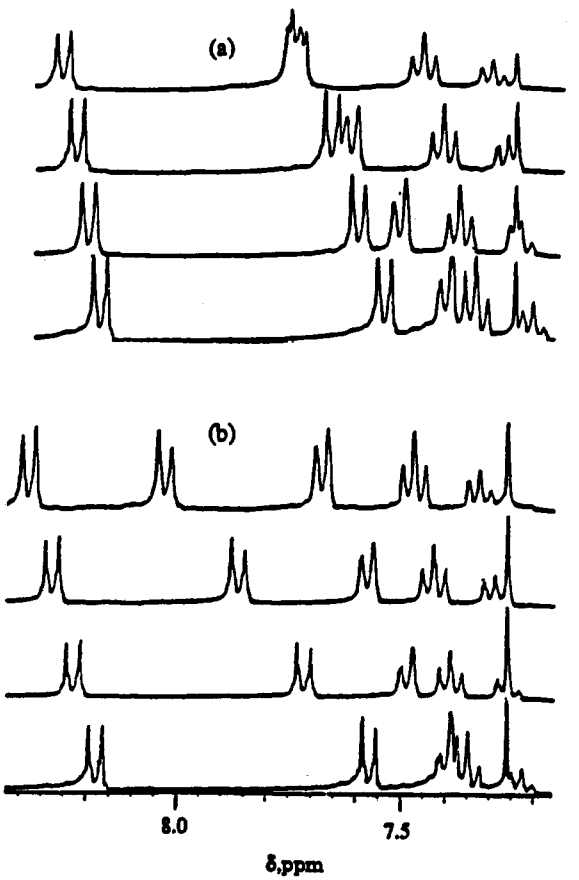


Figure 2. The effect of increasing concentrations of Eu(fod)$_3$ on the aromatic region of the ^1H NMR spectra of (a) (*E*)-5-(*p*-nitrophenyl)-7-phenyladamantan-2-ol, (b) the *Z*-isomer. Note that without shift reagent the spectra are virtually identical. The doublets due to the ortho protons in the proximal phenyl moiety are clearly the more strongly shifted in both compounds.

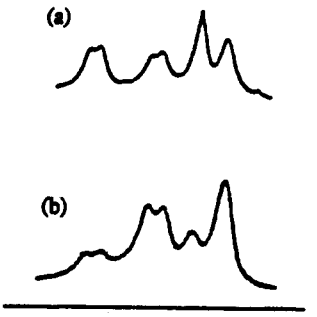


Figure 3. The $H_{4,9\text{-}ax}$ doublets and $H_{1,3}$ singlets of mixtures of (*E*)- and (*Z*)-5-(*p*-nitrophenyl)-7-phenyl-2-adamantanol in the presence of Eu(fod)$_3$. (a) Mixture obtained in reduction of 4-(H, NO_2) (b) Artificial mixture containing a 5:1 excess of *Z*-isomer.

with the hydroxy function for the shift reagent. However, analysis proved possible by HPLC as the two amino alcohols can be nicely separated that way. Since the nitrophenyl alcohols are easily reduced to the amino alcohols with zinc and acetic acid, the assignment of the HPLC peaks was trivial. We note here in passing that the more polar of the epimers, i.e., *E*-4-(H, NH_2) had the higher R_f value (more polar because the OH and NH_2 dipoles point in the same direction).

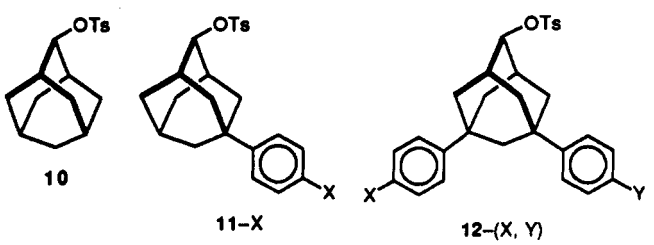
As in our previous study with 2-NH_2,[12] we found the results to be variable when the para substituent is amino; in fact, in the present work, either epimer could be made the dominant one by our choice of conditions. The simple

use of sodium borohydride in 2-propanol gave a mixture in which the *E*-epimer was the major one, with a ratio of 1.5:1 in the same direction as and even larger than what was observed with *p*-nitro! We attribute this to the presence of an equilibrium concentration of the anilinium cation. While this is presumably small, its reduction should be more rapid than that of the neutral species, thus disproportionately affecting the outcome. We therefore did the final experiments in the presence of a small amount of sodium 2-propoxide; this gave a clean and reproducible ratio of 1.28, with the *Z*-isomer the major one.

This same base could not be used in the reduction of 4-(NH_2, NO_2) as it was expected to induce reduction of the nitro group itself. Triethylamine proved to be a satisfactory substitute. Again, HPLC became the analytical means of choice. In this case, the more polar of the epimers is the *Z*-isomer, which we therefore assume to correspond to the peak with higher R_f value. We could not confirm this assignment spectroscopically. The ratio was found to be 1.64 in favor of the "slower" *E*-isomer, which means that the effects of the amino and nitro groups are almost perfectly additive (1.30 × 1.28 = 1.66). Finally, we wished to rule out any possibility that the hydrogen bond forming solvent might have affected the results or that the use of different bases in two of the measurements might have played a role. The entire series of reductions was therefore repeated in THF, with lithium borohydride, and triethylamine; the *E*/*Z* product ratios in this case with **4** were 1.27:1 (4-(H, NO_2), 1:1.23 (4-(H, NH_2)), and 1.58:1 (4-(NH_2, NO_2)).

Solvolysis

The preparations of the various 2-adamantyl tosylates, the solvolyses of which are reported below, were quite difficult and some remarks concerning them are recorded here to help make sense of the procedures described in the Experimental Section. The parent tosylate **10** has been reported[23] to form slowly from 2-adamantanol and tosyl chloride in pyridine at 0 °C. We found the yield to be just as high at room temperature and reached in 3 days. The 5-phenyl analogs (*E*)- and (*Z*)-11-H were prepared in the same way from the alcohols, which were obtained as before.[1] For the tosylates 11-NO_2, difficulties in separating the alcohols and a very slow tosylation reaction giving rise to many side products led us to try various changes in procedure. *tert*-Butyllithium in THF was found to be an excellent base that can be used instead of pyridine, and thence all of our tosylates were prepared that way.



10 **11-X** **12-(X, Y)**

Tosylates 11-NO_2 proved to be obtainable in best yields and purities by nitration of a mixture of esters 11-H followed by column chromatographic separation. The 5-anilinyl alcohols are easily separable, but tosylation of the hydroxy functions in the presence of the amino group was not possible and we resorted to catalytic reduction of a mixture of (*E*)- and (*Z*)-11-NO_2. No way to separate (*E*)- and (*Z*)-11-NH_2 could be found, and it was necessary to reduce the nitro esters separately.

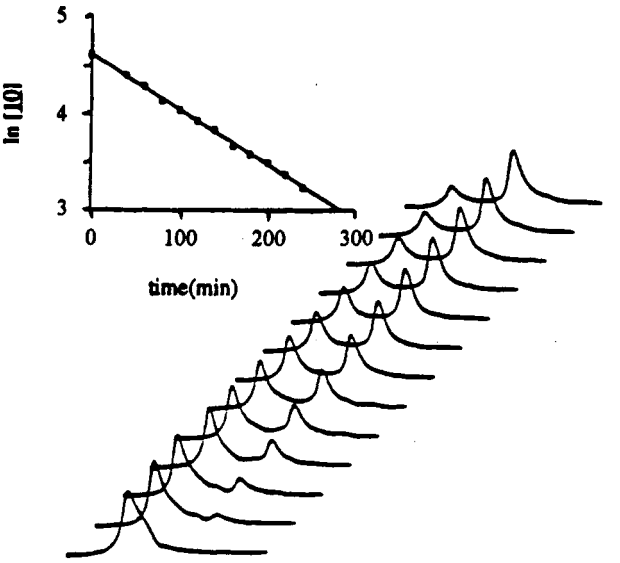


Figure 4. The methyl resonances of **10** and of tosylate anion in 97% hexafluoro-2-propanol-d_2 at 25 °C as a function of time.

The parent 5,7-diphenyl ester **12**-$(H)_2$ was prepared from the alcohol by way of *tert*-butyllithium in a reaction that was remarkably slow (more than 1 h to go to completion). (*E*)- and (*Z*)-**12**-(H, NO_2) could be separated by chromatography from a mixture of the parent and dinitro esters but not from one another; thus, separation of the alcohols by preparative TLC was necessary prior to tosylation. The amino tosylates **12**-(H, NH_2) did prove to be separable by means of preparative TLC, and hence they were obtained by reducing mixtures of the nitro esters. (*E*)- and (*Z*)-**12**-(NH_2, NO_2) were obtained from the parent tosylate by dinitration followed by selective reduction with hydrogen and a platinum-on-carbon catalyst in benzene. TLC monitoring showed the presence of unreacted, monoreduced, and direduced products, and multiple development on preparative TLC plates eventually yielded small samples of both epimers.

The 2-adamantyl system is relatively inert in solvolysis and the 5- and 7-phenyl substituents slow it down even more, requiring an efficient solvolysis medium; 3% aqueous hexafluoro-2-propanol was chosen. No solubility difficulties were encountered. Most of the reactions were followed by means of ^1H NMR, since the methyl resonances of the ester and anion can be seen separately (Figure 4). In same cases, the reaction was also studied by conductance measurements (Guggenheim method;[24] see Figure 5). The results were in good agreement. The correlation coefficients averaged 0.9995 in the conductance experiments and 0.99 in the NMR measurements. 2-Adamantyl and 5,7-diphenyl-2-adamantyl tosylate were measured at several temperatures to allow comparison of all results (Figure 6).

When the data of Table 1 are compared with the reduction results, one of the principal differences is that whereas the 5-anilinyl group acts as a donor in reduction, at least in a basic medium, it causes small retardations in

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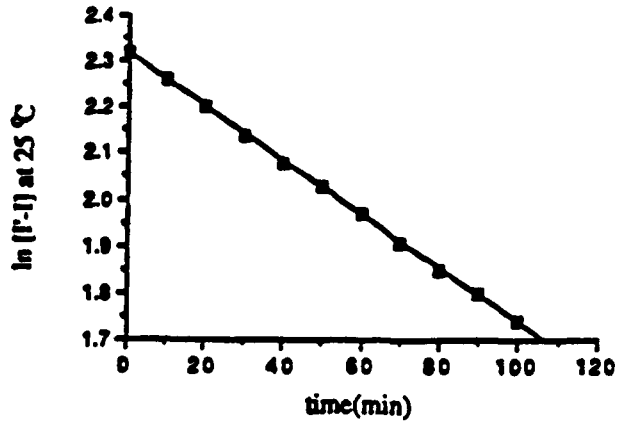

Figure 5. Guggenheim plot of the conductance of a solution of 10 in hexafluoro-2-propanol at 25 °C.

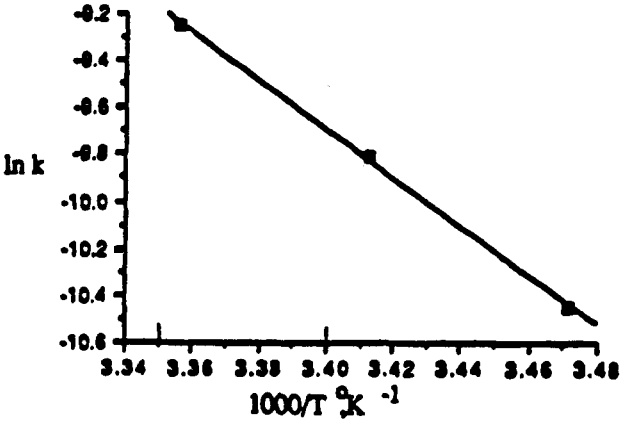

Figure 6. Arrhenius plot of the rate constants of solvolysis of 10 in hexafluoro-2-propanol. The data are summarized in Table I.

Table 1. Summary of Solvolysis Data

substrate tosylate	temp, °C	method	10^5 k, s^{-1}	r
10	15	cond	2.90	0.9996
	20	cond	5.50	0.9999
	25	cond	9.64	0.9998
	25	NMR	9.53	0.999
	56	calcd	255	-
	89	calcd	4400	-
(*E*)-11-H	56	NMR	5.02	0.998
(*Z*)-11-H	56	NMR	8.54	0.999
(*E*)-11-NO_2	56	NMR	0.61	0.997
(*Z*)-11-NO_2	56	NMR	1.53	0.994
(*E*)-11-NH_2	56	NMR	4.64	0.998
(*Z*)-11-NH_2	56	NMR	6.84	0.999
12-$(H)_2$	80	cond	7.74	0.9983
	85	cond	8.85	0.9998
	89	calcd	9.80	-
(*E*)-12(H, NO_2)	89	NMR	0.42	0.947
(*Z*)-12(H, NO_2)	89	NMR	0.87	0.965
(*E*)-12-(H, NH_2)	89	NMR	2.22	0.996
(*Z*)-12-(H, NH_2)	89	NMR	4.57	0.987
(*E*)-12-(NH_2, NO_2)	89	NMR	0.19	0.986
(*Z*)-12-(NH_2, NO_2)	89	NMR	0.40	0.990

solvolysis. We attribute this difference to the unavoidably acidic medium used in the solvolysis; the pK_a of hexafluoro-2-propanol is 5.4 at room temperature.[25] If a significant portion of the aniline is protonated, that portion is unavailable for the solvolysis reaction. In all other respects, however, the solvolysis and reduction data are in agreement. The 5-phenyl group retards the rate of the former reaction by a factor of about 50 when it is in the *anti*-position, or 30 when it is *syn*. The *p*-nitro group reinforces this effect and does so more strongly in the *anti*-phenyl than in the *syn*-phenyl group. The effects are roughly additive; thus, both phenyls together retard the rate by about 500 whereas 30 × 50 ≈ 1500 might have been expected. The slowest of all compounds examined is (*E*)-12-(NH_2, NO_2); roughly in line with the other data in Table I, it is about 20000 times slower than the parent compound 10. We note in this connection that it is conceded in the current literature that the solvolysis of 10 is not a pure k_c process and that it is subject to weak anchimeric assistance. Since it is clearly possible to reduce the rate by means of remote substituents as strongly as shown in this work, we feel that the assistance is not all that weak. Even much stronger deactivation of the vicinal bonds may well be possible, as we hope to determine in future investigations.

We conclude as follows. It is indeed possible to tune both faces of a trigonal carbon independently and observe the added effects of both, as we have seen both in the borohydride reduction of a ketone and in the generation of a cation. Thus, the product ratio in the reduction, which is 1.64, is basically the result of the difference in electronegativity between the nitrogen-bound oxygen and hydrogen atoms separated from the carbonyl carbon by 9 bonds each and from each other by 14 bonds.

Experimental Section

Syntheses. 2,5,7-Tribromoadamantane (3). *endo*-2,3-Trimethylenenorbornane (3 g, Aldrich) was added to a stirred solution of 6 g of anhydrous $AlBr_3$ in 27 mL of Br_2 at −12 to −15 °C over 4 h. Stirring was continued at −12 °C for 5 h, and at −7 °C for 48 h, the mixture was poured onto ice and treated with 200 mL of CCl_4 followed by saturated aqueous sodium bisulfite to remove the yellow color. Filtration yielded 1,2,3,5,6,7-hexabromonaphthalene[17] (3.5 g). The filtrate was separated and the aqueous layer extracted with $CHCl_3$; the combined organic solution was washed with water and dried over $MgSO_4$. Solvent evaporation gave a mixture of 1,5,7- and 2,5,7-tribromoadamantane (crude weight 3.2 g). Elution from silica gel with petroleum ether gave 3 (0.58 g) followed by a mixture of the two compounds. The solvent was removed from the mixture fractions and recrystallization from absolute ethanol gave 2.32 g of 3 (28% overall: mp 169–170 °C, lit.[18] 168–170 °C); ^1H NMR δ 4.45 (s, H_2, 1H), 2.90 (d, $H_{4,9a}$, 2H, J = 13.2 Hz), 2.86 (s, H_6, 2H), 2.42 (s, $H_{1,3}$, 2H), 2.49–2.38 (m, $H_{8,10a,a}$, 4H), 2.15 (d, $H_{4,9e}$, 2H, J = 13.2 Hz); ^{13}C NMR δ 59.40 (C_7), 58.89 (C_6), 58.21 (C_5), 55.06 (C_2), 47.26 ($C_{8,10}$), 42.17 ($C_{1,3}$), 40.96 ($C_{4,9}$).

2,5,7-Triphenyladamantane (5). Into a 25-mL flask, 0.15 g (0.68 mmol) of $AlBr_3$ was measured in a dry box. A benzene (20 mL) solution of 3 (84 mg, 0.23 mmol) was added slowly under nitrogen at 0 °C. The mixture was warmed to rt and after 1 h of stirring, poured over 30 g of ice. The organic layer was separated, 1 N NaOH solution was added to clear up the emulsion, the aqueous layer was extracted with benzene, and the combined organic layer was washed with H_2O and brine, dried over $MgSO_4$, and evaporated to give crude 5 which was purified through a silica gel column (56 mg, 68%, colorless oil): ^1H NMR δ 7.54–7.25 (m, 15H), 3.17 (s, H_2, 1H), 2.99 (s, $H_{1,3}$, 2H), 2.29 (bs, $H_{8,10}$, 4H), 2.17 (s, H_6, 2H), 2.14 (d, $H_{4,9a}$, 2H, J = 12 Hz), 1.90 (d, $H_{4,9e}$, 2H, J = 12 Hz); ^{13}C NMR δ 149.91, 150.13, 143.02, 128.31, 128.22, 128.08, 126.77, 125.84, 125.73, 125.46, 124.96, 124.76, 49.46 (C_6), 45.09 (C_2), 43.62 ($C_{8,10}$), 37.18, 37.04 ($C_{5,7}$), 36.48 ($C_{4,9}$), 32.33 ($C_{1,3}$).

2-Bromo-5,7-dichloroadamantane. In a flask containing 50 mg of 3 (0.13 mmol) in 10 mL of dry benzene was added dropwise 0.47 mL (4.0 mmol) of dry $SnCl_4$ (refluxed over P_2O_5 and distilled under nitrogen). The mixture was allowed to reflux overnight: the reaction was monitored with GC. The intermediate 2,5-dibromo-7-chloroadamantane was recognized by GC and mass

(25) McMurry, *Organic Chemistry*, 3rd ed.; Wadsworth, Inc.: Belmont, CA, 1992, p 630.

spectrum (M - Br at $m/3$ = 247, 249, and 251 in 3:4:1 ratio). Quenching with H_2O, extraction with CH_2Cl_2, washing with water and brine, drying over $MgSO_4$, and evaporation gave 33 mg (87%) of a crude yellow solid that was not purified: ^1H NMR δ 4.38 (s, 1H), 2.68 (d, 2H, J = 12.9 Hz), 2.49–2.39 (m, 4H), 2.21 (d, 4H), 1.94 (d, 2H, J = 12.6 Hz); MS, M - Br, 203, 205, 207 (9:6:1); M - HBrCl, 167, 169 (3:1).

Attempted Oxidation of 5 to 4-(H)$_2$. AIBN (5×10^{-3} g) was added under dry oxygen to column-purified **5** (0.12 g) in 5 mL of dry chlorobenzene. The same amount of AIBN was added every 2 h; TLC showed that **5** had almost disappeared after 30 h. A test with KI/starch confirmed the presence of peroxide, H_2SO_4 (10 mL, 50%) was added and the mixture stirred overnight at 80 °C, extracted with benzene, washed with 15% NaOH solution and H_2O, and dried over $MgSO_4$. Evaporation gave 40 mg of product. TLC showed three major spots and many minor ones; the NMR spectrum of column-separated material corresponding to the three spots showed the presence of the adamantane skeleton and of phenyl rings, but no trace of a carbonyl group was revealed by IR.

5,7-Dihydroxyadamantan-2-one (6). A mixture of **3** (0.45 g), 98% $AgSO_4$ (0.9 g), H_2SO_4 (2.7 mL), and 0.9 mL of H_2O was stirred at 100 °C for 3 h, cooled to rt, and neutralized with KOH pellets. Evaporation of all solvent gave a brown residue which was continuously extracted with ethanol for 10 h. The ethanol was evaporated to give 0.22 g of light-brown solid 2,5,7-trihydroxyadamantane which was dissolved in acetone; Jones' reagent was added dropwise with vigorous stirring until a permanent red color appeared. The stirring was continued overnight. The solution was treated with anhydrous K_2CO_3 and filtered. The pale yellow solution was evaporated and the residue sublimed at 160 °C under vacuum to give 0.15 g of white solid **6**; the total yield from **2** was 69% (mp > 350 °C, lit.[18] >350 °C): ^1H NMR δ 4.88 (s, OH, 2H), 2.24 (s, $C_{1,3}$, 2H), 1.73–1.59 (m, 10H); ^{13}C NMR, δ 215.76 (C_2), 68.10 ($C_{5,7}$), 52.51 ($C_{1,3}$), 49.57 (C_6), 44.44 ($C_{4,8,9,10}$).

(*E*)- and (*Z*)-9-Bromo-7-methylenebicyclo[3.3.1]nonan-3-one (7 and 8). A solution of **3** (200 mg) in 10 mL of pentane was treated with 1.1 g of $AgClO_4$. After 10 min of stirring, the flask was firmly stoppered, sealed with paraffin, wrapped with aluminum foil, and put aside for 2 days. The solution was decanted, 14 mL of dioxane was added, approximately 10 mL of pentane was removed by evaporation, and H_2O was added. The mixture was stirred overnight and extracted with CH_2Cl_2. A crude solid (170 mg) was obtained. Silica gel column separation gave **8** as the major isomer (63 mg, 51%): mp 93–95 °C, and **7** as the minor isomer (31 mg, 25%) mp 97–100 °C. **8**: HRMS, 228.0149, theor 228.0147; ^1H NMR δ 4.83 (s, vinyl H, 2H), 4.64 (s, H_9, 1H), 2.88 (d, J = 17 Hz, $H_{2,4a}$, 2H), 2.63 (s, $H_{1,5}$, 2H), 2.47–2.22 (m, $H_{6,8}$, $H_{2,4e}$, 6H); ^{13}C NMR δ 208.24 (C_3), 137.66 (C_7), 117.06 (vinyl C), 55.61 (C_9), 42.75 ($C_{2,4}$), 42.00 ($C_{6,8}$), 38.87 ($C_{1,5}$). **7**: ^1H NMR δ 4.84 (s, vinyl H, 2H), 4.80 (s, H_9, 1H), 2.99 (d, $H_{6,8a}$, 2H, J = 14.1 Hz), 2.65–2.15 (m, 8H); ^{13}C NMR δ 209.00 (C_3), 139.69 (C_7), 115.62 (vinyl C), 54.69 (C_9), 47.76 ($C_{2,4}$), 37.91 ($C_{6,8}$), 35.99 ($C_{1,5}$). The assignments are based on an application of additivity and resonances of the parent enone.[26]

5,7-Diphenyladamantane-2-carboxylic Acid (9). Adamantane-2-carboxylic acid was prepared from 2-adamantanol in 85% yield as described by Farcasiu;[27] mp 130–133 °C, lit.[27] 137–142 °C; ^1H NMR δ 2.66 (s, H_2, 1H), 2.35 (s, $H_{1,3}$, 2H), 1.93–1.62 (m, 12H); ^{13}C NMR δ 181.57 (C=O), 49.37 (C_2), 38.00 ($C_{8,10}$), 37.26 (C_6), 33.49 ($C_{4,9}$), 29.25 ($C_{1,3}$), 27.33 ($C_{5,7}$). This product was converted into the 5,7-dibromo acid in 65% yield according to Stetter:[21] mp 253–255 °C, lit.[21] 269–271 °C; ^1H NMR δ 2.79–2.14 (m); ^{13}C NMR δ 173.20 (C=O), 61.58 (C_7), 61.38 (C_5), 58.61 (C_6), 46.57 ($C_{8,10}$), 45.09 (C_2), 42.98 ($C_{4,9}$), 36.46 ($C_{1,3}$). A mixture of anhydrous $AlBr_3$ (5 g, 0.02 mol) and dry benzene (100 mL) was treated quickly with 4.5 g (0.013 mol) of the acid under nitrogen at 0 °C, and the mixture was then stirred 18 h at rt. Ice was added to quench the reaction. The solution was acidified with 2 N HCl to dissolve the $Al(OH)_3$ emulsion. The benzene layer was separated and washed twice with 80 mL of water and 80 mL of brine and dried over $MgSO_4$; 4.03 g of yellow crystals were obtained after evaporation. Recrystallization with ethanol and H_2O gave white crystals of **9** (3.41 g, 77%): mp 193–195 °C; ^1H NMR δ 7.42–7.20 (m, 10H), 2.78 (s, $H_{1,3}$, 2H), 2.76 (s, H_2, 1H), 2.14–1.89 (m, 10H); ^{13}C NMR δ 180.45 (C=O), 149.69, 149.40 (C_i), 128.26 (C_m), 125.97 (C_p), 124.83 (C_o), 49.06 (C_6), 47.98 (C_2), 42.63 ($C_{8,10}$), 38.10 ($C_{4,9}$), 36.84, 36.65 ($C_{5,7}$), 30.73 ($C_{1,3}$). Anal. Found: C, 83.17; H, 7.44. Theor: C, 83.10; H, 7.28.

2-(5,7-Diphenyladamantyl) Phenyl Ketone. Acid **9** (2.00 g, 6.0 mmol) and dry ether (45 mL) were placed in a small flask at 0 °C flushed with N_2; 10 mL of 1.8 M PhLi was added dropwise with vigorous stirring at 0 °C over 30 min and then at rt for another 3 h. The reaction was quenched with water followed by 1 N HCl to clear the emulsion. The organic layer was washed with H_2O and brine, dried over $MgSO_4$ and evaporated to small volume. The residue was chromatographed over silica gel with 20% hexane in methylene chloride to give 1.3 g of the white solid ketone which was further purified by washing with minimal amounts of hexane: 0.96 g (41%) was obtained; mp 118–119 °C; HRMS 392.2143, theor 392.2133. 2D NMR was used to assign the peaks: ^1H NMR δ 7.98 (d, 2H, J = 7.2 Hz), 7.64–7.28 (m, 13H), 3.61 (s, H_2, 1H), 2.82 (s, $H_{1,3}$, 2H), 2.42–1.90 (m, 10H); ^{13}C NMR δ 203.36 (C=O), 149.84, 149.57 (5,7-C_i), 137.00 (benzoyl C_i), 132.40 (benzoyl C_o), 128.54, 128.28, 128.15, 128.05, 125.97, 125.83, 125.59, 124.88, 50.51 (C_2), 48.89 (C_6), 43.38 ($C_{8,10}$), 37.42 ($C_{4,9}$), 37.38 (C_7), 36.81 (C_5), 31.72 ($C_{1,3}$). Diphenyl[2-(5,7-diphenyladamantyl)]carbinol (0.3 g) was obtained as a side product: mp 138–141 °C, HRMS, $M^+ - H_2O$ 452.2495, theor 452.2496; ^1H NMR δ 7.79–7.47 (m, 20H), 2.99 (s, 1H, H_2), 2.93 (d, 2H, J = 12 Hz, $H_{4,9a}$), 2.53 (s, 2H, $H_{1,3}$), 2.30 (s, 2H, H_6), 2.32–2.23 (m, 4H, $H_{8,10}$), 1.94 (d, 2H, J = 12 Hz, $H_{4,9e}$); ^{13}C NMR δ 150.54, 149.83, 147.38, 128.18, 128.08, 126.39, 125.68, 125.62, 125.50, 124.91, 124.84, 82.44, 49.62, 48.33, 45.49, 37.81, 37.71, 36.31, 30.58.

5,7-Diphenyladamantan-2-one (4-(H)$_2$). In a 10-mL flask, a mixture of 24.5 mg of 50% NaH (0.51 mmol), 100 mg of 2-(5,7-diphenyladamantyl) phenyl ketone (0.26 mmol) and 5 mL of dry DMF was stirred under nitrogen for 8 h at rt and then dry air was passed through while stirring was continued for 13 h. Quenching with H_2O and extraction with ether followed. Silica gel column chromatography gave 53 mg of white solid 4-(H)$_2$ (69%): mp 139–140 °C; 2 D NMR was used to assign the peaks: ^1H NMR δ 7.37–7.21 (m, 10H), 2.76 (s, $H_{1,3}$, 2H), 2.33 (s, H_6, 2H), 2.28–2.20 (m, $H_{4,8,9,10}$, 8H); ^{13}C NMR δ 217.31 (C=O), 147.31 (C_i), 128.41 (C_m), 126.36 (C_p), 124.77 (C_o), 48.00 ($C_{1,3}$), 46.31 (C_6), 43.58 ($C_{4,8,9,10}$), 37.07 ($C_{5,7}$). Anal. Found: C, 87.03; H, 7.46. Theor: C, 87.37; H, 7.34.

5,7-Diphenyladamantan-2-ol (15 mg) was obtained as a side product: ^1H NMR δ 8.1–7.8 (m, 10H), 3.97 (m, 1H), 2.38–1.20 (m, 12H); ^{13}C NMR δ 150.03, 149.44, 128.27 (2 C's), 125.94, 125.89, 124.96, 124.91, 72.90, 49.08, 41.19, 36.82, 36.60, 35.84, 35.74. After accumulation from several experiments, it was oxidized to 4-(H)$_2$ in 70% yield with Jones' reagent.

A solution of the diphenyl[2-(5,7-diphenyladamantyl)]carbinol (500 mg) in acetic acid (20 mL) and acetic anhydride (20 mL) was allowed to reflux overnight, cooled, and left in the open flask to crystallize for 2 days. The white crystals were filtered and washed with cold petroleum ether to give 0.48 g of [2-(5,7-diphenyladamantylidene)]diphenylmethane (99%): mp 169–170 °C; ^1H NMR δ 7.41–7.18 (m, 20H), 3.14 (s, $H_{1,3}$, 2H), 2.18–2.07 (m, 10H); ^{13}C NMR δ 149.51, 143.94, 142.60, 129.46, 128.25, 128.15, 128.06, 126.27, 125.92, 124.95, 48.58, 44.03, 37.49, 35.11. Anal. Found: C, 92.38; H, 7.21. Theor C, 92.87; H, 7.13.

A Welsbach ozonator (Model T-23) was used to ozonize this olefin (0.7 g) in methylene chloride solution at -78 °C. When TLC showed that the olefin was gone, the solution was flushed with nitrogen at 0 °C until it become colorless. Evaporation of the solvent gave 0.2 g of 4-(H)$_2$ together with 0.3 g of 3′,3′,5,7-tetraphenylspiro[adamantane-2,2′-oxirane] M.P. 85 °C. MS. 468. ^1H NMR, δ 7.74–7.32 (m, 20H), 2.45 (d, J = 12 Hz, 2H, $H_{4,9e}$), 2.26 (d, J = 12.3 Hz, 2H, $H_{8,10e}$), 2.18 (s, H_6), 2.06 (d, J = 12.9 Hz, $H_{8,10e}$), 1.91 (d, J = 12.3 Hz, $H_{4,9e}$), 1.78 ($H_{1,3}$). ^{13}C NMR, δ 149.07 (C_i), 139.68 (C_i), 128.33, 128.16, 127.19, 126.63, 126.10, 125.88, 124.92, 124.87, 73.26 (C_2), 48.35 (C_6), 40.29 ($C_{8,10}$), 40.14 ($C_{4,9}$), 36.62 (C_5), 36.34 (C_7), 33.25 ($C_{1,3}$), 31.52.

(26) Whitesell, J. K.; Minton, M. A. *Stereochemical Analysis of Alicyclic Compounds by ^{13}C NMR Spectroscopy*; Chapman & Hall: London, 1987.

(27) Farcasiu, D. *Synthesis* **1974**, 615.

Nitration of 2-H. HNO_3 (70%, 10 mL) and concd H_2SO_4 (10 mL) were added to 2-H (50 mg) at −78 °C. The solid mixture slowly liquified as the temperature was allowed to increase to −10 °C. After 30 min of stirring, quenching with H_2O and extraction with methylene chloride gave mainly 2-NO_2 together with small amounts of unreacted 2-H and 5-(2,4-dinitrophenyl)-adamantan-2-one. 2-NO_2: ^1H NMR δ 8.17 (d, H_m, 2H, J = 9 Hz), 7.51 (d, H_o, 2H, J = 9 Hz), 2.68 (s, $H_{1,3}$, 2H), 2.38–2.05 (m, 11H); ^{13}C NMR, δ 216.50, 155.34, 129.90, 125.85, 123.58, 46.29, 43.89, 41.65, 38.20, 36.70, 27.90. Conducting the reaction at room temperature overnight gave the (dinitrophenyl)adamantanone alone: ^1H NMR δ 8.31 (dd, H_5, 1H, J = 8.7, 2.4 Hz), 8.20 (d, H_3, 1H, J = 2.4 Hz), 7.78 (d, H_6, 1H, J = 9 Hz), 2.66 (s, $H_{1,3}$, 2H), 2.42–2.00 (m, 11H); ^{13}C NMR δ 215.35, 151.05, 146.14, 144.88, 129.92, 125.24, 119.92, 46.02, 42.25, 39.53, 38.50, 37.79, 27.74.

5,7-Bis(*p*-nitrophenyl)adamantan-2-one ((4-NO_2)$_2$). At −78 °C, 10 mL of 70% HNO_3 was added to 50 mg of 4-$(H)_2$ (0.16 mmol), followed by 10 mL of 98% H_2SO_4 to form a solid mixture. As the temperature was raised, the solid mixture liquefied to a pale yellow solution which was stirred until the temperature reached −10 °C. H_2O was added slowly to quench, and after workup, 4-$(NO_2)_2$ was obtained as the sole product. It was chromatographed (silica gel, 30% ethyl acetate and 0.2% methanol in hexane). The light-yellow product was dissolved in benzene, decolorized with charcoal, and obtained as a white solid by adding hexane (84%): mp 240–245 °C; HRMS M^+ 392.1370, theor 392.1367; ^1H NMR δ 8.21 (d, H_m, 4H, J = 9 Hz), 7.58 (d, H_o, 4H, J = 9 Hz), 2.87 (s, $H_{1,3}$, 2H), 2.39–2.28 (m, 10H); ^{13}C NMR δ 154.08, 131.25, 125.93, 123.85, 47.46, 45.82, 43.14 ($C_{4,8,9,10}$), 37.84, (due to the low solubility, the C_2 peak could not be detected).

5-Phenyl-7-(*p*-nitrophenyl)adamantan-2-one (4-(H, NO_2)). A solution of 0.74 g (2.45 mmol) of 4-$(H)_2$ in 7 mL of acetic anhydride and 7 mL of CH_3NO_2 was heated in a 50 °C oil bath. A second mixture of 0.11 mL of fuming HNO_3 (2.69 mmol), 2.5 mL of acetic anhydride, and an equal volume of CH_3NO_2 was prepared at rt and added dropwise with vigorous stirring, a rinse of 2 mL of a 1:1 mixture of acetic anhydride and CH_3NO_2 being used to complete the addition. After 2 h of stirring, H_2O was added dropwise to quench, and after workup, the residue was chromatographed (silica gel, 30% ethyl acetate and 0.2% methanol in hexane) to give 0.94 g of white solid 4-(H, NO_2): mp 157–8 °C; HRMS 347.1521, theor 347.1516; ^1H NMR δ 8.20 (d, nitroph H_m, 2H, J = 8.4 Hz), 7.58 (d, nitroph H_o, 2H, J = 8.4 Hz), 7.42–7.28 (m, Ph, 5H), 2.83 (s, $H_{1,3}$, 2H), 2.38 (s, H_6, 2H), 2.34–2.26 (m, 8H); ^{13}C N MR δ 216.09, 154.73, 146.73, 146.42, 128.56, 126.60, 125.94, 124.71, 123.65, 47.71, 46.02, 43.34, 43.21, 37.83, 37.09. Unreacted 4-$(H)_2$ (0.54 g) but no dinitro compound 4-$(NO_2)_2$ was observed.

5-(*p*-Aminophenyl)-7-phenyladamantan-2-one (4-H, NH_2). Zinc dust (30 mg) and 10 mL of acetic acid were added to 50 mg of crystalline 4-(H, NO_2) in a 25-mL flask stoppered with a rubber septum and stirred for 7 h. The reaction mixture was filtered and the unreacted zinc washed with CH_2Cl_2. The combined filtrate was evaporated to dryness. The residue was treated with NaOH solution and extracted with CH_2Cl_2 to give the product as a yellow oil. Oven-baked (380 °C for 8 h) or freshly opened activated neutral alumina was used to chromatograph it with a well-dried solvent system of 1% methanol in CH_2Cl_2. Colorless oil: HRMS 317.1770, theor 317.1774.

Alternatively, 50 mg of 4-(H, NO_2) and 30 mg of 5% Pt/C were added to a flask containing 25 mL of dry benzene at room temperature under nitrogen; the flask was quickly attached to the hydrogenation apparatus. After evacuation, it was filled with H_2 (1 atm) and the reaction allowed to go on until no further H_2 uptake was observed. Approximately 3 h reaction time was allowed. After filtration, solvent evaporation and chromatography (neutral alumina, 1% methanol in CH_2Cl_2, 50% ethyl acetate in hexane) gave pure 4-(H, NH_2): ^1H NMR δ 7.42–7.36 (m, Ph, 5H), 7.19 (d, anilinyl-H_o or -H_m, 2H, J = 8.7 Hz), 6.68 (d, anilinyl-H_o or -H_m, 2H, J = 8.4 Hz), 3.64 (s, NH_2, 2H), 2.77 (s, $H_{1,3}$, 2H), 2.32–2.22 (m, 10H); ^{13}C NMR δ 217.74, 147.53, 144.69, 137.52, 128.41, 126.32, 125.64, 124.83, 115.04, 48.28, 46.45, 43.91, 43.67, 37.17, 36.42.

5-(*p*-Aminophenyl)-7-(*p*-nitrophenyl)adamantan-2-one (4-NH_2, NO_2). In a 100-mL flask were added 100 mg (0.26 mmol) of 4-$(NO_2)_2$, 10 mg of 5% Pt/C, 50 mL of absolute ethanol, and 3 mL of CH_3Cl. Afterwards, the reaction mixture was cooled to 10 °C with cold water bath. The hydrogenation apparatus used allowed the amount of H_2 taken up to be measured; a drying tube was used. The system was flushed with H_2 (1 atm). After about 15 mL of H_2 had been absorbed, the reaction was stopped. Approximately 1 h of reaction time was required. The mixture was filtered and chromatographed over silica gel with 50% ethyl acetate in hexane and then neutral alumina with 1% methanol in CH_2Cl_2 to give 8 mg of a yellow oil, 25 mg of unreacted 4-$(NO_2)_2$, and several unidentified compounds.

Alternatively, use of dry benzene as a solvent gave the oil in better yields (>15%): HRMS M^+ 362.1631, theor 362.1625; ^1H NMR δ 8.20 (d, nitroph, 2H, J = 9 Hz), 7.57 (d, nitroph, 2H, J = 8.7 Hz), 7.19 (d, aminoph, 2H, J = 8.7 Hz), 6.60 (d, aminoph, 2H, J = 8.7 Hz), 3.60 (bs, NH_2, 2H), 2.80 (s, $H_{1,3}$, 2H), 2.32–2.25 (m, 10H); ^{13}C NMR δ 135.45, 129.42, 125.99, 125.55, 123.68, 112.72, 48.14, 46.22, 43.73, 43.38, 38.54, 36.32.

Reductions. The general reduction was performed with $NaBH_4$ in 2-propanol and $LiBH_4$ in THF. Generally, an excess of the reducing agent was added to the flask containing the ketone and excess of base in a well-dried solvent. In the $NaBH_4$ reduction no base was used for 4-(H, NO_2) and sodium 2-propoxide was used for 4-(H, NH_2). In all other cases, TEA was used. The reaction mixture was stirred overnight at room temperature, quenched with water, and extracted with methylene chloride. After drying over $MgSO_4$, the solvent was evaporated giving two isomeric alcohols. The yield was more than 90% in all cases. This mixture was passed through a short silica gel column and identified with ^1H NMR. Then it was injected into an HPLC column (5 μm Dupont Zorbax Silica) connected with a Waters Lambda-Max Model 481 spectrophotometer. The areas were calculated manually from the width at half-height and height of each peak. To assure accuracy, the peaks were also copied, cut out, and weighed. The ^1H NMR spectrum was taken with increasing amounts of Eu(fod)$_3$ to see the effect of shift reagent on each isomer. To determine the ratio, a curve analysis program (1280 Data Station Gencap) was also used.

(*E*)- and (*Z*)-5-(*p*-Nitrophenyl)-7-phenyladamantan-2-ol ((*E*)- and (*Z*)-12-(H, NO_2)). Following the general reduction with 4-(H, NO_2) gave a light-yellow solid mixture of two alcohols. A 0.25 M Eu(fod)$_3$ solution in $CDCl_3$ was added in 50-μL increments, and a ^1H NMR spectrum was taken each time. The ratio of two isomers was determined from the well-separated $H_{4,9}$ peaks in one of these mixtures, and the configuration was determined by means of the effect of Eu(fod)$_3$ on each isomer separately. The effect of Eu(fod)$_3$ on an artificial mixture allowed us to confirm the major component as *E*. *E*-isomer: ^1H NMR δ 8.18 (d, 2H, J = 9 Hz), 7.55 (d, 2H, J = 9 Hz), 7.40–7.22 (m, 5H), 4.01 (bs, H), 2.41–1.26 (m, 12H). *Z*-isomer δ 8.17 (d, 2H, J = 9 Hz), 7.56 (d, 2H, J = 9 Hz), 7.40–7.26 (m, 5H), 4.02 (bs, 1H), 2.41–1.25 (m, 12H). ^{13}C NMR spectra were measured of the mixture but too little material was available to determine the spectra of the separate alcohols.

A sample of the original mixture (10 mg) was reduced to the corresponding isomeric anilinyl alcohols with Zn dust (15 mg) in acetic acid (5 mL) with stirring overnight. After filtration, the solvent was evaporated and the residue injected into the HPLC column; it gave the same ratio of products which were identified as the *E*- and *Z*-anilinyl alcohols (see below).

(*E*)- and (*Z*)-5-(*p*-Aminophenyl)-7-phenyladamantan-2-ol ((*E*)- and (*Z*)-12-(H, NH_2)). Following the general reduction procedure with 4-(H, NH_2) gave a yellow oil consisting of a mixture of two isomeric alcohols. After short column chromatography, the mixture was injected into HPLC giving a 1:1.28 ratio for $NaBH_4$ reduction and 1:1.23 for $LiBH_4$ reduction, with the *Z*-isomer as the major one in both cases. Considerable side products were observed under the condition open to the air or without base to guarantee free amine. However, under basic condition, the reaction gave a very clean mixture of two products as judged by HPLC. The NMR spectra were essentially identical: ^1H NMR δ 7.42–7.18 (m, 7H), 6.68 (d, 2H, J = 8.4 Hz), 3.97 (bs, 1H), 3.60 (vbs, 2H), 2.32–1.21 (m, 12H); ^{13}C NMR, δ 149.46, 144.08, 140.40, 139.73, 128.15, 125.71, 125.62, 115.00, 72.90, 49.12, 41.27, 41.08, 36.50, 35.84, 35.74.

(*E*)- and (*Z*)-5-(*p*-Aminophenyl)-7-(*p*-nitrophenyl)adamantan-2-ol ((*E*)- and (*Z*)-12-(NH_2, NO_2)). With the general

reduction procedure, the product was a yellow oil consisting of two isomeric alcohols. The ^{1}H NMR spectrum showed doublets centered at δ 8.17 and 6.60 and quartets at 7.55 and 7.25. The reaction mixture was separated by HPLC and gave a 1:1.64 ratio for the $NaBH_4$ reduction and 1:1.58 for the $LiBH_4$ reduction.

Preparation of Tosylates. 2-Adamantyl Tosylate (10). 2-Adamantanol (0.2 g, 1.32 mmol) was placed in a 25-mL flask flushed with nitrogen, and 10 mL of freshly distilled THF was added. A tosyl chloride solution of 1.97 mmol (0.576 g) in 2 mL of dry THF solution was prepared separately. *tert*-BuLi (1 mL, 1.7 M) was added dropwise into the former solution at 0 °C, the ice bath was removed, and the mixture was stirred vigorously at room temperature. After 1 h, the tosyl chloride solution was added and stirring was continued for 3 h. The mixture was quenched with H_2O and extracted with ether; after workup, **10** was purified on a silica gel column with 30% ethyl acetate and 0.2% methanol in hexane: a colorless oil (0.29 g, 72%) was obtained which solidified upon exposure to air; mp 79–80 °C, lit.[23] 82.7–83.7 °C; ^{1}H NMR δ 7.76 (2H, d, J = 8.1 Hz, H_α), 7.29 (2H, d, J = 8.4 Hz, H_β), 4.64 (1H, s, H_2), 2.40 (3H, s, CH_3), 2.01 (2H, d, $H_{4,9e}$), 1.93 (2H, s, $H_{1,3}$), 1.76–1.59 (6H, m, $H_{8,10e,a}$, H_6), 1.47 (2H, d, $H_{4,9e}$); ^{13}C NMR δ 144.12 (C_i with SO_2), 134.83 (C_i with CH_3), 129.57, 127.32, 86.15 (C_2), 36.94 (C_6), 36.25 ($C_{8,10}$), 32.53 ($C_{1,3}$), 30.97 ($C_{4,9}$), 26.67, 26.41 ($C_{5,7}$), 21.44 (CH_3).

5-Phenyladamantan-2-yl Tosylate ((*E*)- and (*Z*)-11-H). $NaBH_4$ (12 mg) was added to 70 mg (0.31 mmol) of 5-phenyladamantanone **2**-H in 2-propanol. A drying tube was used. The reaction mixture was stirred overnight and quenched with H_2O. The usual aqueous workup and extraction with CH_2Cl_2 gave the white powdery 5-phenyladamantanols quantitatively: ^{1}H NMR δ 7.43–7.24 (m, 5H, Ph), 4.04 and 3.96 (s and s, 1H, H_2), 2.38–1.59 (m, 13H); ^{13}C NMR 150.55 (C_i), 128.10, 128.04 (C_m), 125.64, 125.56 (C_p), 124.79, 124.72 (C_o), 73.92, 73.31 (C_2), 43.17, 42.98 (C_6), 41.99, 36.42, 35.64, 35.53, 35.42, 35.29, 34.96, 28.15, 27.69 (C_7). The tosylates were prepared as described for **10**. The yellow oil was column purified with 20% ethyl acetate in hexane. The two isomers were separated by means of multiple development of preparative TLC. White solid materials were obtained (69% overall, with 25% unreacted starting material). (*E*)-11-H: ^{1}H NMR δ 7.83 (d, J = 8.4 Hz, 2H, Tos-Ph), 7.33 (d, J = 8.4 Hz, 2H, Tos-Ph), 7.30–7.28 (m, 5H, Ph), 4.79 (s, 1H, H_2), 2.45 (s, 3H, CH_3), 2.14–1.55 (m, 11H), 1.91 (s, 2H, $H_{1,3}$). (*Z*)-11-H: ^{1}H NMR δ 7.83 (d, J = 8.1 Hz, 2H, Tos-Ph), 7.36–7.28 (m, 7H), 4.73 (s, 1H, H_2), 2.46 (s, 3H, CH_3), 2.26–1.68 (m, 13H).

5-(*p*-Nitrophenyl)adamantan-2-yl Tosylates ((*E*)- and (*Z*)-11-NO_2). 5-(*p*-Nitrophenyl)adamantanone (100 mg, 0.37 mmol) was reduced with 20 mg of $NaBH_4$ in 15 mL of 2-propanol; a drying tube was used. Aqueous workup gave 98.3 mg of a mixture of alcohols in 97.3% yield. They were separated by means of multiple development of preparative TLC with 40% ethyl acetate and 1.3% methanol in hexane. Both isomers are white solids, available in amounts too small to warrant further purification and ^{13}C NMR measurement. *E*-isomer: ^{1}H NMR δ 8.16 (d, J = 9 Hz, 2H, C_o-nitroph), 7.51 (d, J = 9 Hz, 2H, C_m-nitroph), 3.98 (s, 1H, H_2), 2.18 (d, J = 13.8 Hz, 2H, $H_{8,10e}$), 2.09 (s, 2H, $H_{1,3}$), 1.99–1.93 (m, 8H), 1.55 (d, J = 12.9 Hz, 2H, $H_{8,10e}$). *Z*-isomer: ^{1}H NMR δ 8.16 (d, J = 9 Hz, 2H, C_o-nitroph), 7.51 (d, J = 9 Hz, 2H, C_o-nitroph), 3.92 (s, 1H, H_2), 2.31 (d, J = 12.3 Hz, 2H, $H_{4,9a}$), 2.12 (s, 2H, $H_{1,3}$), 2.06 (s, 1H), 1.89–1.62 (m, 9H).

The isomeric 5-(*p*-nitrophenyl)-2-adamantyl tosylates were prepared separately with the same procedure as for **10** except that CH_2Cl_2 was used to extract instead of ether. The product was isolated from many side products by means of flash column chromatography with 30% ethyl acetate and 0.2% methanol in hexane. A second column separation gave both tosylates as light yellow oils (35%).

Alternatively, a mixture of the tosylates was prepared by mononitration of a mixture of (*E*)- and (*Z*)-11-H. The nitration procedure was the same as that used for 12-$(NO_2)_2$ (see below). The two isomers were separated by silica gel column with 30% ethyl acetate and 0.2% methanol in hexane (yellow oils, >70%); HRMS, M^+ – TosOH 255.1266, theor 255.1259. (*E*)-11-NO_2: ^{1}H NMR δ 8.15 (d, J = 9 Hz, 2H, nitroph), 7.82 (d, J = 8.4 Hz, 2H, tosylph), 7.44 (d, J = 9 Hz, 2H, nitroph), 7.34 (d, J = 8.7 Hz, 2H, tosylph), 4.73 (s, 1H, H_2), 2.45 (s, 3H, CH_3), 2.17–1.52 (m, 13H); ^{13}C NMR δ 148.33, 129.78, 127.79, 127.52, 126.29, 125.78, 123.47, 84.54 (C_2), 42.49, 41.50, 32.83, 30.04, 27.22, 21.58. (*Z*)-11-NO_2: ^{1}H NMR δ 8.16 (d, J = 9 Hz, 2H, nitroph), 7.81 (d, J = 8.1 Hz, 2H, tosylph), 7.47 (d, J = 8.7 Hz, 2H, nitroph), 7.34 (d, J = 8.1 Hz, 2H, tosylph), 4.69 (s, 1H, H_2), 2.45 (s, 3H, CH_3), 2.24–1.67 (m, 13H), 1.88 (s, 2H, $H_{1,3}$).

5-(*p*-Aminophenyl)adamantyl Tosylates ((*E*)- and (*Z*)-11-NH_2). These tosylates were separately prepared form the corresponding nitrophenyl tosylates. To well-purified samples of 15 mg of (*E*)- and (*Z*)-11-NO_2, 5 mg of Pt/C catalyst and 15 mL of dry benzene were added. Each reaction mixture was connected to a hydrogenation apparatus and stirred for 3 h in a cold water bath (~10 °C). The reaction mixture was filtered and dried to give the anilinyl tosylate. The product was column purified with 1% methanol in methylene chloride (brownish oil, >80%), HRMS M^+ 397.1715, theor 397.1705. (*E*)-11-NH_2: ^{1}H NMR δ 7.82 (d, J = 8.1 Hz, 2H, tosylph), 7.33 (d, J = 8.4 Hz, 2H, tosylph), 7.07 (d, J = 8.7 Hz, 2H, anilinylph), 6.63 (d, J = 8.4 Hz, 2H, anilinylph), 4.73 (s, 1H, H_2), 3.57 (bs, 2H, NH_2), 2.44 (s, 3H, CH_3), 2.11–1.85 (m, 13H). (*Z*)-11-NH_2: ^{1}H NMR δ 7.80 (d, J = 8.1 Hz, 2H, tosylph), 7.31 (d, J = 7.5 Hz, 2H, tosylph), 7.06 (d, J = 8.4 Hz, 2H, anilinylph), 6.62 (d, J = 8.4 Hz, 2H, anilinylph), 4.69 (s, 1H, H_2), 3.58 (s, 2H, NH_2), 2.44 (s, 3H, CH_3), 2.14–1.63 (m, 13H).

5,7-Diphenyladamantan-2-yl Tosylate (12-$(H)_2$). Purified 4-$(H)_2$ (0.1 g, 0.33 mmol) was placed in a small flask; 0.025 g (0.66 mmol) of $NaBH_4$ and 15 mL of HPLC grade 2-propanol were added. After overnight stirring, H_2O was added until a white cloudiness formed. Extraction with methylene chloride and usual aqueous workup gave 0.102 g (0.33 mmol) of the white solid alcohol: mp 84–86 °C, 100% yield; ^{1}H NMR 7.40–7.19 (m, 10H, ph), 3.96 (s, 1H, H_2), 2.35 (d, 2H, $H_{4,9a}$, J = 12.6 Hz), 2.25 (s, 2H, $H_{1,3}$, J = 2.4 Hz), 2.05 (s, 2H, H_6), 2.01–1.97 (m, 4H, $H_{8,10e,a}$), 1.72 (d, 2H, $H_{4,9e}$, J = 12.6 Hz); ^{13}C NMR δ 149.92, 149.34 (C_i), 128.17 (C_m), 125.84, 125.79 (C_p), 124.86, 124.81 (C_o), 72.80 (C_2), 48.98 (C_6), 41.09 ($C_{8,10}$), 36.72, 36.50 ($C_{5,7}$), 35.70 ($C_{1,3}$), 35.64 ($C_{4,9}$). Anal. Found; C, 86.26; H, 7.91. Theor C, 86.79; H 7.95.

In a 25-mL flask, 0.102 g (0.335 mmol) of this alcohol and 10 mL of dry THF were added under nitrogen. In a separate flask, a tosyl chloride solution was prepared by adding 2 mL of THF to 0.10 g (0.52 mmol) of tosyl chloride that had been recrystallized from chloroform and hexane. *tert*-BuLi (0.5 mL, 1.7 M) was added dropwise into the reaction flask at 0 °C; the contents became yellow. After 1 h stirring at room temperature, the tosyl chloride solution was added dropwise over 5 min. In the beginning, the solution became colorless and then yellow again at the end. After further stirring for 3 h at rt, the mixture was quenched with H_2O and extracted with ether. The crude product was purified by means of flash column chromatography with 30% ethyl acetate and 0.2% methanol in hexane to give 0.096 g of tosylate 12-$(H)_2$ (62.5%): mp 173–174 °C, HRMS M^+ 458.1905, theor 458.1908. Some unreacted alcohol (26 mg) was recovered: ^{1}H NMR δ 7.88 (d, J = 8.1 Hz, 2H, tosylph), 7.32–7.18 (m, 12H), 4.75 (s, 1H, H_2), 2.41 (s, 3H, CH_3), 2.32 (s, 2H, $H_{1,3}$), 2.27 (d, J = 13.8 Hz, 2H, $H_{4,9a}$), 2.01 (s, 2H, H_6), 1.94 (q, J = 9.6 Hz, 4H, $H_{8,10}$), 1.71 (d, J = 12.6 Hz, 2H, $H_{4,9e}$); ^{13}C NMR δ 149.06, 148.31 (C_i), 144.38, 140.00 (tosylph, C_i), 129.74, 128.25, 128.20, 127.48, 126.08, 126.00, 124.71, 84.05 (C_2), 48.75 (C_6), 40.92 ($C_{8,9}$), 36.24 ($C_{5,7}$), 35.73 ($C_{4,9}$), 33.87 (C_1), 21.53 (CH_3).

2-[5-(*p*-Nitrophenyl)-7-phenyladamantyl]Tosylate ((*E*)- and (*Z*)-12-(H, NO_2)). The procedure is same as that for 12-$(NO_2)_2$ (see below) except for the amount of fuming nitric acid. In this case, 1.5 equiv of fuming nitric acid was used to avoid dinitration. By means of column chromatography with 30% ethyl acetate and 0.2% methanol in hexane, 45% of (*E*)- and (*Z*)-12-(H, NO_2) (white solids), 10% of unreacted starting material, and 10% of dinitrated compounds were collected as well as an unidentified impurity. Alternatively, these tosylates were prepared separately from the corresponding alcohols with *tert*-BuLi and tosyl chloride. The procedure is the same as that used for **10**. *E*-Isomer: HRMS M^+ – TosOH 331.1580, theor 331.1573; ^{1}H NMR δ 8.17 (d, J = 9 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.7 Hz, 2H), 7.31–7.18 (m, 7H), 4.76 (s, 1H, H_2), 2.46 (s, 3H, CH_3), 2.39 (s, 2H, $H_{1,3}$), 2.32 (d, J = 13.2 Hz, 2H), 2.05 (s, 2H, H_6), 2.02–1.75 (m, 6H). *Z*-Isomer: ^{1}H NMR δ 8.18 (d, J = 9 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 9 Hz, 2H), 7.35–7.33 (m, 7H), 4.77 (s, 1H, H_2), 2.46 (s, 3H, CH_3), 2.39 (s, 2H, $H_{1,3}$), 2.31

(d, 2H), 2.05 (s, 2H, H_6), 2.02–1.73 (m, 6H); ^{13}C NMR of mixture δ 156.53, 129.86, 128.47, 127.58, 126.42, 125.88, 124.68, 123.58, 123.54, 83.42 (C_2), 48.54, 40.79, 37.15, 36.26, 35.64, 33.81, 21.60 (CH_3).

2-[5,7-Bis(*p*-nitrophenyl)adamantyl] Tosylate (12-$(NO_2)_2$). 5,7-Diphenyl-2-adamantyl tosylate (12-$(H)_2$) (100 mg, 0.22 mmol) was placed in a small flask and 5 mL of a 50/50 mixture of nitromethane and acetic anhydride was added. A nitric acid solution was made separately by adding 0.05 mL (1.1 mmol) of fuming nitric acid into 5 mL of the same mixed solvent system. The nitric acid solution was added to the reaction flask and stirred for 10 h at room temperature. The reaction was quenched with H_2O and the mixture extracted with methylene chloride. Routine workup gave a yellow oil. Flash column chromatography with 30% ethyl acetate and 0.2% methanol in hexane gave 8 mg of unreacted starting material, 26 mg of a mixture of an unidentified side product and 12-$(NO_2)_2$ (they had almost same R_f), and 65 mg of pure 12-$(NO_2)_2$ as a colorless oil (53.9%). An APT was made to help assign the peaks: ^1H NMR δ 8.15 (d, J = 9 Hz, 2H, nitroph), 8.14 (d, J = 8.7 Hz, 2H, nitroph), 7.82 (d, J = 8.4 Hz, 2H, tosylph), 7.51 (d, J = 8.4 Hz, 2H, nitroph), 7.48 (d, J = 8.4 Hz, 2H, nitroph), 7.35 (d, J = 7.8 Hz, 2H, tosylph), 4.74 (s, 1H, H_2), 2.45 (s, 3H, CH_3), 2.42 (s, 2H, $H_{1,3}$), 2.32 (d, J = 13.2 Hz, 2H, $H_{4,9a}$), 2.04 (s, 2H, H_6), 2.04–2.00 (m, 4H, $H_{8,10}$), 1.79 (d, J = 12.6 Hz , 2H, $H_{4,9e}$); ^{13}C NMR δ 155.83, 155.12 (C_i-nitroph), 146.43, 146.35 (C_i-nitroph), 144.80 (tosylph, C_i), 129.90, 127.52, 125.84, 123.59, 82.59 (C_2), 47.92 (C_6), 40.39 ($C_{8,10}$), 36.92 ($C_{5,7}$), 35.28 ($C_{4,9}$), 33.49 ($C_{1,3}$), 21.58 (CH_3).

2-[5-(*p*-Aminophenyl)-7-phenyladamantyl] Tosylates ((*E*)- and (*Z*)-12-(H, NH_2)). The mixture of the corresponding nitro tosylates was reduced with a procedure which was the same as that for 2-[5-(*p*-aminophenyl)] tosylate. Silica gel column chromatography with 1% methanol in methylene chloride gave a light-brown oil (>65%), HRMS M^+ 473.2020, theor 473.2017. The NMR spectra, appended as part of the supplementary material, are essentially identical.

2-[5-(*p*-Aminophenyl)-7-(*p*-nitrophenyl)adamantyl] Tosylates ((*E*)- and (*Z*)-12-(NO_2, NH_2)). Well-purified 12-$(NO_2)_2$ was selectively reduced with 10 mg of Pt/C in 20 mL benzene at 5–10 °C. The reaction was traced with TLC and stopped when most of the starting material was reduced. The mixture was filtered and the solvent was evaporated. A long silica gel column with 0.5% of methanol in CH_2Cl_2 gave 12 mg of a mixture of the two tosylates as a yellow oil. HRMS M^+ – TosOH 346.1683, theor 346.1681. Direduced compound (15 mg) and unreacted tosylate (10 mg) were also obtained. The epimers were separated by repeated TLC development; both had only 6 doublets in the aromatic region at virtually identical chemical shifts (see supplementary material).

Solvolyses. For the kinetic NMR study, a Bruker AC-250 was used; the WIN NMR deconvolution program was used to measure the areas under the peaks. Hexafluoro-2-propanol-d_6 was purchased from Cambridge Isotope Labs. For the conductance measurements, a Wheatstone Bridge system, Hewlett-Packard Model 120B was used. Distilled hexafluoro-2-propanol and deionized water were used to prepare the solvent.

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Supplementary Material Available: Spectral data of all new compounds described in this paper (100 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.