Stereoselectivity of Destabilized Carbocations: 1-Cyano-2-adamantyl and 3-Cyano-4-protoadamantyl Cations

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Received May 8, 1998

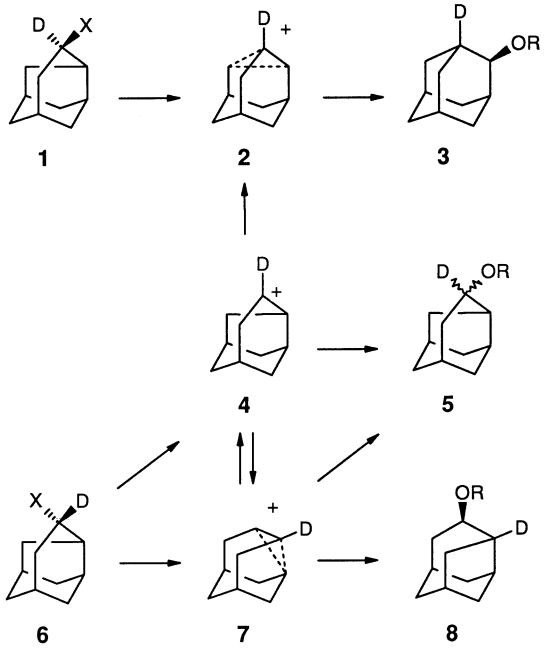
Keywords: Carbocations / Ion pairs / Rearrangements / σ Delocalization / Solvolysis

Nonracemic and ^{18}O-labeled 4-tosyloxyprotoadamantane-4-carbonitriles **10c**, **11c** were prepared. In 60 % dioxane, the *exo*-OTs isomer **10c** afforded ca. 97% of 2-tosyloxyadamantane-1-carbonitrile (**14**) with *ee* = 98% and with 23% equilibration of the tosylate oxygen atoms. The data point to a tight ion pair which undergoes nearly complete and stereospecific recombination. The *endo*-OTs isomer **11c** underwent internal return to give *endo*-4-tosyloxyprotoadamantane-3-carbonitrile (**20**, 60% yield, 51% equilibration of the tosylate oxygen atoms), elimination (6%), and solvolysis (34%) competitively. 2-Hydroxyadamantane-1-carbonitrile (**15**) and 4-hydroxyprotoadamantane-3-carbonitrile (*exo*/*endo* = **18**/**22** ≈ 2.8) were formed with *ee* ≥ 97%. According to these results, the chirality (unsymmetrical bridging) of the parent 2-adamantyl cation is not detectably affected by 1-CN whereas the *endo* selectivity of the parent 4-protoadamantyl cation (symmetrical bridging) is eliminated by 3-CN.

The influence of electron-withdrawing substituents on the generation of carbocations has been studied extensively[1][2]. Much less attention has been directed to 1,2-carbon shifts of destabilized carbocations. A fundamental question regards the degree to which σ delocalization is affected by destabilizing substituents. In previous approaches to the problem, cyano and/or perfluoroalkyl groups were attached to bicyclo[2.1.1]hex-2-yl[3], 2-norbornyl[4], bicyclo[3.2.0]hept-2-yl[5], and 2-norpinyl substrates[6]. The present work extends our studies to the 4-protoadamantyl → 2-adamantyl rearrangement.

The 4-protoadamantyl → 2-adamantyl rearrangement, constituting an important step in the synthesis of adamantoid hydrocarbons[7], has been investigated experimentally[8][9] as well as computationally[10]. The stereochemistry of the rearrangement was elucidated by means of deuterium-labeled, nonracemic substrates (Scheme 1)[11]. The *exo* substrate **1** was found to give 2-adamantyl products **3** with *ee* ≥ 97%. The *endo* substrate **6** afforded 4-protoadamantyl products rather unselectively (*exo*-**5**, 8.1% ; *endo*-**5**, 3.9% ; **8**, 3.6%), along with **3** (76%, *ee* ≥ 97%). The data indicate that the chiral, bridged 2-adamantyl cation **2** does not significantly interconvert with an achiral, open species whereas both versions of the 4-protoadamantyl cation, **4** and **7**, intervene. We have now replaced the deuterium labels of these intermediates with cyano groups.

Scheme 1



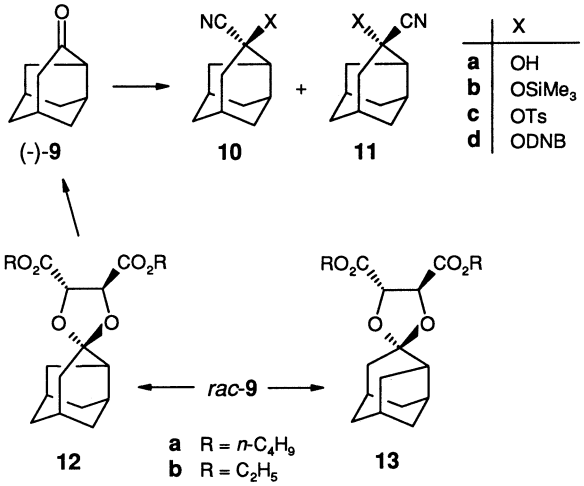
Preparation of Substrates

The addition of hydrogen cyanide to 4-protoadamantanone (**9**)[12] was reported to give a mixture of the cyanohydrins **10a** and **11a**[13]. The isomers were now separated by HPLC, and the configuration was assigned by X-ray analysis of the 3,5-dinitrobenzoate **11d**[14]. When the standard procedure was applied to [^{18}O]-**9**, substantial oxygen exchange was observed. However, the reaction of [^{18}O]-**9** with trimethylsilyl cyanide and subsequent hydrolysis of the silyl ethers **10b**, **11b**[13b] proceeded without significant loss of ^{18}O. In order to resolve the enantiomers of **9**, the ketone was treated with (−)(2*S*, 3*S*)-dibutyl tartrate to give the spiroacetals **12a** and **13a** which were separated by reversed-phase chromatography. The peaks of the butyl esters **12a**, **13a** overlapped less than those of the ethyl esters **12b**, **13b**; the isomer eluting first was obtained with good purity. Hydrolysis afforded (−)-**9** whose *ee* (95.2 ± 0.2%) was esti-

  1434−193X/98/1010−2245 $ 17.50+.50/0

mated by GC on a chiral phase. The optical rotation of (−)-**9** ($[\alpha]_D^{25}$ = − 8.3 ± 0.1, $CHCl_3$) was in good agreement with data from an enzymatic resolution[15]. The configuration (1*R*,3*R*,6*S*,8*R*), shown in Scheme 2, was previously assigned to (−)-**9**[16].

Scheme 2

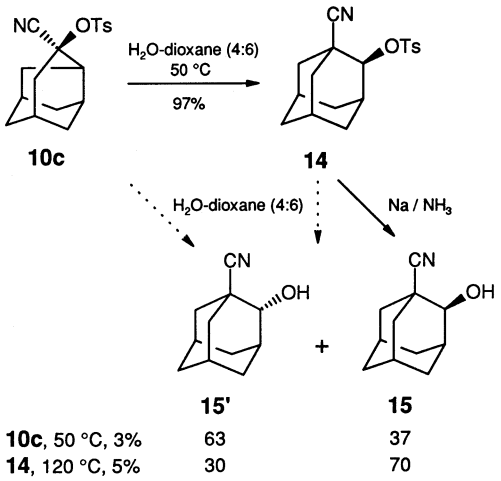


The tosylation (TsCl, pyridine) of **10a** proceeded reluctantly to give the corresponding tosylate **10c** with 20−25% yield. Extended reaction times and elevated temperatures led to rearrangement of **10c** (see below) while stronger bases induced decomposition of **10a**. The isomer **11a** reacted more smoothly with formation of the sterically less congested tosylate **11c** (64%). It should be noted that the substituent X of **10** assumes the "flagpole" position of a slightly distorted cyclohexane boat, as compared to the equatorial (linear) orientation of X in **11**. Force-field calculations (MM3) indicate that the energy difference between **10** and **11** is very small (< 1 kJ/mol) for X = OH but increases with increasing bulk of X.

Rearrangement/Solvolysis of *exo*-4-Tosyloxyprotoadamantyl-*endo*-4-carbonitrile (10c)

The reaction of **10c** in 60% dioxane at 50°C was monitored by HPLC. First-order kinetics were observed, k = (6.32 ± 0.17)·10^{-4} s^{-1}. The predominant product was 2-tosyloxyadamantane-1-carbonitrile (**14**) which is stable at 50°C. Only 3% of 2-hydroxyadamantane-1-carbonitrile (**15**) was detected by GC after complete conversion of **10c**. The rearrangement of [^{18}O]-**10c** (49.4 ± 0.5% ^{18}O) gave **14** with 41.8 ± 0.5% "ester"-^{18}O, i.e. with 23% equilibration of the sulfonate. The amount of "ester"-^{18}O was estimated by means of ^{13}C NMR, utilizing the isotopic shift of the carbon atom attached to ^{18}O.[17] Complete equilibration is assumed to distribute the label equally between the "ester" and "sulfonyl" oxygen atoms of the tosyloxy group. Partial scrambling of the ^{18}O label indicates that the **10c** → **14** transformation proceeds by way of an ion pair. Analogous dissociation-recombination processes of tosylates have been reported[18] although nearly complete recombination, as

Scheme 3



observed for **10c**, is exceptional. The analogous rearrangement of the parent *exo*-4-protoadamantyl tosylate was associated with 52% equilibration of the tosyloxy group[19] even though the conditions (pyridine, 0°C) were milder than those applied to **10c**. Comparison of the data points to tighter ion pairing in the case of the less stable, CN-substituted carbocation.

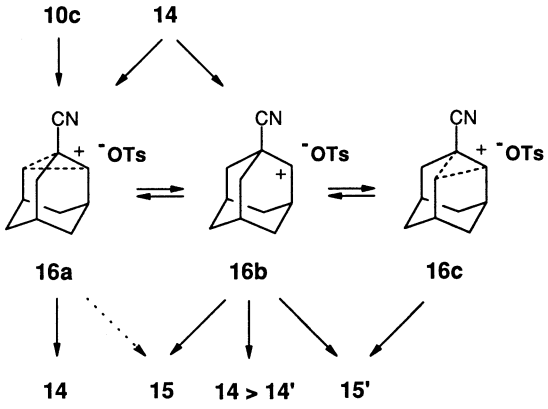
The rearrangement of (+)-**10c** (*ee* = 95.5 ± 0.3%) afforded (+)-**14** (*ee* = 93.6 ± 0.5%) with 98% retention of the enantiomeric purity. The *ee* of **14** was estimated by ^{1}H NMR in the presence of the chiral shift reagent Eu(hfc)$_3$ which splitted the signals of 2-H and *o*-ArH. In ion-pair recombination processes, the counterion returns preferentially to the side of the molecular framework from which it departed[18][19]. Hence the (2*R*) configuration is assigned to **14** and to the alcohol **15** (*ee* = 86%) which was obtained by reductive cleavage of (+)-**14** with sodium in ammonia. The small amount of alcohol formed by solvolysis of (+)-**10c** was analyzed by GC on a chiral phase. The enantiomer **15′** prevailed although the *ee* was only 26%.

The tresylate of **15** was solvolyzed previously but neither the stereochemistry nor ion pairing were addressed.[20] The solvolysis of (+)-**14** (*ee* = 94%) in 60% dioxane required 5 days at 120°C to give 5% of the alcohol **15** with *ee* = 41%. The enantiomeric purity of recovered (+)-**14** (*ee* = 90%) was close to that of the starting material whereas the scrambling of ^{18}O in [^{18}O]-**14** increased substantially (the "ester"-^{18}O decreased from 41.8% to 34.6%, which means 22% of *additional* equilibration). Obviously, dissociation of **14** generates an ion pair which recombines with predominant retention of configuration. MS analysis of the alcohol obtained from [^{18}O]-**14** indicated the presence of little, if any, ^{18}O (1 ± 1%). S−O cleavage is thus excluded as a significant route to **15**.

The stereochemistry of ion-pair recombination does not reveal the nature of the intervening carbocation. Even if the cation originating from **10c** is achiral, the ion pair **16b** will be chiral, and collapse of **16b** will give **14** in excess over **14′**. Since the front side of **16b** is shielded by the counterion (as indicated by bold print in Scheme 4), attack of the solvent

from the rear will be preferred to give **15′** > **15**. However, a chiral carbocation undergoing a small amount of inversion is also compatible with our data. In this case, the ion pair **16a** will undergo collapse (→ **14**) in strong preference to solvent capture (→ **15**) while the reverse holds for the ion pair **16c** (where the counterion is improperly oriented for return). The ionization of **14** is energetically more demanding than that of **10c**, i.e., the ion pair **16a** arising from **14** will be less tight than that arising from **10c**. Hence the ratio of solvent capture to inversion should be more favorable for **16a** from **14**, leading to **15** > **15′**. The solvolytic displacement of labeled 2-adamantyl tosylates is known to proceed with partial retention of configuration[21]; the 1-cyano derivative conforms to the rule.

Scheme 4



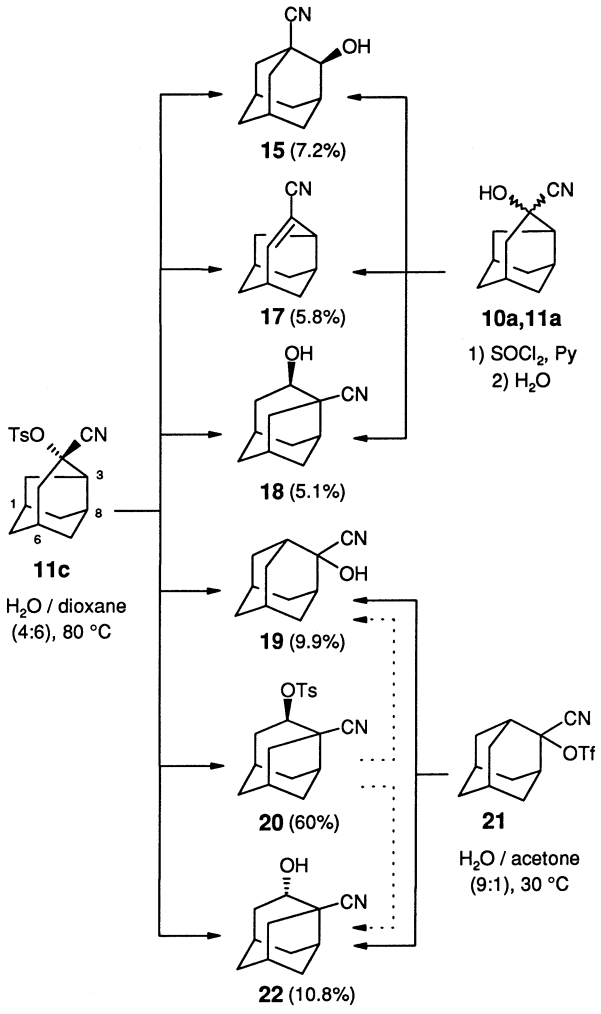
Rearrangement/Solvolysis of *endo*-4-Tosyloxyprotoadamantane-*exo*-4-carbonitrile (11c)

The reaction of **11c** in 60% aqueous dioxane at 50°C proceeded slowly, $k = (1.90 \pm 0.06) \cdot 10^{-6}\ s^{-1}$. The *exo*/*endo* rate ratio $k_{\mathbf{10c}}/k_{\mathbf{11c}} = 3.3 \cdot 10^2$ can be explained in terms of σ participation, as was suggested for the parent 4-protoadamantyl substrates[8a] (see **1** → **2**). However, ground-state effects (steric congestion) would also account for the faster reaction of **10c**, although the close agreement of $\Delta\Delta G^{\neq} =$ 15.6 kJ/mol with ΔE(MM3) = 16.2 kJ/mol may be fortuitous.

All product studies were performed in 60% dioxane at 80°C where **11c** decreased at a more convenient rate, $k = (6.1 \pm 0.2) \cdot 10^{-5}\ s^{-1}$. Under these conditions, *endo*-4-tosyloxyprotoadamantane-3-carbonitrile (**20**) was formed with the rate constant $k = (3.7 \pm 0.3) \cdot 10^{-5}\ s^{-1}$, i.e., with 60% yield. The rearrangement of [^{18}O]-**11c** (49.0 ± 0.5% ^{18}O, exclusively in the "ester" position) afforded **20** with 32.4 ± 0.5% "ester"-^{18}O (51% equilibration). Both the scrambling of ^{18}O and the fraction of internal return indicate that the ion pair generated from **11c** is less tight than that originating from **10c**. Yet ion-pair recombination is highly stereoselective; the *exo* isomer of **20** was not observed. At 80°C, the solvolysis of **20**, $k = (4.7 \pm 0.2) \cdot 10^{-7}\ s^{-1}$, did not compete significantly with that of **11c**. The rate ratio $k_{\mathbf{11c}}/k_{\mathbf{20}} = 1.3 \cdot 10^2$ (80°C) conforms with published data for $k_{\alpha\text{-CN}}/k_{\beta\text{-CN}}$[1][6][22]. These rate ratios do not reflect the relative stabilities of the intervening carbocations since α-cyano sulfonates are destabilized by the geminal interaction of two electron acceptors[23].

The solvolysis products arising from **11c** (60% dioxane, 80°C, 19 h) were analyzed by GC, with the results shown in Scheme 5. (The relative yields of the volatile products were normalized to 40%, taking into account 60% of **20**). 4-Protoadamantanone (1.2%) and 2-adamantanone (9.9%) were detected by GC although ketones were not present in the original mixture. Controls revealed that the cyanohydrins **10a**, **11a**, and **19** decomposed on our GC columns. Isolation of the more abundant cyanohydrin **19** was achieved by HPLC. In contrast to the tosylate **20**, the analogous alcohols **18** and **22** were formed rather unselectively (ca. 1:2). *exo*-4-Hydroxyprotoadamantane-3-carbonitrile (**22**) was previously obtained, along with **19**, by solvolysis of **21**[22]. The configuration of **22** was assigned unequivocally from the X-ray crystal structure[22]. The coupling pattern of **22** ($J_{4\text{-H},endo\text{-5-H}} = 6.5$ Hz, $\Phi_{MM3} \approx 27°$; $J_{4\text{-H},exo\text{-5-H}} \approx 0$ Hz, $\Phi_{MM3} \approx 89°$) is characteristically different from that of the

Scheme 5



endo isomer **18** ($J_{4\text{-H},endo\text{-5-H}} \approx J_{4\text{-H},exo\text{-5-H}} = 8.5$ Hz, $\Phi_{MM3} \approx 33$ and 149°). For a selective approach to **18**, the mixture of 4-protoadamantanone cyanohydrins (**10a**, **11a**) was treated with thionyl chloride (15 h at room temperature). It was anticipated that the chlorosulfites of **10a** and **11a** would rearrange to give the more persistent chlorosulfites of **15** and **18**, respectively. In fact, hydrolysis of the product mixture afforded **15** and **18** (5:1) in addition to the alkene **17**.

Nonracemic **11c** (*ee* = 94.4 ± 0.3%) was solvolyzed (60% dioxane, 100°C, 19 h) to give, among other products, **15** (*ee* = 92.2 ± 1.8%), **18** (*ee* = 93.6 ± 1.2%), and **22** (*ee* = 91.6 ± 2.0%). The *ee* data were obtained by chiral-phase GC; they agree within experimental error. Little, if any, racemization would be expected en route to **18** and **22**. However, the formation of **15** with almost complete (97−98%) retention of enantiomeric purity is a most remarkable result, assigning chirality to the 1-cyano-2-adamantyl cation. An analogous solvolysis (60% dioxane, 100°C, 19 h) of the tosylate **20** proceeded to only 5% conversion, giving rise to **19** and **22** (6.4:1).

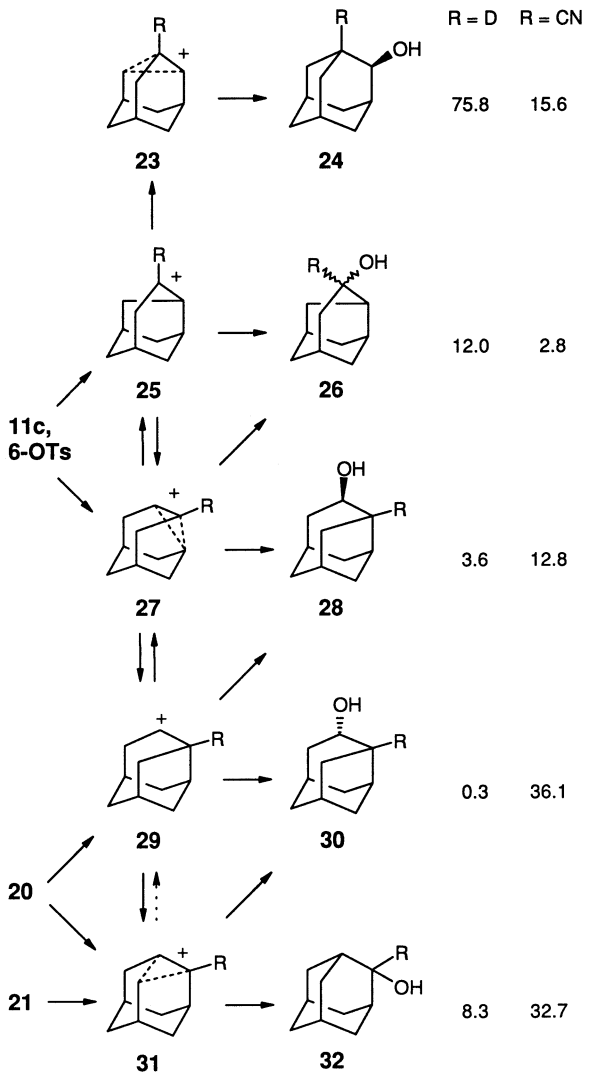
Discussion

4-Protoadamantyl tosylates, both parent and CN-substituted, rearrange with formation of less reactive isomers. Dissociation-recombination processes are involved, as attested by the scrambling of ^{18}O labels. The tightness of the intervening ion pairs is reflected by more or less equilibration of the tosylate oxygen atoms. The rate of ion-pair recombination appears to increase with the exothermicity of the overall rearrangement. In the conversion of **11c** into **20** (51% equilibration), the protoadamantyl framework is retained while the tosylate group is relocated from the α to the β position, relative to CN (−40 kJ/mol[3a]). The substituent effect is reinforced by the release of ring strain (−47 kJ/mol[24]) in the rearrangement of **10c** to give **14** (23% equilibration). Varying tightness of the ion pairs does not affect the stereoselectivity (≥ 98%) of recombination. The counterion returns to the same side of the molecular framework from which it departed.

In 60% dioxane, rearrangement of **10c** (ca. 97%) occurs to the virtual exclusion of solvolysis (ca. 3%). As was pointed out above, the nature of the intervening carbocation(s) cannot be derived from the stereochemistry of internal return (→ **14**) nor from that of the very minor hydrolysis (→ **15**). Therefore, our discussion focuses on the solvolysis of **11c** where partitioning between ion-pair recombination (60%) and solvent capture (34%) is less extreme. The present results for R = CN, obtained with **11c**, will be compared to those previously reported for R = D, from the solvolysis of **6**-OTs[11] (Scheme 6). To simplify matters, alcohols were normalized to 100% while internal return and elimination were disregarded.

The bridged ion **27** is symmetrical for R = H and nearly so for R = D. If the ionization of **6**-OTs produced **27** exclusively, the "upward" (**27** → **25** → **23**) and "downward"

Scheme 6



(**27** → **29** → **31**) routes of Scheme 6 would differ but marginally (by a secondary isotope effect). However, a strong preference (ca. 9:1) for the "upward" route was observed experimentally[11]. Therefore, the open ion **25** must be formed, at least in part, from **6**-OTs. The direction of the favored reaction path is reversed upon introduction of a cyano group. With R = CN, the "downward" route of Scheme 6 predominates (ca. 4.5:1). The dramatic change is readily understood if CN destabilizes **25** more strongly than **29**. We have demonstrated prevoiusly that α-cyano-substituted carbocations are less stable than their β-cyano-substituted analogs, although rates of solvolysis suggest the opposite[3a].

Cyano substitution also affects the *exo*/*endo* ratio of 3-R-protoadamantan-4-ols, **30**/**28**, which is ca. 0.08 for R = D and ca. 2.8 for R = CN. The bridged ion **27** gives rise to **28** whereas a mixture of **28** and (predominantly) **30** is expected from the open ion **29**. Clearly, the contribution of **29** increases at the expense of **27** if R = D is replaced with R = CN.

There is one remarkable point of agreement between R = D and R = CN. In each case, **24** arises with *ee* ≥ 97%, pointing to the chiral, bridged intermediate **23**. The precursor to the achiral product **32** is less definitely assigned. However, **31**-D and **23**-D differ only in the position of D and must be constituted analogously. The stereoselective formation of **30**-CN from **20** and **21** suggests that the bridged structure **31** is retained for R = CN.

Conclusion

The stereoselective capture of 2-adamantyl cations is not detectably affected by CN substitution at C-1. This result conforms with previous data on 1-CN-7-norbornyl cations[5] and 1-CN-2-norpinyl cations[6]. On the other hand, the *endo* preference of the parent 4-protoadamantyl cation is lost on introduction of 3-CN. Analogous findings were reported for bicyclo[2.1.1]hex-2-yl cations and their 1-CN analogs[3a]. It appears that unsymmetrical bridging is not very sensitive to cyano substitution. In contrast, σ delocalization is seriously impaired by attaching *one* cyano group to symmetrically bridged carbon atoms. The behavior of potentially symmetrical cations with *two* CN groups would be of interest but our attempts to generate such species have not been successful.

Experimental Section

^{1}H NMR: Bruker WP 80 and Bruker AM 400; δ = 0 for tetramethylsilane as internal standard, δ = 7.26 for chloroform. − ^{13}C NMR (100.6 MHz) and ^{2}H NMR (61.4 MHz): Bruker AM 400. Analyses of ^{18}O by means of ^{13}C isotopic shifts are most accurate if ^{13}C-^{18}O and ^{13}C-^{16}O signals are of similar intensity. Therefore, $^{18}OH_2$ with 50−55% ^{18}O was used for the preparation of labeled compounds. − IR: Perkin−Elmer 881. − MS: Varian MAT CH 5 (70 eV). − Gas chromatography (GC): Siemens Sichromat 1, equipped with glass capillary columns. The chiral phases heptakis(3-*O*-acetyl-2,6-di-*O*-pentyl)-β-cyclodextrin and octakis(3-*O*-butyryl-2,6-di-*O*-pentyl)-γ-cyclodextrin served to estimate the distribution of enantiomers. − High-pressure liquid chromatography (HPLC): Constametric I and II (LDC) with refractometric or UV detection. − Low-pressure liquid chromatography (LPLC): Glass columns, 30 × 3 cm, 4.5 bar, refractometric dectection. − Melting points: Kofler hot plate (Reichert); not corrected.

[^{18}O]-Tricyclo[4.3.1.0^{3,8}]decan-4-one ([^{18}O]-**9**): Tricyclo[4.3.1.0^{3,8}]decan-4-one[12] (**9**, 0.90 g, 6.0 mmol), anhydrous THF (3 ml), $^{18}OH_2$ (2 ml, ca. 55% ^{18}O), and concentrated HCl (1 μl) were heated at 80°C for 12 h. After cooling to room temp., the mixture was extracted with pentane. The extracts were dried ($MgSO_4$) and concentrated to give 0.85 g (94%) of crude [^{18}O]-**9**. − IR ($CDCl_3$): $\tilde{\nu}$ = 1721 (C=O) and 1686 (C=^{18}O) cm^{-1}. − ^{13}C NMR ($CDCl_3$): δ = 216.901 (C=^{18}O) and 216.953 (C=O).

(−)-Tricyclo[4.3.1.0^{3,8}]decan-4-one [(−)-**9**]: To a solution of **9** (3.0 g, 20 mmol) in $CHCl_3$ (10 ml) was added (−)-(2*S*, 3*S*)-dibutyl tartrate (13.1 g, 50 mmol) and *p*-toluenesulfonic acid (19 mg, 0.1 mmol). The mixture was heated at reflux for 30 h; water was removed by azeotropic distillation. After cooling to room temp., the solution was washed with 0.2 N NaOH and water, dried (K_2CO_3), and concentrated in vacuo. Unreacted ketone was largely removed by short-path distillation to give 6.1 g (77%) of dibutyl spiro[1,3-dioxolane-2,4′-tricyclo[4.3.1.0^{3,8}]decane]-4,5-dicarboxylate (**12a**, **13a**). On HPLC (Polygosil 60-10-C_{18}, methanol/water, 85:15), **12a** was eluted first with *de* ≈ 95%, $[\alpha]_D^{24}$ = 6.7 ± 0.1 (*c* = 2.25 in $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 0.92 (t, *J* = 7.2 Hz, 6 H), 1.31−1.48 (m, 7 H), 1.62 (quint, *J* = 7.2 Hz, 4 H), 1.55−1.79 (m, 4 H), 1.87 (m, 1 H), 1.92−2.03 (m, 2 H), 2.10−2.17 (m, 2 H), 2.29−2.35 (m, 2 H), 4.16 (t, *J* = 6.8 Hz, 2 H), 4.17 (t, *J* = 6.8 Hz, 2 H), 4.67 (AB, *J* ≈ 5.2 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 13.82 (CH_3), 19.21 (CH_2), 28.73 (CH), 30.74 (CH_2), 32.44 (CH_2), 34.39 (CH), 35.26 (CH_2), 36.26 (CH), 39.58 (CH_2), 41.66 (CH_2), 42.07 (CH_2), 43.98 (CH), 65.70 (CH_2), 65.72 (CH_2), 76.40 (CH), 77.66 (CH), 118.33 (C), 170.00 (CO), 170.37 (CO).

To a solution of **12a** (0.80 g, 2.03 mmol) in ethanol (10 ml) was added 2 N HCl (10 ml). The mixture was stirred at 80°C for 7 h and was then extracted with ether. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo to give 0.30 g (98%) of (−)-**9**, *ee* = 95.2 ± 0.2% (GC), $[\alpha]_D^{25}$ = −7.9 ± 0.1 (*c* = 0.94 in $CHCl_3$). For the enantiomerically pure ketone, $[\alpha]_D^{25}$ = −8.3 ± 0.1 is estimated, in reasonable agreement with reported values of −8.7 and +7.5 from an enzymatic resolution[15]. The configuration (1*R*,3*R*,6*S*,8*R*) was assigned to (−)-**9**[16].

4-Hydroxytricyclo[4.3.1.0^{3,8}]decane-4-carbonitriles **10a**, **11a**: To a solution of **9** (6.0 g, 40 mmol) in methanol (150 ml) was added a solution of sodium cyanide (20.0 g, 408 mmol) in water (60 ml). Concentrated sulfuric acid (30 ml) was added dropwise with vigorous stirring. The mixture was heated at reflux for 3 h, and stirring was continued for 3 h at room temp. Nitrogen was then passed through the solution for 2−3 h to remove residual hydrogen cyanide. The mixture was partitioned between diethyl ether and water. The combined ether solutions were washed with aqueous $NaHCO_3$ and aqueous NaCl, dried ($MgSO_4$), and concentrated in vacuo to give 6.8 g of a residue which consisted of **10a** (39%), **11a** (34%), and unreacted **9** (27%). Repeated HPLC (LiChrospher Si 100-5, pentane/ether, 4:1) afforded 2.03 g (29%) of **10a** and 1.35 g (19%) of **11a** with *de* ≥ 99%. − *exo*-4-Hydroxytricyclo[4.3.1.0^{3,8}]decane-*endo*-4-carbonitrile (**10a**): M.p. 133−134°C. − IR (KBr): $\tilde{\nu}$ = 3400 (OH), 2240 (CN) cm^{-1}. − ^{13}C NMR ($CDCl_3$): δ = 27.44 (CH), 30.97 (CH_2), 32.40 (CH), 35.44 (CH), 35.64 (CH_2), 38.89 (CH_2), 42.13 (CH_2), 42.46 (CH_2), 45.04 (CH), 71.08 (C), 123.74 (CN). − *endo*-4-Hydroxytricyclo[4.3.1.0^{3,8}]decane-*exo*-4-carbonitrile (**11a**): M.p. 197−198°C. − IR (KBr): $\tilde{\nu}$ = 3395 (OH), 2240 (CN) cm^{-1}. − ^{13}C NMR ($CDCl_3$): δ = 28.50 (CH), 31.08 (CH_2), 32.94 (CH_2), 33.49 (CH), 35.04 (CH), 39.27 (CH_2), 41.33 (CH_2), 41.92 (CH_2), 45.91 (CH), 68.20 (C), 124.65 (CN). − $C_{11}H_{15}NO$ (177.3): calcd. C 74.54, H 8.53, N 7.90; found for **10a** C 74.53, H 8.59, N 7.96; found for **11a** C 74.58, H, 8.56, N 7.98. − Analogous treatment of (−)-**9** afforded (+)-**10a**, $[\alpha]_D^{20}$ = 64.7 ± 0.5 (*c* = 0.89 in $CHCl_3$), and (+)-**11a**, $[\alpha]_D^{20}$ = 70.4 ± 0.3 (*c* = 0.55 in $CHCl_3$).

[^{18}O]-4-Hydroxytricyclo[4.3.1.0^{3,8}]decane-4-carbonitriles [^{18}O]-**10a**, **11a**: To a mixture of [^{18}O]-**9** (3.0 g, 20.0 mmol), zinc iodide (60 mg, 0.19 mmol), and dichloromethane (60 ml) was added dropwise cyanotrimethylsilane (2.25 g, 22.7 mmol). After the mixture was heated at reflux for 24 h, it was washed with aqueous $Na_2S_2O_3$ and water. The organic phase was dried ($MgSO_4$) and concentrated in vacuo to give 4.7 g (94%) of [^{18}O]-4-trimethylsilyloxytricyclo[4.3.1.0^{3,8}]decane-4-carbonitrile (**10b**/**11b** = *exo*-$OSiMe_3$/*endo*-$OSiMe_3$ = 38:62, as estimated by GC: 25-m OV1, 160°C). A sample was purified by HPLC (LiChrospher 100-5, pentane/2-methoxy-2-methylpropane, 99:1) for mass-spectrometric analysis (*m*/*z* = 234, 236 [$M^+ - CH_3$]) which indicated 50.3% ^{18}O. − ^{1}H NMR ($CDCl_3$): δ = 0.265 (s, 5.5 H), 0.270 (s, 3.5 H), 1.32−1.47

(m, 2 H), 1.51−1.58 (m, 1 H), 1.63−1.76 (m, 2 H), 1.78−1.91 (m, 2.6 H), 2.02−2.14 (m, 2 H), 2.18−2.32 (m, 2 H), 2.47 (q, J = 6 Hz, 0.7 H), 2.57 (dd, J = 14.0/8.5 Hz, 0.7 H), 2.66 (br. t, J = 9 Hz, 1 H). − ^{13}C NMR (C_6D_6, excerpt): δ = −0.257, 0.000 (CH_3), 69.24, 71.48 (C), 122.17, 123.21 (CN). The spectrum of the unlabeled mixture has been published[13b].

A mixture of [^{18}O]-**10b**, **11b** (4.0 g, 16.0 mmol) and 2 N HCl (60 ml) was stirred vigorously at 35−40°C for 10 h and was then extracted with diethyl ether (3 × 50 ml). The extracts were washed with water, dried ($MgSO_4$), and concentrated in vacuo to give 2.75 g (97%) of a residue containing 9% of ketone, 27% of **10a**, and 64% of **11a** (MS: m/z = 177, 179 [M^+], 50.0% ^{18}O). The isomeric cyanohydrins were separated by HPLC (LiChrospher 100-5, pentane/2-methoxy-2-methylpropane, 85:15) to give 506 mg (18%) of [^{18}O]-**10a** and 1.17 g (41%) of [^{18}O]-**11a**.

4-(3,5-Dinitrobenzoyloxy)tricyclo[4.3.1.0^{3,8}]decane-4-carbonitriles **10d**, **11d**: To a solution of **10a** (0.13 g, 0.73 mmol) in anhydrous pyridine (1.5 ml) was added 3,5-dinitrobenzoyl chloride (205 mg, 0.89 mmol). The mixture was stirred for 24 h at room temp. and was then diluted with diethyl ether (10 ml). The solution was washed with 10% HCl, aqueous $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by HPLC (LiChrospher Si 100-5, hexane/ether, 9:1) to give 212 mg (78%) of **10d**, m.p. 128−129°C. − IR (KBr): $\tilde{\nu}$ = 2245 (CN), 1730 (CO) cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 1.51−1.67 (m, 3 H), 1.78−1.95 (m, 4 H), 2.09 (dddd, J = 16.0/11.0/5.2/2.0 Hz, 1 H), 2.21 (m, 1 H), 2.35 (m, 1 H), 2.40 (q, J = 6.2 Hz, 1 H), 2.50 (dd, J = 16.2/1.5 Hz, 1 H), 2.73 (ddd, J = 16.2/8.0/1.5 Hz, 1 H), 3.28 (br. t, J = 9.5 Hz, 1 H), 9.13 (d, J = 2.0 Hz, 2 H), 9.28 (t, J = 2.0 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 27.38 (CH), 31.70 (CH_2), 32.58 (CH), 35.36 (CH_2), 35.49 (CH), 38.67 (CH_2), 40.16 (CH_2), 42.13 (CH_2), 42.50 (CH), 77.15 (C), 119.18 (CN), 122.93 (CH), 129.32 (CH), 133.21 (C), 148.90 (C), 160.56 (CO). − $C_{18}H_{17}N_3O_6$ (371.4): calcd. C 58.22, H 4.61, N 11.32; found C 58.27, H 4.58, N 11.34.

Analogous treatment of **11a** (85 mg, 0.48 mmol) afforded 133 mg (75%) of **11d**, m.p. 154−155°C. − IR (KBr): $\tilde{\nu}$ = 2245 (CN), 1735 (CO) cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 1.48 (dm, J = 13.5 Hz, 1 H), 1.55−1.62 (m, 2 H), 1.78−1.93 (m, 4 H), 2.03 (dd, J = 15.2/2.0 Hz, 1 H), 2.18 (dm, J = 14.0 Hz, 1 H), 2.27−2.34 (m, 2 H), 2.64 (q, J = 6.2 Hz, 1 H), 3.10−3.19 (m, 2 H), 9.11 (d, J = 2.1 Hz, 2 H), 9.26 (t, J = 2.1 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 28.84 (CH), 30.89 (CH_2), 33.58 (CH), 33.94 (CH_2), 35.26 (CH), 39.02 (CH_2), 40.30 (CH_2), 41.69 (CH_2), 43.48 (CH), 75.69 (C), 120.00 (CN), 122.90 (CH), 129.44 (CH), 133.00 (C), 148.72 (C), 160.55 (CO). − $C_{18}H_{17}N_3O_6$ (371.4): calcd. C 58.22, H 4.61, N 11.32; found C 58.18, H 4.69, N 11.28. − The assignment of configuration was confirmed by the crystal structure analysis of **11d**[14].

exo-4-(p-Tolylsulfonyloxy)tricyclo[4.3.1.0^{3,8}]decane-endo-4-carbonitrile (**10c**): To a solution of **10a** (100 mg, 0.56 mmol) in anhydrous pyridine (1 ml) was added *p*-toluenesulfonyl chloride (534 mg, 2.8 mmol) and one drop of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene). The mixture was stirred at 35°C for 3 d. Prolonged reaction and higher temperatures led to partial rearrangement of **10c**. The mixture was diluted with diethyl ether (15 ml) and washed with 10% HCl, aqueous $NaHCO_3$, and water. The organic phase was dried ($MgSO_4$), and concentrated in vacuo. HPLC (LiChrospher 100-5, hexane/ether, 9:1) of the residue afforded 50 mg (50%) of unreacted **10a** and 48 mg (26%) of **10c**, m.p. 112−113°C. − ^{1}H NMR ($CDCl_3$): δ = 1.42−1.51 (m, 2 H), 1.58 (dd, J = 11/3 Hz, 1 H), 1.72−1.80 (m, 2 H), 1.85 (dm, J = 13 Hz, 1 H), 1.94−2.06 (m, 2 H), 2.13 (m, 1 H), 2.28 (m, 1 H), 2.37 (dd, J = 16/2 Hz, 1 H), 2.41 (q, J = 7 Hz, 1 H), 2.47 (s, 3 H), 2.69 (ddd, J = 16/9/2 Hz, 1 H), 3.13 (ddm, J = 10/8 Hz, 1 H), 7.38 and 7.86 (AA′BB′, 4 H). − ^{13}C NMR ($CDCl_3$): δ = 21.96 (CH_3), 27.48 (CH), 30.97 (CH_2), 33.01 (CH), 35.76 (CH_2), 35.81 (CH), 39.99 (CH_2), 41.81 (CH_2), 42.30 (CH_2), 44.30 (CH), 81.36 (C), 119.59 (CN), 128.07 (CH), 130.05 (CH), 134.72 (C), 145.46 (C). − $C_{18}H_{21}NO_3S$ (331.4): calcd. C 65.23, H 6.39, N 4.23; found C 65.18, H 6.31, N 4.35.

The same procedure was applied to (+)-**10a** to give 19% of (+)-**10c**, m.p. 108−109°C, $[\alpha]_D^{25}$ = 32.8 ± 0.1 (c = 1.15 in $CHCl_3$). The enantiomeric purity of this sample is assumed to equal that of (−)-**9**, 95.2 ± 0.2%. Analogous tosylation of [^{18}O]-**10a** afforded 18% of [^{18}O]-**10c**; ^{13}C NMR ($CDCl_3$): δ = 81.295 (C-^{18}O, 49.4 ± 0.3%), 81.336 (C-^{16}O, 50.6 ± 0.3%).

A solution of **10c** (0.15 g, 0.45 mmol) in dioxane/water (3:2, 10 ml) was heated at 50°C for 3 h. The mixture was partitioned between water and diethyl ether. The combined ether solutions were dried ($MgSO_4$) and concentrated in vacuo. HPLC (LiChrospher Si 100-5, pentane/ether, 3:2) afforded 112 mg (75%) of 2-(*p*-tolylsulfonyloxy)tricyclo[3.3.1.1^{3,7}]decane-1-carbonitrile (**14**), m.p. 153−154°C. − ^{1}H NMR ($CDCl_3$): δ = 1.53 (br. d, J = 13 Hz, 1 H), 1.63−1.88 (m, 5 H), 1.90−2.00 (m, 3 H), 2.03−2.13 (m, 2 H), 2.28 (br. d, J = 13 Hz, 1 H), 2.37 (m, 1 H), 2.42 (s, 3 H), 4.69 (br. d, J = 3 Hz, 1 H), 7.34 and 7.86 (AA′BB′, 4 H). − ^{13}C NMR ($CDCl_3$): δ = 21.94 (CH_3), 26.17 (CH), 26.20 (CH), 29.58 (CH_2), 32.49 (CH), 34.82 (CH_2), 35.25 (CH_2), 35.59 (CH_2), 35.67 (C), 40.29 (CH_2), 82.74 (CH), 121.89 (CN), 128.35 (CH), 130.07 (CH), 133.61 (C), 145.3 (C). − $C_{18}H_{21}NO_3S$ (331.4): calcd. C 65.23, H 6.39, N 4.23; found C 65.17, H 6.30, N 4.23. − Tosylation of 2-hydroxytricyclo[3.3.1.1^{3,7}]decane-1-carbonitrile (**15**)[20], as described for **10a** (35°C, 6 d), afforded 53% of **14**, m.p. 153−154°C.

A solution of **10c** (5.08 mg, 15.3 μmol) and 4-methylbenzophenone (3.07 mg, 15.6 μmol; internal standard) in dioxane/water (3:2, 0.5 ml) was heated in a thermostat at 50.1°C. Samples, taken every 10 min, were analyzed by HPLC (LiChrospher Si 100-5-C_{18}, methanol/water, 3:1). First-order kinetics were obeyed up to 4 half-lives. **10c** decreased with k = (6.32 ± 0.17)·10^{-4} s^{-1} while **14** was formed with k = (6.13 ± 0.17)·10^{-4} s^{-1} (97% yield). After ≥ 95% conversion, GC (25 m OV17, 160°C) of the solution indicated the presence of **15** (2.5 ± 0.5%) and of **9** (1.0 ± 0.5%).

The rearrangement of [^{18}O]-**10c** (170 mg, 0.51 mmol) in 60% dioxane (11 ml, 50°C, 3 h) gave rise to [^{18}O]-**14**. − ^{13}C NMR ($CDCl_3$): δ = 82.704 (C-^{18}O, 41.8 ± 0.3%), 82.746 (C-^{16}O, 58.2 ± 0.3%). −Analogously, (+)-**10c** afforded (+)-**14**, m.p. 127−128°C, $[\alpha]_D^{20}$ = 36.2 ± 0.1 (c = 0.74 in $CHCl_3$). The ^{1}H-NMR ($CDCl_3$) spectrum of (+)-**14** was recorded in the presence of an equimolar amount of the chiral shift reagent Eu(hfc)$_3$ [hfc = heptafluoropropylhydroxymethylene-(+)-camphor], which caused "splitting" of the signals for 2-H (δ = 5.59 and 5.69) and for *o*-Ar-H (δ = 8.47 and 8.54). From the ratio of these peaks, (96.8 ± 0.3):(3.2 ± 0.3), the *ee* is estimated as 93.6 ± 0.5%. Reduction of (+)-**14** with sodium in liquid ammonia[18h] led to **15** with *ee* = 86 ± 1% (chiral-phase GC, the predominant enantiomer eluting first). The "second enantiomer" (**15′**) was the major component (*ee* = 26 ± 2%) of the alcohol (ca. 3%) formed by solvolysis of (+)-**10c**.

Rearrangement/Solvolysis of 2-(p-Tolylsulfonyloxy)tricyclo[3.3.1.1^{3,7}]decane-1-carbonitrile (**14**): A solution of [^{18}O]-**14** (41.8% "ester"-^{18}O, as obtained from [^{18}O]-**10c**) in 60% dioxane was heated at 120°C (sealed ampule) for 5 d. Unreacted [^{18}O]-**14** (90−95%) was recovered by HPLC. − ^{13}C NMR ($CDCl_3$): δ = 82.727 (C-^{18}O, 34.6 ± 0.5%), 82.769 (C-^{16}O, 65.4 ± 0.5%). The solvolysis of [^{18}O]-**14** gave ca. 5% of **15** whose mass spectrum (m/z = 177, 179

[M^+]) indicated 1 ± 1% of ^{18}O. − A sample of (+)-**14** [*ee* = 93.6%, as obtained from (+)-**10c**] was treated analogously. The *ee* of recovered (+)-**14** was 90 ± 1% (NMR) and that of **15** was 41 ± 2% (**15**/**15′** = 70.5:29.5).

Rearrangement/Elimination of 4-Hydroxytricyclo[4.3.1.0^{3,8}]decane-4-carbonitriles **10a**, **11a**: To a solution of the cyanohydrins **10a** and **11a** (53:47, 2.60 g, 14.7 mmol) in anhydrous pyridine (3.5 ml) was added at 0°C thionyl chloride (3.2 ml, 43.7 mmol). The mixture was stirred at room temp. for 15 h and was then added to ice-cold water (50 ml). The aqueous dispersion was extracted with diethyl ether. The combined extracts were washed with aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated in vacuo. HPLC (Polygosil 100-5, pentane/ether, 4:1) of the residue led to fractions of **17** (321 mg, 17%) and **15** + **18**. The mixture of alcohols was separated by HPLC (LiChrospher Si 100-5, pentane/ether, 3:2) to give **15**[20] (427 mg, 16%) and **18** (80 mg, 3%). − Tricyclo[4.3.1.0^{3,8}]dec-4-ene-4-carbonitrile (**17**), m.p. 100−101°C. − IR (KBr): $\tilde{\nu}$ = 2205 (CN), 1620 (C=C) cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 1.41 (m, 1 H), 1.48 (dm, *J* = 13.5 Hz, 1 H), 1.53 (dd, *J* = 12.0/3.5 Hz, 1 H), 1.60−1.68 (m, 2 H), 1.72−1.78 (m, 2 H), 1.84 (dddd, *J* = 12.0/9.5/4.8/1.5 Hz, 1 H), 2.33 (m, 1 H), 2.48−2.57 (m, 2 H), 2.87 (t, *J* = 8.2 Hz, 1 H), 7.24 (dd, *J* = 7.9/1.8 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 30.17 (CH_2), 32.95 (CH), 33.58 (CH), 37.84 (CH_2), 38.80 (CH), 39.07 (CH), 41.70 (CH_2), 42.73 (CH_2), 119.64 (C), 121.86 (CH), 155.00 (C). − $C_{11}H_{13}N$ (159.2): calcd. C 82.97, H 8.23, N 8.80; found C 82.86, H 8.20, N 8.72. − *endo*-4-Hydroxytricyclo[4.3.1.0^{3,8}]decane-3-carbonitrile (**18**): m.p. 185−186. − IR (KBr): $\tilde{\nu}$ = 3450 (OH), 2235 (CN) cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 1.37−1.47 (m, 3 H), 1.54 (dd, *J* = 11.5/3.0 Hz, 1 H), 1.68 (dm, *J* = 13.5 Hz, 1 H), 1.77 (dm, *J* = 13.5 Hz, 1 H), 1.88−1.95 (m, 2 H), 2.08 (m, 1 H), 2.22 (br. s, 1 H), 2.27−2.38 (m, 3 H), 2.67 (t, *J* = 8.5 Hz, 1 H), 4.18 (t, *J* = 8.5 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 28.42 (CH), 31.04 (CH_2), 35.90 (CH), 35.96 (CH_2), 37.70 (CH_2), 38.82 (CH_2), 40.96 (CH_2), 42.27 (CH + C), 68.42 (CH), 125.76 (CN). − $C_{11}H_{15}NO$ (177.3): calcd. C 74.54, H 8.53, N 7.90; found C 74.47, H 8.58, N 7.85.

endo-4-(p-Tolylsulfonyloxy)tricyclo[4.3.1.0^{3,8}]decane-exo-4-carbonitrile (**11c**): To a solution of **11a** (100 mg, 0.56 mmol) in anhydrous pyridine (1 ml) was added *p*-toluenesulfonyl chloride (135 mg, 0.71 mmol) and one drop of DBU. The mixture was stirred at 35°C for 12 d to achieve ca. 90% conversion of **11a**. Workup, as described for **10c**, afforded 119 mg (64%) of **11c**, m.p. 102−102°C. − ^1H NMR ($CDCl_3$): δ = 1.39−1.48 (m, 2 H), 1.53 (dd, *J* = 11.2/3.0 Hz, 1 H), 1.67−1.75 (m, 2 H), 1.80 (dm, *J* = 13.5 Hz, 1 H), 1.87 (dm, *J* = 13.9 Hz, 1 H), 2.06 (dm, *J* = 13.9 Hz, 1 H), 2.12−2.24 (m, 2 H), 2.23 (dd, *J* = 15.0/2.0 Hz, 1 H), 2.44 (s, 3 H), 2.50 (q, *J* = 6.3 Hz, 1 H), 2.82 (ddm, *J* = 15.0/8.8 Hz, 1 H), 2.94 (ddm, *J* = 10.0/8.2 Hz, 1 H), 7.35 and 7.86 (AA′BB′, 4 H). − ^{13}C NMR ($CDCl_3$): δ = 21.96 (CH_3), 29.23 (CH), 31.01 (CH_2), 34.20 (CH), 34.33 (CH_2), 35.36 (CH), 39.35 (CH_2), 40.99 (CH_2), 42.14 (CH_2), 45.04 (CH), 80.25 (C), 120.44 (CN), 128.16 (CH), 130.04 (CH), 134.73 (C), 145.44 (C). − $C_{18}H_{21}NO_3S$ (331.4): calcd. C 65.23, H 6.39, N 4.23; found C 65.12, H 6.31, N 4.29.

The same procedure (5 d) was applied to (+)-**11a** to give 49% of (+)-**11c**, $[\alpha]_D^{25}$ = 33.0 ± 0.2 (*c* = 1.09 in $CHCl_3$). The enantiomeric purity of this sample is assumed to equal that of (−)-**9**, 94.4 ± 0.2%. Analogous tosylation (3 d) of [^{18}O]-**10a** afforded 40% of [^{18}O]-**10c**. − ^{13}C NMR ($CDCl_3$): δ = 80.168 (C-^{18}O, 49.0 ± 0.3%), 80.212 (C-^{16}O, 51.0 ± 0.3%).

A solution of **10c** (0.25 g, 0.75 mmol) in dioxane/water (3:2, 15 ml) was heated at 80°C for 19 h. The mixture was partitioned between water and diethyl ether. The combined ether solutions were dried ($MgSO_4$) and concentrated in vacuo. HPLC (LiChrospher Si 100-5, pentane/ether, 4:1 → 3:2) did not separate **15**, **18**, and **22** but afforded 9 mg (7%) of 2-hydroxytricyclo[3.3.1.1^{3,7}]decane-2-carbonitrile (**19**)[25] and 94 mg (38%) of *endo*-4-(*p*-tolylsulfonyloxy)tricyclo[4.3.1.0^{3,8}]decane-3-carbonitrile (**20**), m.p. 144−145°C. − ^1H NMR ($CDCl_3$): δ = 1.38−1.48 (m, 2 H), 1.52 (dd, *J* = 12.0/3.0 Hz, 1 H), 1.63 (dm, *J* = 13.5 Hz, 1 H), 1.68−1.79 (m, 2 H), 1.92 (m, 1 H), 1.97 (ddm, *J* = 13.5/5.5 Hz, 1 H), 2.22 (m, 1 H), 2.34 (dd, *J* = 13.5/3.0 Hz, 1 H), 2.37 (m, 1 H), 2.44 (s, 3 H), 2.53 (dt, *J* = 14.5/9.0 Hz, 1 H), 2.68 (t, *J* = 5.5 Hz, 1 H), 4.83 (t, *J* = 8.5 Hz, 1 H), 7.34 and 7.87 (AA′BB′, 4 H). − ^{13}C NMR ($CDCl_3$): δ = 21.89 (CH_3), 28.55 (CH), 30.94 (CH_2), 35.41 (CH_2), 36.08 (CH), 38.45 (CH_2), 39.27 (CH_2), 40.57 (CH_2), 43.21 (C), 43.37 (CH), 78.43 (CH), 123.61 (CN), 128.40 (CH), 130.01 (CH), 133.64 (C), 145.21 (C). − $C_{18}H_{21}NO_3S$ (331.4): calcd. C 65.23, H 6.39, N 4.23; found C 65.12, H 6.36, N 4.25. − The analogous reaction of [^{18}O]-**11c** gave [^{18}O]-**20**. − ^{13}C NMR ($CDCl_3$): δ = 78.409 (C-^{18}O, 32.4 ± 0.3%), 78.453 (C-^{16}O, 67.6 ± 0.3%).

The volatile products formed from **11c** were analyzed by GC (32 m OV17, 170°C): **9** (3.0%), 2-adamantanone (24.8%), **15**[20] (18.0%), **17** (see above, 14.5%), **18** (see above, 12.7%), and **22**[22] (27.0%). The cyanohydrins **11c** and **19**[25] were found to decompose on this column with formation of **9** and 2-adamantanone, respectively. In an analogous experiment with (+)-**11c**, the peaks of the relevant products were transferred separately to a "chiral-phase" GC column for estimates of the enantiomeric ratios: **15** (*ee* = 92.2 ± 1.8%), **18** (*ee* = 93.6 ± 1.2%), and **22** (*ee* = 91.6 ± 2.0%). The errors of these estimates are affected by partial overlap of the enantiomers.

A solution of **11c** (10.16 mg, 30.6 μmol) and 4-methylbenzophenone (5.87 mg, 29.9 μmol; internal standard) in dioxane/water (3:2, 1.0 ml) was heated in a thermostat at 50.1°C. Samples, taken every day, were analyzed by HPLC (LiChrospher Si 100-5-C_{18}, methanol/water, 3:1). **11c** decreased with $k = (1.90 \pm 0.06) \cdot 10^{-6}\ s^{-1}$ while **20** was formed with $k = (1.06 \pm 0.08) \cdot 10^{-5}\ s^{-1}$ (56% yield). At 79.9°C, **11c** decreased with $k = (6.07 \pm 0.19) \cdot 10^{-5}\ s^{-1}$ while **20** was formed with $k = (3.67 \pm 0.32) \cdot 10^{-5}\ s^{-1}$ (60% yield). Under the same conditions, **20** decreased with $k = (4.7 \pm 0.2) \cdot 10^{-7}\ s^{-1}$ to give **19** and **22** in the ratio of 86:14 (GC).

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