Base-Promoted 1,2-Eliminations from *endo*-2-Bicyclo[2.2.1]heptyl Halides and Arenesulfonates

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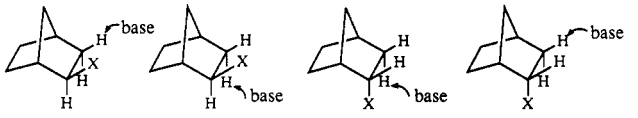
Base–solvent systems that provide clean bimolecular 1,2-elimination from *endo*-2-bicyclo[2.2.1]heptyl halides and arenesulfonates by suppressing competitive solvolysis and nortricyclene-forming 1,3-elimination are developed. The stereochemistries of elimination from *exo*-3-deuterio-*endo*-2-bromobicyclo[2.2.1]heptane (**10**) and *exo*-3-deuterio-*endo*-2-bicyclo[2.2.1]heptyl 2,4,6-triisopropylbenzenesulfonate (**11**) are assessed using these base–solvent systems. The competitive syn-endo and anti-exo-H elimination modes are found to be strongly influenced by base association. However, for dissociated alkoxide bases, the elimination stereochemistry is unaffected by changes in leaving group from halide to arenesulfonate, in base strength, and in base size.

Introduction

Base-promoted elimination from *exo*-2-bicyclo[2.2.1]-heptyl halides and arenesulfonates have been studied rather extensively.[3-7] The reactions exhibit a clear preference for syn-exo over anti-endo-H elimination (**1** and **2**, respectively). In contrast, reports of the elimination



1 (syn-exo) **2** (anti-endo-H) **3** (syn-endo) **4** (anti-exo-H)

stereochemistry for *endo*-2-bicyclo[2.2.1]heptyl halides and arenesulfonates are scarce. Stille and co-workers[8] estimated a 14:86 preference for syn-endo and anti-exo-H elimination (**3** and **4**, respectively) in dehydrochlorination of *exo*-2,3-dideuterio-*endo*-2-chlorobicyclo[2.2.1]heptane promoted by potassium 2-methyl-2-pentoxide in 2-methyl-2-pentanol at 130 °C. The stereochemistry of base-promoted 1,2-elimination from *endo*-2-bicyclo-[2.2.1]heptyl arenesulfonates has not been reported.

An important factor in determining the elimination stereochemistry for 2-substituted bicyclo[2.2.1]heptanes is the ground-state geometry. An antiperiplanar orientation of the β-hydrogen and the leaving group is prohibited, but a synperiplanar arrangement is already present.[3] DePuy and Bishop[9] proposed that E2 reactions will show maximum rates when the dihedral angle between the C_β–H and C_α–X bonds is 180° or 0°, with the former having the higher maximum. Theoretical studies also reveal a preference order for bimolecular 1,2-eliminations of antiperiplanar > synperiplanar > nonplanar.[10] However, when this theory is applied to *endo*-2-chlorobicyclo[2.2.1]heptane, the predominance of anti-exo-H over syn-exo elimination observed by Stille and co-workers[8] cannot be rationalized.

The stereochemistry of elimination from *exo*-2-bicyclo-[2.2.1]heptyl halides and arenesulfonates has been attributed to a preference for syn-exo over anti-endo-H elimination that results from greater steric hindrance for attack at the endo hydrogen.[5] This steric theory[5] would also seem to explain the preference for anti-exo-H over syn-endo elimination in base-promoted dehydrochlorination of *endo*-2-chlorobicyclo[2.2.1]heptane.[8]

The two factors mentioned above are both structural features of the elimination reaction substrates. The identity of the base–solvent system should also be important. A striking change in the propensity for competitive syn- and anti-elimination pathways may take place when an associated base (ion pairs and/or aggregates of ion pairs) is replaced with the corresponding dissociated base.[11,12] For example, in competitive syn and anti elimination from *trans*-2-phenylcyclopentyl tosylate, the relative percentage of syn-elimination product 1-phenylcyclopentene drops from 89% when the base–solvent system was *t*-BuOK–*t*-BuOH (associated base) to 30% when an equivalent of dicyclohexano-18-crown-6 was added to produce the dissociated base.[13] A similar effect has been noted for *exo*-2-bicyclo[2.2.1]heptyl tosylate.[6] Therefore the relative propensities for syn-endo and anti-exo-H elimination from *endo*-2-bicyclo[2.2.1]heptyl halides and arenesulfonates may be influenced by the nature of the base–solvent system.

In this study, base-promoted 1,2-eliminations from *endo*-2-bicyclo[2.2.1]heptyl halides and arenesulfonates have been investigated to determine the factors that control the stereochemical course of these eliminations.

Results and Discussion

Base–Solvent Systems for Clean 1,2-Eliminations. Two problems have been encountered in previous investigations of base-promoted eliminations from *endo*-2-bicyclo[2.2.1]heptyl halides[8] and arenesulfonates.[15] One is competing 1,3-elimination to give nortricyclene and the other is a marked tendency for unimolecular processes (E1 and S_N1) to take place. In general, only low yields of bicyclo[2.2.1]hept-2-ene are obtained.[3,8,15]

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Table I. Elimination Products from Reactions of ROK with *endo*-2-Bromobicyclo[2.2.1]heptane

entry	RO^- of ROK	solvent	18-crown-6 present[a]	temp, °C[b]	hydrocarbon yield, %[c]	relative proportion of nortricyclene, %
1	*tert*-butoxide	*p*-cymene	no	100	0.8	65.2
2	*tert*-butoxide	*p*-cymene	yes	80	82.8	0.8
3	2,3-lutidine	triglyme	no	100	ND[d]	
4	*tert*-butoxide	triglyme	no	100	81.8	0.2
5	*tert*-butoxide	triglyme	yes	80	83.6	0.2
6	isopropoxide	triglyme	yes	80	64.4	0.5
7	tri-2-norbornylmethoxide	triglyme	yes	80	73.3	0.2
8	*tert*-butoxide (29.2)[e]	DMSO	no	80	84.8	0.3
9	*n*-propoxide (28.0)[e]	DMSO	no	80	72.5	0.1
10	ethoxide (27.4)[e]	DMSO	no	80	66.7	0.1
11	trifluoroethoxide (21.6)[e]	DMSO	no	80	25.5	1.0
12	phenoxide (18.0)[e]	DMSO	no	80	9.7	1.7
13	*tert*-butoxide[f]	*t*-BuOH	no	100	ND[d]	
14	*tert*-butoxide[f]	*t*-BuOH	yes	80	14.1	6.0

[a] Equimolar 18-crown-6 and ROK. [b] Reactions at 100 and 80 °C were conducted for 3.0 and 5.0 h, respectively. [c] Combined yield of bicyclo[2.2.1]heptene and nortricyclene. [d] Not detectable. [e] pK_a of ROH in DMSO.[25] [f] Reaction conducted in a stoppered vessel and product extracted into pentane.

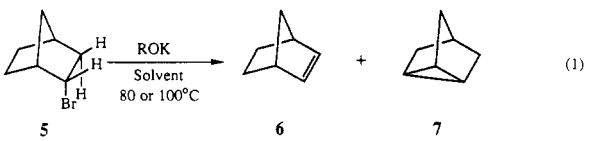
Table II. Elimination Products from Reactions of *t*-BuOK with *endo*-2-X-bicyclo[2.2.1]heptanes

entry	X	solvent	18-crown-6 present[a]	temp, °C[b]	hydrocarbon yield, %[c]	relative proportion of nortricyclene, %
1	I	*p*-cymene	no	100	3.5	33.3
2	I	*p*-cymene	yes	80	65.3	1.4
3	I	triglyme	no	100	78.5	0.7
4	I	triglyme	yes	80	82.0	0.5
5	I	DMSO	no	80	88.7	0.7
6	OTs	triglyme	no	100	1.7	ND[d]
7	OTs	triglyme	yes	80	11.5	ND[d]
8	OTs	DMSO	no	80	13.3	ND[d]
9	OTibs[e]	triglyme	yes	80	19.2	ND[d]
10[f]	OTibs[e]	triglyme	yes	80	16.2	ND[d]
11	OTibs[e]	DMSO	no	80	24.2	ND[d]

[a] Equimolar 18-crown-6 and *t*-BuOK. [b] Reactions at 100 and 80 °C were conducted for 3.0 and 5.0 h, respectively. [c] Combined yields of bicyclo[2.2.1]hept-2-ene and nortricyclene. [d] Not detected. [e] 2,4,6-Triisopropylbenzenesulfonate. [f] The base was tri-2-norbornylmethoxide.

An appropriate base–solvent system for inducing clean bimolecular 1,2-elimination from *endo*-2-bicyclo[2.2.1]-heptyl halides and arenesulfonates was suggested in a reported study of eliminations from *endo*-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl tosylate (bornyl tosylate),[16] a substrate prone to undergo solvolytic elimination producing rearranged hydrocarbon products.[17] Reactions conducted with *t*-BuOK in benzene in the presence of 18-crown-6 gave hydrocarbon products consisting of 95% or greater of 1,7,7-trimethylbicyclo[2.2.1]hept-2-ene,[16] the product of 1,2-elimination.

Reactions of *endo*-2-bromobicyclo[2.2.1]heptane (**5**) with several base–solvent combinations were conducted to determine systems that would provide clean 1,2-elimination (eq 1). Use of the high boiling solvents *p*-cymene (4-isopropyltoluene), triglyme (triethylene glycol dimethyl ether), and DMSO (dimethyl sulfoxide) allowed a slow sweep of nitrogen to carry the hydrocarbon products bicyclo[2.2.1]hept-2-ene (**6**) and nortricyclene (**7**) from the reaction vessel into a chilled receiver for analysis by gas chromatography. Results are presented in Table I.



5 6 7 (1)

Reaction of **5** with *t*-BuOK in *p*-cymeme (associated base) gave only a low yield of hydrocarbon products of which nortricyclene was the major constituent (entry 1). On the other hand, with 18-crown-6 present to produce the dissociated base (free alkoxide or solvent-separated ion pairs), the reaction yielded 82.1% of the 1,2-elimination product **6** and only 0.7% of nortricyclene (entry 2).

In the more polar solvent triglyme there was no evidence for solvolytic elimination (entry 3). Nearly identical results were obtained for reactions of **5** with *t*-BuOK in triglyme in the absence and presence of 18-crown-6 (entries 4 and 5, respectively), which suggests that the polyether solvent is also effective in producing the dissociated base species. Reactions of **5** with the somewhat weaker base *i*-PrOK gave a slightly enhanced proportion of nortricyclene (entry 6). Clean 1,2-elimination was observed with the sterically demanding base tri-2-norbornylmethoxide [tris(*exo*-2-bicyclo[2.2.1]heptyl)methoxide] (entry 7).

Although *t*-BuOK in DMSO gave some product from solvolytic elimination of bornyl tosylate,[16] it produces clean 1,2-elimination from **5** (entry 8). Due to the high polarity of the solvent, crown ether is not needed to produce the dissociated alkoxide bases in DMSO. As the strength of the oxyanion base is decreased, the hydrocarbon yield diminished and the relative proportion of nortricyclene increased (compare entries 8–12).

For comparison with protic solvent of low polarity, reactions of **5** with *t*-BuOK in *t*-BuOH in the absence and presence of 18-crown-6 were conducted (entries 13 and 14, respectively). In these cases, the reactions were conducted in sealed vessels. Extraction with pentane gave no detectable hydrocarbon products in the absence of crown ether. For reaction in the presence of 18-crown-6, the hydrocarbon yield was low and the proportion of nortricyclene was very significant (entry 14). These results show

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that dissociated alkoxide bases in the aprotic solvents of *p*-cymene, triglyme, and DMSO are much more effective in producing clean 1,2-elimination than the tertiary alkoxide in tertiary alcohol combinations that have been used previously to promote eliminations from *endo*-2-bicyclo[2.2.1]heptyl derivatives.[8,15]

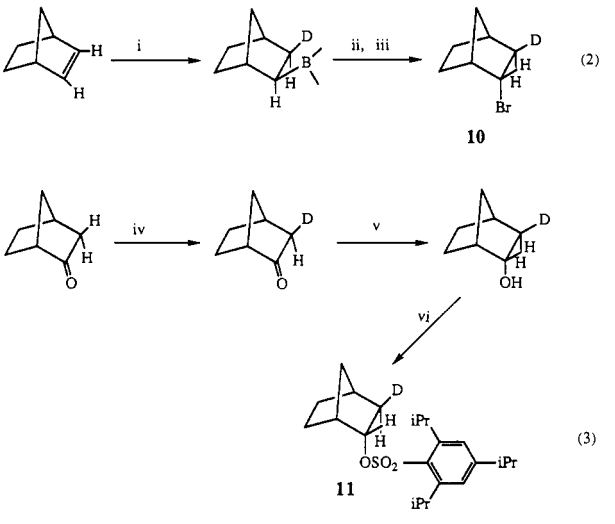
Results recorded in Table II demonstrate that dissociated *tert*-butoxide in *p*-cymene, triglyme, and DMSO (entries 2, 4, and 5) also give clean 1,2-eliminations from *endo*-2-iodobicyclo[2.2.1]heptane, a substrate that should have an even higher propensity for solvolytic elimination than the corresponding bromide **5**.

In extending the studies to *endo*-2-bicyclo[2.2.1]heptyl arenesulfonates, it was noted that Sonnenberg and Stille[15] reported only 5–15% yields of bicyclo[2.2.1]hept-2-ene in reactions of *endo*-2-bicyclo[2.2.1]heptyl brosylate with 2-methyl-2-pentoxide in 2-methyl-2-pentanol at 100–120 °C with a ratio of bicyclo[2.2.1]hept-2-ene to nortricyclene of 94:6. Results from elimination reactions from *endo*-2-bicyclo[2.2.1]heptyl tosylate (**8**) and *endo*-2-bicyclo[2.2.1]heptyl 2,4,6-triisopropylbenzenesulfonate (**9**) promoted by tertiary alkoxide bases in triglyme and DMSO are presented in Table II (entries 6–11). In contrast with the results obtained in elimination from the endo bromide **5** (Table I, entries 4 and 5), reactions of the endo tosylate **8** with *t*-BuOK in triglyme gave a much higher yield of bicyclo[2.2.1]hept-2-ene when 18-crown-6 was present (Table II, entries 6 and 7). When *t*-BuOK in DMSO was utilized (entry 8), the yield of 1,2-elimination product was enhanced even further. For none of these three reactions could nortricyclene be detected.

Anticipating that the low yields of 1,2-elimination product (11–13%) obtained in reaction of *endo*-tosylate **8** might be due to competitive nucleophilic attack of the oxyanion at sulfonyl sulfur, eliminations from the corresponding 2,4,6-triisopropylbenzenesulfonate **9** were studied. In **9** nucleophilic attack of the oxyanion at the sulfur of the sulfonyl group should be sterically retarded compared with **8**. In agreement, the yield of bicyclo[2.2.1]-hept-2-ene increased to 19 and 24% for reactions of the *endo*-2,4,6-triisopropylbenzenesulfonate **9** with dissociated *tert*-butoxide in triglyme and in DMSO (entries 9 and 11, respectively). Reaction of **9** with the highly ramified dissociated base tri-2-norbornylmethoxide in triglyme produced a 16% yield of the 1,2-elimination product (entry 10). In none of these three reactions was any nortricyclene detected.

Synthesis of Specifically Deuterated Substrates. The substrates must be free from the corresponding exo isomer and deuterium should be quantitatively and stereospecifically incorporated at either the 3-exo or 3-endo position to study competitive syn and anti elimination reactions in base-promoted, 1,2-eliminations from *endo*-2-bicyclo[2.2.1]heptyl halides and arenesulfonates. Stereospecifically labeled *endo*-2-bromo-*exo*-3-deuterobicyclo[2.2.1]heptane (**10**) and *exo*-3-deuterio-*endo*-2-bicyclo[2.2.1]heptyl 2,4,6-triisopropylbenzenesulfonate (**11**) were synthesized as shown in eq 2 and 3.

The *exo*-3-deuterio-*endo*-2-bromobicyclo[2.2.1]heptane (**10**) was prepared by adaptation of the methods of Brown and Lane[18] and Brown, De Lue, Kabalka, and Hedgecock.[19] The crude product was contaminated with a fair amount of the exo isomer, which was removed by partial hydrolysis in aqueous methanol to give the pure endo bromide as



(2)

10

(3)

11

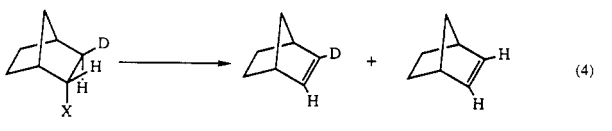
i) $LiAlD_4$-BF_3 etherate, THF. ii) Br_2, THF. iii) MeONa - aq. MeOH.

iv) NaOD - D_2O. v) $LiAlH(OMe)_3$, THF. vi) 2,4,6-$(iPr)_3C_6H_2SO_2Cl$, pyridine.

verified by gas chromatography. Since deuterioboration is highly stereospecific[20] and conversion of the organoborane into the bromide does not affect carbon-3,[18,19,21] the extent of deuterium incorporation at the 3-exo position should be controlled by the level of deuterium present in the sodium borodeuteride (>98%) from which the deuterioborane is generated. As expected, the complicated multiplet for the 2-exo proton in the ^1H NMR spectrum of *endo*-2-bromobicyclo[2.2.1]heptane collapsed to a narrowed singlet for the exo-3-deuterated compound **10**.

exo-3-Deuteriobicyclo[2.2.1]heptan-2-one was prepared by base-catalyzed deuterium exchange.[22] By mass spectrometry the deuterated ketone was shown to be contaminated with 2.5% of undeuterated compound but free of dideuterated product. Reduction with $LiAlH(OMe)_3$[23] gave *exo*-3-deuterio-*endo*-2-bicyclo[2.2.1]heptanol, which was converted into *exo*-3-deuterio-*endo*-2-bicyclo[2.2.1]heptyl 2,4,6-triisopropylbenzenesulfonate (**11**) by reaction with the appropriate arenesulfonyl chloride. As before the complicated multiplet for the 2-exo proton in the ^1H NMR spectrum of *endo*-2-bicyclo[2.2.1]heptyl 2,4,6-triisopropylbenzenesulfonate collapsed to a narrowed singlet for the exo-3-deuterated compound **11**.

Stereochemistry of Elimination from *endo*-2-Bicyclo[2.2.1]heptyl Bromide (10) and *endo*-2-Bicyclo-[2.2.1]heptyl 2,4,6-Triisopropylbenzenesulfonate (11). For base-promoted eliminations from **10** and **11**, syn-endo elimination will yield 2-deuteriobicyclo[2.2.1]hept-2-ene (**12**) and anti-exo-H elimination will produce bicyclo-[2.2.1]hept-2-ene (**13**) (eq 4). The anti-exo-H elimination



(4)

10 X=Br-
11 X=2,4,6(iPr)$_3$C$_6$H$_2$SO$_3$-

12 (from syn-endo elimination)

13 (from anti-exo-H elimination)

mode is retarded by a primary deuterium isotope effect. Therefore the ratio of products **12** and **13** does not directly reflect the relative propensities for syn-endo and anti-

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Table III. Products of 1,2-Elimination from Reactions of ROK with *exo*-3-Deuterio-*endo*-2-X-bicyclo[2.2.1]heptane

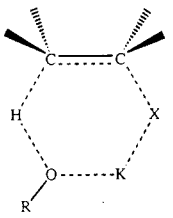
entry	X	RO^- of ROK	solvent	18-crown-6 present[a]	temp, °C	time, h	relative proportion of 2-deuteriobicyclo[2.2.1]hept-2-ene, %
1	Br	*tert*-butoxide	triglyme	no	100	7.0	71.7
2	Br	*tert*-butoxide	triglyme	yes	80	3.0	13.4
3	Br	isopropoxide	triglyme	yes	80	3.0	17.9
4	Br	tri-2-norbornylmethoxide	triglyme	yes	80	3.0	15.1
5	Br	*tert*-butoxide	*p*-cymene	yes	80	3.0	19.1
6	Br	*tert*-butoxide (29.2)[b]	DMSO	no	80	3.0	13.0
7	Br	*n*-propoxide (28.0)[b]	DMSO	no	80	3.0	13.5
8	Br	ethoxide (27.4)[b]	DMSO	no	80	3.0	14.8
9	Br	2,2,2-trifluoroethoxide (21.6)[b]	DMSO	no	80	3.0	10.7
10	OTibs[c]	*tert*-butoxide	triglyme	no	100	7.0	31.8
11	OTibs[c]	*tert*-butoxide	triglyme	yes	80	5.0	9.0
12	OTibs[c]	tri-2-norbornylmethoxide	triglyme	yes	80	5.0	7.0

[a] Equimolar 18-crown-6 and ROK. [b] pK_a of ROH in DMSO.[25] [c] 2,4,6-Triisopropylbenzenesulfonate.

exo-H elimination. In this study no effort was made to correct for the deuterium isotope effect.

With endo bromide **10** and endo arenesulfonate **11**, the effects of such variables as base association, base size, base strength, and the nature of the leaving group upon competitive syn-endo and anti-exo-H elimination pathways were assessed. Since reactions conducted with the undeuterated substrates demonstrated that much higher yields of 1,2-elimination products could be obtained from the bromide (Table I) than the arenesulfonate ester (Table II), most investigations of elimination stereochemistry were conducted with the deuterated bromide **10**. Results are recorded in Table III.

Effects of Base Association and Leaving Group Identity. For both the bromide **10** and the arenesulfonate **11**, addition of 18-crown-6 markedly reduces the amount of syn-endo elimination product formed by reaction with *t*-BuOK in triglyme (compare entries 1 and 2 and entries 10 and 11 in Table III). In the absence of 18-crown-6, interactions of the associated base with the leaving group as depicted in **14** lowers the energy of the syn-endo transition states.[24] Since such interactions are spatially impossible for the anti-endo-H transition states, the relative proportions of product arising from the syn-endo elimination mode are artificially enhanced by base association. In the presence of 18-crown-6, the potassium ion is coordinated by the crown ether, which produces the dissociated base species. Therefore both elimination modes utilize the same (dissociated) base species.



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The effect of 18-crown-6 is particularly striking for bromide **10** as the proportion of 2-deuteriobicyclo[2.2.1]-hept-2-ene (**12**) plummets from 72% (predominant syn-endo elimination) in the absence of crown ether to 13% (predominant anti-exo-H elimination) when the crown ether is present. Presumably the somewhat smaller change observed in the proportion of **12** for elimination from the arenesulfonate **11** (32% and 9% in the presence and absence of 18-crown-6, respectively) results from greater charge dispersal within the arenesulfonate leaving group, which diminishes the interaction between the leaving group and the associated base.

Once the complicating influence of base association is removed, the elimination stereochemistries for bromide **10** and arenesulfonate **11** are nearly the same, which suggests that the timing of bond breaking and bond breaking in the competitive elimination transition states are nearly identical for these two leaving groups. If one assumes a deuterium isotope effect of 3.0 for the anti-exo-H eliminations from **10** and **11** promoted by dissociated *tert*-butoxide, the ratios of anti-exo-H/syn-endo elimination are calculated to be 19 and 30, respectively.

For reactions of bromide **10** with *t*-BuOK in DMSO in the absence of 18-crown-6, the proportion of deuterated alkene **12** was the same as that observed in triglyme with the crown ether present (entries 2 and 6, Table III). With the base–solvent system of *t*-BuOK and 18-crown-6 in *p*-cymene, the proportion of **12** was slightly enhanced, which may indicate that 1 equiv of the crown ether is insufficient to totally disrupt the base association in a solvent of such low polarity.

Effect of Base Strength. The effect of base strength upon the stereochemistry of elimination from bromide **10** was examined for a series of dissociated alkoxide ion bases in DMSO (entries 6–9, Table III). For oxyanions with base strengths varying by nearly 8 pK units,[25] the proportion of deuterated alkene **12** was in the range of 11–15% with no discernible trends. Hence it appears that base strength variation has no significant influence upon the two competitive elimination pathways.

Effect of Base Size. There is manifold evidence that reactions which involve the exo faces of bicyclo[2.2.1]-heptane systems are overwhelmingly faster than those which require approach from the endo direction. For example, base-catalyzed deuterium exchange of the 3-exo proton of bicyclo[2.2.1]heptan-2-one is 715 times faster than that of the 3-endo proton.[22] A >5000:1 preference for exo over endo hydration of bicyclo[2.2.1]heptyl carbocations is also reported.[24] It has been proposed by Brown and Liu[5] that preferential attack at the less hindered 3-exo proton is responsible for the preferred anti-exo-H dehydrochlorination of *exo*-2,3-dideuterio-*endo*-2-chlorobicyclo[2.2.1]heptane. If this were the case, the change from a dissociated alkoxide ion base of modest dimensions to a highly ramified dissociated base would be expected to further accentuate the preference for anti-exo-H over syn-endo eliminations from bromide **10** and arenesulfonate **11**.

Reactions of bromide **10** with dissociated isopropoxide, *tert*-butoxide, and tri-2-norbornylmethoxide in triglyme

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gave relative proportions of deuterated alkene **12** in the range of 13–18% with no apparent relationship between the proportion of **12** and the base size (entries 2–4, Table III). For reactions of arenesulfonate **11** with *tert*-butoxide and tri-2-norbornylmethoxide in triglyme, there was a small decrease in the proportion of **12** when the highly ramified tertiary alkoxide ion base was employed (entries 11 and 12, Table III). However, when taken together the results for **10** and **11** fail to make a convincing case for the postulated steric control of stereochemistry for elimination from *endo*-2-bicyclo[2.2.1]heptyl compounds.

Conclusions

Association of potassium alkoxide bases strongly influences the competition between syn-endo and anti-exo-H elimination from *endo*-2-bicyclo[2.2.1]heptyl bromide and *endo*-2-bicyclo[2.2.1]heptyl 2,4,6-triisopropylbenzenesulfonate by enhancing the proportion of the syn-endo elimination product. For dissociated alkoxide ion bases, anti-exo-H elimination is strongly favored over the competitive syn-endo elimination mode and the elimination stereochemistry is found to be unaffected by changes in leaving group from bromide to arenesulfonate, in base strength, and in base size.

Experimental Section

General Methods. All melting points and boiling points are uncorrected. ^{1}H NMR spectra were recorded on the Varian EM-360 and Varian XL-100 instruments (with $CDCl_3$ as the solvent and TMS as the internal standard). For analysis of hydrocarbon reaction products, an Antek Model 400 gas chromatograph was utilized. GC-MS was conducted with a Varian Aerograph Series 2700 gas chromatograph interfaced with a Varian MAT-311 mass spectrometer and a Varian 620-I data system. *endo*-Bicyclo-[2.2.1]heptan-2-ol, bicyclo[2.2.1]hept-2-ene, 2,4,6-triisopropylbenzenesulfonyl chloride, 18-crown-6, 40% NaOD in D_2O (99+ atom % D), $NaBD_4$ (98 atom % D), and KH (22% dispersion in mineral oil) were purchased from Aldrich and used as received. The *endo*-2-iodobicyclo[2.2.1]heptane was prepared by the reported method.[19]

***endo*-2-Bromobicyclo[2.2.1]heptane.** Hydroboration of bicyclo[2.2.1]hept-2-ene was accomplished by following the procedure and scale described for the synthesis of *endo*-2-iodobicyclo[2.2.1]heptane.[19] The excess hydride was quenched by addition of 2 mL of MeOH. The flask and two pressure-equilibrating dropping funnels were wrapped with aluminum foil. One dropping funnel was charged with 12 mL (0.22 mol) of bromine and the other funnel with 45 mL of 4.75 M MeONa–MeOH. The bromine and methoxide solutions were added simultaneously during 45 min. The reaction mixture temperature was maintained at 5–10 °C during the addition. The excess bromine was destroyed by addition of 10–15 mL of saturated aqueous $Na_2S_2O_3$ solution. Extraction with pentane and distillation of the extract gave a mixture of *endo*- and *exo*-2-bromobicyclo[2.2.1]heptane from which the exo isomer was selectively hydrolyzed by reflux with 5 g of Na_2CO_3 in 200 mL of 80% aqueous MeOH. This partial hydrolysis was repeated, if necessary. Extraction with pentane, washing the pentane extract with H_2O, and distillation gave 3–5 g of pure *endo*-2-bromobicyclo[2.2.1]heptane with bp 69–70 °C/15 Torr. Absence of the exo isomer was demonstrated by ^{1}H NMR. The exo-2-proton of *endo*-2-bromobicyclo[2.2.1]heptane appears at δ 4.32, whereas the endo-2-proton of the exo isomer was observed at δ 3.91. Product purity >99.5% was demonstrated by GC ($^1/_8$ in. × 5 ft column of 20% SE-30 on Chromosorb P).

***exo*-3-Deuterio-*endo*-2-bromobicyclo[2.2.1]heptane (10).** Bicyclo[2.2.1]hep-2-ene was deuteroborated in a similar manner using externally generated diborane-d_6 (from $NaBD_4$ and BF_3·Et_2O). The remainder of the procedure was identical with that described above. Pure *exo*-3-deuterio-*endo*-2-bromobicyclo-[2.2.1]heptane (bp 68–71 °C/16 Torr) was obtained in 15–27% yield. (Only one bicyclo[2.2.1]heptyl group is converted to the alkyl bromide[18].) ^{1}H NMR ($CDCl_3$): δ 1.00–2.10 (m, 7 H), 2.21 (s, 1 H), 2.43 (s, 1 H), 4.30 (s, 1 H).

***exo*-3-Deuterio-*endo*-bicyclo[2.2.1]heptan-2-ol.** Bicyclo-[2.2.1]heptan-2-one (10.0 g) was dissolved in 500 mL of a dioxane–deuterium oxide solution (2:1) that contained 1.90 g of 40% NaOD in D_2O.[22] After being stirred for exactly 2.5 h at room temperature, the reaction solution was poured into a mixture of 250 mL of 0.25 M HNO_3 and 250 mL of pentane. The pentane layer was separated, washed twice with H_2O, and dried over $MgSO_4$. The extract was carefully concentrated using an efficient fractionating column. GC-MS analysis showed that the *exo*-3-deuteriobicyclo[2.2.1]heptan-2-one was contaminated with 2.5% of undeuterated bicyclo[2.2.1]heptan-2-one but was free of dideuterated product. The crude product (4.20 g) was reduced with $LiAlH(OMe)_3$ according to the procedure by Brown and Deck.[23] The crude *exo*-3-deuterio-*endo*-2-bicyclo[2.2.1]heptanol (3.0 g, 70%) was used to prepare the sulfonate ester without further purification.

***exo*-3-Deuterio-*endo*-2-bicyclo[2.2.1]heptyl Triisopropylbenzenesulfonate (11).** *exo*-3-Deuterio-*endo*-2-bicyclo-[2.2.1]heptanol (3.0 g) was treated with 10% excess of 2,4,6-triisopropylbenzenesulfonyl chloride in pyridine.[27] The mixture was kept at 5 °C for 3 days. Usual workup and purification produced 5.6 g (56%) of fluffy white solid (mp 140–141 °C). ^{1}H NMR ($CDCl_3$): δ 1.26 (d, J = 7.0 Hz, 18 H), 1.10–2.70 (m, 10 H), 2.96 (pen, J = 7.0 Hz, 1 H), 4.27 (pen, 2 H), 4.90 (s, 1 H), 7.25 (s, 2 H).

***endo*-2-Bicyclo[2.2.1]heptyl Arenesulfonates.** *endo*-Bicyclo[2.2.1]heptan-2-ol was converted to arenesulfonates by similar procedures.[27] *endo*-2-Bicyclo[2.2.1]heptyl tosylate was obtained in 88% yield after 2 days at 0 °C, mp 33–34 °C. ^{1}H NMR ($CDCl_3$): δ 1.00–1.65 (m, 6 H), 1.75–2.00 (m, 2 H), 2.17 (s, 1 H), 2.34 (s, 1 H), 2.45 (s, 3 H), 4.70–4.85 (m, 1 H), 7.33 (d, 2 H), 7.79 (d, 2 H). Anal. Calcd for $C_{14}H_{18}O_3S$: C, 63.13; H, 6.82. Found: C, 63.31; H, 7.02. *endo*-2-Bicyclo[2.2.1]heptyl 2,4,6-triisopropylbenzenesulfonate was obtained in 60% yield after 5 days at 0 °C, mp 148–149 °C. ^{1}H NMR ($CDCl_3$): δ 1.15–1.75 (m, 24 H), 1.85–2.05 (m, 2 H), 2.20 (s, 1 H), 2.51 (s, 1 H), 2.91 (pen, 1 H), 4.17 (pen, 2 H), 4.75–4.90 (m, 1 H), 7.17 (s, 2 H). Anal. Calcd for $C_{22}H_{34}O_3S$: C, 69.80; H, 9.06. Found: C, 70.09; H, 9.29.

Preparation of Base–Solvent Solutions. KH (0.815 g of 22% dispersion in mineral oil, 2.5 mmol) was weighed into a glass tube (180 mm × 18 mm) with a 19/38 glass joint. The tube was stoppered with a rubber septum and continuously flushed with dry nitrogen, which entered and exited through syringe needles. After removal of the protecting mineral oil by repeated washings with dry pentane using a syringe, the KH was dried in the stream of dry nitrogen and 10.0 mL of purified solvent was added with a syringe. Addition of 2.5 mmol of the appropriate alcohol and an equimolar amount of 18-crown-6 (if needed) produced a 0.25 M solution of the potassium alkoxide in the solvent. The base–solvent solution was allowed to stand for 30–60 min before addition of the elimination substrate.

Isolation of Hydrocarbon Products from Elimination Reactions. A. Nitrogen Gas Sweep Technique.[28] An appropriate amount of the *endo*-2-bicyclo[2.2.1]heptyl halide or arenesulfonate was added to the prepared base–solvent solution to give a 0.125 M concentration. The glass tube was connected to an apparatus by which a slow stream (about 20 mL/min) of dry nitrogen was continuously bubbled through the reaction solution. The sweeping nitrogen subsequently passed through a connection at the top of the glass tube and into a glass cold trap. The bottom of the glass reaction tube and glass cold trap were immersed in a constant temperature bath and a Dewar flask filled with dry ice–acetone, respectively. After the desired time period, the cold trap was disconnected and a small amount of pentane and a weighed amount of cyclohexane (internal standard) were added. The pentane solution was transferred to a sample vial and kept in a freezer until GC analysis.

B. Extraction Technique. For reactions conducted in *t*-BuOH, the base–solvent solution was prepared as before. After addition of the *endo*-2-bicyclo[2.2.1]heptyl halide or arene-

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(28) When bicyclo[2.2.1]hept-2-ene was added to the base–solvent solution in a control experiment, it was quantitatively recovered with the nitrogen gas sweep technique.

sulfonate, the glass tube was tightly stoppered with a glass stopper and the lower portion of the reaction tube was immersed in a temperature bath. After the desired time period, the reaction mixture was poured into water. A weighed amount of cyclohexene (internal standard) was added and the mixture was extracted with pentane. As before, the pentane solution was kept in a freezer until analysis.

Gas Chromatographic Analysis of Hydrocarbon Products. The pentane solutions were analyzed on a $^1/_8$ in. × 10 ft column of 20% SE-30 on Chromosorb P operated at 70–80 °C, which gave satisfactory separation of cyclohexene (internal standard), bicyclo[2.2.1]hept-2-ene (**6**), and nortricyclene (**7**). Relative peak areas were determined by integration and were corrected for molar response, if necessary. The molar responses of cyclohexene to **6** and **7** were both 0.973. Relative peak areas from 2–5 chromatograms were averaged.

Deuterium Analysis. The pentane solutions of hydrocarbon products were injected onto a $^1/_8$ in. × 10 ft column of 20% SE-30 on Chromosorb P operated at an appropriate temperature and the bicyclo[2.2.1]hept-2-ene peak was introduced into the mass spectrometer to determine the deuterium content of the bicyclo[2.2.1]hept-2-ene obtained in elimination from the deuterated bromide **10** and arenesulfonate **11**. Relative intensities of the M^+ and $(M + 1)^+$ peaks from 10–40 mass spectra were averaged as a data set. Several (2–5) data sets were averaged in the determination of deuterium content for which it was assumed that relative intensities of M^+ and $(M + 1)^+$ peaks are the same for bicyclo[2.2.1]hept-2-ene and 2-deuterobicyclo[2.2.1]hept-2-ene.

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The Effect of Conjugation on Hydrogen Iodide and Hydrogen Fluoride Elimination from 1-(*F*-Alkyl)-2-iodoalkenes: From 5-(*F*-Butyl)-4-iodo-1-pentene to 5-(*F*-Butyl)pentadienes and Further to 1-Fluoro-1-(*F*-propyl)-1,3,5-hexatrienes[1]

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Dehydrohalogenation of homologous 1-(*F*-butyl)-2-iodoalkenes, [$R_FCH_2CHI(CH_2)_nCH{=}CH_2$ (n = 2–4)] under defined conditions gave (*F*-butyl)-substituted alkadienes [$R_FCH{=}CH(CH_2)_nCH{=}CH_2$] in high yield. By contrast, $R_FCH_2CHICH_2CH{=}CH_2$ (**1**) gave *E,Z* isomers of 1-fluoro-1-(*F*-propyl)-1,3,5-hexatriene (**3**) in 95% yield by way of isomeric 5-(*F*-butyl)pentadienes (**2** and **4**). Trapping and identification of organic products by GC/MS and FT/IR gave rate of conversion of **1** to intermediate dienes **2** and **4** and of dienes to triene isomers **3**. Samples were separately titrated for HI and HF. Kinetic order of reactions and rates by these independent methods were concordant. IR, UV, and mass spectra were useful in identifying separated GC peaks, and NMR spectra of isolated triene **3** confirmed its structure. Conjugated diene 3*E*-**2** was the major intermediate on the path from **1** to **3**; rate of disappearance of **2** and formation of **3** were almost identical. Surprisingly, elimination of HF from **2**, and its unconjugated isomer 4*E*-**4**, occurred at similar rates. Elimination from 4*E*-**4** may have involved a *concerted* loss of proton and fluoride ion, with a shift of the double bond to give the all-conjugated triene **3**. Novel stereochemistry in these elimination reactions, mass spectrum fragmentation patterns, and other spectroscopic results are reported.

Introduction

Chemistry of perfluoroalkyl-substituted compounds is not well-known and frequently cannot be predicted from analogous hydrocarbon compounds. The integrity of the perfluoroalkyl (*F*-alkyl or R_F) group is usually assumed, since an R_F group remains unaffected by common chemical reactions such as reduction,[2,3] elimination,[4] substitution,[4,5] and other modifications of functional derivatives. In two homologous series of R_F-substituted alkanes [R_F-$(CH_2CH_2)_nI$ and $R_FCH_2CHI(CH_2)_nCH_3$, n = 0–5], elimination and substitution reaction rates and products differed greatly depending on proximity of the iodine and R_F substituents,[4] but in no case was HF lost. Conditions of reaction were used that had given reproducible, clean hydrogen iodide elimination from several classes of R_F-substituted iodoalkanes[4,6] and had been originally chosen to conform to classical studies. Previously, in one specific instance, facile elimination of HF occurred during reaction of excess base with 4-(*F*-alkyl)-3-iodobutanoic acids.[6] Initial attack of base to eliminate HI occurred at the C-2 proton, and not α to the R_F group as in previous cases, and the intermediate reacted further with base to eliminate HF. Though apparently the rate of HF elimination was

$$R_FCF_2CH_2CHICH_2COOH \xrightarrow[-HI]{} R_FCF_2CH_2CH{=}CHCOO^- \xrightarrow[-HF]{} R_FCF{=}CHCH{=}CHCOO^-$$

slower than HI, what factors were responsible for the differing behaviors of these compounds? The answers are important to an understanding of fluorinated compounds.

Free-radical addition of iodo-*F*-alkanes (R_FI) to terminal alkadienes gave good yields of mono- and bis-adducts in two homologous series.[7] Dehydrohalogenation of the

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