Stereochemistry of $LiNR_2$-Induced 1,4-Elimination of Allylic (Benzylic) Ethers

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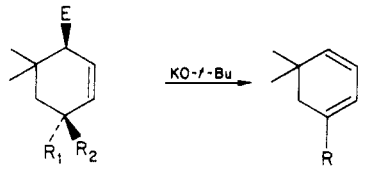
The stereochemistry of base-induced 1,4-elimination of H,D-substituted allylic (benzylic) ethers is examined. The substrates used are structurally similar (cyclohexenyl systems) but differ significantly in the nature of the "diene" product which is generated, forming naphthalene in one case and a very reactive intermediate *o*-xylylene in the other. These differences are reflected in the ease of elimination, allowing in the naphthalene-forming system examination of a range of bases/conditions. Preferential syn elimination, ranging from 87% to ≥99%, depending upon the solvent, substrate, and base employed, is found. An H/D kinetic isotope effect of approximately 3.4 is observed for the LDA-induced reaction in hexane; in spite of this, syn elimination of cis-deuterated substrate is strongly preferred, with no detectable diminution of selectivity under these conditions. Very high syn selectivity is found for reaction of potassium *tert*-butoxide and also when a quaternary ammonium hydroxide is employed, showing that, although lithium coordination may be important for $LiNR_2$-induced elimination, other factors must contribute to this stereochemical course. The substrate which generates an *o*-xylylene intermediate also does so with very high syn selectivity. Conformational effects may dictate the syn preference of these and related cyclohexenyl systems.

Although there are several examples of (formal) base-induced 1,4-elimination in the literature, in only a few instances have these reactions been subjected to mechanistic scrutiny, and in fewer still have stereochemical features been examined. This was a focus of Cristol's work with 9,10-disubstituted dihydroanthracenes, where the evidence indicated that syn elimination was preferred, even though an overall E1cB process was implicated.[1] Hill and Bock, as part of a stereochemical study[2] of various 1,4-eliminations, included the base-induced example shown in eq 1. Again, preferred syn (85–90%) elimination stereochemistry was observed.



(1)

E = 2,6-Cl_2PhCO$_2$
R_1 = H or D
R_2 = D or H

R = H or D

Some time ago we found that allylic ethers undergo a remarkably general 1,4-elimination reaction when treated with lithium dialkylamides.[3] The impetus for examining such systems arose from the observation that certain 1,3-diene monoepoxides, which could otherwise have given a facile 1,2-elimination, instead reacted by very rapid 1,4-elimination.[4] Evidence was obtained which indicated that the epoxide 1,4-elimination involved preferential proton abstraction from a cisoid carbon, although the stereochemical (syn/anti) features remain unexplored. We have also demonstrated that the 1,2-elimination of cyclohexene oxides occur by syn quasi-axial proton abstraction,[5] and it has been tempting to rationalize this selectivity by calling upon coordination of the lithium ion with the epoxy oxygen. Other parallels between the epoxide reactions and those of allylic ethers exist, e.g., the preference for proton abstraction from a cisoid carbon[3] and a study of *cis*- and *trans*-1-methoxy-4-methyl-2-cyclohexene indicated that syn elimination was preferred,[3b] although unusual solvent dependence and generally low syn/anti ratios were found. This was a rather poor model for the study of stereochemistry because of yet another parallel; the 1,4-elimination here required the abstraction of a tertiary proton, and this so slowed the reaction that much of the product 1-methyl-1,3-cyclohexadiene was converted to toluene.[6]

Subsequent studies have reinforced the view that the 1,4-elimination of ethers is indeed quite general; not only can the procedure be used to form cyclic and acyclic dienes (some specifically substituted materials which are difficult to prepare by other methods) but also the propensity extends to benzylic ether analogues, which we have used to advantage to form isobenzofurans,[7] and even *o*-xylylenes[8] (the latter examples are indeed remarkable, given the facility of the alternative base-induced Wittig ether rearrangement).

The $LiNR_2$-induced 1,4-elimination of allylic and benzylic ethers is clearly the most general such reaction known. As such, a study of the mechanism of this process takes on greater import, and the stereochemistry of the reaction is obviously a significant aspect of this question. Consequently, considerable effort has been devoted to devising procedures for the preparation of suitable substrates. Stereoisomers differing only in H,D configuration were needed in order to avoid the problem of slow tertiary proton transfer noted above; such materials have the important added advantage of incorporating the minimal structural perturbation that can constitute a pair of diastereomers (cis/trans isomers). The preparation of such materials has presented an interesting and often frustrating challenge.

Results and Discussion

(a) Preparation of Substrates. A major hurdle in the synthesis of stereoisomerically labeled (H,D) substrates was overcome with the demonstration that the very potent

(1) Cristol, S. *Acc. Chem. Res.* **1971**, *4*, 393.
(2) Hill, R. K.; Bock, M. G.; *J. Am. Chem. Soc.* **1978**, *100*, 637.
(3) (a) Williams, B. Ph.D. Dissertation, UCSB, 1974. (b) Blonski, K. Ph.D. Dissertation, UCSB, 1978.
(4) Thummel, R. P.; Rickborn, B. *J. Org. Chem.* **1972**, *37*, 4250.
(5) Thummel, R. P.; Rickborn, B. *J. Am. Chem. Soc.* **1970**, *92*, 2064.
(6) Cyclohexadienes are slowly converted to aromatics on exposure to $LiNR_2$, under the usual conditions used for eliminations; this procedure can in fact be used to synthesize unusual aromatic systems (unpublished work with D. P. Svedburg: Svedburg, D. P. Ph.D. Dissertation, UCSB, 1979.
(7) (a) Naito, K.; Rickborn, B. *J. Org. Chem.* **1980**, *45*, 4061. (b) Makhlouf, M. A.; Rickborn, B. *J. Org. Chem.* **1981**, *46*, 2734. (c) Cornejo, J.; Ghodsi, S.; Johnson, R. D.; Woodling, R.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 3869. (d) Crump, S. L.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 304. (e) Crump, S. L.; Netka, J.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 2746.
(8) (a) Tuschka, T.; Naito, K.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 70. (b) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 3694. (c) Moss, R. J.; White, R. O.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 5132.

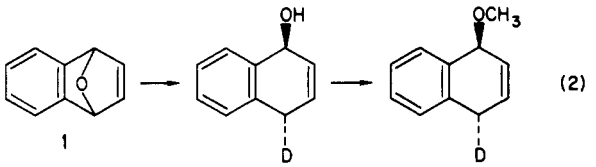
0022-3263/86/1951-1992$01.50/0

Table I. Deuterium Content of Naphthalene and Percent Syn Elimination from 3 and 5[a]

entry	substr	solvent	base	addend	naphthalene d_0	naphthalene d_1	naphthalene d_2	% syn elim
1	3	hexane	LDA		2	98		≥99
2	3	ether	LDA		4	96		98
3	3	THF	LDA		5	95		97
4	3	THF[b]	LDA		5	95		97
5	3	THF	LDA	$(iPr)_2NH$[c]	5	95		97
6	3	hexane	LDA	$(iPr)_2NH$[c]	2	98		≥99
7	3	THF	LDA	LiOMe[c]	6	94		96
8	3	HMPA	LDA		7	93		95
9	3	hexane	LDA	TMEDA[c]	4	96		98
10	3	hexane	LTMP		2	98		≥99
11	3	ether	LTMP		5	95		97
12	3	THF	LTMP		5	95		97
13	3	hexane	LTMP	TMEDA[c]	8	92		94
14	3	*t*-BuOH	KO-*t*-Bu[d]		2	98		≥99
15	3	THF	$R_4N^+OH^-$[e]		3	97		99
16	5	hexane	LDA		2	97	1	99
17	5	ether	LDA		nd	99	1	99
18	5	THF	LDA		1	86	13	87
19	5	hexane	LTMP		2	93	5	95
20	5	ether	LTMP		2	96	2	98
21	5	THF	LTMP		2	91	7	93
22	5	*t*-BuOH	KO-*t*-Bu[d]		2	92	6	94

[a] All reactions were carried out by adding the substrate to the basic solution at ca. 5 °C. The total volume of solvent employed was 10 mL (0.05 M initial substrate), and 3.0 equiv of base were employed unless otherwise noted. [b] The amount of solvent THF was reduced to 2.0 mL in this run to examine concentration dependence. [c] Three equivalents of diisopropylamine, lithium methoxide, or tetramethylethylenediamine, respectively, were added prior to the addition of substrate. [d] Potassium *tert*-butoxide (4.5 equiv), 25 °C. [e] Three equivalents of Triton B (trimethylbenzylammonium hydroxide, 40% in methanol) was used in this reaction.

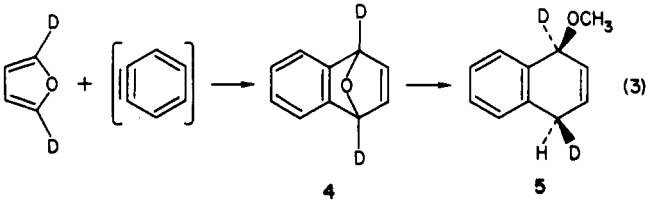
mixed hydride reagent (generated from $LiAlH(O\text{-}t\text{-}Bu)_3$ and Et_3B) developed by Brown and co-workers[9] reductively cleaves 1,4-epoxides with high inversion of configuration.[10] In the two cases where this result has been confirmed, lower limits of 96% and 98% inversion at the cleaved center were found, and the reactions may indeed be completely stereospecific. One of the two materials used in this study[10] was the readily available 1,4-dihydro-1,4-epoxynaphthalene (1), which gave the allylic alcohol 2 when the analogous mixed deuteride reagent was employed. Although 2 is extremely sensitive to both acids and bases



1 2 3 (2)

(preventing use of common variants of the Williamson ether synthesis), it was possible to prepare the ether 3 by the use of silver oxide/CH_3I. Compound 3 presents a particularly interesting model for study of the 1,4-elimination, since the product of such reactions is naphthalene, and, as anticipated, widely different bases are effective in causing the elimination.

With the trans-deuterated material (3) in hand, we turned to the more difficult problem of preparing the cis-deuterated analogue. Although it is possible to prepare this material as a mixture of 1- and 4-monodeuterated products,[10] better control of product is possible by working with the doubly bridgehead deuterated analogue of 1. This was prepared by forcing the double lithiation of furan, quenching with D_2O, and using the 2,5-dideuteriofuran in a cycloaddition reaction with benzyne (this sequence has been used previously by Vernon and co-workers[11]). The 4 prepared in this manner had very high isotopic enrichment (≳98% D at each bridgehead site). Reduction and conversion to the methyl ether 5 was accomplished with the mixed hydride reagent and conditions otherwise identical with those used to form 3.



4 5 (3)

The second deuterium at the methoxy substituted position of 5 should have at most a very slight (secondary kinetic isotope effect) influence on the stereochemistry of the 1,4-elimination, while at the same time serving as a probe for a possible competing process of proton (deuteron) abstraction from this 1-position.

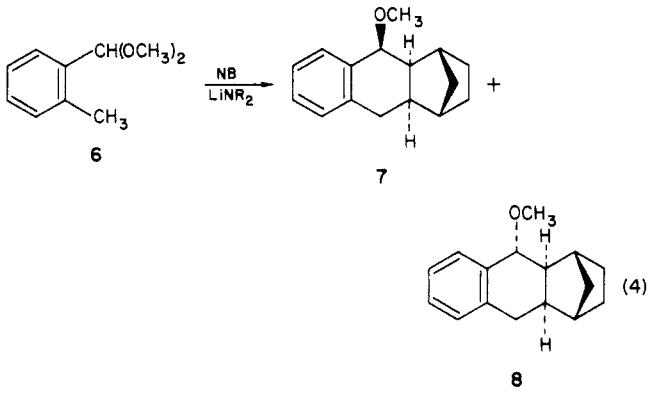
The second substrate (11) used in this study was chosen to differ greatly in the nature of the "diene" which would be formed by 1,4-elimination. Whereas 3 (and 5) form the very stable aromatic naphthalene system, 11 generates a very reactive *o*-xylylene intermediate by this process; these represent close to the limiting extremes of "diene" stability that can be envisaged, and we were particularly interested in determining whether this would influence the mechanism in a manner that might be reflected in the stereochemical outcome.

It has recently been shown that the acetal 6 will undergo $LiNR_2$-induced 1,4-elimination to generate (*E*)-α-methoxy-*o*-xylylene; when carried out in the presence of norbornene (NB), the two cycloadducts 7 and 8 are formed.[8b] The cis isomer 7 proved to be very resistant to further reaction with base, whereas the trans isomer 8 was found to undergo another 1,4-elimination, which in the presence of NB led to the formation of a novel 2:1 cycloadduct. On

(9) Brown, H. C.; Krishnamurthy, S.; Coleman, R. A. *J. Am. Chem. Soc.* **1972**, *94*, 1750. See also: Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1979**, *44*, 3678.

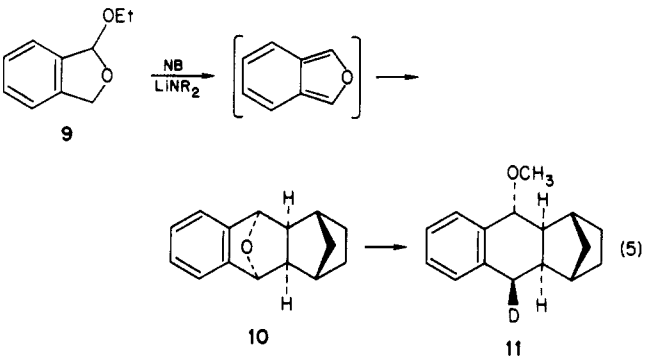
(10) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 1381.

(11) Cooke, M. D.; Dransfield, T. A.; Vernon, J. M. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1377.



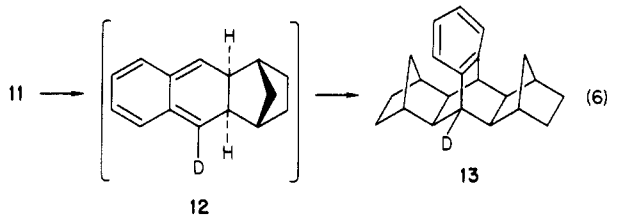
the basis of these observations, the preparation of a specifically deuterated analogue of 8 was undertaken.

The previously reported[7b] base-induced elimination of the acetal 9 in the presence of norbornene was repeated,[12] giving a mixture of exo,exo and endo,exo cycloadducts, from which the latter (10) was isolated by chromatography. Interestingly, the complex metal deuteride reductive cleavage of 10 proceeded well (93%), in spite of potential



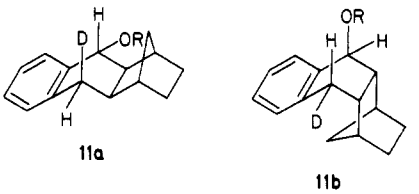
steric problems introduced by the norbornyl group. Conversion of the product alcohol to the ether 11 was accomplished by treatment of a solution in HMPA with *n*-butyllithium (orange endpoint), followed by excess methyl iodide. The structure of 11 was confirmed by comparison with the properties of the nondeuterated analogue,[8b] which established that the methoxy group is trans to the norbornyl fusion. The stereochemistry at the benzylic methylene site was easily determined in this instance, since the protons of the undeuterated material have chemical shifts differing by nearly 0.5 ppm.[13] In 11, only the downfield benzylic methylene proton was evident in the ^{1}H NMR spectrum, as a broadened (coupled to the deuteron) doublet (coupling to the ring fusion proton, ca. 6 Hz) at 2.7 ppm. The absence of detectable absorption at 2.24 ppm showed that this site is completely (≥97%) deuterated. In addition to establishing the stereochemistry of 11, this result adds a third example to the list of materials which have been shown to undergo complete inversion at the reductively cleaved center.[10]

(b) Stereochemistry of 1,4-Elimination. Since only one reaction was carried out with 11, this will be described first. Treatment with lithium diisopropylamide (LDA) in refluxing hexane (5 M in NB, temperature ca. 75 °C) effected elimination to the reactive intermediate *o*-xylylene analogue 12, which was trapped by NB to give the cycloadduct 13 in ca. 50% yield.



The ^{1}H NMR of 13 was identical with that of the previously described undeuterated analogue, except for the appropriately diminished bridgehead singlet. The MS of 13, taken at 6 eV ionizing potential, showed that the contribution of undeuterated material was ≤2%; since this level is identical, within experimental uncertainty, with that found in the starting material 11, it is concluded that the 1,4-elimination in this instance occurs with ≥99% syn selectivity and may be completely stereospecific.

The NMR spectrum of 8 has been interpreted[8b] as showing that the extended conformer corresponding to **11a** is preferred. In order to align the orbitals of the pertinent C–H and C–OCH_3 bonds for concerted elimination with maximum overlap of the π system as the *o*-xylylene 12 is formed, the transition state would require the geometry of the less stable conformer **11b** (the enantiomer is shown



for ease of viewing). It is interesting to note that the (by NMR, more stable) extended conformer of compound 7 has this proper geometry for syn concerted elimination but as noted above 7 is stable to base; presumably this reflects steric interference by the norbornyl group to attack by base.

The high retention of the isotopic label in product 13 clearly rules out mechanisms for the elimination involving a carbanion intermediate which loses its stereochemical integrity, but cannot further distinguish between a concerted process and a some variants of an E1cB process.

The stereochemical results obtained with the naphthalene-forming substrates 3 and 5 are displayed in Table I. Early in the study of 3 it became evident that these reactions were occurring with generally high syn selectivity and that assessment of any differences associated with changing variables would require accurate analyses. The NMR spectra of product from several runs were examined and confirmed that residual deuterium (by integration, 1 D/mol within the limits of measurement uncertainty) was in the 1-position of naphthalene. More accurate analysis required MS, and, to avoid possible differential fragmentation associated with isotope effects,[14] a low ionizing potential (6 eV) was used. This technique is time-consuming because of the low ion current that is generated but avoids essentially all cracking of the naphthalene. Instrument variables were assessed by examining the M+1 and M+2

(12) The preparation and isolation of 10 was skillfully carried out by Robert Sullivan. In order to obtain reasonable yields of cycloadducts, it is necessary to run the reaction above ambient temperature (the cycloaddition of isobenzofuran and norbornene is relatively slow at 25 °C; see ref 7b) and to add the base slowly (to avoid lithiation of the isobenzofuran[7d]); syringe pump addition of LDA to a refluxing hexane solution of NB and 9 was used.

(13) Because of a mistaken internal reference signal, the description of the undeuterated analogue of 11 given in ref 8b is in error; the ^{1}H NMR absorptions reported there are all too large by 0.14 ppm. The stereochemical descriptions of the benzylic methylene protons were also inadvertently exchanged; these should read: 2.24 (dd, appar. t, 1 H, benzylic methylene trans to methoxy, J = 14, 12 Hz) and 2.71 (dd, 1 H, benzylic methylene cis to methoxy, J = 14, 6 Hz). None of the substantive arguments in ref 8b are altered by these changes.

(14) Milliard, B. J. *Quantitative Mass Spectrometry*, Heydon and Son, Ltd.; London, 1978.

percentages for natural abundance naphthalene; these were reproducibly higher than theory by ca. 0.5%. Since this was within the range of reproducibility of measurement, no correction was applied for this instrument sensitivity factor. The values obtained for deuterium content listed in Table I are believed to be accurate within ±1%. In order to calculate the % syn elimination data in Table I, the measured values were adjusted to take into account the ca. 2% of nondeuterated starting material present in **3** and **5**. It was not possible to analyze **3** or **5** by MS, since all procedures examined caused extensive degradation to naphthalene; the isotopic enrichment of **3** and **5** therefore rests on inherently less accurate NMR measurements. Entries of ≥99% syn elimination of Table I may reflect "complete" stereospecificity.

Any process that leads to replacement of D by H at C-1 of compound **5**, if followed by syn elimination, would result in the formation of naphthalene-d_0. In fact, the amount of d_0 product observed in all runs with **5** corresponded (±1%) to the amount of monodeuterated (2%) starting material present, showing that there is no (irreversible) loss of D from this position. These results also rule out the possibility that the data are distorted by base-catalyzed D,H exchange of the product naphthalene from **5** and thus also from **3**.

The most selective reactions with $LiNR_2$ are found in hexane solvent with LDA, where both substrates **3** and **5** gave ≥99% syn elimination, making this the simplest set of conditions for examination of kinetic isotope effects. This was done by a competition kinetics experiment, treating an equimolar mixture of **3** and **5** with insufficient base for complete reaction and using NMR analysis of recovered starting material to determine the extent of reaction of each substrate. This gave $k_3/k_5 = 3.4 \pm 0.3$, supporting the view that proton (deuteron) transfer is occurring in the rate-determining step. This places the activation energy for deuterium abstraction ca. 0.7 kcal/mol higher than that of the corresponding proton transfer process. Since **5** nonetheless reacts with a minimum of 99% selectivity, this shows that the syn elimination pathway for **3** must be favored by at least 3.2 kcal/mol over competing processes.

The most striking generalization of the data in Table I is that high syn elimination preference is seen in all of the reactions examined. Are the small differences meaningful? Certain comparisons suggest they are. For example, entries 1 and 3 indicate that the reaction of **3** with LDA is more selective in hexane (≥99%) than that in THF (97%). This conclusion is reinforced by entry 18, in which substrate **5** with LDA/THF gave the lowest selectivity observed (87–88%). This is the appropriate magnitude (and direction) of change expected if an already energetically modest competition is altered by the introduction of a kinetic isotope effect which disfavors syn elimination from **5**.[15]

The other products of elimination (diisopropylamine and $LiOCH_3$) have no effect on the stereochemical outcome, as shown by entires 5–7, in which amounts of these materials equivalent to the LDA present were added prior to addition of the substrate. The amine alone does not cause elimination of **3** under the usual reaction conditions, and the $LiOCH_3$ appeared to have limited solubility; these experiments were done to query the possibility that incorporation into, or disruption of, LDA aggregates by these addends might occur and influence the stereoselectivity of the elimination. However, within measurement limits, the results are identical with those obtained without these addends. In contrast, tetramethylethylenediamine (TMEDA) does appear to lower the syn selectivity for both LDA and LTMP reactions in hexane (entries 9, 13.) This conclusion is tentative, since only substrate **3** was used with TMEDA present, and the possibility of enhanced product D,H exchange rates was not experimentally excluded.

The solvent is an important variable in determining the level of selectivity found in these eliminations. Reactions in hexane lead to higher or equivalent syn selectivity compared to those in ether in all instances except with **5** and LTMP (entries 19, 20), where the hexane value is uncharacteristically low. Reactions in THF are invariably less selective. We suspect that these observations are related to changes in structure or dissociation of $LiNR_2$ aggregates but have no direct evidence on this point. Interestingly, the use of HMPA as solvent (entry 8) still leads to 95% syn selectivity, essentially identical with the outcome in THF.

While lithium ion coordination to the departing methoxide group is almost certainly required in the less polar solvents employed in this study, it is not clear that suprafacial ("intramolecular" after coordination of Li to O) proton abstraction is the cause of syn elimination preference. Although such a depiction is appealing in its simplicity, the reactions with K-O-*t*-Bu (in *t*-BuOH), and especially with the quaternary ammonium hydroxide Triton B (in THF), both of which are highly syn selective for reactions with **3**, indicate this is not a requirement for selective syn 1,4-elimination. It is instructive to compare our results with those of Hunter and co-workers,[16] who reported striking counterion effects on the stereochemistry of D,H exchange and 1,2-elimination for the base-induced reactions of 1-methoxyacenaphthene in *t*-BuOH, showing that the better oxygen coordinating cations had a major role in the selectivity of proton abstraction and subsequent fate of the carbanion intermediate as it apportioned between reprotonation and elimination pathways. These reactions exhibited moderate to high syn elimination preference which paralleled the coordinating ability of the counterion, indicating that the cation both directed the base to the suprafacial proton and assisted in the departure of methoxide. In contrast to this characteristic E1cB behavior, we find no indication of D,H exchange in the substrates **3**, **5** and **11**, and our results can be accommodated by a concerted syn elimination process, accompanied by an energetically accessible (except with LDA in hexane and a few other conditions) competing anti elimination pathway. Note again that the stability of the diene product has no influence on the syn preference. Substrate conformation may play a decisive role in determining this stereochemical outcome. Our starting materials as well as those studied by Cristol[1] have preferred or accessible boat conformers which offer favorable developing π overlap features, and this may also be significant in the system studied by Hill.[2] Further work is required to determine if there is an intrinsic stereochemical preference in the $LiNR_2$-induced 1,4-elimination of allylic (and benzylic) ethers or if this mechanistic feature is highly substrate dependent.

Experimental Section

NMR spectra (in $CDCl_3$) were recorded on Varian FT-80 or

(15) More precisely, one would expect a net $\Delta\Delta G^*$ of 2 × 0.7 kcal/mol to be introduced by kinetic isotope effects, since syn elimination is presumably favored in **3** to the same extent that it is disfavored in **5** by this factor. The calculation is necessarily imprecise, because of uncertainties in the isotope effect value and product analyses, in addition to requiring the assumption that the isotope effect is the same in THF and hexane.

(16) Hunter, D. H.; Sheering, D. J. *J. Am. Chem. Soc.* **1971**, *93*, 2348. Hunter, D. H.; Lin, Y-T. *Ibid.* **1968**, *90*, 5921.

Nicolet NT-300 instruments. MS were obtained on a VG 70-250 instrument, operating at 6–7 eV ionizing potential for deuterium analyses. Diisopropylamine, 2,2,6,6-tetramethylpiperidine, hexamethylphosphoramide (HMPA), and hexane were distilled from CaH_2. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl immediately before use. Ether was distilled from $LiAlH_4$, and tetrahydropyran (THP) was purified by distillation from sodium, followed by vacuum (ca. 100 torr) distillation from $LiAlH_4$. The $LiAlD_4$ (labeled 98 atom % D) and the triethylborane (1 M in THP) were obtained form the Aldrich Chemical Co.

***trans*-4-Deuterio-1,4-dihydro-1-hydroxynaphthalene (2).** This material was prepared as described previously[10] by reduction of 1[17] with $LiAlD(O\text{-}t\text{-}Bu)_3/Et_3B$ in THP. Both ^1H and ^2H NMR analyses indicated that **2** contained 98 ± 2% D in the designated position; the ^2H result was obtained by using a weighed amount of naphthalene-*1-d* (98%) as an internal quantitative standard.

***trans*-4-Deuterio-1,4-dihydro-1-methoxynaphthalene (3).** A mixture of 1.5 g of **2**, 2.8 g of Ag_2O (freshly prepared, washed with water and acetone, air dried), and 2.5 mL of CH_3I in 15 mL of CH_2Cl_2 was stirred at ambient temperature for 20 h. Distilled Skellysolv (15 mL) was added, and the entire mixture was directly chromatographed on 250 g of activity grade III neutral alumina with graded elution from Skellysolv (400 mL) to 20% ether/Skellysolv. Vacuum evaporation of the later combined fractions gave 1.3 g (80%) of **3** as a colorless liquid: ^1H NMR (80 MHz) δ 3.14 (s, 3 H), 3.40 (br. s, $w_{1/2}$ = 11 Hz, 1 H, C*H*D),[18] 5.07 (dd, apparent t, 1 H, *J* = 3.5 Hz, C*H*OCH_3), 6.00 (ddd, 1 H, *J* = 10, 3.5, 2 Hz), 6.25 (dd, 1 H, *J* = 10.3 Hz), and 7.15–7.54 (m, 4 H; the aromatic region has one proton more downfield than the other three, behavior which we have associated with preferred "equatorial" methoxy conformers in related systems[10]).

***cis*-1,4-Dideuterio-1,4-dihydro-1-methoxynaphthalene (5).** The procedure of Vernon et al.[11] was modified by the use of 10.1 M *n*-butyllithium in hexane to generate 2,5-dilithiofuran. Vacuum evaporation and quenching with D_2O gave 2,5-dideuteriofuran of high isotopic purity. Cycloaddition with in situ generated benzyne afforded 1,4-dideuterio-1,4-epoxy-1,4-dihydronaphthalene (**4**), which by ^1H NMR contained 98 ± 2% D at each designated site. Reduction ($LiAlH(O\text{-}t\text{-}Bu)_3/Et_3B$) gave the dideuterio alcohol (90%), mp 47–48 °C, after recrystallization from ether/petroleum ether: ^1H NMR δ 2.0 (br s, 1 H, OH), 3.3 (m, 1 H, C*H*D), 6.1 (br s, 2 H, vinyl), and 7.1–7.7 (m, 4 H).

Methylation of this alcohol by the procedure described for **3** gave **5** (86%) as a colorless liquid: ^1H NMR (80 MHz) δ 3.14 (s, 3 H), 3.30 (br s, 1 H, C*H*D), 6.01 (dd, 1 H, *J* = 10.2 Hz), 6.24 (dd, 1 H, *J* = 10.3 Hz), 7.24 (m, 3 H), and 7.44 (m, 1 H).

Preparation of 11. Reduction of 500 mg of **10**[7b,12] with 4.3 equiv of $LiAlD(O\text{-}t\text{-}Bu)_3$ and 3.9 equiv of Et_3B in 7.0 mL of THP for 2 h at room temperature gave, after normal workup,[10] 471 mg (93%) of the alcohol as a colorless crystalline solid, mp 162.5–164 °C (lit.[8b] mp 158–159 °C): ^1H NMR (300 Mz) δ 1.0–1.9 (m, 9 H), 2.10 (br s, 1 H, distal bridgehead), 2.52 (br s, 1 H, proximal bridgehead), 2.67 (br d, 1 H, *J* = 6 Hz, C*H*D), 4.32 (d, 1 H, *J* = 10 Hz, C*H*OH), 7.0–7.4 (m, 3 H), and 7.49 (d, 1 H, *J* = 8 Hz).

A portion (400 mg) of this alcohol was taken up in 7.0 mL of HMPA and, after cooling in an ice bath, titrated with *n*-butyllithium in hexane until an orange-brown endpoint was reached. Excess CH_3I was added, and after 0.5 h the mixture was poured into water (50 mL) and extracted with Skellysolv (4 × 20 mL.) The combined organic phase was washed repeatedly with water, dried over K_2CO_3, and evaporated. The residue was chromatographed (silica gel, 10% ether/Skellysolv) to give **11** in quantitative yield as a colorless oil which crystallized on standing, mp 60–62.5 °C: ^1H NMR (300 MHz) δ 1.23 (m, 3 H, syn methano bridge and endo ethano bridge), 1.57 (m, 4 H, anti methano bridge, proximal ring fusion, and exo ethano bridge), 1.70 (m, 1 H, distal ring fusion), 2.09 (br s, 1 H, distal bridgehead), 2.45 (br s, 1 H, proximal brigehead), 2.68 (br d, 1 H, *J* = 6 Hz, C*H*D), 3.63 (s, 3 H), 3.83 (d, 1 H, *J* = 10 Hz, C*H*OCH_3), 7.2 (m, 3 H), and 7.35 (br d, 1 H, *J* = 7 Hz); ^2H NMR (CCl_4 with $CDCl_3$ internal standard) δ 2.28. From integration of the ^1H spectrum, an upper limit of product containing benzylic methylene H trans to the methoxy group was established as 3 ± 2%. Integration of the ^2H spectrum established an upper limit of benzylic methylene D cis to the methoxy group of 2 ± 2%.

1,4-Elimination of 11. Formation of 13. A mixture of 229 mg of **11** and 3 equiv of LDA in 11.5 mL of 5 M norbornene in hexane was refluxed for 13.5 h. After cooling, water was added and the organic material taken up in ether, which was washed with water and brine, dried over K_2CO_3, and evaporated. Chromatography (silica gel, Skellysolv) gave 148 mg (51%) of colorless solid **13**, mp 118–126 °C (lit.[8b] mp for undeuterated analogue, 127–128 °C); the ^1H NMR of **13** was identical with that of the undeuterated analogue reported earlier[8b] except for integration of the benzylic bridgehead absorption at 2.94 ppm (for **13**, s, 1 H.) The MS (6 eV ionizing potential) of **13** exhibited peaks of *m/z* (relative intensity) 290 (2.1), 291 (100.0), 292 (24.2), and 293 (3.1), indicating 98.0 ± 0.3% D/mol.

1,4-Elimination of 3 and 5. (a) With $LiNR_2$. All reactions were carried out under N_2 in an ice bath (measured internal temperature of ca. 5 °C) and quenched after 0.5 h. The base, lithium diisopropylamide (LDA) or lithium tetramethylpiperidide (LTMP), was prepared by dropwise addition of the appropriate amine (1.5 mmol) to 0.94 mL of 1.6 M *n*-butyllithium (hexane.) The solvent (10.0 mL) was then added, followed by addends (if any) as listed in Table I. The substrate **3** or **5** (0.5 mmol) was then added rapidly. After 0.5 h, the reactions were quenched by addition of water (brine when THF was used as the solvent) and extracted with pentane. The organic phase was dried over K_2CO_3 and evaporated. NMR examination at this stage indicated (in agreement with TLC) that all reactions had gone to completion. The solid residue was chromatographed (silica gel, Skellysolv) to isolate the naphthalene, which was then sublimed prior to MS analysis.

(b) With KO-*t*-Bu. Identical conditions and isolation procedures were employed, except for the use of 4.5 equiv of KO-*t*-Bu (Aldrich) and ambient reaction temperature. TLC examination indicated rapid loss of substrate.

(c) With Triton B. Three equivalents of commercial benzyltrimethylammonium hydroxide (40 wt % in methanol) in 10 mL of THF, ice bath temperature, were employed.

Competition Kinetics. 3 and 5 with LDA in Hexane. To each of three flasks containing approximately 1.3 mmol of LDA in 9 mL of hexane (ice bath) was added 0.5 mL of a hexane solution containing 0.65 mmol of **3** and 0.66 mmol of **5**. The reactions were quenched after 2, 5, and 10 min, respectively; subsequent analyses indicated that all were complete within 2 min, giving 65 ± 5% naphthalene in each case (presumably some LDA was lost to adventitious moisture).

The amounts of residual **3** and **5**, and product naphthalene-*1-d*$_1$, were determined by ^1H NMR analysis as follows. The relative amount of naphthalene-*1-d*$_1$ was obtained by integration of the downfield aromatic multiplet (3 H), which was cleanly separately from other absorptions. Residual **3** was given by integration of the H-1 absorption at 5.1 ppm (dd, apparent t, C*H*OCH_3), since **5** has no peak in this region. Residual **5** was obtained by integration of the benzylic methylene absorption, corrected by subtraction of the 1 H contribution of **3** to this area. The values, normalized to 100%, for the three reactions were identical within measurement error limits; **3** (7.1 ± 1.5%), **5** (28.4 ± 3.1%), and naphthalene-*1-d*$_1$ (64.5 ± 3.8%). These values were used to calculate the relative rate ratio (H/D isotope effect) from the equation $k_3/k_5 = \log (3/3_0)/\log (5/5_0) = 3.4 \pm 0.3$.

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(18) The very broad nature of the benzylic methylene proton absorption of **3** has an interesting origin; we attribute it to coupling with H-1, H-2, H-3, and D, all with similar *J* values (3 ± 1 Hz). In the undeuterated analogue of **3**, H-1 appears as an approximate q (*J* = 3.5 Hz). This simplifies to an approximate t for **3**, showing that at least one of the three couplings in the undeuterated material is due to a long range cis 1,4-interaction. Examination of the vinyl proton patterns for undeuterated material, **3**, and **5** indicates that the other two couplings of H-1 are with H-3 (vinyl) and a long range trans 1,4 interaction, rather than with H-2. This interpretation is in keeping with a boatlike preferred conformer for these materials in which the methoxy group is equatorial, leading to an H-1, H-2 dihedral angle approaching 90°.