2. Apparatus and Procedure. The apparatus used for kinetics experiments included a batch reactor in glass with valves allowing argon purges, evacuation, and introduction of the various reagents. Various gases syringes as well as burets allowed given amounts of olefin, O_2, alkylaluminum, or solvent to be introduced into the reactor. A sampling valve was connected to the reactor in order to analyze the gaseous phase or liquid phase at any time during the reaction. Analysis of the olefins required was performed on an Intersmat IGC 120 flame ionization chromatograph.

In the case of the $M(CO)_{6-x}L_x$ catalyst, the precursor complex was introduced into the reactor, which was then evacuated and carefully purged with argon before the solvent was introduced. Then, the olefin, O_2, and the cocatalyst were introduced. In the case of $M(NO)_2X_2(PPh_3)_2$, the catalyst and cocatalyst were allowed to react for 30 min before introducing the olefin.

3. Experimental Conditions. All the experiments were carried out at 25 °C. In all cases 60 mL of chlorobenzene was used. Owing to the various activities observed, the olefin, catalyst and cocatalyst amounts could vary with the catalytic systems. The following experimental conditions were used.

$W(CO)_5PPh_3$, $EtAlCl_2$, O_2: W = 0.167×10^{-2} mol/L, olefin/W = 100, Al/W = 4, O_2/W = 0.5 except for the metathesis of 4,4-dimethyl-2-pentene, where Al/W = 8 and O_2/W = 2.

$Mo(CO)_5PPh_3$, $EtAlCl_2$, O_2: Mo = 0.333×10^{-2} mol/L, olefin/W = 50, Al/Mo = 3, O_2/Mo = 3.

$M(CO)_3$(mesitylene), $EtAlCl_2$, O_2: M = W, W = 0.167×10^{-2} mol/L, olefin/W = 100, Al/W = 2; M = Mo, Mo = 0.167×10^{-2} mol/L, olefin/Mo = 100, Al/Mo = 10, O_2/Mo = 10; M = Cr, Cr = 0.333×10^{-2} mol/L, olefin/Cr = 50, Al/Cr = 4, O_2/Cr = 1.

$M(NO)_2X_2(PPh_3)_2$ (M = W, Mo; X = Cl, Br, I), $EtAlCl_2$: M = 0.167×10^{-2} mol/L, olefin/M = 100, Al/M = 6 except in the case of $Mo(NO)_2I_2(PPh_3)_2$ and branched olefins: Al/M = 10.

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(23) Note that all drawings and discussion assume for clarity a greater degree of ring puckering than is observed in X-ray structure.[17b]

Allenes and Acetylenes. 22. Mechanistic Aspects of the Allene-Forming Reductions (S_N2' Reaction) of Chiral Propargylic Derivatives with Hydride Reagents[1]

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Abstract: Four chiral 3-decyn-2-yl derivatives (**1a–d,** Scheme I) were treated in THF with various aluminum hydride reagents selected to give high yields of 2,3-decadiene. The preferred mode of substitution was deduced from the known absolute configurations of starting material and product. The effect of the temperature on the stereoselectivity was also studied and the thermodynamic parameters were calculated. The use of hydroxy, tertiary amine, or bromide as the leaving group (in compounds **1a**, **1c**, and **1d**, respectively) yielded the allene in a preferred overall syn mode of substitution, the degree of which increased with temperature. The mesylate (**1b**) with lithium trimethoxyaluminum hydride yielded the allene in an anti displacement which was more preferred at lower temperatures. The mechanisms of these reductions are discussed. The chiral allenic alcohols (**11** and **12**) were also prepared via lithium aluminum hydride reductions of chiral acetylenic derivatives (Schemes III and IV).

Introduction

The stereochemical course of the allene-forming 1,3-substitution reactions (S_N2') of chiral propargylic derivatives presents a problem which is analogous to the S_N2' reactions in allylic systems. These reactions of allylic derivatives have been of synthetic and mechanistic interest for years.[3,4] However, it is only during the last 3 or 4 years that definitive experimental evidence of the stereochemistry, in cyclic as well as acyclic systems, has been collected. It is now apparent that

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Table I. Reduction of Acetylenic Derivatives **1a–d** with Hydride Reagents in THF into 3-Decyne (**3**) and/or 2,3-Decadiene (**2**)

entry	compd	reagent (mol)	temp, °C	time, h	**3** yield,[a] %	**2**, (*R*)-(−) or (*S*)-(+) yield,[a] %	$[\alpha]^{22}_D$, deg (*c*, methanol)	ee, %	$-\Delta\Delta G^{\ddagger}$, kcal/mol	$\Delta\Delta H^{\ddagger}$, kcal/mol	$\Delta\Delta S^{\ddagger}$, cal/deg·mol
1	(*S*)-**1a** (X = OH	AlH_3 (3)	0	120	6[b]	53[b]	−55.1 (5.2)	76.0	1.20	0.60	6.6
2	(*S*)-**1a** (X = OH)	AlH_3 (3)	20	20	5	73	−56.4 (7.7)	77.8	1.21		6.1
3	(*S*)-**1a** (X = OH)	AlH_3 (3)	65	2	10	81	−58.1 (5.8)	80.1	1.34		5.3
4	(*S*)-**1a** (X = OH)	$LiAlH_4$–$AlCl_3$ (2:0.2)	65	5	3[b]	68[b]	−47.0 (6.5)	64.8			
5	(*S*)-**1a** (X = OH)	$LiAlH_4$–$AlCl_3$ (2:0.04)	65	24	2[b]	32[b]	−12.6 (6.9)	17.4			
6	(*S*)-**1a** (X = OH)	$LiAlH_4$–$AlCl_3$–LiCl (2:0.04:1)	65	24	2[b]	26[b]	−53.7 (4.1)	74.1			
7	racemic **1a**	$LiAlH(OCH_3)_3$ (3)	65	24	5	16					
8	(*S*)-**1b** (X = OSO_2CH_3)	$LiAlH(OCH_3)_3$ (3)	−20	48	15	79	+52.9 (2.0)	73.0	0.93		0.15
9	(*S*)-**1b** (X = OSO_2CH_3)	$LiAlH(OCH_3)_3$ (3)	0	24	5	59	+51.3 (4.4)	70.8	0.96	−0.90	0.22
10	(*S*)-**1b** (X = OSO_2CH_3)	$LiAlH(OCH_3)_3$ (3)	30	12	30	56	+49.5 (2.8)	68.3	0.96		0.23
11	(*S*)-**1b** (X = OSO_2CH_3)	$LiAlH(OCH_3)_3$ (3)	65	2	16	21	+44.5 (2.9)	61.4	0.96		0.19
12	racemic **1b**	$LiAlH_4$ (2)	20	24	85						
13	racemic **1b**	AlH_3 (2)	20	18	89						
14	(*R*)-**1c** (X = $^{\oplus}NEt_2Me$)	$LiAlH_4$ (1.2)	−40	48		96	+45.9 (5.5)	63.3	0.70		4.7
15	(*R*)-**1c** (X = $^{\oplus}NEt_2Me$)	$LiAlH_4$ (1.2)	0	7		93	+51.9 (7.0)	71.6	0.98	0.68	5.3
16	(*R*)-**1c** (X = $^{\oplus}NEt_2Me$)	$LiAlH_4$ (1.2)	65	1		95	+53.5 (8.1)	73.8	1.27		5.5
17	(*R*)-**1d** (X = Br)	AlH_3 (2)	0	48	19	51	+26.6 (1.5)	45.1[c]	0.53	0.67	4.0
18	(*R*)-**1d** (X = Br)	AlH_3 (2)	20	24	13	74	+28.0 (2.3)	47.4[c]	0.60		4.0
19	(*R*)-**1d** (X = Br)	AlH_3 (2)	65	2	15	25	+31.0 (1.8)	52.6[c]	0.78		4.0
20	(*R*)-**1d** (X = Br)	$LiAlH(OCH_3)_3$ (3)	0	24	23	54	−0.8 (6.7)	1.1			
21	(*R*)-**1d** (X = Br)	$LiAlH(OCH_3)_3$ (3)	65	2	16	45	−1.1 (8.6)	1.5			
22	racemic **1d**	$LiAlH_4$ (1)	20	24	75	8					

[a] The figures for the alcohol **1a** represent GLC yields and the remaining figures isolated yields. [b] The following amounts of (*E*)-3-decen-2-ol were also formed: entry (%), 1 (24); 4 (10); 5 (60); 6 (70). [c] Stereochemical yield when corrected for the optical purity (81.4% ee) of the starting bromide.

the long-held view based on earlier experiments that the S_N2' reactions proceed with preference for syn substitution is not valid. Both experiments[3c] and theory[5] show that the whole spectrum of substitution, spanned by the syn (cis) and anti (trans) extremes, can be expected depending in any particular case on the displacing and displaced groups and, probably, on other factors.[3,5] In addition very high preference for attack anti to the leaving group is shown when allylic compounds react with organocuprates[6] or a palladium(0) complex.[7]

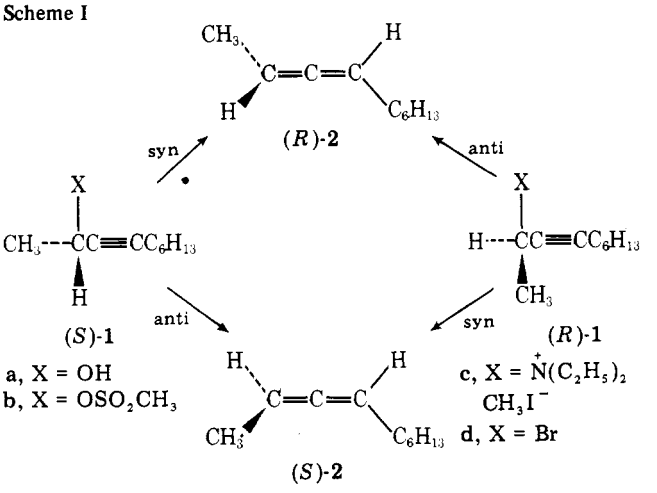
Only hydride[8-10] and organocuprate reactions[11] have been studied in this respect for the propargylic system. No systematic study on the stereochemical aspects of these hydride reactions has been undertaken so far.

The allene-forming reductions of tertiary propargylic alcohols and their acetates with $LiAlH_4$ and $LiAlH_4$–$AlCl_3$ indicate a preference for the syn mechanism.[9a,c] A syn substitution mechanism was also observed in the ring opening of a 4,5-epoxy-2-alkyn-1-ol derivative with $LiAlH_4$.[9b] Borden and Corey[8] reported, however, that the allene-forming hydride reactions of sulfonates of 1,3-di-*tert*-butylpropargyl alcohol follow a preferred anti mechanism.

As reported earlier, a method for the preparation of chiral α-allenic alcohols of excellent enantiomeric purity was discovered when chiral 4-(2-tetrahydropyranyloxy)-2-alkyn-1-ol derivatives (**10** and **17**, Schemes III and VI) are reduced by $LiAlH_4$.[10] One β-allenic alcohol was obtained analogously (Scheme VI) in lower stereochemical yield (75% ee).[10] We have tentatively reported the formation of enantiomerically enriched α- and β-allenic alcohols from $LiAlH_4$ reductions of 4-(trialkylammonio)-2-alkyn-1-ol (**7**) and 5-(trialkylammonio)-3-alkyn-1-ol (**9**) derivatives, respectively.[9d] We found the stereochemical course to be a predominant overall syn substitution in all of these reactions. Alkoxy derivatives react, however, by stepwise addition and elimination[10] (cf. Discussion).

This report describes some of the factors, particularly leaving-group effects, that influence the stereochemical course of the conversion of propargylic derivatives to allenic alcohols

Scheme I



and hydrocarbons by hydride reductions. We have found that mesylates are the only propargylic substrates, out of an alcohol, three quaternary ammonium compounds, two mesylates, and one bromide, which at all temperatures react in an anti mode; the other compounds undergo preferred syn substitutions in most cases. Some of the results presented here have been reported in a preliminary form.[9d]

Results

A. Formation of Allenic Hydrocarbons. We allowed the chiral 3-decyn-2-yl derivatives (**1**) to react with various hydride reagents in THF at different temperatures (Scheme I). The optical rotations of the isolated 2,3-decadiene (**2**) have been used to establish the stereochemistry and stereoselectivity of the reactions (Table I).[12] The estimated enantiomeric purities of 2,3-decadiene in Table I are based on the assumption that the enantiomerically pure allene should have $[\alpha]^{22}_D$ ±72.5°.[13-15]

The difference in free energy of activation ($\Delta\Delta G^{\ddagger}$) was calculated[16] from the optical purity of the product, according

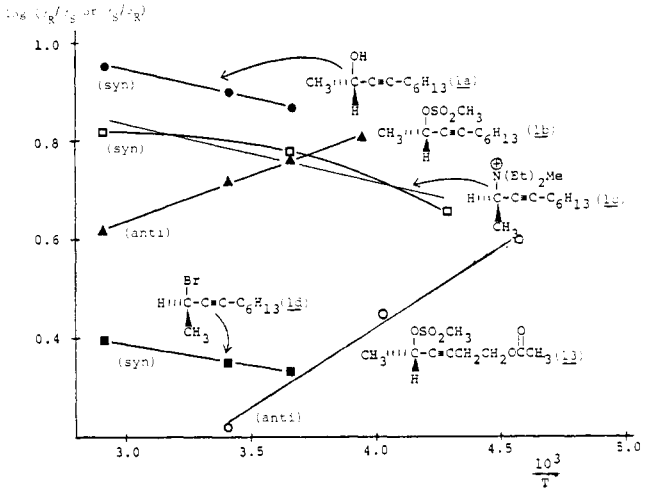


Figure 1. Influence of temperature on the enantiomeric product ratio in the formation of 2,3-decadiene according to Scheme I and in the formation of 3,4-hexadienol from mesylate **13** (Scheme IV). Syn and anti denote the preferred mode of substitution.

to eq 1, where Q is the ratio of produced enantiomers (c_R/c_S or c_S/c_R).

$$\Delta\Delta G^{\ddagger} = \Delta G^{\ddagger}_{R\,(\text{or } S)} - \Delta G^{\ddagger}_{S\,(\text{or } R)} = RT \ln Q \qquad (1)$$

The relationship between log Q and the reaction temperature ($1/T$) is shown in Figure 1. From the slope of the line the difference in enthalpy of activation term ($\Delta\Delta H^{\ddagger}$) was obtained according to the equation

$$\text{slope of the line} = -\Delta\Delta H^{\ddagger}/2.303R \qquad (2)$$

The reaction of (*S*)-3-decyn-2-ol (**1a**) with 3 equiv of AlH_3 in THF at 0, 20, and 65 °C (Table I, entries 1–3) afforded an increasing yield of 2,3-decadiene with temperature. A small amount of 3-decyne (**3**, <10%) was also formed at all temperatures. The allene was isolated by preparative GLC and polarimetric measurements showed that the stereoselectivity of the reaction increased slightly with temperature (76 → 80% ee). Since (*S*)-3-decyn-2-ol gave (*R*)-2,3-decadiene, it can be concluded that the hydride attacks preferentially on the same side of the propargylic system from which the leaving group departs, i.e., a syn substitution mechanism predominates.

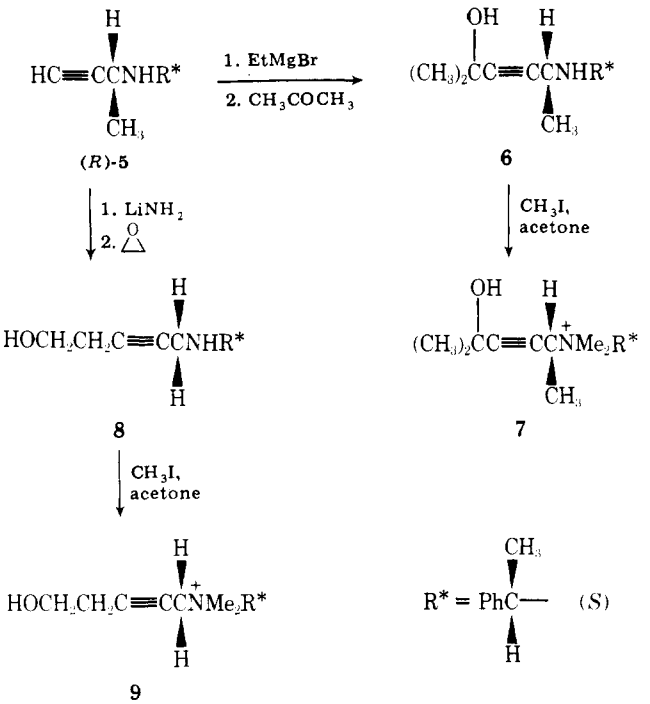
$C_2H_5C{\equiv}CC_6H_{13}$ (**3**) $\qquad$ $CH_3CHCH{=}CHC_6H_{13}$ (**4**)

One reaction gave after 5 days at 0 °C another product (24% isolated yield) besides 2,3-decadiene (53%, entry 1). The compound was proved to be *trans*-3-decen-2-ol (**4**) by spectroscopic identification and by GLC comparison with the cis isomer. This indicates that at this temperature the reaction proceeds via an organometallic intermediate having trans stereochemistry over the double bond.

When the alcohol **1a** was reacted with 2 equiv of $LiAlH_4$ and refluxed in THF in the presence of 0.2 and 0.04 equiv of $AlCl_3$, the allene of lower enantiomeric purity, 65 and 17% ee, respectively, was formed (entries 4 and 5). $LiAlH_4$ reduction according to the latter conditions (0.04 equiv of $AlCl_3$), but in the presence of 1 equiv of LiCl (entry 6), increased the stereoselectivity of the reaction to 74%. In all of these reactions substantial amounts of 3-decen-2-ol (**4**) were formed.

The reaction of the (*S*)-(−)mesylate **1b** with 3 equiv of $LiAlH(OCH_3)_3$ at temperatures between −20 and 65 °C (entries 8–11) resulted in the formation of (*S*)-2,3-decadiene as the main product via a preferred anti substitution mechanism. In this case both the isolated and the stereochemical yield of the allene decreased with increasing temperature. In contrast, only 3-decyne (**3**) was formed in good yield by direct substitution (entries 12 and 13) when the mesylate was treated with 2 equiv of $LiAlH_4$ or AlH_3 at room temperature.

Scheme II



The quaternary ammonium compound **1c** was obtained by reaction of the mesylate **1b** with diethylamine, followed by quaternization with methyl iodide. Excellent yields of allene were obtained when **1c** was reduced with $LiAlH_4$. The enantiomeric yields of (*S*)-2,3-decadiene varied between 63 and 74%, increasing with increasing temperature (entries 14–16). The preferred mode of substitution was found to be syn.

(*R*)-(+)-2-Bromo-3-decyne (**1d**) was prepared by modification of a known procedure for the preparation of chiral bromides from chiral alcohols.[18] Its substitution product with diethylamine was (*S*)-*N*,*N*-diethyl-2-amino-3-decyne ($[\alpha]^{22}_D$ −45.4°, MeOH), thereby establishing that bromination using triphenyl phosphite and *N*-bromosuccinimide proceeds by inversion of the configuration. If (*R*)-(+)-*N*-*N*-diethyl-2-amino-3-decyne prepared from the mesylate (*S*)-**1b** and with optical rotation $[\alpha]^{22}_D$ +52.9° is considered as optically pure, the bromide **1c** has an optical purity of 81.4%. This enantiomeric yield is typical of other related conversions.[18]

The reaction of 2-bromo-3-decyne with $LiAlH_4$ yielded only small amounts of 2,3-decadiene with 3-decyne as the main product (entry 22). The use of $LiAlH(OCH_3)_3$ resulted in higher yields of 2,3-decadiene which, however, was nearly racemic (entries 20 and 21). Reduction with AlH_3 yielded 2,3-decadiene as the main product which was formed in a preferred syn mode of substitution. The stereoselectivity increased slightly (45 → 53% ee) with temperatures from 0 to 65 °C (entries 17–19).

B. Formation of Allenic Alcohols. Reduction of the chiral propargylic trialkylammonio derivative **7** (prepared according to Scheme II) with $LiAlH_4$ yields the α-allenic tertiary alcohol 2-methyl-3,4-hexadien-2-ol (**11**, Scheme III) in a reaction where the optical rotation of the product changes drastically with the reaction temperature (Table II, entries 23 and 23). At 20 °C the allene-forming reaction proceeds via a predominant syn displacement of the tertiary amine, whereas at −70 °C an anti mechanism is preferred. The highest stereochemical yield (69% ee) was obtained at the lower reaction temperature.

Table II. Chiral Allenic Alcohols **11, 12,** and **19** from $LiAlH_4$ Reductions of Acetylenes **7, 9, 10, 14, 17,** and **22**

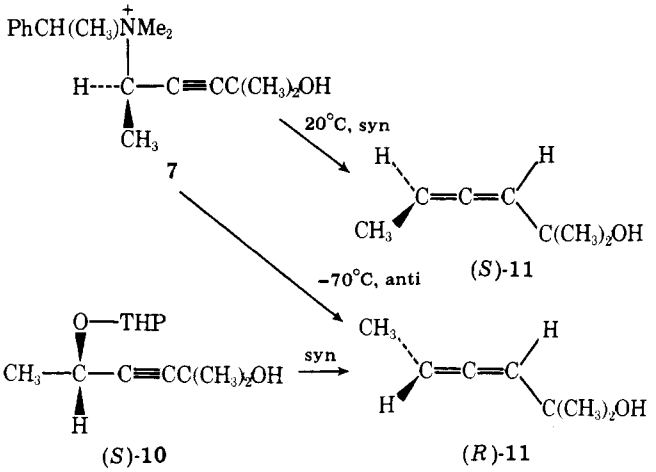
entry	compd	solvent	temp, °C	time, h	allene (yield, %)	$[\alpha]^{22}_D$, deg (*c*, methanol)	% ee
23	**7**	THF	−70	48	(*R*)-**11** (73)	−68.8 (10.5)	69
24	**7**	THF	20	5	(*S*)-**11** (80)	+32.9 (9.4)	33
25[a]	**10**	Et_2O	0	20	(*R*)-**11** (54)	−87.4 (12.3)	90[a]
26[a]	**10**	Et_2O	35	2	(*R*)-**11** (60)	−87.1 (12.2)	90[a]
27[a]	**17**	THF	24	32	(*R*)-**19** (50)	−90.7 (9.5)	95-100[a]
28[a]	**17**	Et_2O	35	3	(*R*)-**19** (65)	−87.6 (9.5)	85-95[a]
29[a]	**17**	$(i\text{-}C_3H_7)_2O$	20	24	(*R*)-**19** (50)	−83.9 (9.1)	80-90[a]
30[a]	**22**	Et_2O	35	8	(*R*)-**19** (40)	−73.6 (8.4)	80[a]
31[a]	**14**	THF	65	24	(*S*)-**12** (35)	−62.5 (7.7)	75[a]
32	**9**	THF	−70	54	(*S*)-**12** (70)	+10.7 (5.5)	14
33	**9**	THF	20	3	(*S*)-**12** (80)	+12.0 (2.8)	16

[a] Data taken from ref 10.

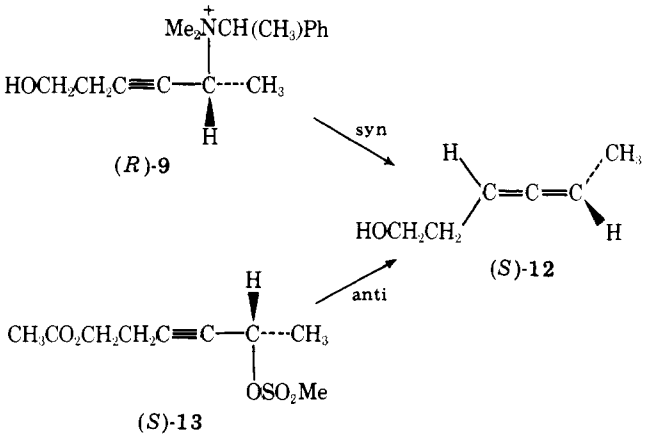
Table III. Formation of 3,4-Hexadien-1-ol (**12**) from $LiAlH_4$ Reduction of the Mesylate **13** in THF (Scheme IV)

entry	temp, °C	time, h	yield, %	$[\alpha]^{22}_D$, deg (*c*, methanol)	% ee	$-\Delta\Delta G^{\ddagger}$ kcal/mol	$\Delta\Delta H^{\ddagger}$, kcal/mol	$\Delta\Delta S^{\ddagger}$, cal/deg·mol
34	−55	96	75	+44.8 (2.6)	60	0.60	−1.4	−3.9
35	−25	96	75	+35.8 (2.1)	48	0.51		−3.8
36	20	12	55	+18.7 (2.0)	25	0.30		−3.9

Scheme III



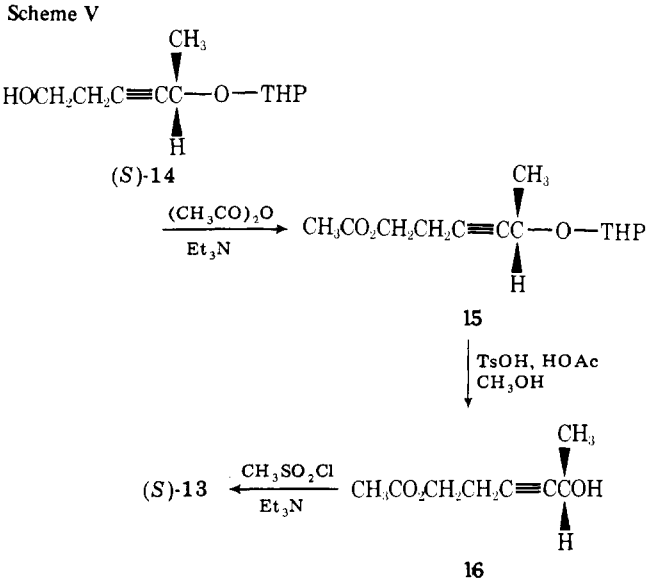
Scheme IV



The absolute configuration at the propargylic carbon of the starting amine (**5**, prepared from (*S*)-(−)-α-methylbenzylamine and the racemic tosylate of 3-butyn-2-ol) was established as *R* by hydrogenation-hydrogenolysis[19] of the enantiomer of **5**.

The chiral β-allenic alcohol 3,4-hexadien-1-ol (**12**) was prepared by $LiAlH_4$ reduction of two different propargylic

Scheme V

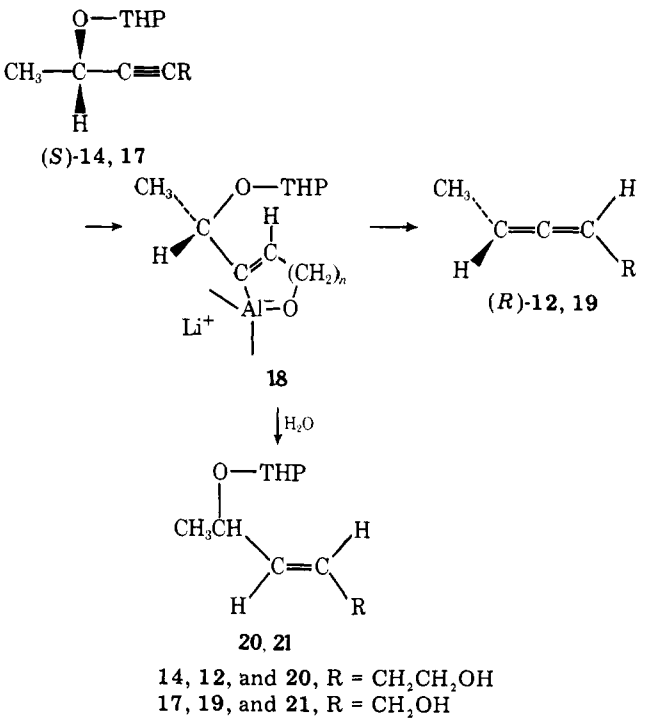


derivatives (**9** and **13**, Scheme IV) according to the conditions given in Tables II (entries 31-33) and III (entries 34-36). (Compound **9** was prepared according to Scheme II and compound **13** according to Scheme V.) The ammonium compound **9** gave (*S*)-3,4-hexadien-1-ol of low optical purity (14-16%). The tertiary amine is replaced via a syn mechanism. Only a very small temperature effect on the optical purity of the product was observed (entries 32 and 33).

In an attempt to demonstrate the existence of an organometallic intermediate in the reaction of **9**, reaction mixtures run at −70 °C for 5 and 30 h, respectively, were hydrolyzed with methanol plus water. GLC analysis indicated that 3,4-hexadien-1-ol had been formed in both runs. Quaternary salts were extracted into CH_2Cl_2 as ion pairs with the sodium salt of benzenesulfonic acid. NMR of the isolated salts indicated the presence of the starting acetylene **9** but no olefinic hydrogens resulting from a protonation product from a conceivable intermediate (cf. Scheme VI) could be detected (<5%).

Treatment of the propargylic (*S*)-mesylate **13** (prepared according to Scheme V) with $LiAlH_4$ gave (*S*)-3,4-hexadien-1-ol (**12**) in an anti substitution reaction (Scheme IV). A variation of the optical yield with temperature was observed

Scheme VI



14, 12, and 20, R = CH_2CH_2OH
17, 19, and 21, R = CH_2OH

(Table III, entries 34–36). From these values the $\Delta\Delta G^{\ddagger}$, $\Delta\Delta H^{\ddagger}$, and $\Delta\Delta S^{\ddagger}$ values were calculated according to eq 1 and 2.

Discussion

The present results demonstrate that the leaving group has a decisive influence on the stereochemistry of 1,3 substitutions with hydride in propargylic systems. In other words, the reaction mechanism changes with the type of leaving group. However, in many of the experiments we had to use different hydride reagents in order to obtain sufficient amounts of allene for reliable measurements of optical rotations. Clearly, results obtained with different hydride reagents are not directly comparable and we will therefore separate the detailed discussion accordingly.

In the case of the formation of the allenic hydrocarbon **2** we have studied the effect of temperature on the enantiomeric yield (Table I). This allowed the activation energy difference ($\Delta\Delta H^{\ddagger}$) to be differentiated into changes in enthalpy and entropy ($\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$, respectively) between the two reaction pathways leading to overall syn or anti displacement. It should be noted that the calculations of $\Delta\Delta S^{\ddagger}$ are based on the slope of each curve with an accompanying uncertainty due to the few experimental points. Furthermore, part of this problem is that the slope of each curve (Figure 1) may very well be different at different temperatures. The phenomenon is well known from studies of the temperature dependence of stereodifferentiating reactions[16] and is indicated in Figure 1 in the case of the reaction of **1c** by the drawing of one curved and one straight line. In spite of the drawback for the thermodynamic calculations we preferred to chose rather large temperature spans in order to observe the temperature dependence more clearly.

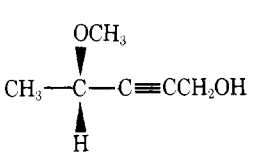
Our calculations of enantiomeric yields of 2,3-decadiene, which give the syn:anti ratio for the displacement, are based on a maximum specific rotation of $[\alpha]^{22}_{D} \pm 72.5°$.[13-15]

The question of absolute configuration of the present allenes is uncomplicated since the Lowe-Brewster rule is valid[17] and, futhermore, the absolute configuration of the alcohol **12** has been determined chemically.[20]

We take a unifying view of the mechanisms of allene-forming hydride reactions in the present discussion and will therefore include some pertinent, already published results, i.e., the conversions **10** → **11** (Scheme III), **14** → **12**, and **17** → **19** (Scheme VI); compound **22** was also converted into **19**.[10]

Metal Oxide or Alkoxide as Leaving Group. The following discussion refers to the reactions of compounds **1a** (Table I), **10, 14, 17,** and **22** (Table II).

The enantiomeric yield of 80.1% obtained when the alcohol **1a** was reduced with AlH_3 in refluxing THF represents the highest figure observed in the present work. As verified by the isolation of the corresponding trans allylic alcohol (**4**) the reduction proceeds at lower temperatures (0 °C) via an organometallic intermediate (**23**) which eliminates metal oxide



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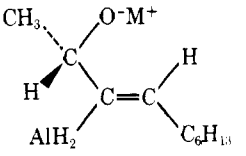


23

in a preferential anti manner. This mode of 1,2 elimination is deduced from the overall syn stereochemistry observed for the displacement reaction (syn:anti ratio 88:12). It was not possible to detect an organometallic intermediate at higher temperatures (20 and 65 °C). As indicated, however, by the virtually unchanged enantiomeric yield (entries 1–3), the mechanism might be essentially the same over the whole temperature range; i.e., at higher temperatures there would be a minimum, corresponding to the intermediate **23,** along the reaction coordinate.

Borden and Corey[8] also noted a syn substitution in the allene-forming reduction of chiral 1,3-di-*tert*-butylpropargyl alcohol with $LiAlH_4$–$AlCl_3$ (mole ratio 3:1, i.e., AlH_3), although the enantiomeric yield was lower (ca. 35% ee) than ours. When these authors used $LiAlH_4$–$AlCl_3$ in a ratio of 13:1, the opposite mode of displacement, i.e., anti, was observed to a similar extent (ca. 40% ee). This last result is partly consistent with ours (entries 3–5), as we also observed an increase in the anti:syn substitution ratio when the amount of $AlCl_3$ was decreased; we did not, however, note a reversal of the predominant mode of substitution. The $LiAlH_4$ reduction, without added $AlCl_3$, of chiral 2,2,3-trimethylhex-4-yn-3-ol in refluxing diglyme has been reported to give an allene in an overall syn displacement (the syn:anti ratio is unknown).[9c] Since Corey and co-workers[21] have observed the regioselective formation of an organometallic intermediate (like **23**) when primary propargylic alcohols are treated with $LiAlH_4$–$AlCl_3$ (60:1), Borden and Corey conclude "that the allene is formed, at least in part, from decomposition of an organoaluminum intermediate".[8] Our experiments provide detailed information in this respect. The reaction of **1a** with AlH_3 proceeds at 0 °C via an organometallic intermediate (**23,** M = Li or Al). The preferred mode of anti 1,2 elimination of metal oxide from this intermediate, when substantial amounts of LiCl (from $LiAlH_4$ and $AlCl_3$) are present in the solution, may possibly be explained in terms of facilitated bridging (coordination of Li^+ with the leaving oxygen) within an aggregation. This theory is strongly supported by the observation that the gradual depletion of reaction mixtures of LiCl (by decreasing the amount of $AlCl_3$) causes a decrease in the overall syn:anti displacement ratios (entries 3–5), but that the original high syn:anti ratio can be almost restored by adding LiCl to the solution containing the least amount of $AlCl_3$ (entry 6). The salt effect of LiCl seems only to influence the syn:anti elimination ratio but not the overall reaction rate since the yield of allene is as poor as with only a small amount of $AlCl_3$ present (entries 5 and 6).

As reported earlier, the formation of α- and β-allenic alcohols by $LiAlH_4$ reduction of monoethers (THP or methyl) of chiral alkynediols (**14, 17,** and **22**) proceeds at lower temperatures (around 0 °C) by an analogous stepwise reaction as shown in Scheme VI,[10] i.e., trans addition followed by preferred anti elimination (overall syn displacement). The enantiomeric yield in the case of **10** → **11** (Scheme III) is unaffected by temperature (entries 25 and 26) and, furthermore, it was noted (entries 27–29) that increasing donor properties of the solvent increased the degree of anti elimination from the intermediate **18** (n = 1, assumed to be present also at room temperature).

The intermediate **18** (n = 2, Scheme VI) exhibits an unusual stability and only slowly undergoes predominant anti elimination to a β-allenic alcohol even in refluxing THF. The enantiomeric yield is also lower than the corresponding formation of α-allenic alcohols from THP derivatives (syn:anti substitution ratio 87:13) whereas **17** → **19** in THF (entry 27) has a ratio higher than 98:2. The syn:anti substitution ratio for the methyl ether **22** is also lower, i.e., 90:10.[10]

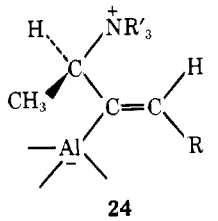
The primary cause of the high degree of anti as opposed to syn 1,2 elimination in all these addition–elimination reactions should be the facile interaction of the carbanion center with the antibonding orbital of the C–O bond, that is, the mechanism of preferred backside attack by an electron pair which is implicit in the usual picture of the concerted E2 reaction. However, as revealed through the experiments with gradual depletion of LiCl (entries 3–6), the catalysis of metal salts seems to be essential for the anti elimination to operate in a low-polarity solvent like THF.

It is probably less meaningful to try to relate the stereochemistry of the present 1,2 eliminations from configurationally stable organometallic intermediates (**18** and **23**) to the E1cB reactions of the irreversible type in which proton abstraction precedes the elimination.[22] However, it is interesting that different types of ionic association in solvents of low polarity strongly affect the stereochemistry of base-promoted 1,2 eliminations.[23]

Allenes from Quaternary Ammonium Compounds. The reduction of quaternary ammonium compounds with $LiAlH_4$ in THF (entries 14–16) is a remarkably efficient way to obtain allenic hydrocarbons uncontaminated with isomeric acetylenes.[24] The reaction has already been used for preparing α- and β-allenic alcohols in high yields[25] (entries 23, 24, 32, and 33).

A predominant syn displacement of tertiary amine is observed in all cases except one, viz., formation of the α-allenic alcohol **11** at −70 °C, where a very high anti:syn ratio of 85:15 is observed. Furthermore, increased temperature increases the syn:anti ratio (entries 14–16 and Figure 1).

Our unsuccessful attempt to detect a reaction intermediate (**24**) in the $LiAlH_4$ reduction of the alcohol **9** at −70 °C is not



24

surprising in view of the recent finding that a tertiary amine is an excellent leaving group in reactions of the E1cB type.[26] The result therefore does not exclude the addition–elimination mechanism in some of these reactions, e.g., the reaction **7** → **11** (Scheme III) at −70 °C, which exhibits an anti stereochemistry in contrast to all the other reductions of quaternary ammonium compounds (including **7** → **11** at 20 °C). It is obvious that the adjacent hydroxy group (as an alcoholate) determines the outcome of this particular reaction and one might speculate what the role of the alcoholate could be. We believe that it could be to promote an addition–elimination reaction whose reaction profile changes drastically with the reaction temperature; i.e., at −70 °C the elimination step would be relatively slow while at room temperature there is not time for the intermediate (**24,** R = CMe_2O^-) to evolve fully, thus leading to a more concerted type of reaction in which the transition state for the attack of the hydride lies much closer to the product. This picture would imply that the intermediate (**24,** R = CMe_2O^-; the trans geometry is postulated) from addition of hydride to **7** undergoes syn 1,2 elimination in preference to anti, since the overall stereochemistry of substitution is anti at −70 °C. Although not wholly applicable to the present case, it is at least interesting to note that studies on the stereochemistry of base-promoted 1,2 eliminations of quaternary ammonium compounds indicate that syn elimination is highly favored in aprotic solvents.[27,23] Therefore, there is at the moment nothing which contradicts the possibility of **7** undergoing a reaction at −70 °C in which the intermediate **24** is "frozen out".

As in the previous case with metal oxide as the leaving group, the entropy portion $\Delta\Delta S^{\ddagger}$ is the major term of the activation energy difference $\Delta\Delta G^{\ddagger}$ (entries 14–16). The present reactions occur between two charged species which also have salt character. The large value of $\Delta\Delta S^{\ddagger}$ is therefore not surprising, although it is not easily interpreted. We can speculate, however, that since this displacement parallels closely the temperature dependence seen with reduction of the propargylic alcohol **1a** (Figure 1) similar mechanism are perhaps involved; i.e., the association of the leaving group with the hydride reagent plays an essential role, perhaps to make these reactions S_Ni' like. In the present case it is probable that AlH_4^- combines with R_4N^+ to an ion pair prior to hydride attack on the triple bond.

Methanesulfonate as the Leaving Group. The mesylate group differs from the general pattern exhibited by the other leaving groups studied in that a predominant anti displacement is exhibited in both the formation of hydrocarbons (to an extent of 80–87%, entries 8–11) and alcohols (60–80%, entries 34–36) by reductions with $LiAlH(OCH_3)_3$ and $LiAlH_4$, respectively. Sulfonates are excellent leaving groups and we are somewhat reluctant to accept that an addition–elimination mechanism is operating. We are then left with mechanisms involving a concerted anti displacement of sulfonate by hydride or possibly a rate-determining formation of an ion pair which is then attacked by hydride.[28] Our experiments, however, do not allow conclusions about the concertedness of the reaction.

Our finding of anti displacements with propargylic mesylates is in agreement with the results of Borden and Corey, who reduced the tosylate and camphorsulfonate of chiral 1,3-di-*tert*-butyl-2-propyn-1-ol with various hydride reagents and found predominant anti substitution in all cases.[8]

The reagent $LiAlH(OCH_3)_3$ is a bulky nucleophile which is advantageous in stereoselective reductions of ketones. This might not only explain the preference for an S_N2' mechanism over an S_N2 in the reduction of the present acetylenes,[30] but also account for the observed anti stereochemistry, since there should be considerable electrostatic repulsion between the entering and leaving groups in the transition state leading to syn substitution. A recent paper reporting theoretical calculations on S_N2' reactions in the allylic system predicts that anti displacements may be preferred when the nucleophile has a negative charge and the leaving group is a halide.[5] The calculations indicate, however, that the syn mode of displacement is usually preferred through "nonbonded attraction".

The reaction of the mesylate **1b** not only exhibits an exceptional preferred stereochemistry of displacement but also a different influence of temperature on the competition between anti and syn substitution (Figure 1, Table I). It appears that

the reaction is "enthalpy controlled" which results in an apparent linear correlation between stereodifferentiation and temperature.[31] Such reactions are rare according to Izumi and Tai.[32] The temperature dependence of the anti:syn ratio of the mesylate **13** (entries 34-36) is similar to that for the mesylate **1b.** However, $LiAlH_4$, not $LiAlH(OCH_3)_3$, was used as reducing agent here. The presence of the alcohol group, as alkoxide, seems to make stereodifferentiation more dependent on differences in the entropy factors.

The comparatively large difference in enthalpy of activation ($\Delta\Delta H^{\ddagger}$) coupled with the small difference in entropy of activation ($\Delta\Delta S^{\ddagger}$) between the competing syn and anti displacement reactions might be interpreted in favor of electrostatic repulsion as the determining factor for faster anti displacement.[33] At the same time the syn mechanism is not favorable, compared, e.g., to the reaction of the quaternary ammonium compound **1c** with $LiAlH_4$, since there are no strong attraction forces between the leaving and entering groups. Thus, only nonbonded attraction favors the syn mechanism.[5] The negligible difference in entropy ($\Delta\Delta S^{\ddagger}$) probably suggests that this reasoning is correct.[33]

Bromide as the Leaving Group. There is a striking difference in enantiomeric yield between the mesylate **1b** and the bromide **1d** when $LiAlH(OCH_3)_3$ is used (Table I). The bromide, however, still gives a much higher anti:syn ratio (~50:50) than the alcohol **1a** and the quaternary ammonium compound **1c,** which both undergo preferred syn displacements. If electrostatic repulsion in the transition state can explain the preferred anti substitution, we can speculate on the relevant differences between bromide and mesylate as leaving groups. Firstly, the mesyloxy group is both larger and more electronegative and the electrostatic repulsion is therefore stronger; secondly, it is a better leaving group than bromide and therefore might not be as dependent on some sort of coordination with the nucleophile as the bromide still appears to be.[51]

Significant enantiomeric yields of allene are obtained from the bromide **1d** only when AlH_3 is the reducing agent (entries 17-19). The preferred syn displacement can be explained by an initial coordination of the electrophilic AlH_3 with the bromine atom followed by an intramolecular attack by hydride from the same side from which bromide departs. This concerted S_Ni' mechanism, as opposed to a stepwise, is reasonable considering the good leaving-group properties of bromide. This route, however, is not overwhelmingly preferred (syn:anti ~70:30). The identical reaction mechanism was suggested for the reduction of allylic halogenides with $LiAlH_4$.[34]

The influence of temperature on the syn:anti ratio (increasing with increasing temperature, Figure 1) shows the same tendency observed for the alcohol **1a** and the quaternary ammonium compound **1c.** It is of interest that the differences in the thermodynamic parameters $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ are very similar in the present case and for compound **1c;** both reactions are "entropy controlled".

Conclusion

In summary the results demonstrate, as one might expect, that the mechanisms of the present 1,3 substitutions are strongly dependent on both the type of leaving group and the nature of the hydride reagent. In addition, a neighboring-group effect on the overall stereochemistry was observed for the alcohols **7** and **9.** The highest enantiomeric yield was obtained in an addition-elimination reaction of a propargylic alcohol (**1a**) with AlH_3 (entry 3). Earlier results had shown that another stepwise reduction of a propargylic derivative (**17**) also gave a very high enantiomeric yield of an allene (Scheme VI).[10] The high degree of stereodifferentiation in these reactions is thus dependent on two selective reactions, i.e., the trans addition of aluminum hydride reagents over the triple bond and the anti 1,2 elimination from the organometallic intermediates **18** and **23.** The overall stereochemistry of this mechanism coincides with the expected syn displacement of the S_Ni' reaction which in fact might be the best way to describe the reaction **1a** → **2** at higher temperatures since no organometallic intermediate can be detected.

An S_Ni' mechanism is also probable when the 2,3-decadiene is formed from the bromide **1d** in a syn substitution on reduction with AlH_3. Furthermore, the charged group of the quaternary ammonium compound **1c** should also interact strongly with the hydride complex, possibly leading to an S_Ni' type of reaction.

The reduction of the sulfonate **1b** with $LiAlH(OCH_3)_3$ probably presents the most remarkable result in the present investigation. It reinforces the preliminary result of Borden and Corey[8] and suggests that the stereochemistry might be determined by electrostatic repulsive forces between the leaving and entering groups. The temperature dependence of the stereodifferentiation can support this view.[33] The preferred anti mechanism of this reaction and the pure nucleophilicity of the $LiAlH(OCH_3)_3$ reagent[35] are reminiscent of the organocuprate reactions of propargylic derivatives since all types of leaving groups, even a tertiary amine in a quaternary ammonium compound,[11b] are displaced in an anti manner.[11] Furthermore, it might be recalled that the organocuprate reactions of allylic derivatives are exclusively anti selective.[6] The relevance, however, of these reactions to the present hydride reductions and other "normal" nucleophilic reactions is questionable since, although organocuprates may be considered to have a highly nucleophilic character,[36] they are one-electron transfer reagents[37] and hence may be difficult to assess in the present context.[11b] However, a completely different but related reaction of inorganic cuprate (from copper(I) chloride and an excess of chloride) with a chiral propargylic chloride resulted in a chloroallene by an anti displacement.[38,52]

Another stereochemical study from the organometallic field demonstrated a preferred anti relationship (anti:syn ratio 70:30) between the migrating alkyl group and the leaving acetate in the allene-forming rearrangement of a trialkyl (3-acetoxy-1-alkynyl)borate.[39]

The only example of a nonorganometallic S_N2' reaction with a preferred anti mechanism in an allylic system has been reported by Stork and Kreft; an almost exclusive anti displacement of mesitoate with alkyl thiolate was demonstrated in an "open" allylic system whereas in a cyclohexenyl system an anti:syn ratio of 65:35 was observed.[3c]

These above-mentioned experimental results taken together with ours might indicate a preferred anti mode of displacement in S_N2'-type reactions when the incoming nucleophile is anionic and when, at the same time, the leaving group is bulky and has a negative charge.[51] Experiment would thus be in agreement with theory (predicted for an allylic system).[5] However, although the chiral propargylic system, as shown here, lends itself to convenient stereochemical studies of the S_N2' reaction, the situation regarding concertedness may also be more critical than in allylic systems since the addition-elimination route may be preferred with poor leaving groups.[10,40]

Up to now there have been no reports on the dependence of the syn:anti selectivity in S_N2' reactions upon temperature.[41] Our experiments do not allow penetration in greater depth, but it may be noted that since entropy factors are not important for determining the syn:anti dichotomy for the sulfonate **1b** we believe that this indicates the existence of electronic repulsive forces in both modes of substitition with the least repulsion in the anti geometry. The result needs confirmation in an allylic system.

Further work on the S_N2' reaction would seem warranted since, as stated by Stork and Kreft,[3c] there is great synthetic potential in this reaction. As an addition to earlier knowledge

we would like to emphasize that the properties of the leaving group appear very important in determining the orientation of approach by the nucleophile.

Experimental Section

Proton magnetic resonance spectra were recorded on a Perkin-Elmer R-12 B, a JEOL JNM-FX 100, or a Varian XL-100 spectrometer. Chemical shifts are reported in parts per million on the δ scale relative to tetramethylsilane internal standard. IR spectra were run on a Perkin-Elmer Infracord 157 G spectrophotometer using liquid films between NaCl disks. These spectra were recorded routinely and are in full agreement with the proposed structures. Optical rotations were obtained on a Perkin-Elmer 141 spectropolarimeter in methanol solution unless otherwise stated. Concentrations are recorded in g/100 mL.

Melting points were taken in open capillary tubes using a heated metal block equipped with calibrated Anschütz thermometers.

Vapor phase chromatography was performed on a Varian 1700 chromatograph, equipped with flame ionization detectors, using the following 2.7-m columns; 5% OV-25 on Gas Chrom Q (100/120) or 5% SE-30 on Chromosorb W (60/80). Individual compounds were isolated on 20% Carbowax 20M (300 or 600 × 0.94 cm) or 20% SE-30 (300 × 0.94 cm), all on Chromosorb W (60/80). Preparative column chromatography was performed on Merck silica gel 60 (230–400 mesh), using the indicated solvent.

All reactions involving hydride or Grignard reagents were performed in a nitrogen atmosphere.

(*S*)-(−)-3-Decyn-2-ol (1a).[42] The resolution and the determination of the enantiomeric purity of (*S*)-(−)-3-butyn-2-ol have been reported.[10] The title compound **1a** was prepared according to standard procedures,[43] from the lithium acetylide of resolved 3-butyn-2-ol and hexyl bromide in liquid ammonia. Distillation gave the alcohol in 87% yield, bp 102 °C (12 mm), $[\alpha]^{22}_D$ − 23.7° (*c* 10.2).

Methanesulfonate Ester of (*S*)-(−)-3-Decyn-2-ol (1b). This mesylate was prepared according to a published procedure.[44] To a stirred solution of 3.0 g (19.5 mmol) of (*S*)-(−)-3-decyn-2-ol (**1a**) and 3.0 g (29.3 mmol) of triethylamine in 50 mL of methylene chloride at −10 °C was added 2.5 g (21.5 mmol) of methanesulfonyl chloride during 15 min. The solution was stirred for another 15 min, and then 50 mL of methylene chloride was added. The organic phase was washed in turn with 10% HCl, saturated $NaHCO_3$ solution, and brine. After drying over anhydrous magnesium sulfate the solvent was removed under vacuum. The product was purified on silica gel 60, using ether–light petroleum (2:3) as the eluent: yield 94%; $[\alpha]^{22}_D$ −79.8° (*c* 10.9, dioxane); NMR ($CDCl_3$) δ 5.29 (m, 1), 3.08 (s, 3), 2.23 (t, 2), 1.67 (d, 3), 1.37 (m, 8), 0.89 (t, 3).

(*R*)-*N,N*-Diethyl-*N*-methyl-3-decyn-2-ammonium Iodide (1c). (*R*)-(+)-*N,N*-Diethyl-2-amino-3-decyne was prepared by treating 2.0 g (8.6 mmol) of the mesylate **1b** with 1.2 g (16.4 mmol) of diethylamine in 40 mL of methylene chloride for 3 days at room temperature. The reaction mixture was diluted with ether and washed with 10% K_2CO_3 solution. The organic phase was dried with potassium carbonate and the solvent was removed under vacuum. Purification on silica gel 60 with ether–light petroleum (1:1) gave the amine in 90% yield, $[\alpha]^{22}_D$ +52.9° (*c* 5.1). Treatment of 2.4 g (11.5 mmol) of this amine with 3.3 g (23.2 mmol) of methyl iodide in 30 mL of acetone for 24 h at room temperature yielded the title compound **1c.** The quaternary salt was purified by washing it several times with ether, yield 68%, mp 60°C. Anal. ($C_{15}H_{30}IN$) C, H, N.

(*R*)-(+)-2-Bromo-3-decyne (1d). This compound was prepared by modification of a published procedure:[18] 4.0 g (26.0 mmol) of (*S*)-(−)-3-decyn-2-ol was treated with 8.9 g (28.6 mmol) of triphenyl phosphite and 5.1 g (28.6 mmol) of *N*-bromosuccinimide at room temperature for 12 h. The reaction mixture was diluted with ether and successively washed with brine and water The ether solution was dried with magnesium sulfate and the solvent evaporated. Purification on silical gel 60 with light petroleum as the eluent gave 4.6 g (82%) of the bromide **1d**: $[\alpha]^{22}_D$ +8.7° (*c* 9.3); NMR ($CDCl_3$) δ 4.60 (m, 1), 2.23 (t, 2), 1.85 (d, 3), 1.36 (m, 8), 0.80 (t, 3).

A sample of this bromide (0.7 g, 3.3 mmol) was treated with 0.5 g (6.8 mmol) of diethylamine in 10 mL of methylene chloride at ambient temperature for 24 h. Purification by GLC on 20% SE-30 gave (*S*)-(−)-*N,N*-diethyl-2-amino-3-decyne, $[\alpha]^{22}_D$ −45.5° (*c* 5.2). It was therefore proved that bromination yields an inverted product with regard to the propargylic starting alcohol **1a.** If (*R*)-(+)-*N,N*-diethyl-2-amino-3-decyne with $[\alpha]^{22}_D$ +52.9°, from the mesylate **1b,** is considered as optically pure, the bromide should have a minimum optical purity of 81.4% (cf. the preparation of **1c**).

Hydride Reagents. Aluminum hydride (AlH_3) was prepared[45] in THF solution from a 3:1 molar ratio of lithium aluminum hydride and aluminum chloride. Lithium trimethoxyaluminum hydride ($LiAlH(OCH_3)_3$) was prepared according to a described procedure[35a] by the addition of methanol to a suspension of lithium aluminum hydride in THF.

Reaction of Propargylic Derivatives 1a–d with Hydride Reagents. Approximately 10 mmol of the appropriate acetylene **1a–d** in 10 mL of THF was added slowly to a stirred suspension of the indicated amount of the appropriate hydride reagent in 50 mL of THF (Table I). The mixture was then maintained at the indicated temperature and the reaction was followed by GLC. After hydrolysis with NH_4Cl solution and extraction with light petroleum, a primary purification of the organic extract was performed on a silica gel column, using light petroleum as the eluent. Decadiene was isolated by preparative GLC on a 6-m 20% Carbowax 20M column before measuring the rotation. The ratio of retention times for 2,3-decadiene/3-decyne at 170 °C was 1:1.16.

Reaction of the alcohol **1a** with AlH_3 at 0 °C for 5 days gave 53% of 2,3-decadiene and 24% of *trans*-3-decen-2-ol, which was isolated as described for decadiene and identified by IR, NMR, and MS.

***cis*-3-Decen-2-ol (4)** was prepared as described[46] by hydrogenation of racemic 3-decyn-2-ol (0.5 g, 3.2 mmol) over Lindlar catalyst (Fluka) in 20 mL of pentane at atmospheric pressure until the calculated amount of hydrogen was absorbed (15 min). The product was isolated and characterized as described above for the trans compound. Comparison of the isomers was made by GLC on a 5% SE-30 column; the ratio of retention times for trans/cis at 100 °C was 1.14.

(1*S*,1′*R*)-*N*-(1-Methyl-2-propynyl)-1-phenylethanamine (5). The reactions of 4.0 g (33.1 mmol) of (*S*)-(−)-phenylethanamine[47] and 7.4 g (33.1 mmol) of the *p*-toluenesulfonate of racemic 3-butyn-2-ol[48] in 50 mL of methanol for 3 days at room temperature afforded a mixture of diastereomeric amines in 70% yield: bp 97–102 °C (12 mm); NMR ($CDCl_3$) δ 7.30 (s, 5), 4.13 (m, 1), 3.55 and 3.12 (two split q, 1), 2.23 (d, 1), 1,30 (two d, 6). The diastereomeric amines were treated with HCl in dry ether to give their hydrochlorides. Two recrystallizations of these salts from chloroform gave enantiomerically pure amine **5**. The progress of the separation of the diastereomeric hydrochlorides could be followed from the ^1H NMR spectra of the free amines. The propargylic protons give rise to two split quartets at δ 3.12 and 3.55 ppm, respectively. The signals at δ 3.55 ppm come from the diastereomer having the least soluble hydrochloride, i.e., the title compound. The amine **5** could also be separated from its diastereomer by GLC on an OV-25 column. The retention time for the amine from the least soluble hydrochloride, i.e., **5**, was 8 min and for its diastereomer 6.8 min at 130 °C. Catalytic reduction of the enantiomer of amine **5** (prepared as described for **5** from (*R*)-1-phenylethanamine) with $Pd(OH)_2$ on activated carbon in ethanol for 48 h at a pressure of 200 psi yielded (*S*)-(+)-2-aminobutane[19] as the levorotatory hydrochloride, $[\alpha]^{20}_D$ −3.2° (*c* 5.0, ethanol). Reaction of this amine hydrochloride with benzoyl chloride in 2 M NaOH yielded the dextrorotatory benzamide,[19] $[\alpha]^{22}_D$ +32.9° (*c* 5.2, ethanol). The amine **5** prepared from (*S*)-1-phenylethanamine should therefore have the indicated *R* configuration at the propargylic carbon.

(5*S*,1′*S*)-5-(1-Phenylethylamino)-2-methyl-3-hexyn-2-ol (6). A Grignard reagent in ether was prepared from 1.6 g (66 mmol) of magnesium and 7.2 g (66 mmol) of ethyl bromide. A solution of 5.7 g (33 mmol) of the amine **5** in 50 mL of THF was added and the mixture was heated to 50 °C for 1 h. Subsequently, 1.7 g (30 mmol) of acetone was added and the mixture was heated for another 7 h. Ether was added and the mixture was treated with 10% K_2CO_3 solution. The organic extract was dried over K_2CO_3 and the solvent was removed under vacuum. Purification on silica gel 60 with ether–light petroleum (1:1) gave 3.5 g (51%) of the amino alcohol **6**: NMR ($CDCl_3$) δ 7.31 (s, 5), 4.00 (q, 1), 3.52 (q, 1), 2.78 (s, 2), 1.47 (s, 6) 1.27 (two d, 6).

(5*S*,1′*S*)-5-Dimethyl(1-phenylethyl)ammonio-2-methyl-3-methyl-3-hexyn-2-ol iodide (7) was prepared from the amino alcohol **6** in analogy with the quaternary salt **9** (vide infra), yield 50%, mp 152 °C. Anal. ($C_{17}H_{26}INO$) C, H, N.

(5*S*,1′*S*)-5-(1-Phenylethylamino)-3-hexyn-l-ol (8). The amine **5** (9.0 g, 52 mmol), dissolved in 50 mL of THF, was added to a stirred sus-

pension of 119 mmol of lithium amide in 400 mL of liquid. After the mixture was stirred for 2 h a mixture of 50 mL of THF and 20 mL of hexamethylphosphoramide (HMPA) was added. Ethylene oxide (4.6 g, 105 mmol) was added over a period of 2 h in small portions. The mixture was stirred overnight and the ammonia was allowed to evaporate. Water was added and the products were taken up in ether, which was washed with 10% K_2CO_3 and dried over K_2CO_3. The solvent was removed under vacuum and the product was purified on a silica gel 60 column using ether–light petroleum (1:1) as the eluent: yield 71%; $[\alpha]^{22}_D$ −5.2° (*c* 4.3); NMR ($CDCl_3$) δ 7.32 (s, 5), 4.02 (q, 1), 3.65 (t, 2), 3.45 (q, 1), 3.00 (s, 2), 2.31 (split t, 2), 1.27 (two d, 6).

(5*S*,1′*S*)-5-[Dimethyl(1-phenylethyl)ammonio]-3-hexyn-1-ol iodide (9). To a solution of 9.4 g (44 mmol) of the amino alcohol **8** in 60 mL of acetone were added 16.1 g (114 mmol) of methyl iodide and 8.3 g (60 mmol) of K_2CO_3. The mixture was stirred for 15 h at room temperature and filtered and the solvent was removed under vacuum. The product was recrystallized from ethanol–ether, yield 65%, mp 146 °C. Anal. ($C_{16}H_{24}INO$) C, H, N.

(*S*)-5-(Tetrahydro-2-pyranyloxy)-3-hexynyl Acetate (15). To a solution of 7.0 g (35.4 mmol) of 5-(tetrahydro-2-pyranyloxy)-3-hexyn-1-ol[49] [(*S*)-**14**] and 1.0 g (9.9 mmol) of triethylamine in 70 mL of pyridine was added 4.3 g (42.2 mmol) of acetic anhydride. The mixture was stirred for 6 h at room temperature, saturated $NaHCO_3$ solution was added, and the solution was extracted three times with 50-mL portions of ether. The combined ether extracts were washed thoroughly with water and the organic phase was dried over sodium sulfate. Distillation at reduced pressure yielded 6.0 g (72%) of the pure ester **15**: bp 96 °C (0.1 mm); $[\alpha]^{22}_D$ −78.8° (*c* 9.6); NMR ($CDCl_3$) δ 4.88 (m, 1), 4.47 (m, 1), 4.16 (t, 2), 3.57 (m, 2), 2.54 (split t, 2), 2.05 (s, 3), 1.65 (m, 6), 1.40 (split d, 3).

(*S*)-5-Hydroxy-3-hexynyl Acetate (16). To 6.0 g (25.0 mmol) of the tetrahydropyranyl derivative **15** in 50 mL of methanol were added 50 mg of *p*-toluenesulfonic acid and 1 mL of acetic acid. The mixture was stirred at room temperature for 4 h and was then diluted with ether–light petroleum (1:1). The organic extract was washed with water and dried over sodium sulfate. Distillation afforded 1.6 g (41%) of the title compound: bp 80 °C (0.1 mm); $[\alpha]^{22}_D$ −29.2° (*c* 5.2); NMR ($CDCl_3$) δ 4.49 (m, 1), 4.15 (t, 2), 2.94 (s, 1), 2.64 (split t, 2), 2.10 (s, 3), 1.45 (d, 3).

(*S*)-(−)-5-Methanesulfonyloxy)-3-hexynyl Acetate (13). This compound was prepared in accordance with the procedure reported by Crossland and Servis,[44] and as described for the methanesulfonate ester **1b**. A methylene chloride solution of 2.2 g (14.1 mmol) of the acetate **16** was treated with 2.1 g (21.0 mmol) of triethylamine and 1.8 g (15.7 mmol) of methanesulfonyl chloride. After drying and solvent removal under vacuum the title compound **13** was purified on a silica gel 60 column using ether as the eluent: yield 91%; $[\alpha]^{22}_D$ −77.3° (*c* 6.1, dioxane); NMR ($CDCl_3$) δ 5.27 (m, 1), 4.17 (t, 2), 3.10 (s, 3), 2.60 (split t, 2), 2.07 (s, 3), 1.61 (d, 3).

Reactions of Acetylenes 7 and 9 with $LiAlH_4$. To 10 mmol of the quaternary salts **7** or **9** in 50 mL of THF was added 12 mmol of $LiAlH_4$ at the temperature indicated in Table II. The mixture was kept at this temperature and the reaction was followed by GLC. After hydrolysis with NH_4Cl solution and extraction with ether, the organic extract was dried with $MgSO_4$ and the solvent was removed under vacuum. The allenic alcohols **11** and **12** were purified by preparative GLC on a Carbowax 20M column before measuring the rotations.

3,4-Hexadienol (12) from $LiAlH_4$ Reduction of the Mesylate 13. To a stirred suspension of 8 mmol of $LiAlH_4$ in 50 mL of THF was slowly added 5 mmol of the acetylene **13** at the temperature given in Table III. The mixture was stirred at this temperature for the time indicated and workup and isolation as described above for the acetylenes **7** and **9** gave the allenic alcohol **12**.

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Ion-Pair Intermediates and Extreme Deuterium Isotope Effects in Partially Diastereospecific Base-Promoted Elimination Competing with Base-Catalyzed 1,3-Proton Transfer

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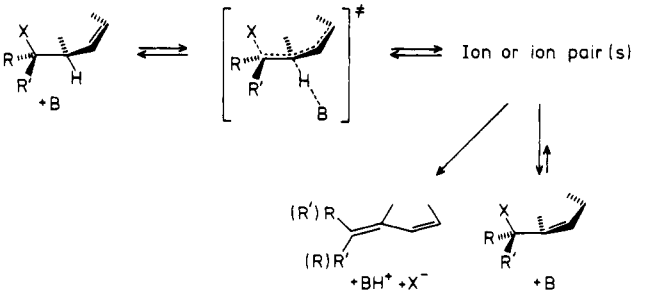
Abstract: Reaction of *threo*- or *erythro*-1-(1-acetoxyethyl)indene (**1**-*h* and **2**-*h*) with quinuclidine (Q) or sodium methoxide (NaOMe) in methanol results in base-promoted 1,2 elimination to give a mixture of (*E*)- and (*Z*)-1-ethylidenindene (**4a**-*h* and **4b**-*h*). In the reactions with Q, base-catalyzed 1,3-proton transfer producing 3-(1-acetoxyethyl)indene (**3**-*h*) competes with the eliminations. The latter compound undergoes base-promoted 1,4 elimination also yielding a mixture of **4a**-*h* and **4b**-*h*. The corresponding 1,3-dideuterated compounds **1**-*d* and **2**-*d* and the 1,1-dideuterated compound **3**-*d* yield, within experimental error, the same ratio of the elimination products (*E*)- and (*Z*)-[3-^{2}H]-1-ethylidenindene (**4a**-*d* and **4b**-*d*) as the protium analogues. With NaOMe, the kinetic isotope effects are $k^H_{14}/k^D_{14} = 6.6 + 1.8$ or -1.4, $k^H_{24}/k^D_{24} = 6.9 \pm 0.3$, and $k^H_{34}/k^D_{34} = 7.5 \pm 1.1$, respectively. The isotope effects measured with Q are $(k^H_{13} + k^H_{14})/(k^D_{13} + k^D_{14}) = 7.1 \pm 0.3$ and $(k^H_{23} + k^H_{24})/(k^D_{23} + k^D_{24}) = 7.3 + 1.6$ or -1.2, respectively. These deuterium isotope effects are composed of unusually large base-catalyzed 1,3-proton transfer isotope effects $k^H_{13}/k^D_{13} = 39 \pm 7$ and $k^H_{23}/k^D_{23} = 30 + 22$ or -11. They are large owing to competition between the 1,2 elimination and 1,3-proton transfer from a common intermediate. The 1,2-elimination isotope effects, on the other hand, have been attenuated by the competition: $k^H_{14}/k^D_{14} = 3.9 \pm 0.3$ and $k^H_{24}/k^D_{24} = 4.4 + 1.2$ or -1.0. Since significant incorporation of protium in **3**-*d* was not observed when starting from **1**-*d*, i.e., the 1,3-proton transfer is highly intramolecular, it is inferred that the 1,2 eliminations and the rearrangements are coupled and that they have at least one irreversibly formed ion pair in common, i.e., the 1,2 eliminations take place with $(E1cB)_{ip,I}$ mechanisms. The isotope effect on the 1,4-elimination reaction of **3** with Q is $k^H_{34}/k^D_{34} = 3.5 \pm 0.1$ and no incorporation of protium in **4a**-*d* and **4b**-*d* was observed. This indicates that the reaction proceeds via partially reversibly formed ion pairs. The ion pair and tightly solvated carbanion elimination reactions are partially diastereospecific. **1**-*h* gives 61 ± 2% syn 1,2 elimination with NaOMe and 94 ± 2% syn with Q while **2**-*h* yields 8 ± 2% syn with NaOMe and 14 ± 2% syn with Q. The 1,4 elimination gives a product ratio **4b**-*h*/**4a**-*h* of 23/77 with NaOMe and 14/86 with Q. The elimination mechanisms of the intermediates and the relationship between deuterium isotope effects and elimination reactions in general are discussed.

Carbanion ion pairs and tightly solvated carbanions are well-established intermediates in many reactions involving proton transfer from carbon.[1] However, the possible role of such intermediates in base-promoted elimination reactions has only recently received attention.[2,3] The intermediacy of reversibly formed ion pairs in some elimination reactions has been proposed. The main criterion for this mechanism $[(E1cB)_{ip,R}]$ has been small kinetic deuterium isotope effects.[3]

Recent work has demonstrated the usefulness of the base-catalyzed 1,3-proton transfer reaction as a probe of intermediates in elimination reactions (Scheme I).[4,5] The elimination of HCl from 1-(2-chloro-2-propyl)indene promoted by tertiary amines in methanol was shown to be stepwise and most likely to involve irreversibly formed ion pairs $[(E1cB)_{ip,I}]$.[4b] With sodium methoxide in methanol the elimination is of the $(E1cB)_I$ type.[4b] The chloro substituent (=leaving group) was found to assist the rate-determining proton transfer (ionization) considerably. The activation energy is lowered by 4 kcal mol^{-1} compared to that of the compound having methyl instead of chloro as substituent.[4b]

Scheme I



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