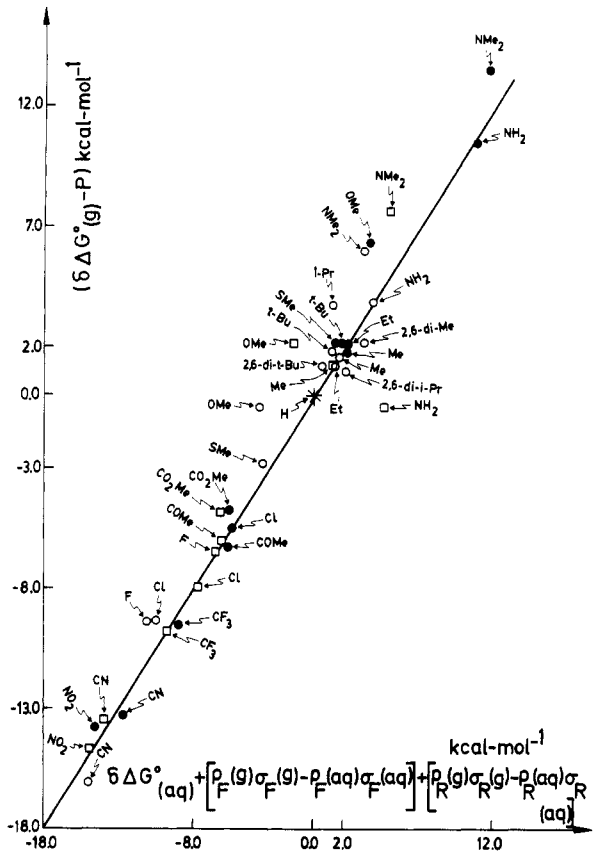

Figure 3. Plot of eq 7: (○) ortho; (□) meta; (●) para.

the same conclusions. Furthermore, should polarizability effects be the only difference between gas-phase and solution basicities of pyridines, then $\delta\Delta G°_{aq}$ values for 2,6-DTBP and 2,6-diisopropylpyridine (2,6-DIPP) should be quite close. In fact, they differ by 1.7 kcal·mol^{-1}, the latter being more basic. Hopkins and Aue[5] have concluded that gaseous 2,6-DTBPH$^+$ suffers a loss of entropy of ca. 6 cal·mol^{-1}·K^{-1} because of hindered rotations of and within the *tert*-butyl groups, while Meot-Ner[4] estimates the entropy loss of aqueous 2,6-DIPPH$^+$ to be small. Thus, a difference of free energy of 1.7 kcal·mol^{-1} can be well accounted for by this entropic effect.

We last notice that eq 3 assumes a constant attenuation factor for resonance and field effects in the ortho, meta, and para positions. As shown in Table II, this is only an approximation. Using eq 2 and keeping in mind that $\rho_\alpha(\text{aq}) \approx 0$, eq 7 obtains.

$$\delta\Delta G°_g - P = \delta\Delta G°_{aq} + [\rho_F(g)\sigma_F(g) - \rho_F(aq)\sigma_F(aq)] + [\rho_R(g)\sigma_R(g) - \rho_R(aq)\sigma_R(aq)] \quad (7)$$

This equation is represented in Figure 3, wherein the line drawn is the theoretical one (zero intercept and unity slope).[18] Notice that for all substituents with the exception of NMe_2 and OMe[17] we have taken $\sigma_F(g) = \sigma_F(aq)$ and $\sigma_R(g) = \sigma_R(aq)$. It is of interest that the points corresponding to the 2-fluoro- and 2-chloropyridines are now close to the theoretical line. On the other hand the amino, *N,N*-dimethylamino, and methoxy derivatives often show significant departures from the behavior predicted by eq 7. This result strongly supports the concept that these departures originate in specific solvent–solute interactions involving the substituents.

Acknowledgment. We would like to thank the Comitê Conjunto Hispano-Norteamericano para la Cooperación, Científica y Técnica for a grant (CCB 84-02-045).

Registry No. Pyridine, 110-86-1; pyridinium ion, 16969-45-2.

(17) Charton, M. *Prog. Phys. Org. Chem.* **1981**, *13*, 119.

(18) The actual correlation equation has an intercept of 0.41 ± 0.57 kcal·mol^{-1} and a slope of 1.01 ± 0.07, with n = 39 (all the available data), r^2 = 0.955, and sd = 1.6 kcal·mol^{-1}. Excluding the data for the 2-OMe, 3-OMe, and 3-NH_2 derivatives, the intercept and slope become, respectively, equal to 0.45 ± 0.36 kcal·mol^{-1} and 1.03 ± 0.05, with n = 36, r^2 = 0.987, sd = 1.0 kcal·mol^{-1}.

Alkylation of Allylic Derivatives. 13. Cross-Coupling Reactions of the Isomeric 2,3,4,4a,5,6-Hexahydro-2-naphthalenyl Carboxylates with Organocopper and Grignard Reagents

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The regio- and stereochemistry of cross-coupling of *cis*- and *trans*-2,3,4,4a,5,6-hexahydro-2-naphthalenyl pivalate (1-OPiv) with organocopper and Grignard reagents has been investigated. Alkylation of *cis*- and *trans*-1-OPiv with $LiCuMe_2$ and $LiCuBu_2$ gives the conjugated product 2,3,4,4a,5,6-hexahydro-2-alkylnaphthalene (**2**) primarily via α-anti-alkylation. Alkylation of *cis*- and *trans*-1-OPiv with LiCu(CN)Me and LiCu(CN)Bu gives both **2** and 3,4,4a,5,6,8a-hexahydro-8a-alkylnaphthalene (**3**). In this case, **2** arises nearly equally from α- and ε-alkylation. Alkylation of *cis*- and *trans*-1-OPiv with $LiCuPh_2$ and LiCu(CN)Ph gives only **2** as a result of α-anti-alkylation. Cross-coupling of *cis*- and *trans*-1-OPiv with Grignard reagents occurs remarkably fast. Reaction of *cis*- and *trans*-1-OPiv with Grignard reagents gives identical product mixtures. Evidence for the intermediacy of radical intermediates and mechanistic implications are discussed.

We have extended our initial studies[1] of the regio- and stereochemistry of alkylation of the *cis*- and *trans*-2,3,4,4a,5,6-hexahydro-2-naphthalenyl system with organocopper reagents. This paper reports an investigation of the regio- and stereochemistry of alkylation of the epimeric pivalates (*trans*-1-OPiv and *cis*-1-OPiv) with $LiCuR_2$ and LiCu(CN)R in which the alkyl groups are methyl and *n*-butyl and with $LiCuPh_2$ and LiCu(CN)Ph. The unexpected proclivity of this system to couple with Grignard reagents in the absence of cuprous salts precluded a study of the copper(I)-catalyzed cross-coupling of 1-OPiv with

(1) Underiner, T. L.; Goering, H. L. *J. Org. Chem.* **1987**, *52*, 897.

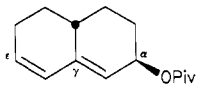
0022-3263/88/1953-1140$01.50/0

Table I. Product Distribution[a] for the Alkylation of *cis*- and *trans*-1-OPiv with $LiCuR_2$ and LiCu(CN)R in Ether

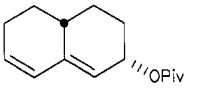
reagent	*trans*-2	*cis*-2	*trans*-3	*cis*-3	yield,[b] %
		trans-1-OPiv			
$LiCuMe_2$	5.2	94.8	0.0	0.0	97
$LiCuBu_2$	5.1[c]	94.9[c]	0.0	0.0	88
$LiCuPh_2$	5.0	95.0	0.0	0.0	96
LiCu(CN)Me	24.5	70.5	3.8	1.2	23
LiCu(CN)Bu	32.3[c]	64.5[c]	2.1	1.1	22
LiCu(CN)Ph	5.0	95.0	0.0	0.0	11
		cis-1-OPiv			
$LiCuMe_2$	81.2	18.8	0.0	0.0	95
$LiCuBu_2$	87.0[c]	13.0[c]	0.0	0.0	86
$LiCuPh_2$	95.0	5.0	0.0	0.0	97
LiCu(CN)Me	35.4	58.0	0.0	6.6	37
LiCu(CN)Bu	72.6[c]	19.1[c]	0.0	8.3	44
LiCu(CN)Ph	96.1	3.9	0.0	0.0	22

[a] Average values from at least two runs. Distribution determined by capillary GC unless noted otherwise. [b] Isolated yields. [c] *trans*:*cis*-2 ratio determined by ^1H NMR.

Grignard reagents.[2] This paper also reports an investigation of the regio- and stereochemistry of coupling of *cis*- and *trans*-1-OPiv with Grignard reagents and provides evidence for involvement of free radical intermediates.



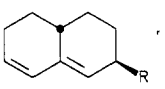
trans-1-OPiv



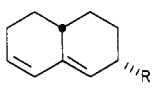
cis-1-OPiv

Alkylation of 1-OPiv with $LiCuR_2$ and LiCu(CN)R. The dialkylcuprates were prepared by adding slightly less[3] than 2 equiv of alkyllithium for each equivalent of cuprous iodide.[4] The alkylcyanocuprates were prepared similarly by using slightly less than 1 equiv of alkyllithium for each equivalent of CuCN.[5] A twofold excess of cuprate in ether was used for alkylation of the pivalates. The initial temperature was −20 °C after which the reaction mixture was stirred overnight at room temperature.

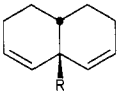
Possible alkylation products include two conjugated isomers, *cis*- and *trans*-2, and two unconjugated isomers, *cis*- and *trans*-3. Product distributions for alkylation of the pivalates with stoichiometric cuprates are presented in Table I. Product compositions were determined by capillary GC, or if baseline resolution was unobtainable, by ^1H NMR. The yields reported in Table I are isolated yields, and product distributions, as determined by capillary GC, were the same before and after isolation.



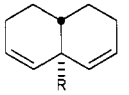
trans-2



cis-2



cis-3



trans-3

(a) R=Me, (b) R=nBu, (c) R=Ph,
(d) R=iPr, (e) R=tBu

Table II. Deuterium Distribution for the Alkylation of α-D-*trans*-1-OPiv with $LiCuR_2$ in Ether

reagent	α-D-2-R[a]	ε-D-2-R[b]
$LiCuMe_2$	88.7	11.3
$LiCuBu_2$	86.2	13.8
$LiCuPh_2$	94.7	5.3
LiCu(CN)Me	57.0	43.0
LiCu(CN)Bu	57.0	43.0
LiCu(CN)Ph	97.1	2.9

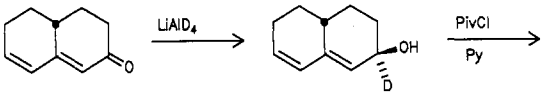
[a] Results from α-alkylation. [b] Results from ε-alkylation.

As shown in Table I, only the two conjugated products, *cis*- and *trans*-2, result from alkylation of 1-OPiv with $LiCuR_2$ or $LiCuPh_2$. The reaction is stereospecific[6] and involves preferential anti-alkylation. Comparison of data for *cis*- and *trans*-1-OPiv shows that with $LiCuR_2$, but not with $LiCuPh_2$, there is a slight stereoselective bias favoring formation of *cis*-2.

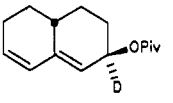
Alkylation of *cis*- and *trans*-1-OPiv with lithium methylcyano- and butylcyanocuprates yielded predominantly the conjugated isomers **2a,b**, with only minor amounts of the unconjugated isomers **3a,b** (Table I). For reasons unclear at this time, these alkylations proceded with less stereospecificity than alkylations with $LiCuMe_2$ or $LiCuBu_2$. Lithium phenylcyanocuprate, however, exhibited excellent stereospecificity, giving ~95% anti-alkylation with both *cis*- and *trans*-1-OPiv. As observed before,[7] the cyanocuprates gave significantly lower yields than dialkylcuprates (Table I). Cyanocuprates are less reactive than dialkylcuprates,[8] and, in this system, the ratio of alkylation to decomposition (of cuprate) is evidently higher for dialkylcuprates than for cyanoalkylcuprates.

The alkylation products were identified by comparison of their ^1H NMR spectra with those of authentic samples of *cis*- and *trans*-**2a** and *cis*- and *trans*-**3a**, whose stereochemistry was established previously.[1] Preparative GC proved ineffective in separating *cis*- and *trans*-2 or *cis*- and *trans*-3; however, characterization of the mixtures was easily accomplished by ^1H NMR because of the preponderance of one isomer and the observation that the resonance for the C-1 vinyl proton of the cis isomer of **2** invariably appeared downfield (0.1 ppm) of the corresponding signal for the trans isomer. The same signal for the cis isomer had a peak width approximately twice as large as the peak width for the trans isomer.[1]

In order to deterine the regiochemistry of alkylation, α-D-*trans*-1-OPiv was prepared by reduction of 2,3,4,4a,5,6-hexahydro-2-ketonaphthalene (**4**)[9] with $LiAlD_4$ followed by esterification with pivaloyl chloride (eq 1).



4 α-D-1-OH



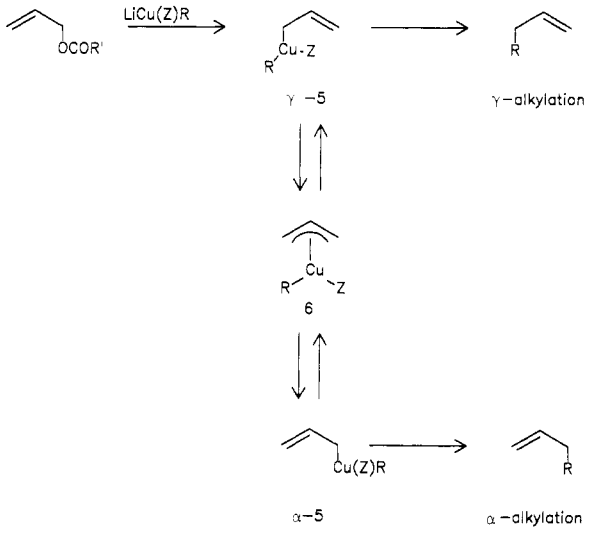
(1)

α-D-1-OPiv

The results for alkylation of α-D-*trans*-1-OPiv with $LiCuR_2$ and LiCu(CN)R are reported in Table II. In these ex-

(2) Tseng, C. C.; Yen, S.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2892 and earlier papers in this series.
(3) Carbonyl attack with formation of the corresponding alcohol accompanies alkylation if the RLi/CuI ratio is >2.
(4) Cuprous iodide (Aldrich) was purified according to the procedure of Kauffman, G. B.; Tetter, L. A. *Inorg. Synth.* **1963**, *7*, 9.
(5) CuCN was prepared according to the procedure of Barber, H. J. *J. Chem. Soc.* **1943**, 79.
(6) Throughout this paper the terms regio- and stereospecific and regio- and stereoselective are used as defined in footnote 3 of ref 10b.
(7) (a) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1984**, *49*, 422.
(8) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005.
(9) Birch, A. J.; Murray, A. R.; Smith, H. *J. Chem. Soc.* **1951**, 1945.

Scheme I. Mechanism for Alkylation of Allylic Carboxylates with Alkylcuprates



periments, product **2** was isolated without fractionation of the cis and trans isomers, and the deuterium distribution at C-2 and C-7 was determined by 30.6 MHz ^{2}H NMR. In a control experiment, reaction of α-D-*trans*-1-OPiv with $LiCuMe_2$ was stopped after ~50% completion, and the unreacted pivalate was found to be unchanged. Analysis by ^{2}H NMR integration gave the same results as ^{1}H NMR integration.

As shown in Table II, the conjugated product **2** obtained with $LiCuR_2$ results mainly from α-alkylation. With LiCu(CN)R there is substantial ε-alkylation as well as α-alkylation. Phenylcyanocuprate is strikingly different in that nearly all of the coupling occurs at the α position.

In earlier work[10] evidence was presented that cross-coupling of allylic carboxylates with alkylcuprates involves oxidative addition with allylic rearrangement to give an S_N2' σ-allylcopper(III) complex (**5**) as shown in Scheme I. This complex either undergoes reductive elimination to give regiospecific γ-alkylation or isomerizes to the π-allyl complex **6** in which case regiospecificity is lost.

The most important evidence for this pathway is that the original double-bond configuration in the ester is not fully preserved in the α-alkylation product[10a] and γ-alkylation inevitably predominates in unbiased systems.[10b]

The regioselective excess α-coupling in the present system is compatible with this mechanistic proposal. As shown in Scheme II, oxidative addition with allylic rearrangement leads to **7** in which the C–Cu bond is allylic with respect to both double bonds. However, the double bonds in **7** are not in the same plane and thus the dihedral angle between the C–Cu bond and the plane of each of the double bonds is different. As shown graphically in Figure 1, MM2 calculations[11] indicate that the dihedral angles are 87° and 67°. We presume a perpendicular orientation is required for facile σ → π isomerization, and, for similar stereoelectronic reasons, we presume the conformation of the initially formed **7** is the one in which the new C–Cu bond is perpendicular to the just shifted double bond. Thus, σ → π isomerization in the direction of the original α position requires no prior conformational adjustment and **7** → **8** isomerization is favored over **7** → **10** isomerization.

Scheme II. Mechanism for the Alkylation of *trans*-1-OPiv with $LiCuR_2$ or LiCu(CN)R

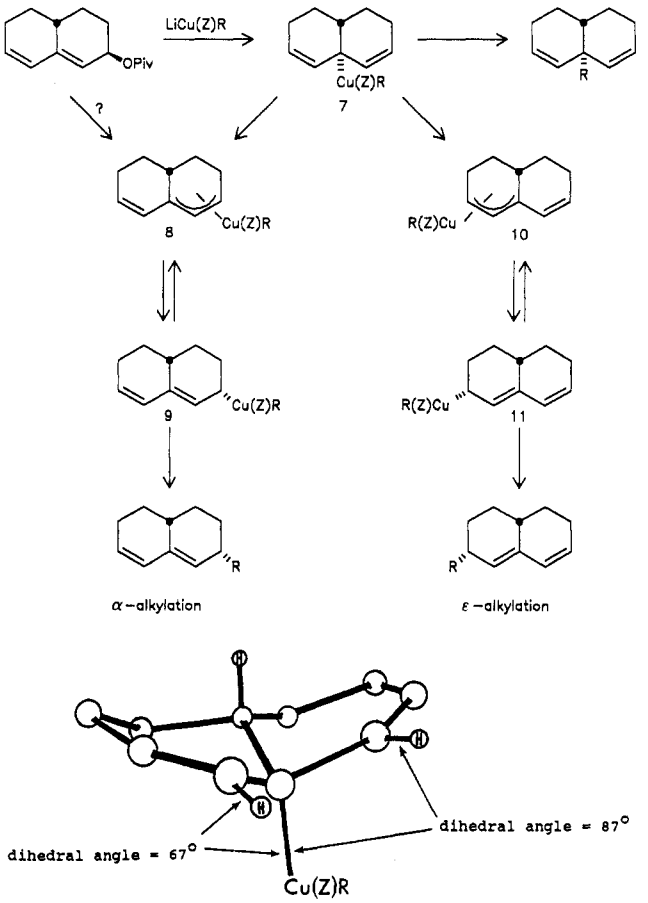


Figure 1. Computer drawing of **7** from MM2 calculation.

As shown in Scheme I, regiochemistry is determined by the reductive elimination to the σ → π isomerization ratio for the σ-allylcopper(III) complex **5**. This ratio depends on the nontransferred ligand (Z) on copper. When Z = CN, the ratio is higher than when Z is a second alkyl group.[7,12] Thus, reactions with LiCu(CN)R are more regiospecific (excess γ-alkylation) than reactions with $LiCuR_2$.

According to mechanistic interpretations in Schemes I and II, the present results in Tables I and II show that σ → π isomerization of the initial σ-allyl complex **7** is faster when Z is a second alkyl group than when Z = CN. Thus, with $LiCuR_2$ there is no detectable reductive elimination to give **3** and the lifetime for **7** is so short that there is only a small amount of conformational change required for formation of the ε-alkylation product. On the other hand, with LiCu(CN)R, the σ → π isomerization of **7** is slowed so that reductive elimination to **3** is observed and conformational change that leads to ε-alkylation product becomes more important.

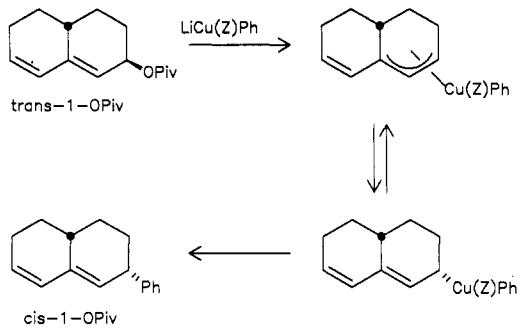
Another explanation for the favored α-alkylation in this system is included in Scheme II. Reaction of *trans*-1-OPiv with the cuprate may lead directly to the π-allylcopper complex **8**. This may be the sole reaction pathway, or this may occur in competition with formation of the σ-allylcopper complex **7**. Subsequent formation of the σ-α-allylcopper complex **9** which retains π-conjugation would be expected to be more favorable than formation of **7** which is unconjugated. The ε-substituted product would then be derived from either rearrangement of **7** to **10** and then

(10) (a) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1983**, *48*, 721. (b) Goering, H. L.; Singleton, V. D., Jr. *J. Org. Chem.* **1983**, *48*, 1531.

(11) Calculations were performed by using K. Steliou's modified version of the MODEL program. An isopropyl group was substituted for the Cu(Z)R group.

(12) Tseng, C. C.; Paisley, S. D.; Goering, H. L. *J. Org. Chem.* **1986**, *51*, 2884.

Scheme III. Mechanism for the Phenylation of *trans*-1-OPiv with $LiCuPh_2$ and LiCu(CN)Ph



to **11**, which could reductively eliminate to yield the observed isomer, or the ϵ-substituted product could arise via direct formation of the π-allyl complex **10**.

Although we cannot rule out any of these possibilities, the first proposal appears the least complicated and is more consistant with previous studies.[10]

In other work[13] we have obtained evidence that reaction of allylic pivalates with a variety of phenylcuprates proceeds via an initial π-allylcopper complex. Presumably, phenylation of *trans*-1-OPiv with either $LiCuPh_2$ or LiCu(CN)Ph proceeds as shown in Scheme III. The 4% ϵ-phenylation can be accounted for by the same arguments used to account for ϵ-alkylation with $LiCuR_2$.

Alkylation of 1-OPiv with RMgX. The unusual reactivity of 1-OPiv with Grignard reagents prohibited isolation of the copper(I)-catalyzed reaction of the ester with Grignard reagents.[2] In addition, use of the cuprate prepared by addition of 2 equiv of Grignard to 1 equiv of CuI yielded a product distribution that was identical with that obtained with the copper-free Grignard reagent.

Cross-coupling of allylic carboxylates with Grignard reagents has been reported;[14] however, it has been found that these reactions are generally much slower than copper(I)-catalyzed Grignard alkylations.[2] Other allylic dienyl pivalates with at least one acyclic double bond have been investigated[15] and found to be similar to ordinary allylic esters, i.e., cross-coupling with Grignard reagents is slow in the absence of copper(I). The reason why 1-OPiv is so reactive toward Grignard reagents remains uncertain but is presumably a result of the geometry of this rigid dienyl system. Copper-free alkylations were accomplished by treating a cold (0 °C) stirred ethereal solution of the pivalates (approximately 1 M) with a 2 M excess of an ethereal solution of Grignard. In order to insure copper-free conditions, each reaction was carried out in a fresh vial with a clean stir bar.[16] The Grignard reagents were prepared at least 1 week before use; under these conditions any copper(I) impurities present from the magnesium turnings would have been reduced to copper(0). After addition, the reactions were warmed to room temperature for 2 h before standard workup. In most cases, it was found that the reaction was complete within 10 min at 0 °C.

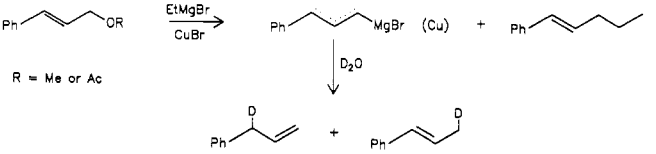
The reaction of *cis*- or *trans*-1-OPiv with a variety of Grignard reagents proceded stereoselectively, and the alkylation product distribution is reported in Table III. Product compositions were determined as described earlier, and the components were isolated by preparative GC. The products were identified by spectral comparisons with fully characterized model compounds (**2a** and **3a**).[1]

Table III. Alkylation Product Distribution[a] for the Reaction of *trans*- and *cis*-1-OPiv with Grinard Reagents in Ether

RMgX	*cis*-3	*trans*-3	*trans*-2	*cis*-2	yield,[b] %
			trans-1-OPiv		
Me	0.0	0.0	14.3	85.7	93
n-Bu	7.1	15.9	31.0[c]	46.0[c]	75
Ph	0.0	0.0	43.0	57.0	97
i-Pr	16.7	10.4	32.5[c]	40.4[c]	76
t-Bu	14.3	38.9	46.7[d]		48
			cis-1-OPiv		
Me	0.0	0.0	12.3	87.7	92
n-Bu	5.3	17.9	24.4[c]	52.4[c]	80
Ph	0.0	0.0	42.0	58.0	96
i-Pr	11.5	12.9	29.9[c]	45.7[c]	85
t-Bu	13.9	37.8	48.3[d]		50

[a] Distribution determined by capillary GC unless noted otherwise. [b] Isolated yields. [c] *cis*:*trans*-**2** ratio was determined by integration of the C-2 protons in the ^1H NMR spectrum of the preparative GC isolated mixture of the two isomers. [d] Ratio of *cis*:*trans*-**2e** could not be obtained since preparative GC isolated samples of **2e** were contaminated with **3e** which interfered with ^1H NMR integration.

Scheme IV



Products arising from carbonyl attack could be detected by capillary GC and isolated by rotary TLC. Alkylation preempted carbonyl attack in most cases. Reacton of *trans*-1-OPiv with MeMgI, or *n*-BuMgI, however, involved ~3% carbonyl attack. The resulting alcohol (1-OH) had its original configuration as determined by ^1H NMR. The more sterically crowded Grignard reagents, *i*-Pr, *t*-Bu, and Ph, did not give detectable carbonyl attack. With *cis*-1-OPiv, carbonyl attack was not observed with any of the Grignard reagents. The speed at which alkylation occurs in this system was demonstrated by treating the corresponding acetate, *trans*-1-OAc, with MeMgI. Only 17% of the acetate underwent carbonyl attack while the remainder underwent coupling. Again, recovered alcohol had retained its configuration.

The relative rates of alkylation of *trans*-1-OPiv with MeMgI in the absence and presence of 1% CuCN (with respect to the Grignard) were determined by spiking an ethereal solution of the pivalate with mesitylene as an internal standard, partitioning the resulting solution amongst two vials (one containing the appropriate amount of CuCN), treating each solution with MeMgI, and measuring product formation as a function of time. In each case the reaction was complete in 10 min at 0 °C, and the ratios of product to mesitylene were the same at intermediate times. Thus, the uncatalyzed cross-coupling is so fast that the CuCN-catalyzed reaction cannot be isolated.

In addition to cross-coupling products **2** and **3**, a reduction product, 2,3,4,4a,5,6-hexahydronaphthalene, **12**, was present in varying amounts depending upon the Grignard reagent used. Methyl and phenyl Grignard produced none of this product, while *n*-butyl, isopropyl, and *tert*-butyl Grignard produced 7%, 8%, and 9%, respectively.

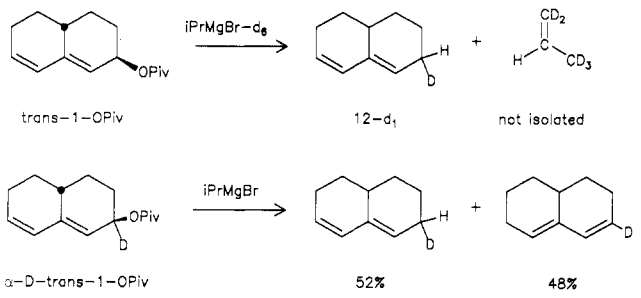
(13) Lesheski, L. E.; Paisley, S. D.; Schmitter, J.; Underiner, T. L., unpublished results.

(14) (a) Arnold, R. T.; Liggett, R. W. *J. Am. Chem. Soc.* **1942**, *64*, 2875; **1945**, *67*, 337. Arnold, R. T.; Searles, S., Jr. *J. Am. Chem. Soc.* **1949**, *71*, 2021. Wilson, K. W.; Roberts, J. D.; Young, W. G. *J. Am. Chem. Soc.* **1949**, *71*, 2019. (b) Higgins, G. M. C.; Saville, B.; Evans, M. B. *J. Chem. Soc.* **1965**, 702.

(15) Underiner, T. L.; unpublished results.

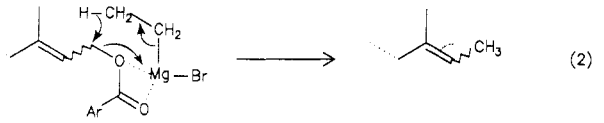
(16) Teflon stir bars were soaked overnight in aqua-regia and then rinsed with NH_4OH.

Scheme V. Reduction of *trans*-1-OPiv with *i*-PrMgBr



Claesson and Sahlberg reported the reduction of the cinnamyl system with EtMgBr and CuBr in THF and ether (Scheme IV).[17] The reduction was thought to occur via a MgBr- or Cu(I)-bound mesomeric anion intermediate which was hydrolyzed to products.

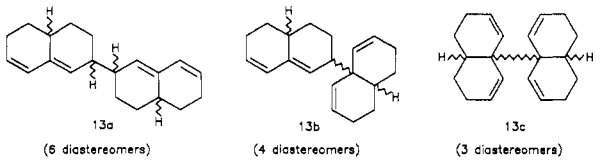
Higgins et al. reported that reaction of geranyl and neryl mesitoates with EtMgBr produced, in addition to coupling product, trace amounts of hydride reduction product.[14b] They proposed the ethyl group of the Grignard functioned as a hydride donor with simultaneous fragmentation to ethylene. This proposal was not verified experimentally (eq 2).



(2)

The reduction of 1-OPiv to yield **12** occurs only with Grignards possessing a β proton. Reaction of *trans*-1-OPiv with *i*-PrMgBr-d_6 produced (in addition to alkylation products) **12**-*d* (Scheme V). Complete incorporation of deuterium was established by ^{1}H NMR. Because of an isotope effect, the amount of reduction leading to **12**-*d* was less by a factor of 1.6 than when nondeuteriated *i*-PrMgBr was used. In addition, reaction of α-D-*trans*-1-OPiv with *i*-PrMgBr produced (in addition to alkylation products) **12**-*d* with the deuterium randomized between the α and ϵ positions (D_{sp^3}/D_{sp^2} = 52/48).[18] Thus, the hydride comes from the Grignard reagent (and not the H_2O quench), and it is delivered equally to both ends of the pentadienyl system.

Another product which had a slightly lower R_f value than products **2**, **3**, and **12** was isolated by preparative TLC. The high resolution mass spectrum of this product had a molecular ion peak corresponding to the dimer of two 2,3,4,4a,5,6-hexahydronaphthyl radicals, $C_{20}H_{26}$. There are three possible regioisomers for such a dimer: **13a** (6 diastereomers), **13b** (4 diastereomers), and **13c** (3 diastereomers). The ratio of alkene protons to alkane protons (3:10) in the ^{1}H NMR spectrum indicated that regioisomer **13a** predominates and presumably is obtained as a mixture of six diastereomers.[19]



(17) Claesson, A.; Sahlberg, C. *Tetrahedron Lett.* **1978**, 5049; J. *Organomet. Chem.* **1979**, *170*, 355.

(18) A small isotope effect in which the deuterium label favors the isomer with the deuterium on an sp^3 carbon was observed; see ref 12.

(19) Analysis of the ^{1}H NMR spectrum of **13a** clearly shows that more than two diastereomers are present. TLC of **13a** gave only one spot, while capillary GC gave three broad overlapping peaks.

Table IV. Product Distribution for the Reaction of *trans*- and *cis*-1-OPiv with Grignard Reagents in Ether

RMgX	2 and 3[a]	12[b]	13[a]	carbonyl attack
		trans-1-OPiv		
Me	93	0	3	3.0
n-Bu	75	7.7	17	3.4
Ph	97	0	0	0
i-Pr	76	6.3	17	0
t-Bu	48	5.5	19	0[c]
		cis-1-OPiv		
Me	92	0	2	0
n-Bu	80	7.7	16	0
Ph	96	0	0	0
i-Pr	85	6.1	14	0
t-Bu	5	9.2	18	0[d]

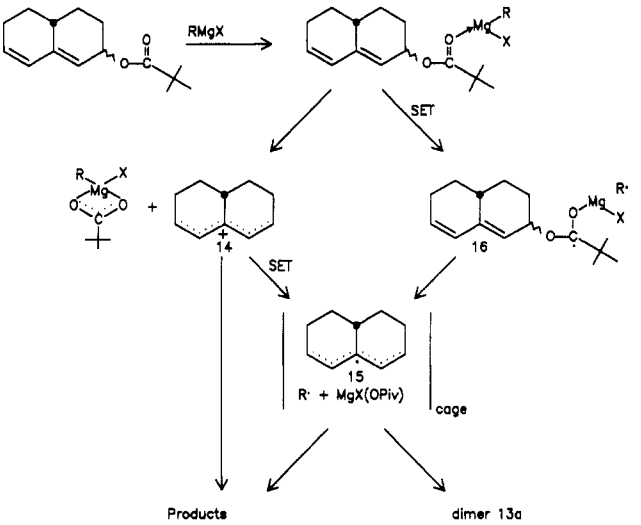
[a] Isolated yields. [b] Percent of **12** present in alkylation product mixture as determined by capillary GC. [c] 22% of unreacted pivalate was recovered. [d] 21% of unreacted pivalate was recovered.

Table V. ^{2}H Distribution in the Alkylation Product for Reaction of *trans*-1-α-D-OPiv with MeMgI and PhMgBr in Ether

reagent	α-D-2[a]	ϵ-D-2[b]
MeMgI	51.8	48.2
PhMgBr	51.9	48.1

[a] Results from α-alkylation. [b] Results from ϵ-alkylation.

Scheme VI. Mechanism for the Alkylation of 1-OPiv with Grignard Reagents



The experimental methods for determining the product distribution did not allow for detection of volatile products arising from dimerization of Grignard reagents. Product distributions for reaction of 1-OPiv with a variety of Grignard reagents are reported in Table IV. The regiochemistry of the reaction of α-D-*trans*-1-OPiv with Grignards was determined in a manner similar to that for the determination of regiochemistry for dialkylcuprates. Methyl and phenyl Grignard were chosen as the alkylating reagent since they yielded **2** with little or none of **12** and **13**. This simplified product isolation. As shown in Table V, alkylation occurs nearly equally[18] at the α and ϵ positions.

Except for the formation of dimer **13a**, all of our results are in accord with the ionic mechanism first proposed by Arnold[14a] and later reexamined by Higgins.[14b] This mechanism involves heterolysis of the coordination compound of the allylic ester with the alkylmagnesium halide to yield the symmetrical pentadienyl cation **14** (Scheme VI). The alkyl group of the complex anion is the source of R^- as well as H^-. In our system, formation of dimer **13a**

evidently arises from coupling of two hexahydronaphthalenyl radicals **15**. The question remains as to whether the other products (**2**, **3**, and **12**) also arise from radical intermediates or if these result from ionic processes. No distinction between these two pathways can be made on the basis of the regiochemistry due to the common symmetry of the pentadienyl cation **14** and radical **15**.

Single electron transfer (SET) in the reaction of Grignard reagents with electrophiles has been extensively studied.[20] Gough and Dixon[21] have provided evidence for a radical mechanism for the coupling of alkylmagnesium halides with allylic bromides. Ashby[22] has presented convincing evidence for SET between ketones and Grignards. Little information concerning the reaction of esters with Grignards is available. The reaction of trityl acetate with phenylmagnesium bromide has been demonstrated to proceed nearly exclusively via a radical intermediate.[23]

Two plausible mechanisms for the formation of a radical intermediate in the reaction of Grignard reagents with 1-OPiv are presented in Scheme VI. SET to the ester would generate intermediate **16** which could then fragment to yield **15**. SET from Grignard reagents to carbonyl compounds has been demonstrated previously.[20,22,23,24] Alternatively, ionizaton of 1-OPiv to the ion pair **14** may initially occur followed by SET to yield **15**.[23,25] Whether all products are derived from **15** or if just **13a** arises via the dimerization of **15** is uncertain. Capture of the ion pair **14** with Grignard reagents via an ionic pathway is certainly possible.

Experimental Section

General Methods. Proton NMR spectra were obtained with a Brucker WP200 instrument; proton-decoupled ^{13}C and ^{2}H NMR spectra were obtained with a JEOLCO FX-200 spectrometer operating at 50.1 MHz (^{13}C) and 30.6 MHz (^{2}H). Chemical shifts for ^{13}C are referenced to the center peak of $CDCl_3$ (77.0 ppm), and chemical shifts for ^{2}H are reported in ppm relative to internal $CDCl_3$ (7.24 ppm). Coupling constants are in hertz. Mass spectra were obtained with an AE1-MS-902 high resolution instrument. IR spectra were obtained with a Polaris FT-IR spectrometer. Product distributions were obtained by capillary GC (175-ft column, UCON-LB-550-X) and products were isolated by preparative GC (4 ft × $^1/_4$ in. column, 20% UCON-LB-550-X on Chromabsorb W).

General Procedure for the Alkylation of Dienyl Pivalates with LiCuR and LiCu(CN)R_2. In a typical experiment the cuprate (1 mmol) was prepared by adding slightly less[3] than a stoichiometric amount of *n*-BuLi (in hexane) or MeLi (in ether) or PhLi (in 7:3 cyclohexane/ether) to a cold (−20 °C) ethereal suspension of CuI[4] or CuCN.[5] An ethereal solution of the pivalate (0.5 mmol) was added to the cuprate at −20 °C, and the reaction was allowed to slowly warm to room temperature overnight. After quenching the reaction with 3 mL of saturated NH_4Cl, the precipitate was filtered and washed well with ether. The ether extracts were combined, shaken with 5% HCl, 10% NaOH, and brine, and then dried over $MgSO_4$. After removal of solvent by fractionation, the alkylation products were obtained by rotary TLC (pentane/silica gel). The spectral properties of the alkylation products are reported below.

***cis*-2,3,4,4a,5,6-Hexahydro-2-butylnaphthalene (*cis*-2b).** The analytical sample was contaminated with 5% of *trans*-**2b**. IR (neat): 3020 (m), 2970 (s), 2940 (s), 2860 (s), 2850 (m), 1480 (m), 1470 (m), 1450 (m), 780 (m), 740 (m). ^1H NMR (δ, $CDCl_3$): 6.00 (d, 1 H, J = 10.1), 5.6–5.7 (m, 1 H), 5.46 (br s, 0.95 H), 5.35 (s, 0.05 H), 2.0–2.2 (m, 3 H), 1.4–1.8 (m, 3 H), 1.0–1.4 (m, 10 H), 0.89 (br s, 3 H). High resolution mass spectrum: calcd for $C_{14}H_{22}$ m/e 190.1722, found m/e 190.1723.

***trans*-2,3,4,4a,5,6-Hexahydro-2-butylnaphthalene (*trans*-2b).** The analytical sample was contaminated with 13% of *cis*-**2b**. ^1H NMR (δ, $CDCl_3$): 6.00 (d, 1 H, J = 10.1), 5.6–5.7 (m, 1 H), 5.46 (br s, 0.1 H), 5.35 (s, 0.9 H), 2.0–2.2 (m, 3 H), 1.4–1.8 (m, 3 H), 1.0–1.4 (m, 10 H), 0.89 (br s, 3 H). High resolution mass spectrum: calcd for $C_{14}H_{22}$ m/e 190.1722, found m/e 190.1723.

***cis*-2,3,4,4a,5,6-Hexahydro-2-phenylnaphthalene (*cis*-2c).** The analytical sample was contaminated with 5% of *trans*-**2c**. IR (CCl_4): 3050 (s), 3030 (s), 2920 (s), 2850 (s), 2810 (s), 1600 (m), 1480 (s), 1450 (s), 1430 (s), 1060 (m), 1000 (m), 850 (m). ^1H NMR (δ, $CDCl_3$): 7.2–7.4 (m, 5 H), 6.12 (d, 1 H, J = 10.1), 5.78 (dt, 1 H, J = 10.1, 4.2), 5.52 (br s, 1 H), 3.57 (br s, 1 H), 1.0–2.4 (m, 14 H). Mass spectrum: calcd for $C_{16}H_{18}$ m/e 210.1408, found m/e 210.1409.

***trans*-2,3,4,4a,5,6-Hexahydro-2-phenylnaphthalene (*trans*-2c).** The analytical sample was contaminated with 5% of *cis*-**2c**. IR (neat): 3050 (s), 2930 (s), 2870 (s), 1610 (m), 1500 (m), 1490 (m), 1450 (m), 1440 (w), 1130 (m), 830 (m), 810 (m), 760 (m), 750 (s), 710 (s). ^1H NMR (δ, $CDCl_3$): 7.2–7.4 (m, 5 H), 6.06 (d, 1 H, J = 8.8), 5.7 (m, 1 H), 5.48 (s, 1 H), 3.5 (br s, 1 H), 1.2–2.4 (m, 14 H). Mass spectrum: Calcd for $C_{16}H_{18}$ m/e 210.1408, found m/e 210.1409.

α-Deuterio-*trans*-2,3,4,4a,5,6-hexahydro-2-naphthalenol (α-D-*trans*-1-OH) was prepared as was *trans*-1-OH[1] except $LiAlD_4$ was used. The NMR spectra was identical with that of *trans*-1-OH except for the sharpening of the alkene proton signals and the absence of a signal at δ 4.4.

Determination of the Deuterium Distribution in the Alkylation of α-D-*trans*-1-OPiv with LiCuR_2 and LiCu(CN)R. The general procedure was followed and the ratio of α to ε alkylation was measured by integration of the corresponding ^2H signals: the α-methylated isomer gave a signal at δ 2.31, while the ε-methylated isomer gave a resonance at δ 5.72; the α-butylated isomer gave a signal at δ 2.11, while the ε-butylated isomer gave a resonance at δ 5.75; likewise the α-phenylated product gave a signal at δ 3.73 and the ε-phenylated at δ 6.00. Duplicate runs gave identical (±1%) results. Electronic integration gave similar results (±1%) as those obtained by manual integration.

General Procedure for the Alkylation of *cis*- and *trans*-1-OPiv with Grignard Reagents. To a cold (0 °C) stirred etheral solution of the pivalate (0.5 mmol) was added 1 mmol of an ethereal solution of Grignard. The mixture was warmed to room temperature and stirred for 2 h before being quenched with 1 mL of NH_4Cl. This mixture was taken up in ether, shaken with dilute HCl, 10% NaOH, and brine, and then dried over $MgSO_4$. Solvent was removed by rotary evaporation, and reaction products were isolated by rotary TLC (pentane/silica gel). The alkylation products were analyzed by capillary GC. **12** contaminated the alkylation products obtained by TLC, and homogeneous samples of isomers **2** and **3** were obtained by preparative GC. When dimer **13** was present, it was separated from the alkylation products by rotary TLC (pentane/silica gel). Duplicate runs gave identical (±2%) results. Spectral properties of the isolated products are reported below or elsewhere in the Experimental Section.

***cis*-3,4,4a,5,6,8a-Hexahydro-8a-butylnaphthalene (*cis*-3b).** IR (neat): 3020 (m), 2980 (s), 2940 (s), 2880 (m), 1480 (m), 1470 (m), 1450 (m). ^1H NMR (δ, $CDCl_3$): 5.60 (dt, 2 H, J = 10.0, 3.7), 5.36 (dt, 2 H, J = 10.0, 1.9), 1.9–2.0 (m, 4 H), 1.0–1.9 (m, 11 H), 0.88 (t, 3 H, J = 6.8). Mass spectrum: calcd for $C_{14}H_{22}$ m/e 190.1722, found m/e 190.1722.

***trans*-3,4,4a,5,6,8a-Hexahydro-8a-butylnaphthalene (*trans*-3b).** IR (neat): 3020 (m), 2940 (s), 2880 (s), 2840 (m), 1475 (m), 1465 (m). ^1H NMR (δ, $CDCl_3$): 5.75 (dt, 2 H, J = 9.9, 2.0), 5.53 (dt, 2 H, J = 9.9, 3.2), 2.0–2.3 (m, 4 H), 1.1–1.9 (m, 11 H), 0.88 (t, 3 H, J = 6.8). Mass spectrum: calcd for $C_{14}H_{22}$ m/e 190.1722, found m/e 190.1723.

***cis*-3,4,4a,5,6,8a-Hexahydro-8a-isopropylnaphthalene (*cis*-3d).** IR (CCl_4): 3000 (m), 2940 (s), 2905 (s), 2820 (m), 1470 (m), 1450 (m), 1430 (m), 1380 (m), 1370 (m). ^1H NMR (δ, $CDCl_3$): 5.65 (dt, 2 H, J = 10.1, 3.7), 5.44 (dt, 2 H, J = 10.1, 1.9), 1.4–2.0 (m, 10 H), 0.87 (d, 6 H, J = 7.2). Mass spectrum: calcd for $C_{13}H_{20}$ m/e 176.1566, found m/e 176.1566.

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(25) Padwa, A.; Goldstein, S. I.; Rosenthal, R. J. *J. Org. Chem.* **1987**, *52*, 3278.

***trans*-3,4,4a,5,6,8a-Hexahydro-8a-isopropylnaphthalene (*trans*-3d).** IR (CCl_4): 3035 (s), 2985 (s), 2950 (s), 2900 (s), 2860 (m), 1480 (w), 1390 (w), 960 (w), 880 (w), 865 (w). ^1H NMR (δ, $CDCl_3$): 5.6–5.8 (m, 4 H), 2.0–2.2 (m, 4 H), 1.4–2.0 (m, 6 H), 0.88 (d, 6 H, J = 6.8). Mass spectrum: calcd for $C_{13}H_{20}$ m/e 176.1566, found m/e 176.1566.

***cis*- and *trans*-2,3,4,4a,5,6-Hexahydro-2-isopropylnaphthalene (*cis*- and *trans*-2d).** A preparative GC isolated sample was a 1.2:1 mixture of *cis*:*trans*-**2d**. NMR (δ, $CDCl_3$): 6.02 (d, 1 H, J = 9.9), 5.6–5.8 (m, 1 H), 5.51 (br s, 0.56 H), 5.37 (br s, 0.44 H), 2.0–2.3 (m, 4 H), 1.0–2.0 (m, 7 H), 0.8–1.0 (6 H, 4 doublets appear at δ 0.95, J = 6.7; δ 0.89, J = 6.8; δ 0.88, J = 6.8; δ 0.87, J = 7.0). Mass spectrum: calcd for $C_{13}H_{20}$ m/e 176.1566, found m/e 176.1565.

***cis*- and *trans*-3,4,4a,5,6,8a-Hexahydro-8a-tertbutylnaphthalene (*cis*- and *trans*-3e).** A preparative GC isolated sample was a 3:1 mixture of trans:cis isomers. IR (CCl_4): 3020 (m), 2960 (s), 2920 (s), 2850 (s), 1470 (m), 1460 (m), 1440 (m), 1390 (m), 1375 (m), 880 (m). ^1H NMR (δ, $CDCl_3$): 5.6–5.8 (m, 4 H), 1.2–2.2 (m, 7 H), 0.93 (s, 2.4 H), 0.88 (s, 6.6 H). Mass spectrum: calcd for $C_{14}H_{22}$ m/e 190.1722, found m/e 190.1723.

***cis*- and *trans*-2,3,4,4a,5,6-Hexahydro-2-*tert*-butylnaphthalene (*cis*- and *trans*-2e).** The analytical sample of the mixture of *cis*- and *trans*-**2e** obtained by preparative GC does not reflect the actual product distribution. The analytical sample was a 4:1 mixture of *cis*:*trans*-**2e**. IR (neat): 3020 (m), 2950 (s), 2870 (s), 2850 (s), 1500 (m), 1450 (m), 1400 (w), 1360 (m), 1130 (w). NMR (δ, $CDCl_3$): 6.05 (d, 1 H, J = 11), 5.65 (m, 1 H), 5.57 (br s, 0.8 H), 5.50 (br s, 0.2 H), 1.2–2.3 (m, 11 H), 0.92 (s, 7.2 H), 0.88 (s, 1.8 H). Mass spectrum: calcd for $C_{14}H_{22}$ m/e 190.1722, found m/e 190.1722.

2,3,4,4a,5,6-Hexahydronaphthalene (12). IR (CCl_4): 3060 (w), 2960 (s), 2920 (m), 2890 (m), 1460 (w), 1400 (w), 1310 (w). ^1H NMR (δ, $CDCl_3$): 6.00 (d, 1 H, J = 10.6), 5.7 (m, 1 H), 5.46 (br s, 1 H), 2.0–2.2 (m, 5 H), 1.7–1.9 (m, 3 H), 1.4–1.6 (m, 1 H), 1.0–1.4 (m, 2 H). Mass spectrum: calcd for $C_{10}H_{14}$ m/e 134.1096, found m/e 134.1096.

2,2′-Bi-2,3,4,4a,5,6-hexahydronaphthyl (13a). NMR (δ, $CDCl_3$): 6.0 (br, s, 2 H), 5.7 (br s, 2 H), 5.3–5.6 (six br signals, 2 H), 2.0–2.4 (m, 8 H), 1.4–1.9 (m, 6 H), 1.1–1.4 (m, 6 H). Mass spectrum: calcd for $C_{20}H_{26}$ m/e 2666.2034, found m/e 266.2033.

Reaction of *trans*-1-OPiv with (Hexadeuterioisopropyl)magnesium Bromide. The Grignard reagent was prepared from acetone-d_6 (99.8% d_6) by using standard procedures. LAH reduction of deuteriated acetone afforded 2-propanol-d_6 quantitatively; subsequent treatment of the alcohol with PBr_3 gave a modest 30% yield of isopropyl-d_6 bromide from which the Grignard was prepared in ether. Following the general procedure, reaction of *trans*-1-OPiv with the deuteriated Grignard produced the normal product mixture of which 4.5% was compound **12**-d_4; this was isolated by preparative GC and had the following: NMR (δ, $CDCl_3$) 6.00 (d, 1 H, J = 9.7), 5.7 (m, 1 H), 5.46 (br s, 1 H), 2.0–2.2 (m, 4 H), 1.7–1.9 (m, 3 H), 1.4–1.6 (m, 1 H), 1.0–1.4 (m, 2 H).

Reaction of α-D-*trans*-1-OPiv with Isopropylmagnesium Bromide. Following the General Procedure, compound **12**-*d* was isolated from the normal array of alkylation products by preparative GC and had the following: NMR (δ, $CDCl_3$) 6.00 (br s, 1 H), 5.7 (m, 0.5 H), 5.46 (br s, 1 H), 2.0–2.2 (m, 4.5 H), 1.7–1.9 (m, 3 H), 1.4–1.6 (m, 1 H), 1.0–1.4 (m, 2 H).

Determination of the Deuterium Distribution in the Alkylation of α-D-*trans*-2-OPiv with MeMgI and PhMgBr. The general procedure was followed and the ratio of α to ϵ alkylation was measured by integration of the corresponding ^2H signals as was done for the determination when dialkylcuprates were used.

***trans*-2,3,4,4a,5,6-Hexahydro-2-naphthyl acetate (*trans*-1-OAc)** was prepared by the addition of 1.73 g of acetyl chloride to a cold (0 °C) stirred solution of 3.00 g of *trans*-1-OH and 3.16 g of pyridine in 6 mL of ether. After addition was complete, the reaction was warmed to room temperature for 2 h. The reaction was transferred to a separatory funnel containing 5% HCl; the aqueous phase was discarded, and the organic phase was washed with saturated $NaHCO_3$ and brine and dried over $MgSO_4$. Solvent was removed by rotary evaporation, and the residue was distilled to give 3.60 g (94%) of *trans*-**1-OAc**, bp 65–67 °C (0.2 mmHg), as a viscous oil which solidified upon sitting at −20 °C. IR (neat): 3030 (m), 2940 (s), 2860 (m), 2840 (m), 1740 (s), 1380 (m), 1250 (s), 1030 (m). NMR (δ, $CDCl_3$): 6.02 (d, 1 H, J = 9.25), 5.83 (m, 1 H), 5.43 (m, 1 H), 5.35 (br s, 1 H), 2.1–2.3 (m, 3 H), 2.06 (s, 3 H), 1.2–1.9 (m, 6 H). Mass spectrum: calcd for $C_{12}H_{16}O_2$ m/e 192.1151, found, m/e 192.1151.

Alkylation of *trans*-1-OAc with MeMgI. The general procedure for the alkylation of dienyl pivalates was followed. A 7.3:1 mixture of *cis*-**2a**:*trans*-**2a** was obtained in 71.4% yield by rotary TLC. Also isolated was *trans*-1-OH in 16.8% yield.