N NaOH (20 mL), cetyltrimethylammonium bromide (0.10 g), and $Co_2(CO)_8$ (10 mmol) was stirred for 3 h at room temperature in a CO atmosphere. Methyl iodide (5 mL) was added to the stirred solution, followed by the allene (10 mmol), and the reaction mixture was stirred for an additional 2–3 h. The reaction mixture was then stirred in air until the decomposition of the organometallic species was complete. The phases were separated (the aqueous phase did not contain any organic products), and the organic phase was washed with water, dried, and concentrated. Separation of the reaction products was achieved by chromatography on silica gel, using hexane–ether as eluant (4 was eluted before 5 in all cases). Phenylallene is cleaved under PTC conditions.[14]

General Procedure for Reaction of Allenes with $Co_2(CO)_8$ in Benzene. To $Co_2(CO)_8$ (10 mmol) in benzene (20 mL) was added the allene (10 mmol). The solution was stirred under CO for 1 day and then exposed to air. Workup was effected as described for the organic phase in the phase transfer catalyzed process.

(14) H. Alper and J. K. Currie, unpublished results.

Acknowledgment. We are grateful to Imperial Oil Ltd, and to the Natural Sciences and Engineering Research Council for support of this research.

Registry No. 3 ($R_1 = C_8H_{17}$; $R_2 = R_3 = H$), 56956-46-8; **3** ($R_1 = R_2 = CH_3$; $R_3 = H$), 598-25-4; **3** ($R_1 = R_2 = (CH_2)_5$; $R_3 = H$), 5664-20-0; **3** ($R_1 = R_3 = (CH_2)_5$; $R_2 = H$), 7124-40-5; **3** ($R_1 = R_3 = CH_3$; $R_2 = H$), 591-96-8; **3** ($R_1 = R_3 = (CH_2)_6$; $R_2 = H$), 1123-11-1; **4** ($R_1 = C_8H_{17}$; $R_2 = R_3 = H$), 76584-04-8; **4** ($R_1 = R_2 = CH_3$; $R_3 = H$), 76584-05-9; **4** ($R_1 = R_2 = (CH_2)_5$; $R_3 = H$), 76584-06-0; **4** ($R_1 = R_3 = (CH_2)_5$; $R_2 = H$), 76599-29-6; **5** ($R_1 = C_8H_{17}$; $R_2 = R_3 = H$), 76584-07-1; **5** ($R_1 = R_2 = CH_3$; $R_3 = H$), 76584-08-2; **5** ($R_1 = R_2 = (CH_2)_5$; $R_3 = H$), 76584-09-3; (*E,E*)-**5** ($R_1 = R_3 = CH_3$; $R_2 = H$), 76584-10-6; (*Z,Z*)-**5** ($R_1 = R_3 = CH_3$; $R_2 = H$), 76584-11-7; (*E,Z*)-**5** ($R_1 = R_3 = CH_3$; $R_2 = H$), 76584-14-0; **6**, 17339-74-1; **7**, 76584-12-8; **12**, 76584-13-9; $Co_2(CO)_8$, 10210-68-1; CH_3I, 74-88-4; CO, 630-08-0.

Alkylation of Allylic Derivatives. On the Regio- and Stereochemistry of Alkylation of Allylic Alcohols by the Murahashi Method

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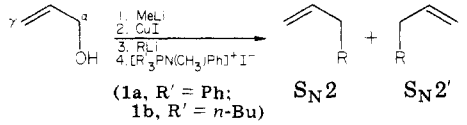
Direct alkylation of allylic alcohols by the Murahashi method has been reinvestigated. This four-step, one-pot process evidently involves formation of the lithium (allyloxy)alkylcuprate (**2**) followed by reaction with (methylphenylamino)triphenylphosphonium iodide (**1a**) or the corresponding tributylphosphonium iodide (**1b**). Contrary to earlier implications, the regiospecific and stereospecific anti γ-alkylation is independent of which aminophosphonium reagent is used. Presumably the final step involves alkylation of the (allyloxy)phosphonium ion (**3**) by $LiCu(R)(N(CH_3)Ph)$. This mixed cuprate also alkylates allylic carboxylates with about the same regio- and stereochemistry as for the Murahashi direct alkylation of the corresponding allylic alcohol. A general mechanism is presented that suggests that the regiochemistry of alkylation of allylic derivatives depends on the nature of the ancillary ligand in the alkylating cuprate.

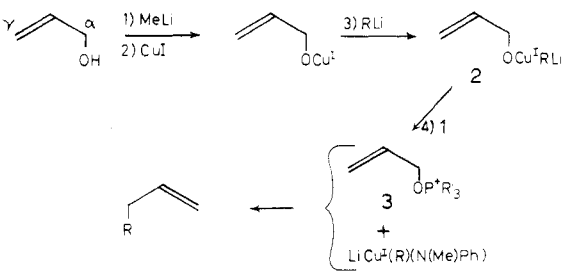
In connection with our investigation of the regio- and stereochemistry of alkylation of allylic carboxylates with dialkyl and mixed cuprates, we were interested in the direct alkylation of allylic alcohols reported by Murahashi and co-workers.[2] This four-step, one-pot process is shown by eq 1.



(1)

In the initial report,[2a] (methylphenylamino)triphenylphosphonium iodide (**1a**) was used in step 4, and there was no indication of regiospecificity—a number of primary allylic alcohols were investigated, and all gave primarily the unrearranged α-alkylation product. More recently,[2b] the tributylphosphonium iodide **1b** was used instead of **1a**, and S_N2' regiospecificity (γ-alkylation) was observed. For example, cinnamyl alcohol and the isomeric α-phenylallyl alcohol undergo 96% and 100% γ-alkylation.[2b] Similarly, 5-methyl-2-cyclohexenol (**4**) undergoes 93% γ-alkylation. In the latter case it was shown that alkylation is also stereospecific and gives the anti alkylation product.

Scheme I. Steps Involved in the Direct Alkylation of Allylic Alcohols



We now report that the difference in regiochemistry in these reports[2] does not result from using different aminophosphonium reagents (**1a** and **1b**) but instead is due to another change in the experimental procedure. In fact, under the same conditions, the regiospecificity and stereospecificity are the same with **1a** and **1b** as would be expected from the mechanistic pathway proposed by Murahashi.[2b]

(1) National Science Foundation Fellow, 1977–1980.
(2) (a) Tanigawa, Y.; Kanamaru, H.; Sonoda, A.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1977**, *99*, 2361. (b) Tanigawa, Y.; Ohta, H.; Sonoda, A.; Murahashi, S.-I. *Ibid.* **1978**, *100*, 4610.

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Table I. Regiochemistry of Alkylation of *cis*-5-Methyl-2-cyclohexenol-α-*d* and -γ-*d* (4-OH) with Methyllithium

cis-4-OH	1	equiv of CH_3Li[a]	% 1-5-*d*[b]	% 3-5-*d*
α-*d*	1a	3	52	48
γ-*d*	1a	3	47	53
α-*d*	1a	1	88	12
γ-*d*	1a	1	12	88
α-*d*	1b	1	93	7[c]
γ-*d*	1b	1	7	93[c]

[a] Equivalents of methyllithium used in step three. [b] This isomer results from α-alkylation of γ-D-4-OH and γ-alkylation of α-D-4-OH. [c] These results are essentially the same as those reported by Murahashi and co-workers.[2b]

This mechanism is outlined in Scheme I. The first two steps lead to the cuprous allyloxide, and the third step gives the (allyloxy)alkylcuprate **2**. The first part of step 4 presumably involves nucleophilic attack by **2** on phosphorus in **1** to give the (allyloxy)phosphonium ion (**3**) and the mixed cuprate, $LiCu(R)(N(CH_3)Ph)$. This is followed by alkylation of **3** by the mixed cuprate. The last step is similar to alkylation of allylic carboxylates with lithium (cyano)alkylcuprates and other mixed cuprates with regard to regio- and stereochemistry (i.e., preponderant anti γ-alkylation).[3,4]

The original procedure[2a] involved use of 3 equiv of alkyllithium in step 3 and **1a** in step 4. In the second report,[2b] 1 equiv of alkyllithium and **1b** were used. In this work we have examined the regiochemistry and stereochemistry in the 5-methyl-2-cyclohexenyl system (**4**) for each procedure. We have also investigated the regiochemistry in the *trans*-(phenyl)methylallyl systems **6**-OH and **10**-OH.

The regiochemistry of alkylation of **4**-OH was examined with *cis*-α- and -γ-D-**4**-OH[5] and the results are presented in Table I. In these experiments the alkylation product, 3,5-dimethylcyclohexene (**5**), was isolated by preparative

4-OH **5**

GC, and the deuterium distribution at C-1 and C-3 was determined by 15.36-MHz deuterium magnetic resonance. A 65–85% conversion of **4**-OH to **5** was observed, and in all cases unreacted **4**-OH remained discretely labeled, which shows there is no rearrangement prior to alkylation.

Results of the stereochemical studies are presented in Table II. In these experiments isomer ratios were determined by capillary GC. It should be noted that the results for reaction of 92% *trans*-**4**-OH with 1 equiv of methyllithium and **1b** overstate the stereospecificity somewhat. In this experiment the unreacted alcohol (~15%) was richer than the starting material in cis isomer (~50%). This results from dissimilar reactivities of the two isomers. Competitive rate studies showed that *trans*-**4**-OH is 3–4 times more reactive than the cis isomer. Thus the alcohol that reacted contained >92% trans isomer. From the data in the tables it is apparent that both α- and γ-alkylation are stereospecifitic; γ-alkylation is anti and α-alkylation results in inversion.

Table II. Stereochemistry of Alkylation of *cis*- and *trans*-5-Methyl-2-cyclohexenol (4-OH) with Methyllithium

4-OH	1	equiv of CH_3Li[a]	prod comp % *cis*-5	prod comp % *trans*-5
99% cis	1a	3	3	97
96% trans	1a	3	93	7
100% cis	1a	1	8	92
99% cis	1b[b]	1	12	88
92% trans	1b	1	91	9

[a] Equivalents of CH_3Li used in step 3 of eq 1. [b] Results similar to those reported for reaction of 92% *cis*-**4**-OH in ref 2b.

The data in Table I show that regiospecificity depends on the amount of methyllithium used in step 3 and not on which aminophosphonium reagent (**1a** or **1b**) is used. With 1 equiv of methyllithium, S_N2' regiospecificity is observed with either **1a** or **1b**. The results of the last two experiments in Table I are in good agreement with those reported by Murahashi and co-workers.[2b] However, regiospecificity is dependent on the procedure and, as shown by the first two experiments in Table I, is essentially lost when 3 equiv of methyllithium is used.

Apparently, with 1 equiv of methyllithium, the only active cuprate species present is the mixed cuprate, $LiCu(CH_3)(N(CH_3)Ph)$, as proposed by Murahashi.[2b] With 3 equiv of methyllithium, presumably $LiCu(CH_3)_2$, or more likely $Li_2Cu(CH_3)_2(N(CH_3)Ph)$,[6] is present and dominates product formation by a nonregiospecific, but stereospecific, process. According to this interpretation, alkylation of (allyloxy)phosphonium ions is similar to alkylation of allylic carboxylates with regard to regiochemistry and stereochemistry, i.e., anti γ-alkylation with mixed cuprates[3,4] and alkylation with inversion but without regiospecificity with dialkylcuprates.[4,5]

The mixed cuprate, $LiCu(CH_3)(N(CH_3)Ph)$, was prepared directly to determine if it alkylates allylic carboxylates. This cuprate was obtained by reaction of lithium methylphenylamide with cuprous iodide followed by treatment of the resulting complex with 1 equiv of methyllithium.

Reaction of $LiCu(CH_3)(N(CH_3)Ph)$ with **4**-OAc results primarily in attack at the carbonyl position to give **4**-OH of the same configuration and *tert*-butyl alcohol; only minor amounts of **5** are formed. Carbonyl attack was effectively eliminated by using the mesitoate (**4**-OTMB) instead of the acetate, and **5** was obtained in ~55% yield. Alkylation of 100% *cis*-**4**-OTMB with the mixed cuprate gives 99% *trans*-**5**, and *cis*-α-D-**4**-OTMB gives **5** with 80% of the deuterium at C-1 (γ-alkylation) and 20% at C-3 (α-alkylation). These experiments show that the regiochemistry and stereochemistry are similar to that for direct alkylation of **4**-OH. This establishes that $LiCu(CH_3)(N(CH_3)Ph)$ is an alkylating reagent and provides supporting evidence for the view[2b] that such mixed cuprates are the alkylating reagents in the regiospecific cross coupling of allylic alcohols with alkyllithium (eq 1).

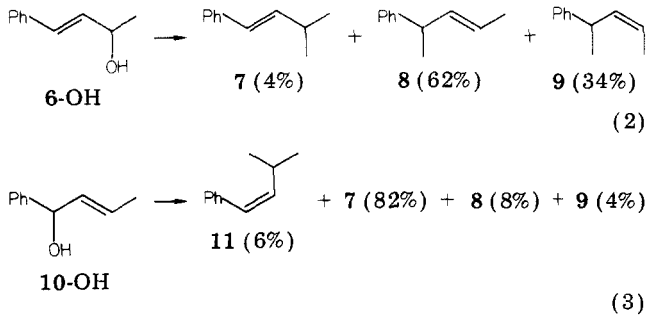
Results for alkylation of *trans*-α-methyl-γ-phenylallyl alcohol (**6**-OH) and *trans*-α-phenyl-γ-methylallyl alcohol (**10**-OH) with 1 equiv of methyllithium are shown in eq 2 and 3. In these experiments, products were isolated in about 84% yield. In other work,[7] we have observed that

(3) (a) Levisalles, J.; Rudler-Chauvin, M.; Rudler, H. *J. Organomet. Chem.* **1977**, *136*, 103. (b) Trost, B. M.; Klun, T. P. *J. Org. Chem.* **1980**, *45*, 4256.

(4) Tseng, C. C., unpublished observations in these laboratories.

(5) Goering, H. L.; Singleton, V. D., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 7854.

(6) Displacement by methylphenylamide has been observed in some cases.[2b] In this work displacement products could not be detected, from which we conclude that free $LiN(CH_3)Ph$ is not present.



alkylation of the isomeric acetates (**6**-OAc and **10**-OAc) with $LiCu(CH_3)_2$ is regioselective but not regiospecific—both isomers give essentially the same product mixture which contains 95% of the conjugated product **7**, ~4% **8**, and minor amounts of other isomers.

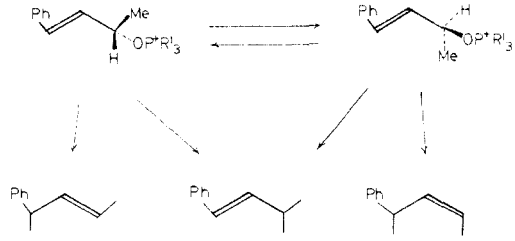
On the other hand, as shown by eq 2 and 3, alkylation of the alcohols by the Murahashi method[2b] is indeed regiospecific—with each isomer, γ-alkylation dominates. The results for **6**-OH are similar to those reported[2b] for alkylation of *trans*-cinnamyl alcohol. In each case 96% γ-alkylation is observed even though this leads to the less stable unconjugated isomer. It is noteworthy that this reaction is more regiospecific than alkylation of **6**-OAc with $LiCu(CH_3)CN$ which gives from 43% to 58% γ-alkylation, depending on conditions.[4]

The results for **10**-OH in eq 3 are misleading with regard to regiospecificity and differ sharply from the 100% γ-alkylation observed with α-phenylallyl alcohol.[2b] In this case the results were variable, and the data presented are for the experiment in which the largest amount of γ-alkylation (~88%) was observed. In another experiment as little as 73% γ-alkylation was observed. As has been noted, the nonregiospecific alkylation of **10**-OAc with $LiCu(CH_3)_2$ gives ~95% γ-alkylation[7] and with $LiCu(CH_3)CN$ ~98% γ-alkylation is observed.[4] The difficulty with **10**-OH is that at some stage there is a variable amount of allylic rearrangement prior to alkylation. This was established by using α-D-**10**-OH and stopping the reaction short of completion. Deuterium magnetic resonance showed that the recovered unreacted alcohol contained ~20% γ-D-**6**-OH. The mechanism for the **10** → **6** isomerization is not clear. It seems unlikely that **10**-OH isomerizes under the reaction conditions (low temperature, basic solution). Possibly the isomerization of the unconjugated (**10**) to the conjugated system (**6**) occurs at the (allyloxy)cuprate (**2**) or (allyloxy)phosphonium ion (**3**) stage. Reconversion of these intermediates to the corresponding alcohols during workup of the incomplete reaction could account for the observed α-D-**10**-OH → γ-D-**6**-OH transformation.

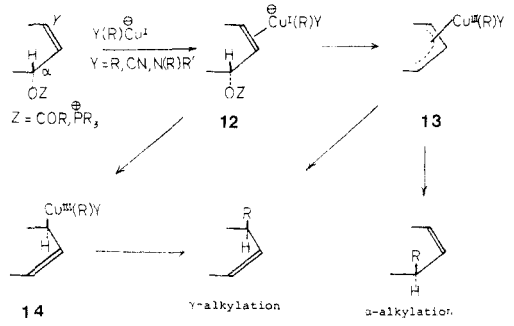
There is another clue that a **10** → **6** isomerization preceeds the alkylation step for alkylation of **10**-OH. In acyclic systems the double bond configuration is fully preserved in the unrearranged α-alkylation product for alkylation of allylic alcohols with 3 equiv of alkyllithium.[2a] For example, alkylation of *cis*-cinnamyl alcohol with 3 equiv of *n*-butyllithium or phenyllithium results primarily in α-substitution, and the cis double bond configuration is preserved.[2a] We[4] and others[3a] have observed that this also is the case for α-alkylation of allylic carboxylates with dialkylcuprates.

On the other hand, γ-alkylation can lead to a mixture of *E* and *Z* isomers.[2,3b] For example, as shown by eq 2, γ-alkylation of **6**-OH gives a mixture of *E* (**8**) and *Z* (**9**) isomers. Presumably this composition is determined by the activation barriers for the two reactive conformations[8] as illustrated in Scheme II. Similarly, with **10**-OH the two reactive conformations are related to the *E* and *Z* γ-alkylation products (**7** and **11**). It is interesting to note that the *Z*/*E* ratio for γ-alkylation of **6**-OH is higher (~0.5) than that observed for γ-alkylation of **6**-OAc with $LiCu(CH_3)CN$ (~0.3).[4] Similarly, the *Z*/*E* ratio for γ-alkylation of **10**-OH is higher (~0.07) than that for γ-alkylation of **10**-OAc with $LiCu(CH_3)_2$ (~0.01).[7]

Scheme II. Conformations Related to Transition States Leading to *E* and *Z* Alkylation Products



Scheme III. Mechanism of Alkylation of Allyl Derivatives with Alkylcuprates



As shown by eq 3, the original double bond configuration in **10**-OH has not been preserved in the apparent α-alkylation products **8** and **9**. In another experiment the alkylation product derived from **10**-OH contained 17% of **8** and 9% of **9**. This is additional evidence that these products result from γ-alkylation of an α-methyl-γ-phenylallyl derivative (**6**) that is formed by allylic rearrangement of the unconjugated isomer (**10**).

The present results (viz., regio- and stereochemistry) suggest that the alkylation step (final transformation in Scheme I) is mechanistically similar to the alkylation of allylic carboxylates with alkylcuprates. A mechanistic outline that correlates the pertinent observations for these alkylations is shown in Scheme III. In this scheme, *Z* in the allyl derivative is a phosphonium group for alkylation of alcohols (**3**) and an acyl group for alkylation of allylic carboxylates, and Y in the cuprate is the unreactive ligand, i.e., either a second alkyl group in a dialkylcuprate or a cyano or imido group in a mixed cuprate.

Specifically, this mechanism accounts for (a) the preservation of double bond configuration in the α-alkylation product, (b) excess γ-alkylation in all cases where regiospecificity is observed,[3,4,9] (c) the dependence of regiochemistry on the ancillary ligand (Y) in the cuprate, and

(7) E. P. Seitz, unpublished work in these laboratories.

(8) Presumably the two reactive conformations are those in which the carbon–leaving group bond is in a plane perpendicular to that of the double bond, i.e., aligned with the C_β and C_γ p orbitals.

(9) Maruyama, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1977**, *99*, 8068. Katzenellenbogen, J. A.; Crumrine, A. L. *Ibid.* **1976**, *98*, 4925. Oshima, K.; Yamamoto, H.; Nozaki, H. *Ibid.* **1973**, *95*, 7926. Yamamoto, Y.; Maruyama, K. *J. Organomet. Chem.* **1978**, *156*, C9. Marino, J. P.; Farina, J. S. *J. Org. Chem.* **1976**, *41*, 3213. Marino, J. P.; Hatanaka, N. *Ibid.* **1979**, *44*, 4467. Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675.

(d) the stereochemistry favoring anti γ-alkylation and α-alkylation with inversion.

The distinguishing feature of this mechanism is that for regiospecific alkylation, oxidative addition of the allyl derivative to the cuprate gives the S_N2' σ-allyl isomer **14** rather than the S_N2 isomer as proposed earlier.[3a] Normally, in unbiased systems, S_N2' displacements are much slower than S_N2 displacements.[10] The reason for the favored S_N2'orientation in the present case is thought to result from a prior complexation of the cuprate with the double bond to give the copper(I)–olefin π complex **12** which is converted to σ-allyl-**14** (regiospecific alkylations) or π-allylcopper(III) species **13** (nonregiospecific alkylations). It should be noted that copper(I)–olefin π complexes have been observed[11] and that this two-step mechanism for oxidative addition of a d^{10} complex is the same as has been proposed for reaction of palladium(0) complexes with allylic derivatives.[12] The mechanistic outline in Scheme III is not meant to imply that only monomeric copper species are involved—it is known that under conditions of these alkylations, dialkylcuprates are dimeric[13] and that other organocopper(I) species exist as aggregates.[14]

This mechanism suggests that the stereochemistry is determined in the initial complexation step which presumably occurs on the least hindered side of the double bond. In sterically unbiased systems this is the side opposite from the leaving group. This configuration leads to anti γ-alkylation via **13** or **14** and α-alkylation with inversion via **13**. In other work we have found that steric hindrance can alter the stereochemistry of α- and γ-alkylation without any important change in regiochemisry. For example, we have observed syn γ-alkylation and α-alkylation with retention in the *exo*-bicyclo[3.2.1]oct-3-en-2-yl system with the same regiochemistry for various alkylations as in the sterically unbiased cyclohexenyl system. In connection with the stereochemistry it should be noted that there is ample precedent for the final reductive elimination with retention of configuration as indicated by the transformation of **13** and **14** to alkylation products.[15]

According to the present interpretation, regiochemistry is determined by the partitioning of the initially formed π complex **12** between the π-allyl complex **13** (nonregiospecific alkylation) and the σ-allyl complex **14** (regiospecific alkylation), and this partitioning is dependent on the nature of the ancillary ligand (Y). In this connection it is significant that oxidative addition reactions of allylic halides to platinum d^{10} complexes give σ-allyl or π-allyl d^8 complexes depending on the ligands on the metal. For example, oxidative addition of allylic halides to $Pt(PEt_3)_4$ gives the σ-allyl complex, $Pt(\eta^1\text{-allyl})X(PEt_3)_2$, whereas with $Pt(PPh_3)_4$, the π-allyl product, $[Pt(\eta^3\text{-allyl})(PPh_3)_2]^+X^-$, is obtained.[16] The regiochemistry observed for the present and related alkylations suggests that a **12** → **13** transformation is favored for alkylation with dialkylcuprates (i.e., Y = alkyl) whereas a **12** → **14** transformation dominates if Y is a cyano or imido group.

The complete preservation of double bond configuration in the α-alkylation product requires that the **12** → **14** transformation is irreversible and that **14** is not converted to the π-allyl complex **13**. Or, to put it another way, the S_N2' σ-allyl complex **14** cannot be an intermediate for formation of the α-alkylation product because in this case the double bond configuration would be lost. We presume that in **13**, as in the case of analogous palladium(II) π-allyl complexes,[12a] the double bond configuration is preserved.

Experimental Section

Materials. Satisfactory spectral data were obtained for all compounds. Proton NMR were obtained with a JEOL MH-100 spectrometer, and deuterium spectra were obtained with a Varian XL-100 spectrometer equipped with Gyro Observe and a deuterium probe. Ethereal MeLi (Ventron, 1:1 LiBr complex) was standardized by double titration,[17] and CuI was purified by a published procedure.[18] Dimethylformamide was purified and dried by distillation from BaO.

(Methylphenylamino)triphenylphosphonium iodide (1a), mp 238.5–241 °C (lit.[19] mp 239.5–241 °C), was prepared[19] from *N*-phenyltriphenylphosphinimine[20] and MeI. This salt was recrystallized from water and dried over P_2O_5 under reduced pressure (0.2 torr).

(Methylphenylamino)tri-*n*-butylphosphonium iodide (1b), mp 122–123.5 °C (lit.[2b] mp 120–120.5 °C), was prepared[21] by reaction of phenyl azide[22] and tri-*n*-butylphosphine followed by reaction of the ethereal solution of unisolated phosphinimine with excess methyl iodide. The product (**1b**) was collected by filtration and purified by recrystallization from ethyl acetate.

***cis*- and *trans*-5-Methyl-2-cyclohexenol (4-OH)[23] and α- and γ-deuterated *cis*-4-OH**[5] were prepared as described earlier except that 1.2 equiv of lithium aluminum deuteride (LAD; instead of 2 equiv[5]) was used in the appropriate hydride reductions. Reduction of 3-ethoxy-5-methyl-2-cyclohexenone[24] with LAH (or LAD) gives 3–7% 4-OH as well as the desired 5-methyl-2-cyclohexenone. The trace amount of 4-OH in the enone was not removed prior to the second reduction (with LAH or LAD) which converts the enone to 4-OH. Thus, γ-D-4-OH was contaminated with a small amount of α,γ-D_2-4-OH. The results in Table I have been corrected for this contamination. The conversion of enone to 4-OH is accompanied by about 3–7% conjugate addition to give 3-methylcyclohexanol. However, the saturated alcohol is inert, and its presence has no effect on the results in Table I.

***cis*-5-Methyl-2-cyclohexenyl mesitoate (4-OTMB)** was prepared from *cis*-4-OH and mesitoyl chloride[25] by the method[23] used to prepare *p*-nitrobenzoate esters. After purification by column chromatography (silica gel with hexane–ether eluent), 4-OTMB was obtained as a light yellow oil: IR (neat) 3030 (w), 2950 (m), 2920 (m), 2870 (m), 2830 (w), 1715 (s), 1650 (w), 1610 (m), 1575 (m), 1275 (s) cm^{-1}; NMR (CCl_4) δ 6.63 (s, 2 H, Ar H), 5.7–5.3 (m, 3 H), 2.17 (s, 6 H, 2 Ar CH_3), 2.11 (s, 3 H, Ar CH_3), 2.1–1.0 (m, 5 H), 0.93 (d, 3 H, J = 6 Hz); mass spectrum, m/e (relative intensity) 258 (M^+, 4), 164 (18), 147 (63), 119 (20), 105 (14), 95 (100), 94 (91), 91 (22), 79 (80), 77 (23), 67 (23), 55 (21), 41 (23); high-resolution mass spectrum, calcd for $C_{17}H_{22}O_2$ m/e 258.1614, found m/e 258.1620. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.0;

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H, 8.6. Found: C, 79.1; H, 8.7.

***trans*-α-Methyl-γ-phenylallyl alcohol (6-OH)**, bp 95–98 °C (1.4–1.6 mm), and ***trans*-α-phenyl-γ-methylallyl alcohol (10-OH)**, bp 81 °C (1.1 mm), were prepared as reported earlier.[26] The characterization of the alkylation products 7–9 and 11 (by NMR, high-resolution mass spectra, and elemental analysis) will be reported elsewhere.[7]

Alkylation of 5-Methyl-2-cyclohexenol (4-OH). In a typical experiment, 1.12 g (10 mmol) of 99% *cis*-4-OH was treated with 6.7 mL of 1.49 M ethereal CH_3Li. The resulting lithium alkoxide was added to a suspension of 1.90 g (10 mmol) of CuI and 20 mL of dry THF which in turn was prepared in a nitrogen-flushed, 250-mL flask equipped with a stirrer and septum. This solution was stirred for 0.5 h, and the resulting homogeneous yellow solution was chilled to −78 °C, after which 6.7 mL of 1.49 M ethereal CH_3Li was added over a period of about 5 min. Then 4.35 g (10 mmol) of (methylphenylamino)tributylphosphonium iodide (**1b**) in 40 mL of dry DMF was added and the cooling bath removed. The brown homogeneous solution was stirred for 3 h at room temperature, after which the reaction was quenched by adding the reaction mixture to a mixture of 30 mL of saturated aqueous NH_4Cl and 50 mL of ether containing 1.08 g of 1,5-cyclooctadiene (internal standard). After being stirred vigorously, the mixture was filtered, and the organic layer was separated, washed with 10 mL of 0.2 M HCl and 10 mL of saturated aqueous $NaHCO_3$, and dried over $MgSO_4$. The dried solution was concentrated by fractional distillation (Vigreux column), and isomer ratios and yields (~70%) were determined by capillary GC (230-ft column, UCON-LB-550-X, 80 °C). The results of these experiments are presented in Table II.

For alkylation of deuterated 4-OH, the products were isolated by preparative GC (10 ft × $^3/_8$ in. column, 20% UCON-LB-550-X on Chromasorb W, 80 °C). Proton-decoupled spectra gave signals at δ 1.28 (3-D-**5**) and 4.67 (1-D-**5**). Results are presented in Table I.

Alkylation of Methylphenylallyl Alcohols 6-OH and 10-OH. These alkylations were carried out on a 10-mmol scale by the procedure described above for alkylation of 4-OH. After concentration of the organic extract of the products, product compositions were determined by capillary GC (94-ft column, UCON LB-550-X, 75 °C). Identification of 7–9 and 11 was made by comparison of retention times with those for authentic samples.[7] In one experiment, the product mixture derived from 6-OH was isolated in 77% yield. Results of these experiments are shown by eq 2 and 3.

In a control experiment α-D-10-OH, prepared by LAD reduction of the corresponding ketone, was alkylated, and the products and unreacted alcohol were isolated as described above, except that the dilute HCl wash was omitted and the unreacted alcohol was isolated by vacuum distillation. Deuterium magnetic resonance showed the recovered alcohol to contain ~20% of the conjugated isomer (γ-D-6-OH).

Alkylation of *cis*-5-Methyl-2-cyclohexenyl Acetate (*cis*-4-OAc) and Mesotoate (*cis*-4-OTMB) with $LiCu(CH_3)(N(CH_3)Ph)$. To 1.90 g (10 mmol) of purified CuI in 20 mL of dry THF was added 10 mmol of lithium methylphenylamide (prepared at 0 °C by adding 8.3 mL of 1.20 M CH_3Li to 1.07 g of *N*-methylaniline), and the resulting solution was stirred 0.5 h at room temperature. The homogeneous clear yellow solution was chilled to −78 °C and changed to a cloudy black mixture. Addition of 8.3 mL of 1.20 M CH_3Li was followed immediately by addition of 1.54 g (10 mmol) of *cis*-4-OAc to the purple inhomogeneous solution. The stirred reaction mixture was warmed to room temperature and became clear yellow and then changed to cloudy green and finally to black. The mixture was quenched and worked up as described above for alkylation of 4-OH. Capillary GC showed the organic extract contained about 5% *trans*-**5**, 95% *cis*-**4**-OH, *tert*-butyl alcohol, and a trace of unreacted *cis*-**4**-OAc.

Alkylation of *cis*-**4**-OTNB by the above procedure gave a 54% yield (GC yield, 1,5-cyclooctadiene internal standard) of *trans*-**5**, and the remaining unreacted **4**-OTNB was ~99.8% cis isomer. No 4-OH (which results from carbonyl attack) was detected.

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Registry No. 1a, 34257-63-1; **1b**, 67660-23-5; *trans*-4-OH, 22031-97-6; *cis*-4-OH, 22049-46-3; *cis*-α-D-4-OH, 73964-44-0; *cis*-γ-D-4-OH, 73964-43-9; *cis*-4-OTMB, 76807-00-6; *cis*-4-OAc, 61221-47-4; *cis*-**5**, 17516-95-9; *trans*-**5**, 56021-63-7; 3-D-**5**, 76807-01-7; 1-D-**5**, 76807-02-8; **6**-OH, 36004-04-3; γ-D-**6**-OH, 76807-03-9; **7**, 15325-61-8; **8**, 42461-65-4; **9**, 76807-04-0; **10**-OH, 52755-39-2; α-D-**10**-OH, 76807-05-1; **11**, 15325-56-1; $LiCu(CH_3)(N(CH_3)_2)Ph$, 76793-71-0; *N*-phenyltriphenylphosphinimine, 2325-27-1; methyl iodide, 74-88-4; phenyl azide, 622-37-7; tributylphosphine, 998-40-3; mesitoyl chloride, 938-18-1.

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Stereoselectivity in the Formation of Heterocyclic Amine Oxides

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The stereoselectivity of the oxidation of *N*-alkylpiperidines was studied with the aid of the conformationally biassing 4-*tert*-butyl substituent. The stereoselectivity was always >95% and showed little sensitivity to the nature of the *N*-alkyl substituent. The axial approach was found to be the predominating stereochemical oxidation path. A brief study of the effects of solvent, temperature, and oxidant on the stereoselectivity was made. The 1,4-dimethylpiperazine system was investigated, and its oxidation at room temperature resulted in 100% of *trans*-1,4-dimethylpiperazine 1,4-dioxide. A method to modulate the stereoselectivity in the formation of saturated heterocyclic amine oxides was developed by inverting the sequence of introduction of the nitrogen substituents. With *cis*-8-methyl-8-azabicyclo[4.3.0]nonane oxidation is preferred from that side of the molecule which is sterically more hindered.

We have demonstrated that amine oxides are excellent reagents in organometallic chemistry.[1] Specifically, they oxidize CO → CO_2 in monomeric and cluster organometallic carbonyl compounds. This reaction facilitates surgical removal of a single CO group. Depending on the nature of the complex, either disengagement of organic ligands or activation of the complex takes place. Indeed, these reactions were usefully exploited by others in organometallic chemistry.[2]

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