Table II. Irradiation of 1-Phenylethyl Pyruvate in Various Solvents

Solvent	Acetophenone yield, %
Benzene	100
Carbon tetrachloride	95
Acetone	86
Pentane	31
Ethyl ether	17

synthesized, irradiated, and found to produce methone (**18**) (Table I) with no detectable isomenthone present.

Oxidation of allylic alcohols can result in attack by the oxidizing agent on the double bond.[10] To investigate whether the pyruvate oxidation sequence avoids this competing pathway, 2-cyclohexen-1-ol (**19**) was studied. Oxidation of **19** proceeded in the normal manner to give 2-cyclohexen-1-one in good yield (Table I).

Pyruvate oxidation was unsuccessful in oxidation of *trans*-cinnamyl alcohol to *trans*-cinnamaldehyde. Although esterification occurred in the normal manner, irradiation of *trans*-cinnamyl pyruvate (**21**) resulted in isomerization to the cis isomer. This is not a surprising result when one considers that esters of pyruvic acid are believed to react via an excited triplet state[2,3] and the triplet state energy of the styrene chromophore should be lower in energy [E_t (styrene) = 61.7 kcal/mol[11]] than that of the keto ester portion [E_t (methyl pyruvate) = 65 kcal/mol[2,12]] of the molecule. Excitation absorbed by the keto ester chromophore would be transferred to the double bond and produce isomerization.

It would be desirable to conduct the pyruvate oxidation process without isolating the intermediate pyruvate ester. This possibility was investigated by irradiating directly the reaction mixture from esterification of 1-phenylethanol (**1**). The yield of acetophenone arising from this abbreviated procedure was good (90%); however, the reaction mixture had become quite dark during irradiation, a result of decomposition of pyridinium hydrochloride.

It is possible to oxidize alcohols to aldehydes and ketones using the pyruvate oxidation sequence described here without allowing the temperature of the reaction mixture to rise above room temperature. Further, no acids or inorganic oxidizing agents ever come in contact with the starting materials or products. Pyridine, the strongest base used, is involved only in the esterfication step. These reaction conditions must be among the mildest available for alcohol to carbonyl oxidations.

Experimental Section

General Procedures. The esterification, irradiation, and isolation procedure used for oxidation of each of the alcohols **1–7, 17,** and **18** was identical. This procedure is described below.

A. Esterfication. The alcohol to be esterified (0.03 mol) and dry pyridine (0.033 mol) were dissolved in 100 ml of anhydrous benzene. Pyruvoyl chloride[6] (0.03 mol) in 50 ml of benzene was added in a dropwise manner with stirring. Precipitation of pyridinium hydrochloride was immediate. Cooling with cold water was necessary to keep the reaction mixture at 25 °C. After stirring for 15 min, the pyridinium hydrochloride was removed by filtration and the benzene distilled in vacuo to yield the pyruvate ester contaminated with pyridinium hydrochloride. The contaminant could be removed by dissolving the reaction mixture in 50 ml of carbon tetrachloride, allowing it to stand for a few hours, and filtering the insoluble material. When the carbon tetrachloride was evaporated from the filtrate, a quantitative yield of the appropriate ester remained.

The identity of each ester was established first by instrumental analysis [NMR (Varian T-60) and GC/MS (Finnigan 1015-D)] and then by saponification to the starting alcohol and sodium pyruvate. Stirring the ester for 12 h in a 1% solution of sodium hydroxide in methanol was sufficient for total saponification.

B. Irradiation and Isolation. The pyruvate ester (4.0 mmol) was dissolved in 350 ml of dry benzene and the solution purged with nitrogen for 1 h. The nitrogen purge was continued during Pyrex-filtered irradiation with a 450-W, medium-pressure Hanovia mercury lamp. After 1 h, the irradiation was stopped, the reaction mixture analyzed by GC/MS, the benzene removed by fractional distillation, and the residual liquid distilled in vacuo using a Buchi/Brinkmann microdistillation oven to give the products shown in Table I. Each product was compared by NMR and GC/MS with a known sample (Aldrich Chemical Co.). In several cases (Table I) small amounts of the starting alcohol were detected. For products **5, 6, 7,** and **19,** noticeable losses occurred during solvent removal; thus, the product yields as determined prior to solvent removal are given in Table I.

Oxidation of Cholesterol (15). Compound **15** was esterified and irradiated in the same manner as the other alcohols; however, the oxidation product **16** crystallized from the reaction mixture following benzene removal and was recrystallized from methanol rather than distilled. Compound **16** was identified by comparison with a known sample.[8]

Effect of Solvent on Pyruvate Oxidation. The effect of solvent change on the pyruvate oxidation process was tested by successively replacing benzene with carbon tetrachloride, acetone, ethyl ether, and pentane as an irradiation solvent in photolysis of 1-phenylethyl pyruvate. The results are shown in Table II. NMR spectra of crude reaction mixtures from irradiations in ethyl ether and pentane showed considerable solvent incorporation.

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Registry No.—**1,** 98-85-1; **2,** 100-51-6; **3,** 111-70-6; **4,** 123-96-6; **5,** 108-93-0; **6,** 96-41-3; **7,** 507-70-0; **8,** 98-86-2; **9,** 100-52-7; **10,** 111-71-7; **11,** 111-13-7; **12,** 108-94-1; **13,** 120-92-3; **14,** 76-22-2; **15,** 57-88-5; **16,** 601-54-7; **17,** 1490-04-6; **18,** 89-80-5; **19,** 822-67-3; **20,** 930-68-7; pyruvoyl chloride, 5704-66-5.

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Stereochemistry of Hydroboration–Oxidation of Terminal Alkenes[1]

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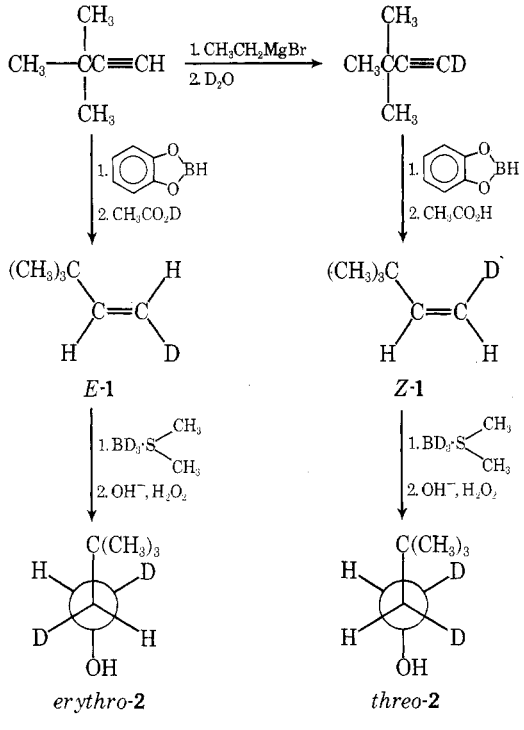
Hydroboration of alkenes followed by alkaline hydrogen peroxide oxidation of the resulting alkylboranes is the method of choice for the anti-Markownikoff hydration of carbon–carbon double bonds.[2] Although mechanistic studies have

been carried out with cyclic[3] and acyclic[4,5] secondary alkylboranes, the stereochemistry of hydroboration of a terminal alkene and the subsequent oxidation of the resulting primary alkylborane has never been determined.[6] The results described below show that these reactions are stereospecific and proceed with net cis addition of H and HO to terminal alkenes. The procedures described below also represent a general, stereospecific route to diastereomeric primary alcohols. Such primary diastereomeric alcohols are of proven utility in organometallic mechanistic studies,[7] and the procedures described below are a substantial improvement over currently available methods for the synthesis of such compounds.

Our results (Scheme I) show that hydroboration and subsequent alkaline hydrogen peroxide oxidation of (*Z*)- or (*E*)-3,3-dimethylbutene-*1*-d_1 (*Z*- or *E*-**1**) proceeds with >95% cis stereospecificity. Assuming cis hydroboration of the alkene, this means that alkaline hydrogen peroxide oxidation of primary alkylboranes occurs with retention of configuration at carbon. The stereochemistry of the products of these reactions, *erythro*- and *threo*-3,3-dimethylbutan-1-ol-*1,2*-d_2 (*erythro*- and *threo*-**2**), was determined by deuterium-decoupled ^{1}H NMR as has been previously described.[7] Non-deuterium-decoupled NMR does not permit a quantitative estimation of the diastereomeric purity of *erythro*- and *threo*-**2**, but approximate coupling constants can easily be obtained which can be used to identify the predominant diastereomer present. The approximate coupling constants obtained in this fashion for *erythro*- and *threo*-**2** are 10.5 and 5.5 Hz, respectively, and agree both with literature values and with those measured in the deuterium-decoupled spectra. The additional observation of a strong ir absorption at 1075 cm^{-1} for *threo*-**2** which is absent in the ir spectrum of *erythro*-**2** and corresponding absorptions at 1120 and 1100 cm^{-1} in the ir spectrum of *erythro*-**2** which are not present in the ir of *threo*-**2** provide further evidence for the purity of these diastereomers. Our experience with these and other similar compounds[8] suggests that in some cases the diastereomeric purity and which diastereomer is present can be determined by ir and ^{1}H NMR without the necessity of deuterium-decoupled ^{1}H NMR. However, deuterium-decoupled NMR is still the most general and best procedure available for determining the diastereomeric purity of 3,3-dimethylbutyl-*1,2*-d_2 derivatives.

Scheme I. Synthesis of *erythro*- and *threo*-3,3-Dimethylbutan-1-ol-*1,2*-d_2



The synthetic procedures leading to the diastereomers **2** are summarized in Scheme I. The straightforward reactions and the ready availability of the deuterated reagents used in this synthesis make these procedures the method of choice for the synthesis of these and similar diastereomeric primary alcohols. Such diastereomeric primary alcohols are of proven usefulness as precursors of ligands in organometallic mechanistic studies.[7,9-12] Synthetic reactions of known stereochemistry could also be used on diastereomeric primary alcohols prepared in this manner to synthesize compounds which would be useful as probes on conformation in simple acyclic systems.[13,14]

The results we have obtained support a concerted mechanism for hydroboration of alkenes. As proposed by Jones,[15] formation of a π complex between the alkene and boron followed by concerted rearrangement yields the alkylborane product. The stereochemical results we have obtained agree with this mechanism and demonstrate that alkylborane formation occurs without significant rotation of the developing carbon–carbon single bond. Although the stereochemistry of the intermediate alkylboranes was not determined in our studies, the paucity of examples of trans addition of metal hydrides to carbon–carbon double bonds and the stereospecificity of the oxidation reaction (vide infra) strongly suggest that hydroboration proceeds through cis addition of hydrogen and boron to the carbon–carbon double bond.

The stereospecificity observed in the alkaline hydrogen peroxide oxidation implies either complete retention or inversion of stereochemistry at the primary alkylborane in the oxidation reaction. Although there are some literature examples of free-radical intermediates in the alkaline hydrogen peroxide oxidation of alkylboronic acids[16] and in the neutral hydrogen peroxide oxidation of alkylboranes,[17] there is not evidence to support an inversion pathway in these oxidation reactions. Intermediate free-radical species would be expected to lead to epimerization which is not observed. We therefore conclude that alkaline hydrogen peroxide oxidation of primary alkylboranes occurs with complete retention of configuration at carbon in accord with Brown's original suggestions.[3]

Experimental Section

General Methods. All reactions of organometallic compounds were carried out in flame-dried glassware under prepurified nitrogen or argon using standard techniques.[2] Tetrahydrofuran and other ethereal solvents were distilled from a purple solution of benzophenone dianion prior to use. Methanol was purified by distillation from a methanol–sodium hypoiodate solution. Routine NMR spectra were recorded on a Varian T-60 NMR spectrometer; chemical shifts are reported in parts per million downfield from tetramethylsilane. Deuterium-decoupled NMR spectra were obtained using a Varian HA-100 spectrometer at the University of Texas at Austin.[18] Routine infrared spectra were obtained using 0.1 mm sodium chloride cells on a Beckman IR-8 spectrometer. Higher resolution infrared spectra were obtained on a Digilab FTS-20 vacuum infrared spectrometer. Raman spectra were recorded on a Cary 82 laser Raman spectrophotometer. A Perkin-Elmer 3920 gas chromatograph was used for GLC analyses. Solutions of deuterioborane–methyl sulfide complex in tetrahydrofuran were purchased from Aldrich Chemical Co. Other solvents and reagents were purchased from commercial sources in reagent quality.

3,3-Dimethylbutyne was prepared in 91% yield by the method of Collier and Macomber:[19] ir (neat) 3300, 2160, and 2110 cm^{-1}; Raman (neat) 2162 (w), 2130 (s), and 1933 cm^{-1} (w).

3,3-Dimethylbutyne-*1*-d_1 was prepared in 96% yield by the method of Zeil, Winnewisser, Bodenseh, and Buchert,[20] ir (neat) 2600 cm^{-1}. The isotopic purity of this compound was determined by the absence of an acetylenic proton in the NMR and by the disappearance of the carbon–carbon triple bond absorption in the ir spectrum (apparently because of coupling of the carbon–carbon triple bond ab-

sorption with the carbon–deuterium absorption). A strong carbon–carbon triple bond stretch was observed at 1982 cm^{-1} in the Raman with a corresponding weak absorption at 1980 cm^{-1} in the infrared.

(*Z*)-3,3-Dimethylbutene-*1*-d_1 (*Z*-1) was prepared in 85% yield from 3,3-dimethylbutyne-*1*-d_1 by the procedure of Brown and Gupta:[21] ir (neat) 2270, 802, 727 cm^{-1}; NMR (neat) δ 5.80 (m, 1, J_{H-H} = 12.0, J_{H-D} = 2.8 Hz), 4.73 (slightly broadened doublet, 1, J_{H-H} = 12.0 Hz), 1.03 (s, 9).

(*E*)-3,3-Dimethylbutene-*1*-d_1 (*E*-1) was prepared in 85% yield by hydroboration of 3,3-dimethylbutyne with 1,3,2-benzodioxaborole followed by deuterolysis of the intermediate at vinylborane with acetic acid-d_1 as has been previously described:[21] ir (neat) 2270, 980, 838 cm^{-1}; NMR (neat) δ 5.76 (m, 1, J_{H-H} = 18.0, J_{H-D} = 1.8 Hz), 4.78 (slightly broadened doublet, 1, J_{H-H} = 18 Hz), 1.01 (s, 9).

***threo*-3,3-Dimethylbutan-1-ol-*1,2*-d_2 (*threo*-2)** was prepared from *Z*-1 following the general procedure of Lane.[22] To a solution of 1.3 ml (10 mmol, 0.85 g) of *Z*-1 in 10 ml of THF in a three-necked, 100-ml, round-bottomed flask equipped with magnetic stirring bar, reflux condensor, and pressure equalized addition funnel was added 3.5 ml of a 0.95 M THF solution of deuterioborane–methyl sulfide at 0 °C dropwise with stirring. This reaction mixture was stirred for 1 h at 0 °C and 3 h at room temperature. Then 0.5 ml of absolute methanol was added by syringe and the reaction mixture cooled to 0 °C. The intermediate alkylborane was then oxidized by addition of 1.1 ml of 3 N aqueous sodium hydroxide followed by addition of 1.2 ml of a 30% hydrogen peroxide solution. After refluxing for 1 h, the reaction mixture was worked up by pouring it into a mixture of 40 ml of ice water and 20 ml of ether. The aqueous phase was separated and washed four times with 25-ml portions of ether. The combined ethereal phase was then washed twice with 10-ml portions of sodium thiosulfate. To ensure complete recovery of all the partially water soluble alcohol, these thiosulfate washes were in turn extracted with four 10-ml portions of ether. The combined ethereal phases were then dried (Na_2SO_4) and the ether was removed by fractional distillation. The resulting yellow oil was purified by a short-path distillation and isolated in 84% yield: bp 140–145 °C (lit.[7] bp 140–145 °C); ir (CS_2) 3350, 1294, 1128, 1075, 1045, 991, and 940 cm^{-1}; deuterium-decoupled NMR ($CDCl_3$) δ 3.65 (d, 1, J = 5.6 Hz), 3.47 (s, 1), 1.49 (d, 1, J = 5.6 Hz), 0.93 (s, 9).

***erythro*-3,3-Dimethylbutan-1-ol-*1,2*-d_2 (*erythro*-2)** was prepared from *E*-1 according to the procedure described for *threo*-**2**. The product alcohol was isolated in 85% yield by distillation: bp 140–145 °C (lit.[7] bp 140–145 °C); ir (CS_2) 3350, 1300, 1120, 1100, 1045, 1000, and 933 cm^{-1}; deuterium- decoupled NMR ($CDCl_3$) δ 3.65 (d, 1, J = 10.2 Hz), 3.52 (s, 1), 1.48 (d, 1, J = 10.2 Hz), 0.94 (s, 9). The infrared spectra for *erythro*- and *threo*-**2** mainly differ in the 1000–1125-cm^{-1} region, *threo*-**2** having a strong peak at 1075 cm^{-1} which is only present as a shoulder in *erythro*-**2**.

Acknowledgments. We are grateful to Drs. E. Kyba and B. Shoulders at the University of Texas at Austin for the deuterium-decoupled NMR measurements. The FTS-20 spectrophotometer was purchased with the aid of NSF Grant GP-37029 to Texas A&M University.

Registry No.—*Z*-1, 6833-43-8; *E*-1, 57002-05-8; *threo*-**2**, 52291-61-9; *erythro*-**2**, 23930-47-4; 3,3-dimethylbutyne, 917-92-0; 3,3-dimethylbutyne-*1*-d_1, 6833-44-9.

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Conformational Isomerism in *o*-Tolyldi-*tert*-butylcarbinol

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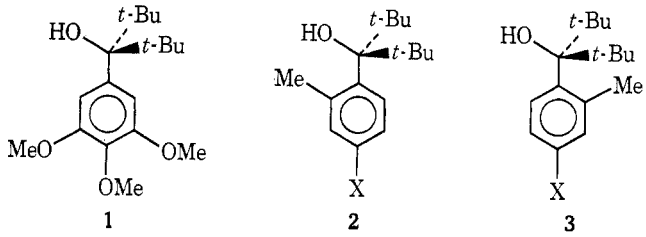
Barriers to rotation about sp^2–sp^3 and sp^3–sp^3 carbon to carbon bonds have been measured mainly by the NMR method[1] for a wide variety of compounds. Among the highest observed for nonbridged structures is the free energy of activation (18.7–21.4 kcal/mol) for rotation of the phenyl ring in 3,4,5-trimethoxyphenyldi-*tert*-butylcarbinol (1).[1c,2]

Our interest in the reactivity of congested tertiary carbinols and their derivatives[3] led us to synthesize *o*-tolyldi-*tert*-alkylcarbinols by condensation of *o*-tolyllithium with di-*tert*-alkyl ketones. GLC analysis of the crude product from the reaction with di-*tert*-butyl ketone revealed the presence of two components, denoted **2a** and **3a**, in the ratio 14:86,



1 2 3

a, X = H; b, X = OMe

whereas after distillation the product was exclusively **2a.** The unstable isomer, **3a** could, however, be isolated by chromatography on alumina in pentane and was found to differ significantly from **2a** in the ir absorption of the hydroxyl group and in the NMR of the aromatic and hydroxyl protons. A more dramatic difference in behavior was found when the dehydration rates were determined: **3a** reacts approximately 10 000 times faster than **2a.**

It is clear that **2a** and **3a** are conformational isomers, "atropisomers".[4] On the basis of kinetic[5] and spectral similarities it can be affirmed that isomer **2a** is of the same type as **2b** whose structure has been determined crystallographically.[7] In this molecule the distance between the carbon of the *o*-methyl group and the hydroxyl oxygen is very small (2.66 Å), this oxygen lying in a plane at 11.6° to the ring plane. Isomer **3a** therefore can only have a structure in which the *o*-methyl group is in the vicinity of the *tert*-butyl groups. The spectral data, as well as the relative amounts of **2a** and **3a** obtained in the synthesis and their relative dehydration rates, are consistent with this assignment. Thus, condensation of the aryllithium with di-*tert*-butyl ketone leads to the lithium