Allyl Alcohol to Saturated Ketone Isomerizations in the Presence of Alkali Metal or *n*-Butyllithium

Donald R. Dimmel,*[1] Wallace Y. Fu, and Shrikant B. Gharpure

Department of Chemistry, Marquette University, Milwaukee, Wisconsin 53233

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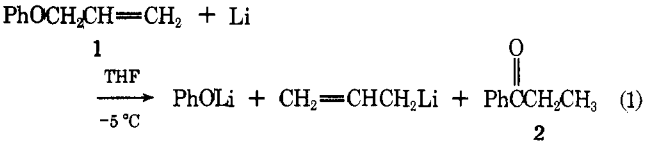
Propiophenone (**2**) is formed when α-vinylbenzyl alcohol (**3**) is treated with 2 equiv of either *n*-butyllithium or sodium–potassium alloy in DME. The mechanism of both reactions appears to be the same; namely, an intermediate dianion **6** is formed which rapidly undergoes intermolecular chain proton transfers with another ion (**5**) generating propiophenone enolate ion.

One of the methods of preparing allyllithium involves treating allyl phenyl ether with lithium metal in THF solvent.[2] In doing this reaction, we observed than a small amount (ca. 5%) of propiophenone was also produced (eq 1). The yield of ketone increased to over 50% when *n*-butyllithium was used in place of the lithium metal.[3] Based on some quenching studies, we proposed the mechanism shown in Scheme I for the *n*-butyllithium reaction.



$$\underset{\mathbf{1}}{\mathrm{PhOCH_2CH{=}CH_2}} + \mathrm{Li} \xrightarrow[-5\,^{\circ}\mathrm{C}]{\mathrm{THF}} \mathrm{PhOLi} + \mathrm{CH_2{=}CHCH_2Li} + \underset{\mathbf{2}}{\mathrm{Ph\overset{\overset{\displaystyle O}{\|}}{C}CH_2CH_3}} \qquad (1)$$

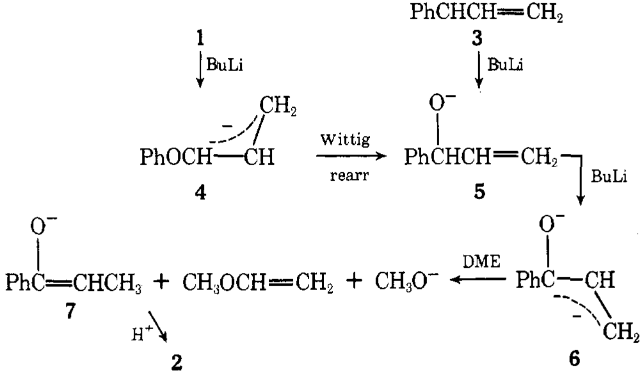
The dianion **6**, which is present in the *n*-butyllithium reaction, could be a useful synthetic intermediate toward the production of specifically alkylated ketones. However, the quenching studies on allyl phenyl ether showed that the dianion (because of its reactivity) never achieved a very high concentration in the reaction mixture. A change to nonpolar solvents, like hexane, changed the whole course of the *n*-butyllithium reactions of allyl phenyl ether[3] and α-vinylbenzyl alcohol (**3**).[4]

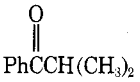
This paper will bring out some additional details about the reactivity of dianion **6** and its conversion (in ether solvents) to propiophenone. Also, some facts concerning the mechanism of the alkali metal promoted isomerizations of **1** and **3** will be presented.

Results

***n*-Butyllithium Reaction.** In order to demonstrate the presence of a dianion intermediate, α-vinylbenzyl alcohol (**3**) was treated with 2 equiv of *n*-butyllithium in DME (dimethoxyethane) and periodically quenched with methyl iodide. Three methylated products, **8–10**, were observed. The results are shown in Figure 1. The starting material had all reacted 1 min after mixing (the first sampling), giving rise to a 80:20 mixture of enolate ion **7** and dianion **6**.[5] There was then a slow conversion of dianion **6** to ion **7**, presumably by way of proton abstraction from the solvent, as shown in Scheme I. None of the expected methylated product, **11**, of alkoxide ion **5** was observed, even in the first sampling.

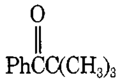
Scheme I





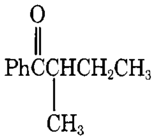
$\mathrm{Ph\overset{\overset{\displaystyle O}{\|}}{C}CH(CH_3)_2}$

8



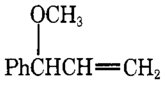
$\mathrm{Ph\overset{\overset{\displaystyle O}{\|}}{C}C(CH_3)_3}$

9



$\mathrm{Ph\overset{\overset{\displaystyle O}{\|}}{C}\underset{\underset{\displaystyle CH_3}{|}}{C}HCH_2CH_3}$

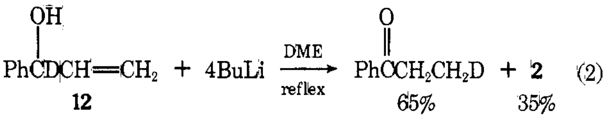
10



$\mathrm{Ph\overset{\overset{\displaystyle OCH_3}{|}}{C}HCH{=}CH_2}$

11

In order to determine what is happening in the first minute of this reaction, the rearrangement of α-deuterio-α-vinylbenzyl alcohol (**12**) was examined. The necessary deuterated alcohol was prepared from α-deuteriobenzaldehyde and vinylmagnesium bromide. Using the conditions normally employed for rearranging **3**, the deuterated analogue gave no ketone and was recovered with deuterium intact. A similar behavior was observed when α,α-dideuterioallyl phenyl ether was treated with *n*-butyllithium.[3,6]



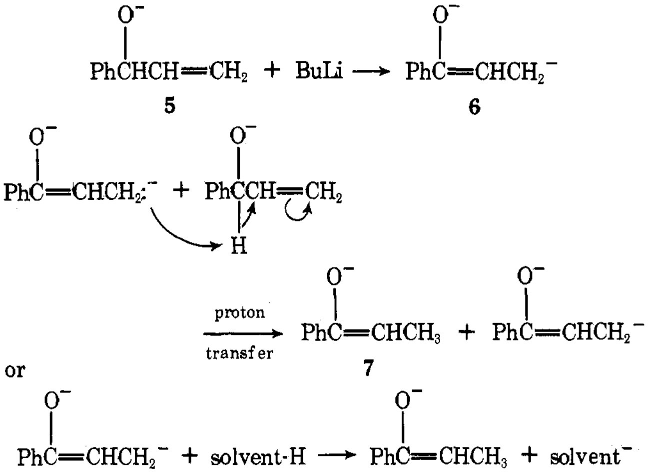
$$\underset{\mathbf{12}}{\mathrm{Ph\overset{\overset{\displaystyle OH}{|}}{C}DCH{=}CH_2}} + 4\mathrm{BuLi} \xrightarrow[\mathrm{reflex}]{\mathrm{DME}} \underset{65\%}{\mathrm{Ph\overset{\overset{\displaystyle O}{\|}}{C}CH_2CH_2D}} + \underset{35\%}{\mathbf{2}} \qquad (2)$$

Under forcing conditions, deuterated alcohol **12** could be rearranged to propiophenone. By a combination of mass and NMR spectra, it was apparent that the propiophenone had 65% of one deuterium atom on the methyl group (eq 2). If the dianion **6** was solely produced by proton abstraction by *n*-butyllithium from alkoxide **5** (Scheme I), there should be no deuterium present in the product ketone. Also, the mechanistically unlikely *intramolecular* 1,3-hydrogen atom transfer within ion **5** can be ruled out in that (a) less than 1 equiv of *n*-butyllithium to α-vinylbenzyl alcohol gives no ketone and (b) excess methyllithium, a base capable of generating **5** from **3**, affords no ketone.

The most plausible explanation of the quenching and deuterium labeling experiments is that the dianion can, in a very rapid reaction, undergo *intermolecular* proton transfers with alkoxide **5**, generating another dianion and propiophenone enolate ion (Scheme II).

For every dianion produced by *n*-butyllithium proton abstraction from **5**, there are many more dianions being produced and destroyed in the chain process. The amount of *n*-butyllithium abstraction vs. chain process can be estimated by (a) the amount of nondeuterated propiophenone produced from **12**, ca. 35%, and (b) the relative amount of dianion remaining (determined by the quenching results) after the first minute of reaction, ca. 20%. The fact that the two estimates do not totally agree can be accounted for by assuming that the dianion, once formed from deuterated alcohol **12**, will be slow to undergo intermolecular deuterium transfer as opposed to reaction with the solvent. Because of this isotope effect, the

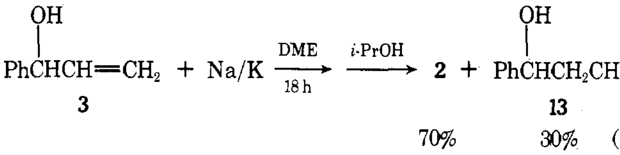
Scheme II



quenching results probably more accurately reflect the degree of proton abstraction by *n*-butyllithium vs. chain process. Even this crude estimate does not depict the true situation in that concentration changes occurring during the course of the reaction disfavor the chain process; i.e., near the end of the reaction, at low alkoxide (**5**) concentrations, the *n*-butyllithium concentration will be high and dianion concentration should still be low.

To summarize, in the reaction of α-vinylbenzyl alcohol with 2 equiv of *n*-butyllithium in DME, a dianion is produced which rapidly undergoes chain proton transfers, followed by a slower reaction with solvent, to give propiophenone (enolate). Based on this conclusion it seems highly unlikely that a dianion like **6** could ever be generated in significant quantities to be a useful synthetic intermediate.

Alkali Metal Reactions. The 5% yield of propiophenone obtained with allyl phenyl ether and lithium metal in THF (eq 1) can be improved to 25% using sodium–potassium alloy in DME. With α-vinylbenzyl alcohol as the starting material, a quantitative production of a 70:30 mixture of propiophenone and 1-phenyl-1-propanol (**13**) was observed (eq 3). The rearrangement of α-vinyl-*p*-methylbenzyl alcohol or allyl *p*-tolyl ether with Na/K alloy in DME gave *p*-methylpropiophenone; consequently, rearrangement occurred without positional changes in the aryl ring.



$$\underset{\mathbf{3}}{\mathrm{PhCH(OH)CH{=}CH_2}} + \mathrm{Na/K} \xrightarrow[18\,\mathrm{h}]{\mathrm{DME}} \xrightarrow{i\text{-PrOH}} \underset{70\%}{\mathbf{2}} + \underset{\underset{30\%}{\mathbf{13}}}{\mathrm{PhCH(OH)CH_2CH_3}} \qquad (3)$$

A methyl iodide quenching study of allyl phenyl ether and Na/K alloy gave anisole, **8**, **9**, **11**, and 1-methoxy-1-phenylpropane (the methylated derivative of **13**). Similarly, α-vinylbenzyl alcohol was methylated at regular time intervals to afford **8**, **9**, and 1-methoxy-1-phenylpropane. This latter reaction was so rapid that no **11** (the methylated product of the starting material) could be detected in the first 2-min sample. The methylated product of dianion **6**, namely **10**, could not be detected (thermal conductivity VPC on concentrated samples) in either case.

The deuterated alcohol **12** was treated with Na/K alloy under the usual room temperature conditions to give, after isopropyl alcohol quenching, unchanged starting material. However, refluxing the mixture for 36 h afforded the usual 70:30 mixture of propiophenone and 1-phenyl-1-propanol. The observed deuterium distribution in the products is shown in eq 4.

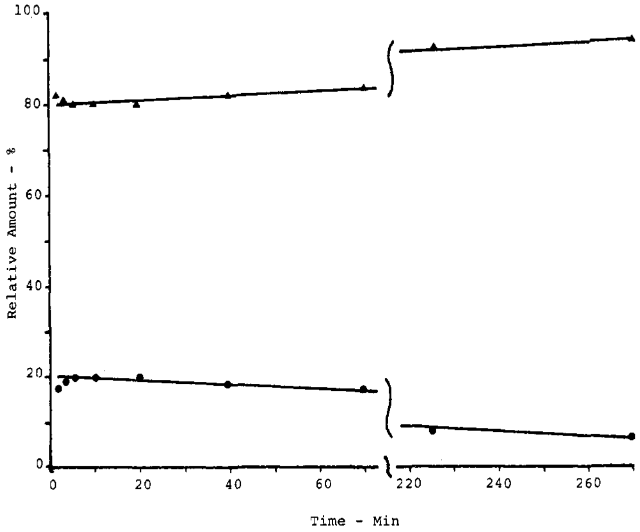
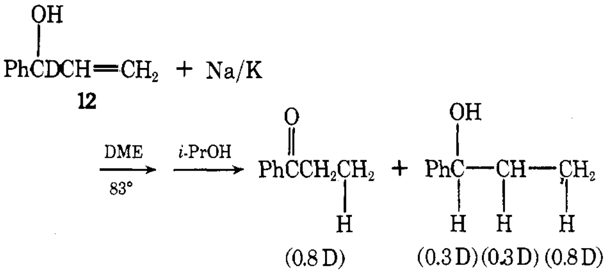


Figure 1. The isomerization of α-vinylbenzyl alcohol (**3**) with 2 equiv of *n*-butyllithium at 25 °C followed by quenching with methyl iodide: ●, amount of α-methylbutyrophenone (**10**); ▲, combined amount of isobutyrophenone (**8**) and pivalophenone (**9**).



$$\underset{\mathbf{12}}{\mathrm{PhCD(OH)CH{=}CH_2}} + \mathrm{Na/K} \xrightarrow[83^\circ]{\mathrm{DME}} \xrightarrow{i\text{-PrOH}} \mathrm{PhC(O)CH_2}\underset{\underset{(0.8\,D)}{H}}{\mathrm{CH_2}} + \mathrm{Ph}\underset{\underset{(0.3\,D)}{H}}{\mathrm{C(OH)}}\!-\!\underset{\underset{(0.3\,D)}{H}}{\mathrm{CH}}\!-\!\underset{\underset{(0.8\,D)}{H}}{\mathrm{CH_2}} \qquad (4)$$

The location of 0.8 of one deuterium in the methyl group of propiophenone was easily deduced by a combination of mass and NMR spectra; there appears to be no deuterium in the ring nor at the methylene position. The deuterium distribution in the alcohol was not as easily arrived at. This alcohol, like most others, has a characteristic weak molecular ion region, populated by M − 1, M − 2, etc., peaks in its mass spectrum which made it practically impossible to get an exact deuterium count. A sample of the alcohol was oxidized with CrO_3–H_2SO_4–H_2O to propiophenone. This latter sample of propiophenone was identical in spectral properties with the 0.8 D sample. The oxidation reaction would not only remove the benzylic hydrogen (or deuterium) but should also effectively exchange, via an acid-catalyzed enolization, any deuterium at the methylene position. However, with the knowledge that 80% of one hydrogen on the methylene group was a deuterium, the NMR spectrum of the deuterated 1-phenyl-1-propanol product became much easier to interpret and clearly showed the approximate 0.3 D at each of the other two aliphatic carbons. A spectrum run in the presence of $Eu(fod)_3$ shift reagent showed no deuteriums atoms at any position in the phenyl ring. Isomerization of α-vinylbenzyl alcohol-*O*-*d* gave nondeuterated propiophenone.

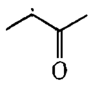
Except for the lack of any methylated product **10** in the quenching studies and the appearance of the saturated alcohol **13**, there seems to be a great deal of similarity in the *n*-butyllithium and alkali metal promoted isomerizations of α-vinylbenzyl alcohol. Both exceptions can be explained while staying in the context of a dianion intermediate.

The dianion produced in the *n*-butyllithium reactions (which can be detected) has lithium for a counterion while the alloy reaction would have sodium or potassium counterions. It is well known that organolithium reagents are more stable than the corresponding organosodium or -potassium reagents, presumably because of a greater degree of covalent bonding in the former case. Conceivably, the alloy reaction could produce a sodium–potassium dianion which is so reactive that it undergoes proton abstraction reactions, as in Scheme II, so rapidly that it never achieves an appreciable concentration or is gone before our first sampling. The greater degree of deuterium found in the propiophenone produced from **12** and Na/K alloy, as compared to the *n*-butyllithium reaction, would indicate that there are more chain proton transfers occurring in the former reaction.

The saturated alcohol **13** is probably a secondary product, arising from the reduction of propiophenone (enolate). This statement is based on the fact that both the alcohol and ketone have the same percent deuterium in their methyl groups. Reducing conditions are present; Na/K alloy in DME is commonly employed in radical anion reactions, where reduction products are frequently observed. Also, sodium hydride or species like this may be present. Sodium hydride has been reported to reduce ketones to alcohols.[7] Treating α-vinylbenzyl alcohol with sodium hydride in refluxing DME afforded nearly a 50:50 mixture of propiophenone and 1-phenyl-1-propanol (**13**).

Some of the saturated alcohol may arise during the isopropyl alcohol quench, via Meerwein–Ponndorf–Verley pathway.[8] Reaction of propiophenone with Na/K alloy, followed by quenching with isopropyl alcohol, gave **13** in yields ranging from 15 to 40% (depending on the order of mixing). It is obvious that all of the saturated alcohol does not result from a reductive quench since methyl iodide quenches show the presence of **13**; also, quenching with *tert*-butyl alcohol (with no α-protons) gave a 80:20 mixture of **2** and **13**.

An alternative mechanism for the alloy-promoted isomerizations could involve radicals or radical anion intermediates. As previously mentioned, the conditions were conducive to this type of reaction; bright colors were observed and a reduction product was isolated. Eadon and Shiekh[9] claim that radicals **14** and **15** are intermediates in the copper-catalyzed rearrangement of 3-buten-2-ol (**16**) to methyl vinyl ketone (**17**). They also observed a 1,3-intermolecular deuterium atom transfer (~80%), showing a large isotope effect.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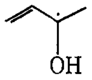
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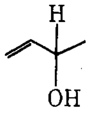
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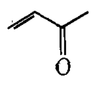
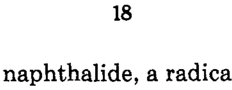
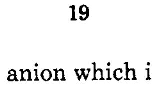

17

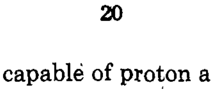
The radical anion **18** could conceivably be an intermediate in the Na/K reactions. A couple of attempts were made to prove its existence in the alloy reactions. One attempt utilized acrylophenone (**19**) (prepared from amine **20**)[10] and sodium naphthalide, a radical anion which is capable of proton abstractions from weak acids.[11] By using 1.1 equiv of sodium naphthalide to 0.1 equiv of α-vinylbenzyl alcohol, the alkoxide ion **5** should be produced with 0.1 equiv of sodium naphthalide remaining. Addition of a small amount of acrylophenone should then generate a low concentration of ketyl **18**. When these conditions were used, no rearrangement products were observed; alcohol **3** was recovered.


$\mathrm{Ph\overset{O^-}{\underset{\cdot}{C}}\!-\!CH\!=\!CH_2}$

18


$\mathrm{Ph\overset{O}{\overset{\|}{C}}CH\!=\!CH_2}$

19


$\mathrm{Ph\overset{O}{\overset{\|}{C}}CH_2CH_2N(CH_3)_2}$

20

Since ketyl **18** should be fairly stable, one may be able to generate it by treating ion **5** with a peroxide. Consequently, α-vinylbenzyl alcohol was mixed with 1 equiv of methyllithium (a reagent which does not rearrange the alcohol) and then a small amount of benzoyl peroxide. Refluxing this solution in the presence of a strong light source gave nothing but recovered starting material.

To summarize, the evidence gathered in the Na/K alloy reactions point toward a mechanism involving a very reactive dianion intermediate which follows the reactions outlined in Scheme II. The fact that a strong base like sodium hydride gives the same reaction products as does Na/K alloy indicates that the latter is also probably acting as a strong base. The yields in the Na/K alloy reaction with allyl phenyl ether suggests that extensions of this reaction for the synthesis of ketones will not prove useful, principally because the accompanying cleavage reactions dominate. However, the yields in the alloy-promoted isomerization of α-vinylbenzyl alcohol hint that extensions of this type of reaction may be synthetically useful.

Experimental Section

All boiling points and melting points were uncorrected. Infrared spectra were determined with a Perkin-Elmer spectrophotometer, Model 137-B. NMR spectra were obtained on a Varian Associates A-60A spectrometer, using Me_4Si as the internal standard and carbon tetrachloride as the solvent. Mass spectra were obtained using a CEC-21-104 mass spectrometer. Gas chromatographic analyses and preparative VPC were performed on a 6 ft × 0.25 in. aluminum column packed with 20% silicon rubber (SE-30) on 60–80 mesh Chromosorb W or a 13 ft × 0.25 in. aluminum column packed with 5% diethylene glycol succinate (DEGS) on 30–60 mesh Chromosorb W, or a 6 ft × 0.25 in. aluminum column packed with 20% Reoplex 400 (polyester) on 60–80 mesh Chromosorb W, using a F & M Model 700 gas chromatograph. Anhydrous solvents, such as dimethoxyethane (DME) and *p*-dioxane, were dried over metallic sodium and potassium and distilled immediately before use.

Propiophenone, allyl phenyl ether, 1-phenyl-1-propanol, and isobutyrophenone were commercially available[12] and *p*-methylpropiophenone has been previously described by us.[3] The procedure of Delaby and Lecomte[13] was used to prepare α-vinylbenzyl alcohol and α-vinyl-*p*-methylbenzyl alcohol.

General Procedure for the Sodium–Potassium Alloy Isomerizations. Sodium (0.36 g, 15.7 mg-atoms) and potassium (0.61 g, 15.6 mg-atoms) were fused together in some refluxing anhydrous DME. After the flask was cooled with an ice–water bath, a solution of 15.7 mmol of allyl phenyl ether (or derivative) or α-vinylbenzyl alcohol (or derivative) in DME was added. The mixture was stirred under a nitrogen atmosphere at room temperature for 18 h. [In the cases of deuterated analogues the mixture was refluxed (83 °C).] The DME solution was then filtered through a fritted funnel and quenched with 15 ml of 2-propanol. The solution was further diluted with water and extracted with 3 × 50 ml of ether. The combined ether extracts were washed with a brine solution, dried over magnesium sulfate, and concentrated on a rotary evaporator. A short-path vacuum distillation afforded a colorless liquid which was analyzed by gas chromatography and NMR. Small samples of the various components of the mixture were usually obtained by preparative VPC and analyzed by ir, NMR, and mass spectra.

The variable time quenching experiments were performed as follows. The substrate to be isomerized, allyl phenyl ether or α-vinylbenzyl alcohol, was added rapidly to a vigorously stirred ice-cold suspension of Na/K alloy in DME in a three-neck round-bottom flask under a nitrogen atmosphere. One minute after initial mixing a sample was withdrawn with a disposable pipet and added to an Erlenmeyer flask containing an excess of methyl iodide in DME. Additional samples were treated the same way at periodic time intervals, i.e., 2, 4, 8, 15, 20, 30, 60, 90, 120, etc., min, after the start. The quenched samples were then analyzed directly by VPC, using retention time comparisons with known samples for identification purposes and the area under the peak for approximate calculation of the relative amounts. The thermal responses of the components, which were generally isomers of each other, in the VPC traces were not calibrated; thus, the relative areas on the traces may not have represented the relative molar proportions of the volatile components. However, our principal objective was to determine the presence of 2-methylbutyrophenone (**10**)[3] in any of the samples and in no case (even in concentrated samples at high attenuation) was a peak indicative of **10** observed.

1-Methoxy-1-phenylpropane. This was the only compound that was observed in the methyl iodide quenches which was not already characterized.[3] It was obtained by preparative VPC (SE-30), as were the other "known" components, to confirm its structure. Subsequently, a sample of the compound was prepared independently as described next.

To a solution of 4.0 g (29.5 mmol) of 1-phenyl-1-propanol in 30 ml of anhydrous ether was added 1.26 g (33 mmol) of commercial sodium amide. After the solution was stirred for 3 h, 3.2 ml (50 mmol) of methyl iodide was added. The solution was stirred for another 4.5 h and then poured into water. The aqueous layer was separated and extracted with two 10-ml portions of ether. The combined ether extracts were dried, flash evaporated, and vacuum distilled to give 2 ml of liquid, bp 48–69 °C (2 mm) [lit.[14] bp 76–77 °C (24 mm)]. On analysis by VPC and NMR, this was found to be a mixture of the starting alcohol and 1-methoxy-1-phenylpropane. The mixture was separated by preparative VPC. The spectral properties of 1-methoxy-1-phenylpropane were ir (film) 9.12 (C–O–C), 13.02, 13.22, and 14.16 μ (Ph); NMR (CCl_4) δ 0.88 (t, 3, $J = 7$ Hz, $C\text{–}CH_3$), 1.70 (m, 2, $\text{–}CH_2\text{–}$), 3.15 (s, 3, $\text{–}OCH_3$), 3.95 (t, 1, $J = 6.5$ Hz, $CHCH_2\text{–}$) and 7.22 (s, 5, Ph).

1-Vinylbenzyl Alcohol-*1-d* (12). The necessary starting material, benzaldehyde-*formyl*-d_1, was prepared by a known procedure[15] and based on NMR and mass spectral analysis was about 98% d_1. A solution of 7.2 g (68 mmol) of vinyl bromide in 20 ml of anhydrous THF was added, with vigorous stirring, to 1.1 g (91 mg-atoms) of magnesium turnings, under nitrogen, over a period of 1 h. An acetone–dry ice cold finger condenser was used to prevent the vinyl bromide from escaping. Formation of the Grignard reagent was completed by external heating (45–55 °C) for an additional 3 h. The Grignard reagent was cooled to room temperature and then a solution of 4.0 g (36 mmol) of benzaldehyde-*formyl-d* in 25 ml of THF was added over the course of 0.5 h. The mixture was stirred under nitrogen for 16 h and decomposed with 10 ml of cold, saturated NH_4Cl. The THF solution was decanted from the caked residue which was triturated with 4 × 25 ml of ether. The combined THF–ether solution was dried over $MgSO_4$, concentrated, and distilled to give 4.0 g (80%) of a colorless liquid: bp 77–85 °C (1.5 mm); ir (film) 3500 (OH), 1060 (C–O), 990 ($C{=}CH_2$), and 700 cm^{-1} (Ph); NMR (CCl_4) δ 7.18 (s, 5, Ph), 5.90 (d of d, $J = 17$ and 9.7 Hz, 1, $\text{–}CH{=}CH_2$), 5.13 (d of d, $J = 17$ and 2 Hz, 1, trans $CH{=}CH_2$), 5.01 (d of d, $J = 9.7$ and 2 Hz, 1, cis $CH{=}CH_2$), and 3.78 (s, 1, OH); mass spectrum (70 eV) *m/e* (rel intensity) 135 (74), 134 (82), 116 (31), 108 (33), 105 (75), 93 (57), 92 (54), 80 (100), 79 (43), 78 (87), 77 (74), 55 (37), 51 (69), 39 (31), and 27 (49).

Isomerization of α-Vinylbenzyl Alcohol (3). A. With Na/K Alloy, Quenched with 2-Propanol. The general procedure afforded a mixture of 70% propiophenone and 30% 1-phenyl-1-propanol, as proven by preparative VPC and comparison of spectral properties to those of known samples.[13]

B. With Na/K Alloy, Quenched with *tert*-Butyl Alcohol. The general procedure was used except for the substitution of *tert*-butyl alcohol for 2-propanol. Analysis by VPC showed 81% propiophenone and 19% 1-phenyl-1-propanol.

C. With Sodium Naphthalide. According to a procedure of Scott,[17] a dark green solution of sodium naphthalide was prepared from 2.5 g (19 mmol) of naphthalene and 0.6 g (26 mg-atoms) of sodium in 25 ml of DME. To this green solution was added 2.2 g (16.4 mmol) of α-vinylbenzyl alcohol and 4 drops of acrylophenone.[10,16] After stirring at room temperature for 18 h the green color was discharged by adding water. The solution was extracted with 2 × 50 ml of ether. The combined ether extracts were dried over $MgSO_4$ and concentrated on a rotary evaporator. VPC analysis showed only naphthalene and α-vinylbenzyl alcohol.

D. With Sodium Hydride. To a suspension of 0.97 g (40 mmol) of sodium hydride in DME was added, with stirring, 5.3 g (40 mmol) of α-vinylbenzyl alcohol. After refluxing for 20 h, the solution was diluted with water and extracted with ether. The ether extract was dried over $MgSO_4$ and concentrated. VPC analysis showed 46% of propiophenone and 54% of 1-phenyl-1-propanol.

E. With *n*-Butyllithium. To a cold (0 °C) solution of 3.0 g (22.4 mmol) of α-vinylbenzyl alcohol in 20 ml of DME was rapidly added 44.8 mmol of *n*-butyllithium in hexane. A vigorous reaction occurred and the reaction mixture became red. The cooling bath was removed and the mixture allowed to warm to room temperature (25 °C). Samples were withdrawn at regular time intervals, quenched with methyl iodide, diluted with ether, and washed with water. The ether solutions were concentrated and chromatographed (SE-30).

From matching retention times, it was possible to prove the presence of isobutyrophenone (8), pivalophenone (9), and α-methylbutyrophenone (10). The results are shown in Figure 1.

Reduction of Propiophenone with Na/K alloy and 2-Propanol. Potassium (0.50 g, 12.8 mg-atoms) and sodium (0.30 g, 12.8 mg-atoms) were fused together in refluxing DME. After cooling to 5 °C, 1.72 g (12.8 mmol) of propiophenone was added. The solution was stirred at room temperature for 18 h. A 5-ml sample was withdrawn, by means of a syringe, and *added* to 1 ml of 2-propanol. Water and ether were added and the ether layer separated, dried over $MgSO_4$, and concentrated. VPC analysis showed 85% propiophenone and 15% α-vinylbenzyl alcohol.

The remaining residue in the flask *was treated with* 15 ml of 2-propanol until all the metal had disappeared (1 h). Ether and water were added and the ether layer separated, dried over $MgSO_4$, and concentrated to give 1.50 g of a colorless liquid: VPC analysis showed 57% propiophenone and 43% α-vinylbenzyl alcohol.

Isomerization of 1-Vinylbenzyl Alcohol-*1-d* (12). A. With Na/K Alloy. The general procedure, employing refluxing DME for 36 h, gave, after quenching with 2-propanol, 1.2 g of colorless liquid. Analysis by VPC showed 70% propiophenone and 30% 1-phenyl-1-propanol. The VPC separated sample of propiophenone showed ir (film) 1710 (C=O), 747 and 692 cm^{-1} (Ph); NMR (CCl_4) δ 7.80–8.05 (m, 2, ortho protons), 7.15–7.55 (m, 3, meta and para protons), 2.70–3.12 (m, 2, $\text{–}CH_2$),[18] and 0.98–1.33 (m, 2.2, $\text{–}CH_D$);[19] mass spectrum (70 eV) *m/e* (rel intensity) 136 (2), 135 (13), 134 (5), 105 (100), 77 (51), 51 (25), 50 (9), 29 (3), and 27 (8). A comparison of this mass spectrum with that of a nondeuterated sample of propiophenone indicated a deuterium distribution of 27% d_0, 69% d_1, and 4% d_2.

The NMR spectrum of the VPC separated sample of the deuterated 1-phenyl-1-propanol showed, in comparison to an authentic, undeuterated sample, a singlet at 7.18 for the aromatic protons (area 110), a broad triplet at 4.38 ($J = 7.0$ Hz, area 14), a singlet at 2.83 (area 26) for the hydroxy proton, a broad multiplet at 1.56 (area 37), and a multiplet at 0.83 ppm (area 49). Sufficient amount of $Eu(fod)_3$ (67.7 mg) was added so that the benzyl, ortho, and meta and para protons were well resolved. The relative integrated areas under ortho:benzyl:meta and para:methylene:methyl were 36:12.3:55:31:40, respectively. Assuming that there are no deuterium atoms in the phenyl ring gives a relative ratio of 2.0:0.7:3.0:1.7:2.2 for the above-mentioned protons.

The NMR sample was concentrated to remove CCl_4 and diluted with ether. The solution was cooled to 0 °C and $CrO_3\text{–}H_2SO_4$ solution was added dropwise until a red color persisted. The red color was discharged by the addition of 2-propanol. The ether solution was filtered, washed with 1 ml of water, dried over $MgSO_4$, and concentrated. A VPC separated sample showed that it was propiophenone; its NMR and mass spectra were identical with those of the deuterated propiophenone. From the NMR spectrum of propiophenone, the deuterium distribution in 1-phenyl-1-propanol was determined: 0.32 at the benzylic position, 0.28 at the methylene position, and 0.80 at the methyl position.

B. With *n*-Butyllithium. To a cold (5 °C) solution of 0.13 g (0.9 mmol) of 1-vinylbenzyl alcohol-*1*-d_1 in 15 ml of anhydrous DME was added a hexane solution of 4.0 mmol of *n*-butyllithium. The mixture was refluxed under nitrogen for 4 h and then stirred at room temperature for 14 h. The mixture was poured into 25 ml of water and extracted with 2 × 50 ml of ether. The combined ether extracts were dried over $MgSO_4$ and concentrated to yield 107 μl of a liquid. VPC analysis (DEGS) showed 87% propiophenone and five other unidentified components totaling 13%. No detectable amount of 1-phenyl-1-propanol was found. After purification by preparative VPC, the sample showed the following spectral characteristics: NMR (CCl_4) 7.78–8.03 (m, 2.0, ortho protons), 7.18–7.53 (m, 3.0, meta and para protons), 2.70–3.12 (m, 2.0, $\text{–}CH_2\text{–}$), and 0.99–1.34 ppm (m, 2.4, $\text{–}CH_2D$);[20] mass spectrum (70 eV) *m/e* (rel intensity) 136 (3), 135 (11), 134 (6), 105 (100), 77 (60), 51 (29), 50 (13), 29 (5), and 27 (8), By comparison to the nondeuterated propiophenone spectrum, a deuterium distribution was arrived at: 34% d_0, 56% d_1, and 9% d_2.

Isomerization of α-Vinylbenzyl Alcohol-*O-d* with Na/K Alloy. To 6 ml of heavy water was added 2 g of α-vinylbenzyl alcohol (3) and a catalytic amount of sodium. This mixture was stirred overnight and extracted with two 8-ml portions of ether. The combined ether extracts were dried, flash evaporated, and vacuum distilled to give **3**-*O-d*. Its NMR spectrum did not show any alcoholic hydrogen. Rearrangement of this by way of the general procedure gave propiophenone containing no deuterium (NMR).

Treatment of α-Vinylbenzyl Alcohol Salt with Benzoyl Peroxide. To a solution of 1.34 g (10 mmol) of **3** in cold DME was added 4.2 ml (10 mmol) of a solution of methyllithium in ether. After the solution was stirred for 15 min, 0.242 g (1 mmol) of benzoyl peroxide was added. A dark red color developed. The solution was then refluxed overnight under a 150-W light bulb. The usual workup, after vacuum distillation, gave 0.4 g of liquid, bp 40–110 °C (2 mm). Based on VPC and NMR, the liquid was principally starting alcohol **3**.

Registry No.—**2,** 93-55-0; **3,** 4393-06-0; **12,** 33716-94-8; 1-phenyl-1-propanol, 93-54-9; sodium amide, 7782-92-5; 1-methoxy-1-phenylpropane, 59588-12-4; benzaldehyde-*formyl-d*, 3592-47-0; α-vinylbenzyl alcohol-*O-d*, 59588-11-3.

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(5) An assumption is made here that the rates of the methyl iodide reactions with each of the intermediates are comparable (and fast). Actually, the dianion would be more reactive than the monoanions; thus, its percentage of the methylated products may be a little higher than its actual percent concentration in solution.

(6) The exact reason for this large isotope effect is unknown. It is conceivable that dianion generation could have a large isotope effect, based on the evidence that certain monoanion formations have exhibited isotope effects of k_H/k_D = 24 at −50 °C [A. Wright and R. West, *J. Am. Chem. Soc.*, **96,** 3227 (1974)]. In the allyl phenyl ether case the α deuteriums appear to not only retart isomerization but also divert the starting material toward competing reactions.

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(18) The multiplet pattern consisted of an intense triplet (J = 7 Hz, vicinal H–H), which was further split (equal intensity triplet, J = 0.7 Hz, vicinal H–D), and a weaker quartet (J = 7 Hz, vicinal H–H).

(19) The pattern is definitely that of a triplet (J ≈ 7 Hz), which is further split. It appears that there is some unsplit triplet superimposed on a triplet which is further split into an equally intense triplet (J ≈ 2 Hz, geminal H–D).

(20) The patterns of the methylene and methyl groups were similar to the previously described deuterated propiophenone,[18,19] but obviously different with the respect to the amount of deuterium on the methyl group. The methylene quartet (reflecting the nondeuterated propiophenone component) and triplet, which was further split (reflecting the –CH$_2$CH$_2$D unit), were closer to the same intensity.

Synthesis of Optically Active Dialkylarylsulfonium Salts from Alkyl Aryl Sulfoxides[1]

Kenneth K. Andersen,* Robert L. Caret,[2] and David L. Ladd[2]

Department of Chemistry, University of New Hampshire, Durham, New Hampshire 03824

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Treatment of alkoxysulfonium salts, prepared by O-alkylation of optically active methyl, ethyl, and *n*-butyl *p*-tolyl sulfoxides, with alkyl Grignard or alkylcadmium reagents gave optically active *n*-butylmethyl-*p*-tolyl-, *n*-butylethyl-*p*-tolyl-, and ethylmethyl-*p*-tolylsulfonium salts. Racemic phenyl-*o*-tolyl-*p*-tolyl- and ethylphenyl-*p*-tolylsulfonium salts were formed from optically active alkoxyphenyl-*p*-tolylsulfonium salts. Trialkylsulfonium salts were not formed when alkoxydialkylsulfonium salts were treated with alkyl Grignard or alkylcadmium reagents. The chiroptic properties of the dialkyl-*p*-tolylsulfonium salts are discussed.

Optically active sulfonium salts, formerly accessible only by resolution, may be synthesized by treating optically active O-alkylated sulfoxides with organocadmium or Grignard reagents (eq 1).[3] This reaction has recently been shown to proceed with inversion of configuration

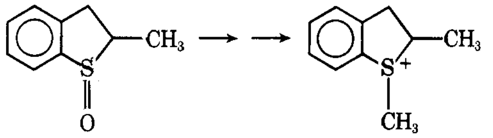
$$RR'S{=}O \rightarrow RR'S^+{-}OR''' \rightarrow RR'R''S^+ \qquad (1)$$

although partial racemization of the alkoxysulfonium salt may lower the enantiomeric purity of the product.[4]

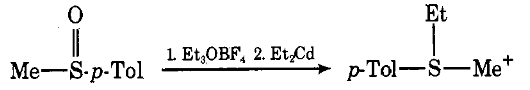
This article reports on the study of this reaction for the synthesis of dialkylaryl-, triaryl-, alkyldiaryl-, and trialkylsulfonium salts and on the chiroptic properties of dialkylarylsulfonium salts. In principle, a given sulfonium salt may be prepared from any one of three sulfoxides. That is, any one of the three groups around sulfur could come from the organometallic reagent while the other two originate from the sulfoxide. But in fact, only alkoxyalkylaryl- and alkoxydiarylsulfonium salts (RArS–OR$^+$, Ar$_2$S–OR$^+$) react as in eq 1; alkoxydialkyl sulfonium salts (R$_2$SOR$^+$) do not.

Results and Discussion

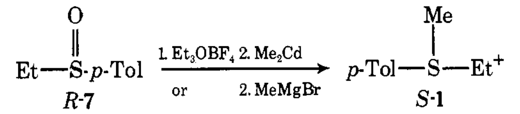
Dialkylarylsulfonium Salts. Treatment of alkoxysulfonium salts, derived from (*R*)-alkyl *p*-tolyl sulfoxides, with alkylcadmium or Grignard reagents yields optically active dialkyl-*p*-tolylsulfonium salts (Table I). Since the cyclic analogues *cis*- and *trans*-**4** yield sulfonium salts *trans*- and *cis*-**5** with predominant inversion at sulfur (eq 2), we assume that acyclic compounds behave similarly.[4] This assumption is strengthened by the reactions depicted by eq 3–6. Enantiomeric sulfonium salts are produced in each pair of reactions (eq 3 and 4, 5 and 6) from sulfoxides of known absolute configuration, thus establishing a common stereochemical process. These results, and the fact that displacement of alkoxy



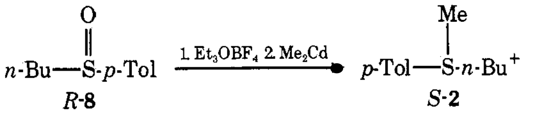
4 **5** (2)



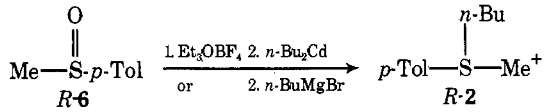
$$\underset{R\text{-}\mathbf{6}}{\mathrm{Me}{-}\overset{\overset{\displaystyle\mathrm{O}}{\|}}{\mathrm{S}}{-}p\text{-Tol}} \xrightarrow{1.\ \mathrm{Et_3OBF_4}\ 2.\ \mathrm{Et_2Cd}} \underset{R\text{-}\mathbf{1}}{p\text{-Tol}{-}\overset{\overset{\displaystyle\mathrm{Et}}{|}}{\mathrm{S}}{-}\mathrm{Me}^+} \qquad (3)$$



$$\underset{R\text{-}\mathbf{7}}{\mathrm{Et}{-}\overset{\overset{\displaystyle\mathrm{O}}{\|}}{\mathrm{S}}{-}p\text{-Tol}} \xrightarrow[\text{or}\quad 2.\ \mathrm{MeMgBr}]{1.\ \mathrm{Et_3OBF_4}\ 2.\ \mathrm{Me_2Cd}} \underset{S\text{-}\mathbf{1}}{p\text{-Tol}{-}\overset{\overset{\displaystyle\mathrm{Me}}{|}}{\mathrm{S}}{-}\mathrm{Et}^+} \qquad (4)$$



$$\underset{R\text{-}\mathbf{8}}{n\text{-Bu}{-}\overset{\overset{\displaystyle\mathrm{O}}{\|}}{\mathrm{S}}{-}p\text{-Tol}} \xrightarrow{1.\ \mathrm{Et_3OBF_4}\ 2.\ \mathrm{Me_2Cd}} \underset{S\text{-}\mathbf{2}}{p\text{-Tol}{-}\overset{\overset{\displaystyle\mathrm{Me}}{|}}{\mathrm{S}}{-}n\text{-Bu}^+} \qquad (5)$$



$$\underset{R\text{-}\mathbf{6}}{\mathrm{Me}{-}\overset{\overset{\displaystyle\mathrm{O}}{\|}}{\mathrm{S}}{-}p\text{-Tol}} \xrightarrow[\text{or}\quad 2.\ n\text{-BuMgBr}]{1.\ \mathrm{Et_3OBF_4}\ 2.\ n\text{-Bu_2Cd}} \underset{R\text{-}\mathbf{2}}{p\text{-Tol}{-}\overset{\overset{\displaystyle n\text{-Bu}}{|}}{\mathrm{S}}{-}\mathrm{Me}^+} \qquad (6)$$