Notes

Allyloxy Carbanions. A Synthesis of 3,4-Dihydroxy-1-olefins from Carbonyl Compounds

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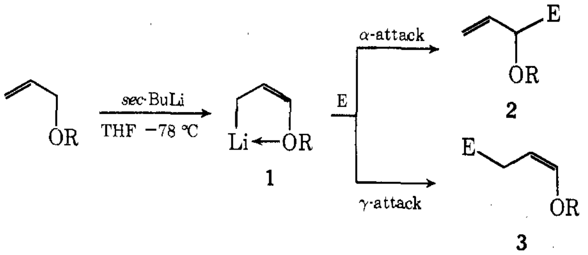
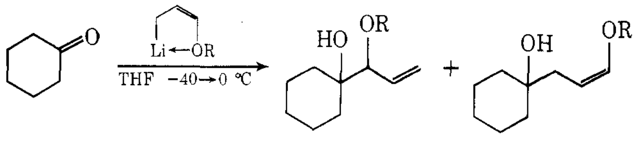
Previous studies have shown that simple allylic ethers are rapidly metalated at low temperature to yield synthetically useful allyloxy carbanions (1).[1] As shown below, reaction of these highly nucleophilic compounds with electrophiles can lead via α-substitution to allylic ethers **2** or via γ-substitution to enol ethers **3**:



With primary alkyl halides, the latter pathway is preferred, and particularly large proportions of alkylated enol ethers are obtained when R = *t*-Bu or SiEt$_3$. Reaction of 1 with carbonyl compounds proceeds mainly by α-attack. Evans and coworkers have reported[1a] that the corresponding allylzinc reagents (**1**, Li = ½Zn, R = alkyl) are useful for effecting regiospecific α-attack on ketones. The work reported here demonstrates that the lithium salt of trimethylalloxysilane (**1**, R = SiMe$_3$) in THF–HMPA also undergoes α-attack on a variety of aldehydes and ketones with 98–100% regioselectivity. Mild acid hydrolysis of the product monosilyl ethers affords 3,4-dihydroxy-1-olefins in high yields.

We have examined the reaction of a number of silicon-substituted allyloxy carbanions with cyclohexanone under various conditions to determine the most effective method for controlling regioselectivity.



	4	5
R = SiEt$_3$	71%	29%
R = SiMe$_3$	95%	5%
R = SiMe$_3$ (5% HMPA)	>99%	

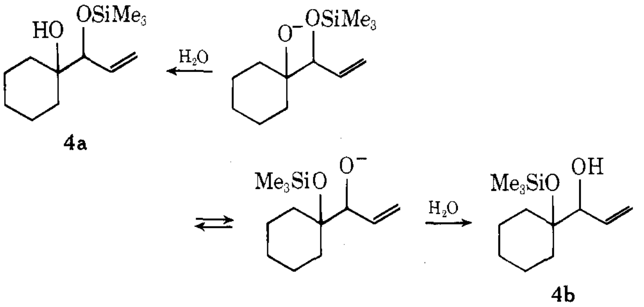
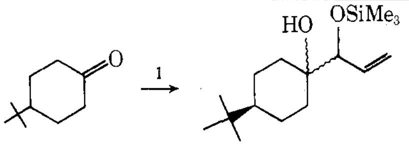
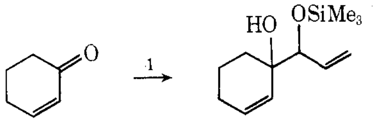
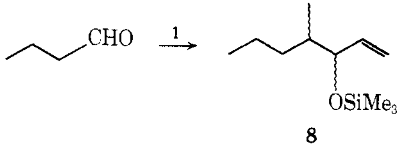
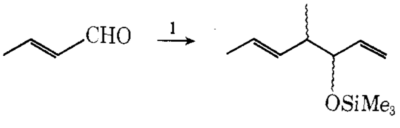


Table I

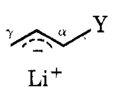
Registry no.		Yield distilled	Purity (VPC)	Registry no.
98-53-3	 **6**	88%	90%	59906-41-1
930-68-7	 **7**	82%	94%	59906-42-2
123-72-8	 **8**	80%	72%	59906-43-3
25447-68-1	 **9**	73%	84%	59906-44-4

As shown above, the trimethylsilyl derivative of **1** in the presence of 5% hexamethylphosphoramide (HMPA) gives very high selectivity for the α-substituted product, **4** (R = $SiMe_3$). The product was obtained in 76% yield after bulb-to-bulb distillation and was readily hydrolyzed (THF–H_2O–HOAc) to the crystalline diol **4** (R = H). One point of ambiguity concerns the site of attachment of the trimethylsilyl grouping in the unhydrolyzed product. Since silicon migration to a vicinal alkoxide could occur, the product could have structure **4a** or **4b** or could be a mixture of the two compounds. Several observations suggest, however, that the product is the initially formed secondary monosilyl ether **4a.** VPC, TLC, and NMR all indicate the adduct to be a single isomer. Thus, it must contain either a tertiary hydroxyl (**4a**) or a secondary allylic hydroxyl (**4b**). These two possibilities should be differentiated by reaction of the product with manganese dioxide or with acetic anhydride/pyridine, since tertiary alcohols are inert to these reagents. We find that the addition product is recovered unchanged on treatment with manganese dioxide/benzene and with acetic anhydride/pyridine under conditions which convert the diol **4** (R = H) to enone and acetate, respectively. These data provide strong support for assignment of structure **4a** to the cyclohexanone adduct.

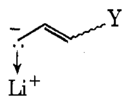
We have also examined the reaction of **1** (R = $SiMe_3$) in 5% HMPA/THF with other carbonyl compounds. In all cases, >98% α-attack was observed. Our results are summarized in Table I.[2]

Like many other allylic organometallics, the allyloxy carbanion reagent exhibits little preference for axial or equatorial attack on 4-*tert*-butylcyclohexanone.[3] The product of this reaction, **6,** was found to consist of a 1:1 mixture of diastereomers. Addition of **1** to α,β-unsaturated carbonyl compounds takes place very largely in the 1,2 sense. Crude **7** and **9,** for example, gave infrared spectra showing a strong hydroxyl band at 3450 cm^{-1} and only weak absorbances in the 1700–1725-cm^{-1} region. Aldehydes generally give larger proportions of by-products than do ketones.[4] These side reactions appear to be due to base-catalyzed self-condensation of the aldehyde group. Although the monosilyl ethers **8** and **9** were not readily purified, the corresponding diols were obtained analytically pure by silica gel chromatography and bulb-to-bulb distillation.

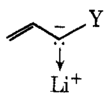
The regioselectivity exhibited by allyloxy carbanions in their reactions with electrophiles is consistent with the behavior of other allyllithiums: *in general,* unsymmetrically substituted allyllithium compounds preferentially react with alkyl halides and protons at the site of higher electron density and with carbonyl compounds, via a rearrangement process[5] involving lithium, at the opposite site. This rule of thumb applies only to compounds in which lithium and the allylic anion are associated;[6] thus, allylic anions substituted by strong electron-withdrawing groups and free allylic anions are excluded. The site of higher electron density is determined by the nature of the substituents on the allylic anion. For an anion like **10** where Y is an anion-destabilizing substituent, higher electron density would be expected at the γ carbon and a structure like **10a** would be preferred over one like **10b.** An allylic anion substituted by an anion-stabilizing group should have complementary charge distribution and favor a structure like **10b** or **10c.** In accord with the general rule above, allyllithium compounds which are terminally substituted by anion-destabilizing groups (Y = alkyl,[7] OR,[1,8] NR_2[9]) undergo preferential protonation and alkylation at the unsubstituted (γ) terminus and reaction with carbonyl compounds at the substituted (α) terminus. Allyllithiums substituted by mild anion-stabilizing groups (Y = SR[10], BR_2[11]) exhibit the opposite behavior: alkyl halides and protons add α and carbonyl compounds add γ to the substituent. Substitution of an allylic anion with stronger anion-stabilizing groups results in less allylic anion–counterion association (**10c**) and gives increased proportions of carbonyl attack by the position (α) of higher electron density.[12] These tendencies may be modified by numerous factors including steric effects, ionizing cosolvents,[6] and use of electrophiles like benzophenone.[13]



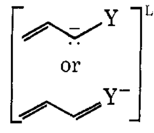
10



10a



10b



10c

Experimental Section

General. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer 727 spectrophotometer. NMR spectra were measured on a JEOL JNM-MH-100 spectrometer and are reported in parts per million downfield from internal tetramethylsilane. Mass spectra were recorded on an LKB-9000 instrument. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Trimethylallyloxysilane. Sodium hydride dispersion (9.2 g, 0.22 mol, 57%) was suspended in 50 ml of anhydrous ether under dry nitrogen. The mixture was stirred while 11.6 g (0.20 mol) of dry allyl alcohol was added over a 2-h period. The resulting slurry was stirred overnight and then all solvents were removed by gentle heating in vacuo. The flask was refilled with nitrogen and 19.5 g (0.18 mol, 23 ml) of trimethylsilyl chloride was added dropwise with stirring. When the addition was complete, the mixture was heated at reflux for 2 h and cooled. The volatile product was isolated by vacuum transfer to a −78 °C trap and was purified by distillation through an 8-in. Vigreux column. The product was a colorless liquid, bp 97–99 °C (760 mm) (lit.[14] 98–99 °C), and the yield was 18.3 g (78% based on trimethylsilyl chloride).

Diol Monosilyl Ether 4 (R = $SiMe_3$). Anhydrous tetrahydrofuran (10 ml) was added to a flame-dried 25-ml flask under nitrogen. The flask was cooled to −40 °C (dry ice/acetonitrile) and 5 mmol of *sec*-butyllithium was injected. The yellow solution was stirred and 1.25 ml (7.5 mmol) of trimethylallyloxysilane and 0.5 ml of dry HMPA were added. The pale yellow to colorless solution was stirred for 5 min and 295 mg (3 mmol) of cyclohexanone in ~2 ml of dry tetrahydrofuran was added over ~30 s. The mixture was stirred for 15 min and the cooling bath was removed. On warming to 0 °C, the mixture was poured into 50 ml of petroleum ether and was thoroughly washed with water (2 × 50 ml) and saturated NaCl. The organic phase was dried (Na_2SO_4) and the solvents were removed at reduced pressure to give a somewhat volatile, colorless oil. Kugelrohr distillation (0.05 mm, oven temperature 110 °C) gave 520 mg (76%) of **4** (R = $SiMe_3$): ir (neat) 3350, 1640 (weak), 1250, 840 cm^{-1}; NMR ($CDCl_3$) δ 5.90 (1 H, ddd, J = 17, 10, 7 Hz), 5.00–5.28 (2 H, m), 3.77 (1 H, d, J = 7 Hz), 2.10 (1 H, br s, OH), 1.10–1.84 (10 H, m), 0.10 (9 H, s); MS (70 eV) *m/e* (rel intensity) 213 (6) (parent − CH_3), 171 (14), 130 (70), 115 (52), 99 (65), 81 (51), 79 (15), 77 (12), 75 (56), 73 (100).

The analytical sample was prepared by hydrolysis of the trimethylsilyl ether in 1:1:6 H_2O/HOAc/THF (1 h, 20 °C). The product was recrystallized from cold pentane to give the pure diol **4** (R = H) as needles, mp 48.5–49 °C.

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.34, H, 10.50.

Diol Monosilyl Ethers 6–9. Compounds **6–9** Compounds were prepared using the procedure above except that, in the preparation of compounds **8** and **9**, the cooling bath was removed immediately after addition of the aldehyde to the −40 °C solution of **1.** This procedure helped limit self-condensation of the starting materials.

All compounds gave satisfactory ir, NMR, and mass spectra. The derived diols also gave satisfactory spectra and elemental analyses.

Acknowledgment. We wish to thank the Research Corporation for their generous support of this work. We would also like to thank Professor Gilbert Stork for his support (NIH GMO5147-18) of some of the early work on this project.

Registry No.—**1** (R = $SiMe_3$), 18146-00-4; **1** (R = $SiEt_3$), 2290-45-1; **4** (R = H), 59906-45-5; **4** (R = $SiMe_3$), 59906-46-6; **4** (R = $SiEt_3$), 59906-47-7; **5** (R = $SiMe_3$), 59906-48-8; **5** (R = $SiEt_3$), 59906-49-9; allyl alcohol, 107-18-6; trimethylsilyl chloride, 75-77-4; tetrahydrofuran, 109-99-9; *sec*-butyllithium, 598-30-1.

References and Notes

(1) (a) D. A. Evans, G. C. Andrews, and B. Buckwalter, *J. Am. Chem. Soc.*, **96**, 5560 (1974); (b) W. C. Still and T. L. Macdonald, *ibid.*, **96**, 5561 (1974); (c) W. C. Still, *Tetrahedron Lett.*, 2115 (1976).

(2) The site of attachment of the trimethylsilyl group was not investigated in these compounds, but has been tentatively assigned by analogy with the cyclohexanone → **4a** conversion.

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(4) Similar behavior has been noted previously with other allyllithiums: V. Rautenstrauch, *Helv. Chim. Acta*, **57**, 496 (1974).

(5) A number of mechanisms have been proposed to explain this rearrangement and are summarized in ref. 4.

(6) Cf. P. M. Atlani, J. F. Biellmann, S. Dube, and J. J. Vicens, *Tetrahedron Lett.*, 2665 (1974); W. H. Glaze, J. E. Hanicak, J. Chaudhuri, M. L. Moore, and D. P. Duncan, *J. Organomet. Chem.*, **51**, 13 (1973).

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(8) C. J. Upton and P. Beak, *J. Org. Chem.*, **40**, 1094 (1975).

(9) H. Ahlbrecht and J. Eichler, *Synthesis*, 672 (1974); M. Julia, A. Schouteeten, and M. Baillarge, *Tetrahedron Lett.*, 3433 (1974); P. Savignac, P. Coutrot, and Y. Leroux, *C. R. Acad. Sci., Ser. C*, **279**, 609 (1974).

(10) J. F. Biellmann and J. B. Ducep, *Tetrahedron Lett.*, 5629 (1968); K. Oshima, H. Takahashi, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **95**, 2693 (1973); P. L. Stotter and R. E. Hornish, *ibid.*, **95**, 4444 (1973); S. Torii, H. Tanaka, and Y. Tomotaki, *Chem. Lett.*, 1541 (1974); ref 6.

(11) R. Kow and M. W. Rathke, *J. Am. Chem. Soc.*, **95**, 2715 (1973).

(12) Anions derived from allylic dithianes [D. Seebach, *Synthesis*, 17 (1969)] and allylic sulfoxides [D. A. Evans, G. C. Andrews, T. T. Fugimoto, and D. Wells, *Tetrahedron Lett.*, 1385 (1973)] give large proportions of α-attack on reaction with ketones. Anions of α,β-unsaturated carbonyl compounds give very high selectivity for α-addition to aldehydes and ketones as well as to alkyl halides and protonating agents; cf., inter alia, H. O. House, "Modern Synthetic Reactions", 2d ed, W. A. Benjamin, Menlo Park, Calif., 1972, Chapter 9; M. W. Rathke and D. Sullivan, *Tetrahedron Lett.*, 4249 (1972); J. L. Herrmann, G. R. Kieczykowski, and R. H. Schlessinger, *ibid.*, 2433 (1973); S. A. G. de Graaf, P. E. R. Oosterhoff, and A. van der Gen, *ibid.*, 1653 (1974).

(13) Simple stabilized allylic anions frequently undergo exclusive γ-attack on benzophenone: R. H. DeWolfe, D. E. Johnson, R. I. Wagner, and W. G. Young, *J. Am. Chem. Soc.*, **79**, 4798 (1957); D. Seebach, *Synthesis*, 17 (1969); E. J. Corey and D. E. Cane, *J. Org. Chem.*, **34**, 3053 (1969); D. Seyferth, G. J. Murphy, and R. A. Woodruff, *J. Am. Chem. Soc.*, **96**, 5011 (1974); D. Seebach and D. Enders, *Angew. Chem., Int. Ed. Engl.*, **14**, 15 (1975).

(14) S. Kohama and S. Fukukawa, *Nippon Kagaku Zasshi*, **81**, 170 (1960); *Chem. Abstr.*, **56**, 496e (1962).

Phenylcinnamalones. 3. Basic Hydrolysis of Phenylcinnamalone[1]

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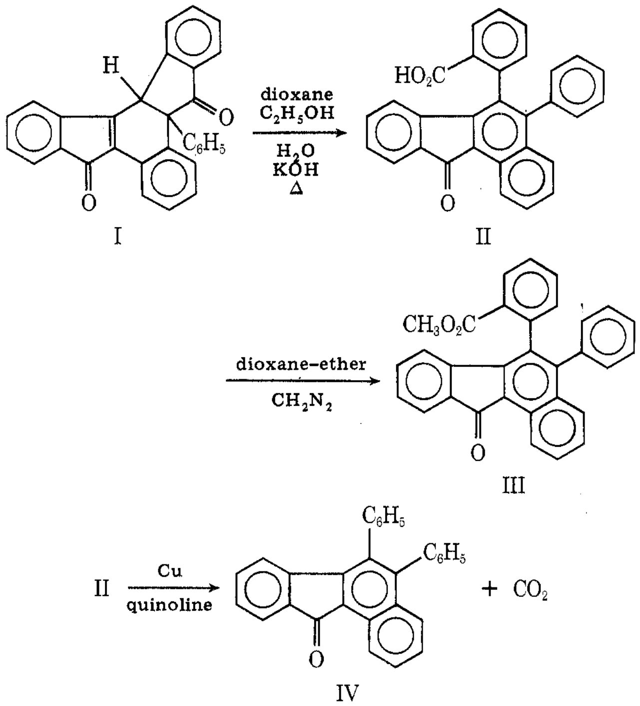
Previous publications in this series have dealt with the preparation and characterization of I,[4] the scope of the preparative reaction,[5] the synthesis of analogues of I,[5] and the nature of some of the potential reaction intermediates.[5] The one-step synthesis of such complicated ring systems utilizing simple starting materials and easily attainable reaction conditions is unusual. Further, we have found that simple single-step reactions allow the conversion of I into a number of compounds also possessing complex ring systems. In this report, we would like to describe the hydrolysis of I to II, the characterization of II, the conversion of II to III, and the decarboxylation of II to IV (see Scheme I).

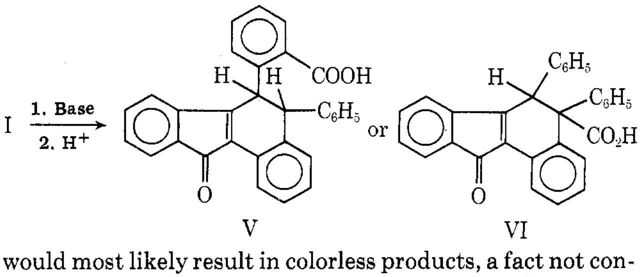
Scheme I



Results and Discussion

It has been found that phenylcinnamalone (I) can be converted to an orange-colored acid (II) by the action of ethanolic potassium hydroxide. Investigation has shown this acid to be of molecular formula $C_{30}H_{18}O_3$. Infrared and proton magnetic resonance (^{1}H NMR) spectral data indicated that the molecular structure of II is that of 6-(*o*-carboxyphenyl)-5-phenyl-11*H*-benzo[*a*]fluoren-11-one (II). ^{1}H NMR spectra of II and its methyl ester (III) reveal it to be a monobasic acid. The spectrum of the acid in Me_2SO-d_6 shows no peak whose chemical shift can be rationalized as resulting from resonance of a carboxyl proton. However, examination of a spectrum of II taken at 120 °C, using protic dimethylformamide (DMF) as the solvent, reveals a singlet, due to the resonance of one proton, at δ 10.03. The spectrum of the methyl ester in Me_2SO-d_6 displays a singlet at δ 3.40. Integration indicates it to be the result of resonance of three protons. The chemical shift of this peak is consistent with those due to resonance of the methyl protons of known carbomethoxy groups.[6] No indication of dibasicity was revealed by the spectra. Neutralization equivalents also confirm monobasicity.

Simple hydrolysis of phenylcinnamalone (I) to form a monobasic acid might be expected to proceed via cleavage of one of the bonds adjacent to one of the two carbonyl groups. Cleavage involving the indanone carbonyl group would result in a monobasic acid (V or VI). Cleavage of the indone grouping would most likely result in colorless products, a fact not consistent with the observed product. Neither V nor VI agree with the parent peak of the mass spectrum of II. This peak appears at *m/e* 426, as opposed to the expected value of 428 for either V or VI.



Thus, dehydrogenation concurrent with the hydrolysis is