

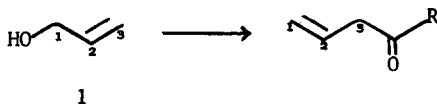
ALLYLOXY KETONE ENOL ETHER-CLAISEN REARRANGEMENT.
REGIOSPECIFIC SYNTHESIS OF ALLYL KETONES FROM ALLYL ALCOHOLS

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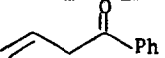
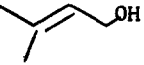
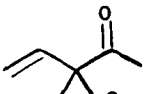
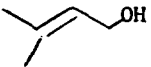
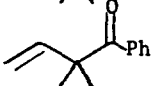
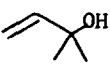
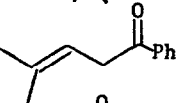
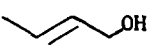
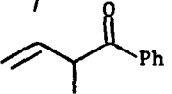
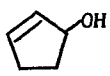
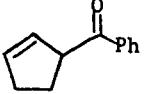
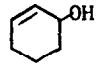
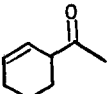
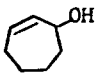
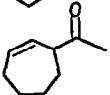
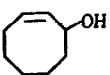
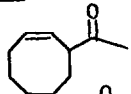
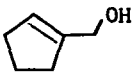
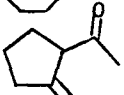
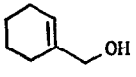
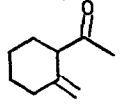
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Claisen rearrangement of allyl vinyl ethers is an important general method of carbon-carbon bond formation for synthesis of γ,δ -unsaturated aldehydes and ketones.¹ Syntheses of γ,δ -unsaturated esters and amides are similarly achieved by rearrangements of 2-alkoxy and 2-amino-3-oxa-1,5-hexadienes.¹ We now report: 1) the first Claisen rearrangements of 1-siloxy-3-oxa-1,5-hexadienes, allyloxy ketone enol silyl ethers², and 2) application of this process to conversion of allyl alcohols into allyl ketones. This new synthesis of allyl ketones has several noteworthy features. Allyl ketones are produced without accompanying formation of the corresponding conjugated vinyl ketones.³ Substitution of an acyl group for the hydroxyl group involves regiospecific carbon-carbon bond formation at the vinyl terminus of the original allyl system and migration of the π -bond.^{4,5}



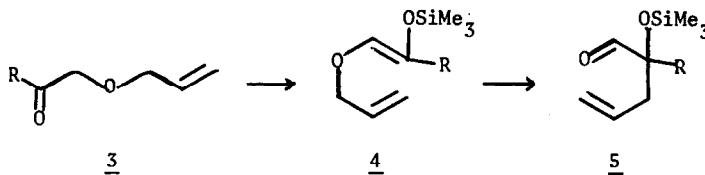
Three methods were examined for the conversion of allyl alcohols 1 into α -allyloxyketones 3 (see table): treatment of 1 with a diazoketone in the presence of boron trifluoride etherate⁶ (method A); treatment of the derived sodium alkoxides with an epoxide⁷ followed by oxidation of the resulting allyloxy alcohol⁸ (method B); and treatment of the derived sodium alkoxide with 2-methoxyallyl bromide⁹ followed by hydrolysis (method C). We found that

Table. Preparation of Allyl Ketones from Allyl Alcohols

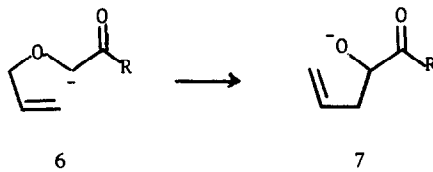
ENTRY	ALLYL ALCOHOL <u>1</u>	ALLYLOXY KETONE <u>3</u> BP(%yield)	α -SILOXY ALDEHYDE <u>5</u> BP(%yield)	ALLYL KETONE <u>2</u>	% YIELD (see ref 14) ^d
1		112-116°/ 3.5mm(79) ^a	70-73°/ 0.05mm(70)		95
2		65-70°/ 5mm(98) ^c	70-75°/ 4.5mm(90)		80
3		120-125°/ 1mm(93) ^a	(99) ^d		83
4		(25) ^b	(99) ^d		81
5		104-110°/ 0.9mm(90) ^a	(98) ^d		83
6		(30) ^b	(80) ^d		93
7		60-62°/ 1mm(97) ^c	67-70°/ 0.6mm(84)		72
8		125-127°/ 10mm(97) ^c	72-74°/ 0.5mm(92)		84
9		136-138°/ 10mm(95) ^c	83-85°/ 0.5mm(91)		98
10		106-108°/ 10mm(83) ^c	52-53°/ 0.5mm(88)		63
11		68-73°/ 1mm(73) ^c	70-75°/ 0.5mm(84)		72

(a) $\text{PhCOCHN}_2/\text{BF}_3/\text{Et}_2\text{O} \rightarrow \text{PhCOCH}_2\text{OR}$; (b) 1.) NaH; 2.) styrene oxide; 3.) pyridinium chloro chromate; purified by molecular distillation; (c) 1.) NaH/THF/HMPA; 2.) 2-methoxyallyl bromide; 3.) H_3O^+ ; (d) not distilled, yields determined with an internal standard by vpc or $^1\text{H-nmr}$; yields for all distilled products are for isolated product.

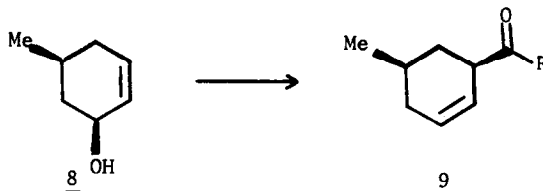
α -allyloxy ketones afford α -allyl- α -aryl (or alkyl)- α -trimethylsiloxy aldehydes 5 upon treatment with chlorotrimethyl silane and triethyl amine in dimethylformamide. This conversion presumably involves Claisen rearrangement *in situ* of intermediate enol silyl ethers 4.¹¹ Alternative reactions, involving [1.2]¹² or [2.3]¹³ sigmatropic rearrangements 6 \rightarrow 7, apparently



are not a problem since yields of 5 are good to excellent (see table). Either silylation of 6 is much faster than rearrangement, or 6 is not an intermediate in the enol silylation of α -allyloxy ketones 3.



The α -siloxy aldehydes 5 were converted to allyl ketones 2 by a one pot hydrolysis-oxidation process with aqueous methanolic periodic acid.¹⁴ The regioselectivity of the overall allyl alcohol to allyl ketone conversion is evident from table entries 2-5, 10 and 11. The present method complements syntheses of allyl ketones involving alkylation of acyl carbanion-equivalents with allylic halides.^{13,15} Furthermore, the new synthetic method should permit stereospecific conversion of allyl alcohols into allyl ketones such as 8 \rightarrow 9.



Acknowledgement. We thank the National Science Foundation for generous support of our research.

References and Notes

1. For a recent review see S.J. Rhoads and N.R. Raulins, "The Claisen and Cope Rearrangements", in "Organic Reactions", Vol. 22, p. 1 ff, John Wiley, New York (1975).
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7. Cf. H.C. Chitwood and B.T. Freure, *J. Am. Chem. Soc.*, 68, 680 (1946); also a complementary procedure involves acid catalyzed alkylation of alcohols with epoxides, Cf. S. Winstein and R.B. Henderson, *J. Am. Chem. Soc.*, 65, 2196 (1943).
8. This was effectively achieved with pyridinium chlorochromate: E.J. Corey and J.W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
9. We prepared this reagent from 2-methoxy propene¹⁰ by reaction with N-bromosuccinimide. Minor amounts of 2-methoxy-1-bromopropene are also produced but this contaminant does not interfere with the desired reaction: G. Greenwood and H.M.R. Hoffmann, *J. Org. Chem.*, 37, 611 (1972).
10. M.S. Newman and M.C. Vander Zwan, *J. Org. Chem.*, 38, 2910 (1973).
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14. The α -siloxy aldehyde 5 (1 mmole) was combined with methanol (5 mL) and water (1 mL). Two phases were initially present, but after boiling under reflux with magnetic stirring for 1 hr, one phase was usually found. The hydrolyzed product was then oxidized *in situ* by addition of aqueous periodic acid (1.3 mL of a 1.0M solution). Reaction progress was monitored by thin layer chromatography on silica gel. The reaction was quenched after complete oxidation (1-10 hrs at 20°C) by addition of ethylene glycol (50 μ l). The mixture was diluted with water and the product extracted into pentane. After washing with NaHCO_3 , then NaCl and drying (Na_2SO_4), solvent was removed. The crude product was generally at least 95% pure β,γ -unsaturated ketone. Samples for analysis were prepared by preparative vapor-liquid phase chromatography. All allyl ketones 2 gave correct elemental analyses, and proton magnetic resonance spectra consistent with the assigned structures.
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