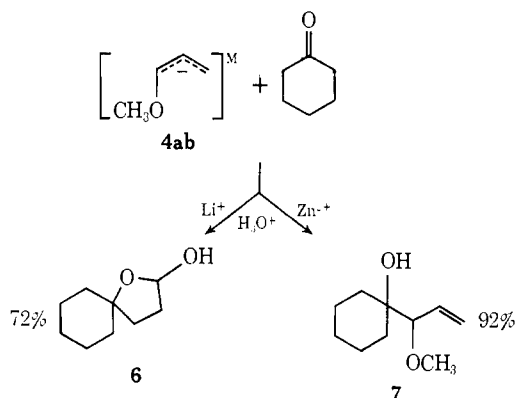


Table I. Reactions of Metalated Ethers with Electrophiles¹¹

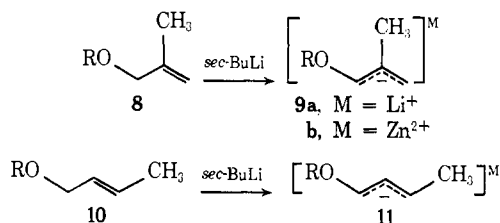
Anion	Electrophile, E ^a	Ratio ^b γ:α	Yield, % ^c γ + α	Product	% yield isolated
4a (R = <i>t</i> -Bu)	<i>n</i> -C ₆ H ₁₃ I	89:11	93	5γ	83
	Br(CH ₂) ₄ Br	80:20	90	5γ	70
	<i>sec</i> -C ₃ H ₇ I	64:36	65	5γ	
	CH ₃ SSCH ₃	>95:5		5γ	80
	Cyclohexanone	27:73	72		
4a (R = CH ₃)	Cyclohexanone	72:28	93	6 ^d	72
4a (R = CH ₃)	(CH ₃) ₂ CHCHO	68:32	99	5γ	
4b (R = CH ₃)	Cyclohexanone	0:100	97	7	92
9a (R = C ₂ H ₅)	<i>n</i> -C ₆ H ₁₃ I	>90:10		12γ	79
	(CH ₃) ₂ C=CHCH ₂ Br	63:37	41	12γ	26
	CH ₃ SSCH ₃	90:10		12γ + 12α	79
	Cyclohexanone	50:50	93	12γ + 12α	
9b (R = C ₂ H ₅)	Cyclohexanone	0:100		12α	97

^a All reactions were carried out at -65°. ^b Both products have been isolated and fully characterized. ^c Determined by nmr relative to an internal standard. ^d Produced by acid hydrolysis (10% HCl-THF) of the enol ether.

the product ratio is highly counterion dependent. The allyl zinc reagent **4b** (R = CH₃), prepared by the addition of 1 equiv of zinc chloride to **4a**, reacts with aldehydes and ketones *exclusively* α to oxygen.¹⁴ This counterion effect is *independent* of the steric bulk of R in metalated ether anion **4b**. Such counterion dependence is illustrated below in the reaction of **4a** and **4b** (R = CH₃) with cyclohexanone. The results of other carbonyl addition reactions are included in Table I.¹¹



In the metalation of methyl-substituted ethers **8** and **10**, it is possible to form two different allylic anions resulting from proton abstraction from either the methyl or methylene positions. However, metalation of **8** and **10** with *sec*-butyllithium (THF, -65°) affords only the allylic anions **9a** and **11a**. The conclusion that, under

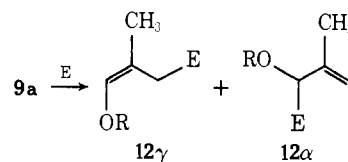


these conditions, the alkoxy substituent *enhances* the kinetic acidity of adjacent positions is interesting in light of other studies which show the opposite to be the case under different conditions.¹⁵

(14) For analogous counterion-dependent processes, see ref 5d and 12a.

(15) D. H. Hunter, Y. Lin, A. L. McIntyre, D. J. Shearing, and M. Zuagulis, *J. Amer. Chem. Soc.*, **95**, 8327 (1973), and references cited therein.

As with anion **4a**, **9a** (R = C₂H₅) reacts regioselectively γ to oxygen in substitution reactions (E = *n*-C₆H₁₃I, 12γ:12α = 90:10). No selectivity was ob-



served in carbonyl addition (E = cyclohexanone, 12γ:12α = 50:50); however, the organozinc reagent **9b** shows exclusive reaction α to oxygen.

The conclusions of this preliminary study are that metalated allylic ethers may be effectively employed as homoenolate anion equivalents in substitution reactions. The present examples point to the fundamental differences in the relative directive effects that are observed in the reactions of oxygen and sulfur-substituted allylic carbanions with electrophiles.

Acknowledgment. We wish to thank the National Science Foundation and the donors of the Petroleum Research fund, administered by the American Chemical Society, for support of this research.

(16) Camille and Henry Dreyfus Teacher-Scholar Recipient (1971-1976), Alfred P. Sloan Fellow (1972-1974). Department of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, Calif. 91109.

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Allyloxy Carbanions. A New Synthesis of Aldehydes via a β-Acyl Carbanion Equivalent

Sir:

The central role of carbonyl compounds in organic chemistry makes new methods for their construction especially valuable. In this communication, we wish to report a new approach to the synthesis of these compounds and its application to a new synthesis of aldehydes.

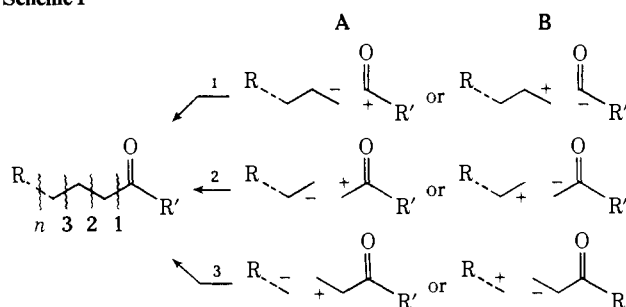
The most useful carbonyl syntheses are generally those which incorporate carbon-carbon bond forma-

Table I

Entry	R	R'-X	% ^a of 11 in alkylated product	% ^a of 12 in alkylated product	% isolated yield of 11 + 12
1	Si(C ₂ H ₅) ₃	CH ₃ -I	97	3	>95
2	Si(C ₂ H ₅) ₃	C ₂ H ₅ -I	83	17	>95
3	Si(C ₂ H ₅) ₃	<i>n</i> -C ₃ H ₇ -I	84	16	>95
4	Si(CH ₃) ₂ - <i>n</i> -C ₄ H ₉	<i>n</i> -C ₃ H ₇ -I	81	19	>95
5	Si(C ₂ H ₅) ₃	(CH ₃) ₂ CH-I	60	40	>95
6	Si(C ₂ H ₅) ₃	Cyclohexyl-I	39	61	80 ^b
7	Si(C ₂ H ₅) ₃	<i>n</i> -C ₃ H ₇ -Br	75	25	>95
8	Si(C ₂ H ₅) ₃	Allyl-Br	68	32	>95

^a Determined by vpc and confirmed by nmr integration. ^b Unidentified high boiling components were formed in this reaction. ^c Prepared by the reaction of the sodium or lithium salt of allyl alcohol and the appropriate trialkylchlorosilane in diethyl ether at room temperature.

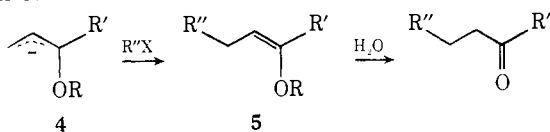
Scheme I



tion. As shown in Scheme I, these may be classified topologically by the position (1, 2, 3, or *n*) of the bond to be made and electronically by the polarity (A or B) of the fragments to be joined. While equivalents of the first five reactions are well documented,¹ general examples of the last category, 3B, are virtually unknown.² Our efforts have been directed toward realization of this latter route, the alkylation of a β -acyl carbanion equivalent.

While a variety of masked β -acyl carbanions may be envisioned, the terminally oxy-substituted allylic carbanion 4 appeared particularly useful. Simple coupling with an alkyl halide would be expected to lead to a β -alkylated aldehyde or ketone *via* the enol ether, 5 (Scheme II).

Scheme II

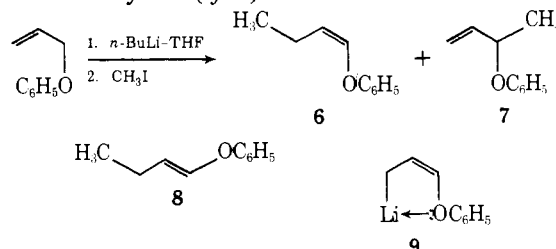


The fact that α -metalloethers are known to be intermediates in the Wittig rearrangement³ suggests that one route to the desired allyloxy carbanion (4) might be *via* low temperature metalation of an allylic ether.^{2e,4}

(1) Examples include: 1A, carbanion + acyl halide; 1B, dithiane or cyanohydrin ether alkylation; 2A, carbanion + epoxide followed by oxidation; 2B, enolate alkylation; and 3A, carbanion + enone.

(2) Several specific examples have been reported: (a) the Grignard reagent of 3-bromopropionaldehyde ethylene glycol acetal is known but is exceedingly sluggish in its reaction with electrophiles, G. Büchi and H. Wüest, *J. Org. Chem.*, **34**, 1122 (1969); (b) β -phenyl enamines have been metalated and alkylated with methyl iodide, H. W. Thompson and B. S. Huegi, *J. Chem. Soc., Chem. Commun.*, 636 (1973); and (c) Δ -3-dihydropyran has been metalated and the anion trapped with trimethylchlorosilane prior to rearrangement, V. Rautenstrauch, *Helv. Chim. Acta*, **55**, 594, 3064 (1972).

This proved to be the case. When, for example, allyl phenyl ether was treated at -78° with *n*-butyllithium in tetrahydrofuran and then with methyl iodide, two new compounds were isolated in 95% yield. These were identified⁵ as the desired enol ether 6 (71%) and the isomeric allylic ether 7 (24%). The *cis* olefin geometry of 6 follows from the 6 Hz coupling⁶ of the vicinal vinyl protons in the nmr. None of the corresponding *trans* enol ether, 8, could be detected. In fact, formation of the *cis* relationship between the vinyl oxygen and the alkylated chain appears stereospecific in all cases studied and suggests that the species undergoing alkylation might better be represented as the internally coordinated metalocycle 9 (*cf.* 4).



In an attempt to increase the proportion of the terminally alkylated enol ether (*e.g.*, 6) in the product of these reactions, the effect of varying the oxygen substituent (R in Scheme II) was investigated. We found that by using the corresponding allyl silyl ethers (Table I, 10, R = Si(C₂H₅)₃ or Si(CH₃)₂-*n*-C₄H₉),⁷ improved yields of the desired product (11) were obtained. Thus, the anion of triethylallyloxysilane (10, R = Si(C₂H₅)₃) was terminally alkylated by methyl iodide in greater than 92% yield (Table I, entry 1). Another feature of

(3) Reviews: U. Schöllkopf, *Angew. Chem., Int. Ed. Engl.*, **9**, 763 (1970); A. R. Lepley and A. G. Giumanini, "Molecular Rearrangements," Vol. 3, B. S. Thyagarajan, Ed., Wiley, New York, N. Y., 1971, p 297.

(4) For recent reports of allylic ether deprotonation with rearrangement see V. Rautenstrauch, G. Büchi, and H. Wüest, *J. Amer. Chem. Soc.*, **96**, 2576 (1974); H. Felkin and A. Tambuté, *Tetrahedron Lett.*, 821 (1969).

(5) All new compounds gave satisfactory infrared, nmr, and mass spectra.

(6) (a) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Oxford, 1969, p 302; (b) H. O. House, *et al.*, *J. Org. Chem.*, **34**, 2324 (1969).

(7) Other silyl ethers, *e.g.*, trimethyl or dimethyl-*tert*-butyl, gave lower proportions of the enol ether and/or significant by-product formation.

this sequence is that the product is an enol silyl ether of known geometry. As such, it can serve as a precursor to a variety of useful synthetic intermediates.⁸

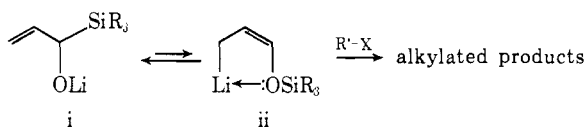
As outlined in Table I, these highly nucleophilic carbanions⁹ can be alkylated by a variety of alkyl iodides and bromides.¹⁰ Yields of aldehydes generally fall in the 80–90% range.¹¹ The only limitation observed thus far lies in the use of highly hindered alkylating agents. Although good yields of alkylated adducts are frequently obtained with these materials, the proportion of enol ether (11) in the product is unacceptably low (entry 6). Examination of other data in Table I reveals several other trends: (1) alkyl iodides give slightly better yields of 11 than do the corresponding bromides and (2) decreased halide substitution likewise leads to higher yields of terminally alkylated product.

The following experimental procedure is representative of the conversion. A solution of 2 mmol of the allyl silyl ether in 1 ml of dry tetrahydrofuran is added dropwise with stirring to a -78° solution of 2.4 mmol of *sec*-butyllithium in 10 ml of anhydrous deoxygenated tetrahydrofuran under a nitrogen atmosphere. When the addition is complete, 0.5 ml of hexamethylphosphoramide (HMPA) is added and the stirring continued for an additional 15 min. The alkyl halide (2.4 mmol) is then added. Stirring is continued for 15 min more and the solution allowed to slowly warm to room temperature. The reaction mixture is then poured into *n*-pentane, washed with saturated ammonium chloride and water (two times), and dried (MgSO_4). Solvent evaporation yields the crude product. Depending on the system, the product may be of sufficient purity to be used directly or may be purified by distillation.

Acknowledgement. The authors would like to thank Professor Gilbert Stork for his support and encouragement.

(8) These include such species as aldols (T. Mukaiyama, *et al.*, *Chem. Lett.*, 1011 (1973)), β -keto ethers (T. Mukaiyama and M. Hayashi, *ibid.*, 15 (1974)), enolates (ref 6b; G. Stork and P. F. Hudrlik, *J. Amer. Chem. Soc.*, **90**, 4462 (1968)), and cyclopropanols (S. Murai, T. Aya, and N. Sonoda, *J. Org. Chem.*, **38**, 4354 (1973)).

(9) Low temperature acid quenching suggests that the alkoxy silane, i, is the major anionic species in solution. Rapid equilibration with ii



and selective trapping presumably gives the observed products. Similar observations have been made with benzyl silyl ethers: A. Wright, D. Ling, P. Boudjouk, and R. West, *J. Amer. Chem. Soc.*, **94**, 4784 (1972).

(10) Chlorides and tosylates give only poor conversion to the desired products.

(11) We have also prepared ketones by this sequence. However, the starting secondary allylic ethers are metalated extremely slowly under our conditions with a corresponding low conversion to alkylated products.

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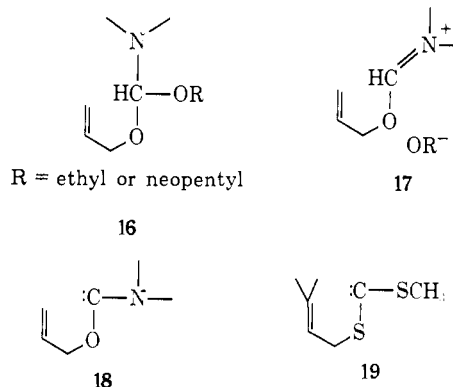
Conversion of Allylic Alcohols to Homologous Amides by *N,N*-Dimethylformamide Acetals

Sir:

A wide variety of allylic alcohols are transformed to γ,δ -unsaturated amides when heated to approximately

160° with *N,N*-dimethylacetamide acetals.¹ We have discovered (see Table I) that certain allylic alcohols when treated similarly with *N,N*-dimethylformamide acetals are converted to homologous β,γ -unsaturated *N,N*-dimethylamides, often in synthetically useful yields. With the tertiary alcohols 1–4, conversions were performed in xylene or collidine solutions. Slightly higher temperatures were required for the secondary alcohols 5 and 6, and in the former case excess reagent had to be avoided because it condensed further with the amide 12 to yield a dimethylaminomethyleneamide. As judged by the behavior of geraniol (7), the method works poorly with γ,γ -disubstituted allylic alcohols.

After incomplete conversion the mixed amide acetals 16 were isolated from 1 and 7. Thermolysis of the former gave the amide 8 while the latter was much more stable. Aqueous work-up regenerated geraniol (7). We assume that the mixed acetals, 16, on being heated loose ethanol or neopentyl alcohol to give imidates, 17, and then carbenes, 18, which undergo a [2,3]sigmatropic rearrangement to produce amides. In support of this hypothesis we cite the facile formyl proton exchange in formamide acetals² and the previously discovered [2,3]sigmatropic rearrangement of a related carbene 19.³ The rate retarding effect of substituents



on the double bond is attributed to nonbonding steric interactions in the transition state and/or the highly nucleophilic character of the carbene 18.

To probe the origin of amide 15 from geraniol 7, (–)-*cis*-carveol (20) [$\alpha]^{25}_{\text{D}} -33.4$ (*c* 5.6, $\text{C}_2\text{H}_5\text{OH}$) was transformed to a 88:12 mixture of diastereomeric amides 22/24 and 26/28, both not epimerized under the reaction conditions. Intensity measurements of *N*-methyl and vinyl protons in the nmr spectrum of the major *cis* diastereomer [$\alpha]^{25}_{\text{D}} -14.8$ (*c* 2.6, $\text{C}_2\text{H}_5\text{OH}$) in the presence of tris[*d,d*-dicampholylmethanato]europium(III)⁴ revealed the presence of two enantiomers in a ratio of 3:1. To determine their absolute configurations the transformation was performed on

(1) H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Justus Liebig's Ann. Chem.*, **641**, 1 (1961); A. E. Wick, D. Felix, K. Steen, and A. Eschenmoser, *Helv. Chim. Acta*, **47**, 2425 (1964); D. Felix, K. Gschwend-Steen, A. E. Wick, and A. Eschenmoser, *ibid.*, **52**, 1030 (1969); H. Muxfeldt, R. S. Schneider, and J. B. Mooberry, *J. Amer. Chem. Soc.*, **88**, 3670 (1966); D. F. Morrow, T. P. Culbertson, and R. M. Hofer, *J. Org. Chem.*, **32**, 361 (1967); W. Sucrow, *Angew. Chem.*, **80**, 626 (1968); D. J. Dawson and R. E. Ireland, *Tetrahedron Lett.*, 1899 (1968).

(2) G. Simchen, S. Rebsdatt, and W. Kantlehner, *Angew. Chem., Int. Ed. Engl.*, **6**, 875 (1967).

(3) J. E. Baldwin and J. A. Walker, *J. Chem. Soc., Chem. Commun.*, 354 (1972).

(4) M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Amer. Chem. Soc.*, **96**, 1038 (1974). We are grateful to Professor Whitesides for a gift of the shift reagent.