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THE AMIDE ACETAL CONDENSATION OF PROPARGYL ALCOHOLS:
SYNTHESIS OF γ-KETO ESTERS AND SILYL ALLENES UNDER MILD CONDITIONS

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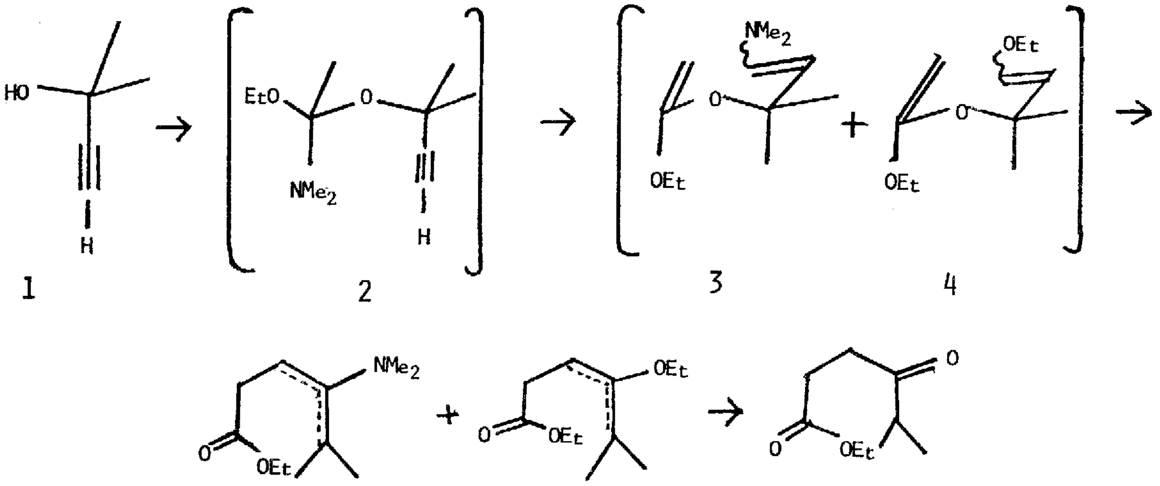
Summary

In this communication we report the first example of a Claisen rearrangement involving an enamine as the allyl double bond and a general, high yield synthesis of silyl allenes.

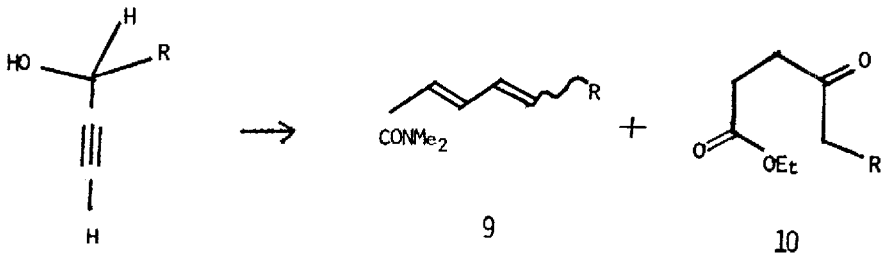
As the amine migration in amide acetals derived from propargyl alcohols[1] seemed to us to have potential as a method of converting acetylenes to enamines[2] under mild conditions, we have investigated the condensation of alcohols 1, 8, and 11 with dimethyl acetamide diethyl acetal.[3]

Nonhydrolytic isolation[4] of the products derived from dimethylacetamide diethyl acetal treatment of 2-methyl-3-propyn-2-ol (1) affords a mixture of enamine 5 and enol ether 6. Enamine 5 presumably results from amine migration in intermediate 2 to afford intermediate 3, followed by Claisen rearrangement involving the enamine double bond. When enamine 5 is stirred



under the reaction conditions with an equivalent of ethanol, no trace of enol ether 6 could be detected, suggesting that enol ether 6 results from the Claisen rearrangement of intermediate 4. To our knowledge, the rearrangements of intermediates 3 and 4 are the first examples of Claisen rearrangements involving enamines and enol ethers, respectively.[5] Hydrolysis (Procedure A) of the reaction mixture affords ketone 7[6] in high overall yield.

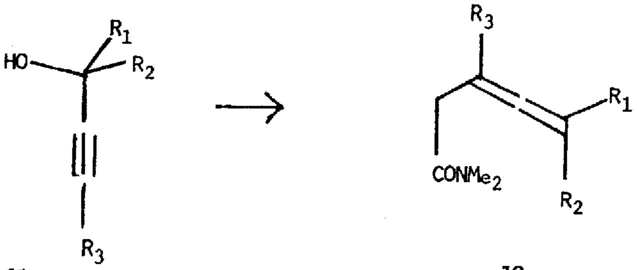
Alcohols 8a and 8b afford low yields of α, β, γ, δ-unsaturated amides 9[7] along with traces of the ketones 10. Alcohols 11a-d[8], however, give allenic amides 12[9] in high yield. The amide acetal Claisen rearrangement of alcohols 11b-d, then provides a facile and general synthesis of 1-substituted silyl allenes.[10]



8 9 10

a R = CH_3

b R = H



11 12

a $R_1 = R_2 = CH_3$, R_3 = nPr

b $R_1 = R_2 = CH_3$, $R_3 = SiMe_3$

c $R_1 = CH_3$, R_2 = H , $R_3 = SiMe_3$

d R_1 = H, R_2 = H, $R_3 = SiMe_3$

Two procedures, outlined below, were used for the reaction of propargyl alcohols with dimethylacetamide diethyl acetal. Procedure A was used for alcohols 1 and 8. This procedure affords some desilylated products from alcohols 11; however procedure B gives high yields of silyl substituted products from these alcohols.

Procedure A: A solution of 1.0 g of propargyl alcohol in 5 ml of N,N-dimethylacetamide diethyl acetal was stirred at 115° for 2-3 hours under nitrogen.

The product mixture was then chromatographed on 60 g of silica gel which had been treated with 6 ml of water. Elution with 5% methanol/chloroform afforded a colorless liquid which distilled over a short path. Isomers were separated by gas chromatography on a 15' x 1/4" Carbowax Column, 20% 20 M on Diatoport S and/or a 20' x 1/4" SE 30 column, 20% on acid-washed DMCS.

Procedure B: A solution of 0.5 g of propargyl alcohol and 0.74 g (1.3 equivalents) of N,N-dimethylacetamide diethyl acetal in 10 ml of xylene was stirred at reflux for 24 hours. After cooling to room temperature, it was poured into 50 ml of water and the resulting mixture was extracted with ether. The organic phase was washed twice with water and dried over magnesium sulfate. Distillation over a short path afforded a colorless liquid.

Yields and product distributions are reported in the Table.

Table - Product Distributions from the Amide Acetal Condensation of Propargyl Alcohols

Alcohol	Procedure	7	9	10	12
1	A	73%	-	-	-
8a	A	-	23%	7%	-
8b	A	-	21%	4%	-
11a	B	-	-	-	81%
11b	B	-	-	-	59%
11c	B	-	-	-	86%
11d	B	-	-	-	80%

The change in major pathway of the reaction (i.e. alcohol 1 vs. alcohols 8 and 11) can be correlated to that observed in the amide acetal condensation of allylic propargylic alcohols[1]; only tertiary alcohols in which the acetylene is terminal afford products resulting from addition to the acetylenic substituent. Further investigation of the mechanism of enamine and enol ether formation is underway. The generality of Claisen rearrangements of enol ethers and enamines is also being investigated.

Acknowledgment:

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References

1. K. A. Parker and R. W. Kosley, Jr., *Tetrahedron Letters,* 3039 (1975).

2. See P. F. Hudrlik and A. M. Hudrlik, *J. Org. Chem.*, 38, 4254 (1973).

3. For reactions of allylic alcohols with dimethylacetamide diethyl acetal, see D. Felix, K. Gschwend-Steen, A. E. Wick, and A. Eschenmoser, *Helv. Chim. Acta*, 52, 1030 (1969).

4. Distillation of the reaction mixture gave a single fraction (95–101° @ 5 mm). The nmr spectrum of this fraction was consistent with a 1:3 mixture of enamine 5 and enol ether 6. For comparison, each component was synthesized independently from ketone 7 (see reference 7); the enamine according to W. A. White and H. Weingarten, *J. Org. Chem.*, 32, 213 (1967) and the enol ether according to U. Schmidt and P. Grafen, *Justus Liebig's Ann Chem.* 656, 97 (1962).

5. For a recent review see S. J. Rhoads and N. R. Raulins, "The Claisen and Cope Rearrangements" in W. G. Dauben, ed. *Organic Reactions*, 22, 1 (1975).

6. Prepared by an independent synthesis from ethyl 4-oxobutyrate (E. R. H. Jones, H. H. Lee, and M. C. Whiting, *J. Chem. Soc.*, 3483 (1960)) according to H. J. Bestmann and B. Arnason, *Chem. Ber.*, 95, 1513 (1972).

7. The thermal rearrangement of propargyl vinyl ethers affords α, β, γ, δ-unsaturated ketones. See R. Marbet and G. Saucy, *Chimia*, 14, 362 (1960).

8. Alcohols 11b-d were synthesized according to M. F. Shostakovskii, I. A. Shikhiev, and N. V. Komarov, *Izvest. Akad. Nauk. SSSR, Otdel. Khim. Nauk*, 1956, 1271 (*Chem. Abstr.*, 51, 5689i).

9. The condensation of a propargyl alcohol with triethyl orthoacetate or with an ynamine affords an allenic ester or amide, respectively, by rearrangement of an intermediate propargyl vinyl ether. See J. K. Crandall and G. L. Tindell, *Chem. Comm.*, 1411 (1970) and J. Ficini, N. Lumbroso-Bader and J. Pouliquen, *Tetrahedron Letters*, 4139 (1968). Also, the condensation of 2-butyn-1-ol with dimethylacetamide diethyl acetal has been reported; J. Corbier, P. Cresson, and P. Jelenc, *C. R. Acad. Sci., Paris*, 270, 1890 (1970).

10. 1,1-Disubstituted allenes have been prepared recently by the conjugate addition of 1-trialkylsilylpropynyl copper derivatives. See B. Ganem, *Tetrahedron Letters*, 4467 (1974).