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A GENERAL SYNTHESIS OF TERTIARY ALLENIC AMIDES: THE REACTION OF PROPARGYL ALCOHOLS WITH DIETHYLFORMAMIDE ACETALS

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Among the syntheses of functionalized allenes[1] are a number of methods based on the rearrangement of a propargyl system. Sigmatropic shifts of both the (3,3)- and (2,3)-varieties have afforded hetero-substituted allenes,[2] and the (3,3)-sigmatropic rearrangement has been used to synthesize carbon-chain substituted allenes (Claisen and Cope rearrangements[3]).

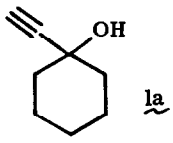
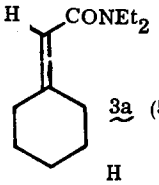
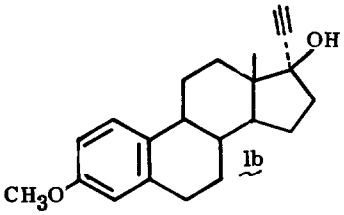
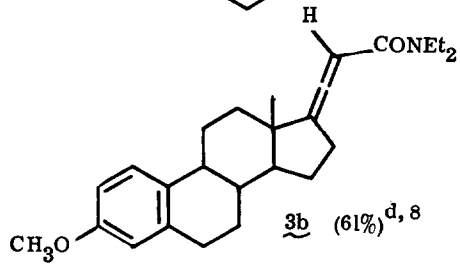
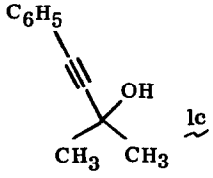
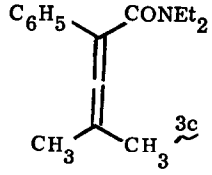
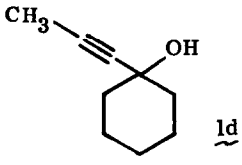
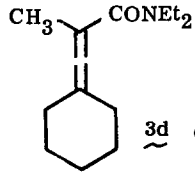
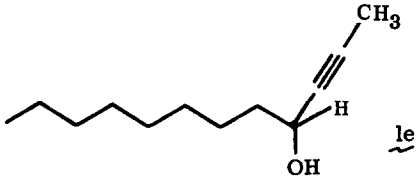
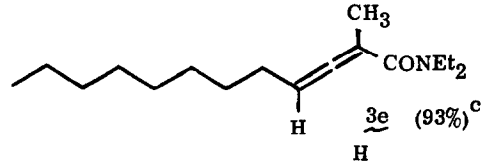
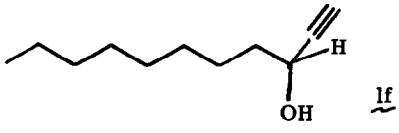
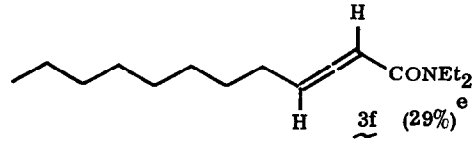
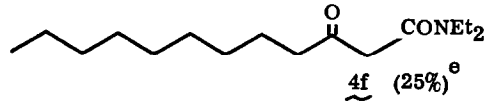
Although the (2,3)-sigmatropic rearrangement has been utilized as a method of carbon chain extension in allylic systems,[4] attempts to apply these rearrangements to propargyl systems have resulted in procedures which are successful only when certain substituent requirements are met.[5] We now report that the reaction of propargyl alcohols with diethylformamide acetals in refluxing hydrocarbon solvents to form allenic amides[6] is general and that good to excellent yields of these products can be obtained (Table).

The exception to be noted is 1-undecyn-3-ol (1f) from which, in addition to allenic amide 3f, a significant amount of keto amide 4f was isolated. Amide 3f is in fact converted to 4f under the conditions of the reaction. The instability of unhindered allenic amides toward nucleophilic addition has been previously noted;[6a] we assume that ethanol generated in the reaction medium is trapped by reaction with 3f, and that silica gel hydrolysis affords 4f.

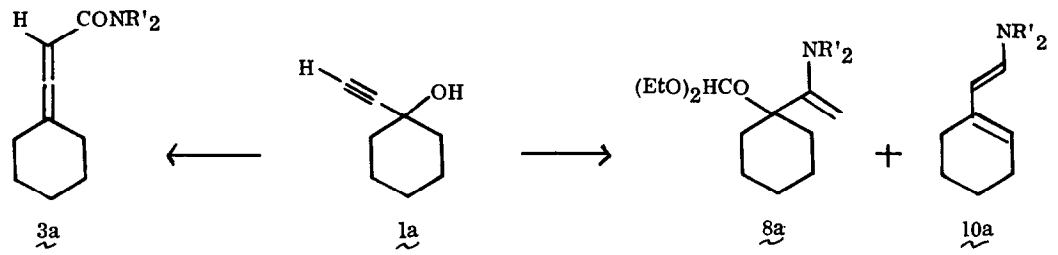
In a typical experiment, the propargyl alcohol is heated under nitrogen with 1-2 equivalents of diethylformamide diethyl acetal[7] in refluxing xylene or dichlorobenzene; ethanol is removed by means of a Dean-Stark trap. Optimum reaction time varies with the substrate. The product is isolated by chromatography on silica gel and then crystallized or distilled. Experimental details and yields for a number of propargyl alcohols are shown in the Table.

The course of the reaction of propargyl alcohols with formamide acetals is heavily dependent on both the structure of the reagent and on the reaction conditions. This dependence is exemplified by the reactions of 1-ethynylcyclohexanol (1a). When 1a was treated with dimethylformamide diethyl acetal (2, R'=Me) in ethanol or in xylene with distillative removal of ethanol, enamine orthoformate 8a (R'=Me) and dienamine 10a (R'=Me) were produced.[5a] When 1a was treated with diethylformamide diethyl acetal (2, R'=Et) in ethanol, a mixture of the corresponding diethylamine enamine orthoformate (8a, R'=Et) and diethylamine dienamine (10a, R'=Et) was obtained. However, when 1a was treated with the diethyl reagent 2 (R'=Et) in xylene with distillative removal of ethanol, only allenic amide 3a (R'=Et) was observed.

TABLE 1 REACTION WITH DIETHYLFORMAMIDE DIETHYL ACETAL

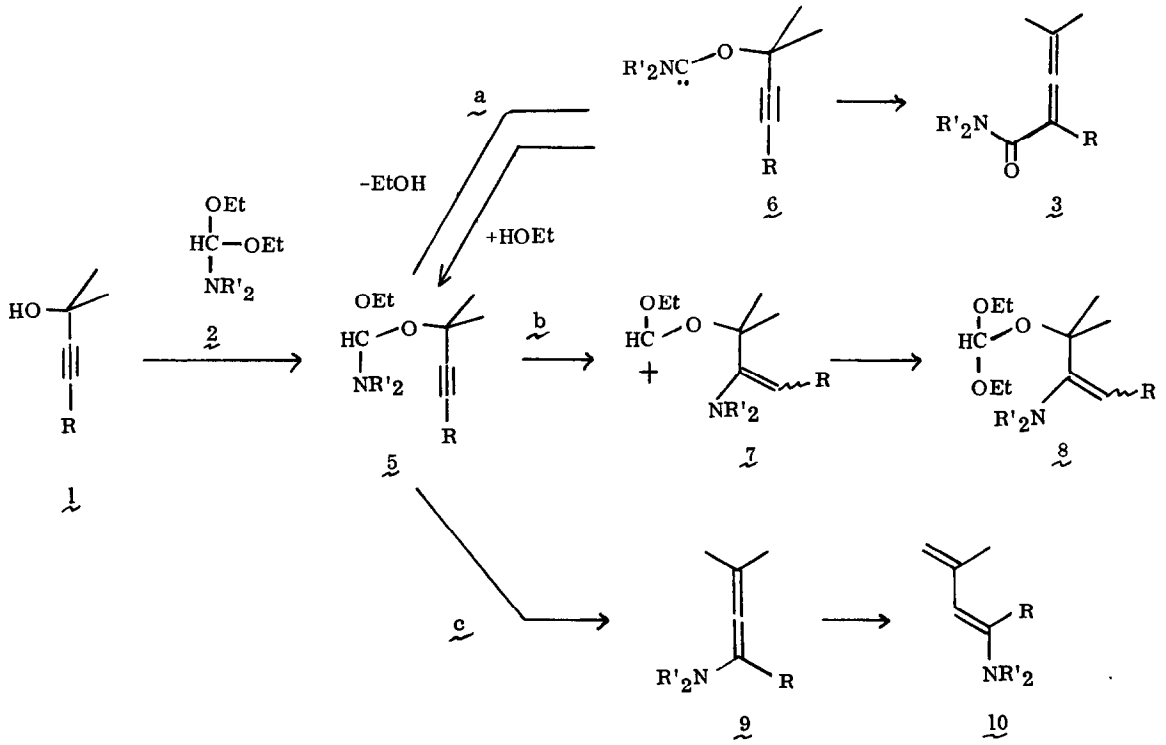
ALCOHOL 1	SOLVENT[a] (°C, HR)	PRODUCT[b] (YIELD)
 1a	A 140, 1.5	 3a (50%)[c]
 1b	A 140, 3	 3b (61%)[d,8]
 1c	A 140, 3	 3c (84%)[d]
 1d	B 170[f], 0.5	 3d (92%)[c]
 1e	B 170[g], 1	 3e (93%)[c]
 1f	A 140, 6	 3f (29%)[e]
		 4f (25%)[e]

a. Solvent: A=xylene, B=o-dichlorobenzene. b. All products gave satisfactory ir and nmr spectra as well as elemental analyses. c. Distilled. d. Recrystallized. e. Separated by chromatography. Yields are of distilled material. f. The reaction mixture was initially heated to 140° for 1 hour. g. The reaction mixture was initially heated to 140° for 0.5 hour.



3a 1a 8a 10a

A mechanistic summary of possible reaction pathways is shown below. When R is alkyl, only pathway a is viable; the rate of reaction along pathway a is presumably dependent on the amount of ethanol present. When R=C_6H_5 and R'=Me, only product 8, derived from pathway b is observed; when R=H and R'=Me, products from both pathways b and c are seen. The rates of reaction along pathways b and c should depend on the ease of migration of the dialkylamino group and may be independent of ethanol concentration. When R=H or C_6H_5 and R'=Et, reaction along pathways b and c is apparently slowed down by the increased steric bulk around the nitrogen; if ethanol is removed from the reaction, the rate along pathway a increases; enamine orthoformate and dienamine are not observed and only allenic amide is isolated.



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