

A VERSATILE METHOD FOR THE PREPARATION OF ALLENIC ALCOHOLS

Gary E. Keck*¹, and R.R. Webb, II

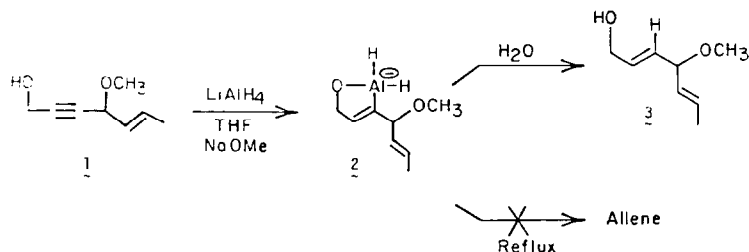
Department of Chemistry

The University of Utah

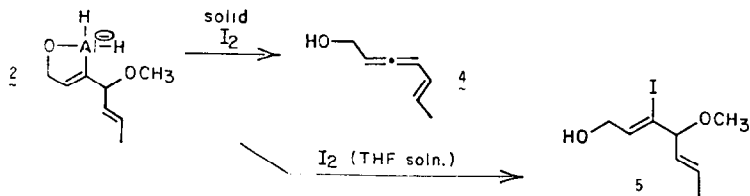
Salt Lake City, Utah 84112

Summary: A convenient three step procedure to a variety of allenic alcohols is described, which relies on a highly unusual partitioning between two reaction pathways depending on the mode of addition of a reagent.

In connection with synthetic studies in progress in our laboratories, we required an efficient preparation of hydroxymethyl allenes, especially hydroxymethylvinyl allenes. Although numerous preparative routes to allenes have been recorded², many of these procedures are of limited utility for the synthesis of potentially sensitive vinyl allenes.³ After several failures to adapt other known procedures to this problem, we were attracted to the lithium aluminum hydride reduction of acetylenic alcohols having the general structure 1 below, since such alcohols were expected to be very readily available, and good literature precedent was available for their reductions to the desired allenic alcohols.⁴ The substrate 1 was readily prepared (vide supra) and its reduction via the general procedure described by Corey⁵ was then investigated. Although 1 was reduced very rapidly by lithium aluminum hydride in THF at 23° to afford the alenate 2, this species (characterized by isolation of the expected trans allylic alcohol 3 upon hydrolysis) proved resistant to elimination at temperatures up to 67° (THF/reflux), and the use of higher temperatures with dioxane as solvent resulted only in the slow production of several unidentified materials.



We next attempted to utilize 2 as a precursor to the corresponding vinyl iodide 5, which could then be employed to secure the desired allene 4 via a reductive elimination process. To our complete surprise, a remarkable observation was made, in that *addition of iodine to 2, as a THF solution at -78°, afforded the expected vinyl iodide 5, whereas addition of iodine as the solid at -78° led directly to allene 4*:



Although the reasons for this result were far from clear, systematic variation of reaction conditions quickly yielded an optimal protocol (vide supra) for production of the allene 4 to the virtual exclusion of 3 and 5, which has proven to be of general utility for the synthesis of such hydroxymethyl allenes. The cases we have examined, using the general experimental procedures provided, are detailed in Table I below.

Table I: Preparation of Allenic Alcohols

Substrate	(yield%)	Allene	(yield%)	Substrate	(yield%)	Allene	(yield%)
	93		60		97		97
<u>1</u>		<u>4</u>		<u>12</u>		<u>16</u>	
	82		70		86		93
<u>6</u>		<u>7</u>		<u>13</u>		<u>17</u>	
	82		40		89		98
<u>8</u>		<u>9</u>		<u>14</u>		<u>18</u>	
	81		70		87		85
<u>10</u>		<u>11</u>		<u>15</u>		<u>19</u>	

(a) Preparation of substrates and conversion to allenes was performed by the general procedures detailed in the experimental section; (b) All allenes were characterized by $^1\text{H NMR}$, $^{13}\text{C NMR}$, IR, and mass spectra. In addition, allenes 11, and 16-19 returned satisfactory C,H combustion analyses. We were unable to obtain satisfactory combustion analyses on the more sensitive vinylallenes; in-house high resolution mass spectrometry was used to confirm elemental composition in these cases. (c) All yields are isolated yields of chromatographically homogeneous materials isolated by column chromatography or Kugelrohr distillation.

The results in Table I above reveal this procedure to be a highly efficient allene synthesis provided that the allene produced is reasonably stable (isolated yields 70-98%), and an acceptable approach even for the synthesis of more labile allenes such as vinylallenes (yields 40-70%). In addition, the simple two pot procedure utilized for the preparation of the requisite acetylenic substrates makes the overall process attractive for its brevity and simplicity.

The mechanism of this intriguing process, is, at present, totally unknown, although some experimental observations are relevant. We currently believe that the experimental observations above point to the production of an intermediate organoaluminum compound from 2 which partitions between conversion to 3 and conversion to 4 based upon the availability of free iodine in solution. Since the "kinetic" solubility of solid iodine in ether at -78° is very low, elimination can take place from this intermediate prior to addition of iodine across the carbon-aluminum bond. With high solution iodine concentrations as are achieved by addition of THF solutions of iodine, this (presumably) intramolecular elimination process is superceded by a bimolecular reaction with iodine. Under "intermediate" conditions with respect to iodine solubility (or availability) mixtures of products were obtained.

Investigations on the mechanism of this process, particularly with respect to stereochemistry, are in progress.

Experimental Section:

Representative Procedure for Preparation of Acetylenic Alcohols: 3-methoxy-undec-2-yn-1-ol. To a solution of n-butyllithium (Alfa, 1.3 M in hexane, 30.20 mL, 0.0393 mol) in dry THF (100 mL) at -78°C under argon was added dropwise a solution of 5.00 g (0.0357 mol) of the THP-ether of propargyl alcohol (3-(1-oxacyclohex-2'-yloxy))-propyne in 20 ml of THF. After stirring for 10 min at -78° , octyl aldehyde (5.57 mL, 0.0357 mol) dissolved in 10 mL THF was added dropwise via syringe. After 20 min at -78° , iodomethane (8.89 mL, 0.1428 mol) was then added neat, and the cold bath removed. After warming to -20°C , HMPA (10 mL) was added and the resulting solution allowed to warm to room temperature. After 1 h at 23° , alkylation was complete, the THF was removed in vacuo, and the residue remaining was diluted with brine and extracted 3 times with ether. The combined ether extracts were then washed with water, brine, dried (K_2CO_3), and

concentrated in vacuo. The crude product was dissolved in methanol (50 mL) and treated with 100 mg pyridinium-p-toluene sulfonate. After stirring for 3 h, tlc indicated complete hydrolysis. Neutralization with saturated, aqueous NaHCO₃, removal of the methanol in vacuo, and standard extractive workup yielded 6.00 gm (86%) of colorless liquid: bp 198-200°C @ 1.1 mm Hg; ¹H NMR (CDCl₃) δ4.50 (d, J=6Hz, 2H), 4.10 (t, J=6Hz, 1H), 3.86 (t, J=6Hz, 1H), 3.55 (s, 3H), 1.78 (m, 2H), 1.45 (8H), 0.95 (3H); IR (neat) 3150-3560(s, br), 2920(vs), 2856, 1460, 1333, 1091(vs), 1018 cm⁻¹; ¹³C NMR (CDCl₃) δ84.59, 84.01, 71.51, 56.30, 50.59, 35.65, 31.92, 29.42, 29.32, 25.39, 27.73, 14.10; MS (EI, probe) 167.0 (2.3), 114.0 (4.0), 98.9 (100), 71.0 (12.0), 69.0(22.3), 43.1(15.6), 40.9(29.4); Anal. (C₁₂H₂₂O₂) C, H.

Representative Procedure for Preparation of Allenes: 2,3-Undecadien-1-ol.

A solution of 3-methoxy-undec-2-yn-1-ol (1.00 g, 5.04 mmol) in ether (20 mL) was added dropwise to a suspension of LiAlH₄ (Alfa, 0.755 g, 20.16 mmol) in ether (350 mL). After 10 min the solution was cooled to -78°C and treated in one batch with solid I₂ (3.83 g, 15.12 mmol) and the resulting suspension stirred for 2 h at -78°C. TLC analysis indicated the reaction to be complete. The cold bath was removed and a saturated solution of Rochelle salt was added cautiously, followed by 20 mL of saturated aqueous sodium thiosulfate. After stirring for 1 h at 5°C (cold room), the phases were separated and the aqueous layer extracted with ether. The combined ether layers were dried (K₂CO₃) and concentrated in vacuo to yield 0.809 g (95.5%) of a colorless liquid: bp 178°C @ 0.45 mm Hg; ¹H NMR(CDCl₃) δ5.58 (m, complex (5 lines), 2H), 4.2 (t, J=4 Hz, 2H), 2.33 (br s, 1H, disappears w/D₂O), 2.05 (m, 2H), 1.34 (8H), 0.9 (3H); IR (neat) 3150-3560 (s,br), 2935(br,vs), 2850, 1961(s), 1460, 1009(vs), 865 cm⁻¹; ¹³C NMR (CDCl₃) δ 203.34, 93.48, 91.72, 60.88, 31.94, 29.25, 28.76, 22.73, 14.11; MS (EI, probe) 107.0, 84.0, 83.0, 78.9, 67.0, 55.1 (P); Anal. (C₁₁H₂₀) C, H.

Acknowledgement: We are indebted to the National Science Foundation, the National Institutes of Health (Grant #GM-28961) and the Alfred P. Sloan Foundation for financial support.

References and Notes:

- 1) Fellow of the Alfred P. Sloan Foundation, 1981-1983.
- 2) For a review, see: Murray, M. in "Methoden der Organischen Chemie," (Houben-Weyl), George Thieme Verlag: Stuttgart, 1977, Vol. 5, pt. 2a.
- 3) For some recent synthetic uses of vinylallenes, note: Condran, P.; Hammond, M.L.; Mourino, A.; Okamura, W. H. J. Am. Chem. Soc. 1980, 102, 6259.
- 4) Cowie, F. S.; Landor, P.D.; Landor, S.R. J. Chem. Soc. Perkin I. 1973, 720.
- 5) Corey, E.J.; Katzenellenbogen, J.A.; Posner, G.H. J. Am. Chem Soc. 1967, 89, 4245.

(Received in USA 23 April 1982)