SYNTHESIS OF β,β-DISUBSTITUTED ACROLEINS VIA VINYL SILANE INTERMEDIATES

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The utility of the tetrahydropyranyl ether of (E)-3-bromo-3-trimethylsilyl-2-propen-1-ol as a single precursor for the synthesis of β,β-disubstituted acroleins is demonstrated.

INTRODUCTION

There are a number of reagents and processes for preparing substituted acroleins [1-5] (α, β-unsaturated aldehydes). These approaches vary greatly in stereochemical control and there is still no general approach to the stereospecific preparation of both E and Z-β, β-disubstituted acroleins. Furthermore, there is always a need for new methods which are stable toward various reaction conditions. It was decided to investigate this problem using a single precursor for the preparation of both E and Z substituted acroleins.

EXPERIMENTAL

Only representative examples are described
(R = n-Bu, R' = Me).

Preparation of the Tetrahydropyranyl Ether of (Z)-3-Trimethylsilyl-2-hepten-1-ol Using sec-Butyllithium (2; R=n-Bu):

23.9 g (81.6 mmol) of (E)-bromo-vinylsilane (1) in 160 ml of dry tetrahydrofuran was treated with 78 ml of 1.25 M sec-butyllithium (97.9 mmol, 1.2 eq). Following treatment with 18.6 ml (163.2 mmol, 2 eq) of n-butyl iodide at -78°C for 3 hours, the mixture was warmed to room temperature, stirred for 30 minutes and worked-up. The solvent was removed by rotary evaporation (warm water bath) to afford a residue which was distilled at reduced pressure to yield 16.5 g (61.1 mmol, 75% yield) of colorless product. Examination by GLPC (50 m SE-30 glass capillary column) revealed that the product was greater than 99% of the (Z)-isomer; bp. 124-127°C/2.5 mm; IR (neat) 2980(s), 2890(s), 1620(m, C=C), 1450(s), 1380(m), 1250(s, CH3Si), 1030 and 1200(s, C-O), and 850 cm⁻¹(s); ¹H NMR (CDCl₃) δH 0.00 (singlet, 9H, (CH3)₂Si), 0.75 (broadened triplet, 3H, J= 6Hz, CH₃), 1.00-1.5 (multiplet, 10H), 1.87 (broadened triplet, J= 6Hz, 2H, C=C-CH₂), 3.1-4.1 (multiplet, 4H, CH₂-O-CH₂), 4.35 (multiplet, 1H, O-CH-O), and 5.3 ppm (triplet, J= 7Hz, 1H, HC=C).

Preparation of the Tetrahydropyranyl Ether of (E)-3-Bromo-2-hepten-1-ol (3; R=n-Bu):

In a 250 ml round-bottomed flask, 11.55 g (42.78 mmol) of the tetra-hydropyranyl ether of (Z)-3-trimethylsilyl-2-hepten-1-ol (2; R = n-Bu) was dissolved in 43 ml of methylene chloride and cooled to -78°C (dry ice/acetone bath). A solution of 8.88 g (55.6 mmol, 1.3 eq) of bromine in 43 ml of methylene chloride was slowly added by an additional funnel. To the red-orange solution was added 25 ml of methanol and about 0.5 g of sodium sulfite and the result was vigorously stirred until the mixture became light yellow in color. While still cold (-78°C), the reaction mixture was quickly poured into a separatory funnel containing 10% sodium sulfite solution and shaken until all color had disappeared. After separation, the aqueous layer was thoroughly extracted with diethyl ether and then the combined organic extracts were dried over anhydrous sodium sulfate. In the absence of light, the solvent was removed by rotary evaporation at room
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Synthesis of β,β-Disubstituted Acroleins Via Vinylsilane Intermediates

The flask was thoroughly purged of air by repeatedly pumping (vacuum pump) then flushing with nitrogen. Addition of 20 ml of dry diethyl ether resulted in a slurry which was cooled to 0°C and treated with 7.5 ml of 1.45 M methylolithium (10.9 mmol, 2 eq). The clear solution was stirred a few minutes at 0°C to afford the copper reagent to which 1.51 g (5.45 mmol) of the tetrahydropyryln ethyl ether of (E)-3-bromo-2-hepten-1-ol (3; R=n-Bu) was added with a few ml of diethyl ether. After stirring 30 minutes at 0°C, the solution was allowed to warm to room temperature and stirred further for 24 hours. The dark reaction mixture was partitioned between concentrated ammonia solution and pentane and shaken until all solids dissolved. After separation, the aqueous layer was extracted with fresh pentane and the combined organic extracts were dried over anhydrous sodium sulfate. The solvent was removed by rotary evaporation at room temperature to afford 1.10 g (5.18 mmol, 95% yield) of the crude olefin (The spectra have been previously recorded).

The crude olefin was dissolved in 10 ml of methanol, treated with a few drops of 0.1N hydrochloric acid stirred for 3 hours at room temperature, and worked-up as previously described. The solvent was removed by rotary evaporation at room temperature to afford a residue which was chromatographed. Elution from 30 g of silica gel with [50% hexane 50% methylene chloride] gave 0.558 g (4.36 mmol, 80% yield) of colorless product. The spectra have been previously recorded.

Preparation of (Z)-3-Methyl-2-heptenal (5, R=n-Bu, R'=Me): To a magnetically stirred solution of 0.512 g (4 mmol) of the corresponding alcohol (4; R=n-Bu, R'=Me) in 29 ml of methylene chloride, 4.32 g of dry powdered barium manganate was added at room temperature. The reaction mixture was stirred for 12 hours and then filtered. The filter cake was washed with methylene chloride. Combination of the filtrates and removal of the solvent at atmospheric pressure afforded a residue which was chromatographed. Elution from 16 g of silica gel with 30% methylene chloride -70% hexane gave 0.212 g (1.68 mmol, 84% yield) of colorless product: IR (neat) 3080(w, H-C=C), 2985(s), 2895(s), 2750(m), 1685(s, C=O), 1640(m, C=C), 1450(m), 1385(m), 1130(s), and 740 cm⁻¹(s); NMR (CDCl₃, internal TMS) δ 0.95 (broadened triplet, J = 6.5Hz, 3H, CH₃), 1.45(multiplet, 4H, -(CH₂)₃), 1.93 (doublet, J=1.0Hz, C=C-CH₂), 2.53 (multiplet, 2H, C=C-CH₂), 5.74 (doublet of doublet, J = 8.5Hz, 1H, CH, CHO); high resolution mass spectrum, calculated (m/e) for C₇H₁₄O: 128.1202; found: 128.1213. An isomeric ratio of 90%(Z): 10%(E) was determined by GLPC (30 m SE-54 glass capillary column).

RESULTS AND DISCUSSION

The development of a synthetic equivalent of acrolein which the terminal end of the carbon-carbon bond can have different polarities was achieved. Intensive studies carried out showed that the tetrahydropyryl ether of (E)-3-bromo-3-trimethylsilyl-2-propen-1-ol (1), prepared by hydroalumination-bromination of the tetrahydropyryl ether of 3-trimethylsilyl-2-propyn-1-ol, [6,7] could serve as a single precursor for all of the synthetic equivalents of acrolein.

\[
\text{THPOCH₃} \quad \text{C} \equiv \text{C} \quad \text{SiMe₃} \\
\text{H} \quad \text{I} \quad \text{Br}
\]

The utilization of (1) as a synthon for the (E)-β-formylvinyl anion involved conversion of the bromovinylsilane (1) to a vinyl lithium reagent via halogen-metal exchange with sec-butyllithium (1.2 eq) in tetrahydrofuran at -78°C followed by alkylation with either methyl iodide or n-butyl iodide at -78°C. The desired alkylated products (2) were obtained in 75% isolated yield with 99% of the (Z)-isomer present with no noticeable amount of the (Z)-isomer present with no noticeable amount of the protonated material (2, R=H) being formed [6,7].
To use (1) as a synthon for the (E)-β-formylvinyl cation, it was necessary to reverse the polarity utilized in the alkylation process. This was accomplished by coupling the bromovinylsilane (1) with cuprate reagents [6,7]. Thus, (1) upon reaction with (PhS)(sec-Bu)CuLi in tetrahydrofuran gave (2, R = sec-Bu) in 65% isolated yield and upon reaction with methyl lithium and 20 mol % copper iodide in diethyl ether gave (2, R = Me) in 75% isolated yield [6,7].

a. 2.5 eq (PhS) (sec-Bu) CuLi, THF
b. 2 eq MeLi, 0.4 eq CuLi, Et O

Further elaboration of vinylsilanes allowed functionalization of the other β-position in the acrolein synthon by a bromination/desilicobromination procedure [6] which gave vinyl bromides (3) in a highly stereoselective manner. Since the tetrahydropropyryl ether group on these vinylsilanes (2) very sensitive to bromine, a significant amount of the cleaved products was observed. Therefore, the cleaved products had to be reprotected by treatment of the crude vinyl bromides with dihydropyran and a catalytic amount of phosphorus oxychloride. The overall yield of this process was quite reasonable (60-65%) with greater than 98% of the E-isomer being obtained.

Subsequent alkylation [6,7] or coupling [6,7] of these vinyl bromides (3), as has been described for bromovinylsilane(1), followed by hydrolysis of the tetrahydropropyryl group (using methanol/0.1N hydrochloric acid) led to isomerically pure allylic alcohols (4) [7] in good yields (80-85%).

The final step in the sequence involved oxidation of the allylic alcohols to the β, β-disubstituted acroleins (5). It was found that barium manganate [8] gave the highest stereo-selectivity in these oxidations and the reaction proceeded quite well at room temperature in ten hours to afford the desired products in good yields (85-88%).
REFERENCES


