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STEREOSELECTIVE SYNTHESIS OF FUNCTIONALIZED OLEFINS: THE ORTHOESTER CLAISEN REARRANGEMENT OF ALKYNYL ALLYLIC ALCOHOLS

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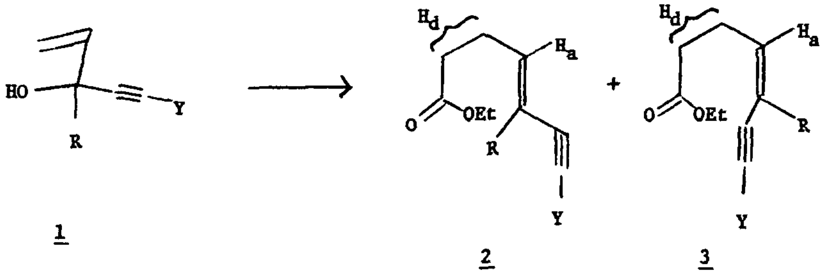
The orthoester Claisen rearrangement[1] sterospecifically converts secondary allylic alcohols to trans-γ,δ- olefinic esters. However, preliminary investigations indicate that tertiary allylic alcohols do not undergo this rearrangement.[2]

In an effort to broaden the scope of the orthoester Claisen rearrangement to afford functionalized di- and trisubstituted olefins, we have investigated the reactions of allylic alkynyl alcohols 1a-d with triethyl orthoacetate. We have found that the orthoester Claisen reactions of these alcohols proceed to give olefinic products 2 and 3 and that in each case, the predominant isomer is that with the bulkier substituent trans to the ester side-chain.



a. $R = H_b$ $Y = H_c$
b. $R = H_b$ $Y = (CH_3)_3Si$
c. $R = CH_3$ $Y = H_c$
d. $R = CH_3$ $Y = (CH_3)_3Si$

The yields and product distributions for the orthoester Claisen rearrangements of alcohols 1a-d are listed in Table I.

TABLE I

Yields[a] and Product Distributions of the Orthoester Claisen Rearrangement of Allylic Alkynyl Alcohols

Alcohol	R	Y	Yield (%, 2 + 3)	Ratio 3/2[b]
1a	H	H	44	10/90
1b	H	$Si(CH_3)_3$	41	20/80
1c	CH_3	H	30	84/16[c]
1d	CH_3	$Si(CH_3)_3$	50[d]	90/10

a. All products were isolated by distillation. b. Isomer mixtures were analyzed by gas chromatography on a 15' x 1/4" Carbowax 20M column. c. Partially equilibrated; with shorter reaction times which effect lower yields, ratios approaching 90:10 were observed. d. This yield is based on unrecovered starting material; 16% of alcohol 1d was recovered by distillation.

The conversion of 1a to a mixture of 2a and 3a was accomplished according to the following procedure. A 0.528g sample (6.5mmol) of alcohol 1a, 10 ml of triethyl orthoacetate and 17 µl of propionic acid was heated at reflux for 1 hour, as ethanol was removed by distillation. After cooling to room temperature the reaction mixture was stirred for 1/2 hour with 750 ml. of 5% KH_2PO_4, and extracted with ether. The ether was washed with 10% $NaHCO_3$ and the product mixture (2a + 3a) was isolated by distillation.

The rearrangement of alcohol 1b was effected by a modification of this procedure. A solution of 0.38g (2.5mmol) of alcohol 1b, 10 ml of triethyl orthoacetate and 17 µl of propionic acid was stirred at reflux for 3 hours as ethanol was removed by distillation. Product isolation was the same as for the products from 1a.

The orthoester Claisen rearrangement of alcohols 1c and 1d was found to require prolonged heating (2 days) with distillative removal of ethanol and repeated additions of triethyl orthoacetate and propionic acid. The workup was the same as above. The isomeric products of each rearrangement were separated by preparative gas chromatography. The geometry of each olefin was assigned on the basis of its nuclear magnetic resonance spectrum; the significant features of these spectra[3] are recorded in Table II.

TABLE II

Correlation of Geometry and NMR Spectrum

δ (ppm), multiplicity

	Ha	Hb	Hc	Hd	vinyl methyl
2a	6.26, d of t J = 16, 6.5 Hz	5.49, d, J = 16 Hz	2.77, d	2.43, unsym. d	
3a	6.04, d of t, J = 12, 6.5 Hz	5.47, broad d, J = 12 Hz	3.10, broad s	2.52, m	
2b	6.11, d of m, J = 16, 6 5 Hz	5.50, d, J = 16 Hz		2.37, unsym. d	
3b	5.92, d of t, J = 11, 6.2 Hz	5.50, d, J = 11 Hz		2.50, m	
2c	5.92, t		2.78, s	2.40, unsym. d	1.82, s
3c	5.79, t		3.13, s	2.47, m	1.86, d
2d	5.85, t			2.35, unsym. d	1.79, d
3d	5.72, t			2 45, m	1.82, d

The geometry of each product was assigned on the basis of the following evidence· in the cases where the products are disubstituted olefins (a and b) the product with the larger ethylenic H-H coupling constant was assigned the trans structure,[4] in cases where the products contain vinyl methyl groups (c and d) the product with the higher field methyl absorption was assigned the structure with the methyl group trans to the vinyl proton[5]. These assignments are consistent with the observation that the olefinic proton H_a suffers a downfield shift when it is cis to the acetylene group. The acetylenic protons in products 3a and 3c absorb at 0.3 ppm lower field than the acetylenic protons in the isomeric products (2a and 2c).

The geometries of enynes 3c and 3d were experimentally correlated by the conversion of 3d to 3c. Treatment of silyl acetylene 3d with silver nitrate in aqueous ethanol for 6 hours at room temperature followed by treatment with potassium cyanide[6] afforded terminal acetylene 3c, containing 5% of isomeric 2c. Treatment with silver nitrate at elevated temperatures, however, a 67:33 mixture of 3c 2c.

We are currently investigating this method as a means of synthesizing di- and trisubstituted olefinic moieties with novel substitution patterns as well as a means of stereoselectively producing tetrasubstituted olefins.

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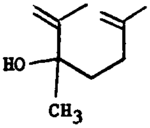

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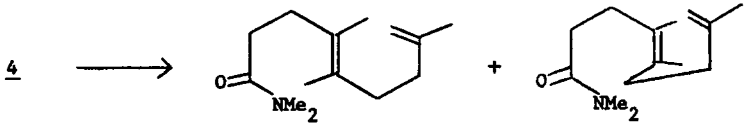
with triethyl orthoacetate under acidic conditions. With dimethyl acetamide diethyl acetal (see reference 1, footnote 1) alcohol 4 afforded a 98% yield of a mixture of the expected amides 5 and 6 in a ratio of 58:42.



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