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THE SYNTHESIS OF ALKENES FROM CARBONYL COMPOUNDS AND CARBANIONS α TO SILICON

V. STEREOSELECTIVE SYNTHESIS OF E- AND Z-DISUBSTITUTED ALKENES.[1]

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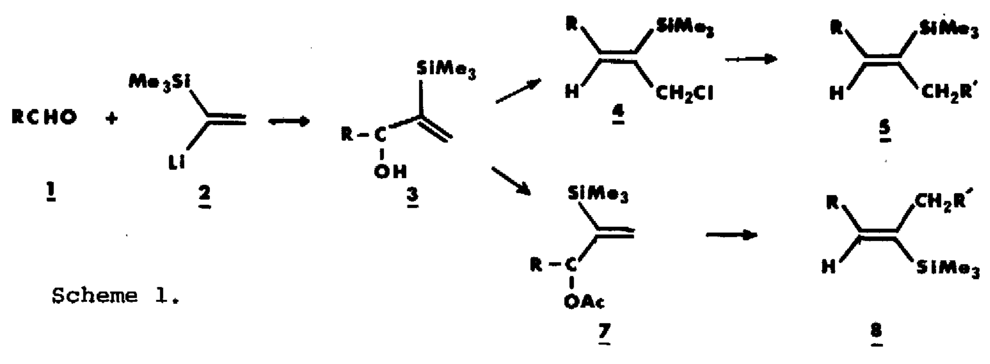
The recognition that β-functionalized organosilanes can eliminate to give carbon-carbon double bond forms the basis of an alkene synthesis which has been reported by us[1,2] and others[3,4]. It involves the condensation of carbonyl compounds with α-silyl carbanions. However, when the alkenes to be synthesized can display geometric isomerism, the alkenes obtained by this reaction have often been found to be a mixture of E and Z isomers in nearly equal proportions.[2,4,5] We wish to propose a general solution to the problem of stereoselectivity in alkene synthesis which has the virtue of being applicable to the preparation of di- and tri-substituted alkenes. We have also demonstrated the utility of our approach in a new synthesis of the sex pheromone of Gypsy Moth (disparlure).[2]

The overall transformations can be illustrated by scheme 1. Reaction of aldehydes (1) with α-trimethylsilylvinyl lithium[6] (2) at -78°C afforded the alcohols 3 in good yields.[1] The stereoselective conversion of the alcohols 3 into predominantly the Z-isomer of the allylic chlorides 4 has been reported by us.[1] Reaction with organocopper lithium reagents at room temperature[7] gave cleanly the vinylsilanes 5 in ∿80% yields with the same stereochemical purity as the precursor chlorides (usually ∿85-90% Z). The vinylsilanes 5 can be protodesilylated with acid to give the E-alkenes stereospecifically in nearly quantitative yields.[8]

The isomeric vinylsilanes 8 can also be prepared. Acetylation of the alcohols 3 gave in a straightforward manner the acetates 7. Reaction of 7 with organo-copper reagents can give stereoselectively the vinylsilanes 8 (>85% E).[7] The reaction is extremely sensitive to the size of the alkyl group R, the temperature of the reaction as well as the choice of copper reagent. When the alkyl group R is iso-propyl or cyclohexyl, reaction of the acetates 7 with organocopper lithium reagents at -78° gave the vinylsilanes 8 in good



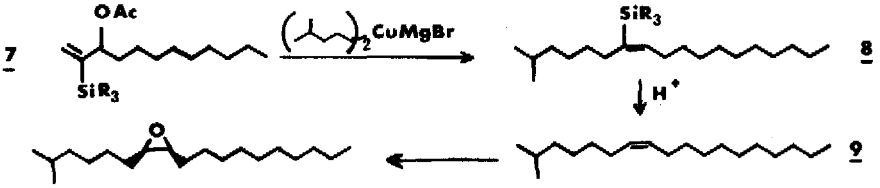
Scheme 1.

yields with high stereoselectivity. The same reactions, if carried out at room temperature, gave mixture of products including those of direct substitution of the acetate group by R'. When the alkyl group is n-$C_{10}H_{21}$, the reaction of 7 with organocopper lithium reagents, even at -100°, gave both isomers of vinylsilanes 5 and 8 with low stereoselectivity. It is obvious therefore that the stereochemistry of the product is governed by the steric interaction of the R group and the trimethylsilyl group. We are able to improve the stereoselectivity of the reaction by using a less reactive organocopper reagent - organocopper magnesium compounds. Thus, treating of 7 (R = n-$C_{10}H_{21}$) with "(n-Br)$_2$CuMgBr"[9] at -78° gave predominantly the *E*-isomer of 8 (R = n-$C_{10}H_{21}$) in 80% yield. The vinylsilanes 8 can be protodesilylated stereospecifically to the corresponding *Z*-alkenes.[8]

It is interesting to note that the stereochemical outcome of the sequence $7 \rightarrow 8 \rightarrow$ *Z*-alkene is opposite to that expected from the reaction of allylic acetate with organocopper lithium reagent which normally gives the *E*-alkene.[7] This illustrates the useful role of the silyl group in controlling the stereochemistry of a reaction.

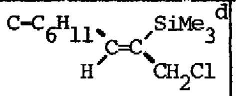
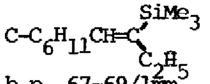
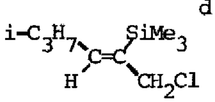
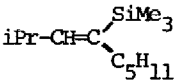
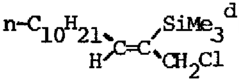
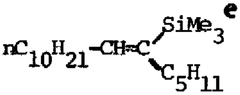
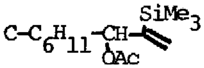
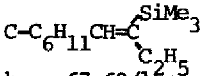
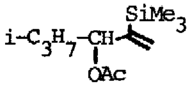
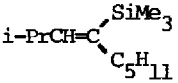
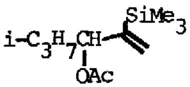
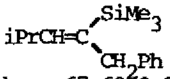
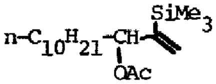
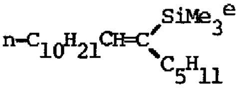
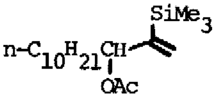
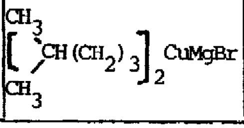
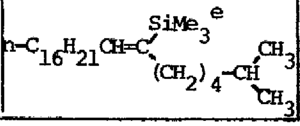
We had previously reported a non-stereoselective synthesis of the sex pheromone of gypsy moth (disparlure).[2] With the present approach outlined in scheme 2, we have now achieved a stereoselective synthesis of disparlure (*Z*:*E* = 87:13) in 65% overall yield calculated from the starting undecanal. In terms of yield, isomeric purity as well as simplicity of operations, the present synthesis appears to be superior to the Wittig reaction.[10]

Scheme 2



Thus, 3 (R = n-$C_{10}H_{21}$), prepared from undecanal in 80% yield,[1] was acetylated with acetic anhydride to give quantitatively the acetate 7 which was purified by column chromatography on silica gel (benzene). To a solution of 2-methylpentylmagnesium bromide (0.015 mole) in ether (25 ml) at 0°, anhydrous cuprous iodide (0.0075 mole) was added. The mixture was warmed to room temperature for 1/4 hr and then cooled to -78°. To the mixture, the acetate 7 (0.006 mole) in ether was added dropwise. The mixture was allowed to warm to room temperature slowly with stirring for 16 hrs. On work-up, there was obtained in 82% yield the vinylsilane 8 (E:Z=87:13) after purification by column chromatography on silica gel (hexane). The vinylsilane 8 (0.50 g) was treated with 15 ml of methylene chloride and 0.10 ml 57% hydriodic acid at room temperature for 30 minutes. The mixture was neutralized and the olefin 9 isolated in quantitative yield. The structure and isomeric ratio of 9 was established by comparison with authentic sample.[10] Epoxidation of 9 by established procedures[2,10] gave disparlure in quantitative yield.

Table: Reaction of organocopper reagents with allylic chlorides and acetates.

Precursor	Reagent	Temp. °C	Product	Yield[a] (E:Z)
 [d]	$(CH_3)_2CuLi$	r.t.	 b.p. 67-69/1mm	80(15:85)
 [d]	$(n\text{-}C_4H_9)_2CuLi$	r.t.	 b.p. 78-80/5mm	80(10:90)
 [d]	$(n\text{-}C_4H_9)_2CuLi$	r.t.	 [e]	80[b](11:89)
 b.p. 76-78/0.1mm	$(CH_3)_2CuLi$	-78°	 b.p. 67-69/1mm	78[b](94:6)
 b.p. 54-56/0.75mm	$(n\text{-}C_4H_9)_2CuLi$	-78°		78[b](92:8)
	Ph_2CuLi	-78°	 b.p. 67-69/0.25mm	61(100:0)
 b.p. 104-106/0.1mm	$(n\text{-}C_4H_9)_2CuLi$	0°	 [e]	-[c](30:70)
		-78°		-[c](53:47)
	$(n\text{-}C_4H_9)_2CuMgBr$	-78°		80(86:14)
		-78°	 [e]	82(87:13)

(a) Isolated yield (b) Contains <5% terminal isomer (c) Yield not determined
(d) See Reference 1 (e) Purified by column chromatography over silica gel (hexane)

With both geometrical isomers of the vinylsilanes available[11], it should be possible to replace the silyl groups stereospecifically with halogens[12] or other electrophiles[13], thus giving tri-substituted alkenes of defined stereochemistry. These reactions are under active investigation in our laboratories.

Acknowledgement

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References and Footnotes

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