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Isoprenoid Chain Elongations by Claisen Rearrangements Using Acetals as Precursors of Vinyl Ethers

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Abstract: Claisen rearrangements of allyl vinyl ethers, formed in situ by the acid catalyzed reaction of dimethyl acetals of acetaldehyde, acetone and isopropenyl methyl ketone with different types of allylic alcohols, have been compared. The primary, secondary and tertiary allylic alcohols used in the investigation were selected to serve as models for isoprenoid synthesis. The basis for two feasible methods that can be iterated to create isoprenoid chains has been investigated.

Introduction and background.

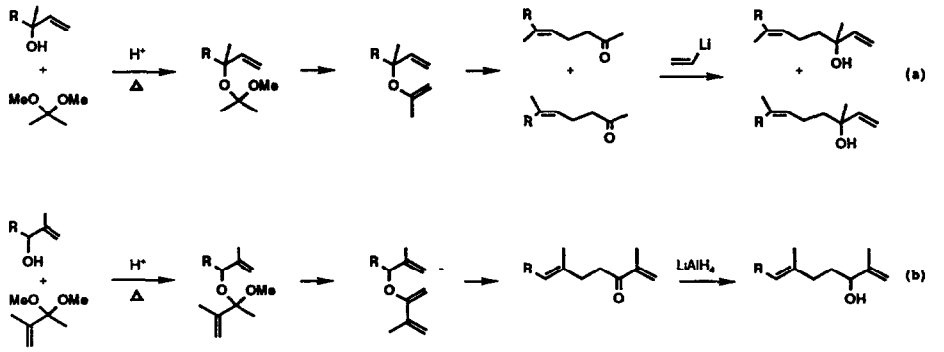
One of many reactions that is likely to be identified by retrosynthetic computer programs as a general method for carbon-carbon bond formation and chain elongation is the Claisen rearrangement. Detailed information on the scope and limitations of such reactions is necessary in order to evaluate the feasibility of progressing from the general case to the specific. We have combined our interest in Claisen rearrangements and terpenoid synthesis[1] with providing additional information on the use of acetals as precursors of vinyl ethers.

The thermal rearrangements, in the gas phase, of allyl vinyl ethers were investigated by Hurd and Pollack.[2] In their investigation, allyl isopropenyl ether was made from acetone allyl acetal, derived from acetone diethyl acetal and allyl alcohol in acid catalyzed reactions. During distillation of the allyl isopropenyl ether, a small amount of the rearrangement product was obtained. This result indicates that three consecutive steps, namely, transacetalation, loss of alcohol and rearrangement, should be feasible in a one-pot reaction by simply mixing and heating the reactants.

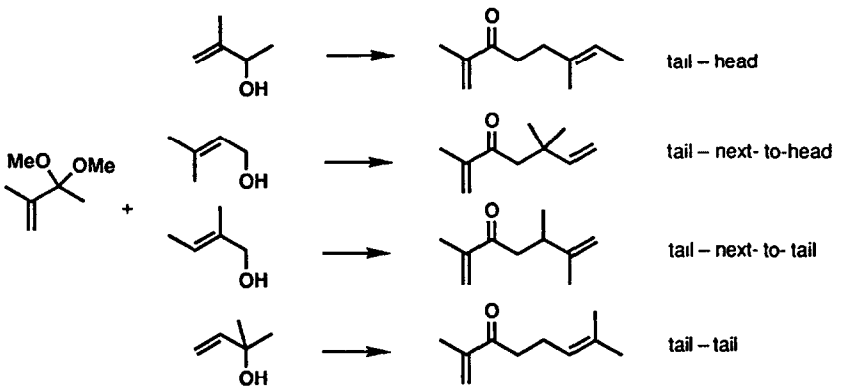
In 1967 Marbet and Saucy published extensive studies on one-pot Claisen rearrangements by heating mixtures of vinyl ethers, allylic alcohols and acid catalysts.[3] Mixed acetals were proposed as intermediates and the use of acetals instead of vinyl ethers was briefly investigated. In these investigations the allylic alcohol moieties were restricted to tertiary alcohols. In 1970, Johnson et al. reported on the use of triethyl orthoacetate (1) for producing γ, δ-unsaturated esters via mixed ketene acetals.[4] Shortly thereafter, the use of isopropenyl methyl ketone dimethyl acetal (2) for isoprenoid synthesis was elegantly demonstrated by Johnson et al.[5] The use of acetals of saturated ketones other than acetone have also been

reported but the applications are limited since unsymmetrical aliphatic ketones leads to ambiguous vinyl ether formation.[6]

Acetals (ketals) as precursors of vinyl ethers in Claisen rearrangements has been covered in several recent reviews[7] and the orthoacetate methodology has become a standard procedure, while the use of acetals of isopropenyl methyl ketone, acetone and acetaldehyde has mostly been left idle.[8]



Scheme 1



Scheme 2

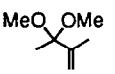
Isoprenoid compounds are formally recognized to consist of isoprene units, most commonly connected by head to tail bonds but other types of connections appear occasionally. The Claisen rearrangement has great potential in isoprenoid synthesis, and Scheme 1 shows two sequences that can be iterated for head to tail type chain elongation. The Claisen rearrangement can be performed on a tertiary allylic alcohol with an acetal of acetone followed by addition of a vinyl Grignard reagent to the resulting ketone. In this case the new

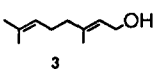
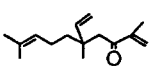
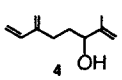
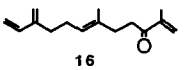
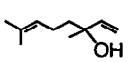
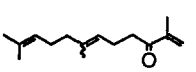
isoprene unit will be attached to the growing chain by a head bond (Scheme 1, (a)) Addition of an isoprene unit by the tail bond can be accomplished by using the dimethyl acetal of isopropenyl methyl ketone (**2**) and reduction of the rearranged product with $LiAlH_4$. (Scheme 1, (b)).

Scheme 2 illustrates the junctions that could be made with the dimethyl acetal of isopropenyl methyl ketone (**2**) and four isoprenoid types of allylic alcohols.

Results.

Three model allylic alcohols, i.e. geraniol (**3**) (2,3,3-trisubstituted allylic alcohol), 2-methyl-6-methylene-1,7-octadien-3-ol (**4**) (secondary allylic alcohol, isopropenyl type) and linalool (**5**) (tertiary allylic alcohol, dialkyl vinyl type) were used to investigate reactions of the dimethyl acetals of isopropenyl methyl ketone (**2**), acetone (**6**) and acetaldehyde (**7**). Two methods were used to perform the reactions. The reagents were mixed with an acid catalyst followed by method **A**: heating the reaction mixture to reflux temperature at atmospheric pressure with or without an additional solvent, or method **B**: heating the neat reaction mixtures in sealed tubes.

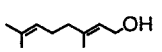
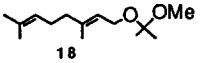
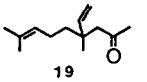
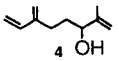
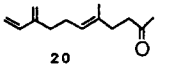
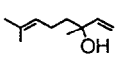
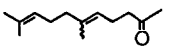
Table 1. Results with 

Allylic alcohol	Acetal 2[a] (mmole)	Catalyst[a] (mmole)	Solvent	Temp (°C)	Time (h)	Products	Yield (% iso)	Method
 3	1	o-NO_2PhCOOH 0 2	1,2,4-trimethyl benzene	180	4	 15	23	A
"	1	CH_3CH_2COOH 0 15	–	150	15	no main product		B
 4	5	o,p-$(NO_2)_2$PhOH 1	toluene	105	8	 16	93	A
 5	6	o,p-$(NO_2)_2$PhOH 1	toluene	105	8	 17 *Z*/*E* = 1 2	24	A
"	1	H_3PO_4/CH_3COOH (4%, v/v) 10 µl	–	150	24	no main product		B

a) To 1 mmole of the alcohol

It should be pointed out that the reactions were sensitive to the nature and amount of catalyst used. In each case an effort had to be made to select an appropriate catalyst and vary the amounts to enable the reactions. The selection was made from the following catalysts: CH_3CH_2COOH[4], H_3PO_4/CH_3COOH[9], H_3PO_4/HCOOH, *o,p*-dinitrophenol[5a] and *o*-nitrobenzoic acid[6g]. The results are presented in Tables 1–3.

Table 2. Results with 

Allylic alcohol	Acetal 6[a] (mmole)	Catalyst[a] (mmole)	Solvent	Temp (°C)	Time (h)	Products	Yield (% iso)	Method
 3	7	H_3PO_4/HCOOH (4%, v/v)100µl	toluene	105	24	 18	–	A[b]
"	5	CH_3CH_2COOH 0 3	–	150	15	 19	35	B
 4	7	H_3PO_4/HCOOH (4%, v/v) 50 µl	toluene	105	24	 20	3	A
"	5	CH_3CH_2COOH 0 3	–	150	15	"	33	B
"	6	o,p-$(NO_2)_2$PhOH 0 1	–	150	8	"	40	B
 5	4	H_3PO_4/HCOOH (4%, v/v)10µl	toluene	105	75	 21 *Z/E* =1 2	6	A
"	3	H_3PO_4/CH_3COOH (10%, v/v) 20µl	–	150	18	" *Z/E* =43 57	64	B

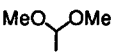
a) To 1 mmole of the allylic alcohol b)The product decomposed on the silica gel column during isolation

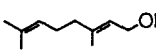
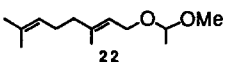
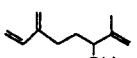
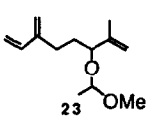
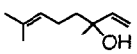
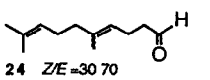
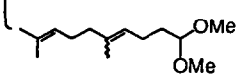
Discussion.

Formation of the mixed acetals seems to occur in all cases. Elimination of alcohol appears to occur most readily from the mixed acetals of isopropenyl methyl ketone which gives a vinyl ether conjugated with a double bond.[5a] In light of this, the dimethyl acetal of methyl vinyl ketone (**8**) would have been an interesting candidate for investigation. Unfortunately, no simple method for the synthesis of acetal **8** has been found.[10]

The difficulty of forming vinyl ethers from acetals of acetaldehyde is well documented in early literature;[11] and accordingly, Bertrand and Viala[12] found that the mixed acetal formed from

allene alcohol and ethyl vinyl ether was stable under both acid and neutral conditions. Hence, it is not surprising that in our investigation the mixed acetals of acetaldehyde were found to be quite stable when formed from primary and secondary alcohols. However, vinyl ether formation does occur readily from mixed acetals of acetaldehyde when tertiary alcohols are involved (Table 3, last entry; and ref. 3b). Small amounts of rearranged products were formed from the reactions of acetals of acetone when toluene was used as a solvent. Better results were obtained in the sealed tube reactions at 150 °C .

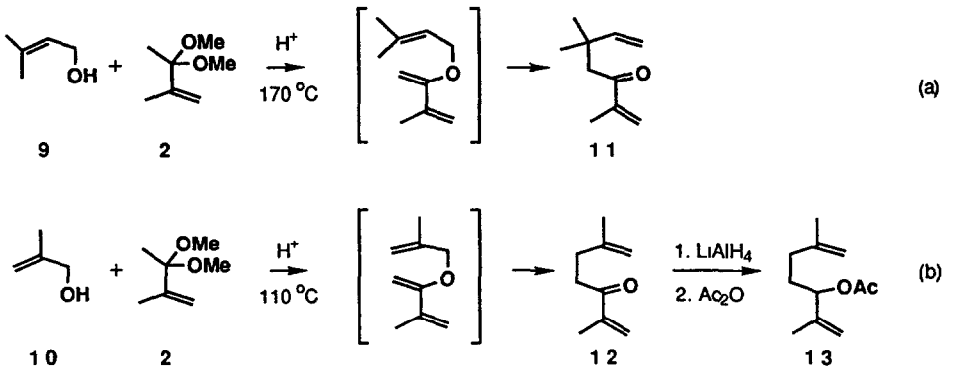
Table 3. Results with 

Allylic alcohol	Acetal 7[a] (mmole)	Catalyst [a] (mmole)	Solvent	Temp (°C)	Time (h)	Products	Yield (% iso)	Method
 3	3	H_3PO_4/HCOOH (10 %, v/v), 10µl	xylene	140	7	 22	57	A
"	5	CH_3CH_2COOH 0 3	–	150	16	"	56	B
 4	3	H_3PO_4/CH_3COOH (4 %, v/v), 5µl	toluene	105	20	 23	70	A
"	5	o,p-$(NO_2)_2$PhOH 0 1	–	150	6	"	36	B
"	1	" 0 1	–	120	24	"	40	B
 5	5	H_3PO_4/CH_3COOH (4 %, v/v), 10 µl	–	150	15	 24 Z/E =30 70	13	B
						 25 Z/E = 37·63	49	

a) To 1 mmole of the alcohol

Products of rearrangements leading to quaternary carbons (geraniol type) were difficult to obtain. At lower temperatures only mixed acetals were formed. At higher temperatures the reaction mixtures became complex in most cases. In separate experiments the reactions of acetal **2** with the alcohols 3-methyl-2-buten-1-ol (**9**) (geraniol type) and 2-methyl-2-propen-1-ol (**10**)[8b] (isopropenyl type) were compared. In the first case, the reaction temperature had to be raised to 170 °C to achieve the rearranged product **11** (Scheme 3, a). In the case of alcohol **10**,

the ketone **12** was readily formed at 110 °C. Ketone **12** was further used to synthesize the mealybug pheromone analog **13**[13] (Scheme 3, b).

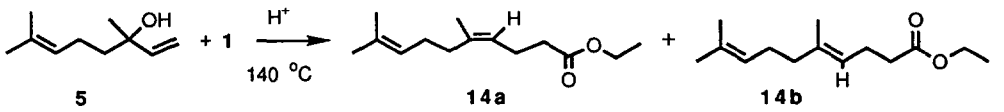


Scheme 3

The stereochemistry of the newly formed double bond in reactions with secondary allylic alcohols has a high selectivity for the *E* isomer, consistent with previous investigations.[14] The suggested mechanism is that the reaction mainly proceeds through a chair-like transition state in which the alkyl substituent takes the equatorial position. The reactions with tertiary alcohols gave poor *E*/*Z* selectivity in all cases. This can be interpreted by assuming that there is only a small preference for the larger substituent to take the equatorial position in the transition state (see below).

Reaction of triethyl orthoacetate and linalool.

We have noted that Kang et al.,[15] in the synthesis of *(E)*-β-farnesene, claimed a 97% yield of the *E* ester **14b** from the reaction of the tertiary alcohol linalool and triethyl orthoacetate (**1**). Since this result is not consistent with our findings we have repeated the reaction. Analysis by capillary gas chromatography showed that the rearrangement produced a 42:58 mixture of two main products that were isolated by performing repeated column chromatography on silica gel. The *Z* and *E* structures **14a** and **14b**, respectively, were assigned by ^{13}C NMR data.[16]



Scheme 4

Summary.
In one-pot Claisen rearrangements starting from allylic alcohols and simple acetals, the substitution pattern of the mixed acetals, formed during the course of the reactions, is crucial for the ease of vinyl ether formation. Mixed acetals of α,β-unsaturated ketones appear to form vinyl ethers with an efficiency similar to that of mixed ortho esters. Acetals of acetone need somewhat elevated temperatures to form vinyl ethers. Acetals of acetaldehyde only form vinyl ethers when one of the moieties originates from a tertiary alcohol.

Secondary alcohols give rise to products with high selectivity for *E* double bonds, while the *E*/*Z* selectivity is poor when tertiary allylic alcohols are involved. In reactions with 3,3-disubstituted allylic alcohols the rearrangements were found to be sluggish.

The basis for two feasible methods that can be iterated to create isoprenoid chains has been investigated. The synthetic value of the method requiring a tertiary alcohol as a starting material is restricted by the stereochemical outcome. An excellent method for chain elongation with an isoprene unit is available through the use of acetals of isopropenyl methyl ketone. This type of reaction has been used in the synthesis of several all-trans isoprenoid pheromone components that will be described in a separate paper.[17]

EXPERIMENTAL

NMR spectra were recorded in $CDCl_3$ on a Bruker WP 200 and AM 400 spectrometer. Analytical GC was performed with an FID detector and a 25 m DB-5 or a DB-23 capillary column. All liquid chromatography was performed on silica gel (Merck 60, 0.040 - 0.063 mm) and gradient elution was used with increasing amounts of ethyl acetate in hexane.[1a] TLC was performed on silica gel (Merck 60, precoated aluminum foil) eluted with 20% ethyl acetate in hexane and developed with vanillin and sulfuric acid in ethanol.

General procedures. Method **A**: In a flask equipped with a distillation set for the removal of MeOH formed during the reaction, the starting alcohol (1 mmol) and the acetal (for acetal **2**, 2 or 3 mmol; for acetal **6** and **7**, 3-5 mmol) were mixed in a solvent (for acetal **6** and **7**, no solvent was used; for acetal **2**, toluene, xylene and 1,2,4-trimethylbenzene were used depending on the desired reaction temperature). The acid catalyst (CH_3CH_2COOH, 0.06 mmol; 2,4-dinitrophenol, 1 mmol; *o*-nitrobenzoic acid, 0.2 mmol; H_3PO_4/CH_3COOH (4% v/v), 10 µl or H_3PO_4/HCOOH (4% v/v) 10 µl)) was added to the mixture. The mixture was heated and then cooled to room temperature. The products were isolated by column chromatography by loading the whole reaction mixture on a column and further purified by repeated chromatography.

Method **B**: The starting alcohol, the acetal and the acid catalyst were mixed and heated in a

sealed tube at 150 °C and then cooled to room temperature. The reaction mixture was worked up as in method **A**.

^1H and ^{13}C NMR data for compounds **15-25**:

5-Allyl-2,5,9-trimethyl-1,8-decadien-3-one (15). δ 1.11 (3H, s, $-CH_3$), 1.40-1.46 (2H, m, $-CH_2-$), 1.58 (3H, s, $-CH_3$), 1.67 (3H, s, $-CH_3$), 1.85 (3H, s, $-CH_3$), 1.84-1.92 (2H, m, $-CH_2-$), 2.65 (1H, d, J = 14.5 Hz $-CH_2CO-$), 2.75 (1H, d, J = 14.5 Hz, $-CH_2CO-$), 4.93 (1H, d, J = 17.4 Hz, $=CH_2$), 4.99 (1H, d, J = 10.8 Hz, $=CH_2$), 5.08 (1H, t, J = 7 Hz, =CH-), 5.73 (1H, s, $=CH_2$), 5.87 (1H, s, $=CH_2$), 5.84 (1H, dd, J = 17.4, 10.8 Hz, -CH=); δ 17.62 (CH_3), 17.76 (CH_3), 22.96 (CH_2), 23.17 (CH_3), 25.71 (CH_3), 39.65 (C), 40.76 (CH_2), 46.53 (CH_2), 111.73 (CH_2), 124.40 (CH_2), 124.62 (CH), 131.33 (C), 146.18 (CH), 146.18 (C), 201.36 (CO).

(*E*)-2,6-Dimethyl-10-methylene-1,6,11-dodecatrien-3-one (16). δ 1.62 (3H, s, $-CH_3$), 1.87 (3H, s, $-CH_3$), 2.16-2.23 (4H, m, br,.$-CH_2-$), 2.28 (2H, t, J = 8 Hz, $-CH_2-$), 2.78 (2H, t, J = 8 Hz, $-CH_2-$), 4.98 (1H, s, $=CH_2$), 5.01 (1H, s, $=CH_2$), 5.06 (1H, d, J = 10.9 Hz, $=CH_2$), 5.17 (1H, t, J = 6.6 Hz, -CH=), 5.24 (1H, d, J = 17.7 Hz, $=CH_2$), 5.76 (1H, s, $=CH_2$), 5.95 (1H, s, $=CH_2$), 6.37 (1H, dd, J = 10.9, 17.7 Hz, -CH=); δ 16.19 (CH_3), 17.71 (CH_3), 26.63 (CH_2), 31.33 (CH_2), 34.39 (CH_2), 36.37 (CH_2), 113.13 (CH_2), 115.81 (CH_2), 124.38 (CH_2), 124.61 (CH), 134.40 (CH), 138.98 (C), 144.61 (C), 146.08 (C), 201.96 (CO).

(*Z*)-2,7,11-Trimethyl-1,6,10-dodecatrien-3-one (17a). δ 1.61 (3H, s, $-CH_3$), 1.69 (6H, s, $-CH_3$), 1.88 (3H, s, $-CH_3$), 2.05 (4H, br, $-CH_2-$), 2.30 (2H, dt, J = 7, 7 Hz, $-CH_2-$), 2.70 (2H, t, br, J = 7 Hz, $-CH_2-$), 5.12 (2H, br, -CH=), 5.76 (1H, s, $=CH_2$), 5.95 (1H, s, $=CH_2$); δ 17.69 (CH_3 x 2), 22.95 (CH_2), 23.40 (CH_3), 25.75 (CH_3), 26.59 (CH_2), 31.91 (CH_2), 37.92 (CH_2), 123.75 (CH), 124.24 (CH), 124.40 (CH_2), 131.70 (C), 136.37 (C), 144.59 (C), 201.83 (CO).

(*E*)-2,7,11-Trimethyl-1,6,10-dodecatrien-3-one (17b). δ 1.59 (3H, s, $-CH_3$), 1.61 (3H, s, $-CH_3$), 1.67 (3H, s, $-CH_3$), 1.88 (3H, s, $-CH_3$), 1.91-2.13 (4H, m, $-CH_2-$), 2.30 (2H, dt, J = 7 Hz, $-CH_2-$), 2.70 (2H, t, J = 7 Hz, $-CH_2-$), 5.07 (1H, t, J = 7 Hz, -CH=), 5.11 (1H, t, J = 7 Hz, -CH=), 5.75 (1H, s, $=CH_2$), 5.95 (1H, s, $=CH_2$); δ 16.02 (CH_3), 17.68 (CH_3), 17.70 (CH_3), 23.15 (CH_2), 25.72 (CH_3), 26.69 (CH_2), 37.66 (CH_2), 39.71 (CH_2), 122.92 (CH), 124.28 (CH), 124.41 (CH_2), 131.43 (C), 136.24 (C), 144.63 (C), 201.92 (CO).

Acetone 3,7-dimethyl-2,6-octadienyl methyl acetal (18). δ 1.36 (6H, s, $-CH_3$), 1.59 (3H, s, $-CH_3$), 1.66 (3H, s, $-CH_3$), 1.67 (3H, s, $-CH_3$), 2.00-2.10 (4H, br, $-CH_2-$), 3.22 (3H, s, $-OCH_3$), 3.98 (2H, d, br, J = 7 Hz, $-CH_2O-$), 5.10 (1H, br, -CH=), 5.34 (1H, t, J = 7 Hz, -CH=); δ 16.41 (CH_3), 17.69 (CH_3), 24.51 (CH_3), 24.58 (CH_3), 25.69 (CH_3), 26.14 (CH_2), 39.69 (CH_2), 48.44 (CH_3), 57.69 (CH_2), 100.03 (C), 121.31 (CH), 124.12 (CH), 131.58 (C), 138.96 (C).

4-Allyl-7-methyl-7-nonen-2-one (19). δ 1.10 (3H, s, $-CH_3$), 1.37-1.46 (2H, m, $-CH_2-$), 1.58 (3H, s, $-CH_3$), 1.66 (3H, s, $-CH_3$), 1.83-1.91 (2H, m, $-CH_2-$), 2.10 (3H, s, $-CH_3$), 2.39 (1H d J = 15 Hz, $-CH_2-$), 2.44 (1H, d, J = 15 Hz, $-CH_2-$), 4.95 (1H, d, J = 17 Hz, $=CH_2$), 5.04 (1H, d, J = 11 Hz, $=CH_2$), 5.06 (1H, t, J = 7 Hz, -CH=), 5.80 (1H, dd, J = 17, 11 Hz, -CH=); δ 17.62 (CH_3), 22.82 (CH_3), 22.87 (CH_2), 25.71 (CH_3), 32.43 (CH_3), 39.58 (C), 40.86 (CH_2), 53.64 (CH_2), 112.28 (CH_2), 124.47 (CH), 131.47 (C), 145.86 (CH), 208.20 (CO).

(*E*)-8-Methylene-5-methyl-5,9-decadien-2-one (20). δ 1.60 (3H, s, $-CH_3$), 2.14 (3H, s, $-CH_3$), 2.21 (4H, br, $-CH_2-$), 2.25 (2H, t, J = 7 Hz, $-CH_2-$), 2.53 (2H, t, J = 7 Hz, $-CH_2-$), 4.98 (1H, s, $=CH_2$), 5.01 (1H, s, $=CH_2$), 5.05 (1H, d, J = 11 Hz, $=CH_2$), 5.16 (1H, br, -CH=), 5.24 (1H, d, J = 17 Hz, $=CH_2$), 6.38 (1H, dd, J = 17, 11 Hz, -CH=); δ 16.12 (CH_3), 26.57 (CH_2), 29.92 (CH_3), 31.30 (CH_2), 33.57 (CH_2), 42.44 (CH_2), 113.14 (CH_2), 115.84 (CH_2), 124.65 (CH), 134.02 (C), 138. 95 (CH), 145.97 (C), 208.85 (CO).

(*Z*)-6,10-Dimethyl-5,9-undecadien-2-one (21a). δ 1.61 (3H, s, $-CH_3$), 1.68 (6H, s, $-CH_3$), 2.04-2.05 (4H, s, br, $-CH_2-$), 2.13 (3H, s, $-CH_3$), 2.25 (2H, dt, J = 7, 7 Hz, $-CH_2-$), 2.44 (2H, t, J = 7 Hz, $-CH_2-$), 5.08 (1H, t, br, J = 7 Hz, -CH=), 5.10 (1H, br, -CH=); δ 17.68 (CH_3), 22.33 (CH_2), 23.39 (CH_3), 25.75 (CH_3), 26.54 (CH_2), 29.95 (CH_3), 31.91 (CH_2), 44.06 (CH_2), 123.36 (CH), 124.21 (CH), 131.72 (C), 136.55 (C), 208.83 (CO).

(*E*)-6,10-Dimethyl-5,9-undecadien-2-one (21b). δ 1.59 (3H, s, $-CH_3$), 1.61 (3H, s, $-CH_3$), 1.68 (3H, s, $-CH_3$), 1.97 (2H, t, J = 7 Hz, $-CH_2-$), 2.05 (2H, dt, J = 7, 7 Hz, $-CH_2-$), 2.13 (3H, s, $-CH_3$), 2.26 (2H, dt, J = 7 Hz, $-CH_2-$), 2.45 (2H, t, J = 7 Hz, $-CH_2-$), 5.07 (2H, t, with small splits, J = 7 Hz, -CH=); δ 16.01 (CH_3), 17.71 (CH_3), 22.52 (CH_2), 25.72 (CH_3), 26.66 (CH_2), 29.98 (CH_3), 39.68 (CH_2), 43.81 (CH_2), 122.57 (CH), 124.23 (CH), 131.47 (C), 136.43 (C), 208.93 (CO).

Acetaldehyde 3,7-dimethyl-2,6-octadienyl methyl acetal (22). δ 1.32 (3H, d, J = 5 Hz, $-CH_3$), 1.61 (3H, s, $-CH_3$), 1.69 (6H, s, $-CH_3$), 2.08 (4H, br, $-CH_2-$), 3.32 (3H, s, $-OCH_3$), 4.10 (2H, m, $-OCH_2-$), 4.70 (1H, q, J = 5 Hz, -OCHMeO-), 5.10 (1H, br, -CH=), 5.36 (1H, t, J = 7 Hz, -CH=); δ 16.43 (CH_3), 17.71 (CH_3), 19.32 (CH_3), 25.72 (CH_3), 26.41 (CH_2), 39.64 (CH_2), 51.95 (CH_3), 62.00 (CH_2), 99.64 (CH), 120.65 (CH),124.04 (CH), 131.68 (C), 140.15 (C).

Acetaldehyde 1-isopropenyl-4-methylene-5-hexenyl methyl acetal (23).[18] δ 1.28 (1.30) (3H, d (d), $-CH_3$), 1.66 (1.74) (3H, s (s), $-CH_3$), 1.62-1.86 (2H, m, $-CH_2-$), 2.15-2.32 (2H, m, $-CH_2-$), 3.29 (3.31) (3H, s, $-CH_3$), 4.05 (3.87) (1H, t, (t), J = 7 (7) Hz, -CH-O-), 4.62 (4.59) (1H, q (q), J = 5 (5) Hz, -O-CHMe-O-), 4.89-5.27 (6H, m, $=CH_2$), 6.38 (1H, dd, J = 18, 11 Hz, -CH=); δ 16.68 (CH_3), 17.21 (CH_3), 19.56 (CH_3), 20.00 (CH_3), 27.25 (CH_2), 27.51 (CH_2), 32.05 (CH_2), 50.99 (CH), 53.66 (CH), 80.06 (CH), 97.40 (CH), 100.29 (CH), 112.85 (CH_2), 113.23 (CH_2), 113.30 (CH_2), 114.01 (CH_2), 115.64 CH_2), 115.70 (CH_2), 138.87 (CH), 138.92 (CH), 144.42 (C), 145.29 (C), 146.04 (C).

(*Z*)-5,9-Dimethyl-4,8-decadien-1-al (24a). δ 1.63 (3H, s, -CH_3), 1.70 (6H, s, -CH_3), 2.01-2.08 (4H, br, -CH_2-), 2.32-2.48 (4H, m, -CH_2-), 5.12 (2H, t, br, J = 6.7 Hz, -CH=), 9.78 (1H, t, J = 1.7 Hz, -CHO); δ 17.68 (CH_3), 20.73 (CH_2), 23.37 (CH_3), 25.74 (CH_3), 26.47 (CH_2), 31.95 (CH_2), 44.23 (CH_2), 122.84 (CH), 124.08 (CH), 131.85 (C), 137.01 (C), 202.62 (CO).

(*E*)-5,9-Dimethyl-4,8-decadien-1-al (24b). δ 1.60 (3H, s, -CH_3), 1.64 (3H, s, -CH_3), 1.69 (3H, s, -CH_3), 1.99-2.10 (4H, m, -CH_2-), 2.31-2.46 (4H, m, -CH_2-), 5.07 (2H, br, -CH=), 9.77 (1H, t, J = 1.7 Hz, -CHO); δ 16.08 (CH_3), 17.72 (CH_3), 20.90 (CH_2), 25.72 (CH_3), 26.61 (CH_2), 39.65 (CH_2), 44.00 (CH_2), 122.04 (CH), 124.13 (CH), 131.56 (C), 136.87 (C), 202.72 (CO).

(*Z*)-5,9-Dimethyl-4,8-decadien-1-al dimethyl acetal (25a). δ 1.61 (3H, s, -CH_3), 1.69 (6H, s, -CH_3), 1.62-1.68 (2H, br, -CH_2-), 2.03 (6H, br, -CH_2-), 3.31 (6H, s, -OCH_3), 4.36 (1H, t, J = 6 Hz, -$CH(OMe)_2$), 5.12 (2H, t, br, J = 6.5 Hz, -CH=); δ 17.67 (CH_3), 23.02 (CH_2), 23.44 (CH_3), 25.74 (CH_3), 26.62 (CH_2), 31.92 (CH_2), 32.79 (CH_2), 52.61 (CH_3 x 2), 104.11 (CH), 124.29 (CH x 2), 131.62 (C), 135.90 (C).

(*E*)-5,9-Dimethyl-4,8-decadien-1-al dimethyl acetal (25b). δ 1.61 (6H, s, -CH_3), 1.69 (3H, s, -CH_3), 1.62-1.66 (2H, br, -CH_2-), 2.03 (6H, br, -CH_2-), 3.32 (6H, s, -OCH_3), 4.36 (1H, t, J = 6 Hz, -$CH(OMe)_2$), 5.09 (1H, t, br, J = 6 Hz, -CH=), 5.12 (1H, t, br, J = 6 Hz, -CH=); δ 15.95 (CH_3), 17.72 (CH_3), 23.14 (CH_2), 25.74 (CH_3), 26.70 (CH_2), 32.53 (CH_2), 39.72 (CH_2), 52.69 (CH_3 x 2), 104.13 (CH), 123.47 (CH), 124.34 (CH), 131.39 (C), 135.78 (C).

Preparation of ethyl 5,9-dimethyl-4,8-decadienoate (14). Linalool (770 mg, 5 mmol), triethyl orthoacetate (5.67 g, 35 mmol) and propionic acid (22 mg, 0.30 mmol) were mixed in a flask, equipped with a distillation set for the removal of MeOH formed during the reaction, and heated (oil bath 140 °C) for 24 h, then cooled to room temperature. The products were isolated by column chromatography and two compounds (42:58, by GC) were obtained in a combined yield of 74 % (772 mg). Further separation was done by repeated chromatography, and NMR spectra showed them to be the *Z* and *E* isomers **14a** and **14b**.

(*Z*)-14a. ^{1}H NMR δ 1.25 (3H, t, J = 7 Hz, -CH_3), 1.61 (3H, s, -CH_3), 1.68 (6H, s, -CH_3), 2.05 (4H, t, J = 3 Hz, -CH_2-), 2.32 (4H, t, J = 3 Hz, -CH_2-), 4.13 (2H, q, J = 7 Hz, -OCH_2-), 5.11 (2H, br, -CH=). ^{13}C NMR δ 14.26 (CH_3), 17.64 (CH_3), 23.39 (CH_3), 23.43 (CH_2), 25.71 (CH_3), 26.52 (CH_2), 31.89 (CH_2), 34.74 (CH_2), 60.23 (CH_2), 123.13 (CH), 124.15 (CH), 131.72 (C), 136.70 (C), 173.46 (CO).
(*E*)-14b. ^{1}H NMR δ 1.26 (3H, t, J = 7 Hz, -CH_3), 1.60 (3H, s, -CH_3), 1.62 (3H, s, -CH_3), 1.68 (3H, s, -CH_3), 1.95-2.10 (4H, m, -CH_2-), 2.32 (4H, t, J = 3 Hz, -CH_2-), 4.13 (2H, q, J = 7 Hz, -OCH_2-), 5.05–5.12 (2H, br, m, -CH=). ^{13}C NMR δ 14.27 (CH_3), 16.00 (CH_3), 17.70 (CH_3), 23.58 (CH_2), 25.70 (CH_3), 26.63 (CH_2), 34.56 (CH_2), 39.65 (CH_2), 60.24 (CH_2), 122.32 (CH), 124.18 (CH), 131.44 (C), 136.60 (C), 173.50 (CO).

Preparation of the mealybug pheromone analog.

2,6-Dimethyl-1,6-heptadien-3-one (12). In a flask fitted with a distillation set for the removal of MeOH, 2-methyl-2-propen-1-ol (4.31 g, 60 mmol), acetal **2** (5.27 g, 40.5 mmol) and *o*-nitrobenzoic acid (0.338 g, 2 mmol) were dissolved in xylene (10 ml), and the mixture was heated to 140 °C (oil bath) for 3 h, then cooled to room temperature. The product was separated by column chromatography and further purified by repeated chromatography (4.01 g, 72 %). ^{1}H NMR δ 1.75 (3H, s, -CH_3), 1.88 (3H, s, -CH_3), 2.32 (2H, t, J = 8 Hz, -CH_2-), 2.84 (2H, t, J = 8 Hz, -CH_2-),4.68 (1H, s, =CH_2), 4.74 (1H, s, =CH_2), 5.77 (1H, s, =CH_2), 5.98 (1H, s, =CH_2). ^{13}C NMR δ 17.63 (CH_3), 22.64 (CH_3), 32.15 (CH_2), 35.72 (CH_2), 110.04 (CH_2), 124.32 (CH_2), 144.53 (C), 144.80 (C), 201.46 (CO).

2,6-Dimethyl-1,6-heptadien-3-ol and its acetate (13, mealybug pheromone analog). To a suspension of $LiAlH_4$ (380 mg, 10 mmol) in dry diethyl ether (20 ml) was added dropwise ketone **12** (1.38 g, 10 mmol) in dry diethyl ether (10 ml) at room temperature and stirred for 0.5 h. The disappearance of the ketone was monitored by TLC, a mixture of $Na_2SO_4 \cdot 10H_2O$ and celite (4 g, 4:1, by weight) was added and stirred until the color turned to white after approx. 0.5 h. The mixture was filtered and dried with $MgSO_4$. The ether was evaporated to give the alcohol product,[8b] which was then mixed with $(CH_3CO)_2O$ (5 ml) and pyridine (4 ml) and left overnight. After column chromatography acetate **13** was obtained (1.65 g, 91%).

^{1}H and ^{13}C NMR for the alcohol: δ 1.58 variable.(1H, s, -OH), 1.65-1.72 (2H, m, -CH_2-), 1.74 (6H, s, -CH_3), 2.02-2.10 (2H, m, -CH_2-), 4.07 (1H, t, J = 6 Hz, -CHOH-), 4.71 (1H, s, =CH_2), 4.73 (1H, s, =CH_2), 4.85 (1H, s, =CH_2), 4.95 (1H, s, =CH_2). δ 17.61 (CH_3), 22.55 (CH_3), 32.87 (CH_2), 33.80 (CH_2), 75.67 (CH), 110.12 (CH), 111.16 (CH), 145.66 (C), 147.47 (C).
^{1}H and ^{13}C NMR for acetate **13**: δ 1.73 (6H, s, -CH_3), 1.78 (2H, m, -CH_2-), 2.00 (2H, t, J = 7 Hz, -CH_2-), 2.07 (3H, s, -CH_3), 4.68 (1H, s, =CH_2), 4.73 (1H, s, =CH_2), 4.90 (1H, s, =CH_2), 4.96 (1H, s, =CH_2), 5.17 (1H, t, J = 7 Hz, -CHOAc-). δ 18.11 (CH_3), 21.22 (CH_3), 22.52 (CH_3), 30.63 (CH_2), 33.46 (CH_2), 77.04 (CH), 110.29 (CH_2), 112.89 (CH_2), 143.08 (C), 144.86 (C), 170.34 (CO).

Preparation of 2, 5, 5-trimethyl-1, 6-heptadien-3-one (11). 3-Methyl-2-buten-1-ol (432 mg, 5 mmol), acetal **2** (670 mg, 5 mmol) and *o*-nitrobenzoic acid (168 mg, 1 mmol) were mixed with 1, 2, 4-trimethylbenzene (2 ml) in a flask fitted with a distillation set for the removal of methanol. The mixture was heated gradually to 170 °C, then cooled to room temperature. Product **11** (365 mg, 48 %) was isolated by column chromatography. ^{1}H NMR δ 1.12 (6H, s, -CH_3), 1.85 (3H, s, -CH_3), 2.68 (2H, s, -CH_2-), 4.91 (1H, d, J = 17 Hz, =CH_2), 4.93 (1H, d, J = 11Hz, =CH_2), 5.75 (1H, s, =CH_2), 5.88 (1H, s, =CH_2), 5.91 (1H, dd, J = 17, 11 Hz, -CH=). ^{13}C NMR δ 17.73 (CH_3), 27.21 (CH_3 x 2), 36.58 (C), 48.16 (CH_2), 110.39 (CH_2), 124.63 (CH_2), 146.03 (C), 147.52 (CH), 201.37 (CO).

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