Electrophilic cyclization of polyene allylsilanes. Synthesis of albicanyl acetate

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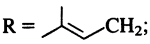
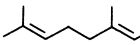
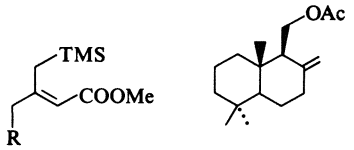
The allylsilanes **5** (*a*, R =  ; *b*, R = ) were prepared by a nickel(II) catalyzed coupling of trimethylsilylmethylmagnesium chloride with the enol phosphate of the corresponding β-keto esters. Stannic chloride and mercuric trifluoroacetate effected a cyclization of **5**. The product from **5***b* was converted into the marine natural product, albicanyl acetate (**1**).



5 **1**

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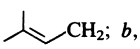
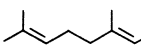
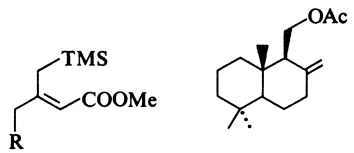
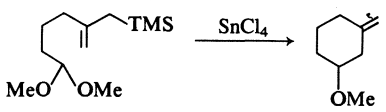
On a préparé les allylsilanes **5** (*a*, R =  ; *b*, R = ) grâce à un couplage, catalysé par le nickel(II), du chlorure de triméthylsilylméthylmagnesium avec le phosphate de l'énol des β-cétoesters correspondants. Le chlorure stannique et le trifluoroacétate mercurique ont un effet sur la cyclisation du composé **5**. On a transformé le produit obtenu à partir du composé **5***b* en acétate d'albicanyle (**1**), un produit naturel marin.



5 **1**

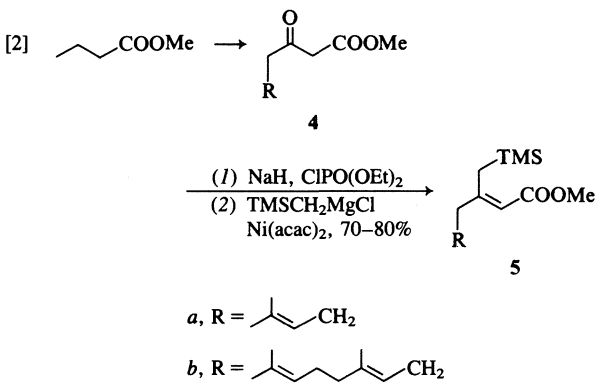
[Traduit par le journal]

Recent studies on the synthesis of allylic silanes and their cyclization (1) prompt us to report our results on the synthesis of carboxylated allylsilanes and their cyclization which has led to a synthesis of the marine sesquiterpene, albicanyl acetate (**1**) (2). In 1975, Fleming and co-workers found that the allylsilane **2** cyclized cleanly to the exocyclic product **3** (eq. [1]) (3). We were intrigued about the possibility of extending this concept to the cyclization of polyolefinic esters and acids.

[1] 

2 **3**

The esters **5***a* and **5***b* were synthesized from methyl acetoacetate as shown in eq. [2]. The β-keto esters **4** (4) were prepared by the alkylation of the dianion of methyl acetoacetate (5) with γ,γ-dimethylallyl bromide and geranyl bromide respec-

[2] 

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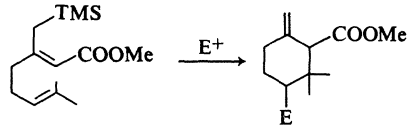
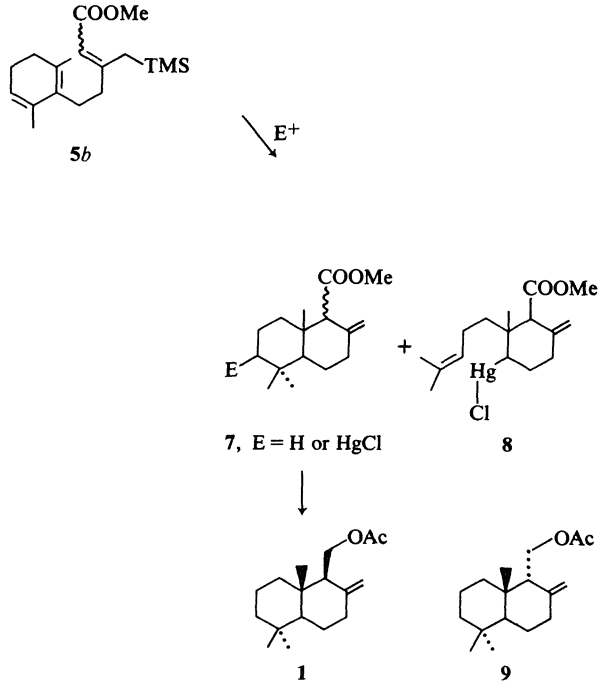
tively. Compounds **4***a* and **4***b* were converted into the *Z*-enol phosphates (6) in 95–100% yield. The enol phosphates were reacted with trimethylsilylmethylmagnesium chloride and nickel(II) bisacetylacetonate catalyst[3] (7) to give mainly the *Z*-allylsilanes **5** in 70–80% yield. The stereoselectivity was estimated from the ^{1}H nmr of **5***a* (*E*/*Z* = 1:20) and **5***b* (*E*/*Z* < 1:20). In addition we have prepared the *E*-enol phosphate from β-keto ester **4***b*[4] and coupled it with trimethylsilylmethylmagnesium chloride using $Ni(acac)_2$ catalyst to give **5***b* in 76% yield (*E*/*Z* = 7:3). The stereospecificity in this coupling is very different from that recently reported by Casey *et al.* for β-halo enoate esters (8).

We have studied a variety of electrophilic cyclizations of **5** and at this time note the results with Lewis acids and mercuric trifluoroacetate. Treatment of a CH_2Cl_2 solution of ester **5***a* with stannic chloride at 0°C gave the exocyclic alkene **6** (E = H) in ca. 90% yield. A gc analysis of the crude reaction product showed that ratio of exocyclic to endocyclic product was 7:1. Prolonged exposure of the reaction mixture to stannic chloride lead to isomerization of **6** (E = H) to the endocyclic β,γ-unsaturated compound. The ester **5***a* gave the organomercury product **6** (E = HgCl) in 84% yield on cyclization with mercury trifluoroacetate in nitromethane followed by an aqueous brine workup (9).



5*a* **6**, E = H or HgCl

Cyclization of **5***b* (>95% *Z*) in CH_2Cl_2 with stannic chloride at −56°C gave the 9β- and 9α-isomers **7** (E = H) in almost quantitative yield. The ratio of 9β-**7**/9α-**7** as determined by gc was 4:1. The structure of the major isomer was determined by reduction ($LiAlH_4$), chromatographic purification (10), and acetylation (Ac_2O, py, DMAP) to give (±)-albicanyl acetate (**1**) in 70% yield. The synthetic albicanyl acetate was identical to a natural sample (2) in spectral and chromatographic comparisons. The mercuric trifluoroacetate cyclization (9) of **5***b* gave a mixture of 9β- and 9α-**7** (E = HgCl) and monocyclic product **8**. The mixture could be purified by flash chromatography (10) to give 55–65% of the bicyclic products **7** (E = HgCl) and ca. 10% of **8**. The bicyclic products were analyzed by reduction ($LiAlH_4$) and acetylation (Ac_2O, py, DMAP) to give a mixture of (±)-albicanyl acetate (**1**) and its C-9 epimer **9** in a yield of 65–70% (**1**/**9** = 73:27).



5*b* **7**, E = H or HgCl **8** **1** **9**

The mixture of **5***b* containing mainly the 2*E* isomer (*E*/*Z* = 7:3) was cyclized with mercuric trifluoroacetate, reduced, and acetylated as above in 85% overall yield. A vpc analysis of the acetates showed that the ratio of **1**/**9** was 18:82. Thus the Hg^{2+} cyclization of the 2*E* and 2*Z* isomers of **5***b* is stereospecific and it would appear that the 9β-ester partially isomerizes to the 9α-ester under the cyclizing conditions or in the hydride reduction.

In summary the allylsilane activates conjugated esters in polyene cyclizations and they can be used to selectively produce exocyclic alkenes in electrophilic cyclizations initiated by protons or mercuric trifluoroacetate.[5]

[3]The coupling of β-phosphoryloxy alkenoate esters with Grignard reagents can be effected with Cu(I) or Ni(II) catalysts (J. P. Barnier, F. L. Harris, and L. Weiler, unpublished results). This extends the utility of our earlier reported alkene synthesis (ref. 6).

[4]The *E*-enol phosphates of β-keto esters can be prepared from the corresponding β-keto esters using triethylamine or 4-dimethylaminopyridine as base and a small amount of HMPA in the solvent system (F. W. Sum, Ph.D. Thesis, University of British Columbia, Vancouver, B.C., 1979 and W. McKay, F. W. Sum, and L. Weiler, unpublished results).

[5]All new compounds were characterized by ir, nmr, mass spectroscopy, and high resolution mass measurement or elemental analysis.

Acknowledgements

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Total synthesis of racemic 2-desoxystemodinone and stemodinol; the identity of natural "stemodinol" with stemarin

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Total syntheses of the naturally occurring diterpenoid 2-desoxystemodinone (**3**) and the diterpenoid structure **2** ("stemodinol") are described. The synthetic diterpenoid **2** was not identical to an authentic sample of "stemodinol". The authentic sample was found to be stemarin to which structure **2** had been erroneously assigned in the literature. It would appear that the diterpenoid represented by **2** has not been isolated from natural sources.

Ronald B. Kelly, Mary Lou Harley, Sandra J. Alward et Percy S. Manchand. Can. J. Chem. **60**, 675 (1982).

On décrit la synthèse totale du diterpènoïde naturel désoxy-2 stémodinone (**3**) et celle du diterpènoïde ayant la structure **2** ("stémodinol"). Le diterpène synthétique **2** ne correspond pas tout à fait à un échantillon authentique du "stémodinol". On a trouvé que l'échantillon authentique est de la stémarine à laquelle on a attribué par erreur la structure **2** dans la littérature. Il semble donc que le diterpène représenté par la structure **2** n'est pas d'origine naturelle.

[Traduit par le journal]

Recently we described (1) a total synthesis of the structurally unique diterpenoid stemarin (**1**) (2). This synthesis featured photoaddition of allene to an α,β-unsaturated ketone and two subsequent skeletal rearrangements. At the same time (1) we anticipated the completion of syntheses of stemodinol (**2**) (3) and related terpenoids (3, 4) and alphidicolin (5) by a similar strategy.[1] We now wish to describe syntheses of (±)-stemodinol (**2**) and the related diterpenoid (±)-2-desoxystemodinone (**3**) (2) as anticipated.

[1]For syntheses of aphidicolin and the stemodane diterpenoids by entirely different approaches see refs. 6 and 7 respectively.

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