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INTRAMOLECULAR DIELS–ALDER REACTIONS OF SILICON SUBSTITUTED DIENES
SYNTHESIS WITH HOMO-ALLYL SILANES

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Abstract—Metallation of 3-vinyl-5-trimethylsilyl-1-pentene (**16**) with *n*-BuLi gives a Si substituted pentadienyl anion reagent for bisannelation of *ortho*-alkenyl benzaldehydes. Tricyclic olefin **23b** produced by this method is a homo-allylsilane which undergoes protodesilylation to 4-vinyl-12-methoxy-18,19-bisnor-podocarpa-8,11,13-triene **24b**. The addition of β-(trimethylsilyl)ethyl magnesium bromide (**12**) to 12-methoxy-18,19-bisnor-5β-podocarpa-8,11,13-triene-4-one **27** gave the corresponding alcohol **29**. When **29** and related γ-hydroxy silanes are treated with acid, dehydration to allylsilane and protodesilylation to exocyclic vinyl compounds result. Alcohol **29** produces **24b** in 93% yield. Compound **24b** can be converted in several steps to podocarpic acid.

The Diels–Alder reaction is one of the most useful reactions in Organic Synthesis and in recent years the intramolecular variant has found increasing application.[1] Our own attention has focussed on the development of a general bisannelation strategy for the synthesis of polycyclic compounds.[2,3] This method involves the reaction of 3-substituted pentadienyl anions with suitable unsaturated aldehydes (eqn 1) to produce in one step, trienes capable of intramolecular Diels–Alder cyclization. We have applied the method to the synthesis of several sesquiterpenes.[3] While the general method proceeds admirably, the elaboration of tricyclic diterpenoid materials, such as **3**, poses a strategic problem. Most known diterpenes possess geminal-disubstitution at C-4 as exemplified by **4a,b**. The Diels–Alder construction requires, however, that C-4 be sp^2. The problem can be formulated as in eqn (2).

We felt that this problem might have a silicon solution that moreover would not compromise the flexibility of the Diels–Alder approach. The unique reactivity of allyl silanes has proven them to be functional groups with considerable potential for synthesis.[6] While quite stable thermally and unreactive toward many reagents, they react with electrophiles with well established allylic rearrangement. Thus they figured prominently in our early effort[7] to expand the scope of the Diels–Alder reaction by merging these two important chemistries. The Diels–Alder reaction of trimethylsilyisoprene **5** generates an allylic silane in the Diels–Alder adduct **6**. Thus protodesilylation produces an exocyclic olefin **7**. In principle this approach could provide a solution to the problem outlined in eqn (2) and we have carried out the preliminary experiment in eqn (3).[8]

A more intriguing possibility for geminal elaboration was suggested by the report of Sakurai[9] that homo-allyl silanes react with electrophiles to produce cyclopropyl compounds. This process would be ideal in the present case since the catalytic hydrogenation of spirocyclopropanes is a known method[10] for geminal dimethylation. When homo-allyl silane **8** was treated with acid, however, no cyclopropane **9** was formed (Scheme 1). The product was vinyl cyclohexane **10** (100% yield), formed by a very general protodesilylation reaction pathway for homo-allyl silanes which involves formation of a γ-silyl cation (**11**). *Loss of TMS as reported by Sakurai is not observed.* Instead the loss of a proton gives an intermediate allylsilane[11] **14** which undergoes subsequent protodesilylation to **10**. An alternate approach to the same cation **11** is also possible *via* γ-hydroxy silanes[12] now readily available using the new silicon reagent **12** we recently have reported.[13]

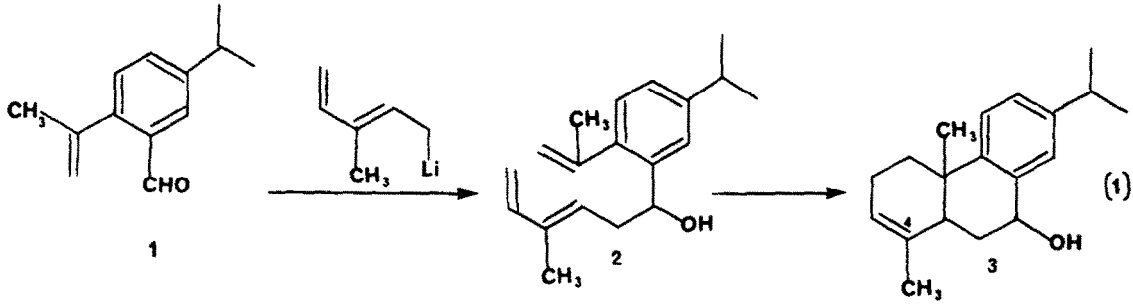
In the event, the protodesilylation of homo-allyl silanes can be seen to provide a solution to the problem posed in eqn (2).

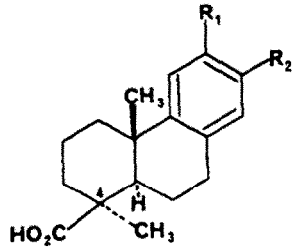
RESULTS

Application of this silicon methodology to the synthesis of podocarpic acid is now described. Podocarpic acid[5] **46** is a cheap and abundant natural product that has been synthesized many times[14] but serves in the present connection as a target for testing our Diels–Alder approach to Ring A via homo-allyl silanes. The bisannelation route (eqn 1) to polycyclic compounds requires an efficient method for the synthesis of 3-substituted-1,4-pentadienes. As a general rule, this is easily accomplished by alkylation of the parent anion at the central carbon.[3b] Conditions can usually be found for predominant C-3 alkylation. In the present case the reaction of **31** with (2-bromo ethyl)trimethylsilane **32** (0°, THF) gave 60% **16**, 40% **34** and a small amount of **33**, a not uncommon result for such an alkylation. Purification of **16** is however readily achieved by treatment of the crude reaction mixture with excess maleic anhydride. trans-Diene **33** disappears instantly (GC) while the reaction of **34** takes a few hours at room temperature. After the unwanted isomers have reacted, the mixture is extracted several times with NaOH to remove the anhydrides formed. In this way **16** can be obtained readily in 51% yield.

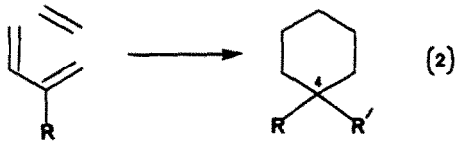
The key bisannelation reagent **15** can be prepared by metallation of 1,4-diene **16**. Reaction of **15** with 2-adamantanone yields **17** (28%), whose *E*-double bond can be established by comparison with many compounds in the 3-methyl series.[15] The reaction of reagent **15** with benzaldehyde also gives **18** (48%) as well as a small amount of the corresponding C-3 product. Thus silyl anion **15** is established as a viable reagent for the bisannelation outlined in eqn (1).

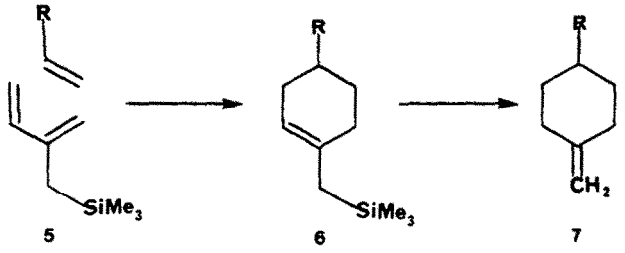
Applying the new approach we developed to *ortho*-alkenyl benzaldehydes,[16] **19a** and **19b** were prepared. When **19a** was allowed to react with **15**, **20a** was produced in 57% yield. Heating **20a** in toluene at 100° for

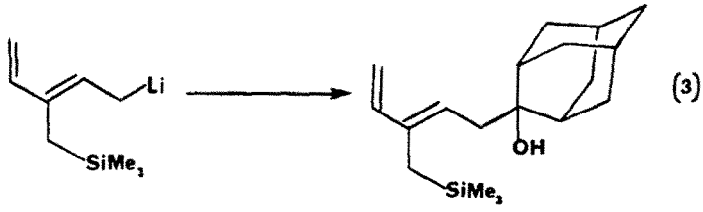




4a. callitrisic acid[4] (R_1=H, R_2=$CHMe_2$)
4b. podocarpic acid[5] (R_1=OH, R_2=H)

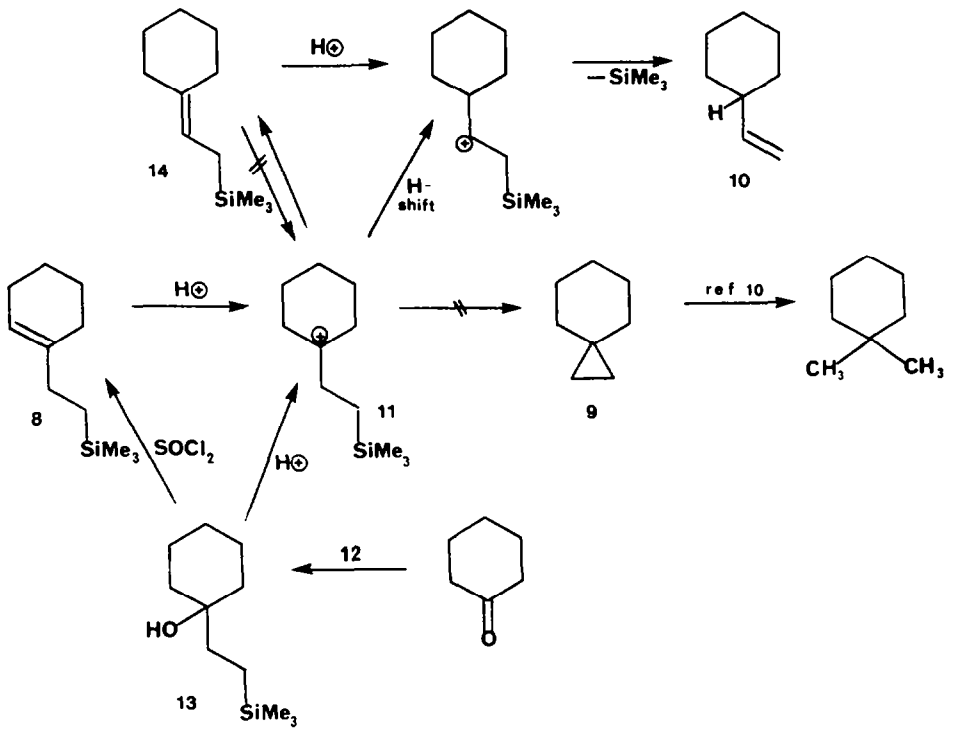




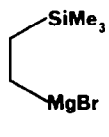


5.5 hr leads to smooth and quantitative cyclization to **21a** (isomers) as expected.[2] Acid treatment, however, did not give the expected loss of TMS but a compound (**22**) corresponding to dehydration of the benzylic alcohol followed by double bond isomerization. Fortunately, removal of the benzylic alcohol ($Na/NH_3/EtOH$) gave a hydrocarbon **23a** (85%) that underwent rapid protodesilylation giving **24a** (80%). The product **24a** is a mixture of isomers at C-4 and C-5 (*vide infra*).

Beginning with aldehyde **19b**, the addition of **15** gave alcohol **20b** as the exclusive product (37%). In this case protection of the benzylic alcohol as the OTMS group ($TMSCl/Et_3N$) was necessary before Diels–Alder cyclization. The benzylic TMS ether was directly removed yielding **23b** (30% overall from **20b**). Unfortunately **23b** proved to be a 4:1 mixture of *cis*/*trans*-isomers in which the *cis*-isomer predominates.[2] The structural assignment is discussed in more detail below, but for present pur-



Scheme I.



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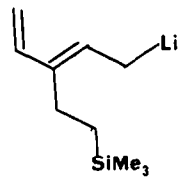

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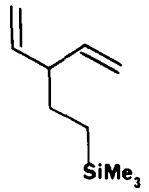

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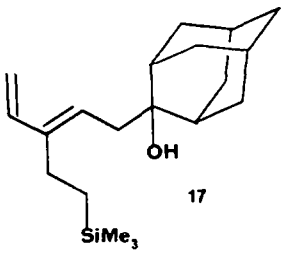

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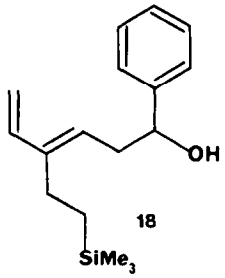

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poses the mixture was carried forward. When **23b** was treated with trifluoroacetic acid (25°, 1 hr) or with $BF_3 \cdot AcOH$ (−20°, 40 min) protodesilylation to **24b** occurred in 93% yield (4 isomers, 5:65 (two unresolved isomers): 30 ratio).

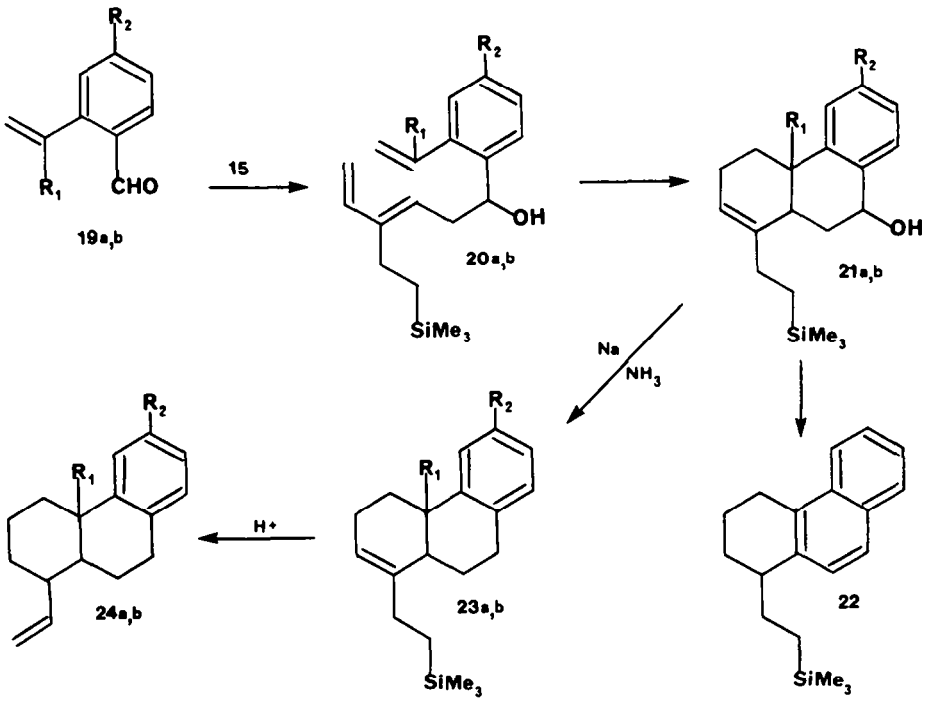
The stereochemical assignment of these isomers was possible when our alternate route to γ-silyl cations was discovered. We have recently reported[13] the preparation and use of a novel reagent **12**, that represents an "umpolung" of normal organo-Si reactivity (i.e. anions α to Si, cations β to Si). Compound **12** reacts with carbonyl electrophiles such as 2-adamantanone to produce γ-hydroxy silane **25**. Such alcohols serve as excellent precursors for the same γ-silyl cations available from homoallyl silanes. Treatment of **25** with $BF_3 \cdot AcOH$ thus provides **26** in 100% yield.

In the context of the present synthesis of podocarpic acid, known[17] ketones **27** and **28** were therefore required. Each corresponds to a configuration at C-5 present in the isomer mixture **23b**. When **27** was treated with "β-silyl anion" **12**, a single alcohol (**29**) could be isolated in 89% yield. The expected axial disposition of the OH group in **29** was confirmed by the chemical shift of the angular Me (δ 1.3) compared to the corresponding known[17] methyl carbinol isomers (δ 1.27 for axial alcohol, δ 1.15 for equatorial alcohol). When **29** was treated with $BF_3 \cdot AcOH$, **24b** was produced in 100% yield. GC and GC/MS analysis revealed that the major product from **29** (*trans* ring fusion) corresponds to the isomer from **23b** that comprises 30% of the mixture (*vide infra*).

Conversion of *trans*-**24b** (from **29**) into ester **42** proceded smoothly (71% overall). Compound **24b** was converted by oxidation of the vinyl to carboxylic acid ($KMnO_4/IO_4^-$) followed by diazomethane to ester **42**. The enolate of **42** has been alkylated to give **30**. Since **30**[14] has been converted into podocarpic acid **4b** this constitutes a formal synthesis of that substance.

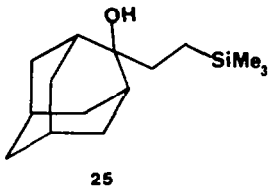
DISCUSSION

Preparation of the pentadienyl anion **15** is achieved by reaction of **16** with n-BuLi/THF. Over the course of 2–3 hr at 25° the red color characteristic of such delocalized anions (in THF) develops. We have reported[2,3,15] a



a. $R_1 = R_2 = H$
b. $R_1 = CH_3$, $R_2 = OCH_3$

Scheme II.



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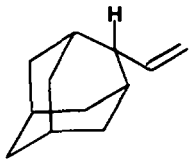

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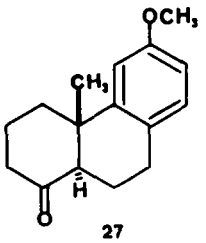

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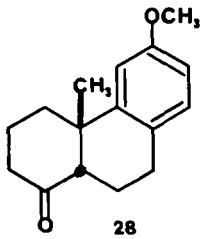

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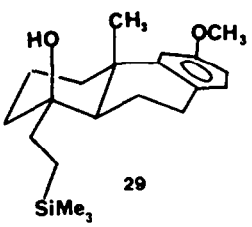

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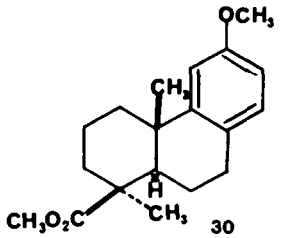

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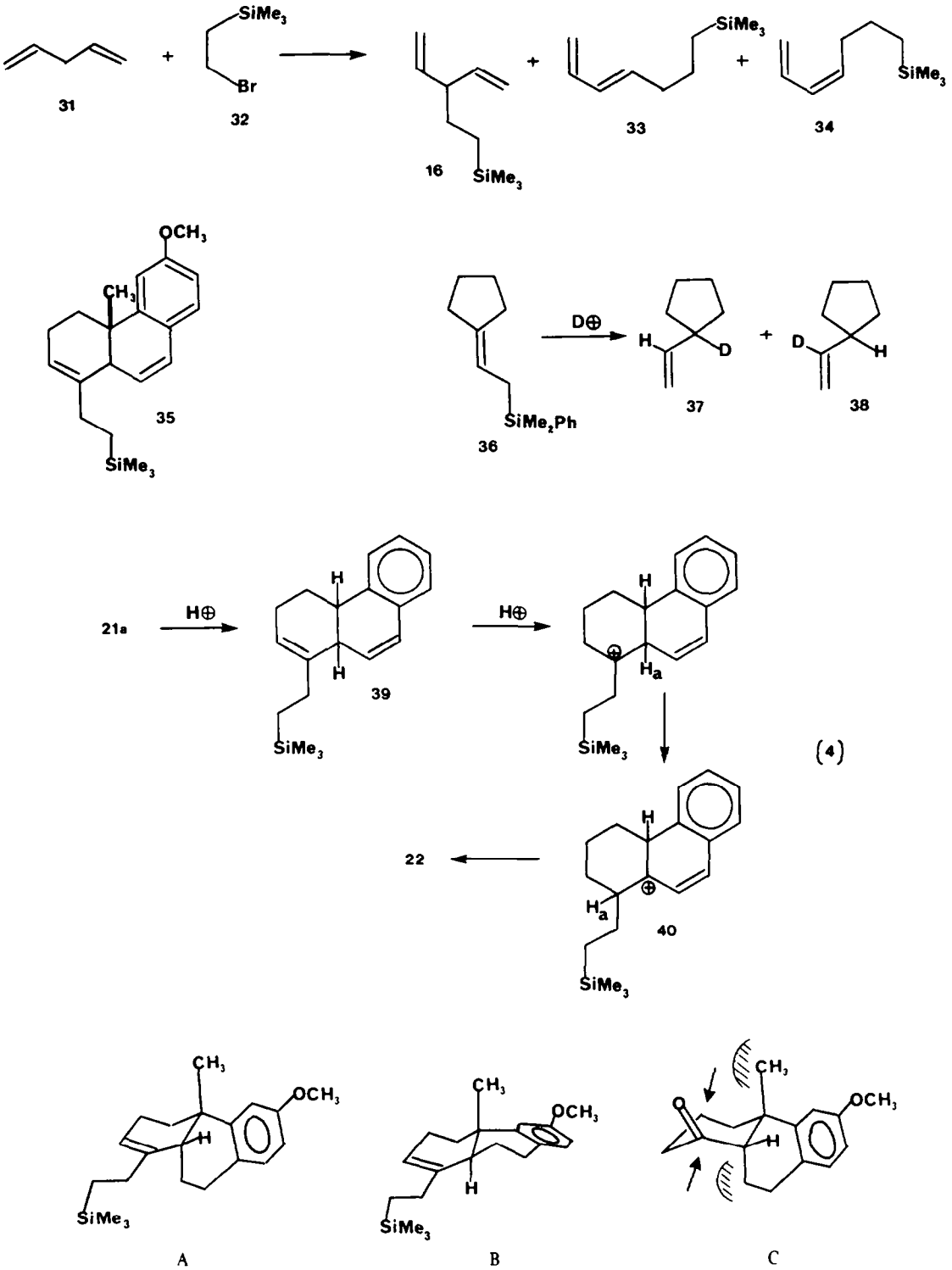
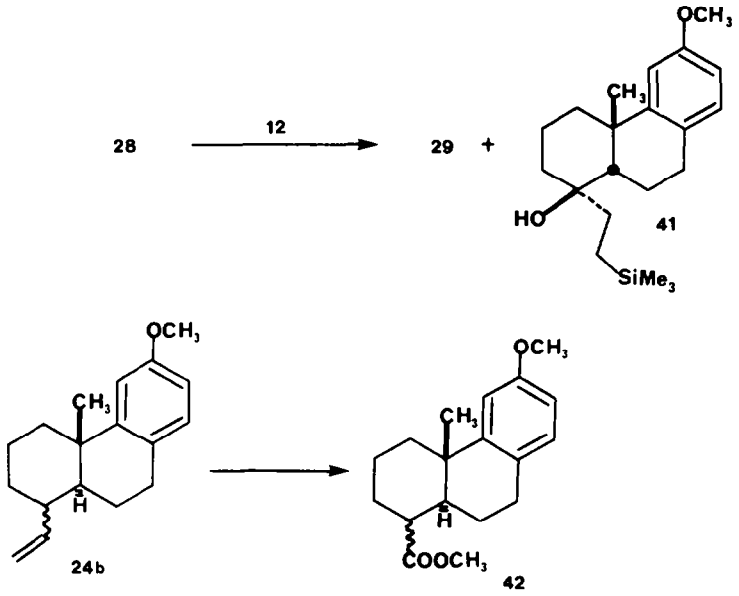


number of other 3-substituted pentadienyl anion reactions and **15** behaves similarly. Thus, with hindered electrophiles (2-adamantanone) only reaction at C-1 is observed, whereas unhindered electrophiles often give mixtures. *ortho*-Substituted benzaldehydes **19a** and **19b** however give >90% of the C-1 adduct. The *E*-double bond geometry of the dienes produced in this reaction is well precedented. The 220-MHz NMR spectrum of the dienes reveal a doublett-of-doubletts at δ 6.2–6.3 (J = 11, J = 17) of *E*-dienes and a very small < 5% doublett of doubletts at δ 6.5–6.6 (J = 11, J = 17) for the *Z*-diene.

Very conveniently, the C-1 adducts **18**, **20a**, **20b** also separate widely by tlc from the corresponding C-3 adducts, the latter being neopentyl. Thus, chromotagraphic separation of the isomers is easy if required.

The intramolecular Diels–Alder process has been discussed in similar systems.[2] The only comment that is necessary regards the ready loss in this system of the C-7 substituent during thermolysis to produce varying amounts of **35**. This is undoubtedly due to the *p*-OMe



group assisting formation of benzyl cation. Since the C-7 substituent was removed by Na/NH_3 reduction (a process that also reduces the C_6–C_7 double bond of **35**) no overall material loss was observed.

The central question of homo-allyl silane protodesilylation is now addressed. When **8** or **13** is treated with acid, vinyl cyclohexane **10** is produced in quantitative yield (Scheme 1). This compound is also formed from protonation of allysilane **14**.[19] Although it has been generally assumed that allyl silanes react *exclusively* to produce cations β to Si, Fleming[20] has recently established that in certain cases, when for instance the alternative cation is tertiary, protonation can occur to produce initially a γ-cation which undergoes hydride shift followed by loss of TMS. Compound **14** does not behave in this way but **36** was reported by Fleming[20] to produce **37** and **38** in 50:50 ratio.

In the tricyclic cases, attempted protodesilylation of **21a** gave instead compound **22** with no loss of TMS. One explanation involves rapid dehydration of the C-7 OH to give **39** (eqn 4). Protonation of **39** yields a γ-silylcation which now has the opportunity to migrate a tertiary allylic H (Ha) giving cation **40**. Proton loss gives the aromatized compound **22**. When the C-7 OH group is removed (i.e. **23a**) this pathway is no longer so favorable and the γ-silyl cation rearranges to a β-silyl cation which loses the TMS group.

Protonation of **23b** was studied most carefully since it serves as the nucleus for podocarpic acid. Compound **23b** was obtained as an 80:20 mixture of *cis*/*trans*-isomers at the ring fusion. The stereochemistry was established by comparison of the NMR signals of the angular Me group (δ 1.28 for the *cis*-isomer and δ 1.05 for the *trans*-isomer) with a number of known derivatives of this type.[21] The lower field Me signal in *cis*-**23b** is attributed to deshielding by the aromatic C-ring (Fig. A) relative to that of *trans*-**23b** (Fig. B).

When this 80:20 mixture is protodesilylated, an olefin mixture **24b** is formed that shows three peaks by GC (OV101, programmed at 120° (1 min) then 5°/min to 300°) at retention time = 10.4, 11.9 and 12.6 min (5:65:30) ratio. When alcohol **29** is treated with acid only two isomers (*trans*-ring fusion but epimeric vinyls) are formed at retention time = 11.9 and 12.6 min (1:2 ratio).

The γ-hydroxy silane with *cis*-ring fusion (corresponding to the major isomer of **23b**) was difficult to obtain. Although ketone **28** is more stable than **27**, the CO group is evidently more hindered, due to an axial β-Me on one side and an axial α-ring carbon[22] on the other (Fig. C). Thus, *enolization* is the major pathway of reaction of **28** with Grignard **12** (62% recovered **28**). Two alcohols could be isolated, however, in 20% and 18% yield. The first of these proved to be *cis*-isomer **41** while the second was identical with *trans*-alcohol **29**: Epimerization and reaction of the epimeric ketone with Wittig reagents or MeLi is known.[23] Protodesilylation of **41** occurs smoothly to produce two **24b** isomers at retention time = 10.4 min (15%) and 11.9 min (85%) with a *cis*-ring fusion but epimeric vinyls. Thus, the GC peak of **24b** at 11.9 is shown to consist of 2 unresolved isomers.[27]

In summary, we have established that cations generated γ-to Si, whether derived via homoallylsilanes or γ-hydroxysilanes, protodesilylate in the same manner as allyl silanes. The inert-CH_2CH_2TMS grouping thus may serve as a vinyl synthon in certain cases.

EXPERIMENTAL

NMR spectra were recorded on Varian HR-220, T-60A or EM360 spectrometers. Chemical shifts are reported in ppm downfield from internal TMS (or the trimethylsilyl of the CH_2CH_2TMS present in the molecule). Mass spectra were recorded on a Hewlett-Packard 5992 GC/MS or Dupont 21-4928 mass spectrometers and IR spectra on a Perkin–Elmer 137. Analytical gas chromatography was performed with a Varian Model 3700 with a 1.5% OV-101 (Chromasorb G) column (5′ × 1/8″) with the temp or program indicated. Distillations were performed with a Buchi/Brinkman microdistillation oven and b.ps are approximate. TLC used Baker-flex silica gel plates and R_f values are followed by the eluting solvent in parentheses.

Preparation of compound **16**. A soln of 1,4-pentadiene (1.7 g, 17.2 mmol) in 2 ml dry THF was cooled to −78° under N_2. To this magnetically stirred soln was added 6 ml n-BuLi (2.4 M, 14.4 mmol) dropwise. The mixture was warmed to room temp, stirred 1 hr, diluted with 8 ml THF and then cooled to 0°. A soln of **32**,[24,25] (2.07 g, 11.4 mmol) in 10 ml dry THF was added dropwise

over a period of 30 min. After stirring for a further 15 min the mixture was quenched with water. Usual workup gave after bulb-to-bulb distillation 1.65 gm (86%) colorless liquid containing 60% **16** and 40% of a mixture of *E*-and *Z*-isomers (**33**, **34**). The mixture was stirred overnight at room temp with excess maleic anhydride in ether. The Diels–Alder adducts and excess maleic anhydride were hydrolyzed by stirring with 1N NaOH soln. Bulb-to-bulb distillation gave pure **16** (51%) R_f = .88 (pentane), GC (80°): 2.4 min. IR(neat) 6.12, 8.05, 10.95 μ, NMR ($CDCl_3$) δ 5.8 (2H, m), 5.1 (4H m), 2.65 (1H m), 1.41 (2H m), .55 (2H m), 0 (9H S), MS m/e (rel, intensity) (M^+ not observed), 140 (7), 125 (15), 101 (62), 74 (28), 73 (100), 59 (36), Calc. for $C_{10}H_{20}Si$: 168.13342. Found: 168.13304.

The ratio of the *E*-and *Z*-isomers **33** and **34** varies slightly depending on the reaction conditions. The *Z*-isomer **34** predominates and reacts with maleic anhydride much more slowly than **33**. In one experiment, pure **34** was isolated by preparative GC and its structure was established by the following spectral data: IR(neat) 6.05, 8.0, 10.0 μ, NMR ($CDCl_3$) δ 6.32 (1H m), 6.07 (d, d J = 16, 11 Hz, 1H), 5.7 (1H m), 5.02 (2H m), 2.1 (2H m), 1.43 (2H m), .53 (2H m), 0 (9H S), MS *m/e* (rel. intensity) 168 (14), 140 (15), 125 (15), 101 (46), 74 (31), 73 (100), 59 (47) Calc. for $C_{10}H_{20}Si$: 168.13342. Found: 168.13337.

Preparation of 3(2' *trimethylsilylethyl*) *pentadienyl anion* **15**. A soln of 168 mg (1 mmol) of **16** in dry THF was cooled to −78° under N_2 and stirred magnetically. To this soln was added .33 ml n-BuLi soln (2.4 M in hexane, .8 mmol) dropwise. Stirring was continued at this temp for 15 min, then for 30 min at 0°, and finally for 2 hr at room temp. When the stirring was stopped, two layers formed. The upper layer contains mostly hexane and was discarded. The lower THF layer containing the anion **15** was diluted with 0.5 ml THF and cooled to −78° before use.

Preparation of compound **17**. A soln of 2-adamantanone (90 mg, .6 mmol) in .5 ml THF was added dropwise to a THF soln containing .8 mmol of the anion **15** at −78°. The mixture was warmed up to 0°, stirred 15 min and then quenched with 1 ml cold water. GC of the crude product showed the formation of a single compound. The crude product was purified by preparative tlc (10% Et_2O/pentane) to give 50 mg (28%) **17**.

R_f = .2(10% Et_2O/pentane), GC(100°) 4.95 min. IR (heat) 2.8, 6.22, 6.85, 8.02, 11.6, 11.95 μ NMR ($CDCl_3$) 6.3 (1H dd J = 17 and 11 Hz) 5.5 (1H t, J = 8 Hz) 4.85–5.22 (2H, m), 2.5 (2H d J = 8Hz), 2.04–2.2 (2H m) 1.6–1.9 (14H m), 1.05–1.5 (2H m), 0.45–0.65 (2H, M) 0 (9H s) calc. for $C_{20}H_{34}OSi$-H_2O (M^+ absent): 300.22733. Found: 300.22733.

Preparation of compound **18**. Benzaldehyde (distilled, 42.5 mg, 0.4 mmol) was reacted with **15** as described for 17. The crude product was purified by short column chromatography to give pure **18** (48%).

R_f = 0.38 (20%Et_2O/pentane) GC (80°) 6.5 min. IR (neat 2.85, 6.1, 6.2, 8.02, 11.6, 11.95 μ NMR ($CDCl_3$) δ 7.35 (5H, bs.) 6.26 (dd J = 17 and 10 Hz, 1H) 5.4 (1H, t J = 8 Hz), 4.68–5.05 (3H m), 2.57 (2H t J = Hz) 0.55 (H, m) 0(9H, s). Calc. for $C_{17}H_{26}OSi$: 274.17529. Found: 274.17516.

Preparation of compound **20a**. A soln of *ortho*-vinyl benzaldehyde **19a**[16] (400 mg, 3 mmol) in 10 ml dry THF was reacted with **15** as described for **17**. The product mixture was purified by short column chromatography to give 492 mg pure **20a** (54%).

R_f = .32 (10% ether/pentane) GC (150°–5 min.–25°/min–300°) 8.7 min. IR (neat) 2.9, 6.3, 8.1, 9.15, 10.15, 11.7, 12.1 μ NMR ($CDCl_3$), δ 7.38 (m 2H) 7.16 (m 2H) 6.95 (dd, J = 17 and 11 Hz, 1H), 6.14 (dd, J = 17, 11 Hz, 1H) 5.52 (d, J = 17 Hz 1H) 5.36 (t, J = 3.5 Hz, 1H) 5.2 (d, J = 11 Hz, 1H) 4.93 (m, 3H), 2.45 (t, J = 5 Hz, 2H), 2.3 (m 1H), 2.08 (t, J = 7, 2H), 1.11 (t, J = 5 Hz, 2H), 0.51 (m 2H), O (S, 9H).

MS *m/e* (rel intensity), 300 (9) 283 (26) 282 (100) 208 (50) 181 (87) 180 (58) 167 (33) 141 (48) 128 (25). Cacl. for $C_{19}H_{28}SiO$: 300.19092. Found: 300.19070.

Preparation of **20b**. A soln of **19b**[16] (2.51 g, 14.3 mmol) in 10 ml dry THF was reacted with **15** as described for **17**. GC analysis showed the formation of a single isomer **20b**. The crude product was passed through a bed of silica gel to remove polymeric dienes and other polar impurities and was further purified by short column chromatography to yield 1.82 g (37%) compound **20b**

R_f (10% ether/pentane) = 0.31, GC (200° – 2 min–25°/min–300°) 4.2 min. IR(neat), 2.82 (broad), 6.15, 6.65, 6.82, 7.7, 8.0, 8.2, 9.55 (broad), 10.05, 11.6 (broad), 12.0 (broad) μ NMR ($CDCl_3$), δ 7.45 (d J = 9 Hz, 1H), 6.82 (dd, J = 9 and 3 Hz, 1H), 6.63 (d, J = 3 Hz 1H), 6.24 (dd, J = 17, 11 Hz, 1H), 5.4 (t, J = 7 Hz 1H), 4.7–5.3 (m, 4H) 3.8 (s, 3H) 2.75 (t, J = 7, Hz 2H), 1.8–2.3 (m, 1H) 2.05 (s, 3H), 1.2 (t, J = 7, Hz 2H) 0.4–0.7 (m, 2H) 0.0 (s, 9H).

Preparation of compound **21a**. 800 mg (2.66 mmol) of **20a** was dissolved in 12 ml distilled toluene and sealed under N_2 in a pyrex tube prewashed with conc NH_4OH aq. The tube was heated at 100° for 5 hr to produce *ca* 800 mg **21a** as a mixture of isomers (The *cis*/*trans* ratio was determined after conversion to **23a**). R_f (10% ether/pentane) = 0.22 GC (150°–5 min–25/min–300°) 8.2 min (plus shoulders) IR(neat) 2.80 6.9, 7.24, 8.0, 8.94 (strong), 11.55, 11.82 μ NMR ($CDCl_3$) δ 7.55 (m, 1H) 7.36 (m, 1H) 7.18 (m, 2H) 5.5 (bs., 1H) 4.75 (dd, J = 10, 6 Hz, 1H) 2.77 (m, 1H) 2.38 (m, 1H), 1.16–1.24 (m, 2H) 0.47–0.78 (m, 2H) 0.0 (s, 9H) MS. *m/e* (rel. intensity) 300.2 (0.4), 282 (10.5) 181 (16) 180 (11) 141 (11) 75 (15) 73 (100) 57 (9) 45 (12) Calc. for $C_{19}H_{28}OSi$: 300.19092 Found: 300.19098.

Attempted protodesilylation of **21a**. A soln of 15 mg of **21a** was dissolved in 2 ml ice-cold ether saturated with HCl. After stirring at room temp for 1 hr the mixture was washed twice with 2 ml portions of 5 $NaHCO_3$ aq and water, dried over $MgSO_4$ and the solvent evaporated. GC showed the absence of the starting material and formation of a single compound (**22**).

GC (200°—2 min—25/min—300°) 3.6 min (vs starting material at 4.2 min) GCMS *m/e* (rel. intensity). 282 (3.4) 181 (6.6) 180 (5.7) 141 (8.3) 73 (100) 59 (15.3) 45 (16.6).

Preparation of compound **23a**. Anhyd ammonia was condensed in a 3-necked 50 ml flask with dry ice condenser (10 to 12 ml). A soln of **21a** (300 mg, 1 mmol) in about 2 ml dry THF and 0.3 ml (5 mmol) EtOH was added. Metallic Na (0.115 g, 5 mmol) was added to the flask in small portions over a period of 15 min. After each addition, a blue color developed that disappeared after several minutes of stirring. After 1 hr the mixture was allowed to warm to room temp as the ammonia evaporated, and was subsequently quenched with 10 g ice. The product was extracted three times with 10 ml portions of ether and the ether washed with water, dried over $MgSO_4$ and evaporated to yield 240 mg compound **23a** (85%).

R_f (10%Et_2O/pentane) = 0.9. GC (150°—5 min. 25°/min.—300°) *cis* = 8.2 min, *trans* = 8.4 min (the *cis*/*trans* ratio ~65.35) IR (neat) 6.72, 6.92, 8.05, 11.6, 12.0 μ NMR ($CDCl_3$) 7.0–7.3 (m, 4H) 5.5 (bs, 1H) 2.73–2.95 (m, 2H), 2.38–2.6 (m, 1H) 0.47–0.79 (m, 2H) 0.0 (s, 9H) MS *m/e* (rel. intensity) *cis*: 284 (9) 210 (5) 183 (6) 141 (5) 73 (100) 59 (16) *trans*: 184 (13) 210 (3) 183 (19) 141 (7) 73 (100) 59 (16) Calc. for $C_{19}H_{28}Si$: 284.19601 Found: 284.19605.

Preparation of compound **24a**. Compound **23a** (540 mg 1.9 mmol) was cooled to 0° under N_2 and 5 ml trifluoracetic acid was added. After stirring for 2 hr, the mixture was diluted with 15 ml ether, washed three times with 10 ml portions of 5% $NaHCO_3$ aq and twice with water, dried over $MgSO_4$, and the solvent evaporated. The crude product was purified by preparative TLC to give 322.5 mg (1.52 mmol, 80%) compound **24a**.

R_f (pentane) = 0.49 GC (120°—1 min 20°/min—300°) 4.14 min (at least three isomers) IR (neat) 6.1, 6.72, 6.9, 8.04, 11.0, 13.18, 13.62 μ NMR ($CDCl_3$) 6.91–7.22 (m, 4H) 5.70–5.84 (m, 1H) 4.86–5.15 (m, 2H) 2.50–2.88 (m, 3H) MS *m/e* (rel. intensity) 212 (100) 183 (42) 144 (36) 143 (30) 142(66) 141 (53) 130 (37) 129 (70) 128 (48) 117 (41) 115 (37) 91 (20) Calc. for $C_{16}H_{20}$: 212.15650 Found: 212.15301.

Preparation of **23b** *from* **20b**. To an ice-cooled soln of **20b** (1.8 g, 5.24 mmol) in 25 ml dry THF was added 7 ml (~50 mmol) of distilled Et_3N followed by 6.5 ml (~50 mmol) of freshly distilled trimethylsilyl chloride. After warming to room temp, the contents were stirred for 4 hr at which time GC analysis showed complete disappearance of the starting material. Volatile materials were removed on a rotary evaporator and the residue extracted four times with 15 ml portions of dry toluene. The extracts were filtered through celite, concentrated to about 10 ml and transferred to a

pyrex tube (prewashed with conc NH_4OH). The tube was sealed and heated at 170° for 20 hr. GC analysis showed complete conversion of the starting material to the Diels–Alder adduct. The trimethylsiloxy group was then removed by Na in liquid ammonia as described for **23a**. The crude product was purified by short column chromatography to give pure **23b** in 30% overall yield.

R_f (2% Et_2O/pentane) = 0.55 GC (150°—1 min 20/min—300°) *cis*/*trans* ratio 4:1, *cis* = 5.67 min *trans* = 5.87 min IR (neat) 6.22, 6.35, 6.7, 6.85, 7.85, 8.08, 8.3, 8.56, 9.62, 11.65, 12.05. NMR ($CDCl_3$) 6.6–7.1 (m 3H), 5.35–5.55 (m 1H) 3.8 (S 3H) 2.55–2.8 (m 2H) 1.28 (s, 12/5 H), 1.05 (s, 3/5 H) MS *m/e* (rel. intensity) cis: 328.2 (100) 314 (16) 313 (61) 239 (17.4) 227 (34) 174 (30) 121 (6) 73 (81) *trans*: 328.2 (100) 314 (20) 313 (73) 239 (23) 227 (24) 174 (10) 121 (22) 73 (80). Calcd. for $C_{21}H_{32}SiO$: 328.22232 Found: 328.22223.

Preparation of **24b** *by protodesilylation of* **23b**. A soln of 200 mg of **23b** in 20 ml CH_2Cl_2 was cooled to −20° under N_2 and stirred magnetically. About 250 mg of BF_3-AcOH complex[26] was added and the stirring continued for 1.5 hr at which time GC analysis showed the absence of starting material. The mixture was quenched with 5 ml 5% $NaHCO_3$ aq, diluted with 15 ml Et_2O, washed with 5% $NaHCO_3$ aq, water, dried over K_2CO_3, filtered and evaporated yielding 93% (GC) of compound **24b** as a mixture of isomers.

R_f (2% ether/pentane) = 0.53, (pentane) = 0.16. GC (150°—1 min 20°/min 300°) isomers: 3.2, 4.2, 4.6 min (120°—1 min 5°/min—300°) isomers: 10.48, 11.9, 12.6 min. (5:65: 30 ratio) IR (neat) 6.1, 6.2, 6.35, 6.7, 6.85, 7.8, 8.05, 9.62, 11.05, 13.7, NMR ($CDCl_3$) 6.6–7.1 (m 3H), 5.7–6.3 (m 1H) 4.85–5.25 (m 2H) 3.81 (S 3H) 2.7–3.0 (m 2H) MS *m/e* (rel intensity): 256 (100) 241 (38) 227 (20) 185 (19) 174 (39) 173 (30) 171 (33) 156 (20) 147 (32) 121 (32) for the isomer at 11.9 min. Calcd. for $C_{18}H_{24}O$: 256.18271 Found: 256.17600.

Preparation of ester **42**. To a soln of *trans*- **24b** (51 mg 0.2 mmol; from **29**) in 10 ml t-BuOH was added a soln of 9 mg $KMnO_4$, 396 mg K_2CO_3, 520 mg $NaIO_4$, and 10 ml water. The mixture was stirred at room temp overnight (16 hr). The mixture was then diluted with 10 ml water, washed with CH_2Cl_2 and acidified with conc HCl. The acid was then extracted 3 times with 10 ml portions of CH_2Cl_2, washed with sat NaCl aq, dried over $MgSO_4$ and solvent evaporated to give 48 mg crude solid acid (88%). The acid was then converted to ester with diazomethane. Separation by prep. tlc gave 71% yield of the ester **42** (based on **24b**).

R_f (*20% ether/pentane*) = 0.41 GC (150°—1 min. 20°/min—300°) 5.22 min. IR (neat): 5.84, 6.2, 6.65, 6.68, 8.02, 8.98, 9.62, 9.8 μ NMR ($CDCl_3$): 6.6–7.1 m 3H), 3.80 (S, 3H) 3.72 (s, 3H) 2.60–2.95 (m 3H) 1.36 (s, 3H) MS *m/e* (rel. intensity):288 (M^+; 100) 257 (1) 256 (38) 229 (26) 228 (62) 213 (64) 185 (23) 173 (22) 171 (24) 134 (78) 128 (11) Calc. for $C_{18}H_{24}O_3$: 288.1725. Found: 288.0955.

Preparation of Grignard **12**. 96.3 g **32**[24,25] was dissolved in 200 ml dry ether and added dropwise to a mixture of 18 g Mg and 300 ml dry ether. The temp increased rapidly and ice cooling was required. After 1.5 hr the reaction was complete and 5.2 g unreacted Mg remained. The supernatant ether solution of **12** was transferred to serum-capped bottles and kept at −10° in the the freezer. The reagent is stable at this temp for months.

Preparation of compound **25**. A soln of 500 mg (3.33 mmol) 2-adamantanone (Aldrich) was added dropwise at room temp to 15 ml of the soln of Grignard reagent prepared above. After 15–20 min stirring the mixture was poured into 10% H_2SO_4/ice and extracted twice with ether. The ether layer was dried ($MgSO_4$) and evaporated and the residue chromatographed (1:9, EtOAc: hexane) to yield 35% **25**, m.p. 87–89°. GC (60°—1 min—20°/min—300°) 8.57 min NMR (CCl_4) 1.5–2.3 (m, 15H), 1.1–1.5 (m, 2H), 0.2–0.6 (m, 2H), 0.0 (s, 9H). MS: *m/e* (rel. intensity) no M^+, 237 (2), 233 (20), 151 (100), 150 (22), 91 (18), 75 (56), 73 (45) Calc. for $C_{15}H_{28}OSi$: 11.11 H, 71.43 C, Found: 11.12 H, 71.51 C.

Preparation of compound **29**. A soln of 220 mg (0.9 mmol) of **27**[17] was reacted with Grignard **12** in the same manner as in the preparation of **25**. Alcohol **29** was produced quantitatively. GC (120°—1 min—20°/min—300°) 8.08 min NMR ($CDCl_3$) δ 6.5–7.2 (m, 3H), 3.7(s, 3H), 1.3 (s, 3H), 1.0–2.0 (m), 0.8–1 (m, 2H), 0.1–0.5 (m, 2H), 0 (s, 9H). MS *m/e* (rel. intensity) 346 (39), 246 (20), 245 (97), 244 (69), 229 (23), 227 (100), 173 (29), 161 (43), 73 (32). Calc. for $C_{21}H_{34}SiO_2$: 346.23279. Found: 346.22538.

Preparation of compound **41**. A soln of 70 mg (0.3 mmol) *cis*-**28**[17] was reacted with Grignard **12** in the usual manner. GC analysis of the product showed (program 120°—1 min—20°/min—300°). 62% recovered starting **28**, 20% *trans*- **29** (8.08 min.) and 18% *cis*- **41** (7.60 min.). Tlc (5: 95 ethyl acetate: hexane) showed three spots for **28** (R_f = 0.21), **29** (R_f = 0.33) and **41** (R_f = 0.47). Preparative tlc gave pure **41** *ca.* 15 mg. MS *m/e* (rel. intensity) 346 (7), 329 (30), 328 (100), 313 (20), 227 (41), 174 (28), 73 (49).

Dehydration/protodesilylation of **29**. A soln of 50 mg (0.14 mmol) **29** in 5 ml CH_2Cl_2 was cooled to −20° and treated with a few crystals of BF_3-AcOH. After 30 min GC analysis showed no starting material remaining. Two peaks were formed in quantitative yield based on an internal GC standard. These peaks were identical with **24b** isomers of retention times 11.9 and 12.6 min (1:2 ratio, program: 120°—1 min—5°/min—300°).

Dehydration/protodesilylation of **25**. Compound **25** was reacted with BF_3-AcOH in CH_2Cl_2 in the same manner as **29** to yield **26** quantitatively. GC (60°—1 min—20°/min—300°) 5.39 min IR (neat) 3.2, 3.3, 6.2, 8.05, 9.1, 10.1, 11.0 μ. NMR ($CDCl_3$) 5.8–8.4 (m, 1H), 4.8–5.1 (m, 2H), 1.5–2.2 (m, 15H). MS *m/e* (rel. intensity) 162 (100), 133 (22), 120 (17), 119 (23), 107 (16), 22 (106), 105 (36), 93 (28), 93 (32), 91 (60), 80 (25), 79 (67), 78 (15), 77 (33). Calc. for $C_{12}H_{18}$ 11.12 H, 88.88 C, Found: 11.31 H, 88.60 C.

Dehydration/protodesilylation of **41**. Treatment of *ca.* 15 mg of **41** with BF_3-AcOH in the same manner as **29** gave the two isomers of **24b** of retention time = 10.4 and 11.9 min (15.85 ratio, program: 120°—1 min—5°/min—300°).

Protodesilylation of **8**. Compound **8** (prepared by $SOCl_2$ dehydration of **13**[13] and containing *ca* 20% of **14**) was treated in CH_2Cl_2 with BF_3-AcOH. After 5 min at 0° no starting material remained. The only volatile product was **10**. MS: *m/e* (rel. intensity) 110 (19), 95 (17), 82 (36), 81 (100), 69 (12), 68 (23), 67 (77), 54 (35), 41 (47). NMR ($CDCl_3$) 5.5–6.2 (1H, m) 4.8–5.3 (2H, m).

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