Syntheses of Theaspirone and Vitispirane *via* Palladium(II)-Catalyzed Oxaspirocyclization

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Total syntheses of theaspirone (A and B) and vitispirane (A and B) are described. The key step in the syntheses is the palladium(II)-catalyzed intramolecular oxaspirocyclization of diene alcohol **4** to either vitispirane or the allylic alcohol **9**. The outcome of the oxaspirocyclization is very much dependent on the solvent employed. In water−acetic acid (4:1) a 1:1 mixture of the diastereomeric alcohols **9A** and **9B** was exclusively formed. In water with 8 equiv of a strong non-nucleophilic acid, vitispiranes A and B (1:1) were obtained. An alternative procedure to obtain vitispirane with the use of LiCl and K_2CO_3 is described. In the latter reaction vitispirane B is formed preferentially. This result is explained by an equilibrium between the two possible π-allyl complexes **5A** and **5B**, the kinetically favored **5B** being transformed into vitispirane **3B** before isomerization to **5A** occurs.

Introduction

Theaspirone (**1**) was the first spiro ether isolated from black tea.[1] Oak woods used in wine and spirit maturation as well as yellow passion fruit are other sources for theaspirone.[2] In nature, it occurs as a mixture of isomers, A and B. Theaspirone A has a sweet, tea-like odor while theaspirone B has a more earthy smell.[3] Theaspirane (**2**), found for the first time as a naturally occurring substance in raspberry,[4] is also present in yellow passion fruit. Vitispirane (**3**) is a structurally related compound identified among the volatiles of grape juice or distilled white wines.[5] It also occurs in quince fruit and vanilla aroma.[5,6] Vitispirane together with theaspirone and theaspirane belong to a class of norisoprenoid spiro ethers existing in nature in both the A and B forms (Figure 1). Ever since their isolation these compounds have been popular synthetic targets.[4,6,7]

The palladium-catalyzed intramolecular 1,4-addition of nucleophiles to conjugated dienes is a useful method for constructing heterocyclic systems.[8] We have recently developed an oxaspirocyclization of dienes **I** catalyzed by palladium(II), for the formation of [5,6], [5,7], [6,6], and [6,7] spiro ethers (**III**).[9] The first step in the catalytic cycle involves a regioselective oxypalladation of the trisubstituted double bond in **I** to give spirocyclic (π-allyl)-palladium complex **II** as an intermediate. This complex undergoes a *p*-benzoquinone-induced attack by a second nucleophile (AcO^-, Cl^-) resulting in an overall 1,4-oxidation of the diene (Scheme 1).

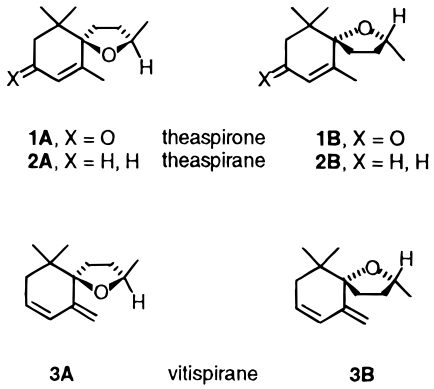

Figure 1.

In a previous study[9b] we made preliminary efforts to apply the palladium(II)-catalyzed oxaspirocyclization toward synthesis of theaspirone. Unfortunately, we were not able to obtain a catalytic reaction for the 1,4-oxidation of **4** to give a spirocycle. However, we did some studies on the stoichiometric reaction using the isolated (π-allyl)-palladium complexes **5A** and **5B**, which were produced in good diastereoselectivity. In a separate reaction they were transformed to **6** (A:B, 93:7) (Scheme 2).

In the present study we have developed a *catalytic* reaction for the formation of the theaspirane skeleton and

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(5) (a) Simpson, R. F.; Strauss, C. R.; Williams, P. J. *Chem. Ind.* **1977**, 663. Wines: (b) Strauss, C. R.; Wilson, B.; Anderson, R.; Williams, P. J. *Am. J. Enol. Vitic.* **1987**, *38*, 23. (c) Winterhalter, P.; Sefton, M. A., Williams, P. J. *Am. J. Enol. Vitic.* **1990**, *41*, 277. Quince fruit: (d) Tsuneya, T.; Ishihara, M.; Shiota, H.; Shiga, M. *Agric. Biol. Chem.* **1983**, *47*, 2495.
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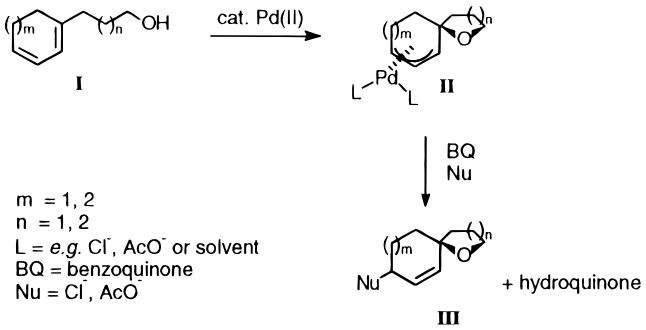
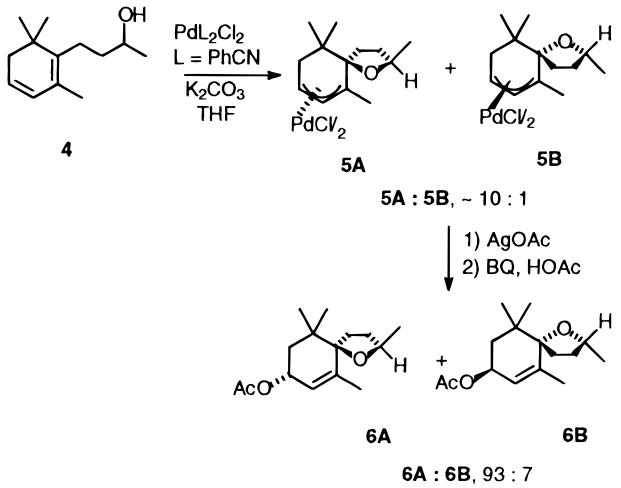
Scheme 1. Palladium(II)-Catalyzed Oxaspirocyclization.



Scheme 2. Stoichiometric Oxaspirocyclization via the Isolated (π-Allyl)Palladium Complex (BQ = *p*-Benzoquinone).



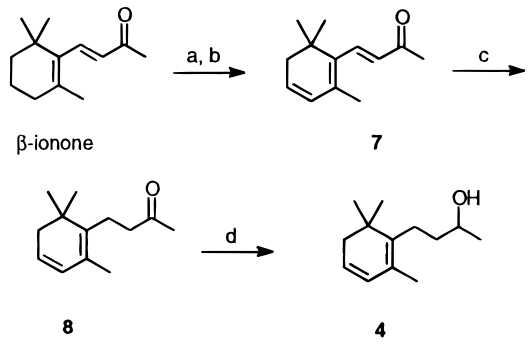
applied it to the total syntheses of theaspirone and vitispirane. With small variations of the reaction conditions in this new palladium-catalyzed reaction, either theaspirone or vitispirane was obtained. We have also discussed the kinetic versus thermodynamic control in the formation of the intermediate π-allyl complex, which will determine whether isomer A or B is formed in the catalytic reaction.

Results and Discussion

Preparation of Starting Materials. The starting material for the oxaspirocyclization was prepared according to ref 9b with some modifications. An improved method for the selective reduction of **7** was achieved by using Bu_3SnH and catalytic amounts of $Pd(PPh_3)_4$,[10] which gave a higher yield than the radical reduction with Ph_3SnH previously employed.[9b,11] $NaBH_4$ reduction of the keto function in **8** gave the requisite diene alcohol **4** in 95% yield (Scheme 3).

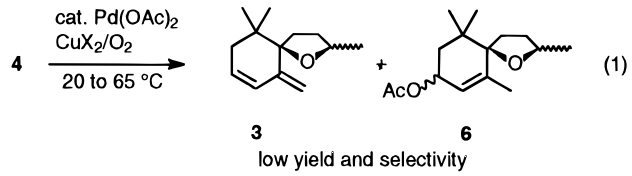
Oxaspirocyclizations toward Theaspirone and Vitispirane. We previously found that the reaction under standard oxaspirocyclization conditions[9b] (5% $Pd(OAc)_2$, 2 equiv of *p*-benzoquinone, 2 equiv of $LiOAc{\cdot}2H_2O$ in acetone−acetic acid, 4:1, room temperature) with slow addition of the diene[12] was unsuccessful.[13] Since it was demonstrated that oxypalladation and nucleophilic attack on the π-allyl complex **5** (Scheme 2) did take place in separate stoichiometric reactions,[9b] although in different solvents, further studies toward developing a catalytic reaction were called for. A change in solvent from acetone−acetic acid to THF−acetic acid did not improve the reaction. Pure acetic acid (using 10% of the catalyst) yielded after 24 h 25−30% of the desired cyclized acetate **6** together with several side products and the Diels−Alder adduct between benzoquinone and diene **4**.

Scheme 3[a]



[a] (a) NBS, *hν*, CCl_4. (b) Na_2CO_3, DMF (77% from β-ionone). (c) Bu_3SnH, $Pd(PPh_3)_4$ (3−5 mol %) $THF/H_2O/NH_4Cl$, 2 h, rt (90%). (d) $NaBH_4$, 0 °C (95%).

Some other oxidation systems such as $Cu(OAc)_2/O_2$ and $CuCl_2/O_2$ were tried in an effort to develop a catalytic reaction. In most of these reactions, mixtures of **3** and **6** were obtained from **4** in low yield (eq 1). With $CuCl_2/O_2$ as the oxidant a prolonged reaction time increased the selectivity for **3**. In all these reactions both the A and B isomers of the products were obtained and no selectivity in the addition of AcO^- was achieved (eq 1).



Discouraged by these results we looked into the benzoquinone reaction in more detail. In this reaction we had observed that alcohol **9** was formed when $LiOAc{\cdot}2H_2O$ was employed, showing that also water is capable of attacking the π-allyl intermediate. We therefore increased the amount of water, and reaction in a 4:1 mixture of water−acetic acid[14] gave mainly the alcohol **9** together with acetate **6**, vitispirane **3**, and Diels−Alder product in a ratio of 85:11:2:2. After workup the alcohol **9** was isolated in 72% yield. In this reaction four diastereomeric alcohols of **9** were observed (eq 2). The ratio A to B of the alcohols was ~1:1, which shows that the catalytic oxaspirocyclization reaction is not diastereoselective. The alcohols were further oxidized by MnO_2 to theaspirones A and B (1:1) in 88% combined yield.

To investigate the reason for the low diastereoselectivity at C-8, a control experiment was carried out in

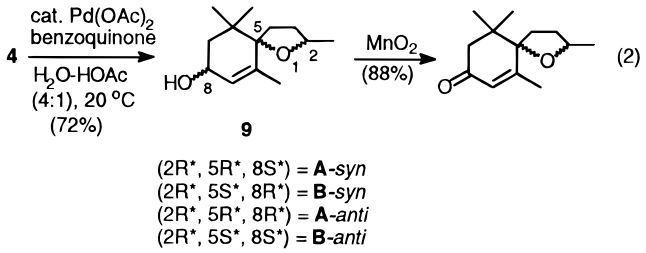
(10) Keinan, E.; Gleize, P. A. *Tetrahedron Lett.* **1982**, *23*, 477.

(11) (a) Wolf, H. R.; Zink, M. P. *Helv. Chim. Acta* **1973**, *56*, 1062. An additional alternative way for the selective reduction of **7**, however in a lower yield (53%), is the reduction with Cu hydride, prepared by mixing a 1.0 M solution of $LiAlH_4$ in THF with CuI. See: (a) Negishi, E.-i.; King, A. O.; Klima, W. L.; Patterson, W.; Silveira, A., Jr. *J. Org. Chem.* **1980**, *45*, 2526. (b) Ashby, E. C.; Lin, J. J.; Kovar, R. *J. Org. Chem.* **1976**, *41*, 1939.

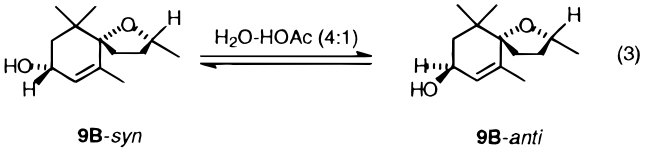
(12) The slow addition of the diene was necessary to avoid Diels−Alder reaction between the diene and *p*-benzoquinone.

(13) Mainly Diels−Alder product and starting material were obtained.

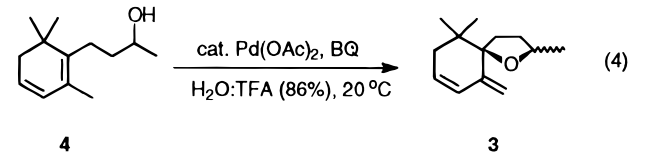
(14) The alcohol was dissolved in acetone (1 M) for the addition.



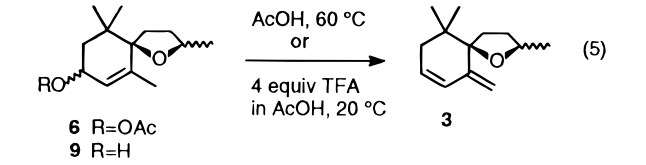
which **9B**-*syn* was treated with aqueous acetic acid (eq 3). After 24 h at room temperature, a mixture of isomers **9B**-*syn* and **9B**-*anti* in a ratio of 1.4:1 was isolated. This shows that the alcohols undergo acid-catalyzed epimerization which would account for the mixture of 1,4-cis and 1,4-trans addition products observed. However, this does not affect the synthetic strategy since the C-8 stereogenic center is eliminated in the oxidation to theaspirone.



The use of a stronger acid led to diene formation. Thus, in water with 8 equiv of methanesulfonic acid, diene alcohol **4** was transformed into vitispiranes **3A** and **3B** in moderate yield after 22 h (**3A**:**3B**, 1:1). When trifluoroacetic acid (TFA) (8 equiv) was employed, the reaction of **4** was complete after 15 h and vitispiranes A and B were isolated in 86% yield (**3A**:**3B**, 1:1) (eq 4).



A likely explanation for the formation of vitispirane (**3**) is that water attacks the intermediate (π-allyl)-palladium complex to give alcohol **9**, followed by elimination of water. In two control experiments, a mixture of the acetate **6** and the alcohol **9** was treated with (i) acetic acid at 60 °C or (ii) with 4 equiv of CF_3COOH in acetic acid at room temperature. Both reactions led exclusively to the formation of vitispirane (**3A**:**3B**, 1:1) (eq 5).



In an alternative procedure for obtaining vitispirane **3**, LiCl was added to the reaction. It was thought that the chloride anion would be a better nucleophile than the carboxylate anion and that the allylic chloride intermediate would directly eliminate hydrogen chloride to form vitispiranes. Different reaction conditions were tried, and the results are listed in Table 1. Reaction at room temperature gave only starting material. However, at 50 °C the anticipated formation of vitispiranes took place (eq 6, Table 1)). It is interesting to note that the diastereomeric ratio between **3A** and **3B** varied with slight changes of the pH. In unbuffered acetic acid the ratio **3A**:**3B** is essentially 1:1, whereas in buffered acetic acid (added K_2CO_3) **3B** is favored over **3A** by a factor of 3 (Table 1, entries 1 and 3). Also the strength of the acid (entries 2−4) influences the ratio between **3A** and **3B**. The isomer preference in entries 2−4 is reversed to that of the stoichiometric reaction. The use of stronger acids (CF_3COOH, CCl_3COOH) did not lead to cyclization products.

Table 1. Palladium(II)-Catalyzed Oxaspirocyclization of 4 with the Addition of LiCl in Acetone in the Presence of Different Acids. All Reactions Were Heated to 50 °C

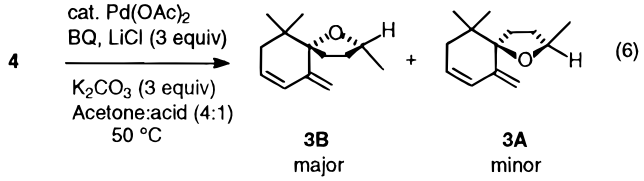
entry	conditions[a] (cosolvent)	additives	product ratio **3A**:**3B**
1	acetic acid		1:1
2	dichloroacetic acid	3 equiv of K_2CO_3	1:2
3	acetic acid	3 equiv of K_2CO_3	1:3
4	isobutyric acid	3 equiv of K_2CO_3	1:3.3

[a] In all reactions 5% $Pd(OAc)_2$ was used as the catalyst. The reactions were run for 48 h at 50 °C with the addition of 3 equiv of LiCl. All reactions were run in acetone together with an acid as a cosolvent in a 4:1 ratio.

Table 2. Different Reaction Conditions for the Formation of π-Allyl Complex 5 from Diene Alcohol 4. The Reactions Were Performed in THF with $Pd(PhCN)_2Cl_2$ as the Source for Pd

entry	additives[a]	reactn time (h)	products **5A**:**5B**
1		3	10:1
2	K_2CO_3[b]	∼14[c]	7:1
3	K_2CO_3[b,d]	3	2:1
4	K_2CO_3[b] and water[e]	3[f]	1:1.3

[a] The additives were added before the palladium complex. [b] 2 equiv. [c] The mixture was stirred 2 h at room temperature and kept overnight in the refrigerator. [d] The reaction was diluted with THF to [substrate] ∼0.006 M (normally 0.06 M). [e] Water (2%) was added to the solvent. [f] Not full conversion (60%).

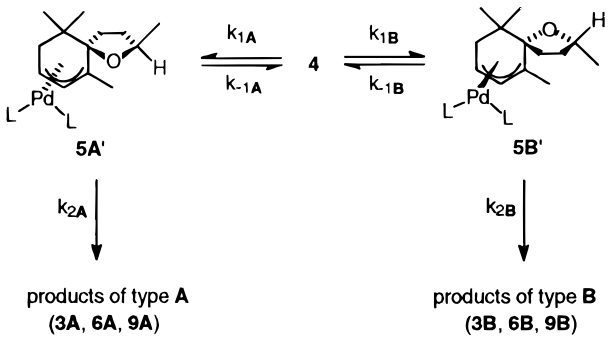


Mechanistic Aspects. In the stoichiometric formation of π-allyl complex **5** from diene alcohol **4**, a proton is liberated, which may induce isomerization by catalyzing the retro-oxypalladation. This was investigated by varying the acidity of the medium in the reaction between $PdCl_2(PhCN)_2$ and **4**, and the results are presented in Table 2. Without base, isomerization is possible and π-allyl complex **5A** predominates (entry 1). Upon addition of K_2CO_3 the **5A**:**5B** ratio decreases (entry 2), and when the same conditions were used in a diluted reaction to slow down the isomerization, **5A** and **5B** were isolated in a 2:1 mixture (entry 3). Finally, in entry 4, water was added to the reaction to dissolve the base which trapped the acid more efficiently, resulting in a 1:1.3 mixture in favor of isomer **5B**.

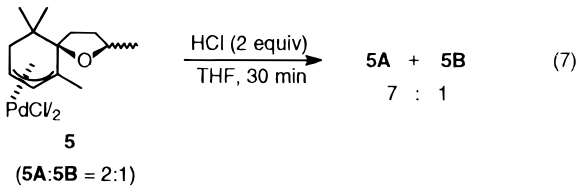
In a control experiment a 2:1 mixture of **5A** and **5B** was treated in THF with HCl (2 equiv) for 30 min at room temperature, which led to isomerization of **5B** to **5A**, giving a ratio **5A**:**5B** of 7:1 (eq 7). The isomerization takes place via an acid-catalyzed retro-oxypalladation to diene alcohol **4** and subsequent recyclization.[15,16] These

(15) For acid-catalyzed retro-oxypalladation, see: Robinson, S. D.; Shaw, B. L. *J. Chem. Soc.* **1963**, 4806.

Scheme 4



results show that complex **5A** is the favored complex under thermodynamic control.



The acid-catalyzed equilibrium between complexes **5** is shown in Scheme 4. In the catalytic reaction the two π-allyl complexes **5A′** and **5B′** generated are trapped by an irreversible nucleophilic attack. Despite the fact that the reaction is run under acidic conditions, the competing nucleophilic attack (k_{2A} and k_{2B}) will trap the π-allyl complexes **5** and hinder equilibration. The results presented in Table 1 show that the ratio **3A**:**3B** decreases with decreasing acidity strength in the medium, in line with a retarded equilibrium between **5A′** and **5B′** at a higher pH. At a slightly increased pH the reaction becomes more kinetically controlled and formation of **3B** is favored.[17]

In the stoichiometric reaction without added base, the π-allyls were allowed to equilibrate, leading to thermodynamical control, and a ratio **5A**:**5B** of 10:1 was obtained.

Conclusions

Palladium(II)-catalyzed oxaspirocyclization can be used for efficient syntheses of theaspirone and vitispirane. The reaction proceeds via oxaspirocyclic (π-allyl)palladium intermediates. An interesting balance between formation of kinetic and thermodynamic (π-allyl)palladium complexes controls the stereochemistry of the tetrahydrofuran ring (A or B isomer). By controlling the reaction the isomeric ratio A:B can be changed from 10:1 to 1:3.3.

Experimental Section

NMR spectra were recorded for $CDCl_3$ solutions (^1H at 400 MHz and ^{13}C at 100.5 MHz) using tetramethylsilane (0.0 ppm, ^1H) or chloroform-*d* (7.26 ppm, ^1H, 77.0 ppm, ^{13}C) as internal standards. Mass spectra were obtained in GC/MS mode (EI, 70 eV). Slow addition was performed by the use of a syringe pump. Commercial acetone (99.5%) was dried over molecular sieves (4 Å). Acetic acid was dried by the addition of 0.5% acetic anhydride. *p*-Benzoquinone was recrystallized from ethanol. Lithium acetate dihydrate, triphenyltin hydride, and 1.0 M $LiAlH_4$ solution in THF were purchased from Aldrich. $Pd(OAc)_2$ was bought from Engelhard. $PdCl_2$ was obtained from Johnson Matthey. Tetrakis(triphenylphosphine)palladium[18] and MnO_2[19] were prepared according to standard procedures. Tributyltin hydride was prepared from Hydrofugeant H68 (Rhône-Poulenc) and bis(tributyltin) oxide (Aldrich).[20] Merck silica gel 60 (240−400 mesh) was used for flash chromatography.

3,4-Dehydro-*β*-ionone (7),[21] **7,8-dihydro-3,4-dehydro-*β*-ionol (4),**[9b] **and *π*-allyl complex (5)**[9b] were prepared according to literature procedures.

7,8-Dihydro-3,4-dehydro-*β*-ionone (8). Bu_3SnH (5.26 g, 1.8 mmol) was added dropwise to a stirred solution of **7** (1.9 g, 10 mmol), $Pd(PPh_3)_4$ (0.34 g, 0.3 mmol), NH_4Cl (1.07 g, 21 mmol), and H_2O (0.5 mL, 27 mmol) in 25 mL of THF under an atmosphere of N_2. After 2 h ether (100 mL) was added and the organic phase was separated and washed with brine. Evaporation of the solvents gave a yellowish oil which was dissolved in EtOAc (100 mL) and stirred with a saturated solution of NaF (20 mL) for 3−4 h. The precipitate formed was filtered off, the solvent was evaporated, and the residue was subjected to flash chromatography (using pentane:ether 85:15 as the eluent), giving 1.7 g (90%) of **8** as a yellow oil. The spectral data were in agreement with previously reported values.[9b] An alternative way for the selective reduction of **7** to **8** was accomplished with triphenyltin hydride as described in ref 11a.

Spiro[4,5]-8-acetoxy-2,6,10,10-tetramethyl-1-oxa-6-decene (6) was prepared from (π-allyl)palladium chloro dimer **5** as described in ref 9b. Spectral data are reported for the three major isomers. MS: *m*/*z* (mixture) 252 (M^+, <1%), 196 (38), 177 (1.4), 154 (100).

(2*R,5*R**,8*S**)-6A-*syn*:**[9b] ^1H NMR (400 MHz) δ 5.33 (m, 1 H), 5.15 (bm, 1 H), 4.15 (m, 1 H), 2.07−1.93 (m, 2 H), 2.02 (s, 3 H), 1.84 (m, 1 H), 1.78 (s, 3 H), 1.77−1.64 (m, 2 H), 1.41 (m, 1 H), 1.26 (d, J = 6 Hz, 3 H), 1.02 (s, 3 H), 0.89 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 171.0, 146.0, 119.5, 88.1, 77.0, 67.4, 39.8, 36.1, 34.8, 32.2, 24.5, 23.8, 21.5, 20.9, 18.7.

(2*R,5*R**,8*R**)-6A-*anti*:**[9b] ^1H NMR (400 MHz) δ 5.35−5.29 (m, 1 H), 5.27 (m, 1 H), 4.17−4.08 (m, 1 H), 2.1 (dd, J = 14.0, 9.5 Hz, 1 H), 2.05 (s, 3 H), 1.91−1.98 (m, 1 H), 1.88−1.81 (m, 2 H), 1.78 (s, 3 H, C=CCH_3), 1.58 (dd, J = 8.0, 6.0 Hz, 1 H), 1.49−1.38 (m, 1H), 1.28 (d, J = 6.0 Hz, 3 H), 1.01 (s, 3 H), 0.93 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 170.8, 145.7, 120.4, 88.3, 77.2, 69.5, 40.8, 39.2, 34.8, 34.3, 24.8, 22.2, 21.4, 20.7, 18.1.

(2*S,5*R**,8*R**)-6B-*anti*:**[9b] ^1H NMR (400 MHz) δ 5.40 (m, 1 H), 5.24 (m, 1 H), 4.00 (m, 1 H), 2.10−1.98 (m, 2 H), 2.02 (s, 3 H), 1.86 (dd, J = 9.2, 12.8 Hz, 1 H), 1.78 (m 1 H), 1.75 (m, 3 H), 1.68 (ddd, J = 1.2, 6.2, 12.5 Hz, 1 H), 1.56 (m, 1 H), 1.26 (d, J = 6 Hz, 3 H), 1.01 (s, 3 H), 0.91 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 171.0, 140.8, 123.1, 86.7, 79.1, 69.0, 39.0, 38.7, 36.2, 30.6, 24.6, 23.0, 21.4, 21.1, 19.1.

Spiro[4,5]-8 hydroxy-2,6,10,10-tetramethyl-1-oxa-6-decene (9). To a stirred mixture of *p*-benzoquinone (0.104 g, 0.96 mmol) and palladium acetate (0.011 g, 0.05 mmol) in water (4 mL) and acetic acid (1 mL) was added diene alcohol **4** (0.093 g, 0.48 mmol) in acetone (0.5 mL) over a period of 12 h. The mixture was stirred for another 3 h until the reaction was complete according to TLC. The reaction was worked up as described below for the preparation of **3**. The crude product contained a mixture of four diastereoisomeric alcohols (85%) together with 11% of the acetate **6** according to NMR. The crude product was heated (60 °C) for 30 min in a mixture of 2 M NaOH (2.4 mL) and MeOH (9.5 mL). The solvents were removed *in vacuo*. Ether (100 mL) was added, and the solution was washed with brine (2 × 15 mL) and dried ($MgSO_4$).

(16) A small amount (<10%) of the diene alcohol **4** was also isolated in this reaction.

(17) In the extreme case if the equilibrium is completely stopped the reaction will be under kinetic control and the product ratio will depend on the ratio k_{1A}/k_{1B}. With a full equilibrium between **5A′** and **5B′** (thermodynamically controlled intermediates) the product ratio will depend on $(k_{1A}k_{-1B}/k_{-1A}k_{1B})(k_{2A}/k_{2B})$.

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Purification by flash chromatography (pentane/ether, 80:20−50:50) gave two fractions, the first containing three isomers and the second one single diastereoisomer (**9B**-*anti*). The combined alcohols were obtained in 72% yield as colorless oils. The isomers were isolated by HPLC.

(2*R,5*R**,8*S**)-9A-*syn*:**[9b] ^{1}H NMR (400 MHz) δ 5.43 (m, 1 H), 4.17 (m, 1 H), 4.09 (bm, 1 H), 2.00 (m, 2 H), 1.81 (m, 1 H), 1.78 (m, 3 H), 1.74 (m, 1 H), 1.66 (m, 1 H), 1.44 (m, 1 H), 1.26 (d, J = 6 Hz, 3 H), 1.05 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 142.4, 124.6, 88.2, 76.8, 64.9, 43.3, 36.4, 34.8, 25.8, 24.6, 22.1, 21.0, 19.1.

(2*R,5*R**,8*R**)-9A-*anti*:**[9b] ^{1}H NMR (400 MHz) δ 5.33 (m, 1 H), 4.23 (bm, 1 H), 4.12 (m, 1 H), 2.08 (dd, J = 8.5, 13.2 Hz, 1 H), 1.93 (m, 1 H), 1.82 (m, 2 H), 1.75 (m, 3 H), 1.44 (m, 2 H), 1.26 (d, J = 6 Hz, 3 H), 0.95 (s, 3 H), 0.91 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 143.3, 124.8, 88.5, 77.0, 65.9, 45.1, 39.2, 34.4, 31.2, 24.8, 22.1, 20.6, 18.0.

(2*S,5*R**,8*S**)-9B-*syn*:**[9b] ^{1}H NMR (400 MHz) δ 5.41−5.38 (m, 1 H), 4.25−4.19 (m, 1 H), 4.17 (dp, J = 8.5, 6.0 Hz, 1H), 2.18 (dt J = 13.0, 8.5 Hz, 1 H), 2.10−2.02 (m, 1 H), 1.87−1.80 (m, 2 H), 1.74 (s, 3 H), 1.57 (ddt, J = 12.0, 9.5, 8.2 Hz, 1 H), 1.44 (dd, J = 13.0, 8.0 Hz, 1 H), 1.25 (d, J = 6.0 Hz, 3 H), 0.99 (s, 3 H), 0.96 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 142.4, 124.7, 88.8, 77.4, 65.9, 44.5, 39.8, 35.1, 33.6, 25.8, 23.1, 21.7, 19.1.

(2*S,5*R**,8*R**)-9B-*anti*:**[9b] ^{1}H NMR (400 MHz) δ 5.50 (m, 1 H), 4.10 (bm, 1 H), 3.98 (m, 1 H), 2.02 (m, 2 H), 1.78 (m, 1 H), 1.74 (dd, J = 2, 1.6 Hz, 3 H), 1.70 (md, J = 8 Hz, 2 H), 1.63 (bm, 1 H), 1.57 (m, 1 H), 1.26 (d, J = 6 Hz, 3 H), 1.00 (s, 3 H), 0.85 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 138.3, 128.3, 86.8, 76.5, 65.9, 43.7, 39.0, 36.3, 30.2, 24.7, 22.7, 21.0, 19.1.

Spiro[4,5]-2,6,10,10-tetramethyl-1-oxa-8-oxo-6-decene (Theaspirone, 1). Oxidation of the alcohols **9** with MnO_2 performed as described in ref 9b afforded theaspirones A and B. The NMR data of theaspirone A were in accord with those reported in ref 9b.

(2*S,5*R**)-Theaspirone B:**[3b] ^{1}H NMR (400 MHz) δ 5.76 (m, 1 H), 4.22 (m, 1 H), 2.40 (m, 1 H), 2.35−2.26 (m, 2 H), 2.15 (m, 1 H), 1.96 (d, J = 1.3 Hz, 3 H), 1.87 (ddd, J = 3, 9.3, 13.5 Hz, 1 H), 1.64 (m, 1 H), 1.30 (d, J = 6 Hz, 3 H), 1.07 (s, 3 H), 1.01 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 198.8, 168.2, 125.3, 88.6, 78.0, 49.9, 41.6, 35.0, 32.7, 24.5, 23.7, 21.3, 20.5.

Spiro[4,5]-2,10,10-trimethyl-6-methylene-1-oxa-7-decene (Vitispirane, 3). To a stirred mixture of *p*-benzoquinone (0.104 g, 0.96 mmol) and palladium acetate (0.011 g, 0.05 mmol) in water (4 mL) and trifluoroacetic acid (0.44 mL) was added diene alcohol **4** (0.093 g, 0.48 mmol) in acetone (0.5 mL) over a period of 12 h. After stirring for another 4 h, the reaction was ready according to TLC. Water (4 mL) was added, and the resulting mixture was extracted with ether (3 × 3 mL). The combined organic layers were washed with 2 M NaOH until the aqueous extract was colorless. The water layers were back-extracted with ether (2 × 10 mL). The combined organic layers were washed with brine (7 mL) and dried ($MgSO_4$). The crude product was purified by flash chromatography (pentane:ether, 95:5) to give 0.079 g (86%) of vitispirane **3** (**3A**:**3B** = 1:1) as a colorless oil. Spectral data (^{1}H NMR, MS, IR) were in accord with those reported in ref 6.

(2*R,5*R**)-3A:**[6] ^{1}H NMR (400 MHz) δ 6.05 (mdd, J = 2.7, 9.5 Hz, 1 H), 5.59 (m, 1 H), 5.06 (s, 1 H), 4.86 (s, 1 H), 4.31 (app hex, J = 6 Hz, 1 H), 2.16 (md, J = 18.5 Hz, 1 H), 2.12−1.89 (m, 3 H), 1.50−1.39 (m, 1 H), 1.24 (m, 1 H), 1.23 (d, J = 6 Hz, 3 H), 0.95 (s, 3 H), 0.89 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 149.5, 128.6, 127.0, 109.0, 88.8, 77.2, 41.1, 36.1, 32.8, 31.6, 23.5, 23.3, 21.4.

(2*S,5*R**)-3B:**[6] ^{1}H NMR (400 MHz) δ 6.07 (mdd, J = 2.9, 9.6 Hz, 1 H), 5.59 (m, 1 H), 5.18 (s, 1 H), 4.89 (s, 1 H), 4.04 (m, J = 6 Hz, 1 H), 2.17 (md, J = 18.2 Hz, 1 H), 2.12−1.82 (m, 3 H), 1.62−1.51 (m, 1 H), 1.34 (d, J = 6 Hz, 3 H), 0.98 (s, 3 H), 0.90 (s, 3 H); ^{13}C NMR (100.5 MHz) δ 150.2, 128.9, 126.8, 110.3, 88.5, 75.6, 40.3, 37.3, 32.8, 32.5, 23.33, 23.28, 20.6.

Oxaspirocyclization of 4 to Vitispirane (3) in the Presence of K_2CO_3 and LiCl. In a two-necked flask fitted with a reflux condenser under nitrogen were successively placed $Pd(OAc)_2$ (20 mg, 0.089 mmol), *p*-benzoquinone (390 mg, 3.61 mmol), potassium carbonate (400 mg, 5.41 mmol), and lithium chloride (128 mg, 3.01 mmol) in acetone−acetic acid (4:1, 7.5 mL). After subsequent addition of the diene alcohol **4** (350 mg, 1.8 mmol), the reaction mixture was heated during 48 h at 50 °C (the reaction was followed by TLC). The usual workup followed by flash chromatography (hexane:ethyl acetate, 90:10) afforded 195 mg (56%) of **3** as a colorless oil (**3A**:**3B**, 26:74). Further experiments to evaluate the influence of the acidity of the medium were conducted employing different acids and K_2CO_3 under similar reaction conditions (Table 1).

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