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Stereocontrolled Formation of *cis* and *trans* Ring Junctions in Hydrindane, Decalin, and Steroid Systems by Palladium-Catalyzed Regioselective and Stereospecific Hydrogenolysis of Allylic Formates

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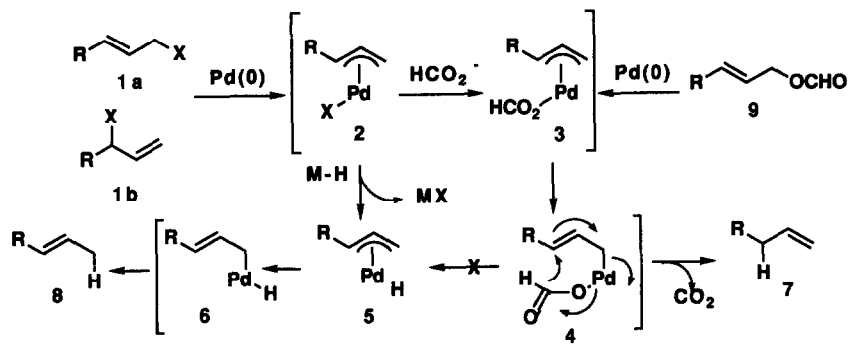
Abstract: Both the *cis* and *trans* ring junctions can be generated selectively in hydrindane, decalin and steroid systems by the palladium-catalyzed regioselective and stereospecific decarboxylation-hydrogenolysis of allylic formates. The *trans* junctions were formed from 3β allylic formates of decalin and steroid and 5β allylic formates of hydrindane. The corresponding 3α and 5α formates generate the *cis* ring junction

INTRODUCTION

Stereocontrolled generation of *cis* or *trans* ring junctions in hydrindane or decalin derivatives is a desirable but elusive synthetic goal. Hydrogenation of 4-olefins of decalin is not reliable, giving a mixture of stereoisomers in many cases. Several stereospecific methods for generation of ring junctions using stereo-defined C-3 allylic alcohols are known. An elegant method for stereospecific generation of *cis* and *trans* ring junctions via free radical cyclization of bromomethylsilyloxy group derived from stereo-defined allylic alcohols in decalin and hydrindane systems has been reported. Namely the *cis* junction is obtained from the 3α alcohol and the trans junction from the 3β alcohol.[1] In this case, however, a carbon unit is introduced at C-4. Also the *trans* junction was generated from 3β steroidal alcohol via [3,3] sigmatropic rearrangement of 5α-hydrazene.[2] The *cis*-fused hydrindane stereochemistry was generated by the treatment of tosylhydrazone of 5-keto hydrindene with catecholborane.[3] We have found a good solution to this general problem based on π-allylpalladium chemistry. A preliminary account has already been given,[4] and the details of this methodology are presented in this paper.

Palladium-catalyzed reaction of allylic esters with formic acid to give a mixture of olefins was reported briefly.[5] We have found that the palladium-catalyzed hydrogenolysis of terminal allylic compounds **1a,b** using $Pd(OAc)_2$ and Ph_3P as a catalyst with ammonium formate proceeds to afford mainly 1-olefins **7**.[6] Then we found that the hydrogenolysis of allylic compounds proceeds more smoothly by the use of allylic carbonates as the substrates and triethylammonium formate as the reductant. In addition, $n\text{-}Bu_3P$ gives better selectivity than Ph_3P.[7] This regioselective hydrogenolysis can be explained by Scheme **1**. The π-allylpalladium complex **2** reacts with formate to form π-allylpalladium formate **3**. The attack of the hydride generated from σ-allylpalladium formate **4** on the more substituted side of the allylic system by the cyclic mechanism shown by **4** affords terminal olefin **7**. The decarboxylation and hydride transfer should be the

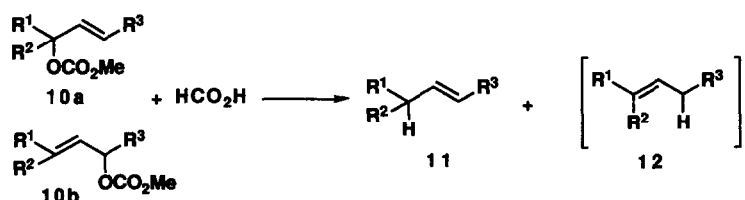
concerted process as shown by **4**. The decarboxylation of **4** to form π-allylpalladium hydride **5** does not take place. π-Allylpalladium formate **3** is the intermediate of the hydrogenolysis, which was confirmed by an NMR spectrum.[8] Expecting that the π-allylpalladium formate **3** should be formed directly from allylic formate **9**, we found that allylic formate **9** can be converted to olefin **7** without the use of ammonium formate. The use of allylic formate **9** is preferrable than other allylic esters, because the reaction is cleaner. Hydrogenolysis of allylic compounds to form olefins is carried out with various hydride sources such as $LiAlH_4$,[9] borohydrides,[10-13] hydrosilanes (polymethylhydrosilane),[14] tin hydride,[15] butylzinc chloride,[16] SmI_2,[17] and electrolysis.[18] These hydrides form the π-allylpalladium hydride **5** by transmetallation, and subsequent transfer of the hydride takes place to the less substituted terminal carbon by the reductive elimination of **6** to give 2-olefin **8** from terminal allylic compounds **1a,b** as the main product, and the reactions are not regioselective. In this sense, formate is a unique reagent, and it is used as either allylic formate or triethylammonium formate. Use of triethylammonium formate for the hydrogenolysis of various substrates is known.[19-22]



Scheme 1

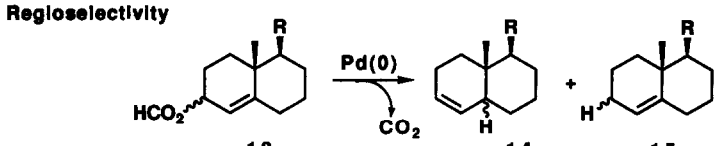
RESULTS AND DISCUSSION

So far we have studied the hydrogenolysis of terminal allylic compounds to prepare terminal olefins. Then we wanted to extend this reaction to internal allylic compounds. "Is the hydrogenolysis of unsymmetrically substituted internal allylic systems **10a,b** regioselective ?" was the question. (Scheme **2**) We expected the formation of **11** by the hydride attack at the tertiary carbon, rather than the seconday carbon to form **12**. Actually we found the reaction is regioselective as expected.



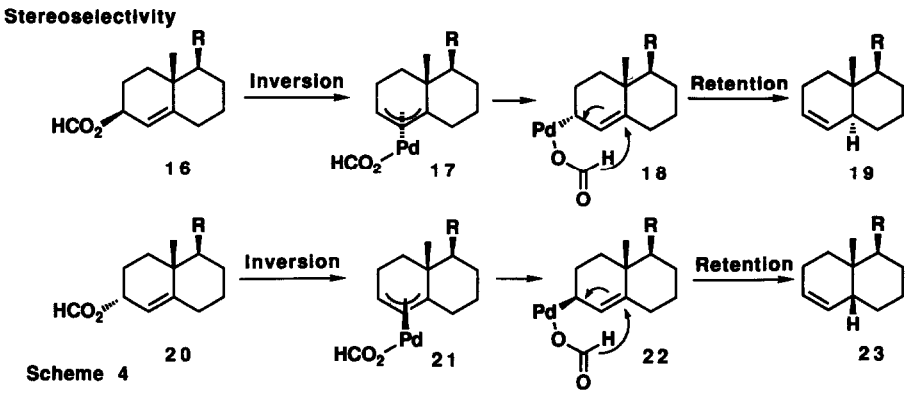
Scheme 2

As one obvious application in this direction, we hoped to apply this regioselective hydrogenolysis reaction to hydrindane and decalin systems, expecting high regio- and stereoselectivities. If the hydride attacks the more substituted tertiary angular carbon of the allylic system in a bicylic system **13**, the 3–olefin **14**, rather than the 4–olefin **15**, should be formed. (Scheme 3)



Scheme 3

In addition to the regioselectivity, we expected the stereospecificity in the cyclic systems based on the following mechanistic considerations.(Scheme 4) In palladium-catalyzed allylation reactions of nucleophiles via π-allylpalladium complexes, it is well-established that the initial step of π-allylpalladium complex formation involves inversion of stereochemistry. The subsequent addition of a soft carbon nucleophile to the π-allyl system takes place from the side opposite to palladium resulting in net retention overall.[23] On the other hand, the addition of a hard nucleophile to a π-allylpalladium complex proceeds from the same side as palladium, and hence the overall inversion takes place. Based on the above-shown stereochemical considerations, we expected that the attack of Pd(0) on the 3β-formate **16** to form the π-allylpalladium formate **17**, in which palladium has α-orientation, would take place with inversion of stereochemistry. The subsequent migration of the hydride from the α-palladium formate **17** to the angular carbon should occur from the α side with retention as shown by **18** to give the *trans* decalin **19**. Therefore, overall inversion is expected.[24] Similarly the 3α–formate **20** undergoes the hydride transfer from the β side as shown by **22** to give the *cis* decalin **23**. Thus the stereospecific formation of the *trans* octahydronaphthalene **19** is expected from the 3β-allylic formate **16**, and the *cis* compound **23** would be formed from the 3α-allylic formate **20**. We were pleased to find that these reactions in fact proceeded as expected.



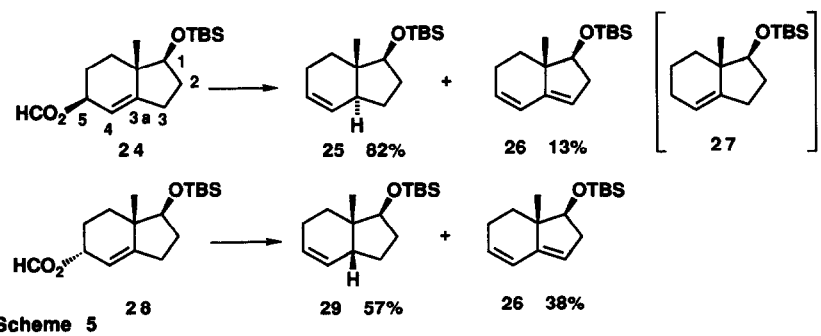
Scheme 4

The Preparation of the Catalyst. It should be noted that the preparative method of the active catalyst used in this hydrogenolysis is crucial. The catalyst active for the hydrogenolysis is prepared by mixing $Pd(acac)_2$ or $Pd(OAc)_2$ and n-Bu_3P in 1:1 ratio in THF. It is expected that bivalent Pd(+2) salt is reduced to Pd(0) by the reaction with n-Bu_3P, which is oxidized to butylphosphine oxide. Therefore, the

active catalytic species is a phosphine-free Pd(0) species, ligated by the weakly coordinating tributylphosphine oxide, and easily becomes ligand-free by approach of the allylic substrates.[25] Recently, the reduction of $Pd(OAc)_2$ with Ph_3P to form Pd(0) and triphenylphosphine oxide was reported.[26,27] When $Pd_2(dba)_3$, which is a conventional Pd(0) complex and used frequently in many palladium-catalyzed reactions, was used with $n\text{-}Bu_3P$ for the present reaction, no reaction took place. The ligand dba (dibenzylideneacetone) is a strongly coordinating bidentate olefin ligand, and seems to inhibit the coordination of hindered olefins of the allylic substrates. In addition, the purity of $Pd(OAc)_2$, $Pd(acac)_2$ and $n\text{-}Bu_3P$ is crucial for consistent results. We obtained satisfactory results by the use of $n\text{-}Bu_3P$ in a "Sure-Seal" bottle, purchased from Aldrich. No or poor results were obtained when slightly impure $n\text{-}Bu_3P$ purchased from other companies was used even after distillation. $Pd(acac)_2$ was used after recrystallization from benzene. Hot benzene-insoluble material was removed from $Pd(OAc)_2$ before the use. This is a good prepartative method for phosphine-free Pd(0) species *in situ* which is a highly active catalyst.

$$Pd(OAc)_2 + n\text{-}Bu_3P \longrightarrow Pd(0)\cdots O{=}PBu_3 + Ac_2O$$

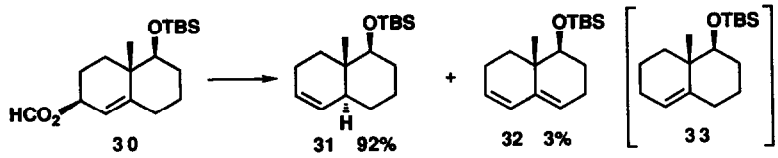
Application to Hydrindane and Decalin Systems. At first we examined the reaction of hydrindane. (Scheme **5**) 5-Keto hydrindane was prepared and its reduction gives mainly 5β allylic alcohol. The 5β-alcohol was inverted to the 5α-allylic benzoate by the Mitsunobu reaction. The 5α-allylic alcohol was obtained after hydrolysis of the benzoate. Then both the 5β- and 5α-formates **24** and **28** were prepared by the treatment of the allylic alcohols with a mixture of formic acid, acetic anhydride, and pyridine. They were subjected to the palladium catalysis. The catalyst solution was prepared by mixing $Pd(acac)_2$ and $n\text{-}Bu_3P$ (1:1) in THF. The initially pale yellow solution turned to brown during the reaction. The reaction proceeded in 30 min at room temperature to give only the 4-hydrindenes **25**(82%) from **24,** and **29** (57%) from **28** with no regioisomeric 3a-hydrindene **27** being formed. In addition, the *trans* fused product **25** (^1H NMR, angular CH_3, δ, 0.73) was obtained from the β–formate **24,** and the formation of the *cis* junction **29** (^1H NMR, CH_3, δ, 0.89) from the α-formate **28** was confirmed. This result shows that the hydrogenolysis is stereospecific. The palladium-catalyzed elimination reaction to give conjugated dienes is competitive with the hydrogenolysis.[28] Thus, the heteroannular conjugated 3,4-diene **26** was formed (13% from **24** and 38% from **28**) as a byproduct by the elimination.



Scheme 5

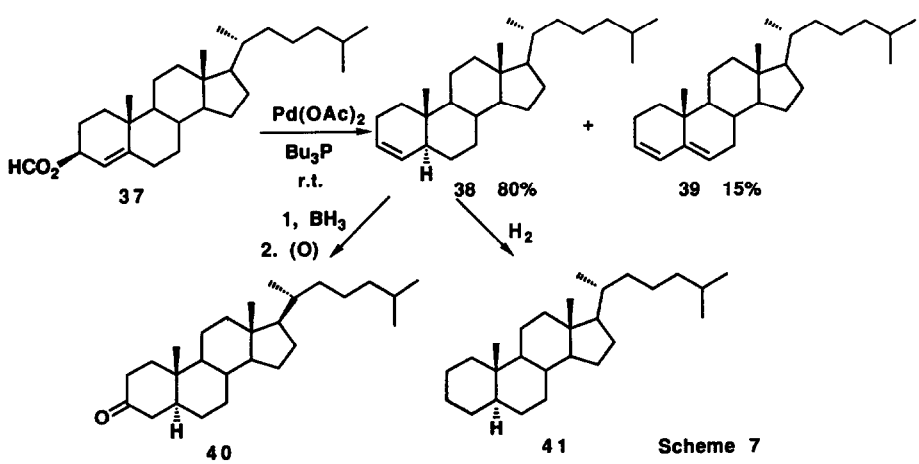
Then we studied the reaction of decalin system. (Scheme **6**) The 3β-allylic alcohol was obtained by the reduction of the 3-keto group, and the 3α-allylic alcohol was prepared by the Mitsunobu inversion reaction via the benzoate. The 3β and 3α allylic formates **30** and **34** were prepared by the reaction with a mixture of

formic acid, acetic anhydride, and pyridine. Their palladium-catalyzed reaction proceeded smoothly at room temperature in one hour. Only the 3-olefins **31** and **35** were formed regioselectively. Formation of 4-olefin **33** was not detected. The reaction was stereospecific. The *trans* junction **31** (^{1}H NMR, angular CH_3, δ, 0.77) was formed in 92% yield from the β-formate **30**, and the α-formate **34** was converted to the *cis* junction **35** (^{1}H NMR, angular CH_3, δ, 0.94) in 89% yield. As byproducts, the heteroannular conjugated 3,5-diene **32** (3%) was produced from **30**, and the homoannular 2,4-diene **36** (6%) from **34**. This interesting regioselective elimination reaction was discussed in a separate paper.[29]



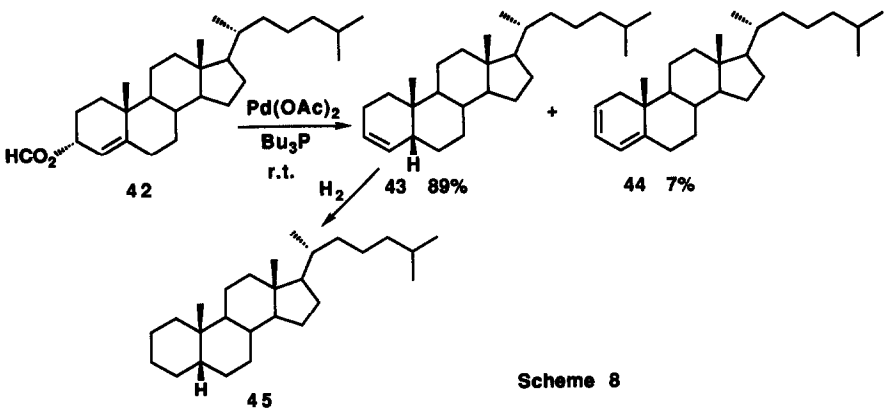
Scheme 6

Application to Steroids. So far we observed highly regioselective and stereospecific hydrogenolysis with the hydrindane and decalin systems. One important application of this methodology is the stereoselective generation of both *cis* and *trans* AB ring junctions in steroids. At first we studied the hydrogenolysis with 4-cholesten-3(α or β)-ols. (Scheme **7**) The 3β-formate **37** and the 3α-formate **42** were prepared and subjected to the palladium catalysis prepared from $Pd(OAc)_2$ and n-Bu_3P (1 : 1) at room temperature for 1.5 - 2 h. The 3β-formate **37** was converted to the AB *trans*-3-cholestene (**38**) (80%, ^{1}H NMR, 19 CH_3, δ, 0.77),[30] with high regioselectivity and stereospecificity. The byproduct in this case was the heteroannular conjugated 3,5-dienes **39** (5%). 3-Cholestene (**38**) was converted to 3-chlolestanone (**40**) by hydroboration [31] and oxidation. In this way, reduction of 4-chlosten-3-one to *trans*-fused 3-cholestanone (**40**) was achieved. Also 5α-cholestane (**41**) was obtained by the hydrogenation of **38.**



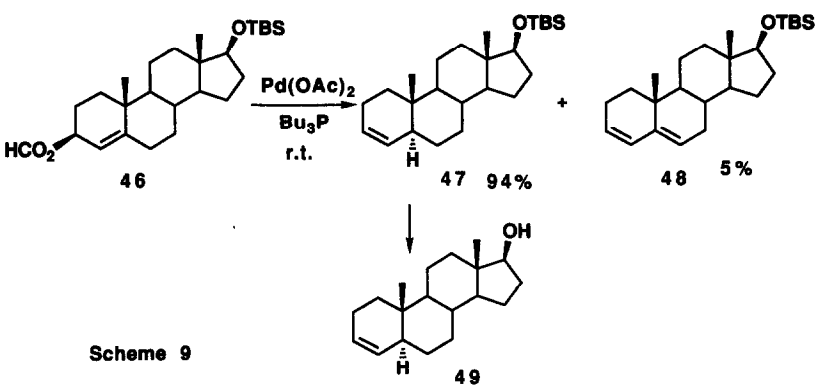
Scheme 7

Similarly, AB *cis*-3-cholestene (**43**) (89%, ^{1}H NMR, 19 CH_3, δ, 0.95) [32] was obtained cleanly from the 3α-formates **42**. (Scheme **8**) The homoannular 2,4-dienes **44** (7%) was the byproduct. *cis*-3-Cholestene (**43**) was converted to *cis*-fused 5β-cholestane (**45**) by hydrogenation.



Scheme 8

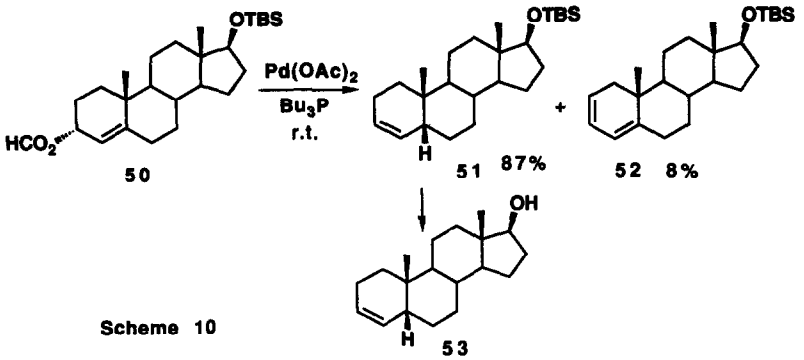
Then similar reaction was carried out with 4-androstene-3-(α or β),17β-diols. (Scheme **9**) The 3β-formate **46** was converted cleanly to the AB *trans* steroid **47** in 94% yield (^{1}H NMR, 19 CH_3, δ, 0.78). A small amount of the hetero-annular conjugated 3,5-diene **48** was obtained (5%). Desilylation of **47** afforded 5α-androst-3-en-17-β-ol (**49**).



Scheme 9

The hydrogenolysis of the corresponding 3α–formate **50** afforded the *cis* steroid **51** in 87% yield (^{1}H NMR, 19 CH_3, δ, 0.96), which was converted to 5β-androst-3-en-17β-ol (**53**) by desilylation. The homo-annular conjugated 2,4-diene **52** (8%) was the byproduct. (Scheme **10**)

In conclusion, the novel method for the preparation of both *cis* and *trans* ring junctions at will in hydrindane and decalin systems was established by the palladium-catalyzed hydrogenolysis of their stereo-defined allylic formates, and the method was successfully applied to steroids. This novel method suggests that the palladium-catalyzed regioselective and stereospecific hydrogenolysis of allylic formates should become a powerful synthetic tool. Assignment of the *cis* and *trans* ring junctions can be done easily by comparing ^{1}H NMR absorption of the angular methyl groups. The absorption of the methyl group in the *trans* isomer appears (about δ, 0.77-0.78) at higher field than that of the *cis* isomers (about δ, 0.94-0.96).



Scheme 10

EXPERIMENTAL SECTION

General methods. The 400 MHz ^1H and 100 MHz ^{13}C NMR spectra were recorded on a JEOL GX-400 instrument. $CDCl_3$ was used as a solvent, where the chemical shifts are given in δ-units relative to internal $CHCl_3$. Optical rotation was measured on a JACSCO DIP-4 digital polarimeter using 10 mm x 0.5 dm pyrex cell. Analytical TLC was executed on precoated Merck silica gel 60 F254 (0.25 mm thickness). Column chromatography was performed on silica gel (230-400 mesh) and eluted with hexane. The yields of the conjugated dienes formed as byproducts by the elimination reaction were estimated from NMR spectra.

Materials. Commercially available $Pd(OAc)_2$ was dissolved in hot benzene and filtered. Pure $Pd(OAc)_2$ was obtained by evaporation of the solvent. Recrystallized (benzene) $Pd(acac)_2$ was used. n-Bu_3P was purchased from Aldrich in a "Sure-Seal" bottle.

Preparation of the Allylic Formates. The formates used in this study were prepared by the treatment of the corresponding allylic alcohols with a mixture of formic acid, acetic anhydride and pyridine (1:1:1.5) at room temperature.

Preparation of the Palladium Catalyst from Pd(acac)$_2$. To a solution of $Pd(acac)_2$ (46 mg, 0.15 mmol) in THF (2 mL) was added n-Bu_3P (0.037 mL, 0.15 mmol) at room temperature under argon and the resulting pale yellow solution was stirred for 5 min.

The hydrogenolyses were carried out as follows.

trans-Hydrindene 25. To a stirred solution of the β-formate **24** (155 mg, 0.5 mmol) in THF (0.5 mL) was added dropwise the stock solution of the catalyst (0.4 mL, 0.025 mmol) at room temperature. The reaction mixture was stirred for 30 min and passed through Florisil using ether (30 mL) as an eluent, and the combined solution was concentrated in vacuo to give a colorless oil (133 mg). The crude product, contaminated with the heteroannular 3,4-diene **26** (13%), was purified by flash column chromatography. The *trans*-hydrindene **25** (109 mg) was isolated in 82% yield. ^1H NMR. δ, 0.01 (s, 3H, $SiCH_3$), 0.02 (s, 3H, $SiCH_3$), 0.73 (s, 3H, angular CH_3), 0.89 (s, 9H, t-Bu), 1.25-2.15 (m, 9H, CH and CH_2), 3.65 (dd, J = 8.98, 7.15 Hz, 1H, OCH), 5.50-5.62 (m, 2H, CH=CH). ^{13}C NMR. δ, -4.8, -4.5, 10.6, 18.1, 24.1, 24.3, 25.9, 31.2, 34.0, 42.9, 42.8, 80.4, 126.6, 128.2.

Confirmation of the *trans* junction was carried out comparing with an authentic sample by gas chromatography. Catalytic hydrogenation of the corresponding hydrindenone with Pd on carbon gave the *cis* product as a main product and the *trans* isomer in a small amount as reported.[33] Hydroboration and PCC oxidation of **25** afforded the 5-ketone, which was identical with the minor product of the hydrogenation.

cis-Hydrindene 29. By the same procedure used for the β-formate **24**, the hydrogenolysis of the α-formate **28** (155 mg) was carried out for 2.5 h to give a colorless oil (133 mg). The product, contaminated with the heteroannular diene **26** (38%), was purified by flash column chromatography. The *cis*-hydrindene **29** (75.8 mg) was isolated in 57% yield. ^{1}H NMR. δ, 0.02 (s, 3H, $SiCH_3$), 0.03 (s, 3H, $SiCH_3$), 0.89 (s, 3H, angular CH_3 and 9H, CH_3 in t-Bu), 1.17-1.56 (m, 4H, CH_2), 1.90-2.18 (m, 5H, CH, and CH_2), 3.77 (dd, J = 7.60, 5.84 Hz, 1H, OCH), 5.54-5.64 (m, 2H, CH=CH). ^{13}C NMR. δ, -4.9, -4.4, 18.1, 20.4, 21.9, 25.9, 28.6, 29.7, 32.4, 43.0, 43.3, 78.3, 124.3, 131.6.

The 5-ketone obtained by hydroboration and PCC oxidation of **29** was identical with the *cis* isomer obtained as the main product of the above-mentioned hydrogenation

trans-Decalin 31. To a stirred solution of the β-formate **30** (162 mg, 0.5 mmol) in THF (0.5 mL) was added dropwise the stock solution of the catalyst (0.4 mL 0.025 mmol) at room temperature. The reaction mixture was stirred for 1 h, and passed through Florisil using ether (30 mL) as an eluent. The combined solution was concentrated in vacuo to give a colorless oil (148 mg). The product was contaminated with the heteroannular 3,5-diene **32** (3%) which was removed by flash column chromatography. The *trans*-decalin **31** (129 mg) was obtained in 92% yield. ^{1}H NMR. δ, 0.03 (s, 6H, $SiCH_3$), 0.77 (s, 3H, angular CH_3), 0.89 (s, 9H, t-Bu), 1.09-2.10 (m, 11H, CH and CH_2), 3.24 (dd, J = 7.70, 7.69 Hz, 1H, OCH), 5.28-5.33 (m, 1H, CH=C), 5.52-5.59 (m, 1H, C=CH). ^{13}C NMR. δ, -4.8, -3.8, 9.7, 18.1, 23.2, 24.6, 25.9, 26.6, 31.0, 33.4, 38.2, 43.0, 78.5, 126.0, 130.3.

The *cis* and*trans* ring junctions were determined in the following way. Catalytic hydrogenation with Pd on carbon of the corresponding 3-octalone afforded a mixture of *cis* and *trans* isomers (2.5:1). Hydroboration and PCC oxidation of **31** afforded a mixture of 3-decalone and 4-decalone (4 : 1). The 3-decalone was identical with the minor product of the hydrogenation by gas chromatographic analysis.

cis-Decalin 35. The hydrogenolsys of the α-formate **34** (162 mg) gave a colorless oil (148 mg). The product contaminated with the homoannular 2,4-diene **36** (6%) was purified by flash column chromatography. The *cis* decalin **35** (125 mg) was obtained in 89% yield. ^{1}H NMR. δ, 0.036 (s, 3H, $SiCH_3$), 0.039 (s, 3H, $SiCH_3$), 0.89 (s, 9H, t-Bu), 0.94 (s, 3H, angular CH_3), 1.08-2.15 (m, 11H, CH and CH_2), 3.62 (dd, J=9.53, 4.03 Hz, 1H OCH), 5.35-5.41 (m, 1H, CH=C), 5.60-5.67 (m, 1H, C=CH). ^{13}C NMR. δ, -4.8, -3.7, 14.1, 18.1, 20.9, 22.6, 25.9, 28.2, 31.0, 31.6, 36.6, 41.3, 70.5, 126.6, 131.9. Hydroboration and PCC oxidation of **35** afforded 3-decalone as a main product, which was identical with the major product of the hydrogenation.

Preparation of the Palladium Catalyst from Pd(OAc)$_2$. To a solution of $Pd(OAc)_2$ (28 mg, 0.125 mmol) in THF (2 mL) was added n-Bu_3P (0.03 mL, 0.125 mmol) at room temperature under argon and the resulting greenish yellow solution was stirred for 5 min.

5α-Cholest-3-ene (38). To a solution of the β-formate **37** (207 mg, 0.5 mmol) in THF (0.5 mL) was added the solution of the palladium catalyst (0.4 mL, 0.025 mmol) at room temperature and the reaction

mixture was stirred for 2 h. The mixture was passed through Florisil using ether (30 mL) as an eluent, and the combined organic layer was concentrated to give crystals (185 mg). The product was contaminated with the heteroannular 3,5-diene **39** (5%) which was removed by flash column chromatography. 5α-Cholest-3-ene (**38**) (148 mg) was obtained in 80% yield. mp. 74.0-74.5°C (n-hexane-ethanol), $[\alpha]_D$ = +60.12° (C = 0.509, $CHCl_3$), lit. 73-74°C, +62° ($CHCl_3$),[34] ^1H NMR. δ, 0.67 (s, 3H, 18-CH_3), 0.77 (s, 3H, 19-CH_3), 0.87 (d, J = 6.60 Hz, 3H, 26- or 27-CH_3), 0.87 (d, J = 6.60 Hz, 3H, 26- or 27- CH_3), 0.91 (d, J = 6.60 Hz, 3H, 21-CH_3), 0.92-2.08 (m, 29H, CH and CH_2), 5.25-5.30 (m, 1H, CH=C), 5.50-5.56 (m, 1H, C=CH). Hydrogenation (room temperature, 1 atm) of **38** in ethyl acetate with Pd on carbon (10%) afforded 5a-cholestane (**41**), mp, 80-80.5°C, lit. 78-79°C,[35]. Hydroboration of **38** with BH_3,[31] followed by oxidation (PCC) afforded 3-cholestanone (**40**), mp, 127.5-128.5°C (ethanol), $[\alpha]_D$ + 39.76° ($CHCl_3$, C = 0.332), lit. 125-126°C,[36] ^{13}C NMR, δ, 11.9, 12.2, 18.7, 21.1, 22.6, 22.8, 23.5, 23.9, 24.2, 27.5, 28.0, 28.3, 32.1, 34.1, 34.9, 35.6, 35.8, 36.2, 39.5, 40.1, 42.8, 45.9, 53.4, 56.3, 56.6, 125.4, 131.5.

5β-Cholest-3-ene (43). The reaction of the α-formate **42** (202 mg, 0.488 mmol) was carried out with the palladium catalyst (0.4 mL, 0.025 mmol) for 2 h to give crude crystals (177 mg) after work-up. The product, contaminated with the homoannular 2,4-diene **44** (7%), was purified by flash column chromatography. 5β-Cholest-3-ene (**43**) (165 mg) was isolated in 89% yield. semi-solid, $[\alpha]_D$ = +19.20° (c = 0.698, $CHCl_3$), lit. mp. 48-50°C, +19.6° (C= 0.63, $CHCl_3$).[32] Anal. Calcd for $C_{27}H_{46}$: C, 87.49; H, 12.51. Found: C, 87.47; H, 12.91. ^1H NMR. δ, 0.66 (s, 3H, 18-CH_3), 0.86 (d, J = 6.60 Hz, 3H, 26- or 27-CH_3), 0.86 (d, J = 6.60 Hz, 3H, 26- or 27-CH_3), 0.90 (d, J = 6.60 Hz, 3H, 21-CH_3), 0.95 (s, 3H, 19-CH_3), 0.96-2.05 (m, 29H, CH and CH_2), 5.31-5.36 (m, 1H, CH=C), 5.62-5.69 (m, 1H, C=CH). ^{13}C NMR. δ, 12.0, 18.7, 21.5, 22.4, 22.6, 22.8, 23.0, 23.8, 24.3, 27.5, 27.7, 28.0, 28.3, 33.5, 34.0, 35.6, 35.8, 36.2, 39.5, 40.3, 40.9, 42.7, 43.5, 56.3, 56.2, 127.0, 132.4. Hydrogenation of **43** afforded 5β-Cholestane (***45***). mp, 70.5°C (EtOH), $[\alpha]_D$ = +25.05° (C = 0.503, $CHCl_3$), lit. 71-72°C (EtOH), +25.07 ($CHCl_3$).[37]

Androst-3-en-17β–ol (49). The reaction of the β-formate **46** (216 mg, 0.5 mmol) in THF (0.7 mL) with the palladium catalyst (0.37 mL, 0.025 mmol) for 1.5 h gave crude crystals (195 mg). The crude product, contaminated with the heteroannular 2,4-diene **48** (5%), was purified by flash column chromatography to give white crystals of **47** (182 mg, 94%). ^1H NMR. δ, 0.00 (s, 3H, Si CH_3), 0.01 (s, 3H, Si CH_3), 0.71(s, 3H, 18-CH_3), 0.78 (s, 3H, 19-CH_3), 0.88 (s, 9H, t-Bu), 0.80-2.09 (m, 20H, CH and CH_2), 3.55 (dd, J = 8.43, 8.43 Hz, 1H, OCH), 5.25-5.30 (m, 1H, CH=C), 5.52-5.58 (m, 1H, C=CH). ^{13}C NMR. δ, -4.8, -4.5, 11.5, 11.9, 18.1, 20.7, 23.52, 23.53, 25.9, 27.4, 31.0, 31.7, 34.2, 35.0, 35.7, 37.3, 43.5, 46.0, 50.8, 53.7, 81.9, 125.5, 131.4. Desilyation of **47** with Bu_4NF afforded 5α-androst-3-en-17β-ol (**49**). mp, 152.5-153.5°C (n-hexane), $[\alpha]_D$ = +55.13° (C = 0.584, $CHCl_3$), lit. 152-153°C, +50° ($CHCl_3$).[37]

5β-Androst-3-en-17β-ol (53). The reaction of the α-formate **50** (75 mg, 0.175 mmol) in THF (0.5 mL) with the palladium catalyst (0.13 mL, 0.0087 mmol) for 1.5 h gave a yellow oil (65 mg). The crude product, contaminated with the homoannular 2,4-diene **52** (8%), was purified by flash column chromatography to give **51** as an oil (47 mg, 87%). ^1H NMR. δ, -0.01 (s, 3H, $SiCH_3$), 0.00 (s, 3H, $SiCH_3$), 0.70 (s, 3H, 18-CH_3), 0.87 (s, 9H, t-Bu), 0.96 (s, 3H, 19-CH_3), 0.75-2.07 (m, 20H, CH and CH_2), 3.53 (dd, J = 8.42, 8.42 Hz, 1H, OCH), 5.30-5.36 (m, 1H, CH=C), 5.62-5.69 (m, 1H, C=CH). ^{13}C NMR. δ, -4.8, -4.5, 11.3, 18.1, 21.1, 22.4, 23.0, 23.6, 25.9, 27.1, 27.6, 31.0, 33.6, 34.1, 35.7,

37.5, 41.2, 43.4, 43.6, 50.5, 81.9, 127.0, 132.3. Desilyation of **51** with Bu_4NF afforded 5β-androst-3-en-17β-ol (**53**) as crystals, mp, 136-137°C, $[\alpha]_D$ = 13.1° (C = 0.107, $CHCl_3$), lit. 132-133°C, +13° ($CHCl_3$).[38]

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