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Stereochemistry of the Palladium Catalyzed Exchange of Deuterium with Allylic Hydrogens[1]

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The stereochemistry of the palladium catalyzed exchange of deuterium with the allylic hydrogens of cholest-8(14)-en-3β-ol, 2, has been examined in a test of the Rooney, Gault, and Kemball hypothesis that a π-allylic surface intermediate is able to react directly with molecular hydrogen. The test compound was selected from evidence that only one face of the double bond is accessible to a catalytic surface. The correlation of mass, ^{13}C nuclear magnetic resonance, and infrared spectral data shows that no more than one hydrogen atom in each allylic methylene group is replaced (C-7 and C-15). Because the RGK mechanism would require that both hydrogens should be replaced, it cannot be operating in this system.

The isomerization of cholest-7-en-3β-ol to **2** is catalyzed in benzene solutions by $PdCl_2(C_6H_5CN)_2$ but not by $HRh(PPh_3)_4$, which lends support to the hypothesis that π-allylic but not "half-hydrogenated" intermediates are involved in the related palladium-catalyzed isomerization and exchange reactions of these steroids.

INTRODUCTION

Some years ago Rooney, Gault, and Kemball (*1*) proposed that π-allylic complexes are intermediates in a variety of reactions involving hydrogen (deuterium) and hydrocarbons which are catalyzed by the surfaces of certain group VIII metals such as palladium and rhodium. The suggestion drew attention to the importance of considering that surface-catalyzed reactions are analogous to the reactions of transition metal complexes; however, the geometry of the transition state which they pictured for the key reaction in their proposal had no clear analogy in any recognized elementary process involving such complexes. They proposed that a π-bonded allylic structure was able to accept a hydrogen atom in two ways: (a) by abstracting a hydrogen atom from the surface to the underside of the adsorbed group, or (b) by abstracting a hydrogen atom from a molecule of hydrogen positioned above the complex, the second atom of this molecule being attracted simultaneously to a surface site (Fig. 1). This theory has been said to explain, for example, "two-set" exchange in cycloalkanes, *cis* to *trans* isomerization in dialkylcycloalkanes, the hydrogenation of

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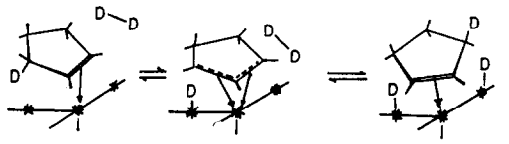

FIG. 1. The alternative paths for the combination of a π-allylic structure with deuterium according to the mechanism of Rooney, Gault, and Kemball (1). (Reproduced by permission of the publishers, Academic Press, Inc., New York.)

1,2-dimethylcyclohexene to a mixture of *cis* and *trans* isomers, and the distribution of deuterium in the products of the deuteration and exchange of *p*-xylene (*1*, *2*). The alternative possibility that desorbed alkenes might be the reactive intermediates which give rise to these phenomena has gained support although the extent of their freedom from the surface remains in question (*3–5*).

A critical test of the Rooney, Gault, and Kemball hypothesis appeared to require the determination of the stereochemistry of the exchange of allylic hydrogens with deuterium. It seemed to us that cholest-8(14)-en-3β-ol, **2**, is suited uniquely for accomplishing this purpose. Apparently only the α-face of the double bond is accessible to a hydrogenation catalyst because **2** cannot be hydrogenated (in neutral or weakly acidic media) nor be isomerized to cholest-14(15)-en-3β-ol, a more stable isomer (*6*, *7*). To form the latter, a hydrogen atom must be attached to C-8 in the β-configuration to produce the *trans* fusion of the B and C rings. Similarly, the approach to the β-face of the double bond in cholest-7-en-3β-ol, **1**, appears to be prohibited although syn addition of hydrogen to it would yield the most stable cholestanol (*7*). **1** can be isomerized to **2**, however, presumably by a transfer of the α-hydrogen at C-14 to the α-face of the double-bonded carbon atom at C-7. This would be consistent with the demonstration by Bream, Eaton, and Henbest (*7*) that the migration of a double bond from the 8(9)- to the 8(14)-position in the isomeric cholestenols, **3** to **2**, occurs by a 1,3-transfer of hydrogen which is restricted to one side of the molecule, the α-face in this instance (Fig. 2). The isomerization of

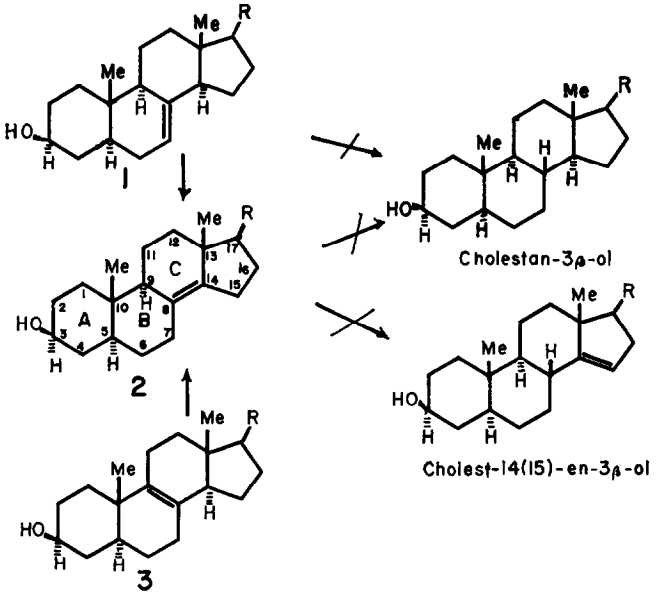

FIG. 2. Allowed and disallowed transformations of 1 and 2 on hydrogenation catalysts (neutral or weakly acidic media) (*3*).

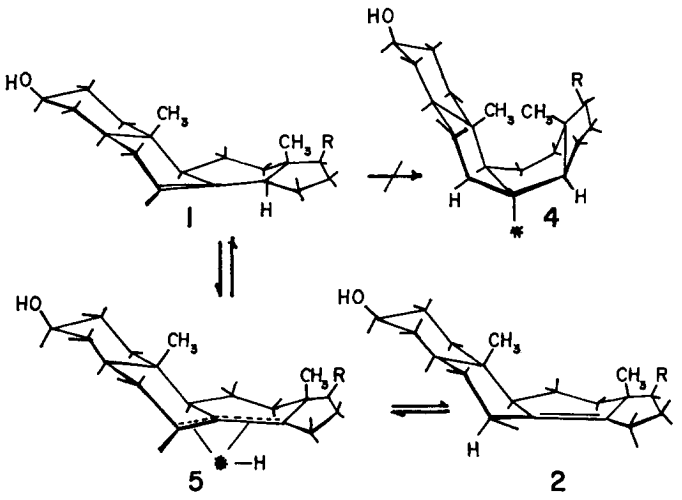

FIG. 3. Intramolecular nonbonded interactions which affect the mechanism of double-bond migration in cholest-7-en-3β-ol (*3*). (Reproduced by permission of the publishers, Academic Press, Inc., New York.)

acyclic tetra-substituted alkenes on palladium catalysts also involves stereo-specific hydrogen transfers presumably with retention of configuration at the tertiary carbon atoms (*8*).

The intermediates in the isomerizations of these steroids almost certainly have π-allylic structures rather than saturated "half-hydrogenated state" structures. The formation of the latter from either **1** or **2** when adsorbed on their α-faces, introduces large intramolecular repulsive interactions between the angular methyl groups at C-10 and C-13. These interactions are avoided if isomerization occurs via the formation of π-allylic intermediates (Fig. 3) (*3*).

Undoubtedly, the exchange of deuterium for the hydrogen atoms at C-7 and C-9 in **2** proceeds via the π-allylic structures which are intermediates in the isomerization of the cholestenes referred to above. In addition, exchange at C-15 could occur through the π-allylic structure formed by abstracting the α-hydrogen atom at C-15.

Although the evidence is clear that the transfer of hydrogen between the catalyst and the carbon atoms at C-8, C-9, and C-14 occurs only to the face of the carbon atom which is directed towards the catalyst, there is no direct evidence that the transfer at C-7 or C-15 is equally restricted (*7*). Furthermore, the later positions are more exposed than those at C-8, C-9, and C-14, and the operation of the RGK mechanism here would be revealed only thorugh exchange experiments.

Accordingly we have sought to determine the rate and stereochemistry of exchange with deuterium of the allylic hydrogen atoms in cholest-8(14)-en-3β-ol. A palladium catalyst was selected because the phenomena which the RGK mechanism presumes to explain are most commonly observed when palladium catalysts are used. In search for supporting evidence that the mechanism of isomerization of **1** to **2** involves the formation of a π-allylic intermediate, **1** was exposed to the action of several transition metal complexes which are believed to catalyze the isomerization of alkenes by different mechanisms (*9*).

EXPERIMENTAL

Materials. Following a procedure described by Birch and Walker for the hydrogenation of ergosterol (*10*), the hydrogenation of 7-dehydrocholesterol, **6** (ob-

tained from Aldrich Chemical Co.), in benzene containing chlorotristriphenylphosphinerhodium(I) as catalyst gave only cholest-7-en-3β-ol, **1**, which on recrystallization from ether-methanol produced fine white needles, mp 122.5–123.5° ((*11*) 122–123°). In comparison, the hydrogenation of **6** in dioxane at 760 Torr (ca. 27°) with a Raney nickel catalyst, according to the procedure of Fieser and Herz (*12*), gave a product which after a single recrystallization from aqueous acetone, produced small white crystals (mp 121–122°) which contained approximately 8% of **2** as estimated from its PMR spectrum. The hydrogenation of **6** in absolute ethanol catalyzed by Pd-black (*13*) gave **2** in 90% yield after recrystallization from anhydrous methanol or chloroform–methanol (1:3); white needles, mp 119.5–120.3°, $[\alpha]_D$ + 20.0° (mp 119–120°, $[\alpha]_D^{21}$ + 20.4°) (*11*).

Cholest-8(14)-en-3β-yl acetate, **7**, was prepared by the Pd-black catalyzed hydrogenation in absolute ethanol of cholest-5,7-dien-3β-yl acetate (International Chemical Co.); mp 76–77° ((*14*, *15*) 77–78°).

The palladium black was purchased from Engelhard Industries (Menlo Park, N.J.) and the complexes palladium chloride bisbenzonitrile (*16*) and hydridotetrakistriphenylphosphinerhodium(I) (*17*) were prepared according to previously described procedures.

Ethanol-OD, prepared from diethyl carbonate and D_2O (Diaprep, 99.7% deuterium) according to the procedure of Streitwieser, Verbit, and Stang (*18*), when used as a solvent for the exchange reactions of **2** with deuterium, resulted in more rapid rates of exchange than when either reagent grade absolute ethanol, which had been distilled from magnesium turnings, or ethanol-OD purchased from Diaprep Corp (99.5 atom % D) were used. Thiophene free benzene (Phillips Petroleum Co.) was percolated through alumina before use as a solvent for experiments with the soluble catalysts.

Procedure for the exchange reactions. The exchange reaction between cholest-8(14)-en-3β-ol, **2**, and deuterium was conducted in a 575-ml flat-bottomed flask which was connected to a gas buret, a mercury manometer, and a cylinder of deuterium (99.6$^+$ atom % D, Bio-Rad Laboratories or Liquid Carbonic Co.). Samples for analysis could be removed by syringe through a septum which closed a 10-mm tube sealed to the side of the flask. The mixture of the catalyst and the solution of **2** was stirred by a Teflon-coated stirring bar which was driven by an external magnet.

In a typical experiment, cholest-8(14)-en-3β-ol (1.54 g, 4×10^{-3} mole), the solvent (90 ml), and palladium black (0.28 g) were placed in the reaction flask; the system was evacuated and flushed three times with D_2 before stirring was begun. Samples were removed at predetermined intervals, filtered, and the solvent was evaporated. The crystalline product was recrystallized from methanol to insure that any -OD remaining in the sterol sample had been replaced by -OH.

Mass spectral analyses. Samples of exchanged **2** were analyzed by mass spectrometry (Hitachi RMU-6E) at 70 eV. The cracking pattern of unexchanged **2** furnished a reference for correcting the relative intensities of the ion currents corresponding to the parent ions of each molecular species in the sample of exchanged **2**. Cholest-4-en-3-one was added to some of these samples to serve as an internal mass marker.

Distribution of deuterium based upon ^{13}C NMR. Advantage was taken of the recent complete peak assignment for the ^{13}C spectrum of cholest-8(14)-en-3β-ol, **2**, which was accomplished by the use of a shift reagent, off-resonance proton decoupling, and a comparison of a series of narrow-frequency proton-decoupled ^{13}C spectra of this steroid (*19*).

The amount and location of deuterium in a sample of **2** which had undergone exchange was determined as follows. The noise-decoupled ^{13}C spectra of protonated and of partially deuterated cholest-8(14)-en-3β-ol were obtained under identical conditions. The intensities of the signals corresponding to that portion of the three allylic carbons which remained fully protonated in the partially exchanged sample were compared with the corresponding peak intensities of the unexchanged sample. From the ratios of the values, the percentage of incorporation of deuterium at each site was calculated. Because under the condition of this spectral determination the decrease in the intensity of a peak given by a particular methylene group in a molecule may be due to the replacement of either one or both hydrogens by deuterium, the estimation of the fractional number of deuterium atoms incorporated at C-7 and C-15 will be low if more than one proton has in fact been replaced at either position.

Infrared spectral analysis. A Perkin-Elmer 457 grating instrument was used to record the spectrum in the region in which the absorption bands are characteristic of the stretching mode of a C–D bond. Ten milligrams of the selected sample of cholest-8(14)-en-3β-ol, **2**, was dissolved in 0.30 ml of CCl_4 with 2 μl of acetonitrile to serve as an internal reference for frequency. The solution was placed in a 0.1025-cm demountable cell whose windows were polished and the spacing checked. A matched cell containing the solvent was used for reference and the region of the spectrum between 2500 and 2000 cm^{-1} was scanned on the slow speed.

Isomerization of cholest-7-en-3β-ol (**1**) *and cholest-7-en-3β-yl acetate catalyzed by* $PdCl_2(C_6H_5CN)_2$. A sample of **1** (0.108 g) and $PdCl_2(C_6H_5CN)_2$ (0.071 g) were placed in an NMR tube which was attached to a vacuum line and evacuated to ca. 1 μm. Purified benzene (0.633 g) was sublimed into the tube which then was sealed *in vacuo*. The solids dissolved when the mixture was warmed to 60°. The course of the isomerization was followed by observing the decrease in the intensity (peak height) of the signal at δ 0.54 (C-18 methyl group of **1**) and the increase in the intensity of the signal at δ 0.68 (C-19 methyl group of **2**). After about 90 min, palladium metal began to separate (ca.15% conversion of **1** to **2**). Similarly cholest-7-en-3β-yl acetate (0.102 g), $PdCl_2(C_6H_5CH)_2$ (0.024 g), and benzene (0.521 g) were heated in an evacuated sealed tube at 60°. The isomerization was much more rapid (96% conversion in 30 min) and palladium metal was not formed for at least 24 h.

A similar procedure was employed when isomerization was attempted with hydridotetrakistriphenylphosphinerhodium(I) as a possible catalyst. No change was observed during a period of 4 days at 60°.

RESULTS

In preliminary exchange experiments, reagent grade ethanol or a commercially available ethanol-OD (see experimental part) was used as a solvent. The results of a typical experiment in which the purchased ethanol-OD was used is given in Table 1. Evidently two hydrogen atoms are exchanged more rapidly than the third and

TABLE 1

The Palladium-Catalyzed Exchange of Cholest-8(14)-en-3β-ol with D_2 in Ethanol-OD (Diaprep Co.)[a]

Relaxation time (min)	Deuterium distribution (%)					ϕ[b]
	d_0	d_1	d_2	d_3	d_4	
16	63.8	30.9	3.9	1.1	0.2	43
45	43.5	43.0	12.0	1.4	0.0	72
180	19.2	51.9	27.2	0.8	0.0	114
2840	1.2	33.5	50.3	13.7	1.0	180
4380	1.2	30.3	51.3	16.1	1.1	186

[a] This experiment (B) was sampled at the times noted. The ^{13}C spectral analysis of the last sample (B-5) is given in Table 2.

[b] The function $\phi = \Sigma id_i$, where d_i is the mole fraction of molecules which contain i deuterium atoms. (See E. Crawford and C. Kemball, *Trans. Faraday Soc.* **58**, 2452 (1962).) The summation includes the d_3 molecules (computed from the mass spectrum), which in this experiment were always less than 1.0%.

TABLE 2

Comparison of ^{13}C NMR Analysis with Mass Spectral Analysis for Deuterium in Exchanged Cholest-8(14)-en-3β-ol[a]

^{13}C NMR		Mass spectrum		^{13}C NMR		Mass spectrum	
Position	%D	Mol. species	%	Position	%D	Mol. species	%
	Sample A-4				Sample B-5		
C-7	59	d_0	28.6	C-7	>95	d_0	1.2
C-9	17	d_1	56.1	C-9	58	d_1	30.3
C-15	7	d_2	15.2	C-15	22	d_2	51.3
		d_3	0.3			d_3	16.1
						d_4	1.1
Average D/mol.	0.83[b]		0.87		1.75+[b]		1.86
	Sample D-1				Sample E-2		
C-7	≥95	d_0	3.3	C-7	≥95	d_0	0.5
C-9	41	d_1	36.8	C-9	85	d_1	2.7
C-15	27	d_2	36.5	C-15	62	d_2	20.6
		d_3	19.2			d_3	48.8
		d_4	3.7			d_4	26.8
		d_5	0.3			d_5	0.0
Average D/mol.	1.68+[b]		1.85		2.42+[b]		3.00

[a] The sample designation refers to a sample obtained in an experiment recorded in Tables 1 or 3 except for A-4 which is mentioned only in the text.

[b] The reported percentage deuterium incorporated at C-7 and C-15 is based upon the assumption that only one deuterium atom is replaced at these positions (see text).

further exchange appears to proceed much more slowly. Similar results were obtained with the undeuterated ethanol which indicated that the exchange of D_2 with **2** is much faster than the exchange with the hydroxyl hydrogens of the ethanol.

The amount and location of deuterium in a sample of **2** which had undergone exchange for 73 hr (Table 1, sample B-5) was determined by ^{13}C NMR as described in the experimental section. Because this method of analysis measures the fraction of carbon atoms located at a particular position which have *not* gained any deuterium, the actual amount of deuterium which was introduced into the C-7 and C-15 methylene groups cannot be determined from this measurement without additional information. If one assumes that only one of the protons in these methylene groups can be exchanged, then the estimate for the fractional incorporation of one deuterium at C-7, C-9, and C-15 are >95, 58, and 22%, respectively, giving an average of 1.75+D per molecule. The mass spectrum of this sample shows the average number of deuterium atoms per molecule is 1.86D. Clearly the agreement between these two estimates excludes any significant amount of doubly deuterated carbon atoms, and therefore, only one of the hydrogen atoms at C-7 or C-15 was in fact replaced in this experiment. Similar results were obtained with a sample which contained a lesser amount of deuterium as a result of a slower exchange rate in ordinary ethanol (Table 2, Sample A-4).

More rapid and more extensive exchange

occurs if the solvent ethanol-OD is prepared from the reaction of D_2O with ethyl carbonate. The results using this solvent are quite reproducible as can be seen by comparing the distribution of deuterium in **2** found in experiments D and E with those found in experiment C for the same period of exposure to the conditions for exchange (Table 3). The deuterium content per molecule, as determined from the mass spectrum, is greater than that which is estimated, by ^{13}C NMR (CMR), to be at C-7, C-9, and C-15 (Table 2). The proton-decoupled CMR spectrum of these samples, however, indicates that deuterium is present at C-6 and C-11, and taking this into account, the comparison of ms and CMR data again indicates that only a single proton has been replaced at a given carbon atom.

The preceding conclusion is supported by the observed changes in the infrared spectra of successively more exchanged samples of **2**. As deuterium becomes incorporated into **2**, absorption bands grow in intensity in the region of 2000–2200 cm^{-1}, which is characteristic of a C–D stretch and a sharp band at about 2800 cm^{-1} disappears (Fig. 4). The first three bands which appear can be assigned to the introduction of deuterium at particular allylic positions in **2** through a comparison of the relative intensities of these bands with the distribution of deuterium given by the CMR spectral analysis. Thus the band at 2065, 2114, and 2169 cm^{-1}, are due to the introduction of deuterium at C-9, C-7, and C-15, respectively. This assignment is consistent with the observed absorptions reported for 5α-deutero-3β-acetoxycholestan-6-one at 2125 cm^{-1} and 7α-deutero-3β-acetoxycholestan-6-one at 2138 cm^{-1} which are due to C–D stretching modes; the lower frequency band is associated with an *axially* attached *tertiary* deuterium atom, the higher frequency with an *axially* attached *secondary* deuterium atom (*20*). The C–D adsorption band for an equatorial deuterium atom occurs at a

TABLE 3

The Palladium-Catalyzed Exchange of Cholest-8(14)-en-3β-ol with D_2 in Ethanol-OD Prepared from Ethyl Carbonate[a]

Expt.	Relaxation time (min)	Deuterium distribution (%)						ϕ[b,c]
		d_0	d_1	d_2	d_3	d_4	d_5	
C	16	26.2	48.5	20.1	4.2	1.0	0.2	106
	45	3.0	37.0	42.4	13.6	4.1	0.0	179
	180	0.5	22.6	20.0	52.4	24.6	0.0	298
	600	0.5	0.8	7.7	60.0	28.7	2.2	322
	780	1.4	1.3	7.5	53.4	31.7	4.5	327
	1020	0.3	0.7	2.6	39.2	43.0	14.2	367
	1200	0.2	0.6	3.9	36.7	48.3	7.5	376
	1590	0.2	0.6	3.8	29.0	49.0	12.5	396
	2190	0.2	0.6	3.4	23.6	50.2	22.0	389
	2880	0.2	0.5	2.9	19.6	50.4	25.7	400
D	45	3.3	36.8	36.5	19.2	3.7	0.3	184
E	45	4.9	35.6	38.7	18.3	2.5	0.0	178
	180	0.5	2.7	20.6	48.8	26.8	0.0	301

[a] Experiments C, D, and E are independent and were sampled at the indicated times.

[b] See footnote *b*, Table 1.

[c] The summation includes the molecules (computed from the mass spectrum) which were more highly deuterated than d_5, although they constituted less than 1.0% of the total number except in samples C-7 and C-8.

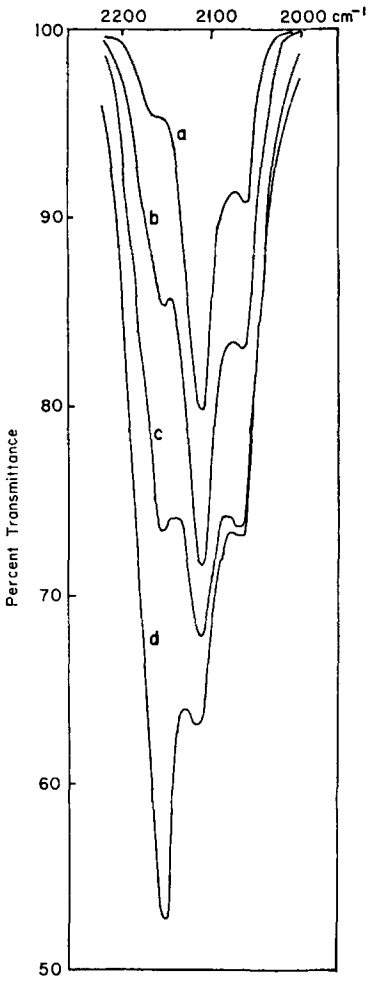

FIG. 4. Correlation of growth in infrared adsorption at 2000–2200 cm^{-1} with the incorporation of deuterium in cholest-8(14)-en-3β-ol (**2**). Curves a–d were given by samples of **2** which contained an average of 1.06, 1.84, 3.01, and 4.00 deuterium atoms per molecule as determined by mass spectrometry. Curves b and c may be compared with the ^{13}C NMR analysis for deuterium in the same samples (Table 3 samples D-1 and E-2).

higher frequency than the absorption band for an axial deuterium atom which is attached to the same carbon atom (*20*). An allylic C–D bond in the five-membered ring can be expected to absorb at a higher frequency than an axial allylic C–D bond in a six-membered ring.

The band at 2065 cm^{-1} reaches a maximum value when the average deuterium content (mass spectral analysis) is about 3.0 deuterium atoms per molecule while the apparent further increase in intensity at 2114 cm^{-1} is due to the growth of a band (or bands) at higher frequencies. Clearly in this process, the character of the band at 2114 cm^{-1} is not changed as would be expected if the -CHD- group at C-7 were being converted to $-CD_2-$ (*20*). In this event, a single C–D stretching frequency would be replaced by two frequencies corresponding to the coupled inphase and out of phase vibrations of the $-CD_2-$ group. Similarly the increase in absorption at about 2169 cm^{-1} seems to be due to an increase in the number of -CHD- groups (apparently the α-H's at C-10 and C-11 which are equatorial are replaced) rather than to the replacement by deuterium of both hydrogen atoms at C-15. This conclusion is consistent with our interpretation of the proton-decoupled CMR spectra of the more highly exchanged sample of **2** as noted above.

The isomerization of cholest-7-en-3β-yl acetate to cholest-8(14)-en-3β-yl acetate proceeds readily in benzene solutions containing the benzo-nitrile complex of palladium chloride. However, no reaction occurs if hydridotetrakistriphenylphosphinerhodium(I), $HRh(PPh_3)_4$, is used in place of the palladium complex. Both complexes are known to be effective catalysts for the isomerization of alkenes albeit by different mechanisms (*9*).

DISCUSSION

Evidently, the exchange of deuterium at the C-7 and C-15 allylic positions of **2**, places no more than one deuterium at each carbon atom. Exchange at the tertiary C-9 carbon atom definitely occurs with retention of configuration on the α-side of the molecule, the side which faces the catalyst. If the same mechanism also accounts for exchange at C-7 and C-15, then the deuterium atoms introduced at the latter positions also must have α-configurations.

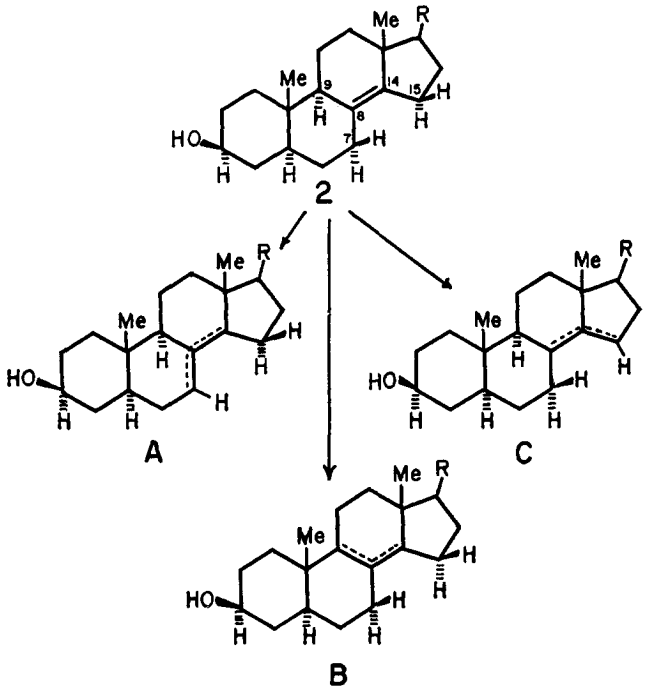

FIG. 5. Alternative π-allylic structures resulting from the abstraction of allylic hydrogen atoms from **2**. Bonding to the catalyst is not symbolized.

This conclusion is supported by the infrared spectral data, however, a more direct basis for making this configurational assignment is being sought by the use of proton magnetic resonance and shift reagents (*21*). Clearly, the RGK mechanism which should lead to the replacement of both α and β hydrogen atoms is not operating here. And because replacement with retention of configuration is the dominant, if not exclusive, mechanism of catalytic exchange in neutral media, one may conclude that the mechanism first proposed by Rooney, Gault, and Kemball, which involves an attack of molecular deuterium upon a π-allylic complex of the catalyst, does not occur in this instance. One might concede that this mechanism might be blocked sterically at C-9, but the C-7 and C-14 positions are exposed.

Interestingly, the relative rates of exchange of the protons at C-7, C-9, and C-15 decrease in that order, although one might have anticipated that exchange at C-9, a tertiary carbon atom, would take place more rapidly than at C-7. Perhaps this indicates that the formation of a π-allylic structure from C-7 to C-14, (**A**), is subject to less catalyst hindrance than the formation of the π-complex **B**, C-9 to C-14 (Fig. 5). The π-complex (**C**) resulting from the abstraction of a hydrogen atom at C-15 would be expected to be strained relative to **A** because unsaturation is extended into a five- instead of to a six-membered ring. Presumably the relative stabilities of these complexes would be reflected in the relative energies of the transition states through which they are formed from **2**.

The finding that the isomerization of the acetate of **1** (cholest-7-en-3β-yl acetate) is readily accomplished in a benzene solution of $PdCl_2 \cdot (C_6H_5CH)_2$ whereas the complex $HRh(PPh_3)_4$ is completely without effect, indicates that the isomerization proceeds via the abstraction of an allylic hydrogen from **1** to form a π-allylic intermediate. Apparently the alternative ad-

dition–elimination mechanism does not take place although $HRh(PPh_3)_4$ is a very effective isomerization catalyst of simple alkenes. The bulky triphenylphosphine ligands might prevent the required coordination of **1**. However, we are inclined to attribute the lack of isomerization in this instance to the reason we have given to explain why neither **1** nor **2** can be hydrogenated, e.g., that the formation of the required half-hydrogenated state is prevented by the large intramolecular repulsive interactions which develop upon forming this saturated structure (Fig. 3).

The failure of cholest-8(14)-en-ol, **2**, to be hydrogenated over a palladium catalyst also indicates that the suprafacial 1,3-sigmatropic hydrogen shift mechanism, which was proposed by Smith and Swoap (*22*) to explain some of the same phenomena for which the RGK mechanism was designed, does not occur with these steroids. The argument is as follows: A molecule of **2** can be absorbed on its α-face forming a π-complex. The presumed suprafacial 1,3-sigmatropic mechanism should permit the transfer of a β-hydrogen at C-15 to the β-position at C-8 with the concomitant formation of the 14(15)-double bond thus yielding cholest-14(15)-en-3β-ol (Fig. 2) which is readily hydrogenated to cholestanol (*6*, *7*). The isomerization is catalyzed by protic acids but not by platinum metal catalysts and hydrogen in neutral media (*6*).

Hilaire and Gault (*23*) have proposed that the double-bond migration in simple alkenes, which occurs on the surface of palladium, prodeeds by a direct intramoledular shift of hydrogen according to the mechanism of Smith and Swoap (*22*). Although structural changes do result in changes in reactivity via a particular mechanism, complete lack of conversion of **2** (although 1-butene, for example, isomerizes readily on palladium catalysts) would be difficult to explain if 1-butene were isomerizing via the suggested 1,3-shift mechanism. One should note that the exchange of allylic hydrogens proceeds readily in either compound on palladium catalysts, although the experimental conditions are not strictly comparable. Accordingly we suggest that alternatives to the 1,3-sigmatropic shift mechanism be sought to rationalize the results of alkene isomerization and exchange experiments.

At one time, the possibility that desorbed alkenes are the reactive intermediates, which give rise to the phenomena which the RGK mechanism was designed to explain, was discounted on the grounds that the enthalpy for the conversion of alkane to alkene plus hydrogen was too unfavorable (*24*). The argument, however, neglected to consider the partially compensating heat of adsorption of hydrogen, an oversight which has since been corrected (*4*). The catalysts (palladium and rhodium) which best promote these phenomena are also catalysts which are particularly active for the isomerization of alkenes, processes which require the ready desorption of alkenes.

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[3] Note added in proof. The use of the shift reagent $Eu(fod)_3$ at 90 MHz did not give an adequate resolution of the desired proton spectrum.

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