Mechanism of Formation of 4–6η-3-Oxo Steroid–PdCl Complexes

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Summary In the formation of the 4α—6α-η-PdCl complex from 2,2-dimethylcholest-4-en-3-one initial π-complexing appears to be rate-limiting, and in the proton elimination step, $k\ 6\beta^2H/k\ 6\alpha^1H$ = *ca.* 1.

A SERIES of 3-oxo-Δ^4-steroids (**1**) have been shown to give 4—6-η-PdCl complexes[1] (**2**) as single substances (t.l.c.), showing a consistent pattern of ^1H n.m.r. signals for 4-H, 6-H, and 19-Me (Table).

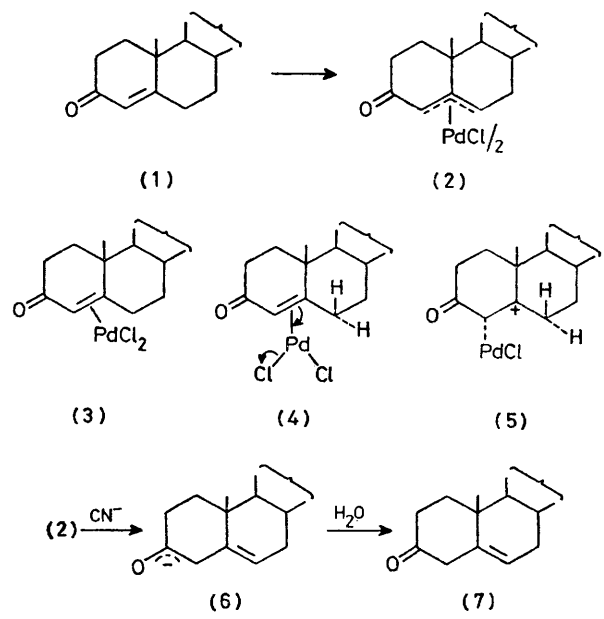
TABLE

	δ				
Substitution	4-H	6-H	19-Me	19-Me[a]	Method[b]
(**2a**) 17β-C_8H_{17}	3·40	4·41	1·23	1·16	(i), (ii), (iii)
(**2b**) 17β-OH	3·43	4·45	1·27	1·18	(i), (ii)
(**2c**) 17α-Me, 17β-OH	3·46	4·42	1·27	1·24	(i)
(**2d**) 17β-COMe	3·34	4·43	1·27	1·16	(i)
(**2e**) 2,2-Me_2, 17β-C_8H_{17}	3·28	4·44	1·27	1·25	(i), (iii)

[a] Parent steroid. [b] (i) Na_2PdCl_4 in MeOH, 72—96 h; (ii) $(PhCN)_2PdCl_2$ in benzene, reflux, 12 h; (iii) $(PhCN)_2PdCl_2$ + steroid in a melt at 90 °C, 0·5 h.

4—6β-η-Co-ordination of the PdCl residue in (**2**) would be expected to deshield the 19-Me group appreciably;[2] in a 4—6β-η-analogue of (**2**) Jones[3] indicates deshielding of 19-Me by 0·4—0·45 p.p.m. We infer that in the above series of complexes (**2**) the PdCl residue is α-co-ordinated.

Formation of the PdCl derivative (**2**) may be followed by t.l.c. separation, and u.v. estimation of the complex formed. Using testosterone and method (i) (Table), we found no catalysis by added HCl, *i.e.* PdCl-co-ordinates to the keto rather than to the enolic form of (**1**), and, as expected, retardation by added LiCl. There remains, however, the question of which step in the sequence (**1**) → (**3**) → (**2**) may be rate determining, and the degree of stereoelectronic discrimination between elimination of 6β-H or 6α-H.



Preliminary experiments with 6β-[^{2}H]cholest-4-en-3-one using method (ii) (Table), with added $CaCO_3$ (4 equiv.) to trap HCl, indicated substantial retention of ^{2}H in the complex (**2a**) formed, but some loss and scrambling of ^{2}H in the unreacted cholest-4-en-3-one. We therefore turned to 2,2-dimethylcholest-4-en-3-one[5] which was found to react by methods (i) and (iii), but not by method (ii), except at very high concentration. Added bases ($CaCO_3$, NaOAc) in methanol solution promote reduction to palladium. We therefore applied method (iii) to 6β-[^{2}H]2,2-dimethylcholest-4-en-3-one (86% ^{2}H, from DCl on 2,2-dimethyl-3-ethoxycholesta-3,5-diene[4]) with dry $CaCO_3$ added to the melt. Recovered 2,2-dimethylcholest-4-en-3-one retained 85% ^{2}H, and a ^{2}H-complex (**2e**) was obtained (n.m.r. integration, 4-H : 6-H = 1 : 0·4).

In the mass spectrometer, complexes (**2**) lose Pd, H, and Cl which makes ^{2}H estimation uncertain. However, we find that these complexes react readily with aqueous KCN, with kinetic protonation of an intermediate carbanion (**6**), and in a two-phase reaction system with benzene the 3-oxo-Δ^5-steroid (**7**) may be isolated without isomerisation. In this way the ^{2}H-complex (**2e**) gave ^{2}H-2,2:dimethylcholest-5-ene-3-one, *m/e* 413 and 412, ν_{CO} 1720 cm^{-1}, δ 5·4 (*ca.* 0·5H), containing 42% ^{2}H, and this result could be duplicated.

By sampling the reaction mixture, t.l.c. separation, and u.v. estimation of both unreacted steroid and complex (**2**), the rate of reaction by method (iii) could be followed. Rate plots for (**1e**) and 6β-[^{2}H]-(**1e**), obtained in this way, showed a little scatter, but a mean ratio of 6β-[^{1}H]-(**1e**) : 6β-[^{2}H]-(**1e**) = 1·1 : 1 indicates essentially no rate difference, *i.e.* step (**1**) → (**3**) appears to be slow relative to (**3**) → (**2**), in this case.

Alkene–$PdCl_2$ complexes undergo *trans*-addition of nucleophilic addends,[6] which suggests that the π-$PdCl_2$ → π-allyl–PdCl transformation may follow from a polarisation step (**3**) ⇌(**4**) or (**5**). However, the orbital overlap requirements for concerted proton loss should then lead to marked discrimination in favour of 6β-H elimination; in base-catalysed enolisation of androst-4-en-3,17-dione, 6β-H is removed 53 times faster than 6α-H. In the case of [^{2}H]-(**1e**) → [^{2}H]-(**2e**), the ^{2}H loss (86 to 42%) indicates a discrimination in favour of 6β-H loss of the same order as the kinetic isotope factor $k6\beta\text{-H}/k6\beta\text{-}^2\text{H}$. Data for enolisation[8] or elimination[9] reactions point to a kinetic isotope factor of 4—6. Discrimination of this order in favour of 6β-H elimination in the reaction (**1e**) → (**2e**) appears to be much too small to be consistent with concerted loss of proton and Cl^- in (**4**). The electrons of the 6α-bond, on the other hand, are not suitably oriented for direct overlap into a π-allyl grouping. However, n.m.r. studies[10] for simple Pd-π-allyl derivatives, indicate a dynamic state between π-allyl and σ-allyl extreme structures. Hence, 6α-H loss, possibly to Pd or to Cl^-, accompanied by Pd insertion into the electrons of the 6α-bond may offer a second route to products of type (**2**). The surprisingly small discrimination in favour of 6β-H loss suggests that this second mechanism may make a significant contribution to formation of the Pd–π-allyl complex in the present case. More generally, the relative extent of *syn* or *anti* hydrogen loss may depend on the solvent and the bases present.

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