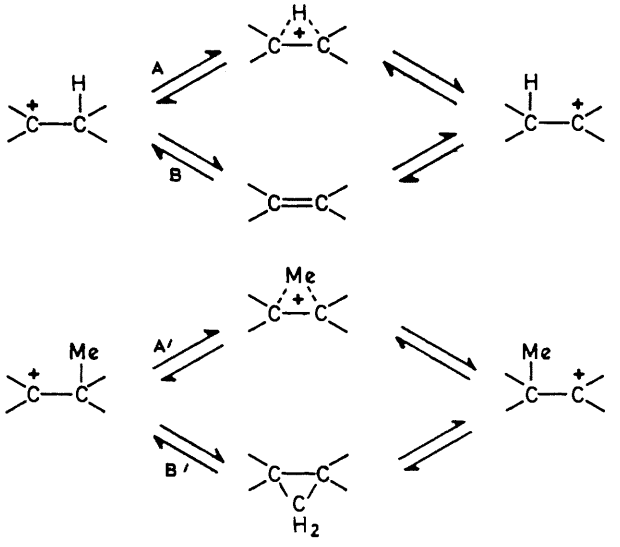
The Backbone Rearrangement of Des-A-steroids: Some Mechanistic Aspects

By J. P. BERTHELOT and J. LEVISALLES*†

(*Laboratoire de Chimie, Faculté des Sciences de Nancy, France*; *Equipe de Recherche Associée au C.N.R.S.*)

Summary Using deuteriated substrate and reagent, it was shown that the backbone rearrangement of des-A-steroidal hydroxy-olefins does not proceed through protonation–deprotonation of intermediate olefins or cyclopropanes.

CHEMICALLY induced backbone rearrangements of steroids[1–4] and triterpenoids[5,6] take place by stereospecific migrations of hydrogen atoms and methyl groups. For each migrating species (H or CH_3) two mechanisms can be envisaged:



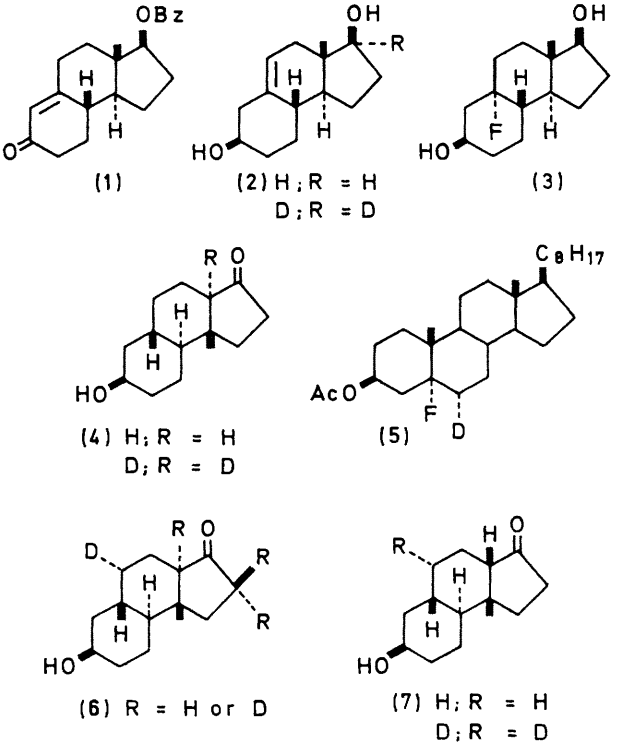
In mechanisms A and A′, the migrating species does not exchange hydrogen with the surrounding medium, but it does so in mechanisms B and B′. It has been previously shown,[2,4] that anhydrous HF is a convenient medium for such rearrangements; and we describe here experiments which were conducted with DF, on a des-A-steroid, the structure of which simplifies the interpretation of deuterium labelling experiments (only one methyl group in the molecule).

The hydroxy-enone (**1**)[7] could be transformed by reduction of the corresponding enol acetate into diol (**2H**). On treatment with anhydrous HF, diol (**2H**) gave a mixture of fluoro-diol (**3**) and hydroxy-ketone (**4H**). Chemical and spectral data, which are omitted for the sake of brevity, fully support the structures assigned.[8] As it had been shown in the androstane series,[2] diol (**2D**), treated under the same conditions, afforded hydroxy-ketone (**4D**) with 97 ± 3% retention of deuterium.

DF was prepared according to the method of Olah and Kuhn,[9]

$$FSO_3H + D_2O \rightarrow DF + HDSO_4,$$

and was found to contain 33% DF by mass spectral analysis of the addition product (**5**) with cholesteryl acetate (see Table).[10,11] Diol (**2H**) was treated with DF, and the resulting hydroxy-ketone (**6**) was heated under reflux with methanolic KOH to remove any deuterium α to the carbonyl group. The resulting epimeric hydroxy-ketone (**7D**) was analysed by mass spectrometry (see Table). Bearing in mind the margin of error in mass spectral measurements (±3%), this leads to the conclusion that only one deuterium has been introduced in the molecule, *i.e.* at C-11. The influence of a possible kinetic isotope effect is cancelled out in this case by the method used for deuterium analysis.



The fluoro-diol (**3**), treated in the same way, afforded hydroxy-ketone (**7H**), analysed by mass spectrometry

Deuterium distribution in various deuteriated samples (as determined by mass spectrometry)

Sample	$^2H_0$	$^2H_1$	$^2H_2$
(**5**)	67	33	0
(**7D**) from (**2H**) ..	68·5	31·5	0
(**7H**) from (**3**) ..	97	3	0

(see Table). Again, this indicates no introduction of deuterium in the molecule.‡

† Present address: Laboratoire de Chimie organique, Faculté des Sciences, 1, rue Victor Cousin, 75-Paris 5ème, France.

‡ It can be shown that the fluoro-diol (**3**) is formed first, and then the hydroxy-ketone (**4H**); the small amount of deuterium found in (**7H**) may be taken as evidence that the reverse reaction from (**3**) to (**2H**) hardly occurs at all. [For similar evidence in the case of cholesterol, see ref. 12. footnote p. 1650].

The above results seem to exclude mechanisms B [13] and B',[14] as both these mechanisms would imply production of multideuteriated species with a binomial distribution. Since this is not the case, it must be concluded that a protonation–deprotonation mechanism is ruled out for the migration of hydrogen atoms and methyl groups. This is in good agreement with experiments described by Coates[6] with $ZnCl_2$–CH_3CO_2D on the friedelene → alnusene → oleanene transformation and also with the recent results of Olah and White[15] concerning the t-butyl-dimethyl- and isopropyl-dimethyl-carbonium ions.

These experiments, however, do not distinguish between a plain 1–2 methyl shift and the intermediate formation of an edge-protonated cyclopropane, which rearranges more rapidly than it exchanges protons with the medium.

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[1] J. W. Blunt, M. P. Hartshorn, and D. W. Kirk, *Tetrahedron Letters*, 1966, 2175.
[2] J. C. Jacquesy, J. Levisalles, and J. Wagnon, *Chem. Comm.*, 1967, 25; *Bull. Soc. chim. France*, 1970, 670.
[3] F. Frappier, Q. K. Huu, F. X. Jarreau, J. Hannart, and R. Goutarel, *Compt. rend.*, 1967, **264**, *C*, 707.
[4] P. Bourguignon, J. C. Jacquesy, R. Jacquesy, J. Levisalles, and J. Wagnon, *Chem. Comm.*, 1970, 349.
[5] J. L. Courtney, R. M. Gascoigne, and A. Z. Szumer, *J. Chem. Soc.*, 1958, 881.
[6] R. M. Coates, *Tetrahedron Letters*, 1967, 4143.
[7] L. Velluz, G. Nomine, J. Mathieu, E. Toromanoff, D. Bertin, J. Tessier, and A. Pierdet, *Compt. rend.*, 1960, **250**, 1084.
[8] J. P. Berthelot, Thesis, Nancy, 1970.
[9] G. A. Olah and S. J. Kuhn, *J. Inorg. Nuclear Chem.*, 1959, **10**, 164.
[10] C. S. Barnes and C. Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1962.
[11] R. Jacquesy and J. Levisalles, *Bull. Soc. chim. France*, 1966, 1884.
[12] J. C. Jacquesy, R. Jacquesy, and J. Levisalles, *Bull. Soc. chim. France*, 1967, 1649.
[13] G. Ourisson, *Proc. Chem. Soc.*, 1964, 274.
[14] G. M. Kramer, *J. Amer. Chem. Soc.*, 1969, **91**, 4819.
[15] G. A. Olah and A. M. White, *J. Amer. Chem. Soc.*, 1969, **91**, 5801.