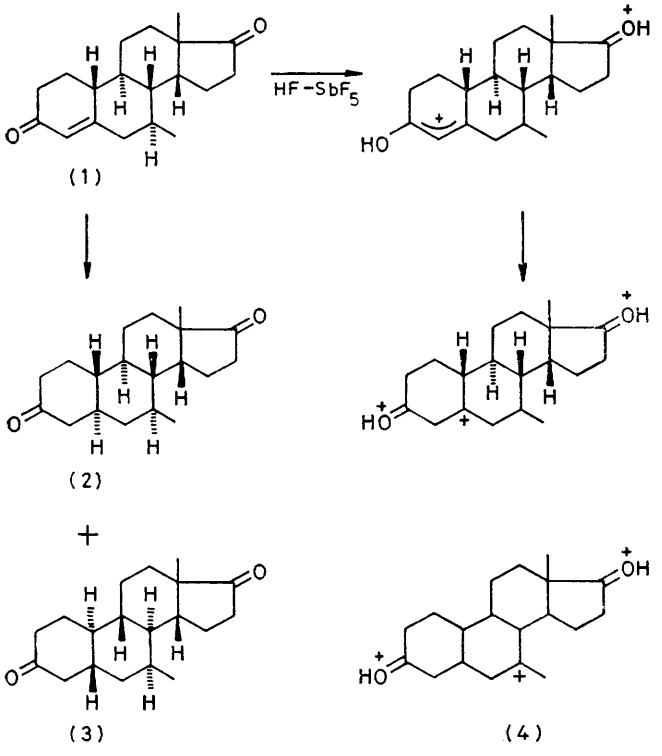
Reductive Isomerisation in Superacidic Media: Evidence for a 1,3 Hydride Shift in a Steroid

By ROSE JACQUESY and CLAUDINE NARBONNE

(*Laboratoire de Chimie XII 'Synthèse et réactivité de produits naturels,' E.R.A. C.N.R.S. No.* 556, 40, *Avenue du Recteur Pineau,* 86022 *Poitiers, France*)

Summary The major component of the reaction of 7β-methyl-14-iso-oestr-4-ene-3,17-dione in HF–SbF_5–methylcyclopentane at 0 °C has been shown to result from 1,3 hydride shift followed by kinetically controlled intermolecular hydride transfer.

IN superacidic media, steroidal keto-enones such as (**1**) can undergo unusual isomerisations *via* triprotonated species. The third protonation on the hydroxyallyl cation is rate limiting and affords a carbenium ion which can be trapped *in situ* by a hydride donor, *e.g.*, a hydrocarbon. The fate of the carbenium ion before trapping is of interest since the isomerisations observed in superacidic media are usually different from those occcuring in other acidic solutions.



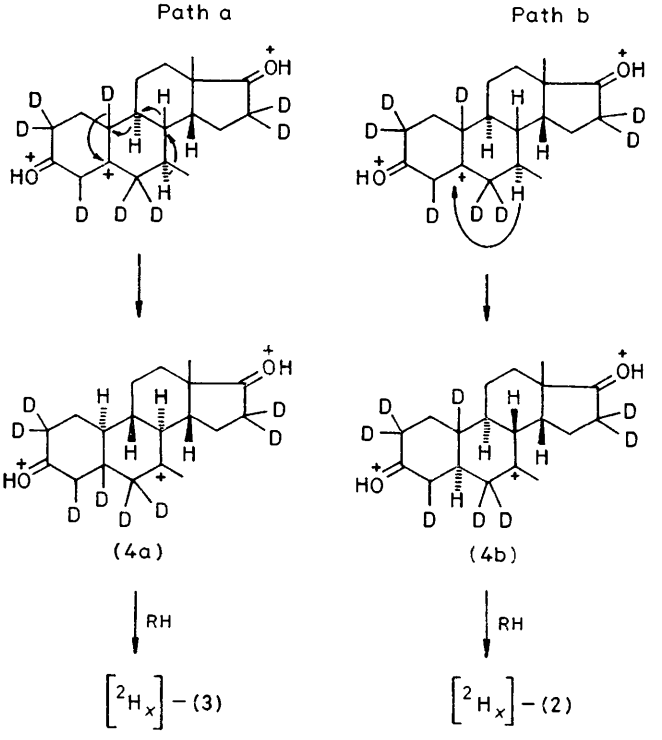
Addition of the enone (**1**) (300 mg) to a solution of HF (5 ml)–SbF_5 (1 ml)–methylcyclopentane (0·2 ml) leads, after 40 min at 0 °C, to a mixture of the ketones (**2**) (60%; already described[1]) and (**3**)† (27%).

Use of perdeuteriated cyclohexane as donor leads to monodeuteriated (**2**) and (**3**) in which the deuterium atom is located at the 7-position implying reduction of a triprotonated species (**4**).‡ At this acidity, the intermolecular hydride transfer is shown to be irreversible.

TABLE 1. Deuterium content and distribution in compounds (**1**), (**2**), and (**3**) (mass spectrometric determination).

Compd.	$^2H_3$	$^2H_4$	$^2H_5$	$^2H_6$	$^2H_7$	$^2H_8$	Total deuterium content
(**1**)	1·5	3	9	25·5	43	18	6·6 atoms
(**2**)	1	3·5	10·5	30	42	13	6·5 atoms
(**3**)	—	1·5	6·5	24	45	23	6·8 atoms

In order to provide some insight into the mechanism of the isomerisation steps, the enone (**1**), extensively deuteriated at the enolisable positions (2, 4, 6, 10, 16), was examined under the same conditions as just described, leading to polydeuteriated ketones (**2**) and (**3**). No loss of deuterium could be detected (Table 1), in agreement with a



SCHEME

† M.p. 100 °C; $[\alpha]_D$ + 25°; ^1H n.m.r.: 1·0 (3H, s) and 0·91 (3H, d, *J* 7 Hz); c.d. (dioxan): $\Delta\epsilon_1$ + 0·2 (320 nm); $\Delta\epsilon_2$ — 1·09 (292 nm).

‡ In superacidic media ($H_0 < -12$), keto groups are 100% protonated as shown by their u.v. and n.m.r. spectra.

mechanism of isomerisation proceeding only *via* intramolecular hydride shifts.

The position of the deuterium atoms in (**2**) and (**3**) was determined unambiguously by comparison between the ^{13}C n.m.r spectra of the non-deuteriated and deuteriated compounds. The chemical shifts were calculated by the semi-empirical method recently described by Saunders *et al.*[2] and showed good agreement with the experimental spectra. Studies of specifically deuteriated compounds and of selected derivatives confirmed the given assignments[3] (Table 2). The complete disappearance in the ^{13}C n.m.r. spectrum of the deuteriated compounds $[^2H_x]$-(**3**) of the signals at 48·6 (C-4), 41·6 (C-6), 41·2 (C-2), 36·7 (C-5), and 33·4 p.p.m. (C-16) and shielding of the signals corresponding to C-10 and C-15 (0·15 p.p.m.) and C-1 and C-7 (0·10 p.p.m.), due to an isotope effect, indicate a classical mechanism proceeding *via* 1,2 hydride shifts (Scheme, path a). In the ^{13}C n.m.r. spectrum of the major component $[^2H_x]$-(**2**), signals at 43·3 (C-6), 41·2 (C-2), and 35·8 p.p.m. (C-16) are totally absent while signals at 46·1 (C-10) and 48·4 p.p.m. (C-4) are of very low intensity. The signals due to C-1, C-5, and C-15 are shifted to high field by 0·15—0·25 p.p.m. and the C-9 signal by only 0·08 p.p.m. These data are only compatible with the reduction of the species (**4b**) resulting from a direct 1,3 hydride shift (Scheme, path b).

TABLE 2. ^{13}C N.m.r. spectra of the ketones (**2**) and (**3**) [$\delta(Me_4Si)$ 0 p.p.m.].

Compd.	C-1	C-2	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-18	7-Me
(**2**)	30·2	41·2	48·4	42·6	43·3	32·9	45·2	39·9	46·1	25·4	27·8	47·7	44·4	19·0	35·8	18·7	19·1
(**3**)	30·2	41·2	48·6	36·8	41·6	28·7	45·3	38·1	47·0	27·5	31·1	50·2	45·3	19·9	33·4	25·2	13·7

Although intramolecular 1,3 hydride shifts in both the acyclic aliphatic and the norbornyl cations are well documented,[4] their occurrence as a major possible pathway in the cyclohexyl system has been questioned.[4,5] It is clear from our results that suitable geometrical conditions and the use of superacid media can indeed favour 1,3 hydride shifts over the usually less energetic 1,2 mechanism. The bulkier the anion, the higher is the rate of interconversion between carbenium ions. Lowering the activation barrier of the corresponding transition states (*e.g.*, only 8·5 kcal/mol was estimated[6] for a 1,3 hydride shift in isobutyldimethyl cation at low temperature in SbF_5–SO_2ClF solution), thus providing unexpected reaction pathways, could be a common feature of superacid and some acid (*e.g.* H_2SO_4 and $HClO_4$) media. Thus the reported evidence for a 1,3 hydride shift in a case where successive 1,2 migrations could also be operative indicates that the more general occurrence of such a mechanism could indeed have been underestimated as far as cationic rearrangements are concerned.

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