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A TRAPPED DERIVATIVE IN STEROID BACKBONE REARRANGEMENT

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.When treated with BCl_3 at -70°C, compound 1 undergoes a backbone rearrangement to give compound 3 (1) *via* the ionic species 2. A second derivative 4, was also obtained (ratio 3/4 : 2/1); fig. 1.

The structure of the latter compound, $C_{21}H_{35}ClO$, investigated by 300 MHz ^1H NMR, indicates a partially rearranged steroid with the same primary alcohol function at C-4, like 3. A tertiary position for the chlorine atom was deduced from its chemical stability.

Up to now, the only partially rearranged compounds to be isolated are those arising from self-stabilization by proton elimination (2) to give olefinic products. Because of poor nucleophilicity, the anionic part of usual acidic reagents to be used (HF (3), H_2SO_4 (4), AcOH/TsOH (5), CF_3COOH (6)..) does not trap any cationic intermediary during the process. The use of BCl_3 gives chlorine ions in the mixture through organoborane formation with the steroidal CH_2O^- moiety. Its nucleophilicity is important enough to stop the rearrangement by trapping one of the cations 2. Based on actual knowledge of the different mechanisms invoked for such rearrangement (7), the chlorine atom is expected to be located at C-8, C-9, C-10 or C-14 position for a half rearrangement, although, the C-17 position, corresponding to a complete rearrangement, could not be firmly rouled out.

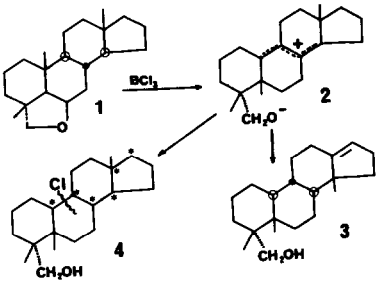


Fig.1

In fact, only one compound is isolated. To determine the position of the chlorine atom, an X-ray analysis of 4 was undertaken.

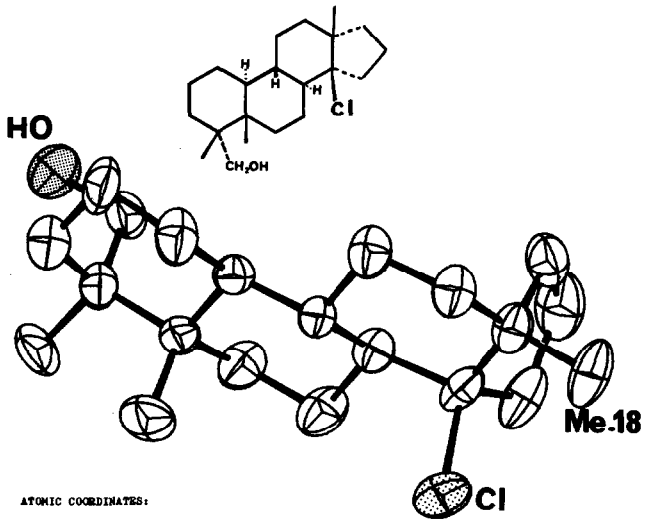
Compound 4, isolated by tlc, crystallizes from $CHCl_3$ as large orthorhombic prisms, space group $P2_12_12$, with $Z = 8$, $a = 11.69$, $b = 23.65$, $c = 14.01$ Å.

3942 reflections were recorded, in the $\theta/2\theta$ mode, on a four-circle computer controlled diffractometer (CuKα radiation, $\lambda = 1.5418$ Å, filtered by a graphite monochromator). The data set was corrected for Lorentz polarization but not for absorption.

The structure was solved by application of the multi-solution method (8) with some difficulty. The refinement of the atomic positional parameters and individual anisotropic thermal factors led to a final R = 5.8 %. All hydrogen atoms, located from difference Fourier synthesis, were included in the final stage of the refinement, but their positions were not refined.

The two molecules of the asymmetric unit have the same conformation. The ORTEP (10) drawing, fig. 2, of one of the molecules, indicates clearly the chlorine atom to be β on the C-14 atom and a *cis* C/D ring junction.

As located, this chlorine atom has strong syn-axial interactions leading to a more strained situation in 4 than in the more flattened compound 3. In the same way, the high value of the 4/3 ratio to be obtained in the final step is rather unexpected on the simple basis of a pure thermodynamic control of the reaction and the hypothesis of a slow Me-18 migration, which has been recently suggested (7) in amino-steroid backbone rearrangement, could be involved in our case to be the most important pathway of the compound 4 synthesis.



ATOMIC COORDINATES:

MOLECULE N° 1 :

ATOM	X	Y	Z	"B"
C- 1	8157	1012	-1958	4.8
C- 2	8781	504	-1536	5.6
C- 3	8004	176	-873	5.6
C- 4	7472	517	-78	4.1
C- 5	6865	1063	-499	3.5
C- 6	6505	1477	311	4.5
C- 7	5953	2012	-73	4.7
C- 8	6774	2330	-721	3.4
C- 9	7189	1951	-1544	3.2
C-10	7692	1395	-1163	3.4
C-11	8068	2276	-2145	4.2
C-12	7606	2836	-2513	4.1
C-13	7154	3230	-1736	4.0
C-14	6323	2915	-1048	4.0
C-15	6245	3317	-195	5.6
C-16	7482	3534	-75	6.6
C-17	8071	3437	-1041	4.8
Me- 4	6592	137	471	5.3
Me- 5	5758	878	-1049	5.9
Me-18	6603	3752	-2225	6.1
Cl-14	4921	2815	-1581	6.4

MOLECULE N° 2 :

ATOM	X	Y	Z	"B"
C- 1	4094	8626	3227	5.3
C- 2	3850	9230	3016	6.9
C- 3	3221	9528	3874	7.4
C- 4	2140	9211	4202	5.7
C- 5	2418	8577	4395	4.8
C- 6	1327	8231	4618	5.7
C- 7	1566	7602	4794	5.1
C- 8	2163	7329	3952	4.1
C- 9	3225	7655	3618	4.2
C-10	2999	8296	3505	4.4
C-11	3612	7400	2685	5.3
C-12	3871	6772	2750	6.1
C-13	2922	6414	3199	5.1
C-14	2395	6698	4084	4.0
C-15	1289	6352	4239	5.8
C-16	838	6257	3256	7.6
C-17	1812	6367	2546	6.5
Me- 4	1657	9539	5079	8.5
Me- 5	3212	8539	5310	6.6
Me-18	3389	5814	3384	7.1
Cl-14	3322	6605	5113	5.7

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