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14ß-HYDROXY STEROIDS - VI. [1]
SYNTHESIS OF DIGITOXIGENIN

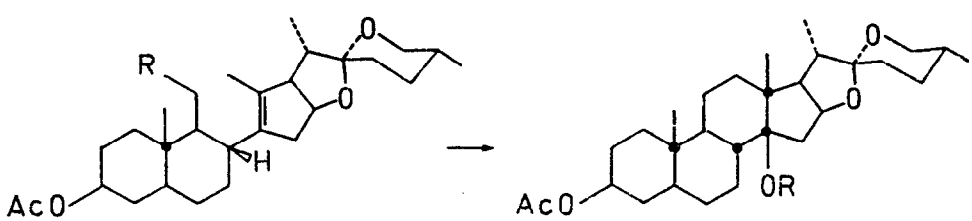
Tsenka Milkova, Hermann Stein, Aranka Ponty, Dirk Böttger,
and Peter Welzel*
Abteilung für Chemie der Ruhruniversität
Postfach 102148, D-4630 Bochum

Abstract: A short and efficient synthesis of digitoxigenin (10) is reported using a new method for the introduction of the 14ß-OH group.

Until now for the introduction of a 14ß-OH group into the steroid nucleus there existed only one general method (independent of the substitution at C-17) : Hydration of a Δ^{14} double bond by HOBr addition followed by hydrogenolysis of the carbon-halogen bond (Bernstein-Engel method). [2]

Recently, we reported on an easy access to 12,14ß-diols. [3] We wish now to disclose a general and efficient method for the formation of 14ß-hydroxy steroids lacking substitution at C-12.

When lumihecogenin acetate (1), which is prepared from hecogenin acetate in 80% yield, [4] was reduced with sodium borohydride (in ethanol, 30 min at 25°C) primary alcohol 2 was obtained in 99% yield. 2 was mesylated (0.5 mmol in 3 ml of CH_2Cl_2 with 100 µl of triethylamine and 50 µl of mesylchloride, 75 min at - 70°C) to furnish after chromatographic separation 3 (70%). Solvolysis of 3 under the conditions reported by Masamune [5] gave 66% yield of the known 14ß-hydroxy tigogenin acetate (4). [3] Using methanol instead of water as nucleophile we were able to isolate 14ß-methoxy compound 5 .

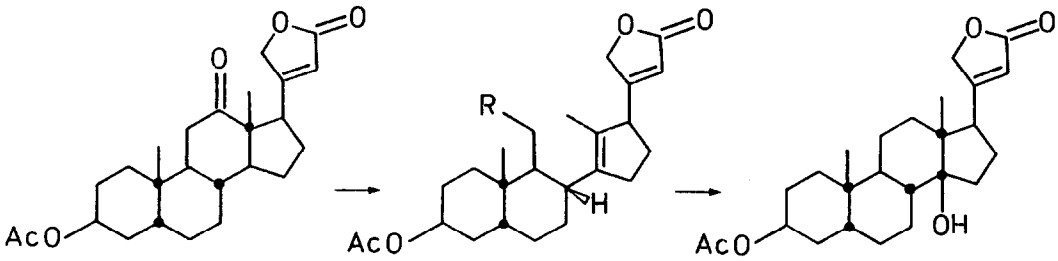


	R
1	CHO
2	CH_2OH
3	CH_2OMs

	R
4	H
5	CH_3

Similarly, photolytic rearrangement of 12-oxo-cardenolide 6 [6] yielded secoaldehyde 7, which on reduction with sodium borohydride (2 equivalents in ethanol, 10 min at 0°C) furnished 8 in 43% yield (based on 6). Mesylation of 8 to 9 as described above followed by solvolysis (0.2 m oxalic acid in acetone/water 1:2, 1h at 50°C) gave 52% yield (based on 8) of digitoxigenin acetate (10), identical with an authentic sample .

6 can be prepared from deoxycholic acid in few steps. [6] The reactions reported in this communication represent, therefore, a short and efficient synthesis of medicinally important digitoxigenin from readily available deoxycholic acid .



6 | 7 | 8 | 9 | 10

	R
7	CHO
8	CH_2OH
9	CH_2OMs

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