Synthesis of human steroid metabolites of interest in doping analysis

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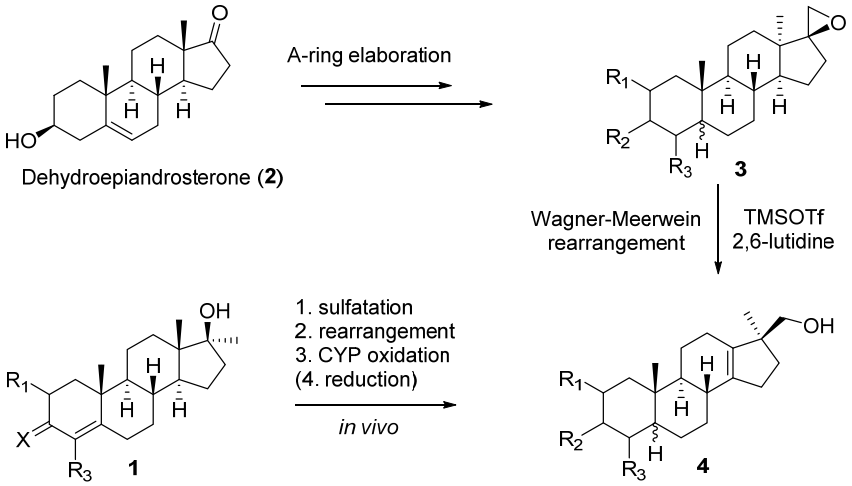
In doping control analysis, the urine samples of athletes are tested for the presence of phase I/II metabolites. To elucidate metabolites' structural identities the synthesis of the most probable stereoisomers is carried out, which are then compared with the real metabolites from an excretion study. Since 2006 a number of steroidal long-term metabolites with a common rearranged D-ring fragment were reported, some of these highly metabolized compounds bear several new stereocenters.

The metabolic transformations leading to these novel D-ring fragments are depicted in the scheme below, as is the biomimetic key step in our synthesis: a Wagner-Meerwein rearrangement. Metabolites (**4**) originating from 5 different anabolic agents (**1**) were synthesized from commercially available **2** and their identity secured.[1] In the later stages of the project Phase II metabolites (glucuronides) were targeted as well.[2]



Scheme 1: Biosynthesis and key step

[1] N. Kratena, V. S. Enev, G. Gmeiner, P. Gärtner, *Monatsh. Chem.*, **2019**, 150, 843.

[2] N. Kratena, S. M. Pilz, M. Weil, G. Gmeiner, V. S. Enev, P. Gärtner, *Org. Biomol. Chem.*, **2018**, 16, 2508.