

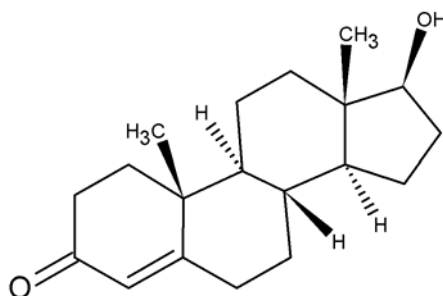
COSI SIMILI, COSI DIVERSE

1. FOR A FEW ATOMS MORE: TESTOSTERONE AND DOPING

A few days ago, the Tour de France winner, Floyd Landis, was found to have a high, indeed impermissible level of testosterone in his urine. Not quite, more of what was actually found in just a while. The sample was taken just after his comeback victory in a critical stage of bicycling's premier race. If a second sample confirms the problem, Landis's victory will be disallowed.

Testosterone is the principal male sex hormone, produced mainly where... you might suspect from its name. And it is also produced in the ovaries of females. Testosterone is a so-called anabolic steroid, a class of molecules that give us a continuing lesson that almost the same is not the same.

All the steroids, the class of molecules that include testosterone, have the same atomic framework – four all-carbon rings, fused together. Three are hexagons, the third ring going off at an angle to the other two. Fused to that last ring is a pentagon of carbon atoms. Call the rings A (6 carbons), B (6), C (6), D (5). Testosterone has an oxygen and a hydrogen (OH) attached to ring D, two CH₃ (methyl) groups, one at the juncture of rings C and D, the other at the juncture of A and B. Finally ring A of testosterone has an oxygen attached to it as well, and there is a double bond in that ring.

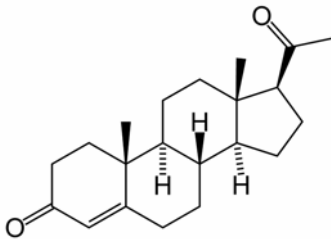


testosterone

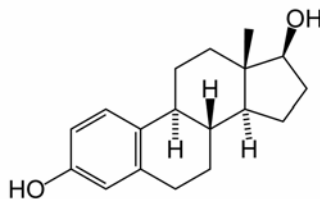
Testosterone is responsible for the secondary sex changes which occur in male puberty – facial and pubic hair, oiliness of skin, body odor, all that teenage boy stuff. But the molecule is also produced by human females, albeit in 1/20th of the amount in males. Testosterone affects energy levels, and protects against osteoporosis, in both sexes. Nothing is

simple in the real world – only human beings want it black or white, male or female.

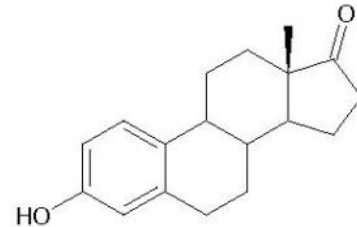
Remarkably enough, the biochemical precursor of testosterone (in both sexes) is progesterone, a female sex hormone. The only difference between progesterone and testosterone is all of four atoms, two carbons and two hydrogens, in what is attached on the five-membered D ring. Two more female sex hormones are estradiol and estrone; these differ from testosterone by the loss of one CH₃ and an H, and, respectively, two more hydrogens. Small changes, indeed. With major consequences.



progesterone

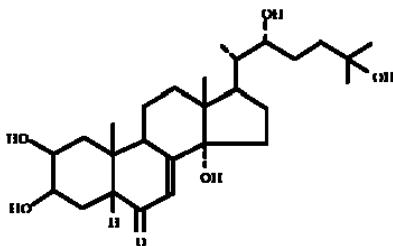


estradiol

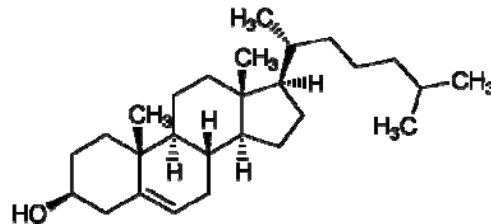


estrone

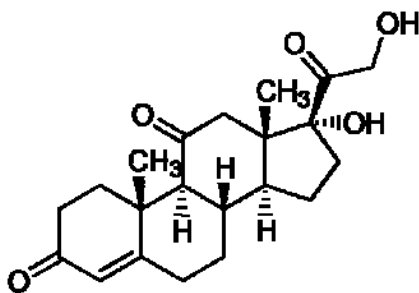
Also in the same family of molecules, all with the same 6:6:6:5 fused ring system pattern are ecdysone, the molting hormone of insects; cholesterol, absolutely essential and present in substantial amounts in our bodies; cortisones, important anti-inflammatory drugs; and the bile acids.



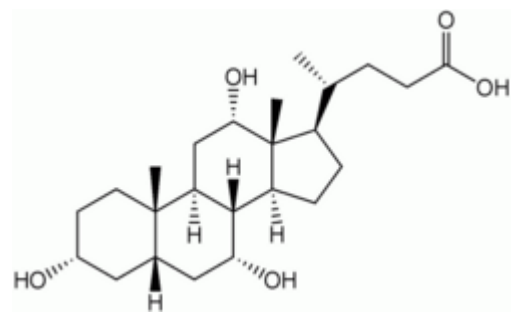
ecdysone



cholesterol



cortisone



cholic acid, a bile acid

A pretty incredible set of biological functions, n'est-ce-pas? All affected by an atom off here, an atom on there. Moreover, as subtle a change as having the mirror image of a molecule serves to change its function.

That's fun for sure, to figure out whence this exquisite biological diversity. But why should a biker take testosterone? More facial hair doesn't help win the Tour de X. Well, testosterone is anabolic – it increases muscle mass and strength, bone density and maturation. Testosterone helps muscles recover from exercise.

Testing for abuse is not simple. There is testosterone. And it happens to have a wide variation of concentrations in the blood of individuals. And within one individual with time. So one cannot conclude from just an elevated level of testosterone that the molecule has been supplemented!

Enter epitestosterone. It is in fact a stereoisomer of testosterone. This means it contains all the same atoms, attached to each other in similar ways, but with a different disposition in space. It turns out that epitestosterone has no apparent physiological effect (the same and not the same redux). But both and testosterone and epitestosterone are produced in the body by parallel biochemical pathways, in about equal amounts. So whereas in the body of any given person there may be a higher absolute concentration of testosterone (and epitestosterone) than in another, the ratio of testosterone to epitestosterone is close to 1.

This is the clue to detecting abuse. Supplementing testosterone, the only isomer which has the desired physiological effects, has no effect on the biological production of epitestosterone. So the sports medical bodies settle on the testosterone/ epitestosterone ratio as an indicator of foul play. 1:1 is normal, 4:1 is when the red card is shown; Landis' sample A apparently had an 11:1 ratio.

I know, I know – you will tell me that the dopers, making big bucks, are not stupid. They'll administer not only testosterone, but also some epitestosterone, so as to keep the ratio of testosterone:E under 4:1. With good science, this strategy too can be countered. Because (see the vanillin story) the natural testosterone (or epitestosterone) is slightly radioactive, and different in its ^{12}C to ^{13}C ratio from the synthetic material. Indeed the results of that test were just announced, and they show that some of the testosterone in Landis' urine was of synthetic origin.

Sample B remains to be tested. Stay tuned.