The purpose of the present study is to answer the question of whether there is a species difference in the effects of a pharmacological dose of dehydroepiandrosterone (DHEA) on the enzymes that participate in olein acid (18:1) formation in the liver. Feeding a diet containing 0.5% (w/w) DHEA for 14 days markedly increased the activities of acyl-coenzyme A (CoA) synthetase, palmitoyl-CoA chain elongase and stearoyl-CoA desaturase in the liver of rats and mice. These enzyme activities, however, were not changed by DHEA in guinea pigs. The treatment of rats and mice with DHEA markedly increased proportions of 18:1 in hepatic lipids, especially phosphatidylcholine (selectively at C-2 position), triacylglycerol and cholesterol ester. DHEA caused no significant change in any acyl compositions of hepatic lipids of guinea pigs. The levels of DHEA or dehydroepiandrosterone sulfate (DHEAS) were markedly increased in serum and livers by DHEA administration to rats, mice and guinea pigs. High correlations were observed between hepatic levels of DHEA or DHEAS and stearoyl-CoA desaturase activity in rats. These results indicate that there are species difference in the inducing effects of DHEA or DHEAS on hepatic formation of 18:1 and that guinea pigs lack the machinery to induce the enzymes.