

STEREOSPECIFIC S-ASSISTED CATIONIC CYCLIZATION
A SYNTHETIC APPLICATION TO THIASTEROIDS

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In connection with our synthetic work on thia steroids, we have investigated a new annelation method for direct conversion of a seco steroid intermediate (e.g. **2**) to an estratetraene (e.g. **6**). The substrates (**1-4**) were prepared from readily available 3-methoxy-8,14-seco-16-thia-D-homoestra-1,3,5(10),9(11)-tetraene-14,17a-dione. We found that acetoxymesylates (**1a-4a**) on acetolysis (60-80°, HOAc) effectively underwent intramolecular cyclization but with stereospecificity to give **5a-8a** (50-70%) as a single product, respectively. Structural proof suggested that the present solvolysis involves cationic olefin cyclization reaction which presumably proceeds via an episulfonium ion intermediate formed by sulfur participation, resulting in retention of configuration at C₁₄. Facile ring closure was also observed on solvolyses of corresponding diols and diacetates as well as dimesylates, although these reactions were accompanied to some extent by a secondary skeletal rearrangement. Strikingly, treatment of cis α,α -diol (**1c**) with methanesulfonic acid in acetic acid (58°, 2.5 h) afforded predominantly C/D-cis **5a** (72%), while cis β,β -diacetate (**2d**) under a slightly vigorous condition (100°, 5 h) resulted in C/D-trans **6a** (70%), directly isolated as crystalline. Formic acid, trifluoroacetic acid, and acetone-perchloric acid were also used for the above cyclization. On the other hand, trans diol derivatives (**3c** and **3d**) led to a complex mixture of possible cyclized products. Thus, the successful cyclization process opened a straightforward route to the preparative synthesis of 16-thia-D-homoestrogens. Transformation of the estratetraenes (**5**, **6**, **7**, and **8**) into 16-thia-D-homoestradiol 3-methyl ether (80%) and its possible stereoisomers was accomplished by lithium-ammonia reduction.

