Azadiradione Analogs from 13α- and 13β-Dehydro-epi-androsterone

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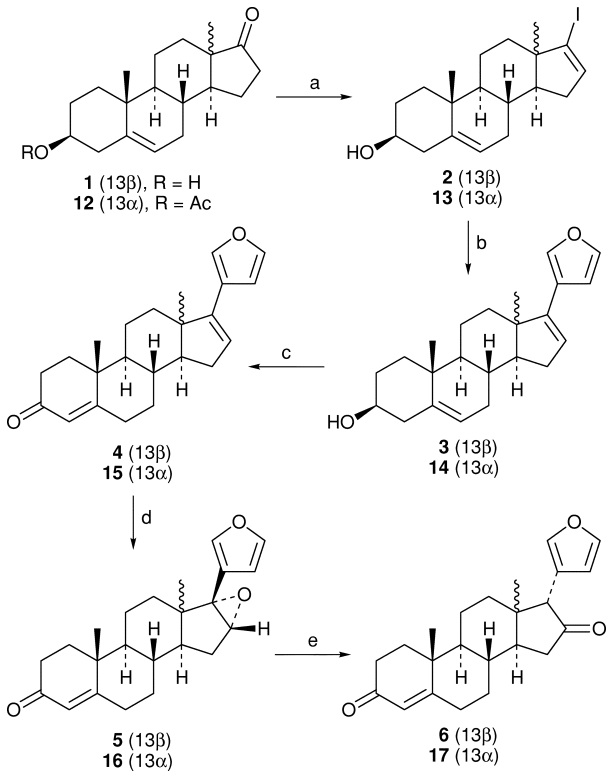
The synthesis of diketones **6**, **11** and **17** related to the limonoid antifeedant azadiradione is achieved in 5, 4 and 5 steps, respectively, involving a Stille type coupling reaction and a stereoselective epoxide rearrangement.

Steroids with a heterocycle as ring E are well known compounds with interesting biological properties. This family of compounds includes cardenolides, and recently, pyridyl, imidazolyl and other derivatives showing anti-prostatic activity.[1] The construction or insertion of ring E in the androstane skeleton has been approached in many different ways, most of them extremely long and tedious.[2] In this context we were interested in a short and efficient synthesis of furyl steroid derivatives related to the limonoid insect antifeedants azadiradione and epiazadiradione,[3] and their deacetyl derivatives nimbocinol and epinimbocinol which exibit anti-arthritic, anti-inflammatory and anti-ulcer properties,[4] for the development of a procedure of general application for the preparation of heterocyclic ring E steroids.

Over the past few years, we have devoted extensive efforts towards the synthesis of limonoid model compounds and have developed short and efficient routes to compounds resembling the CDE portion of azadiradione.[5] The key step of these methods consists in a coupling catalyzed by Pd,



1 (13β), R = H
12 (13α), R = Ac
2 (13β)
13 (13α)
3 (13β)
14 (13α)
4 (13β)
15 (13α)
5 (13β)
16 (13α)
6 (13β)
17 (13α)

Scheme 1 *Reagents and conditions*: a, i, $N_2H_4{\cdot}H_2O$, Et_3N, reflux; ii, I_2, Et_3N, THF, r.t.; b, Bu_3(3-furyl)Sn, $Pd(Ph_3P)_4$, DMF, reflux; c, $Al(OPr^i)_3$, cyclohexanone, toluene, reflux; d, *m*-CPBA, CH_2Cl_2, −40 °C; e, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C

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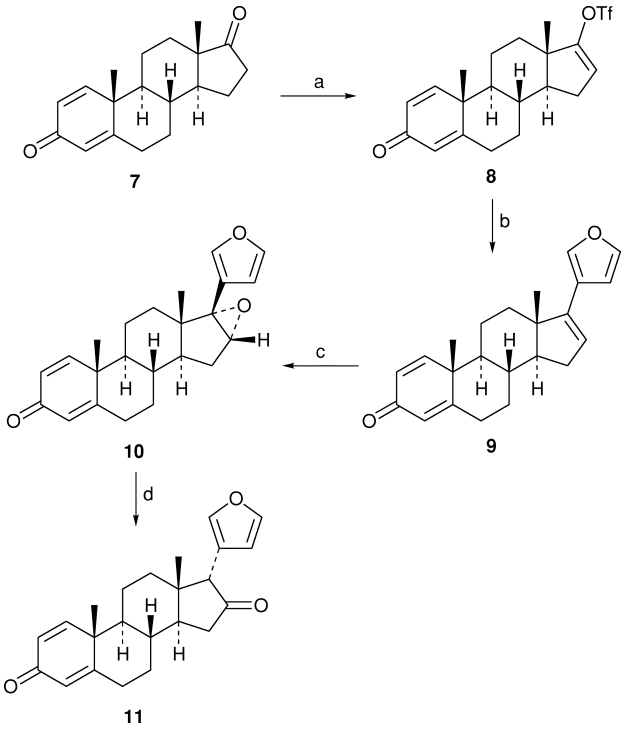

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Scheme 2 *Reagents and conditions*: a, i, LDA, THF, −20 °C; ii, $PhNTf_2$, HMPA, THF, −78 °C; b, Bu_3(3-furyl)Sn, LiCl, $Pd(Ph_3P)_4$, THF, reflux; c, *m*-CPBA, CH_2Cl_2, −20 °C; d, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C

between a vinyl iodide and a stannylfuran. To be considered general, the versatility of the method needs to be tested in androstane derivatives. If some heterocycle ring E steroid were desired, this could be obtained by adequate substitution of the stannylvinyl component. The present paper concerns the chemical synthesis of compounds **6**, **11** and **17** (Schemes 1 and 2).

Configuration of the C-13 methyl group and the furan in diketone **6**, **11** and **17** was assigned on the basis of the ^1H NMR values and there is good concordance with these reported for epiazadiradione and epinimbocinol.[4,11]

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Techniques used: ^1H and ^{13}C NMR, polarimetry, TLC

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