Available online at www.sciencedirect.com
SCIENCE DIRECT®
Steroids 70 (2005) 131–136
Steroids
www.elsevier.com/locate/steroids

Synthesis of biologically active steroid derivatives by the utility of Lawesson's reagent☆

Nadia R. Mohamed[a,*], Gamal A. Elmegeed[b], Hoda A. Abd-ElMalek[c], Magdi Younis[d]

[a] *Photochemistry Department, National Research Centre, Dokki, Giza, Egypt*
[b] *Hormones Department, National Research Centre, Dokki, Giza, Egypt*
[c] *Chemistry of Pesticides Department, National Research Centre, Dokki, Giza, Egypt*
[d] *Botany Department, Faculty of Science, South Valley University, Aswan, Egypt*

Received 21 June 2004; received in revised form 2 November 2004; accepted 8 November 2004

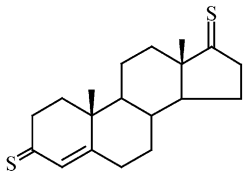
Abstract

Steroid derivatives **V**, **VI**, **VII** and **VIII** reacted with Lawesson's reagent (LR) to produce spiro-oxazaphosphole-4′,17-androstene derivative **XI**, diazaphospholoandrostane **XIV** and the thionated derivatives **XVI** and **XVII**, respectively. The structures of the new compounds were confirmed by analytical and spectroscopic evidence. A mechanism accounting for the formation of the new compounds was given. The in vitro antimicrobial activity of the new compounds were tested.

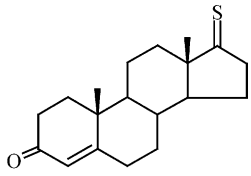
Keywords: Organophosphorus; Steroids; Lawesson's reagent; Bioactivity

1. Introduction

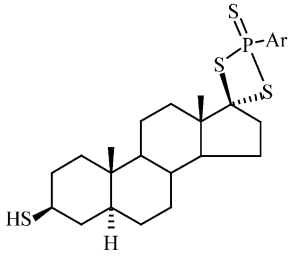
Attention has been devoted in the literature to the synthesis of several steroidal derivatives that exhibit marked medicinal activities [1–3]. In a recent communication from this laboratory, we have reported [4] the synthesis of some thioxosteroids (**I**, **II**), mercaptospirothiones (**III**) and the thiaphosphole steroid derivative (**IV**) derived from 4-androsten-3,7-dione, epi-androsterone and progesterone, respectively. We have shown that some of these new compounds possess marked antibacterial and antifungal activities [4].



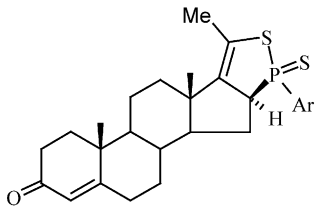
I



II



III



IV

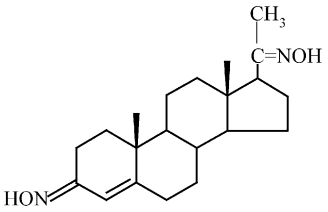
In view of this information and in continuation of our work in this field [5–7], we would like to report here on the formation and characterization of new steroid derivatives derived from 3,20-dioximinoprogesterone (**V**),

☆ Studies on organophosphorus compounds X, cf. Ref. [27].

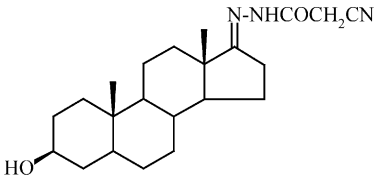
* Corresponding author.
E-mail address: nadia_ragab_m@hotmail.com (N.R. Mohamed).

0039-128X/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.steroids.2004.11.001

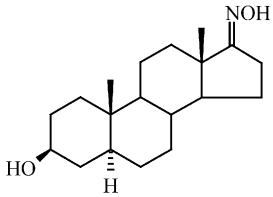
3β-hydroxy-5α-androstan-17-cyanoacetylhydrazone (**VI**), 3β-hydroxy-5α-androstan-17-oxime (**VII**), and 3β-hydroxy-5α-androstan-17-acetylhydrazone (**VIII**) [5]. 2,4-Bis(*p*-methoxyphenyl)-1,3,2,4-dithiaphosphetane-2,4-disulfide (Lawesson's reagent; LR) (**IX**) [8] was used in the present investigation as thiating and/or phosphorylating agent. The in vitro antimicrobial activity of the new steroid derivatives was tested against a wide spectrum of gram positive, gram negative bacteria and fungi.



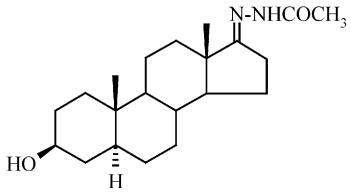
V



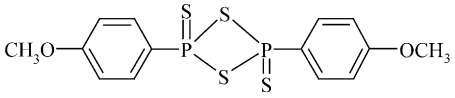
VI



VII



VIII



IX

2. Experimental

Starting steroids were purchased from Sigma Company and compound **V** was prepared according to the literature [9]. Appropriate precautions in handling moisture sensitive compounds were undertaken. All melting points are uncorrected, the IR spectra are expressed in cm^{-1} and recorded in KBr pellets on a Pa-9721 IR spectrometer. ^1H NMR spectra were obtained on a Varian EM-390 (90) MHz spectrometer in DMSO-d_6 as solvent and TMS as internal reference. Chemical shifts (δ) are expressed in ppm. Mass spectra were recorded on Kartos (75 eV) MS equipment. Elemental analyses were carried out by Microanalytical Data Unit at the National Research Centre, Giza, Egypt. All described compounds showed the characteristic spectral data of the cyclopentanoperhydrophenanthrene moiety of steroids similar to those reported in the literature [10,11]. For the nomenclature of steroid derivatives, we used the definitive rules for the nomenclature of steroids published by the Joint Commission on the Biochemical Nomenclature (JCBN) of the International Union of Pure and Applied Chemistry [12–14]. Isolation and identification of bacterial and fungal strains and the antimicrobial study of the new compounds were carried out at the laboratory of Botany Department, Faculty of Science, South Valley University, Aswan, Egypt.

2.1. Synthesis

2.1.1. The reaction of Lawesson's reagent with compounds *V* and *VI*

2.1.1.1. General procedure. To a solution of each of compound **V** (0.68 g, 0.002 mol) or **VI** (0.74 g, 0.002 mol) in dry toluene (30 ml), LR (0.81 g, 0.002 mol) was added. The reaction mixture in each case was heated under reflux for 8 h. The solvent was evaporated under vacuum; the remaining residue was applied to a chromatographic column prepared by packing slurry of silica gel 60-mesh in cyclohexane.

*2.1.1.2. 5′-Methyl-3′-(p-methoxyphenyl)-3′-thioxospiro[2′,1′,3′-oxazaphosphole-4′,17-androst-4-ene]-3-oxime **XI**.* The product was obtained by elution with cyclohexane/ethyl acetate (7:3 v/v), deep red product, crystallized from benzene, yield 0.63 g (62%), mp 229 °C. IR (ν/cm^{-1}): 3555 (NOH), 2970 (CH_3), 2850 (CH_2), 1652,