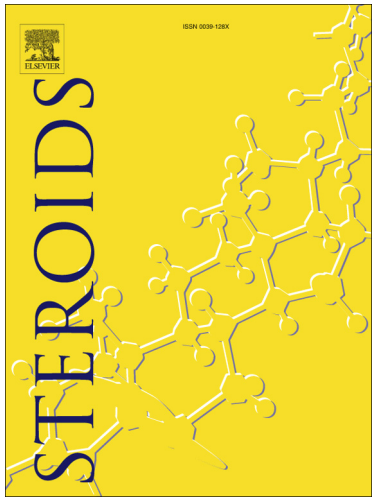

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Stereoselective synthesis of the four 16-hydroxymethyl-3-methoxy- and 16-hydroxymethyl-3-benzyloxy-13*α*-estra-1,3,5(10)-trien-17-ol isomers and their antiproliferative activities

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Abstract

The reduction of 16-hydroxymethylene-3-methoxy-13α-estra-1,3,5(10)-trien-17-one (**14**) and 16-hydroxymethylene-3-benzyloxy-13α-estra-1,3,5(10)-trien-17-one (**16**) yielded a mixture of two diastereomeric diols, the 16α-hydroxymethyl,17β-hydroxy and 16β-hydroxymethyl,17α-hydroxy isomers (**17a–20a**) in a ratio of 6:1. We describe a straightforward synthetic route to transform the isomers with *trans* functional groups attached to ring D (**17a**–**20a**) into isomers with *cis* functional groups (**25a-28a**).

We determined the *in vitro* antiproliferative activities of compounds **17a**–**20a** and **25a**–**28a** by means of MTT assays against a panel of human adherent cancer cell lines HeLa, A2780, MCF-7, T47D, MDA-MB-231 and MDA-MB-361).

Keywords: 13α-Estrone, Stereocontrolled synthesis, Stereoisomers, Antiproliferative activity.

1. Introduction

Breast cancer is the most frequently diagnosed cancer in women worldwide [1]. Since estrogens are known to play a role in the development of many breast cancers, a logical approach to the treatment of estrogen-sensitive breast cancer is the use of anti-estrogens that block the interaction of estrogens with their specific receptor. The literature provides evidence that inversion of the configuration of estra-1,3,5(10)-trien-17-one at C-13 may lead to the loss of estrogenic activity [2, 3]. These investigations revealed that the C-13 epimers of estradiols