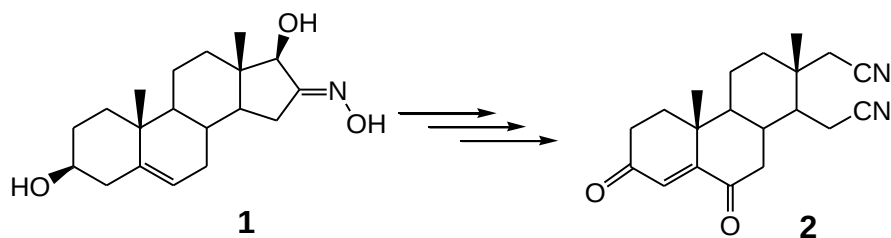


Synthesis of potential antitumor steroid derivatives

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Starting from (16*E*)-3 β ,17 β -dihydroxy-16-hydroxyiminoandro-5-ene (**1**) 3,6-dioxo-16,17-secoandro-4-ene-16,17a-dinitrile (**2**) was synthesized in several steps. First, the Beckmann fragmentation of D ring was conducted and 16,17-seco-16-cyano-17-aldehyde **3** was obtained, the acetylation of which gave 3 β -acetoxy derivative **4**. The reaction of compound **4** with NaBH₄ in ethanol afforded secocyano alcohol **5**. Further esterification carried out with 4-toluenesulfonyl chloride and substitution with potassium cyanide gave 16,17a-dicyano derivative **7**. After transesterification of compound **7** and oxidation of 5-en-3 β -ol steroid **8** into corresponding 4-ene-3,6-dione using Jones reagent compound **2** was obtained.



Compounds **2** and **8** were screened for antitumor activity against human breast adenocarcinoma ER+, MCF-7; human breast adenocarcinoma ER-, MDA-MB-231; prostate cancer AR-, PC-3; human cervix carcinoma, HeLa; and colon cancer, HT-29 cells; as well as one human non-tumor cell line, MRC-5. Compounds **2** and **8** exhibited significant antitumor activity against HeLa cells; while **2** also showed strong cytotoxicity against MDA-MB-231. Both compounds **2** and **8** were not toxic to healthy MRC-5 cells.

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