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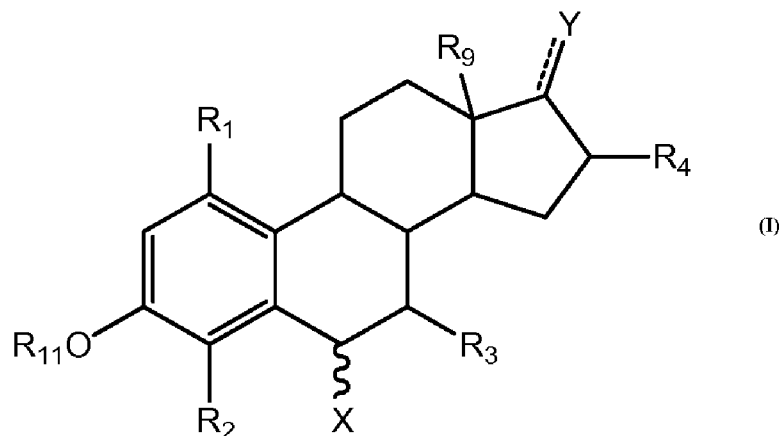
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(54) Title: 6-SUBSTITUTED ESTRADIOL DERIVATIVES AND METHODS OF USE



(57) Abstract: Disclosed are compounds of the formula (I): where in R₁, R₂, R₃ and R₄ are independent l y hydrogen, C₁-C₆ alkyl, halo, a sulfate, a glucuronide, -OH, a bulky group, aryl, cycloalkyl, heteroaryl, heterocycloalkyl, N (CH₂)_n; a phosphate group, and a phosphinate group; R₉ is hydrogen, halogen or alkyl; R₁₁ i s selected from the group consisting of H, C₁-C₆ alkyl, halogen, a sulfate, a glucuronide, -SO₂NH₂, -COOH, -CN, -CH₂CN-, -NHCN-, -CHO, =CHOCH₃, -COO salt, -OSO₂alkyl, -NH₂, and -NHCO (CH₂)_n; R₁₂ is selected from the group consisting o f H, a C₁-C₆ alkyl, a sulfate, a glucuronide, a bulky group, aryl, cycloalkyl, heteroaryl and heterocycloalkyl; X i s selected from the group consisting of C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, halogen, a glucuronide, -NH₂, -SO₂NH₂, -COOH, -CN, -CH₂CN, -NHCN, -CHO, -COOsalt, -OSO₂alkyl, -SH, -SCH₃, -CH [(CH₂)_nCH₃] COOCH₃, - (CH₂)_mCOOCH₃, - (CH₂ U-O-CH₃, - (CH₂)_m-O- (CH₂)_nCH₃, (CH₂)_m-S-CH₃, - (CH₂ U-S- (CH₂)_nCH₃, - (CH₂)_m-NH- (CH₂)_nCH₃, -C₂-C₈ alkenyl -O- (CH₂)_nCH₃, -C₂-C₈ alkenyl -S- (CH₂)_nCH₃, -C₂-C₈ alkenyl -N- (CH₂)_nCH₃, -C₂-C₈ alkynyl -O- (CH₂)_nCH₃, -C₂-C₈ alkynyl -S- (CH₂)_nCH₃, -C₂-C₈ alkynyl -N- (CH₂)_nCH₃, - (CH₂ U-OH, - (CH₂)_m-O-NH₂, - (CH₂)_m-S-NH₂, -NH (CH₂)_mCH₃, -NH (CH₂)_mOCH₃, -NH (CH₂)_mCHOH-COOH, -N (CH₃)₂, - (CH₂)_m (NH) CH₂OH, -NHCOOH, - (CH₂)_mNHCOOH, -NO₂, -SCN, -SO₂alkyl, -B (OH)₂, - (CH₂)_mN (CH₃)₂, -SO₂-NH₃, - (CH₂)_m-NH-SO₂-NH₂, -NHC (=S) CH₃, and -NHNH₂; and Y is selected from hydrogen, =O, -OCO(R₆) and -OH; wherein m is an integer between 0-20, n is an integer between 0-8, the symbol represents either

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a single or a double bond capable of forming a keto group at position 3 or 17; and the Λ /WV symbol represents any type of bond regardless of the stereochemistry; and the respective enantiomers, other stereochemical isomers, hydrates, solvates, tautomers and pharmaceutically acceptable salts of said compounds. The compounds are useful in the treatment of various types of cancer.