stimulation may comprise measuring fold induction by increasing concentrations in an AR response reporter system or a prostate specific antigen secreting system. The method of measuring inhibition and/or stimulation may comprise measuring an effect of the compound on tumor growth in an animal.

BRIEF DESCRIPTION OF THE DRAWINGS

[0045] The following Figures present the results of pharmacological examination of certain compounds.

[0046] Figure 1 is a graph depicting that bicalutamide displays an agonistic effect on LNCaP-AR. Agonistic activities of bicalutamide in AR-overexpressed hormone refractory prostate cancer. LNCaP cells with overexpressed AR were treated with increasing concentrations of DMSO as vehicle or bicalutamide in the absence of R1881. Activities of AR response reporter were measured.

[0047] Figure 2 is a graph depicting an antagonistic assay of bicalutamide on LNCaP-AR. Agonistic activities of bicalutamide in hormone sensitive prostate cancer. LNCaP cells were treated with increasing concentrations of DMSO as vehicle or bicalutamide in the absence of R1881. Activities of AR response reporter were measured.

[0048] Figure 3 is a graph depicting the effect of compounds on LNCaP-AR.

[0049] Figure 4 is a graph depicting the effect of compounds on LNCaP-AR.

[0050] Figure 5 is a graph depicting the inhibition effect on LNCaP-AR.

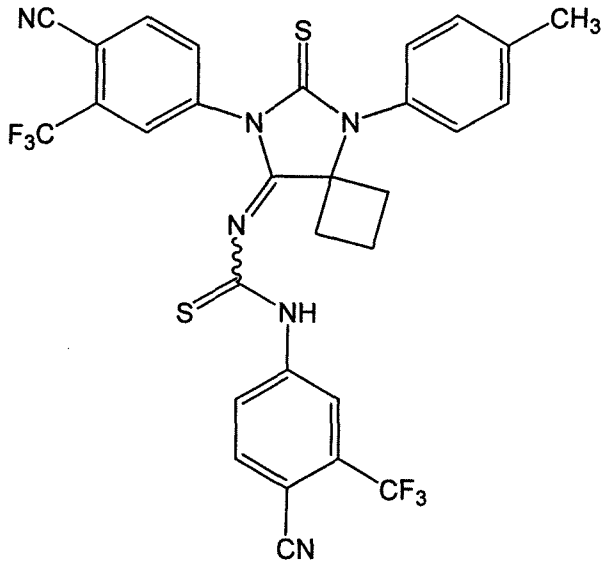
[0051] In Figures 6-10, example 5-3b is RD7 and example 7-3b is RD37.

[0052] Figure 6. Inhibition on growth of AR-overexpressed LNCaP cells. Androgen starved LNCaP cells with overexpressed AR were treated with increasing concentrations of DMSO as vehicle or test substances in the presence of 100 pM of R1881. After 4 days of incubation, cell growth was measured by MTS assay.

[0053] Figure 7. Inhibitory effect on growth of AR-overexpressed LNCaP xenograft model. Mice with established LN-AR xenograft tumors were randomized and treated with indicated compounds orally once daily. Tumor size was measured by caliber. (A), mice were treated with 1 mg per kg of bicalutamide, example 7-3b, or vehicle for 44 days. (B), mice were treated with vehicle, 0.1, 1, or 10 mg per kg of example 7-3b for 44 days.

Claims

1. A compound of the formula



[RD93]

2. Use of the compound of claim 1 in the manufacture of a pharmaceutical drug for the treatment of hormone refractory prostate cancer.

3. Use of the compound of claim 1 in the manufacture of a pharmaceutical drug for the treatment of benign prostate hyperplasia.

4. Use of the compound of claim 1 in the manufacture of a pharmaceutical drug for the treatment of breast cancer.

5. Use of the compound of claim 1 in the manufacture of a pharmaceutical drug for the treatment of ovarian cancer.

6. A composition comprising a compound according to claim 1 for the treatment of hormone refractory prostate cancer.

7. A composition comprising a compound according to claim 1 for the treatment of benign prostate hyperplasia.

8. A composition comprising a compound according to claim 1 for the treatment of breast cancer.

9. A composition comprising a compound according to claim 1 for the treatment of ovarian cancer.