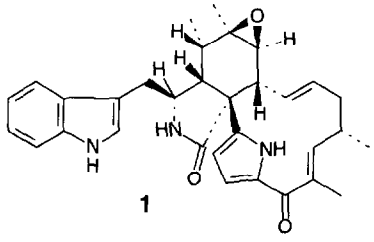
Monitor: molecules, synthesis and profiles

Monitor provides an insight into the latest developments in drug discovery through brief synopses of recent presentations and publications together with expert commentaries on the latest technologies. There are three sections: *Molecules* summarizes the chemistry and the pharmacological significance and biological relevance of new molecules reported in the literature and on the conference scene; *Synthesis* outlines the latest advances in synthetic and separation techniques, approaches to the total synthesis of natural products of pharmaceutical relevance and the screening of new chemical entities; *Profiles* offers commentary on promising lines of research, emerging molecular targets, novel technology and legislative issues.

Penochalasins

A novel class of cytotoxic cytochalasans, penochalasin A **1**, B **2** and C **3**, have been isolated from a *Penicillium* species originally separated from the marine alga *Enteromorpha intestinalis* and fully characterized by Numata, A. and coworkers [*J. Chem. Soc. Perkin Trans. 1* (1996) 239–245]. All of these compounds exhibited potent cytotoxic activity in the P388 lymphocytic leukaemia cell culture-based test system.



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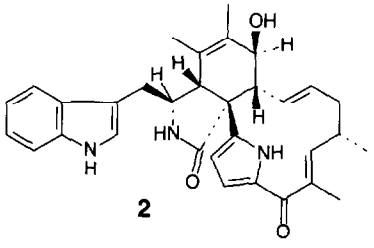

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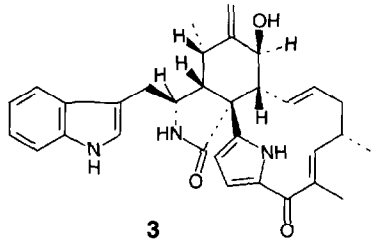

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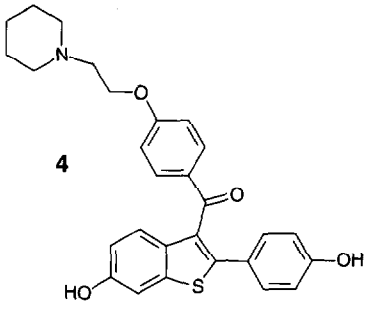
Selective estrogen receptor modulators



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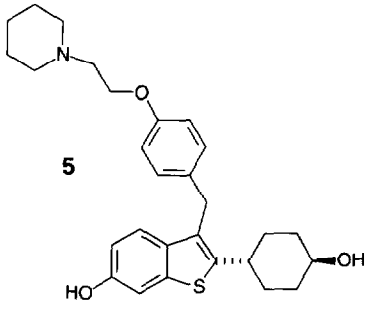

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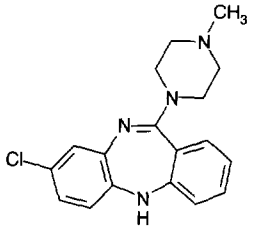
The increased risk of breast cancer associated with estrogen replacement therapy has led to the need for alternative therapies for postmenopausal pathologies, such as osteoporosis and coronary heart disease. One approach has been to design molecules that antagonize the effects of estrogen on uterine and breast tissue, whilst mimicking the effects of estrogens on bone and the cardiovascular system. Raloxifene (LY139481) **4** is presently in clinical trials for the treatment of osteoporosis. Grese, T.A. and coworkers [*Bioorg. Med. Chem. Lett.* (1996) 6, 201–206] describe the synthesis and biological evaluation of a number of 2-alkyl raloxifene analogs.

These studies demonstrate that the 2-cyclohexyl analogs, such as **5**, show particular potential as selective potent estrogen receptor modulators.

Potential atypical antipsychotic agents

It has been suggested that atypical antipsychotic agents, such as clozapine **6**, give rise to fewer CNS side-effects as a consequence of high antagonistic affinity for the serotonin 5-HT_{2A} receptor relative to that for the dopamine D_2 receptor. Howard, H.R. and coworkers [*J. Med. Chem.* (1996) 39, 143–148] report an investigation into a series of substituted phenethyl derivatives of 3-benzisothiazolylpiperazine as potent atypical antipsychotic agents.



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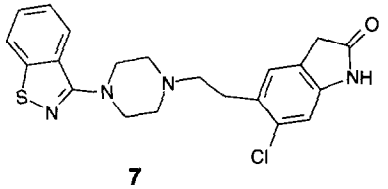

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