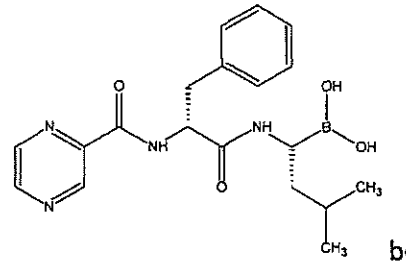
METHOD FOR INHIBITION OF DEUBIQUITINATING ACTIVITY

FIELD OF THE INVENTION

The invention relates to a method of treating cancer in a patient by inhibiting deubiquitinating activity. More particularly, the invention relates to a method of treating a cancer in a patient who has proved resistant to treatment by at least one anti-cancer medicine. Most particularly, the invention relates to a compound for use in the method and to a pharmaceutical composition comprising the compound.

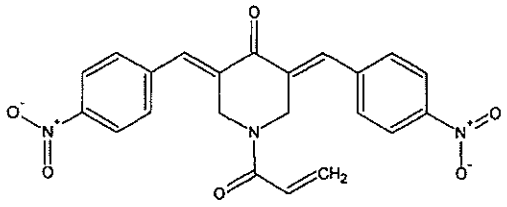
BACKGROUND OF THE INVENTION

Tumor cells display enhanced sensitivity to disruptions in the ubiquitin-proteasome system (UPS) making this an attractive target for the development of anti-cancer therapies (1). Ubiquitin-tagged substrates are degraded by the 26S proteasome, a multi-subunit complex comprising a proteolytic 20S core (20S CP) capped by 19S regulatory particles (19S RP) (2,3). The 20S CP has evolved as an important target for anti-cancer drug development, resulting in the approval of bortezomib (Velcade®) for treatment of myeloic leukemia (4).



bortezomib

The compound b-AP15 (NSC687852) is known to induce p53-independent and cathepsin-D-dependent apoptosis (5,6).



b-AP15 (NSC687852)

OBJECTS OF THE INVENTION

It is an object of the invention to provide a compound for use in a method of treating cancer in a patient by inhibiting deubiquitinating activity, in particular a cancer refractory to state-of-the-art chemotherapy.

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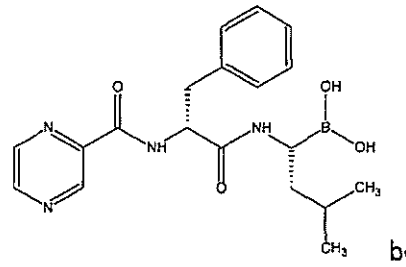

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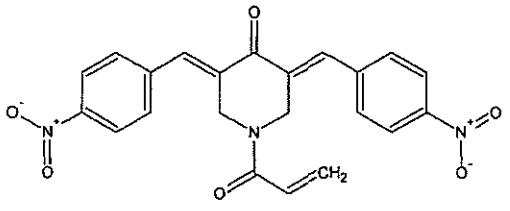

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