



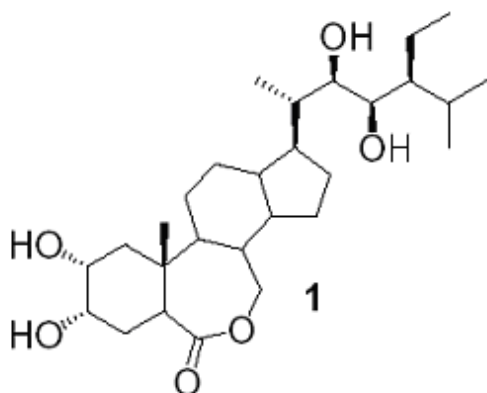
Synthesis of a 4-norsteroid precursor of brassinosteroids

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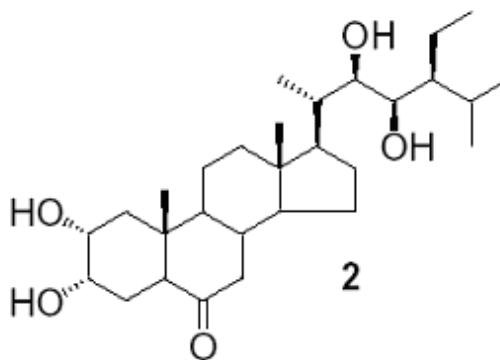
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Introduction

Brassinosteroids (BRs) are a group of plant steroid hormones, which are essential for normal plant development (Khrupach *et al.*, 1999). Brassinolide (**1**), the most active member of this family, is a C₂₈ steroid with an unusual ring B lactone structure. So far more than 60 natural BRs have been described (Bajguz and Tretyn, 2003), among which are C₂₉ homologues, such as



28-homocastasterone (**2**). The C₂₉ BRs are of particular interest because, although in minority in their natural sources, these compounds can be conveniently synthesised from stigmasterol (**3**), which makes them good candidates for application in large scale as agrochemicals (Hayat and Ahmad, 2003).



In recent decades a large number of non-natural BRs analogues has been synthesised, in which both the functional groups present in natural BRs as their carbon skeletons have been changed. We present herein a synthesis of a ring-A contracted steroid, a key precursor in the synthesis of new BRs analogues.

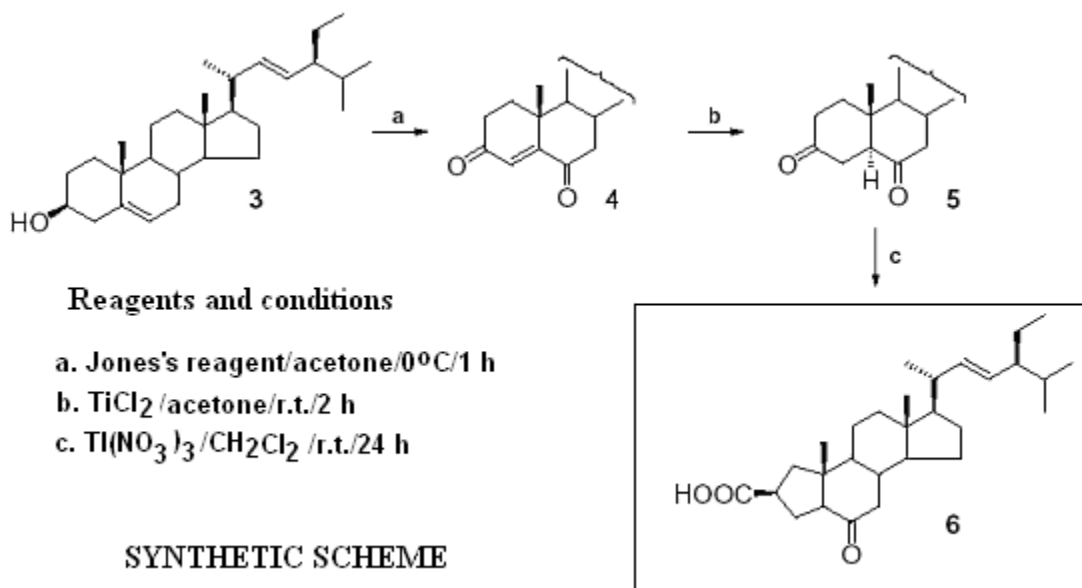
Results and Conclusions

The sequence leading to the target compound is shown in the Synthetic Scheme. The oxidation of stigmasterol with chromium trioxide in an acidic medium (Hunter and Priest, 2006) allowed the simultaneous oxidation of C-3 hydroxyl and the introduction of a carbonyl in C-6, a functionality that, as it is known, it is necessary for a bioactive BRs (Ramírez *et al.*, 2005).

Subsequently the selective reduction of the Δ^4 double bond of the unsaturated diketone was achieved by treatment with Ti (II) chloride. The product showed the right C-5 stereochemistry (*trans* rings A/B fusion).

The contraction of cyclohexanones to carboxycyclopentanes promoted by Ti (III) nitrate (Silva, 2002) is a known reaction, and it is known that the result is widely dependent on the ability of enolizing the ketone.

Previous experience showed that a C-3 ketone in steroids has a higher reactivity than a C-6 ketone. Therefore, the treatment of dione **5** with this reagent led to the desired compound (22(*E*)-6-oxo-4-nor-5 α -stigmast-22-en-2 β -carboxylic acid, **6**) in high yield (85%), the obtained regioselectivity being remarkable.



In addition, the configuration of C-2, bonded to the carboxyl, is compatible with the mechanism proposed for this type of ring contraction (Ferraz and Silva, 1998).

All compounds were structurally characterised by spectroscopic techniques (MS, and mono- and bidimensional NMR). The obtained compound will serve as a starting product for the synthesis of new BRs analogues, which will allow to establish the influence of this novel structural change on bioactivity.

Note: This study was presented at the "XXVI Congreso Argentino de Química", San Luis, Argentina, 2006

References

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