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Total Synthesis of Δ^{12}-Prostaglandin J_3, a Highly Potent and Selective Antileukemic Agent

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Recent reports described Δ^{12}-prostaglandin J_3 (Δ^{12}-PGJ_3) as a potent and selective ablator of leukemia stem cells *in vitro* and *in vivo*. In view of the increasing interest in cancer stem cells as drivers for growth, perpetuation, recurrence, and drug resistance in various types of cancer, Δ^{12}-PGJ_3 may serve as an important tool to decipher cancer biology and a lead compound for drug discovery and development. Naturally formed from ω-3 eicosapentaenoic acid ((5Z,8Z,11Z,14Z,17Z)-5,8,11,14,17-icosapentaenoic acid, EPA), this secondary metabolite was isolated in minute amounts and characterized by UV spectroscopic and mass spectrometric methods. The impressive *in vitro* potency and selectivity of Δ^{12}-PGJ_3 against chronic myelogenous leukemia (CML) stem cells (IC_{50} = 12nm) and its ability to effectively cure this form of leukemia in a mouse model, coupled with its scarcity, prompted us to undertake its total synthesis with the intention of rendering it readily available for thorough biological investigations and full structural characterization.

紹介論文

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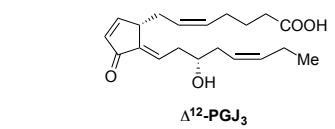
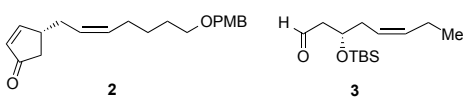
要旨

A catalytic asymmetric total synthesis of the potent and selective antileukemic Δ^{12}-prostaglandin J_3 (Δ^{12}-PGJ_3) is described. The convergent synthesis proceeded through intermediates **2** and **3**, formed enantioselectively from readily available starting materials and coupled through an aldol reaction followed by dehydration to afford stereoselectively the cyclopentenone alkylidene structural motif of the molecule.



Δ^{12}-PGJ_3



2 **3**