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An Approach to the Synthesis of a C_9-C_{15} Fragment of Discodermolide

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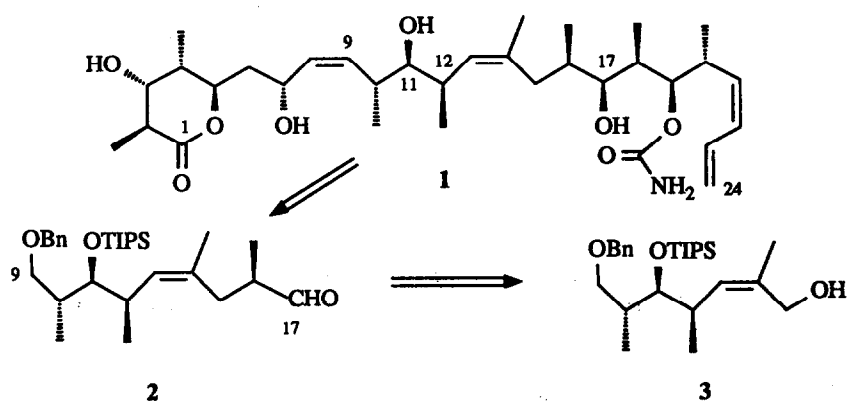
Abstract: The asymmetric synthesis of a synthetically useful fragment corresponding to the C_9-C_{15} region of the immunosuppressant lactone discodermolide is reported.

In the preceding paper we described the synthesis of a synthetically useful fragment **2** corresponding to the C_9-C_{17} region of the of the immunosuppressant lactone discodermolide **1**[1]. A key intermediate in the synthesis of aldehyde **2** was the allylic alcohol **3**. The synthesis of this alcohol **3** relied on a tin(II) triflate mediated aldol condensation of a β-keto imide[2] to set the stereocentres at C_{11} and C_{12}. The double bond geometry arose unambiguously from the ring opening of an unsaturated lactone. We now describe a shortened and more practical approach to this key intermediate **3**.

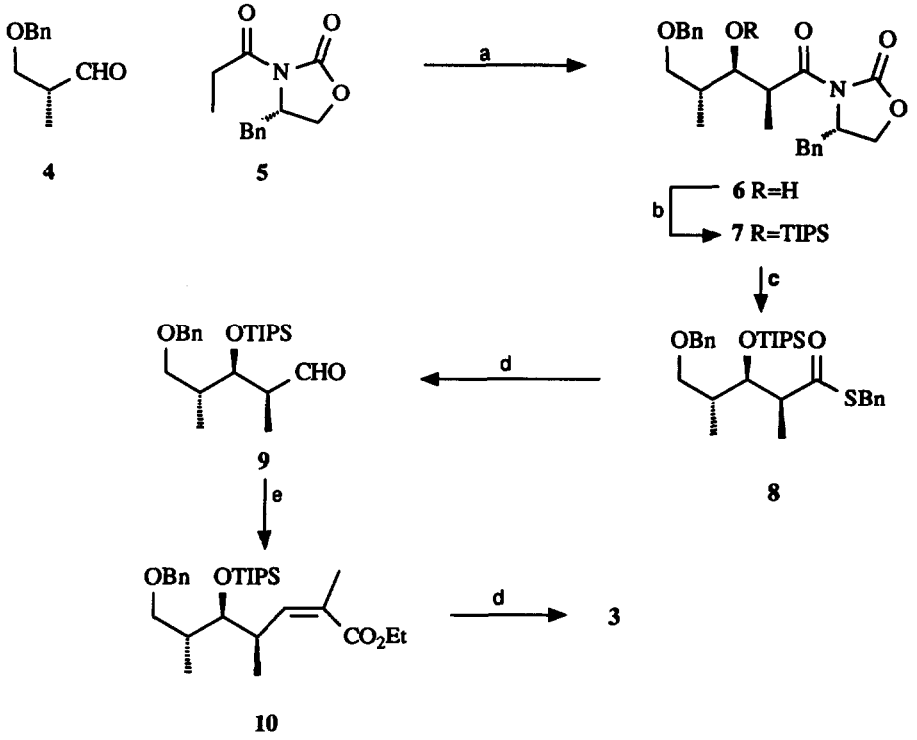


2 **3**

The route (Scheme 1) started with the dibutylboron triflate mediated aldol condensation[3] of aldehyde **4**[4] and oxazolidinone **5**. This gave the chiral aldol product **6** (94%) which was protected (triisopropylsilyl triflate) as the silyl ether **7** (80%). The chiral auxiliary was removed on treatment with benzyl mercaptan and n-butyl lithium to afford the thioester **8** (75%). The thioester **8** was converted to the aldehyde **9** (94%)

on treatment with DIBAL-H. The olefin **10** was prepared as a single geometric Z-isomer[5] *via* the Still modification[6] of the Horner-Emmons reaction. Thus treatment of aldehyde **9** with ethyl 2-[bis(trifluoroethyl)]phosphonopropionate afforded the olefin **10** (92%) which was converted to the key alcohol **3** (93%) on treatment with DIBAL-H.

Scheme 1



a) Bu_2BOTf / NEt_3; b) TIPSOTf / 2,6-lutidine; c) n-BuLi / BnSH; d) DIBAL-H / CH_2Cl_2; e) $KN(TMS)_2$ / ethyl 2-[bis(trifluoroethyl)phosphonopropionate / 18-crown-6

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