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THE TOTAL SYNTHESIS OF (±)ERIGEROL

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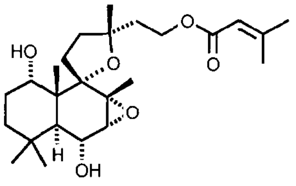
dedicated to Prof. E.C. Taylor on the occasion of his 65th birthday.

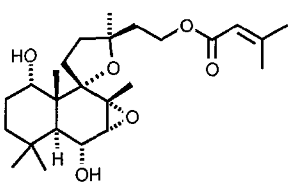
Summary: The labdane diterpenoid Erigerol and diastereoisomers thereof were synthesised in a 23 step sequence.

Erigerol (1) was isolated from the aerial parts of Erigeron philadelphicus L. in a very low yield. Its structure was determined by spectral data and X-ray analysis[3]. The structural complexity of 1 and its similarity to Forskolin (5) a compound which is a unique adenylate cyclase activator[4] and which has attracted recently a number of synthetic chemists[5], made 1 a challenging target for total synthesis. In this preliminary communication[6] we wish to report not only the total synthesis of (±)1 but also of the diastereomeric compounds (±)2, (±)3 and (±)4.

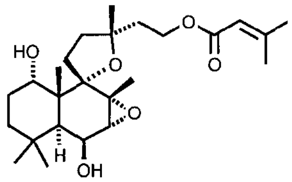
The common starting material was the bicyclic ketone 6 easily available in large quantities through a Diels-Alder-reaction of ethyl 3-cyclopropylidene-propenyl ether and 2,6-dimethylbenzoquinone[7]. The reactions leading to (±)1-(±)4 are outlined in the following schemes. The m.p. of the compounds are thereby indicated in parenthesis of the compound number. All compounds



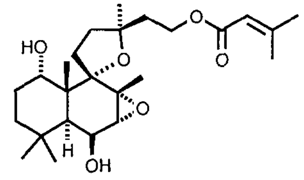
(±) **1**



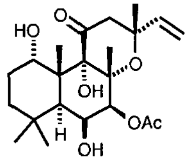
(±) **2**



(±) **3**

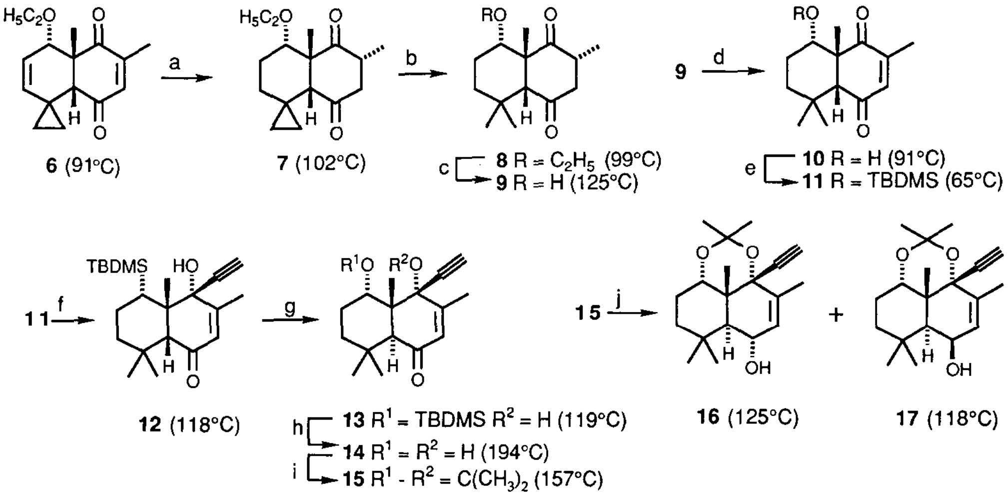


(±) **4**



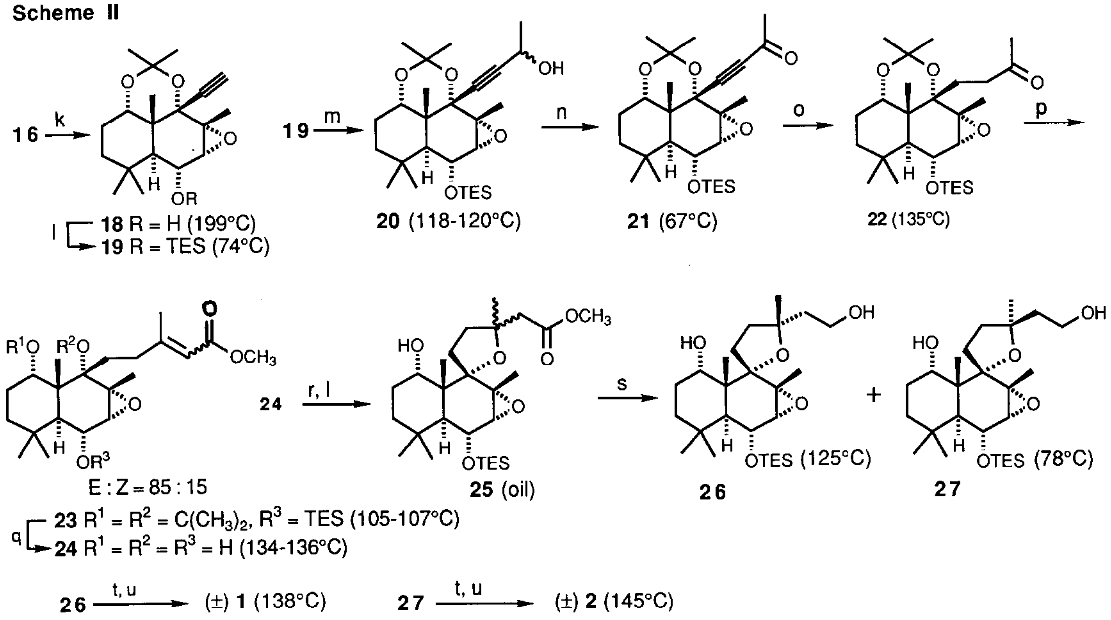
(±) **5**

Scheme I



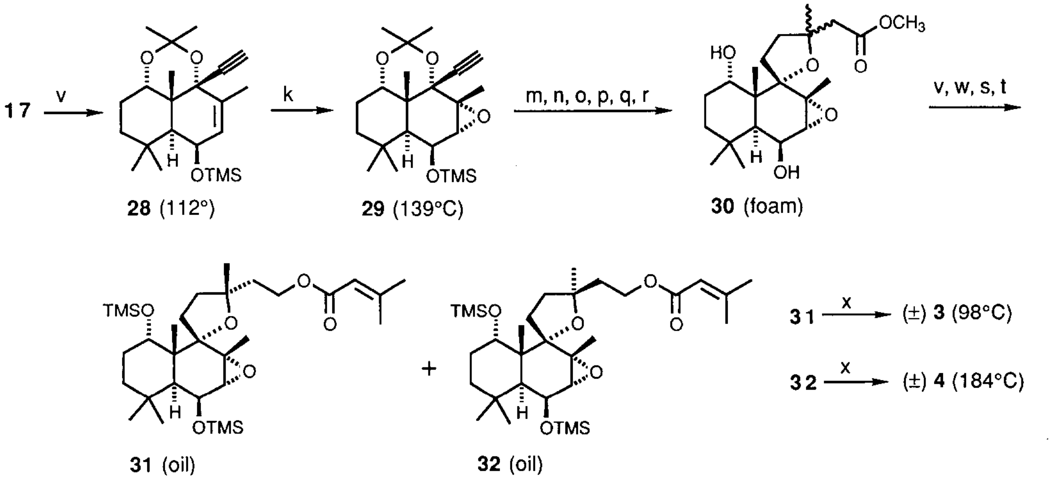
a) Pd($CaCO_3$), H_2, NaOMe followed by AcOH [MeOH, r.t.]; b) Pt, H_2 [AcOEt, AcOH, n.p., r.t.]; c) BBr_3 [CH_2Cl_2, -78°-0°]; d) DDQ, p-TsOH [toluene, refl.]; e) TBDMSi-triflate, 2,6-lut. [CH_2Cl_2, -78°]; f) Li-acetylide [THF, -78°-0°]; g) bas. Al_2O_3 [toluene, refl.]; h) $HF_{aqu.}$ [5% in CH_3CN, 40°]; i) 2,2-diMeOpropane, p-TsOH [acetone, r.t.]; j) $NaBH_4$, LiCl, Li_2CO_3 [DME, r.t.].

Scheme II



k) m-ClpBA [CH_2Cl_2, r.t.]; l) TES-triflate, 2,6-lut. [CH_2Cl_2, -78°]; m) n-BuLi, CH_3-CHO [THF, -78°]; n) MnO_2 [cyclohex., r.t.]; o) Pd-$CaCO_3$, H_2 [AcOEt, 10 bar, 50°]; p) $(MeO)_2P(O)CH_2COOCH_3$, NaH [DME, 60°]; q) 1 N HCl [THF, 35°]; r) DBU [Et_3N, refl.]; s) DIBAH [THF, 0°]; t) $(CH_3)_2C{=}CHCOCl$, DMAP [CH_2Cl_2, 0°]; u) TBAF•$3H_2O$ [THF, r.t.].

Scheme III



v) TMSCl, 2,6-lut. [CH_2Cl_2, 70°]; w) TMS-triflate, 2,6-lut. [(CH_2Cl_2, -78°]; x) TBAF $3H_2O$, $HF_{aqu.}$ [THF, r.t.].

were fully characterized by spectroscopic data (NMR, IR, MS) and microanalyses. Furthermore, the structure of (±)1 and that of some of the intermediates was ascertained by X-ray structural analysis[6]. The yields in all individual steps ranged from 85-98%; the ether cleavage (8 → 9) proceeded only with 68% yield.

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References and Notes.

1. On sabbatical leave from the Dept. of Chemistry, Laurentian University, Sudbury, Ontario, Canada.

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