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Enantioselective Synthesis of (-)-Boschnialactone

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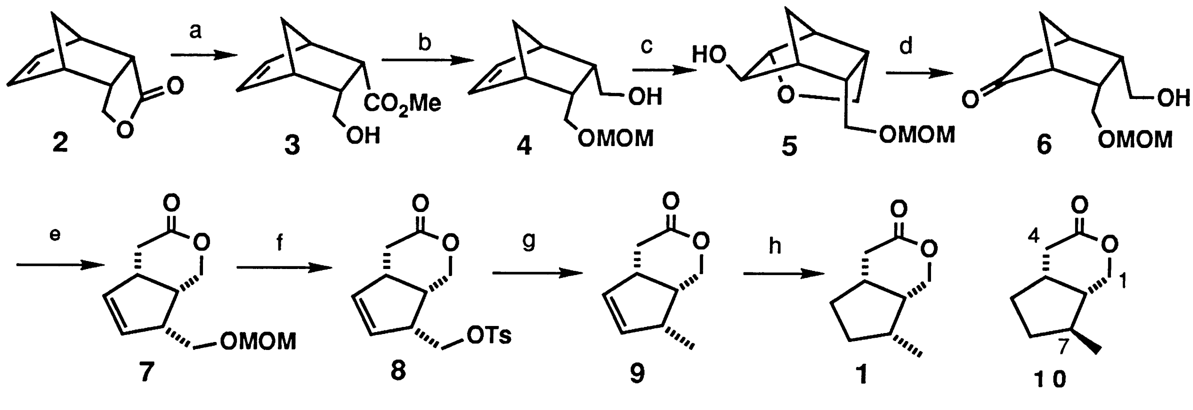
An enantioselective synthesis of (-)-boschnialactone was accomplished starting from a chiral fused bicyclo[2.2.1]heptane lactone readily available *via* an asymmetric Diels-Alder reaction.

Boschnialactone (**1**), one of the iridoids, was isolated from *Boschniakia rossica* Hult. and the absolute stereostructure was determined by Sakan and collaborators.[1)] Because of its unique biological properties such as cat-attracting effect and insect-repellent, several syntheses of (±)-**1** have been reported to date.[1,2)] However, there have been no enantioselective syntheses of (-)-**1**. Recently we reported a facile, enantiodivergent preparation of a chiral bicyclo[2.2.1]heptane lactone **2** available in a short step from the adduct obtained by an asymmetric Diels-Alder reaction.[3)] The lactone **2** is suitable as a synthetic tool for the chiral synthesis of both of the enantiomers of **1**, with natural and unnatural configuration. Herein, we disclose the first enantioselective synthesis of (-)-**1** with natural configuration starting from the (+)-lactone **2**.

The construction of the cyclopentapyranone ring is based upon a ring fission of a bicyclo[2.2.1]heptanone framework. According to the literature method,[4)] saponification of **2** and the subsequent esterification afforded the ester alcohol **3**, which was protected as the methoxymethyl ether (87% yield). Careful reduction of the ester



a) Ref. 4 b) MOMCl, ${}^{i}Pr_2NEt$, CH_2Cl_2, r.t., 12 h, 87%; $LiAlH_4$, THF, -3 °C, 10 min, 73% c) mcpba, CH_2Cl_2, 0 °C, 2.5 h, 59% d) PCC, molecular sieves 4A, CH_2Cl_2, r.t., 5 h, 72%; Al-Hg, THF, EtOH, 0 °C, 3 h, 91% e) *hν* (200 W, low-pressure Hg lamp, quarz filter), CH_3CN, r.t., 4 h, then conc. HCl (cat.), r.t., 1 h; PCC, molecular sieves 4A, CH_2Cl_2, r.t., 7 h, 64% f) PPTS, ${}^{t}BuOH$, reflux, 8 h, 86%; TsCl, pyridine, DMAP (cat.), r.t., 12 h, 93% g) Zn, NaI, dimethoxyethane, reflux, 1 h, q.y. h) H_2 (1 atm), 5% Pt on alumina, ${}^{t}BuOH$, r.t., 5 h, 85%

yielded the alcohol **4** (73% yield). Exposure of **4** to 3-chloroperoxybenzoic acid (mcpba) gave the tricyclic ether **5** in 59% yield. PCC oxidation[5] of **5** followed by reduction with Al-Hg produced the keto alcohol **6** (66% yield). Photolysis of **6**[6] and treatment of a 1:1 mixture of the resulting hemiacetal with PCC gave the lactone **7** in 64% yield. Removal[7] of the methoxymethyl group in **7**, tosylation, and reduction[8] afforded dehydroboschnialactone (**9**)[2a] in 80% yield. Hydrogenation of **9** over Pd-C gave **1** which was contaminated by a certain amount of its epimer. The epimer was inseparable from **1** by chromatography, and the stereochemistry would be assigned to be **10**[2b] on the basis of the NMR spectrum of the crude product. It was assumed that the isomerization of the double bond in **9** should occur during the hydrogenation.[9] Finally, platinium-catalyzed hydrogenation furnished boschnialactone (**1**)[10] without contamination by any stereoisomers in 85% yield.

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10) Selected physical data: **5**: mp 82-84 °C; $[\alpha]_D^{26}$ -30.2° (*c* 1.69, $CHCl_3$). **6**: bp 121-125 °C / 0.15 mmHg (1 mmHg= 133.322 Pa); $[\alpha]_D^{25}$ -5.0° (c 1.90, $CHCl_3$). **7**: mp 42-44 °C; $[\alpha]_D^{25}$ -17.3° (*c* 2.10, $CHCl_3$). **8**: mp 127 °C; $[\alpha]_D^{25}$ +19.9° (*c* 2.73, $CHCl_3$). **9**: mp 90-91 °C; $[\alpha]_D^{26}$ -19.8° (*c* 0.77, $CHCl_3$). **1**: bp 109-115 °C / 13 mmHg (lit.[1] 105-112 °C / 6 mmHg); $[\alpha]_D^{26}$ -21.3° (*c* 0.34, $CHCl_3$) {lit.[1] $[\alpha]_D^{21}$ -18.2° (*c* 2.10, $CHCl_3$)}.

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