purified by flash chromatography on silica gel (Et_2O/hexanes 50/50 →100/0) to give the desired product (205 mg, 0.871 mmol, 88% yield) as a pale yellow oil. $R_f = 0.27$ (Et_2O/hexanes 90/10); IR (neat): $\tilde{\nu} = 3506.1\ cm^{-1}$ (br.), 3115.9, 2921.6, 2710.9, 1692.9, 1648.3, 1605.4, 1512.0, 1404.1, 1345.1, 1237.9, 1106.8, 1063.1, 1019.7, 850.8; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 9.43$ (s, 1H; H-1), AB signals (4H, $\delta = 8.25$, 7.58, $J_{AB} = 8.7$ Hz; aromatic H), 6.56 (tq, 1H, $J = 7.2$, 1.2 Hz; H-3), 5.07 (dd, 1H, $J = 6.2$ Hz; H-5), 2.89 – 2.77 (m, 2H; H-4), 2.20 (br. s, 1H; OH), 1.71 (s, 3H; CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 195.17$, 150.94, 148.99, 147.25, 141.35, 126.46, 123.73, 71.90, 38.37, 9.31; MS: m/z (%) = 218.22 (3.5) [$M^+ - OH$], 152.15 (57.5), 84.13 (100.0); HR-MS: calcd for $C_{12}H_{14}NO_4 = 236.0923$, found = 236.0921; molecular formula: $C_{12}H_{13}NO_4$ (235.23 g mol^{-1}).

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Total Synthesis of (+)-Eurylene and (+)-14-Deacetyleurylene**

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Recently biologically active and structurally novel triterpene polyethers, natural products which are thought to be biogenetically derived from squalene, have been isolated from both marine and terrestrial plants. Among the polyethers are cytotoxic eurylene (**1**) and 14-deacetyleurylene (**2**; see Scheme 1), isolated from the wood of *Eurycoma longifolia* by Itokawa et al.[1] The stereostructures and conformations of **1** and **2** have been elucidated by X-ray crystallographic analysis and spectroscopic methods.[2] The mechanism of action for the cytotoxic activities of these natural polyethers, however, remains to be clarified, because these molecules are available only in restricted amounts from natural sources. Therefore, the development of an efficient synthesis was desired for these polyethers. The novel structures, the cytotoxic activities, and the conformation – activity relationships[2] of **1** and **2** have attracted the attention of many synthetic organic chemists; however, the total synthesis of **2** with potent cytotoxic activity has never been accomplished.[3] Here we report the efficient and stereoselective total synthesis of (+)-eurylene (**1**) and (+)-14-deacetyl eurylene (**2**), featuring monool- and diol-differentiated chemoselective oxidative cyclizations promoted by rhenium(VII) and chromium(VI) oxo species, respectively.

Our retrosynthetic analysis of **1** and **2** is depicted in Scheme 1. The key events for the total synthesis are the stereoselective construction of the *trans* and *cis* tetrahydrofuran (THF) rings and the differentiation of the 14-hydroxy group. To solve this problem, we focused on the hydroxy-directed *syn* oxidative cyclization of acyclic bishomoallylic alcohols promoted by rhenium(VII)[4] and chromium(VI) oxides.[5] Thus, the *trans* THF ring will be constructed by applying our Re^{VII} protocol[6] to the bishomoallylic monool moiety in triol **3**, while the *cis* THF ring is constructed by the Cr^{VI}-induced *cis*-selective cyclization of the bishomoallylic vicinal diol. The pseudo-*meso* triol **3** will, in turn, be derived

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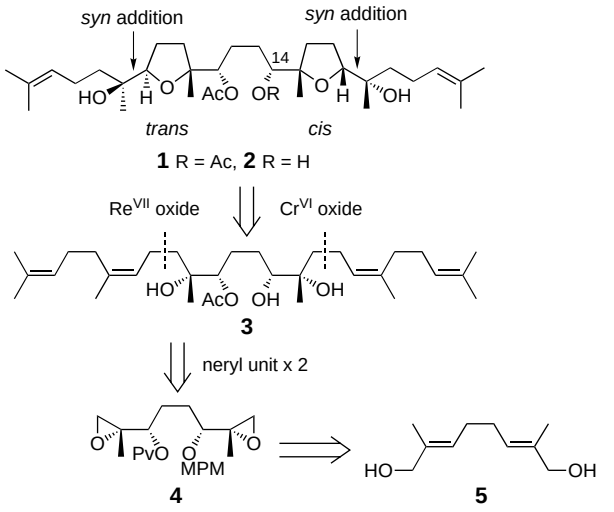
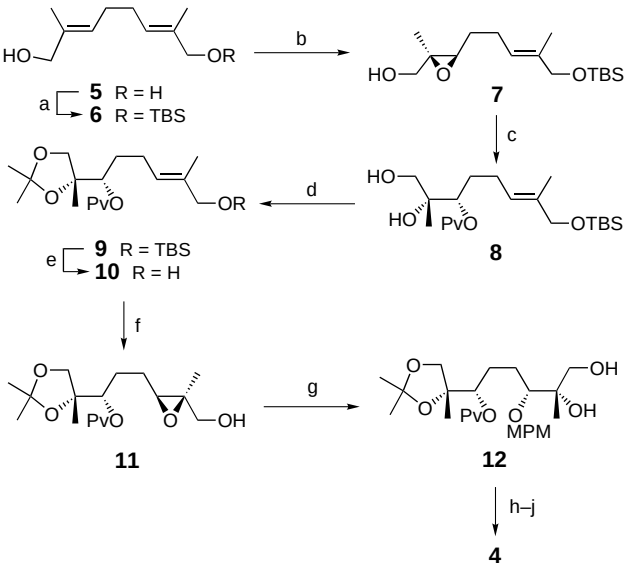


Scheme 1. Retrosynthetic analysis of **1** and **2**. Pv = pivaloyl; MPM = 4-methoxyphenylmethyl.

from the appropriately protected diepoxide **4** by extending the side chains with two neryl units in a bidirectional manner. It was envisaged that the diepoxide **4** can be prepared by Sharpless asymmetric epoxidation of the readily available diol **5** and subsequent regioselective ring-opening reactions.

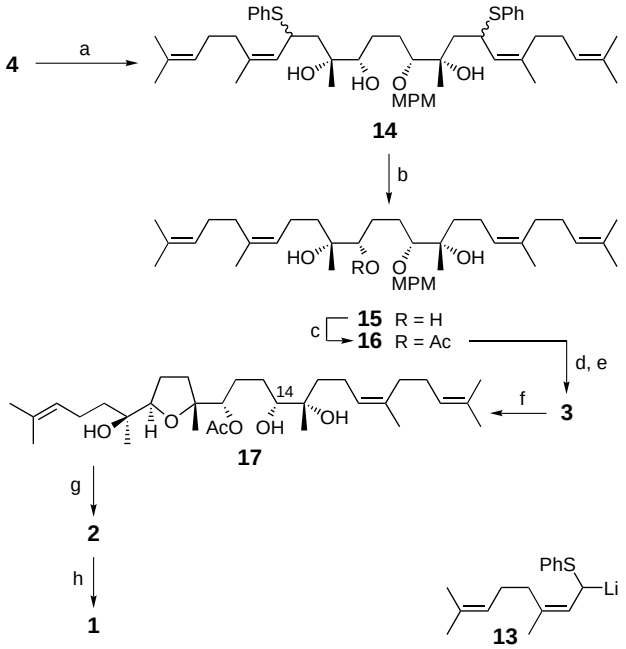
The stereoselective preparation of the diepoxide **4** began with monoprotection of the known diol **5**[7] as a *tert*-butyldimethylsilyl (TBS) ether (→**6**; Scheme 2). Sharpless asymmetric epoxidation[8] of the allylic alcohol **6**[9] using (−)-diethyl D-tartrate (D-(−)-DET) afforded the epoxy alcohol **7** in high optical purity.[10] The pivalate group was introduced regioselectively into **7** by a titanium-assisted epoxide-opening



Scheme 2. a) TBSCl, imidazole, CH_2Cl_2, RT, 1 h, 55%; b) TBHP, $Ti(OiPr)_4$, D-(−)-DET, MS 4 Å, CH_2Cl_2, −20 °C, 2 h, 83% (98% *ee*); c) $Ti(OiPr)_4$, PvOH, benzene, 0 °C, 2 h, 83%; d) 2,2-dimethoxypropane, camphorsulfonic acid, CH_2Cl_2, 0 °C, 2 h, 88%; e) Bu_4NF, THF, RT, 3 h, 99%; f) TBHP, $Ti(OiPr)_4$, L-(+)-DET, MS 4 Å, CH_2Cl_2, −20 °C, 3 h, 89%; g) $Ti(OMPM)_4$, MPMOH, benzene, 60 °C, 12 h; h) AcOH/H_2O (4/1), RT, 5 h; i) MsCl, Py, CH_2Cl_2, 0 °C → RT, 5 h; j) K_2CO_3, MeOH, RT, 1 h, 41% (4 steps). Ms = methanesulfonyl, Py = pyridine, TBHP = *tert*-butyl hydroperoxide.

reaction[11] to yield 1,2-diol **8** as a single diastereomer; subsequent acetonide protection and desilylation furnished the allylic alcohol **10** in good overall yield. The asymmetric epoxidation of **10** using L-(+)-DET provided the epoxy alcohol **11**, which was subjected to a $Ti(OMPM)_4$-mediated epoxide-opening reaction[11, 12] with *p*-anise alcohol to produce the desired 1,2-diol **12** and a 1,3-diol derivative in a ratio of approximately 3:1. Deprotection of the acetonide in 1,2-diol **12**, mesylation of both primary hydroxy groups in the resultant tetraol, and subsequent basic treatment of the dimesylate finally gave the requisite diepoxide **4** in 41% yield (based on four steps from **11**).

The bidirectional chain extension proceeded smoothly by alkylation of **13**, the lithio derivative of neryl phenyl sulfide,[6b] with the diepoxide **4** in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), yielding the bissulfide **14** as a mixture of diastereomers (Scheme 3).[13] Compound **14** was



Scheme 3. a) Compound **13**, TMEDA, THF, −78 °C, 30 min, then 0 °C, 2 h; b) Na, THF/*i*PrOH (2/1), reflux, 15 h, 86% (2 steps); c) Ac_2O, Py, RT, 12 h, 91%; d) DDQ, MS 4 Å, CH_2Cl_2, 0 °C, 2 h, 68%; e) AcOH/H_2O (4/1), RT, 16 h, 89%; f) $[(CF_3CO_2)ReO_3 \cdot 2CH_3CN]$, TFAA, CH_2Cl_2/CH_3CN (9/1), −40 °C, 1.5 h, 84%; g) PCC, CH_2Cl_2, RT, 30 min, 47%; h) Ac_2O, Py, RT, 40 h, 80%.

desulfurized under Bouvault–Blanc conditions[6b, 14] to provide the triol **15**, and selective acetylation of the *sec*-alcohol afforded the diol acetate **16** in good overall yield. The MPM protecting group in **16** was converted into the 4-methoxybenzylidene acetal through interaction of the neighboring hydroxy groups with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).[15] Subsequent acidic hydrolysis furnished the key substrate **3** required for the oxidative cyclizations.

The optimal conditions were determined, and the treatment of triol **3** with eight equivalents of the oxorhenium(VII) complex $[(CF_3CO_2)ReO_3 \cdot 2CH_3CN]$[16] and ten equivalents of trifluoroacetic anhydride (TFAA) in a mixed solvent system (CH_2Cl_2/CH_3CN 9/1)[6] at −40 °C for 1.5 h diastereoselectively

gave the expected *trans* THF product **17** in 84% yield; the right-hand part of the molecule was intact. On the other hand, when **17** was treated with a stoichiometric amount of the oxochromium(VI) complex pyridinium chlorochromate (PCC),[17] in CH_2Cl_2 at room temperature for 30 min,[5] the bishomoallylic vicinal diol moiety was oxidatively cyclized, probably via a chelated dialkoxychromium intermediate,[5a, 18] with complete *cis* diastereoselectivity to produce (+)-14-deacetyleurylene (**2**).[19] The spectral characteristics (^{1}H and ^{13}C NMR, IR, MS, and HRMS) of synthetic **2** were identical to those reported for the natural product.[1b] Finally, selective acetylation of the 14-hydroxy group in **2** afforded another objective, (+)-eurylene (**1**),[19] whose spectral data were also consistent with the ^{1}H NMR spectrum of an authentic sample[3a] and with the data reported for the natural product.[1]

In conclusion, we have accomplished the first total synthesis of (+)-14-deacetyleurylene (**2**), featuring chemoselective THF ring formations stereocontrolled by *syn*-oxidative cyclizations of the bishomoallylic monool and diol induced by oxorhenium(VII) and -chromium(VI) species, respectively. The reason for the intriguing relationship[2] between the conformations and cytotoxicities of **1** and **2** is under investigation.

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[19] **1**: M.p. 145 – 147 °C, $[\alpha]_D^{24} = +4.86$ ($c = 0.275$ in $CHCl_3$); ref. [1] m.p. 146 – 148 °C, $[\alpha]_D = +4.32$ ($c = 0.14$ in $CHCl_3$). **2**: M.p. 64.3 – 67.4 °C, $[\alpha]_D^{25} = +6.02$ ($c = 0.600$ in $CHCl_3$); ref. [1b] m.p. 63 – 65 °C, $[\alpha]_D = +6$ ($c = 1.03$ in $CHCl_3$).

Cuprophilicity: Spectroscopic and Structural Evidence for Cu–Cu Bonding Interactions in Luminescent Dinuclear Copper(I) Complexes with Bridging Diphosphane Ligands**

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Copper(I) – copper(I) bonding interactions have widely been invoked to be a driving force for the self-assembly of copper(I) aggregates and to play an important role with regard to the photoluminescence of polynuclear copper(I) complexes con-

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