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THE STEREOSELECTIVE TOTAL SYNTHESIS OF RACEMIC TELEKIN

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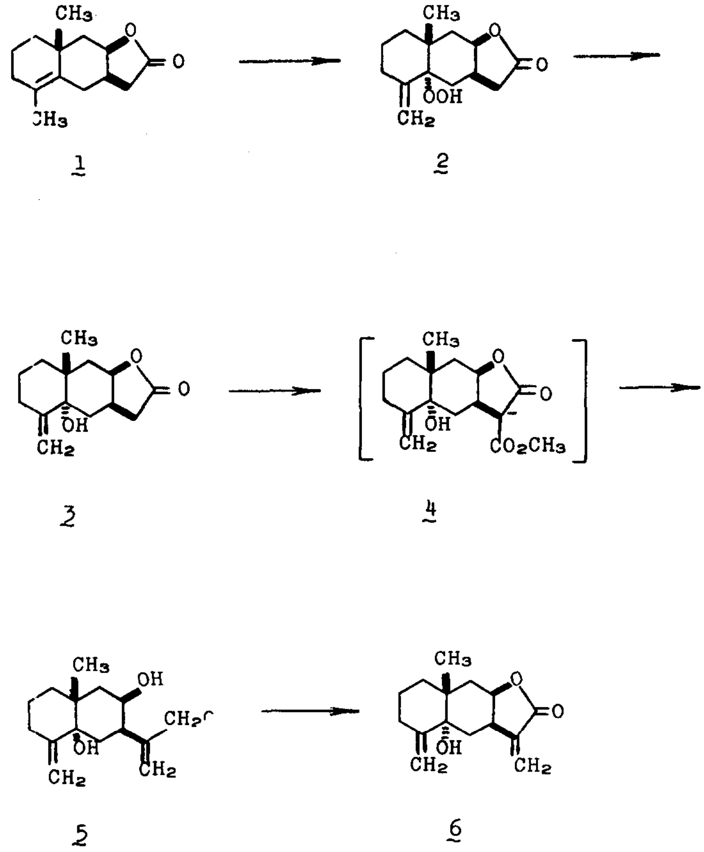
The alantolactone family of sesquiterpenes[1] presents a variety of challenging synthesis problems. Over the past few years, we have investigated various schemes with the aim of solving some of these problems and synthesizing representative members of this eudesmane group. Recent studies[2,3] have yielded important breakthroughs and cleared the way for the attainment of our initial goals. We now report a stereoselective total synthesis of racemic telekin (6) by a straightforward route which corroborates the proposed structure[4] of the naturally occurring sesquiterpene lactone

The preparation of tricyclic lactone 1, a key intermediate in our alantolactone synthesis, from Hagemann's ester has already been described.[3] This substance, upon photooxygenation according to the procedure of Nickon and Bagli,[5] gave hydroperoxide 2 [m.p. 117.5-118.5°; $\lambda_{max}^{CHCl_3}$


CH3
O
O
CH3
1
CH3
O
O
OOH
CH2
2
CH3
O
O
OH
CH2
3
CH3
O
O
OH
CH2
CO2CH3
4
CH3
OH
CH2
OH
CH2
CH2
5
CH3
O
O
OH
CH2
CH2
6

2.86, 3.00 (OOH), 5.67 (lactone CO), 6.08 and 11.0 μ ($C=CH_2$); $\delta_{TMS}^{CHCl_3}$ 5.19, 4.88 p.p.m. ($C=CH_2$)] as the principal product. 4-Cholestene, a steroidal analog of unsaturated lactone **1**, exhibits a marked preference for α-attack by oxygen under these conditions[6] and, on this basis, we assign the *trans* configuration to decalyl hydroperoxide **2**. Reduction with sodium iodide in acetic acid[5] afforded the corresponding alcohol **3** [m.p. 154-158°; λ_{max}^{KBr} 2.90 (OH), 5.72 (lactone CO), 6.08 (C=C), 8.18, 8.43, 8.53, 9.42, 9.85, 10.42, 10.93, and 11.53 μ]. Triol **5** [m.p. 136-139°; λ_{max}^{KBr} 2.9-3.0 (OH), 6.08 (C=C), 8.42, 9.67, 9.97, 10.14, and 10.95 μ] was secured by treating hydroxy lactone **3** with sodium hydride in refluxing dimethyl carbonate, removing the excess dimethyl carbonate, and treating the resulting α-carbomethoxy lactone enolate **4** with lithium aluminum hydride in 1,2-dimethoxyethane.[2] Selective oxidation of triol **5** occurred readily through the action of activated manganese dioxide[2,7] in benzene, and racemic telekin **6** [m.p. 195-196.5°; λ_{max}^{KBr} 2.84, 2.90 (OH), 5.70 (lactone CO), 6.00, 6.07 ($C=CH_2$), 7.92, 8.52, 8.77, 9.71, 9.95, 10.44, 10.97, 11.50, and 12.22 μ] was thereby obtained. The infrared spectrum of this material faithfully reproduced the richly detailed published spectrum[4] of the natural product.

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