

THE SYNTHESIS OF (±)-DIPLODIALIDE C AND (±)-DECAN-9-OLIDE,
THE NATURALLY OCCURRING 10-MEMBERED OLIDES

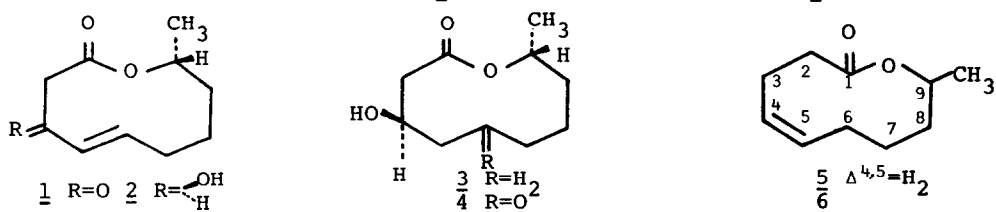
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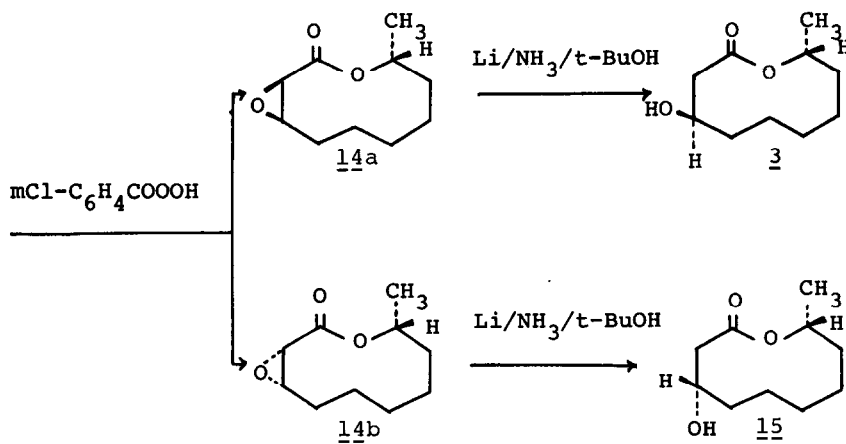
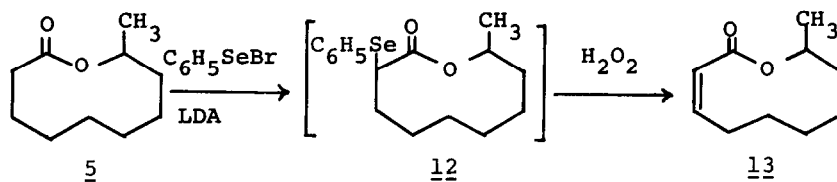
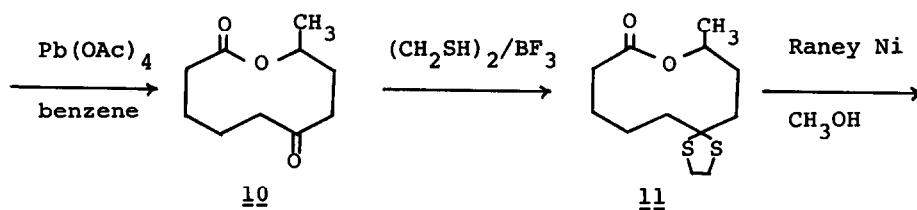
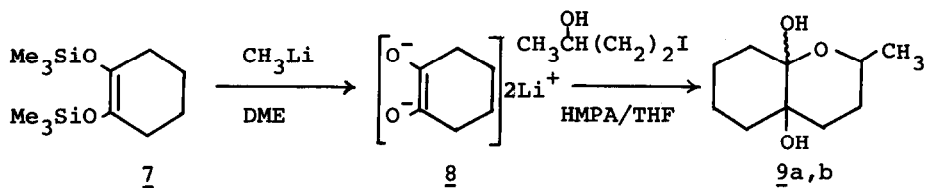
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Diplodialides A(1), B(2), C(3), and D(4), possessed of 10-membered lactone moiety in their structures are the first members of open-chain pentaketoides isolated from *diplodia pinea* (IFO 6472). Wada and co-workers discovered that diplodialide A(1) showed a significant inhibitory activity against 11 α -hydroxylase of progesterone in vegetable cell cultures of *Rhizopus stolonifer* at 125p.p.m.^{1a,b} Subsequently, decan-9-olide (5) and (Z)-dec-4-en-9-olide (6) were isolated from the metasternal gland secretion of *Phoracantha synonyma* by Moore et al.²

We have reported that the lithium 1,2-enediolates [easily available from the reaction of the enediol-bis-trimethylsilyl ethers with 2 equiv. of methyl-lithium] underwent C-alkylation to furnish the α -hydroxy ketones.^{3a,b} Application of this reaction to the synthesis of the medium ketolactonic compounds was indicated in the preceding paper.^{3c} We now wish to report in this communication the synthesis of (±)-diplodialide C(3) and (±)-decan-9-olide (5).



The enediol-bis-trimethylsilyl ether 7,⁴ readily prepared in high yield by the acyloin condensation of diethyl adipate in the presence of trimethylchlorosilane was converted by addition of 2 equiv. of methylolithium in monoglyme into its 1,2-enediolate 8, which was immediately subjected to alkylation with 3-hydroxy-1-iodobutane in THF-HMPA to give two diastereomeric glycols of 9a [mp 110-111°,



ir max(nujol) 3558, 3292 cm^{-1} , ms 168($\text{M}^+ - \text{H}_2\text{O}$)] and 9b [mp 130-132°, ir max(nujol) 3450, 3350 cm^{-1} , ms 168($\text{M}^+ - \text{H}_2\text{O}$)] in 87% yield. Oxidation of a mixture of 9a and 9b ($\text{Pb}(\text{OAc})_4/\text{benzene}$, rt, 1hr) smoothly occurred to give the desired ketolactone 10 [mp 44-44.5° (lit.⁵ 37-37.5°), ir max(nujol) 1716, 1700 cm^{-1} , ms 184(M^+)] in a nearly quantitative yield. Thioketalization of 10 ($(\text{CH}_2\text{SH})_2/\text{BF}_3 - \text{AcOH}$, rt, 5hr) afforded the corresponding thiolactone 11 [mp 71-72°, ir max(nujol) 1720 cm^{-1} , ms 260(M^+)] in 90% yield, which upon desulfurization with Raney nickel in refluxing methanol provided (\pm)-decan-9-olide 5 in 90% yield, which was identical to the natural olide by gas chromatography and mass spectrometry. Treatment^{6a,b} of 5 with phenylselenium bromide-lithium diisopropylamide in THF at -78° followed by oxidation (30% $\text{H}_2\text{O}_2/\text{AcOH}$, 0°, 1hr) gave the cis- $\alpha\beta$ -unsaturated lactone 13 [ir max (neat) 1710, 1621, 814 cm^{-1} , uv λ_{max} (EtOH) 212nm, nmr δ (CCl_4) 0.90-2.30(9H, m), 1.33(3H, d, $J=7\text{Hz}$), 2.50-3.00(1H, m), 5.10(1H, m), 5.72(1H, d-d, $J=11.5\text{Hz}$ and 1Hz), 6.00-6.40(1H, m)] in 82% yield. Epoxidation⁷ of 13 ($\text{mCl} - \text{C}_6\text{H}_4\text{CO}_3\text{H}/4,4'$ -thiobis-(6-t-butyl-3-methyl-phenol)/ $(\text{CH}_2\text{Cl})_2$, refluxing, 24hr) followed by separation on preparative silica gel tlc gave 68% yield of 14a [ir max(neat) 1746 cm^{-1} , nmr δ (CCl_4) 1.31(3H, d, $J=7\text{Hz}$), 2.80-3.05(1H, m), 3.50(1H, d, $J=5\text{Hz}$), 5.50(1H, m)] and 14b [ir max(neat) 1723 cm^{-1} , nmr δ (CCl_4) 1.28(3H, d, $J=7\text{Hz}$), 3.00-3.36(2H, m), 5.10(1H, m)] in a ratio of 1:2. Reduction of 14a ($\text{Li}/\text{liq-NH}_3/\text{t-BuOH}$, -45°, 15min) afforded (\pm)-diplodialide C(3) in 45% yield, whose spectral properties were identical with those of the natural diplodialide C in all respects. A similar reduction of 14b gave epi-diplodialide C 15 [ir max(CCl_4) 3613, 3439, 1723 cm^{-1} , nmr δ (CCl_4) 0.90-2.00(10H, m), 1.22(3H, d, $J=7\text{Hz}$), 2.10-2.70(2H, m), 3.90(1H, m), 4.85(1H, m), ms 168($\text{M}^+ - \text{H}_2\text{O}$)] in 40% yield.

The studies on synthesis of the other diplodialides by this useful method are now in progress.

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