Total Synthesis of (±)-(*E*)-8β,17-Epoxylabd-12-ene-15,16-dial

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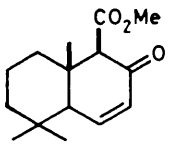
The title labdanoid dialdehyde (**10**) which has high antifungal activity was synthesized stereoselectively from the *trans*-decalone derivative (**1**).

In connection with our previous synthesis[1] of polygodial and warburganal which possess a wide spectrum of biological activity including insect antifeeding, antimicrobial, cytotoxic, plant growth regulation, molluscicidal, and anticomple-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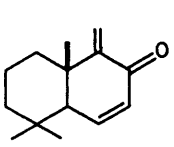
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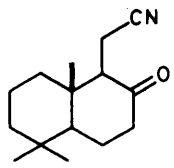
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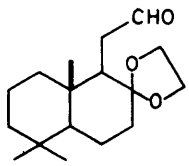
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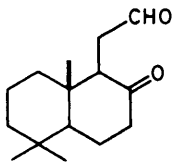
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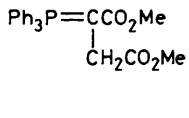
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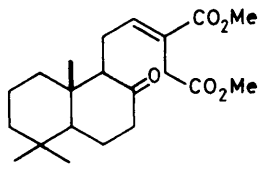
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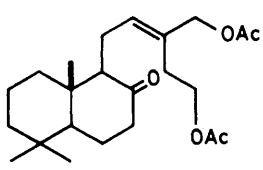
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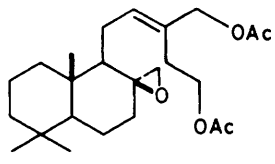
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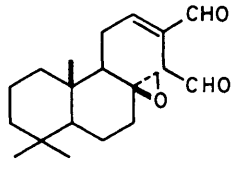
(10)

mental properties, we attempted the synthesis of the labdanoid dialdehyde (**10**) which was isolated from the seeds of *Afromomum daniellii* in 1979[2] and has the same functional groups as polygodial. In this paper, we describe the first synthesis of the labdanoid dialdehyde (**10**) from the *trans*-decalone derivative (**1**).[3]

The cyano-ketone (**3**), m.p. 80—82 °C [ν_{max}(CCl_4) 2250 and 1715 cm^{-1}], was synthesized from the *exo*-methylene enone (**2**)[4] by the Michael addition of a C_1 unit at C-11 (KCN, NH_4Cl, dimethylformamide–H_2O, room temp.) followed by hydrogenation (Pd/C, EtOH) [90% yield from (**2**)]. Compound (**3**) was protected (ethylene glycol, *p*-$MeC_6H_4SO_3H$), reduced (di-isobutylaluminium hydride, hexane), and deprotected with acid (50% acetic acid) to give the keto-aldehyde (**5**) [quantitative yield from (**3**)], [(**5**) (oil): ν_{max}(CCl_4) 1720 and 1710 cm^{-1}; ^{1}H n.m.r. (CCl_4) δ 0.73 (3H, s), 0.88 (3H, s), 1.00 (3H, s), and 9.73 (1H, s)]. Next, (**5**) was treated with the phosphorane (**6**)[5] to give the keto-diester (**7**) having (*E*)-stereochemistry[6] (72.4%, benzene reflux temp., 20 h) [(**7**) (oil): ν_{max} (CCl_4) 1740 and 1710 cm^{-1}; ^{1}H n.m.r. (CCl_4) δ 0.76 (3H, s), 0.89 (3H, s), 0.99 (3H, s), 3.34 (2H, s), 3.65 (3H, s), 3.70 (3H, s), and 6.69 (1H, t, *J* 6 Hz)]. However, the reaction of the acetal-aldehyde (**4**) with the phosphorane (**6**) gave the acetal of the keto-diester (**7**) in only 8% yield owing to the steric hindrance of the bulky ethylene acetal group. Compound (**7**) was converted into the keto-diacetate (**8**) [ν_{max}(CCl_4) 1740 and 1710 cm^{-1}; ^{1}H n.m.r. (CCl_4) δ 0.76 (3H, s), 0.88 (3H, s), 1.00 (3H, s), 2.02 (6H, s), 4.08 (2H, t, *J* 6 Hz), 4.40 (2H, s), 5.42 (1H, t, *J* 7 Hz)] by the usual method [i, ethylene glycol, *p*-$MeC_6H_4SO_3H$; ii, $LiAlH_4$, diethyl ether; iii, Ac_2O, pyridine; iv, 50% AcOH; 65.2% yield from (**7**)]. Treatment of (**8**) with dimethylsulphonium methylide followed by acetylation gave the oxirane (**9**) (78% conversion yield), [(**9**) (oil): ν_{max} (CCl_4) 1740, 1230, and 1025 cm^{-1}; ^{1}H n.m.r. (CCl_4) δ 0.92 (9H, s), 2.00 (3H, s), 2.04 (3H, s), 2.18 (1H, d, *J* 3.5 Hz), 2.43 (1H, d, *J* 3.5 Hz), 4.04 (2H, t, *J* 6 Hz), 4.42 (2H, s), and 5.36 (1H, br. m)]. Finally, hydrolysis (K_2CO_3, aqueous MeOH, room temp.) of (**9**) afforded the corresponding diol, which without purification was oxidized (oxalyl chloride, Me_2SO, CH_2Cl_2, NEt_3 or NCS, Me_2S, $AgBF_4$, NEt_3) to the dialdehyde (**10**) [43% yield from (**9**)] [(**10**) (oil) ν_{max} (CCl_4) 1730, 1690, and 1640 cm^{-1}; u.v.(EtOH) λ_{max} 234 nm; ^{1}H n.m.r. ($CDCl_3$) δ 0.88 (3H, s) 0.91 (3H, s), 0.93 (3H, s), 2.30 (1H, d, *J* 3.5 Hz), 2.44 (1H, d, *J* 3.5 Hz), 3.40 (2H, br. s), 6.62 (1H, t, *J* 7 Hz), 9.32 (1H, s), 9.56 (1H, t, *J* 1 Hz)], which had identical ^{1}H n.m.r. and i.r. spectra with the natural product.

This work was supported in part by a Grant-in-Aid for Scientific Research (1981 to S. I.) from the Ministry of Education, Science and Culture.

Received, 18th February 1983; Com. 232

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