Synthesis of a *trans*-Decalin as a Potential Insect Antifeedant

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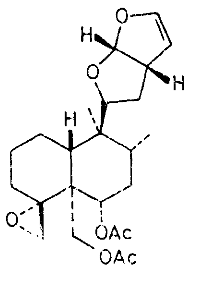
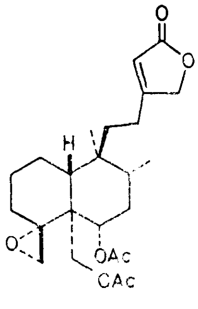
Summary In a model study for the synthesis of clerodane-related insect antifeedants the *trans*-decalin (**3**) was prepared and shown to inhibit feeding of *Locusta migratoria*.

The synthesis of clerodane-related diterpenes has recently attracted considerable attention.[1] However none of the approaches reported so far has achieved the construction of the desired epoxy-diacetate functional group arrangement common to the natural products such as clerodin (**1**)[2] and ajugarin I (**2**)[3] and known to be important for insect antifeedant activity.[4]



(1)



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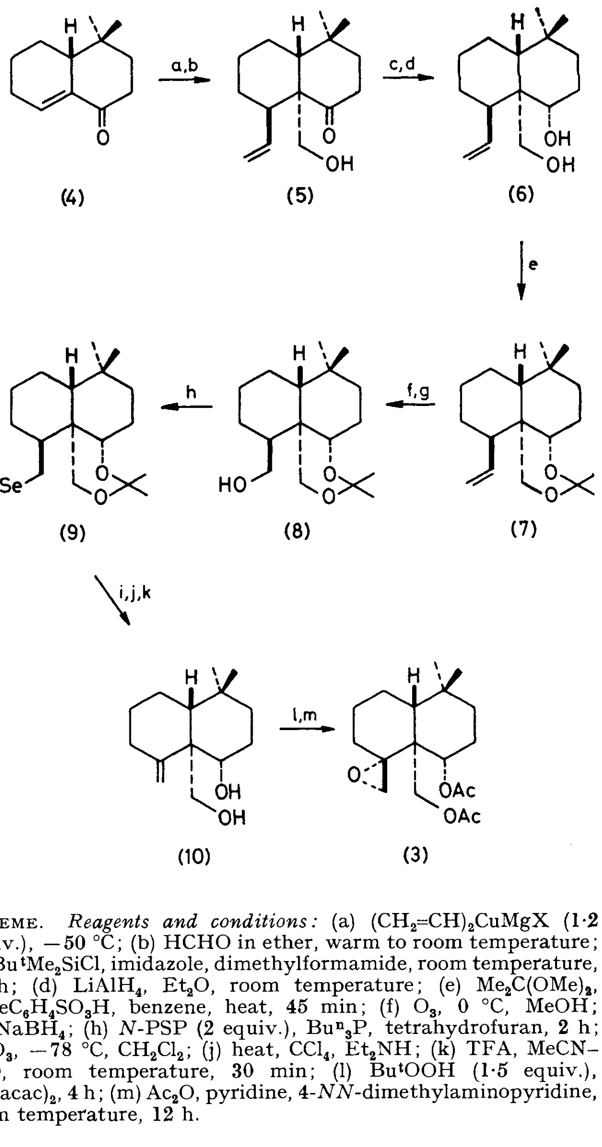

Scheme. *Reagents and conditions:* (a) $(CH_2{=}CH)_2CuMgX$ (1·2 equiv.), −50 °C; (b) HCHO in ether, warm to room temperature; (c) Bu^{t}Me$_2$SiCl, imidazole, dimethylformamide, room temperature, 12 h; (d) $LiAlH_4$, Et_2O, room temperature; (e) $Me_2C(OMe)_2$, *p*-$MeC_6H_4SO_3H$, benzene, heat, 45 min; (f) O_3, 0 °C, MeOH; (g) $NaBH_4$; (h) *N*-PSP (2 equiv.), Bu$^n_3$P, tetrahydrofuran, 2 h; (i) O_3, −78 °C, CH_2Cl_2; (j) heat, CCl_4, Et_2NH; (k) TFA, MeCN–H_2O, room temperature, 30 min; (l) Bu^{t}OOH (1·5 equiv.), VO(acac)$_2$, 4 h; (m) Ac_2O, pyridine, 4-*NN*-dimethylaminopyridine, room temperature, 12 h.

Here we report a synthesis of a suitable model compound (**3**) which allows us both to probe the biological activity of these diterpenes and to develop a strategy which could potentially be applied to the total synthesis of natural compounds.

The readily prepared enone[5] (**4**) reacted with a vinyl cuprate to form an enolate regiospecifically which was trapped with formaldehyde in ether solution to afford the *trans*-decalin keto-alcohol (**5**)† in 65% overall yield. Reactions of methylene equivalents other than the vinyl cuprate with the enone (**4**) were unsuccessful. The stereochemical assignment of (**5**) was expected on mechanistic grounds and was entirely consistent with a detailed high-field ^{1}H n.m.r. spectral analysis.

In order to obtain the stereospecific reduction of (**5**) removal of the directing effect of the primary hydroxy-group was necessary by prior treatment with t-butyldimethylsilyl chloride. Subsequent reaction with excess of $LiAlH_4$ gave the diol (**6**) in 77% yield [^{1}H n.m.r. δ 3·7 (dd, *J* 11·6 and 1·7 Hz, >C*H*OD after D_2O exchange)].

Protection of the 1,3-diol unit using acetone dimethyl acetal gave compound (**7**) in essentially quantitative yield. The vinyl group was subjected to ozonolysis and reductive work-up with $NaBH_4$ to give the alcohol (**8**) (86% yield) which was smoothly converted into the selenide (**9**) using *N*-phenylselenophthalimide (*N*-PSP)–Bu$^n_3$P[6] in high yield (89%) and subsequently oxidised, *syn*-eliminated, and deprotected with aqueous trifluoroacetic acid (TFA) to give the diol (**10**) (m.p. 122—124 °C) (92%).

Directed epoxidation[7] of the diol (**10**) using Bu^{t}OOH–VO(acac)$_2$ (Hacac = acetylacetone) gave an intermediate epoxy-diol which was rapidly acetylated to give the final epoxy-diacetate (**3**) in 52% yield (m.p. 105—106 °C). The ^{1}H n.m.r. spectrum of (**3**) showed characteristic resonances at δ 4·88 (d, *J* 12·3 Hz, 1 H), 4·7 (dd, *J* 11·4 and 4·7 Hz, 1H), 4·36 (d, *J* 12·3 Hz, 1H), 2·99 (dd, *J* 4 and 2·4 Hz, 1H), and 2·22 (d, *J* 4 Hz, 1H), these data being identical to equivalent resonances in the natural products. Additionally the structure of (**3**) is supported by the observation of strong nuclear Overhauser effects between the secondary acetate methine proton and one methine proton on the epoxide ring and between the axial methyl group and one of the methylene protons of the primary acetate unit.

On testing‡ compound (**3**) for insect antifeeding properties with *Locusta migratoria* a 70% inhibition of feeding was obtained at 100 p.p.m. on GF/A discs containing 5% sucrose as the food source. This activity was equivalent to that shown by clerodin hemiacetal.

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† All new compounds were fully characterised by spectroscopic methods and elemental microanalysis.

‡ We thank Dr. E. A. Bernays, Centre for Overseas Pest Research, London, for this result.

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