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Stereochemically Controlled Intramolecular Diels–Alder Reactions: Synthesis of Substituted *trans*-Fused Octahydronaphthalenes Possessing a Bridgehead Methyl Group

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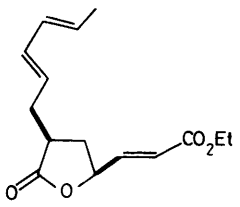
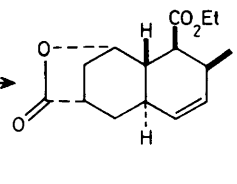
Cyclisation of triene (**5**) gives solely the octahydronaphthalene (**9**).

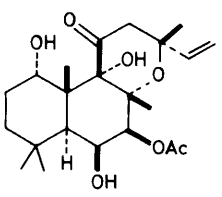
The intramolecular Diels–Alder reaction has proved to be extremely valuable in the synthesis of octahydronaphthalenes[1] as it allows such systems to be constructed efficiently and with a reasonable degree of stereocontrol at the ring junction. However in cases where there are asymmetric centres on the chain linking the diene and dienophile, it is often difficult to control the stereochemistry of the resulting octahydronaphthalene. Previously we reported[2] that such control could be achieved by fusing a lactone ring onto the triene and showed that (**1**) underwent cyclisation to give solely the octahydronaphthalene (**2**). We were therefore interested to see if similar stereocontrol could be achieved in systems leading to compounds with a methyl group at the bridgehead since an approach of this type would be of value in the synthesis of natural products such as forskolin[3] (**3**) and nagilactone-C[4] (**4**). In this communication we describe the synthesis of triene (**5**)‡ and studies on its thermal cyclisation.



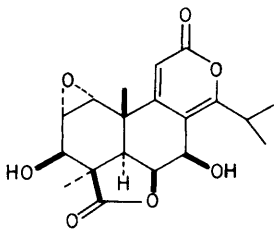
(**1**)



(**2**)



(**3**)



(**4**)

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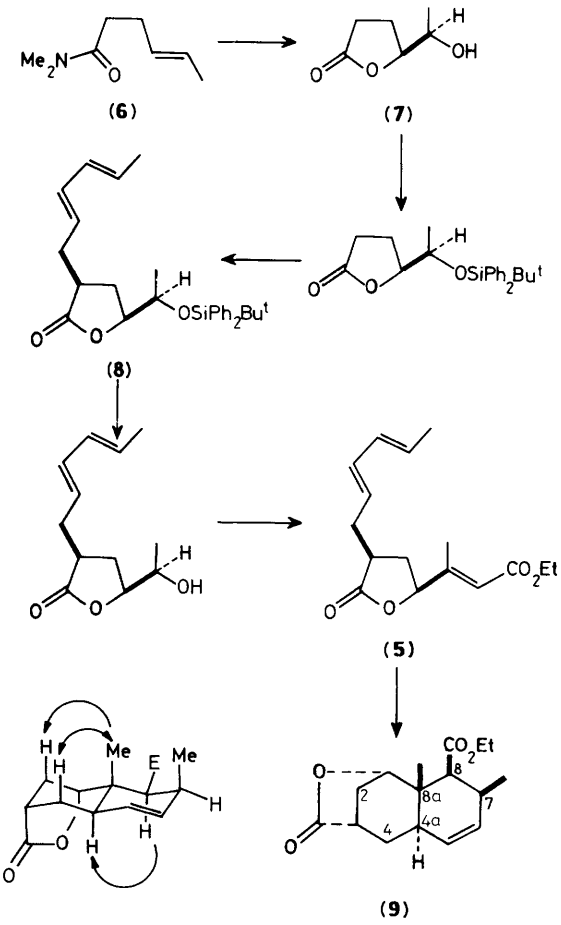
‡ All new compounds gave satisfactory microanalytical or mass spectra data.

Triene (**5**) was synthesised from amide (**6**) by the route shown in Scheme 1. Cyclisation of (**6**) with *m*-chloroperbenzoic acid gave (**7**) which was protected as a t-butyldiphenylsilyl ether [65% overall yield from (**6**)] and alkylated to the *syn*-lactone using our previously described[5] 'one-pot' pro-



Scheme 1

cedure. This gave (**8**) in a ratio of 10:1 *syn* to *anti* and an overall yield of 70%. Straightforward alkylation produced a ratio of 1:8 *syn* to *anti* (80% yield). Deprotection and Swern–Wittig reaction[2,6] then gave triene (**5**) in 74% overall yield from (**8**). Cyclisation was carried out by heating (**5**) in bromobenzene containing butylated hydroxytoluene (BHT) in a sealed tube at 220 °C for 240 h. This gave (**9**) in 70% yield together with 15% unreacted starting material.

The stereochemistry of (**9**) could not be fully assigned from the ^{1}H (360 MHz) n.m.r. spectrum, but decoupling experiments indicated that H-4a was axial and H-7 equatorial. In addition the similarity between the ^{1}H and ^{13}C n.m.r. spectra of (**9**) and (**2**), whose stereochemistry had previously been unambigously assigned,[5] did suggest that (**9**) had the stereochemistry shown. This was confirmed by nuclear Overhauser enhancement (n.O.e.) difference spectroscopy. Irradition of the methyl group at C-8a showed an enhancement of H-2_{ax} and H-4_{ax} and irradiation of H-4_{ax} showed an enhancement of the methyl at C-8a. Irradiation of H-8 showed an enhancement of H-4a. Thus the methyl group at C-8a is on the same face as H-4_{ax} and H-2_{ax} whereas H-8 is on the same face as H-4a. The stereochemistry of (**9**) is therefore as shown.

In conclusion we have described a short and efficient stereocontrolled synthesis of substituted octahydronaphthalenes bearing a methyl group at the bridgehead. The application of this approach to other ring systems and in the synthesis of natural products will be reported in due course.

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