

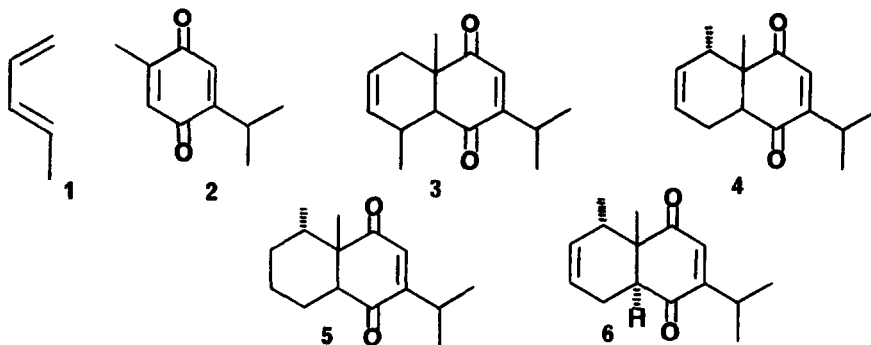
THE STRUCTURE OF THE DIELS-ALDER ADDUCT FORMED FROM THYMOQUINONE AND PIPERYLENE

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In 1935, Fieser and Seligman¹ reported the Diels-Alder reaction of alkylated quinones with dienes leading to mono- and bis-adducts containing angular methyl groups. One of the most interesting adducts obtained was that from piperylene, **1**, and thymoquinone, **2**. It was shown that the oily adduct was a 1:1 addition product. Because it failed to form a semicarbazone, Fieser suggested that the adduct might have structure **3**. However, this question has apparently never been investigated further. In view of the obvious potential of **3** in the synthesis of sesquiterpenes of the eudalene type, we have determined the structure of the adduct. The adduct is represented by **4** and is not a naturally occurring sesquiterpene skeleton.



The adduct was obtained as a yellow oil in good yield as described¹. The question if its structure may be divided into three parts. First, which double bond of thymoquinone reacted? This was quickly established by n.m.r. The crude adduct gave n.m.r. signals for a secondary methyl (0.80 δ , doublet, $J = 7$ Hz), two methyls of an isopropyl group (1.08 and 1.13 δ , doublets, $J = 6.8$ Hz) and a quaternary methyl (1.39 δ , singlet). The disappearance of a vinyl methyl, which occurs in the n.m.r. of thymoquinone, and the appearance of a quaternary methyl in the spectrum of the adduct showed reaction had taken place at the

methyl substituted double bond.

Next, what were the relative position of the methyls; was $\mathfrak{3}$ or $\mathfrak{4}$ formed? An obvious way to answer this would be to observe the n.m.r. resonance of the proton at C-5. Unfortunately, even at 220 MHz the proton at C-5 and the isopropyl septet in the adduct were superimposed. Catalytic hydrogenation of the adduct produced a dihydro compound, $\mathfrak{5}$, (mp 59-60°) in which the n.m.r. signals of C-5 and the isopropyl septet were clearly separated. The C-5 proton appeared as a complex multiplet which would only be expected for the ABX system in $\mathfrak{5}$. Had the compound been derived from $\mathfrak{3}$ a doublet for the C-5 proton should have been observed. The orientation obtained would be predicted on the basis the recent work on the Diels-Alder reaction 1,4-unsymmetrically disubstituted dienes by Schmidt *et. al.*^{2,3,4}.

Last, the stereochemistry of $\mathfrak{4}$ was assigned according to the well established precedents regarding the stereochemistry of addition of 1,4-dienes to dienophiles⁵. Evidence for the ring juncture stereochemistry was obtained by isomerization of $\mathfrak{4}$ (cis) to $\mathfrak{6}$ (trans) which could be carried out by treatment of $\mathfrak{4}$ with triethyl amine in methanol. Compound $\mathfrak{6}$ was crystalline, m.p. 74-5°. Attempts to purify $\mathfrak{4}$ by chromatography, gas and liquid or distillation lead to partial conversion to $\mathfrak{6}$. In practice the best way to obtain pure material was to convert the crude adduct to $\mathfrak{6}$ as above and recrystallize from pentane at low temperature.

Additional evidence for the relative orientation of the methyl groups in the Diels - Alder adduct was obtained from the nmr spectrum of $\mathfrak{6}$ in the presence of the latest Europium shift reagent^{6,7}, Eu (fod-a₉)₃. The data is presented in figure 1. On addition of the Europium reagent, the proton at C-5 shifted downfield and was easily recognized as the X part of an ABX spectrum, which is only possible in compound $\mathfrak{6}$. As can be seen in figure 1, H₈, H₁, H₅, H₁₁ and H₁₂ are the proton which are shifted the most. With a Drieding model one can see that these protons are all close in space to the C₆ carbonyl. This is only true for the stereochemistry and orientation in $\mathfrak{6}$.

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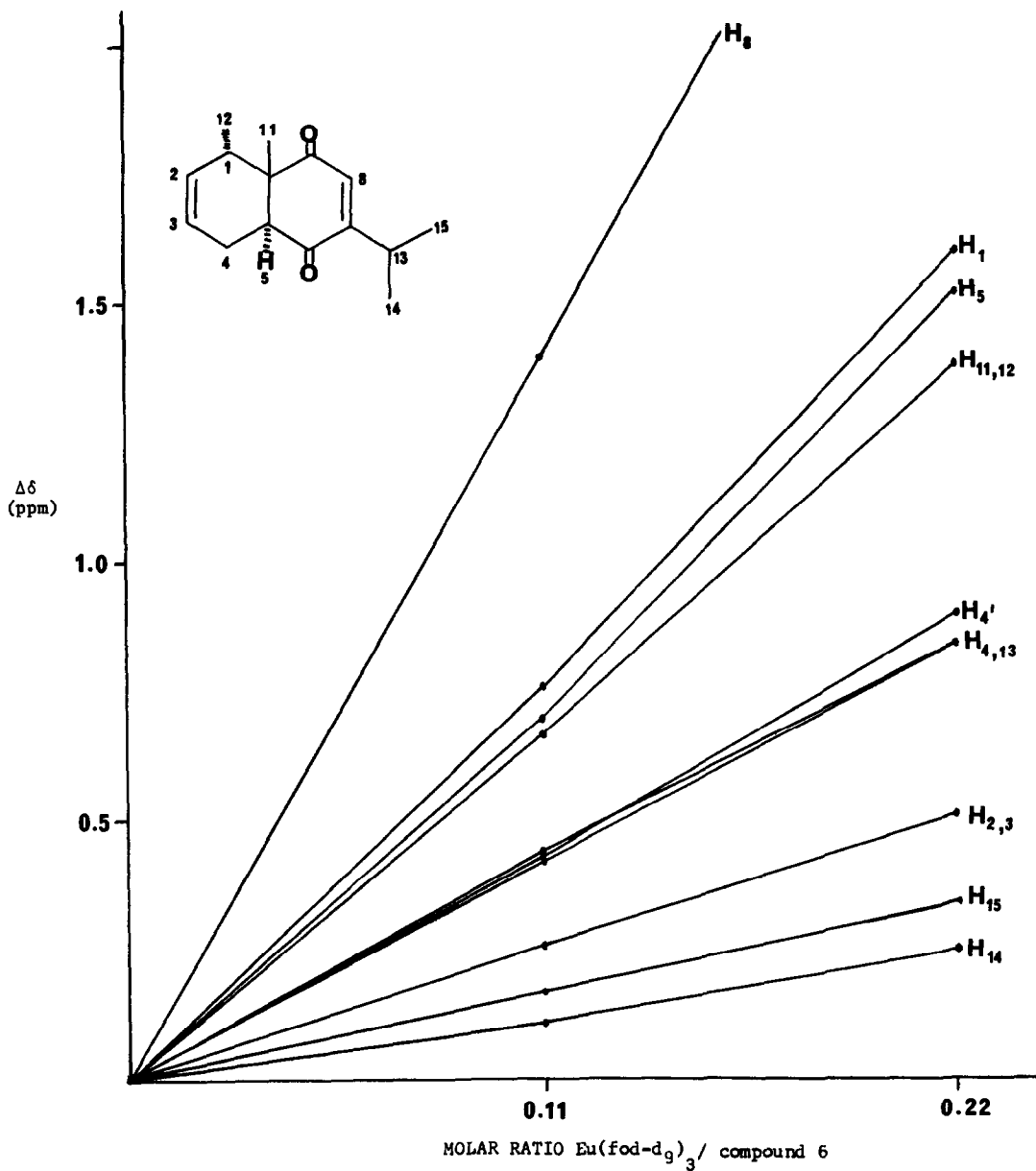


Figure 1. The change in chemical shift ($\Delta\delta$) of the hydrogen atoms of compound 6 upon addition of $\text{Eu}(\text{fod-d}_9)_3$.

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