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THE DIELS-ALDER REACTION OF DIENES WITH A CIS-1-METHYL GROUP

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## Summary: A 1,1,3-trimethyl-2-alkylbutadiene undergoes Diels-Alder reactions far more efficiently than the corresponding 1,1-dimethyl-2-alkylbutadiene.

It is often stated<sup>1</sup> that the Diels-Alder reactions of dienes having a cis-1-methyl group are very slow because steric interactions between the cis-methyl group at C-1 and the cis-H at C-4 in the s-cis conformation (1), which is required for the reaction, lead to this conformation being disfavoured relative to the s-trans conformation (2).



In the Diels-Alder reaction of 1,1-dimethylbutadiene and acrylonitrile this effect is sufficiently large to allow the diene to rearrange to 1,3-dimethylbutadiene which then undergoes Diels-Alder reaction with acrylonitrile.<sup>1a</sup> However, the known Diels-Alder reaction of 1,1,3-trimethylbutadiene (3) with acrolein (4)<sup>2,3</sup> appears to be an exception to this argument, although clearly diene (3) is degenerate to rearrangement.



We have repeated this work to produce (5) which was fully characterised as its DNP derivative; n.O.e. difference spectroscopy was used to show that the expected regioisomer (5) was obtained. A related intramolecular Diels-Alder reaction of a 1,1,3-trimethyl butadiene fragment has also been reported in a route to the taxane ring system. The preceeding Letter describes a method for the synthesis of highly substituted dienes which we have used to prepare dienes (6) and (8) in order to provide further experimental evidence on this situation.

The Diels-Alder reaction of diene (6), which lacks a 3-methyl group, with N-phenyltriazoline dione at room temperature leads to a low yield (33%) of adduct (7).



When diene (6) was reacted with acrolein and  $BF_3OEt_2$  at -78° an as yet unidentified inseparable mixture<sup>1</sup> of compounds in poor yield resulted. In contrast with these results diene (8), which has a 3-methyl group, underwent a much cleaner Diels-Alder reaction with N-phenyltriazoline dione to give (9) in 85% yield, and the  $BF_3 \cdot OEt_2$  catalysed reaction of (8) with acrolein at -78° produced a 52% yield of adduct (10) and 10% yield of hetero Diels-Alder adduct (11).



N.O.e. difference experiments in which the geminal methyl groups were separately irradiated produced enhancements of 4% and 5% to the aldehyde proton and 7% and 2.4% to H-4 which supports the structural assignment of (10).

One possible explanation of the different reactivity of diene (6) and diene (8) may be that (8) can undergo a degenerate rearrangement via a 1,5-hydrogen shift whereas (6) would give different dienes in this process. To test this possibility we synthesised a deuterated diene (12) as shown in the Scheme below.



Diene  $(12)^5$  reacted with acrolein and  $BF_3.OEt_2$  without rearrangement of deuterium according to proton nmr (300) MHz (as shown in the figure) to give the adduct (13) 60% and the hetero Diels-Alder product (14) 5%.



The nmr of (13) in the figure clearly shows the absence of the multiplet at  $\delta$  2.03 and the singlet at  $\delta$ 1.74 assigned to the protons at C-6 and the methyl group at C-1 respectively in (10) along with the undisturbed presence of the methyl groups at C-3.

This result clearly rules out rearrangement of the diene during the Diels-Alder reaction of (12)/(8) with acrolein and  $BF_3.OEt_2$ . In addition, if diene (12) was heated at 100° for 12 hr no evidence for any scrambling of deuterium was observed. The alternative explanation of the more efficient reaction of diene (8) compared to diene (6) concerns the steric and electronic effects of the 3-methyl group. Although it is unlikely that the two double bonds are completely coplanar in diene (8) the unfavourable steric interaction with the 1-methyl group in the approximate s-cis conformation is counter-balanced by the steric interaction between the 1-methyl and the 3-methyl in the approximate s-trans conformation (15).





Figure: The 300 MHz (CDCl<sub>2</sub>)  $^{1}$ H NMR of (10) and (13).

This may lead to a sufficient concentration of the approximate s-cis conformation (8) to give the Diels-Alder reaction. This steric effect of the 3-methyl group is absent from diene (6) which is therefore less reactive. Alternatively it is also possible that the electron donating effect of the 3-methyl group is increasing the rate of the Diels-Alder reaction of (8) with acrolein.

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## References

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 Deuterium nmr (300 MHz) shows three signals for diene (12) and mass spectrum indicates an average of 97% deuterium incorporation at each sight. (Received in UK 15 December 1986)