

Stereochemical Aspects of Diels-Alder Reaction of Substituted Penta-2,4-dienols and Maleic Anhydride Derivatives

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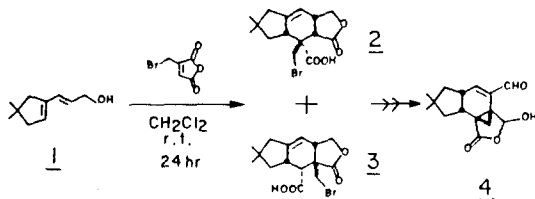
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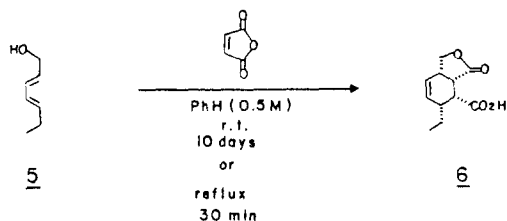
Abstract □ Reaction of diene alcohol **5** and maleic anhydride in benzene at either room temperature or reflux proceeds probably through an intermolecular Diels-Alder cycloaddition followed by lactone formation to give adduct **6**.

Keywords □ Diels-Alder reaction, Penta-2,4-dienols, Maleic anhydride, Intramolecular, Intermolecular.

Diels-Alder reaction of substituted penta-2,4-dienol with maleic anhydride derivative has been employed as an important step in the synthesis of various natural products as illustrated by Greenlee-Woodward synthesis of Marasmic acid **4**.²⁾

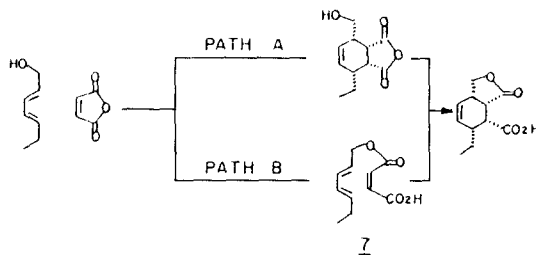


In connection with our research program directed toward synthesis of alkaloids³⁾ we had an opportunity to investigate Diels-Alder reaction of known diene alcohol **5**⁴⁾ with maleic anhydride as shown below.



A priori there are two possible pathways leading to adduct **6** under the reaction condition, i.e. intermolecular Diels-Alder reaction followed by intra-

molecular ester formation (PATH A) or intermolecular esterification followed by intramolecular Diels-Alder reaction (PATH B).⁵⁾



To clarify this point we prepared acid **7** by treatment of alcohol **5** with maleic anhydride in the presence of DMAP (TEA, CH_2Cl_2 , rt, 40 min, 95%).^{6,7)} While intramolecular Diels-Alder reaction of acid **7** in refluxing benzene was quite sluggish, thermolysis of acid **7** in xylene at reflux for four hours produced *cis*-fused adduct **6** in 60% yield.^{6,8)}

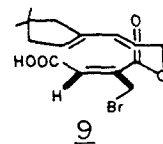
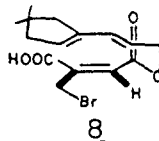
These experiments strongly suggest that reaction of alcohol **5** and maleic anhydride proceeds through intermolecular Diels-Alder cycloaddition followed by lactone formation (PATH A) under the reaction condition. Caution should be exercised in interpretation of stereochemical outcome of thermal cycloaddition between substituted penta-2,4-dienols and maleic anhydride derivatives depending upon experimental parameters

such as temperature and presence of acylation catalyst.

LITERATURE CITED

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- Professor Heathcock and his collaborators speculated that adducts **2** and **3** were formed by intramolecular Diels-Alder reaction of esters **8** and **9** respectively by

way of an endo transition state, which seems to be unlikely under the reaction condition even though unproven (vide infra); ApSimon, J.: *The Total Synthesis of Natural Products*, John Wiley and Sons, Vol. 5, p. 403 (1983).



- Yields were not optimized.
- Satisfactory spectral data were obtained for all new compounds.
- Predominant formation of cis-fused adduct in this reaction constitutes an exception rather than a rule in the intramolecular Diels-Alder reaction of 1,3,8-nonatriene-type system.
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