Stereochemical Control by an Allylic Substituent of an Acyclic Dienophile in the Diels-Alder Reaction

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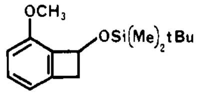
The Diels-Alder reaction of cyclic[1] and, in one case, acylic unsaturated sugars[2] is one of the newest developments coming under the rubric of sugars as starting materials for noncarbohydrate molecules.[3] In an extension of our work on the aureolic acid antibiotics,[1c] we have examined the Diels-Alder reaction of an *o*-quinone methide **2** (derived from benzocyclobutene **1**)[4] with sugars **3–5**. Our substrates presented a choice as to which of two allylic substituents would influence the face selectivity of cycloaddition. If steric effects of the allylic function were to be dominant, then one would predict attack from the face opposite the bulky sugar group (re face) to form the *R* configuration at C-3 of the product. This reasoning parallels the arguments used by Kishi in his research on the hydroboration of acyclic alkenes for the synthesis of polyether antibiotics.[5] On the other hand, a recent theory due to Houk[6] calls into play orbital interactions between the allylic substituent and the vicinal orbitals of the transition state for cycloaddition. Thus, one would assume that the LUMO-HOMO interaction of a syn alkoxy in the cycloaddition transition state (A) is more unfavorable than the syn alkyl interaction (B). As a consequence of this assumption, the Houk theory would predict that the incoming group would bond to the face opposite to the allylic oxygen function (si face) so as to minimize secondary orbital antibonding effects. Figure 1 illustrates the possibilities, with slight distortions, since the alkyl and alkoxyl are staggered and not perfectly syn or anti to the π system when the C–H bond is in the plane of the alkene, as is assumed to be the case in the steric effects argument.[7]



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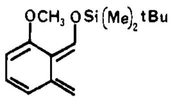

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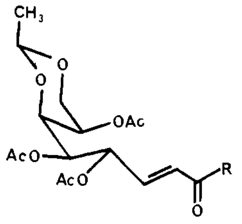
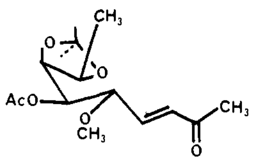


3 $R = OC_2H_5$

4 $R = CH_3$



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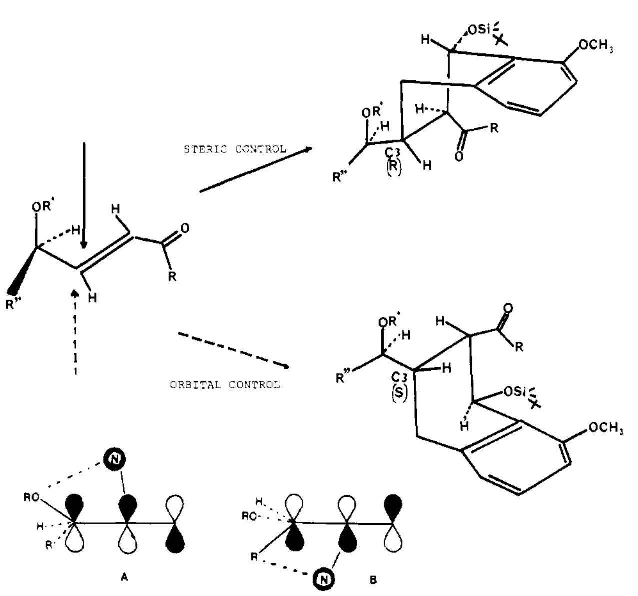
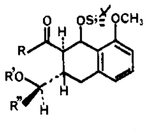
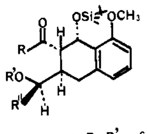


Figure 1.

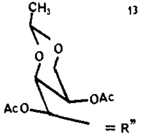
In the event, diene precursor **1** and sugar **3** (prepared by acetylation of a known sugar)[8] were heated in a sealed tube (chlorobenzene solvent) for 3 days. Multiple developments with 9:1 petroleum ether/ethyl acetate on the preparative layer silica plates afforded two adducts **6** (oil) and **7** (mp 103–104 °C), with a selectivity of 4:1 in 71% overall yield. NMR data suggested that both adducts were the result of endo control by the ester function. Careful hydrolysis of major adduct **6** (K_2CO_3 in absolute methanol) followed by epimerization and spontaneous lactonization afforded γ-lactone **8** (IR 1760 cm^{-1}). Acetylation of lactone **8** produced diacetate **9** (mp 148–149 °C). That the stereochemistry at C3 of the major adduct is indeed *S*, the result of addition to the si face of the dienophile, was proven by a single-crystal X-ray structure determination. Interestingly, the exact structure showed us that our tentative stereochemical assignments based on proton–proton coupling in the NMR were not correct.[9] (Figure 2).



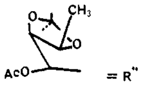
6 $R = OC_2H_5$, $R' = Ac$
10 $R = CH_3$, $R' = Ac$
12 $R = CH_3$, $R' = CH_3$



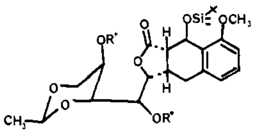
7 R, R' = 6
11 R, R' = 10
13 R, R' = 12



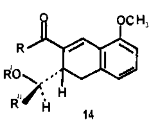
6, 7, 10, 11



12, 13



8 $R' = H$
9 $R' = Ac$



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† On leave 1980–1981 from Department of Chemistry, Warsaw Univeristy, Warsaw, Poland.

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[7] Neither theory serves to predict the useful asymmetric inductions observed in Diels-Alder reactions of fumaric acid esters of chiral alcohols; for a recent example, see: Helmchen, G.; Schmierer, R. *Angew Chem, Int. Ed. Engl.* **1981**, *20*, 205–206.

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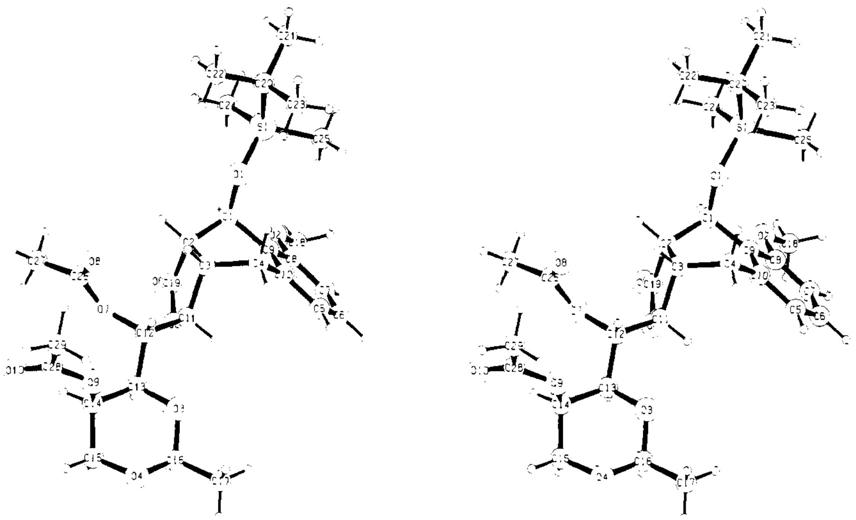

Figure 2. Stereoview of the X-ray structure of lactone **9**.

Table I. Yields of Diels–Alder Adducts

starting material	product (% yield)		selectivity
3	**6** (57)	**7** (14)	4:1
4	**10** (49)	**11** (39)	1.2:1
5	**12** (68)	**13** (17)	4:1[a]

[a] Based on NMR of inseparable mixture.

Ketones **4** and **5** were also successfully condensed with *o*-quinone methide to yield adducts **10**–**13** in good yields (Table I). Evidence that **6**, **10**, and **12** have the identical 3-*S* configuration comes from the nearly identical CD spectra displayed by the products of their BF_3-catalyzed elimination, e.g., **14**. It is clear that the C-3 center is most influential on the CD, because the complementary elimination products derived from **7**, **11**, and **13** displayed CD curves that are the mirror images of those shown by **14**. Thus we can conclude that the face preferences are the same in all our examples, even though the selectivity with ketone **4** is drastically reduced. The sense of preferred addition in our examples of the Diels–Alder reaction not only conform to the predictions of Houk but are also consistent with the results observed by Horton in Diels–Alder reactions of acyclic sugars where the carbonyl of the dienophile is the exo group.[2] On the other hand, our results are opposite in a stereochemical sense to those reported by Liotta[10] for the Diels–Alder addition to dienones with γ-hydroxyl substituents where steric effects seem to be the controlling factor. We can conclude that the use of unsaturated acyclic sugars has great potential for chiral syntheses via Diels–Alder reactions; but caution must be exercised in assuming the sense of asymmetric induction to be obtained.[11]

Supplementary Material Available: Tables of final atomic parameters, final anisotropic thermal parameters, bond lengths, bond angles, and torsion angles (6 pages). Ordering information is given on any current masthead page.

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(9) The crystals were monoclinic, space group $P2_1$, with a = 13.145 (3) Å, b = 7.220 (3) Å c = 17.871 (4) Å, β = 108.10 (2)°, and d_{calcd} = 1.192 g cm^{-3} for Z = 2 ($C_{29}H_{42}O_{10}Si$, M_r = 578.73). The intensity data were measured on a Hilger–Watts diffractometer (Ni-filtered Cu Kα radiation, θ–2θ scans, pulse-height discrimination). The size of the crystal used for data collection was approximately 0.10 × 0.20 × 0.55 mm; the data were corrected for absorption (μ = 10.6 cm^{-1}). A total of 2379 independent reflections were measured for $\theta < 57°$, of which 2096 were considered to be observed $I > 2.5\sigma(I)$. The structure was solved by a multiple-solution procedure (Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *A27*, 368) and was refined by full-matrix least squares. Six reflections which were strongly affected by extinction were excluded from the final refinement and difference map. In the final refinement, anisotropic thermal parameters were used for the nonhydrogen atoms and isotropic temperature factors were used for the hydrogen atoms. The hydrogen atoms were included in the structure factor calculations but their parameters were not refined. The final discrepancy indexes are R = 0.041 and wR = 0.044 for the remaining 2090 observed reflections. The final difference map has no peaks greater than ±0.3 e $Å^{-3}$. The absolute configuration is based on the anomalous scattering of the silicon atom and was established by refining both enantiomers. The final weighted R values were 0.0439 for the configuration shown and 0.0449 for its antipode. Thus, by Hamilton's test (Hamilton, W. C. *Acta Crystallogr.* **1965**, *18*, 506) the configuration shown corresponds to the absolute configuration.

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(11) The research at Fordham was supported by Grants CA 27116 and AM 21888. We wish to thank Professor S. M. Weinreb of Penn State University, through whose courtesy several 360-MHz NMR spectra were obtained. We are grateful to Professor T. T. Herskovits of Fordham for the use of this Cary 60 Co instrument and for his assistance in obtaining useful spectra.

Triplet Exciplex Formation in the External Heavy-Atom Effect

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The interaction of an electronically excited aromatic hydrocarbon with a ground-state molecule containing heavy atoms (external heavy-atom effect) has been the subject of a number of recent investigations.[1] Although the nature of the interaction is unresolved, several authors[2] favor a proposal that formation of an excited-state complex or exciplex is involved even though experimental evidence for such an intermediate is meager. In particular, experimental information regarding the external heavy-atom effect upon the triplet states has not required a new intermediate. In this work evidence is presented that strongly argues for a triplet exciplex intermediate in the external heavy-atom interaction of ethyl iodide (EI) with the first triplet of anthracene ($^3A^*$).

EI has been observed to quench A fluorescence with a corresponding enhancement of triplet production.[3] The heavy-atom solvent also causes a decrease in the triplet lifetime of A. Using the technique of flash photolysis to observe triplet–triplet absorption, the triplet-state decay of A in degassed dilute solution (~10^{-4} M) was characterized and studied as a function of EI concentration. A sum of the first-order triplet decay parameters

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