π-Facial Selectivity in Diels–Alder Reactions of C-2-Vinyl Glycals. Stereocontrolled Route to Annulated *C*-Glycopyranosides

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An allylic methoxy substituent at C-3 in C-2 vinyl glycals (**1b,c**) induces complete *anti* π-facial selectivity in the thermal Diels–Alder reaction with maleic anhydride; in contrast, products resulting from *anti* and *syn* approaches are observed when linear acetylenic compounds are employed as dienophiles; the latter adducts readily aromatize to afford a mixture of products with the pyranose ring unchanged (**8**) and opened (**9**).

Recently, π-facial selectivity in intermolecular Diels–Alder reactions has attracted considerable attention.[1] In particular, the influence of the relative topicity of the Diels–Alder reaction on systems bearing a single allylic heteroatom has been the subject of numerous studies.[2—5] These studies have been restricted to three classes of dienic structures: 5-substituted cyclopenta-1,3-dienes,[2] chiral acyclic dienes,[3,4] and conformationally locked vinyl cyclopentadienes.[5a] The factors governing the facial stereoselection are still not fully under-

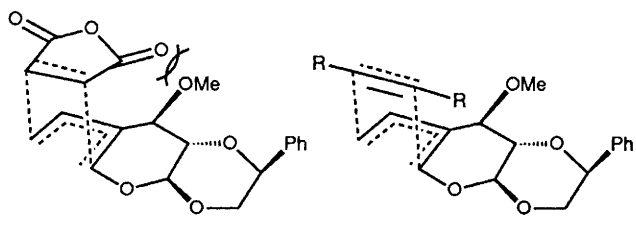
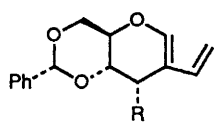
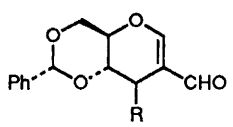


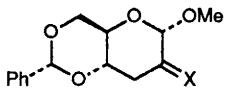
Figure 1



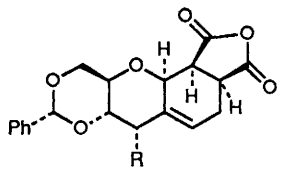
(1)
a; R = α-OH
b; R = α-OMe
c; R = β-OMe
d; R = H



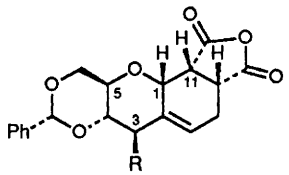
(2)
a; R = β-OMe
b; R = H



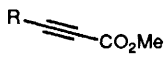
(3)
a; X = O
b; X = CHOMe



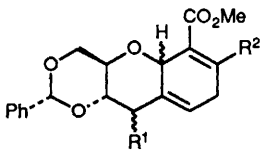
(4)
a; R = OMe
b; R = H



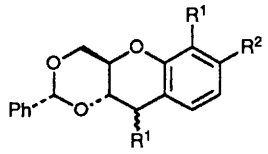
(5)
a; R = OMe
b; R = H



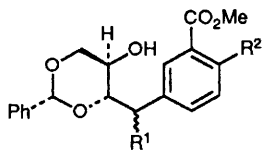
(6)
a; R = CO_2Me
b; R = H



(7)
R^1 = OMe or H,
R^2 = CO_2Me or H



(8)
R^1 = OMe or H,
R^2 = CO_2Me or H



(9)
R^1 = OMe or H,
R^2 = CO_2Me or H

stood[2] and the results of these studies are system dependent.[5a] On the other hand, carbohydrate-derived dienes[6—9] have been shown to give intermolecular Diels–Alder reactions with complete facial selectivity *anti* to the stereogenic allylic alkoxy groups.†

As a continuation of our interest in the scope of cycloaddition reactions in carbohydrate substrates,[9,10] we report herein the results of a study of facial selectivity in Diels–Alder cycloadditions of pyranose dienes (**1b—d**),[11] towards maleic anhydride and symmetrical (**6a**) and nonsymmetrical (**6b**) acetylenic dienophiles. These dienes were chosen for three reasons: (i) they are 3-substituted dienes bearing a chiral centre in their substituent, (ii) the stereogenic allylic heteroatom is attached on the pyranose ring,[5a] and (iii) the products obtained are a new class of *C*-glycosides.‡

Diene (**1b**) (^{13}C NMR δ 64.7, C-5) was prepared by *O*-methylation (90%) of (**1a**),[10] diene (**1c**) (^{13}C NMR δ 69.0, C-5) was obtained by Wittig methylenation (75%) of α,β-unsaturated aldehyde (**2a**),[13] and diene (**1d**) was made from (**3a**)[14] *via* the α-alkoxy vinyl ether (**3b**), followed by mild acidic treatment as described elsewhere[13] and methylenation of the resulting conjugated enal (**2b**) [overall 64% from (**3a**)].

We have found that an allylic methoxy group in dienes (**1b**) and (**1c**) exerts an *anti*-directing effect, giving with maleic anhydride exclusively the products (**4a**) and (**5a**) corresponding to an *endo* approach. Absence of the stereodirecting allylic group in (**1d**) results in a mixture of inseparable α- and β-*endo* products (**4b**) (^{13}C NMR δ 38.0, C-3) and (**5b**) (^{13}C NMR δ 33.2, C-3) in 88% yield in a 3:7 ratio, respectively.§ The contrast in C-5 chemical shift between the spectra of (**1b**) and (**1c**) (*vide supra*) and the similar shifts of C-5 in the spectra of (**4a**) (δ 64.6) and (**5a**) (δ 64.0) fully support the proposed steric structures. The hydrogen at C-5 of (**4a**) and (**5a**) suffers only one γ-axial interaction in both compounds, from the OMe substituent in (**4a**) and from the C-1–C-11 bond in (**5a**).

The adducts are assigned as *endo* owing to the nearly identical size of the coupling constants $^3J_{1,11}$, 8 Hz in (**4a**) and 7 Hz in (**5a**), and the large nuclear Overhauser enhancement (NOE) effects suggesting a *cis*-relationship of these hydrogens. Although small NOE effects between H-1 and H-11 might also be expected if (**4a**) and (**5a**) were *exo*-adducts, this possibility is ruled out in view of the formation of unique Diels–Alder products due to the *anti*-directing effect of the allylic substituent. No such directing effect would be justified in the case of *exo*-adducts.

Linear acetylenic dienophiles react preferentially *anti* to the methoxy group. A rationalisation for such behaviour is shown in Figure 1, where a more significant interaction with the allylic group would be expected for the ethylenic dienophile, through an *endo* transition state in a hypothetical *syn* approach, compared to the linear acetylenic dienophile.¶ Dienes (**1b—d**) react with dienophiles (**6a—b**) to give in every case a mixture of compounds (**7**), (**8**), and (**9**) [^1H and ^{13}C NMR spectroscopy and MS (MH^+) on the crude reaction product]. As expected, reaction of (**1b—d**) with (**6b**) occurs

† In the examples studied by Lipshutz *et al.*[8] and by us,[9] the two stereogenic groups were present in a *syn* relationship in the dienic systems.

‡ We propose the term annulated[12] *C*-glycopyranosides for these structures where the *C*-substituent at the anomeric carbon is part of a cyclic structure involving one of the atoms in the pyranose ring.

§ Results from Franck's[3] and Kozikowski's[4] groups have shown that the nature of the dienophile has a significant effect on the face selectivity in Diels–Alder reactions involving chiral acyclic dienes.

¶ Precise assignment of the C-5 resonances of the components of this mixture is difficult. However, differentiation between the major and minor isomers could be carried out on the basis of their quite different C-3 signals.

with complete regioselectivity to afford compounds (**7**)—(**9**), where R^2 = H. Compounds (**7**) appear as a mixture of epimers at C-1, based on the intensity of the C-5 signals, the majority of products resulting from an *anti*-attack relative to the C-3 substituent. Compounds (**7**) cannot be isolated, as they readily aromatize[15] to (**8**). As expected, aromatic tricyclic products (**8**) resubjected to the reaction conditions are not transformed into bicyclic compounds (**9**).[16] Compounds (**8**) and (**9**) are formed from common intermediates (**7**) under the same reaction conditions as well as by silica gel chromatographic treatment.‖

In conclusion, the *anti*-facial selectivity in the formation of the Diels–Alder adducts reported here appears to be purely of steric origin.

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‖ Spectroscopic and analytical data are in agreement with the proposed structures.