Facial Selectivity in the Diels–Alder Reactions of *cis*-Cyclohexa-3,5-diene-1,2-diol and Derivatives with *N*-Phenylmaleimide

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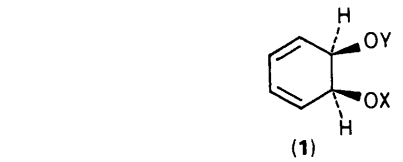
N-Phenylmaleimide adds to *cis*-cyclohexa-1,3-diene-1,2-diol and its derivatives preferentially to the face of the diene *syn* to the oxygen substituents; this effect is less pronounced in the more reactive, cyclic derivatives.

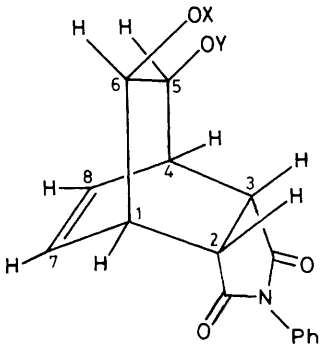
The Diels–Alder reactions of 5-hetero-substituted cyclopenta-1,3-diene derivatives are well known examples of cycloadditions that proceed by attachment of the dienophile to the more sterically hindered, *syn* face of the diene.[1] Orbital calculations have provided various explanations for this[2] and related phenomena,[3] and there seems to be no fundamental reason to expect hetero-substituted cyclohexadienes to behave very differently. However, it has been reported that some derivatives of *cis*-cyclohexa-3,5-diene-1,2-diol (**1a**)[4,5] react with maleic anhydride,[4,6] 4-(*p*-bromophenyl)-1,2,4-triazoline-3,5-dione,[7] and a number of acyclic dienophiles[8] by addition to the *anti* face of the diene. We have compelling evidence that, with *N*-phenylmaleimide as the dienophile, the diene (**1a**) and four of its derivatives add predominantly *syn* to the *cis*-oxygen functions of the dienes.

By stirring a chloroform solution of the *cis*-diol (**1a**) and *N*-phenylmaleimide at room temperature for 24 hours, we obtained an excellent yield of a mixture of two adducts in a 94:6 ratio, as determined by careful integration of the 300 MHz n.m.r. spectrum of the mixture. The diacetate (**1b**), the bis(trimethylsilyl ether) (**1c**), the (dimethylsilylene)bis(oxy)[9] (**1d**), and the isopropylidenedioxy (**1e**) derivatives were prepared from (**1a**) by straightforward methods, and their reactions with *N*-phenylmaleimide were run under similar conditions. Derivatives (**1b**) and (**1c**) reacted more slowly than (**1a**) and gave good yields of one predominant adduct [88:12 adduct ratio for (**1b**); we could find signals for only one adduct in the n.m.r. spectrum of the product obtained from (**1c**)]. The bicyclic derivatives (**1d**) and (**1e**) reacted significantly faster than (**1a**); from the results of competitive reactions we estimated a hundredfold difference in rate between diene (**1c**) and diene (**1d**). Nevertheless, the bicyclic derivatives showed much less facial selectivity in their Diels–Alder reactions [adduct ratios of 65:35 for (**1d**) and 60:40 for (**1e**)], possibly owing to steric factors. Adduct ratios were not the result of equilibration because heating chloroform solutions of isolated, pure adducts for several days did not produce any of the isomeric adducts.

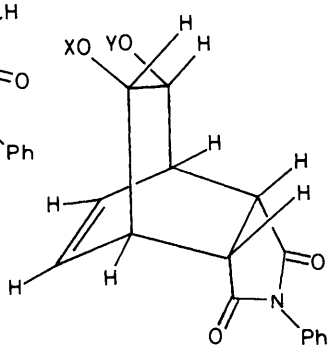
The two adducts derived from (**1e**) were readily separated by column chromatography. The more abundant adduct was shown to have structure (**2e**) by measurement of nuclear Overhauser effects in its n.m.r. spectrum. In particular, the proximity of one of the isopropylidene methyls to the hydrogens on C-2 and C-3 was unequivocally established, and there was also a significant enhancement of the alkene proton signal on irradiation of the signal due to the hydrogens on C-5 and C-6. By similar measurements with the less abundant adduct it was clear that its structure was (**3e**). Conversion of the pure major adduct (obtained by repeated recrystallization) from the reaction of (**1a**) to its isopropylidenedioxy derivative provided pure (**2e**). Also, derivatization of the pure major diol adduct, which must have structure (**2a**), yielded the other major adducts (**2b**), (**2c**), and (**2d**). Hydrolyis of (**3e**) with aqueous HCl afforded (**3a**), which was identical with the



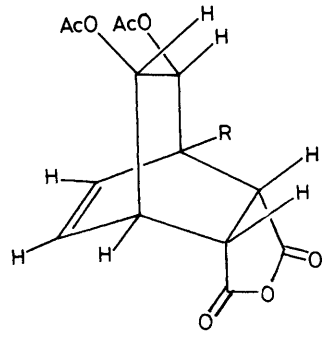
(1)



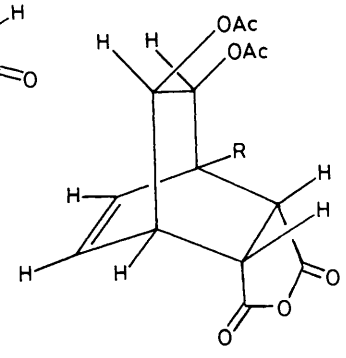
(2)



(3)



(4)



(5)

	X	Y
a	H	H
b	Ac	Ac
c	$SiMe_3$	$SiMe_3$
d	$-SiMe_2-$	
e	$-CMe_2-$	

minor adduct observed in the Diels–Alder reaction with diene (**1a**).† Derivatization of (**3a**) gave the minor adducts (**3b**), (**3c**), and (**3d**). Thus, in every case the major adduct was the result of *endo*-addition *syn* to the *cis*-oxygen face of the diene, and each minor adduct must have arisen from *endo*-addition to the *anti* face of the diene.

Furthermore, similarities between the n.m.r. spectra of our major adduct (**2b**) and the data published[4,6] for the putative major maleic anhydride adducts (**4**) (R = Me and Et) suggest that the correct structures of these adducts are, in fact, the *syn*-addition products (**5**). However, *anti*-addition by 4-(*p*-bromophenyl)-1,2,4-triazine-3,5-dione was established conclusively by *X*-ray analysis.[7] We conjecture that the difference in facial selectivity between this dienophile and *N*-phenylmaleimide arises because an *endo*-approach by the former towards the *syn* face of any of these *cis*-oxygen dienes must lead to unfavourable electrostatic interactions between the dienophile's nitrogen lone pairs and lone pairs on the oxygens of the diene. This is complementary, but opposite in effect, to the observations of Ginsburg[10] with some propellane dienes.

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† The structures of the adducts obtained from (**1a**) have been confirmed by *X*-ray analysis. Details will be published elsewhere.