

Stereospecificity in Diels–Alder Reactions of Dienes and Dienophiles derived from Methyl 4,6-*O*-Benzylidene- α -D-glucopyranoside

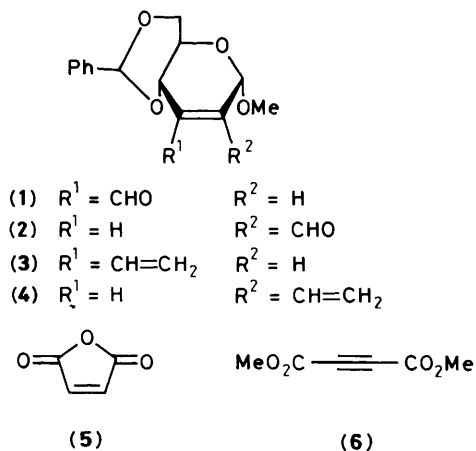
J. Cristobal Lopez,* Eric Lameignere, and Gabor Lukacs*

Institut de Chimie des Substances Naturelles du C.N.R.S., 91190 Gif sur Yvette, France

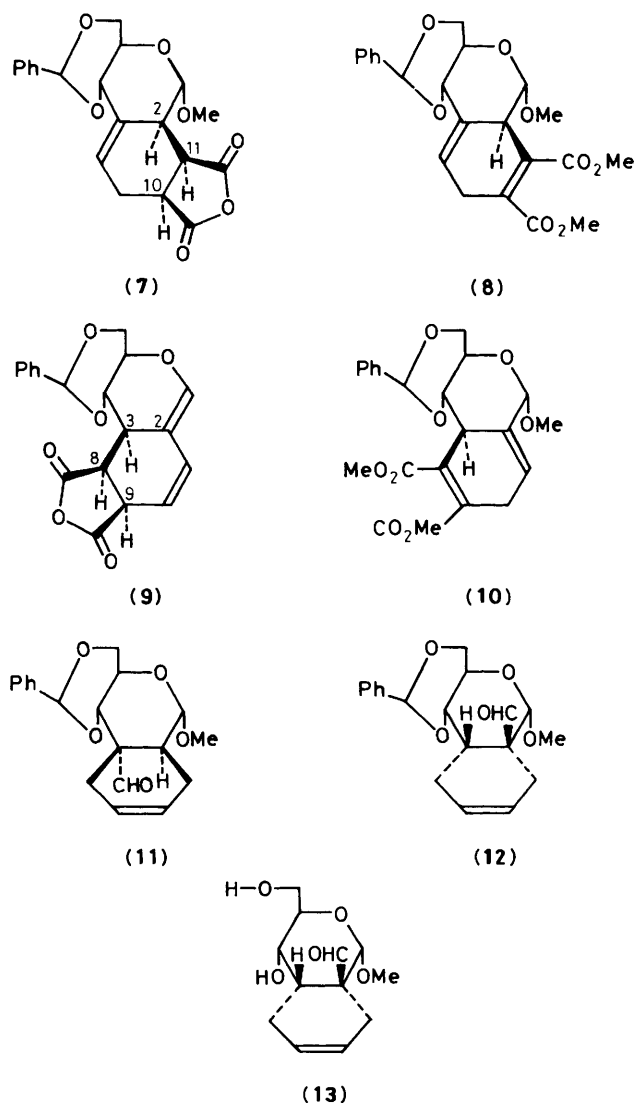
Conjugated enals (1) and (2) and dienes (3) and (4) derived from methyl 4,6-*O*-benzylidene- α -D-glucopyranoside underwent highly efficient (yields ranging from 75 to 95%) Diels–Alder reaction with complete facial specificity with butadiene, dimethyl acetylenedicarboxylate, and maleic anhydride leading exclusively to *endo* adducts with the latter.

There is currently considerable interest in the application of carbohydrates as chiral building blocks for the generation of carbocyclic systems.^{1,2} Pioneering work by Fraser-Reid's group on 'annulated sugars'³ have proved their enormous potential for stereocontrolled access to optically pure cycloalkyl compounds. In the intermolecular cycloaddition route to 'annulated sugars' carbohydrates have been commonly used as dienophiles.⁴ However to our knowledge, only one recent example of Diels–Alder reaction has been reported from pyranoid sugars† incorporating a diene system.⁵ Here we report the efficiency and facial specificity in the intermolecular Diels–Alder reaction of regioisomeric conjugated enals (1) and (2) and dienes (3) and (4).⁸

Pyranose dienes (3) and (4) reacted readily under thermal conditions (dry toluene, reflux overnight, 1.5 equiv.) with maleic anhydride (5) and dimethylacetylene dicarboxylate (6) to afford stereospecifically the condensation products (7)–(10), arising from an exclusive attack on the opposite face to the anomeric methoxy group‡ and in the *endo* mode when maleic anhydride was employed. On the other hand, conjugated enals (1) and (2) also reacted in a stereospecific manner with butadiene in the presence of AlCl_3 as catalyst§ to afford carbocyclic compounds (11) and (12), respectively.



The configuration at C-2 in compounds (7) (78%) ($J_{1,2}$ 5 Hz) and (8) (95%) ($J_{1,2}$ 8 Hz) was as expected on the basis of previous related examples.^{5,6} The large $J_{1,2}$ value found in the case of (8) accounts for a *trans*-diaxial relationship between H-1 and H-2,^{8,10} with the C-2–C-11 bond of the carbocycle equatorially oriented and the pyranose ring in a preferred boat conformation.¹¹ Concerning (7), there are literature precedents¹² for medium range coupling values between H-1 and H-2 involved in a *trans* relationship. These boat-like conformations are confirmed by a diagnostic nuclear Overhauser effect (n.O.e.) obtained between H-2 and H-5 in 1D and 2D experiments. Evidence for the *endo* mode of addition [(7) $J_{2,11}$ 5 Hz, $J_{11,10}$ 10 Hz; (9) $J_{3,8}$ 6 Hz, $J_{8,9}$ 9 Hz] is based on



† Studies of inter-⁶ and intramolecular⁷ Diels–Alder reactions of furanoid dienes have been elegantly exploited by Fraser-Reid's group.

‡ This result is in agreement with previous examples from Fraser-Reid's⁶ and Giuliano's⁵ groups and seems to indicate that electrostatic interactions⁹ are overridden in the cyclic sugar cases by steric influence of the axial alkoxy group.

§ Boron trifluoride–ether can also be used under similar reaction conditions without appreciable variation in the yield of the adduct formed. In a typical experiment the corresponding α -enal was dissolved in dry CH_2Cl_2 under argon atmosphere at -78°C and an excess of butadiene was bubbled through the solution, the catalyst (5 equiv.) was added and after 5 min the temperature was allowed to rise to -50°C . The reaction was usually complete in 3 h. Usual work-up and chromatography yielded the corresponding adduct (76–87%).

n.m.r. data from previous examples.^{5,6} The configuration at C-3 in compounds (9) (75%) and (10) (78%) is deduced from the large triplet signal for H-4 in both compounds ($J_{3,4}$, $J_{4,5}$ 10 Hz). The sharp singlet type anomeric proton affords proof for the diequatorial relationship of H-1 and H-2 in compound (11). The stereostructure of (12) obtained by exclusive α -attack of the diene is of great interest. The vicinal coupling $J_{3,4}$ (5 Hz) in compound (13) obtained from (12) is in agreement with literature data for a reduction product of an adduct formed between 2,3-dimethyl buta-1,3-diene and ethyl 2,3-dideoxy- α -D-glycero-hex-2-enopyranosid-4-ulose.¹⁰

To the best of our knowledge this is the first report on Diels-Alder reaction in pyranosidic α -enal systems. The cycloaddition reaction of such systems allows access to enantiomerically pure carbocyclic structures containing stereochemically defined quaternary carbon centres,¹³ as well as opening new ways to two types of angularly functionalized decalin derivatives *via* appropriate transformations followed by the Ferrier reaction.¹⁴ The benzylidene acetal group confers *conformational rigidity* to the sugar nucleus and further extends¹⁵ the versatility of these glucose derived building blocks.

We thank Drs. C. Fontaine and M. Gonzalez Sierra for carrying out the n.o.e. experiments. J. C. L. thanks the Ministerio de Educacion Y Ciencia, Spain, for a post-doctoral MEC-MRT fellowship.

Received, 29th January 1988; Com. 8/00322J

References

- 1 B. Fraser-Reid and R. C. Anderson, *Fortschr. Chem. Org. Naturst.*, 1980, **39**, 1.
- 2 S. Hanessian, 'Total Synthesis of Natural Products. The Chiron Approach,' Pergamon Press, Oxford, 1983.
- 3 B. J. Fitzsimmons and B. Fraser-Reid, *J. Am. Chem. Soc.*, 1979, **101**, 6123; J. L. Primeau, R. C. Anderson, and B. Fraser-Reid, *ibid.*, 1983, **105**, 5874.
- 4 G. Helmchen, R. Karge, and J. Weetam in 'Modern Synthetic Methods,' ed. R. Scheffold, Springer-Verlag, Berlin, Heidelberg, 1986, vol. 4, p. 261, and references therein.
- 5 R. M. Giuliano and J. H. Buzby, *Carbohydr. Res.*, 1986, **158**, C1.
- 6 K. M. Sun, R. M. Giuliano, and B. Fraser-Reid, *J. Org. Chem.*, 1985, **50**, 4774, and references therein.
- 7 B. Fraser-Reid, Z. Benkő, R. Giuliano, K. M. Sun, and N. Taylor, *J. Chem. Soc., Chem. Commun.*, 1984, 1029.
- 8 J. C. Lopez, E. Lameignere, and G. Lukacs, *J. Chem. Soc., Chem. Commun.*, 1985, 514.
- 9 S. D. Kahn and W. J. Hehre, *J. Am. Chem. Soc.*, 1987, **109**, 663.
- 10 H. Gnichtel, C. Gumprecht, and P. Luger, *Liebigs Ann. Chem.*, 1984, 1531.
- 11 M. Jalili-Nanini, D. Guillerme, and J.-Y. Lallemand, *Tetrahedron*, 1983, **749**, and references therein.
- 12 M. B. Yunker, D. E. Plaumann, and B. Fraser-Reid, *Can. J. Chem.*, 1977, **55**, 4002.
- 13 S. F. Martin, *Tetrahedron*, 1980, 419.
- 14 R. J. Ferrier, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1455.
- 15 S. Hanessian and N. R. Plessas, *J. Org. Chem.*, 1969, **34**, 1035, 1045, 1053; A. Liptak, I. Jodal, and P. Nanasi, *Carbohydr. Res.*, 1975, **44**, 1; S. S. Bhattacharjee and P. A. J. Gorin, *Can. J. Chem.*, 1969, **47**, 1195.