

## Highly Regio- and Stereo-selective Diels–Alder Reactions of 5-(2',3',4',6'-Tetra-*O*-acetyl- $\beta$ -D-glucopyranosyloxy)-1,4-naphthoquinone

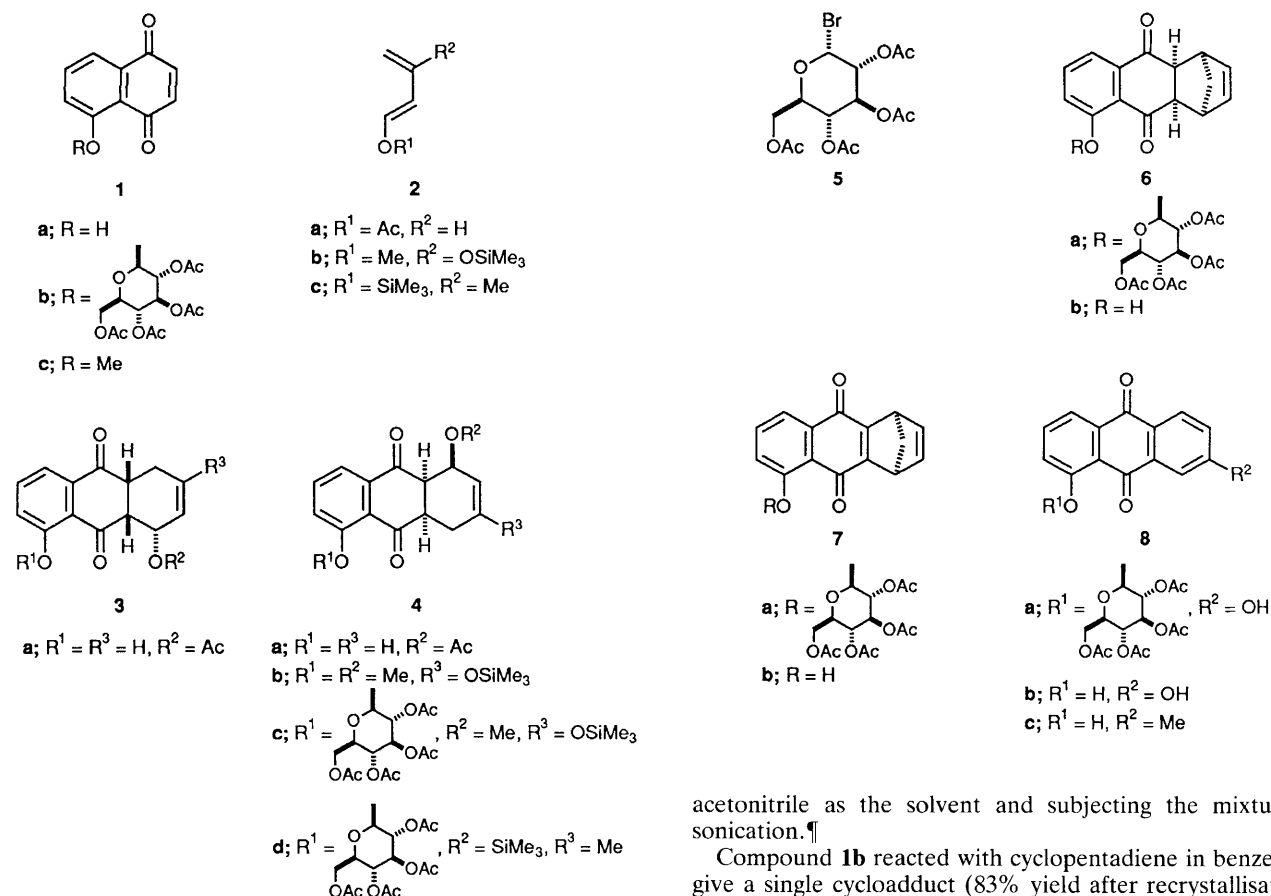
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The title compound **1b** reacts with cyclopentadiene to give a single cycloadduct, assigned the stereostructure **6a** by X-ray crystallography; single cycloadducts, *i.e.* **4c** and **d**, also arise in the corresponding reactions involving the dienes **2b** and **c**.

Diels–Alder cycloadducts of juglone **1a** and its derivatives are of value in the synthesis of quinonoid natural products and their relatives. Not surprisingly, therefore, much attention has been devoted to controlling the regio- and stereo-chemical outcome of such reactions.

The observations of Trost and his coworkers, that the regiochemistry of the cycloaddition of juglone **1a** with the diene **2a** is markedly improved in the presence of boron trifluoride [from a 2:1 mixture to a > 20:1 mixture of the ( $\pm$ )-cycloadducts **3a** and **4a**],<sup>1</sup> has played an important role in



the two strategies that have been successfully developed to derive cycloadducts of type **3** and their enantiomers/diastereoisomers.

One strategy, established by Trost<sup>2</sup> and ourselves,<sup>3</sup> makes use of enantiopure dienes and achiral Lewis acids to generate cycloadducts of type **3** and their diastereoisomers. The other strategy, progressed by the groups of Kelly<sup>4</sup> and Yamamoto,<sup>5</sup> employs enantiopure boron-based Lewis acid complexes of juglone **1a** (produced *in situ*) and achiral dienes to generate cycloadducts of type **3** and their enantiomers.<sup>†</sup>

We now report a third strategy, involving the use of juglone derivatives of type (**1**; R = a detachable enantiopure ligand), which is remarkably effective for the synthesis of cycloadducts of type **4**.

Prompted by our finding that dienes of type (**2**; R<sup>1</sup> = 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl) display a notable diastereofacial reactivity towards cyclic dienophiles,<sup>6,7</sup> we decided to investigate the dienophilic reactivity of the juglone glycoside **1b**.<sup>‡</sup> Initially, the last-cited compound, m.p. 148 °C, [α]<sub>D</sub><sup>20</sup> -80° (1.5% in CHCl<sub>3</sub>) was prepared (78% yield after recrystallisation) by treating a mixture of juglone **1a** and the acetobromoglucose **5**<sup>8</sup> in quinoline with silver(I) oxide.<sup>§</sup> However, the reaction was somewhat capricious and better, and reproducible, results (82% yield) were obtained by using

acetonitrile as the solvent and subjecting the mixture to sonication.<sup>¶</sup>

Compound **1b** reacted with cyclopentadiene in benzene to give a single cycloadduct (83% yield after recrystallisation), m.p. 152–154 °C, [α]<sub>D</sub><sup>20</sup> -114° (0.5% in CHCl<sub>3</sub>) assigned the stereostructure **6a** by X-ray crystallography.<sup>||</sup> Clearly, the diene had added in an *endo*-selective manner to the 'top' face of the alkene moiety of compound **1b**.

Acidic hydrolysis of the glycoside **6a** afforded the aglycone **6b** in a somewhat impure state. However, the dehydro-derivative **7a** (obtained in 72% yield after chromatography and crystallisation by treatment of compound **6a** with Et<sub>3</sub>N in CH<sub>2</sub>Cl<sub>2</sub> under O<sub>2</sub>), m.p. 188 °C (decomp.), [α]<sub>D</sub><sup>20</sup> -72° (0.3% in CHCl<sub>3</sub>), reacted with hot ethanolic hydrochloric acid to give the quinone **7b** (92% yield after crystallisation), m.p. 150 °C, [α]<sub>D</sub><sup>20</sup> +20° (0.2% in CHCl<sub>3</sub>).

Based upon the aforementioned stereochemical result and the finding of Boeckman and his coworkers, that the dienophile **1c** and the diene **2b** react to give only the (±)-cycloadduct **4b**,<sup>9</sup> we hoped that the cycloadduct **4c** would be produced in the Diels–Alder reaction of compounds **1b** and **2b**. Gratifyingly, a single cycloadduct (92% yield after

¶ We thank Dr A. Whiting for suggesting these conditions.

|| Crystal data: C<sub>29</sub>H<sub>28</sub>O<sub>12</sub>, *M* = 568.5, *a* = 6.270(3), *b* = 19.811(9), *c* = 23.162(6) Å, *U* = 2877 Å<sup>3</sup>, space group *P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>, *Z* = 4, *D*<sub>c</sub> = 1.31 g cm<sup>-3</sup>, μ(Mo-Kα) = 0.64 cm<sup>-1</sup>. An Enraf-Nonius CAD-4 diffractometer employing graphite monochromated Mo-Kα radiation (λ = 0.71069 Å) in the ω-2θ scan mode, was used to record 4023 reflections (0 < θ < 25°). Lorentz-polarisation corrections were applied but absorption effects were ignored. The structure was solved by direct methods (P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J.-P. Declercq and M. M. Woolfson, MULTAN-80, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data, Universities of York, England, and Louvain-la-Neuve, Belgium, 1980) and refined by block-matrix least-squares procedures (G. M. Sheldrick, SHELX-76, Program for Crystal Structure Determination, University of Cambridge, 1976) to final residuals of *R* = 0.043 and *R*<sub>w</sub> = 0.041 {*w* = 1.603/[σ<sup>2</sup>(*F*<sub>o</sub>) + 0.002*F*<sub>o</sub><sup>2</sup>] for 2965 observed reflections with *F*<sub>o</sub> ≥ 3σ(*F*<sub>o</sub>)}. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Data Centre. See Notice to Authors, Issue No. 1.

<sup>†</sup> Stoichiometric amounts of the Lewis acids are required. However, bovine serum albumin has been shown to catalyse the Diels–Alder reaction of juglone **1a** and 1-methoxycyclohexa-1,3-diene to give a 2.5:1 mixture of cycloadducts; the major cycloadduct possessed an enantiomeric excess of 38% (S. Colonna, A. Manfredi and R. Annunziata, *Tetrahedron Lett.*, 1988, **29**, 3347).

<sup>‡</sup> Previous attempts to prepare this compound were unsuccessful (N. F. Hayes and R. H. Thomson, *J. Chem. Soc.*, 1954, 904).

<sup>§</sup> Similar conditions were used by Müller to effect the glycosidation of hydroxyanthraquinones (A. Müller, *Chem. Ber.*, 1929, **62**, 2793).

crystallisation), m.p. 182–183 °C (decomp.),  $[\alpha]^{20}_{\text{D}} +51^{\circ}$  (2.2% in  $\text{CHCl}_3$ ) emerged when the reaction was conducted in benzene. It reacted with a few drops of hydrochloric acid (conc.) in chloroform to give the anthraquinone **8a** (93% yield after recrystallisation), m.p. 150 °C,  $[\alpha]^{20}_{\text{D}} -60^{\circ}$  (1% in  $\text{CHCl}_3$ ), which when heated in ethanolic hydrochloric acid afforded compound **8b** (90% after recrystallisation), m.p. 292 °C (lit.,<sup>10</sup> 293–294 °C).\*\* We, therefore, assign the structure **4c** to the cycloadduct.

The diene **2c** reacted with the dienophile **1b** in benzene to give the cycloadduct **4d** (93% yield after recrystallisation), m.p. 158 °C,  $[\alpha]^{20}_{\text{D}} +75^{\circ}$  (0.1% in  $\text{CHCl}_3$ ). In accord with its assigned regiostructure, compound **4d** was converted into the anthraquinone **8c** (77% yield after recrystallisation), m.p. 180 °C (lit.,<sup>11</sup> 183–184 °C),<sup>††</sup> under acidic conditions (conc.  $\text{HCl}-\text{CHCl}_3$ ;  $\text{HCl}-\text{EtOH}$ ).

In addition to their synthetic value, the aforementioned results are of considerable mechanistic interest. Clearly, the sugar is exerting a remarkable stereodirecting effect (a 1,6-relationship exists between the closest stereogenic and reacting centres). The results are not consistent with the model which we have developed<sup>7</sup> to explain the diastereofacial reactivity of dienes of types (**2**;  $\text{R}^1 = 2,3,4,6\text{-tetra-}O\text{-acetyl-}\beta\text{-D-glucopyranosyl}$ ) towards dienophiles.

\*\* The regioisomeric anthraquinone is reported<sup>9</sup> to have an m.p. of 272–275 °C.

†† The regioisomeric anthraquinone is reported to have an m.p. of 147 °C (P. C. Mitter and A. K. Sarkar, *J. Indian Chem. Soc.*, 1930, **2**, 619).

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