

(2Z,4E)-1,3,6-Triacetoxyhexa-2,4-diene a Novel Diels–Alder Diene Precursor of Cyclohexanones

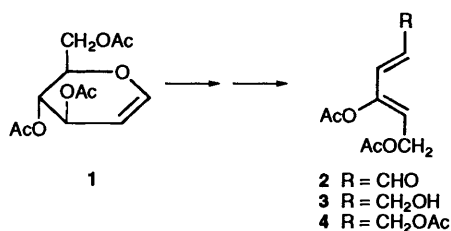
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The novel title diene **4**, prepared from 3,4,6-tri-*O*-acetyl-D-glucal, is a stable compound which undergoes Diels–Alder reactions with electron-deficient dienophiles, to give cyclohexanone derivatives.

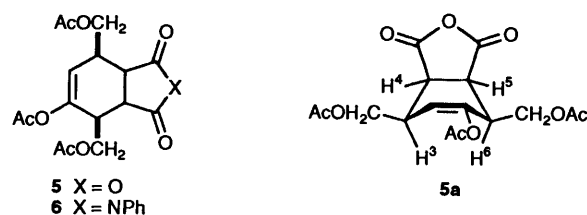
Previous work of our group has been devoted to the use of carbohydrate derivatives in Diels–Alder reactions.¹ In most of the cases, the dienophile was the sugar-derived component, there being fewer examples with sugar-derived dienes. However, although alkoxy- or acyloxy-dienes are useful compounds for the synthesis of cyclohexanones, their availability and stability are rather limited.^{2–4} Here, we report the synthesis of the novel diene (2Z,4E)-1,3,6-triacetoxyhexa-2,4-diene **4**, as well as the results of our preliminary studies on its reactivity with electron-deficient dienophiles.

Compound **4** prepared (64% overall yield†) from easily available 3,4,6-tri-*O*-acetyl-D-glucal⁵ **1** by way of a Perlin

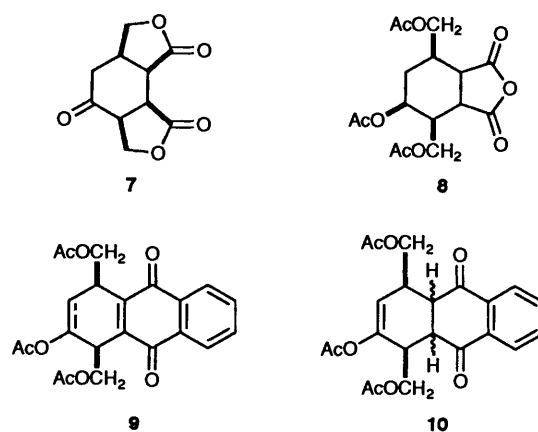


transformation⁶ followed by DBU-promoted elimination of acetic acid⁷ from the resulting α,β -unsaturated aldehyde, gave the dienal **2**. Reduction of the formyl group of **2** with methanolic NaBH₄ gave the alcohol **3**, which afforded the desired diene **4** by acetylation (Ac₂O/py). In fact, compound **4** (as well as compounds **2** and **3**) was an oil that was shown to be (¹H NMR) a 15:1 mixture of 2Z,4E- and 2E,4E-stereoisomers. Although separation of the latter was unnecessary for the Diels–Alder reactions, we report both herein because the minor isomer proved to be unreactive although not interfering in the isolation of the adducts. In contrast to **4**, which could be stored for long periods of time with no observable decomposition or polymerization, the alcohol **3** was rather unstable, leading to complex mixtures when undergoing thermal cycloaddition; the dienal **2** was quite unreactive towards the three dienophiles that we used.

The reaction of the diene **4** with maleic anhydride (1.0 equiv.) in refluxing toluene proceeded in a completely *endo*-stereoselective manner⁸ to give crystalline *cis,cis,cis*-1-acetoxy-3,6-di(acetoxymethyl)cyclohex-1-ene-4,5-dicarboxylic anhydride **5** as the sole product (55% yield). The structure of the adduct **5** was assigned by analogy with other Diels–Alder type reactions^{9–11} involving cyclic dienophiles and acyclic dienes. This was supported by analytical and spectroscopic evidence. Thus, its IR spectrum displayed the expected cyclic anhydride peaks at



1780 and 1840 cm⁻¹, with the former band at higher intensity. In the ¹H NMR spectrum the vinyl proton appeared at δ 5.60, as a double doublet showing a splitting ($J_{2,3}$) of 3.5 Hz and long-range splitting ($J_{2,6}$) of 2.7 Hz. The relative stereochemistry of the substituents in the cyclohexene ring was established from the $J_{3,4}$ and $J_{5,6}$ values (6.0 and 6.1 Hz, respectively), which indicate a *cis* relationship between the hydrogens concerned. These couplings correspond to torsion angles¹² of ca. 45° and are consistent with the adoption of a boat-like conformation of type **5a**.¹³ As a stereochemical consequence of the *endo* addition, the dilactone **7** (IR carbonyl absorptions at 1756 and 1700 cm⁻¹) could be formed in 64% yield by acid hydrolysis from the adduct **5**. Furthermore, steric crowding on the upper face in **5** caused the catalytic hydrogenation of the double bond to occur entirely on its lower face,¹⁴ thus leading quantitatively to the saturated anhydride **8** as a single product. In a similar



way, **4** also underwent Diels–Alder reaction with *N*-phenylmaleimide (boiling toluene, 30 h) to afford **6** (50% yield, m.p. 139–141 °C) as the sole product, and with naphthoquinone (260 h) to yield a mixture from which crystalline **9** (46% yield, m.p. 148–150 °C) was isolated as the major product, together with an oil (3%) containing only *endo*- and *exo*-**10** in a 3.5:1 ratio. Heating of this oil in toluene solution led to its conversion into **9**. Again, the $J_{3,4}$ and $J_{5,6}$ couplings for **6** and **10-endo** showed values of ca. 6 Hz.

† Yields are for isolated purified compounds and have not been optimized.

In conclusion, we describe here a new diene, whose utility is based on its stability, easy availability in gram quantities and on its applicability to the construction of highly useful products, such as cyclohexanone or anthraquinone derivatives. Our current efforts are now directed toward the synthesis of other acetoxy dienes with different substitution (so that it may include chirality) at the terminal carbons of the dienic system.

Experimental

Preparation of the Diene 4.—A stirred solution of the aldehyde **2**⁷ (4.8 g, 22.4 mmol) in methanol (32 cm³) was treated with NaBH₄ (1.1 g, 29.1 mmol) at 0 °C. After 15 min, the mixture was diluted with water (60 cm³) and extracted with dichloromethane (3 × 50 cm³). The combined organic phases were washed with saturated aqueous NaHCO₃ (2 × 50 cm³) and brine (50 cm³), dried (MgSO₄), and concentrated to afford the crude alcohol **3** as an oil (3.95 g, 82%). Treatment of **3** with Ac₂O-py gave diene **4** as an oil (4.13 g, 72% from **2**). Selected NMR data: δ_H(200 MHz; CDCl₃) 6.20 (dt, *J*_{4,5} 15.6, *J*_{4,6} 1.2, H-4), 5.80 (dt, *J*_{5,6} 6.1, 5-H), 4.63 (br d, 6,6'-H) and 4.56 (d, 1,1'-H); δ_C(CDCl₃) 146.9 (C-3), 126.7 (C-4), 125.0 (C-5) and 115.9 (C-2).

Diels–Alder Reaction of the Diene 4 with Maleic Anhydride.—Maleic anhydride (196 mg, 1.96 mmol) and a catalytic amount of hydroquinone were added to a solution of **4** (504 mg, 1.96 mmol) in dry toluene (10 cm³) and the mixture was heated at 104 °C for 48 h. The solvent was evaporated and the residue was purified by flash column chromatography on silica (chloroform–acetone, 9:1) to give the adduct **5** as colourless needles, which were recrystallized from chloroform–ethanol (384 mg, 55%); m.p. 128–130 °C; δ_H(CDCl₃) 5.60 (dd, 2-H), 3.74 (dd, *J*_{5,6} 6.1, 5-H), 3.65 (dd, *J*_{4,5} 9.6, *J*_{3,4} 6.0, 4-H), 2.96 (m, 6-H) and 2.83 (m, 3-H); δ_C(CDCl₃) 147.1 (C-1), 115.5 (C-2), 42.9, 42.2 (C-4,5), 36.7

(C-6) and 34.9 (C-3) (Found: C, 54.0; H, 5.2. C₁₆H₁₈O₉ requires C, 54.23; H, 5.12%).

Acknowledgements

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