## Asymmetric Diels-Alder Reactions of a Chiral Sugar Nitroalkene: Diastereofacial Selectivity and Regioselectivity

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The uncatalysed Diels-Alder addition of 1-(trimethylsilyloxy)- and 1-acetoxybuta-1,3-diene to a sugarderived nitroalkene proceeds with complete regioselectivity and diastereofacial selectivity to yield crystalline, optically pure, cyclohexene derivatives.

Absolute control of the stereochemistry of Diels–Alder reactions has been achieved in the Lewis acid-catalysed reactions of chiral acrylates<sup>1,2</sup> or, with more modest results, by using chiral catalysts,<sup>3</sup> dienes,<sup>4</sup> or dienophiles;<sup>5</sup> only limited success has been achieved in thermal asymmetric synthesis.<sup>1,6</sup> We have reported<sup>7</sup> that nitroalkenes derived from sugars react, as chiral dienophiles, with symmetric dienes to yield optically active norbornene or cyclohexene derivatives.

We describe here our results for thermal reactions between the nitroheptene  $1^8$  and 1-substituted dienes, focussing attention on the regioselectivity and stereofacial selectivity. As a consequence of the effective regiochemical control exerted by the nitro group,<sup>9</sup> we have only isolated and detected those regioisomers in which the nitro and the diene substituent are *ortho*. Diels-Alder reaction of the nitroalkene 1 and the



Scheme I

butadiene 2 gave an inseparable 1:1 mixture of adducts 4 and 5<sup>†</sup> quantitatively [crystallised (ether-light petroleum) in the same ratio]. However, when the product was crystallised from aq. methanol, hydrolysis of the trimethylsilyloxy group occurred to yield compounds 6 and 7, the former being isolated by fractional crystallisation (CCl<sub>4</sub>). The latter isomer could not be isolated due to equilibration between 6 and 7, which occurs during chromatography on silica gel.

Treatment of mixtures of 6 and 7 with pyridinium dichromate in  $CH_2Cl_2$  led to the crystalline cyclohexenone derivative 10 (55%) as the only product, *i.e.* both starting compounds had the same absolute configurations at C-4 and C-5.

Condensation of the nitroalkene 1 and the butadiene 3 led, exclusively, to the adduct 9. This compound showed NMR data identical with those obtained from enriched mixtures of the fully acetylated derivative of compound 7. The relative



configurations at C-3, C-4 and C-5 for 8 and 9 (hence for compounds 4–7) were determined from their coupling constants  ${}^{3}J_{3,4}$  and  ${}^{3}J_{4,5}$ , indicating a *trans,trans* relationship between 3-H, 4-H and 5-H in compound 8, and a *cis,trans* arrangement in compound 9. The proposed absolute stereo-chemistry at the three chiral centres was based on spectral and polarimetric correlations of compound 11 ‡ with the known compound 12 (4S,5S) and its (4R,5R) diastereoisomer.<sup>7c,d</sup>

Concerning the facial selectivity (i.e. 4R,5S vs. 4S,5R adducts), it is remarkable that for the thermal cycloadditions we have only isolated (and detected) those products with the 4R,5Sconfiguration, arising from the attack of diene on the C-1 si-face of the dienophile. This indicates that complete diastereofacial selectivity operates, probably because the si-face in the nitroalkene is the less-hindered one $7^{d,11}$  (in its presumably most stable conformer) and because the approach of the nucleophilic dienes 2 or 3 to the nitroalkene 1 should be<sup>12</sup> anti to an allylic substituent. Here, both steric and electrostatic arguments are consistent with the observed selectivity, which is among the best for uncatalysed Diels-Alder reactions. Another consideration is the endo or exo orientation of the reactants (i.e. the configuration at C-3) during cycloadditions. We conclude that there is no endo/exo selectivity for the reaction with the butadiene 2, whereas for butadiene 3 the selectivity is exclusively endo.13

The synthetic utility of compounds 6 and 9 lies in the fact that they are chiral building blocks readily available in gram quantities and may be converted into a variety of structures of current interest.<sup>6</sup>

## Experimental

Diels-Alder Reaction of the Nitroalkene 1 and 1-(Trimethylsilyloxy)buta-1,3-diene.—To a solution of compound 1 (10.0 g,

 $Compound 11 \{ [\alpha]_D + 37 (c \ 0.55, CHCl_3) \}$  was obtained from compound 9, by treatment with NaBH<sub>4</sub> in 1,4-dioxane.<sup>10</sup>

<sup>&</sup>lt;sup>†</sup> This mixture and other all new compounds displayed satisfactory analytical and spectral data (IR, NMR); yields are not optimized.

23.1 mmol) in dry toluene (100 cm<sup>3</sup>) was added butadiene 2 (20 cm<sup>3</sup>, 112.5 mmol) and hydroquinone (catalytic amount). After the reaction mixture had been heated at 105 °C for 24 h in a closed glass container, its NMR spectra showed disappearance of the starting nitroalkene and formation of the adducts 4 and 5 (1:1). Evaporation of the solvent led to an oily residue that crystallised (ether-light petroleum) to yield a 1:1 mixture of adducts 4 and 5 (7.0 g, 53%) (Found: C, 50.2; H, 5.9; N, 2.4. C<sub>24</sub>H<sub>37</sub>NO<sub>13</sub>Si requires C, 50.07; H, 6.48; N, 2.43%). Crystallisation of the residue from aqueous methanol gave compounds 6 and 7 (1:1 mixture) (7.2 g, 62%). Fractional crystallisation from CCl<sub>4</sub> gave pure adduct 6 (3.1 g, 27%); m.p. 162-164 °C;  $\delta_{\rm H}({\rm CDCl}_3)$  4.99 (dd,  $J_{1',5}$  8.0 Hz, 1'-H), 4.55 (br d, 3-H), 4.37  $(dd, J_{3,4} 8.3, J_{4,5} 11.2, 4-H)$  and 2.65 (br d, 5-H);  $\delta_{C}$  (CDCl<sub>3</sub>) 90.3 (C-4), 71.7 (C-1'), 71.1 (C-3) and 35.8 (C-5) (Found: C, 50.1; H, 5.85; N, 2.8. C<sub>21</sub>H<sub>29</sub>NO<sub>13</sub> requires C, 50.10; H, 5.81; N, 2.78%).

Treatment of adduct 6 with Ac<sub>2</sub>O–Py gave its fully acetylated derivative **8** (75%); m.p. 70–72 °C;  $\delta_{\rm H}$ (CDCl<sub>3</sub>) 5.69 (br d, 3-H), 5.01 (dd,  $J_{1',5}$  8.4, 1'-H), 4.56 (dd,  $J_{3,4}$  8.5,  $J_{4,5}$  8.7, 4-H) and 2.73 (m, 5-H);  $\delta_{\rm C}$  (CDCl<sub>3</sub>) 86.4 (C-4), 72.1 (C-3), 71.6 (C-1') and 35.9 (C-5).

Diels–Alder Reaction of Nitroalkene 1 and Buta-1,3-dien-1-yl Acetate.—Following the procedure described above, cycloaddition of nitroalkene 1 (6.0 g, 13.9 mmol) and the butadiene **3** (4.9 cm<sup>3</sup>, 41.6 mmol) was achieved in 96 h. Evaporation of the toluene led to an oil that crystallised (methanol) to yield the adduct **9** (5.7 g, 75%); m.p. 173 °C;  $\delta_{\rm H}(\rm CDCl_3)$  5.59 (t, 3-H), 5.05 (dd,  $J_{1',5}$  9.0, 1'-H), 4.82 (dd,  $J_{3,4}$  4.6,  $J_{4,5}$  9.0, 4-H) and 2.86 (m, 5-H);  $\delta_{\rm C}(\rm CDCl_3)$  83.1 (C-4), 70.9 (C-1'), 65.2 (C-3) and 32.8 (C-5) (Found: C, 50.9; H, 5.75; N, 2.2. C<sub>23</sub>H<sub>31</sub>NO<sub>14</sub> requires C, 50.64; H, 5.73; N, 2.57%).

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