

COMPLETE STEREOSELECTIVITY IN THE INTRAMOLECULAR DIELS-ALDER REACTION
OF A TRIENE DERIVATIVE FROM D-XYLOSE*

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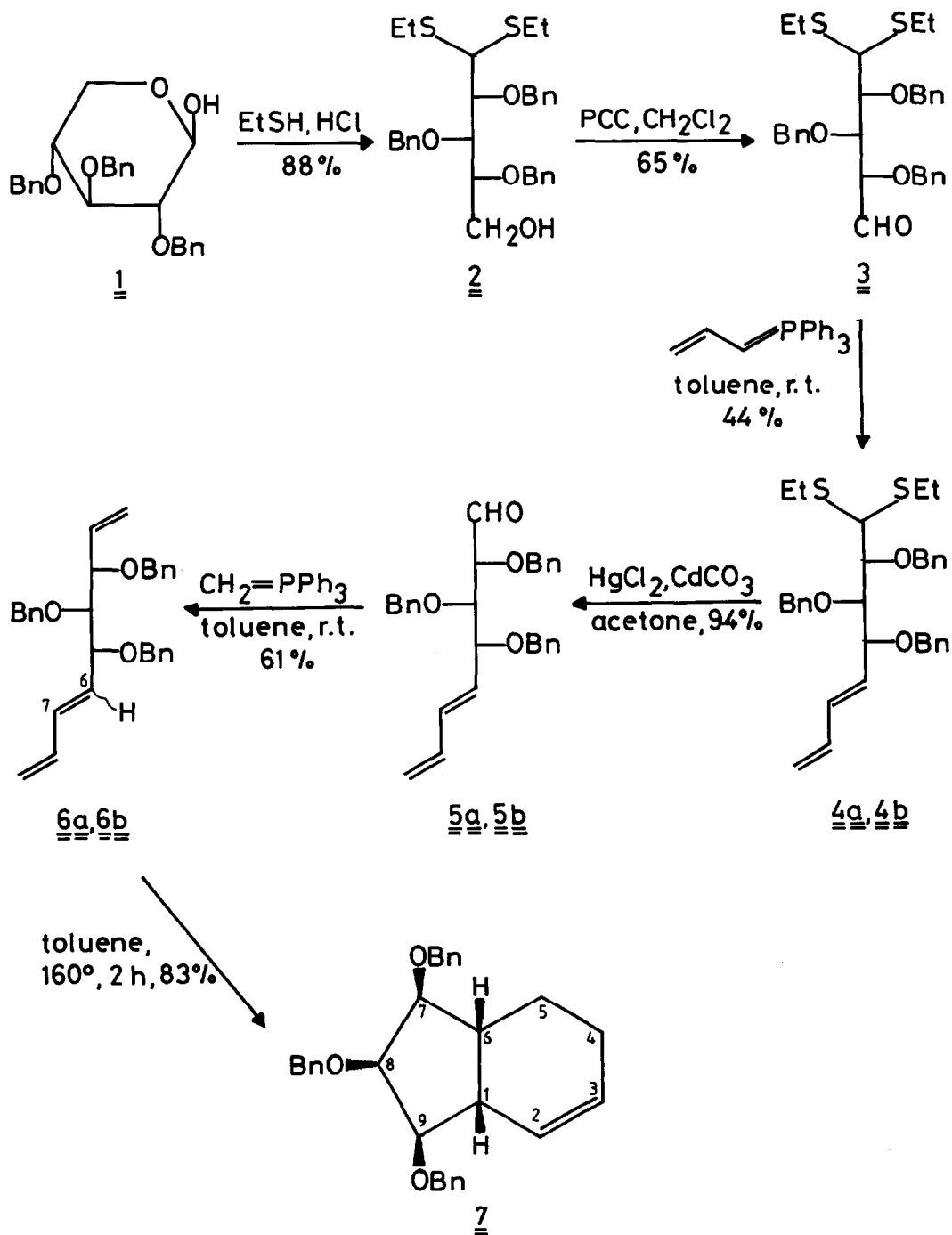
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Summary: Thermal intramolecular Diels-Alder reaction of triene **6** yielded the bicyclic derivative **7** with excellent stereoselectivity.

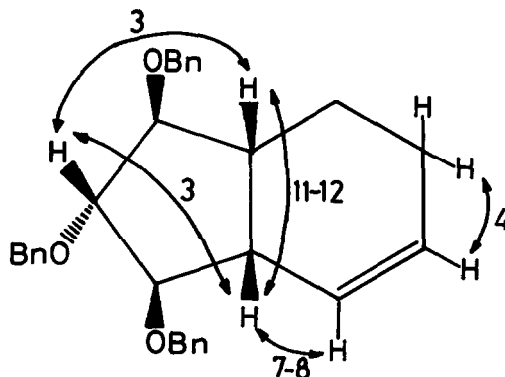
Although intramolecular Diels-Alder reactions have been investigated extensively^{1,2} little attention was paid to reactions where chiral olefins were utilized as starting compounds³. The stereoselectivity with such reactants is generally low and depends strongly on the reaction conditions and on the nature of the chain between the dienophile and philodiene extremities of the molecule. Supposedly the presence of multiple chiral centers in the triene to be cyclized would exert a beneficial influence on the stereochemical outcome of the reaction. Following our previous work⁴ on Diels-Alder reactions with carbohydrates we have tried to test this assumption using triene **6** obtained from D-xylose.

Thioacetalization of 2,3,4-tri-O-benzyl-D-xylose⁵ with ethanethiol gave 2,3,4-tri-O-benzyl-D-xylose diethyl dithioacetal **2** ($[\alpha]_D^{20} = 6.2$ (c 0.21 CHCl₃)) which, on oxidation with pyridinium chlorochromate yielded the compound **3** ($[\alpha]_D^{20} = -6.0$ (c 0.25, CHCl₃)). Wittig reaction with vinylmethylene triphenylphosphorane led to a 4:6 mixture of E:Z dienes **4a** and **4b**, respectively. Removal of the thioacetal protective groups gave a mixture of the E:Z aldehydes **5a** and **5b** in the same ratio. This was treated without separation with methylene triphenylphosphorane to afford, in a second Wittig reaction trienes **6a** and **6b** as an unseparable mixture (E:Z ratio 4:6). When this mixture was heated in toluene at 160°C in sealed tube for 2 h **7** was obtained in 83% yield⁶.

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No other products could be detected in any appreciable amounts in the reaction mixture. The stereochemistry of 7 was deduced from the $^1\text{H}/^1\text{H}$ NOE values arrows pointing from irradiated to detected spins, the number giving the enhancements in per cent as shown below.



Although it is known that bulky benzyloxy group in allylic position to the diene moiety can induce a moderate stereoselectivity in thermal intramolecular Diels-Alder reactions⁷, the virtually complete selectivity observed in the present case appears to be unprecedented. Since the selectivity of the reaction is apparently independent on the configuration of the C6-C7 bond in the trienes 6a, 6b either thermal E-Z isomerisation must take place prior to the intramolecular addition step or else, the latter may proceed through a common transition state from either 6a or 6b.

Bicyclic derivatives like 7 serve as versatile precursors for the synthesis of important natural products such as prostaglandines, enzyme inhibitors, pseudo sugars, and the intramolecular Diels-Alder reaction of appropriate carbohydrate derivatives appears to be promising approach for obtaining such molecules with defined chirality at multiple contiguous chiral centers in a high stereoselective way.

Acknowledgment

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References

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6. The structures of new products were identified by means ^1H - and ^{13}C -NMR spectra, by mass spectrometry and by elemental analysis. All compound gave satisfactory data. Some of important, characteristic data for compound **7** is presented here:
 $[\alpha]_{\text{D}}^{20} = 23.35$ (c 1.11, CHCl_3); ^1H NMR data (C_6D_6) δ 1.40-1.70 (2H, H-5a,5b, $J_{5a,6} = 4.7$ Hz, $J_{5b,6} = 0.0$ Hz); 1.78 (2H, H-4a,4b, $J_{3,4a} = 3.7$ Hz, $J_{3,4b} = 3.7$ Hz); 2.32 (1H, H-6, $J_{1,6} = 0.0$ Hz, $J_{6,7} = 6.1$ Hz); 2.72 (1H, H-1, $J_{1,2} = 3.5$ Hz, $J_{1,9} = 6.0$ Hz); 3.77 (1H, H-9); 3.78 (1H, H-7, $J_{7,8} = 5.5$ Hz); 4.24 (1H, H-8, $J_{8,9} = 5.5$ Hz); 5.52 (1H, H-3, $J_{2,3} = 9.8$ Hz); 5.55 (1H, H-2, $J_{2,4a} = 1.8$ Hz, $J_{2,4b} = 1.8$ Hz) ppm.
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