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A DOUBLE DIELS-ALDER REACTION OF A C_2-SYMMETRIC BIS-DIENOPHILE: A NEW ENANTIOSELECTIVE APPROACH TO NATURAL LOGANIN

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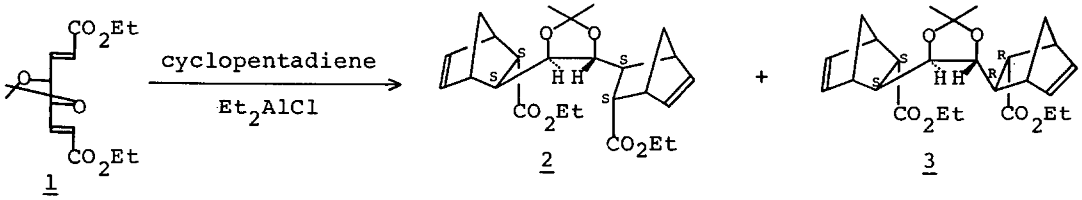
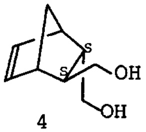
Summary: Reaction of a chiral C_2-symmetric bis-dienophile 1 and cyclopentadiene gave a mixture (3:2) of adducts 2 and 3 of which the major one was converted into the key intermediate 12 of loganin. The formation of the adducts is presumed via the anti-Felkin-Anh type active conformers, 14 and 15, respectively.

Diels-Alder reaction of α,β-unsaturated esters carrying sugar residue on the β-carbon proceeds with high steric control due to stereo and electronic effects of the sugar moiety.[1] In connection with our synthesis of the C_2-symmetric bis-α,β-unsaturated ester[2b] 1 from D-mannitol,[2] we examined the reaction of 1 carrying the sugar residue on the β,β'-carbons with cyclopentadiene.

Reaction of 1 with cyclopentadiene (10 equiv, CH_2Cl_2, -20°C, 20 h) proceeded in the presence of diethylaluminum chloride[3] (2 equiv) to afford a mixture (3:2) of two double adducts 2 and 3 (90%) which could be separated by recrystallization and column chromatography to furnish the major 2[4] as crystals (mp 77-78°C) and the minor 3 as an oil.



Stereochemistry of the adducts was confirmed by converting them into the known trans-2,3-dihydroxymethyl-5-norbornene[1c] (4) via sequential reduction (LAH), hydrolysis (dil. H_2SO_4), and one flask cleavage ($NaIO_4$) and reduction ($NaBH_4$), respectively. The diol 4 from 2 (76%) showed optical rotations ($[\alpha]_D^{24}$ -24.9° ($CHCl_3$)) identical with those reported[1c] for (2S,3S)-4 indicating the (2S,3S;2'S,3'S)-configuration of the progenitor 2. On the other hand, 4 from 3 (60%) showed no optical rotations which indicated the (2S,3S;2'R,3'R)-configuration of 3. Since we have (2R,3R)-(4) from D-mannitol,[2b] both enantiomers of 4 have now been accessible from the same chiral precursor.



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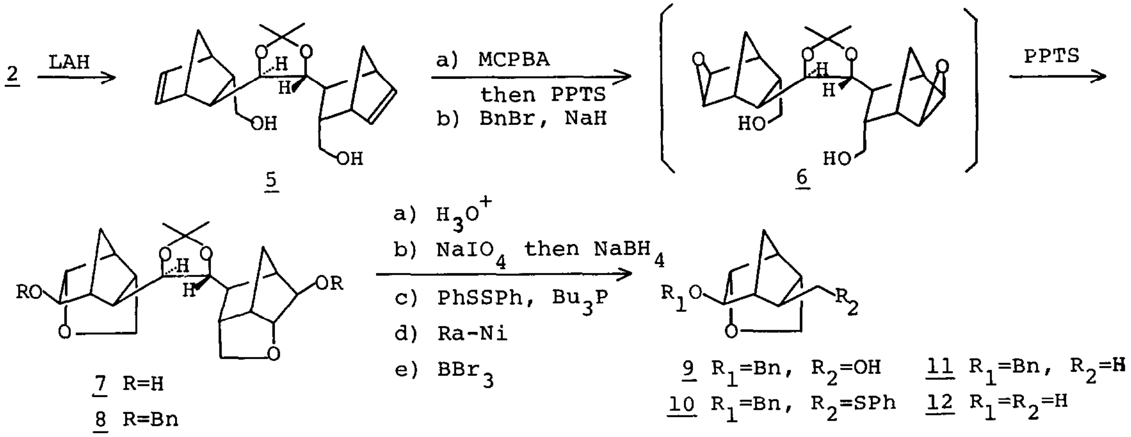
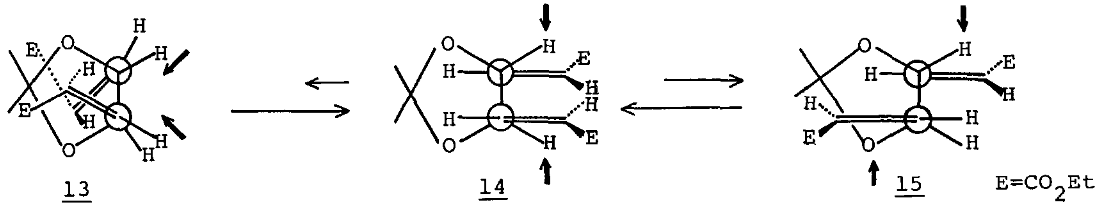
$[\alpha]_D^{24}$ -24.9°($CHCl_3$)

To demonstrate its utility, 2 was transformed into 12, the key intermediate of loganin.[5] Reduction of 2 gave 5 (99%) which was epoxidized, followed by acid treatment to give 7 (71%) *via* 6. The formation of 7 rigorously supported the *endo*-configuration of the ester groups of 2. On sequential benzylation, deketa-



lization, and one flask cleavage and reduction, 7 afforded 9 (77%) which was deoxygenated to give 11 (89%) via 10.[6] Finally, 11 was debenzylated to furnish 12 ($[\alpha]_D^{27}$ -67.18° (CH_2Cl_2); lit.[5] $[\alpha]_D^{18}$ -67.3° (CH_2Cl_2)) (85%).

The formation of the major adduct 2 was presumed via the anti-Felkin-Anh type active conformer 14 rather than via the Felkin-Anh conformer[8] 13 due to a considerable dipole-dipole and non-bonded interections in 13. Similarly, 3 was presumed to be formed via the another anti-Felkin-Anh conformer 15 of which higher steric hindrance compared to 14 was reflected in the product ratio.



References and Notes

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