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Synthesis of α-D-*C*-Glucoside Employing Dichloroketene Cycloaddition and Baeyer-Villiger Oxidation

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Abstract: The cycloaddition of dichloroketene to glucal followed by Baeyer-Villiger oxidation gave a bicyclic γ-lactone, an α-D-*C*-glucoside, which was further transformed to glucitol under the Suárez protocol. © 1997 Elsevier Science Ltd.

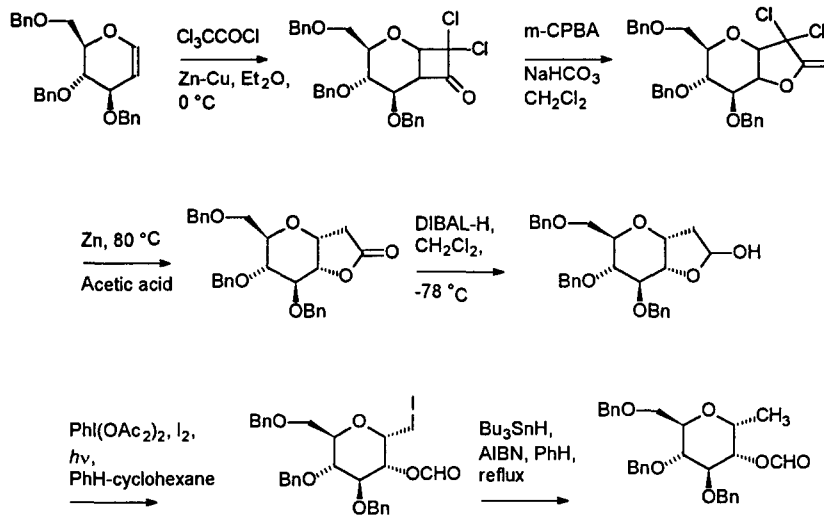
Synthesis of *C*-glycosides attracted much research interest during the past years. Even though there are a number of efficient methods, the regio-and stereospecific *C*-glycosidaton is thought the area to be explored.[1-4]

Dichloroketene is known to react with enol ether to give a dichlorocyclobutanone in a regiospecific manner. Furthermore, the latter can be oxidized under the Baeyer-Villiger conditions to a lactone. Greene *et al.* used this chemistry to acyclic enol ether for the synthesis of natural product.[5,6] Few study was known for the cycloaddition of dichloroketene to cyclic enol ether such as glucal to construct a bicyclic lactone. Herein, we wish to report a short synthetic method of *C*-glucoside using dichloroketene cycloaddition and Baeyer-Villiger oxidation.

Cycloaddition between dichloroketene (generated *in situ* from trichloroacetyl chloride and zinc-copper couple, Zn-Cu)[5] and tri-*O*-benzyl-D-glucal gave a *C*-glucoside with *cis* C-1 and C-2 substituents. The cycloadduct was then converted to bicyclic lactone by Baeyer-Villiger oxidation (metachloroperoxybenzoic acid and sodium bicarbonate) and dechlorination (Zn, acetic acid) in 40% for three steps. The lactone was then reduced by diisobutylaluminum hydride (DIBAL-H) to a lactol in 85% yield and the latter was subject to the α-alkoxy oxyradical fragmentation under Suárez condition[7] to give a *C*-glucoside having iodomethyl on C-1 and formate on C-2 in 90% yield. The *cis* relationship and the stereochemistry of C-1 and C-2 substituents were determined by measuring the coupling constants (dd, J = 7.9 Hz and 5.0 Hz) of the proton on C-2 at 5.20 ppm. The axial-axial and axial-equatorial couplings of proton on C-2 with the protons on C-3 and C-1, respectively, indicate the axial orientation of H-2 and the equatorial orientation of C-2 formate (OCHO).[8] Since the cycloaddition is known to give a *cis* product, the iodomethyl group should have axial orientation, *cis* to the C-2 OCHO group. Based on the stereochemistry and the orientations of the substituents, the cycloaddition of dichloroketene to olefin took place from the α-face of glucal. The glycoside having iodomethyl group on C-1 was then subject to a radical reaction to give a C-1 methyl-D-glucitol drivative[9] (for H-2, δ 5.07, dd, J = 9.3 Hz and 5.6 Hz)[8,10] in 85% yield (Bu_3SnH-AIBN).

In conclusion, dichloroketene cycloaddition to glucal followed by Baeyer-Villiger oxidation provided a new

synthetic method for the α-D-*C*-glucoside.



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8. For the coupling constants of the axial H-2, see reference 3 and 4.
9. For the C-1 β-methyl glycoside, cf. Hanessian, S.; Martin, M.; Desai, R. C. *J. Chem. Soc., Chem. Commun.*, **1986**, 926-927.
10. Spectral Data for the final product; mp 64-65 °C; IR (KBr) 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.03 (s, 1 H), 7.26-7.55 (m, 13 H), 7.13-7.17 (m, 2 H), 5.07 (dd, J = 9.3, 5.6 Hz, 1 H), 4.49-4.80 (3 x ABq, 6 H), 4.34 (m, 1 H), 3.84 (t, J = 8.6 Hz, 1 H), 3.64-3.75 (m, 4 H), 1.24 (d, J = 7.1 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.12, 138.07, 137.95, 137.86, 128.42, 128.38, 127.98, 127.88, 127.84, 127.78, 127.68, 79.58, 77.68, 74.96, 74.80, 73.50, 73.00, 71.81, 68.80, 68.50, 12.58.

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