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Preliminary communication

Opening of epoxides in the presence of iodine

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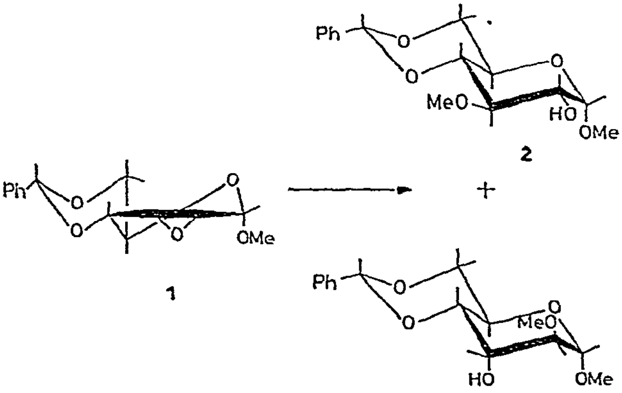
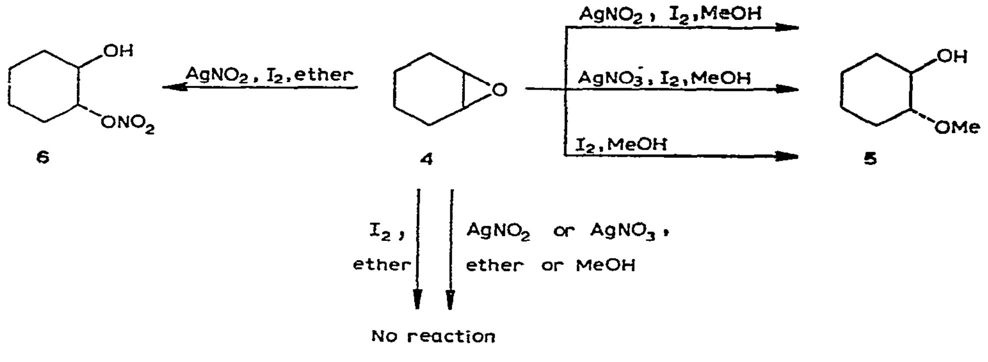
In connection with some studies[1] on the addition of pseudohalogens (produced *in situ* by the reaction of the appropriate silver salts and iodine) to unsaturated carbohydrates, methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (1) was treated with silver nitrite and iodine in methanol for 18 h at room temperature. Besides the formation of some water-soluble material, methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-glucopyranoside (2) and methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-altropyranoside (3) were isolated in 30% and 10% yields, respectively. The same results were obtained when compound 1 was treated with silver nitrate and iodine in methanol for 4 h at reflux temperature. The preponderance of the diequatorial product 2 is remarkable, since compound 1 gives virtually only the diaxial product, methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-altropyranoside (3), with sodium methoxide[2]. It has been well demonstrated[3–5], by the ring-opening reactions of epoxides fused to pyranoid rings that have their conformations stabilized by a "locking" group, that *trans*-diaxial opening of epoxides in the sugar series is favored, in accord with the Furst–Plattner rule[6]. Thus, methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (1) gives, with a wide variety of nucleophilic reagents, predominantly the products of *trans*-diaxial



SCHEME 1

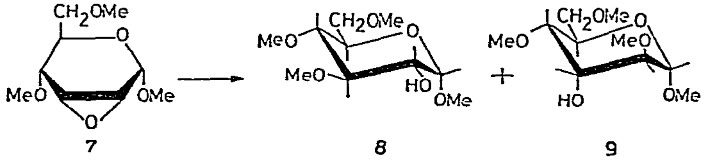


SCHEME 2

ring opening[4]. The present results are an *apparent* infringement of the rule of diaxial cleavage of epoxides★.

In exploratory, model studies, cyclohexene oxide (4) was treated under a variety of conditions. Thus, with silver nitrite (or silver nitrate) and iodine in methanol the main product was *trans*-2-methoxycyclohexanol (5), characterized as the 3,5-dinitrobenzoate[10]. When ether was used as the solvent, with silver nitrite and iodine, the preponderant product was *trans*-1,2-cyclohexanediol mononitrate (6), identified as the known[11] *p*-toluenesulfonate★★. A quantitative yield of compound 5 was obtained when the epoxide 4 was treated with only iodine and methanol. Compound 4 was unaffected, however, by treatment with iodine in ether, or with silver nitrite or silver nitrate in either methanol or ether.

The experiments with cyclohexene oxide indicate that iodine and methanol alone are sufficient for opening of the epoxide ring. Treatment of compound 1 with iodine and



★A preponderance of diequatorial products has been observed from compound 1 in reactions with hydrochloric or hydrobromic acid, to give the methyl 3-deoxy-3-halo-α-D-glucosides and methyl 2-deoxy 2-halo-α-D-altrosides[7], but in these cases the conformation-stabilizing 4,6-*O*-benzylidene group is removed during the reaction, possibly before opening of the epoxide ring. Also, compound 1 gives a diequatorial iodohydrin with methylmagnesium iodide[8]; diaxial halohydrins are obtained, however, with ethylmagnesium iodide, ethylmagnesium bromide, and phenylmagnesium bromide[9]. This formation of different iodohydrins with methylmagnesium iodide and ethylmagnesium iodide has not been explained.

★★The formation of nitrates has been observed[12] previously in reactions involving silver nitrite and iodine. The reaction of silver nitrite and iodine produces nitryl iodide (NO_2I) in solution[1,13]. In polar solvents, particularly, because of the increased solubility of silver nitrite, the nitrite ions can easily be oxidized to nitrates.

methanol, however, afforded only water-soluble material, presumably because of the removal of the 4,6-*O*-benzylidene group. Accordingly, methyl 2,3-anhydro-4,6-di-*O*-methyl-α-D-allopyranoside (7) was treated with iodine and methanol. After 7 days at room temperature, methyl 3,4,6-tri-*O*-methyl-α-D-glucopyranoside (8) and methyl 2,4,6-tri-*O*-methyl-α-D-altropyranoside (9) were formed in a ratio of 66:34, respectively; however, some starting material was still present.

A rationalization is being sought for the preponderance of diequatorial products with compound 1, in which the conformation is fixed by the *trans*-fused 4,6-benzylidene acetal ring. One suggestion is that ring opening occurs, in the presence of iodine, by a reaction of S_Ni character. In this process the epoxide oxygen atom could initially form a complex with iodine. Because of the marked destabilizing effect that the two oxygen atoms, attached to C-1, would have on carbonium-ion formation arising from cleavage of the epoxide C—O bond nearest the anomeric center, attack by methanol could then occur predominantly at C-3, to give the *trans*-diequatorial product of steric development-control.

Full details of these and other examples of the opening of epoxides in the presence of iodine will be published later.

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