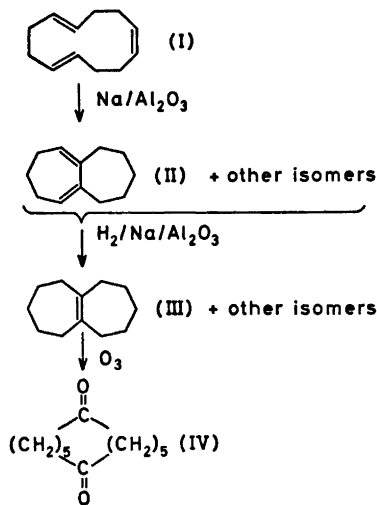


A Simple Synthesis of Cyclo-dodecane-1,7-dione from Cyclododeca-1,5,9-triene

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So far no *in vitro* synthesis for cyclo-dodecane-1,7-dione (IV) has been reported. Ozonolysis of the bicyclo[5.5.0]dodecene isomer (III), having its double bond in the bridge, might constitute an attractive final step in such a synthesis. Since the related bicyclo[5.5.0]dodecadiene (II) is formed¹ by isomerization of commercially available cyclododeca-1,5,9-triene (I) on "high-surface" sodium, and since partial hydrogenation of conjugated dienes can be performed on such catalysts,² the following synthetic route has been tried and found successful:



The isomerization at room temperature of macrocyclic diolefins, such as cyclododeca-1,7-diene, on "high-surface" potassium catalysts, prepared by dispersion of the metal on alumina, leads in the absence of hydrogen to a quasi-equilibrium between monocyclic diolefins.³ On the other hand, cyclododeca-1,5,9-triene, as already mentioned, undergoes a further transannular reaction and is transformed at

higher temperature on "high-surface" sodium catalysts to bicyclic diolefins, a substantial part of which must have the bicyclo[5.5.0]dodeca-1,6-diene structure (II), inferred from the structure of the isolated Diels-Alder adduct.¹ We find by gas-chromatography that at least five compounds are formed, of which the major one amounts to 40%. We also find that this reaction goes fast to the same constituents even at room temperature when potassium on alumina is used. However, the reaction is then difficult to control and continues to compounds of higher saturation.

Monocyclic conjugated diolefins can be partially hydrogenated to mono-olefins over the same potassium-alumina catalysts that produce them from non-conjugated diolefins.² In the present case, sodium-alumina proved to be an effective hydrogenation catalyst for the mixture of bicyclic diolefins and transformed them into bicyclic mono-olefins.

Gas-chromatography shows now only two main peaks, with the major component present in about 60% of the total. It must have the desired bicyclo[5.5.0]dodec-1(7)-ene structure (III) since ozonolysis of the mixture gave cyclododecane-1,7-dione (IV) in good yield.

Experimental. Isomerization step. Woelm aluminium oxide, activity I, (20 g) was dried at 500° for 20 h and transferred to a one-liter round flask under dry nitrogen. Freshly cut sodium (0.9 g) was added and the stirred mixture heated slowly to 200°. The molten metal became dispersed on the alumina surface and assumed a dark blue colour. After cooling, *cis,trans,trans*-cyclododeca-1,5,9-triene (20 g) dissolved in heptane (200 ml) was added, and the mixture refluxed with stirring until the gas-chromatogram showed that all the starting material had been consumed, and that five new main peaks had appeared. This generally required about 4 h.

Hydrogenation step. Into the above mixture hydrogen gas was introduced, and stirring and refluxing continued. After 5–10 h, depending on catalyst activity, the gas-chromatogram showed a simplification into two main peaks, ratio 2:5. The catalyst was then filtered off and washed with heptane. The catalyst should be immediately destroyed with methanol.

Ozonolysis step. The catalyst-free heptane solution (about 200 ml) from the reduction was transferred to an ozonation vessel, and a mixture of acetic acid (100 ml) and water (100 ml) added. After cooling to 0°, about 85% of the

calculated quantity of ozone was bubbled in. Oxidized material passed into the aqueous acetic acid phase, while saturated hydrocarbons stayed in the heptane layer.

The aqueous acetic acid layer was separated from the heptane layer, neutralized with sodium bicarbonate, and extracted three times with ether. The ether solution was dried with CaCl_2 and evaporated. The viscous oily residue (~15 g) soon crystallized. The solid was filtered off and recrystallized twice from methanol to give pure cyclododecane-1,7-dione (4 g), m.p. 133–135° (reported⁴ 134–136°). In addition, the mother liquors contain about the same quantity of diketone, together with a very large number of minor constituents, as shown by gas chromatography. Further crystal crops may be obtained, but tedious and lengthy low-temperature crystallizations are required. A combination with chromatographic methods may seem advantageous, but contact with active alumina provokes transannular condensation of the cyclododecanedione.

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Received March 1, 1971.

Oxidation of Carbohydrate Derivatives with Silver Carbonate on Celite. Oxidation of some Aldose Methyl Ethers

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Silver carbonate on celite has been reported by Fetizon and co-workers to oxidize secondary and, less easily, primary alcohols in benzene solution to ketones and aldehydes, respectively.^{1,2} Primary diols with the hydroxyl groups separated by four to six carbon atoms are, however, oxidized to lactones when treated with the same reagent.³ This behaviour may be explained by a prior cyclization of the initially formed monoaldehydes to hemiacetals,

which subsequently are dehydrogenated to lactones.

Since reducing derivatives of aldoses contain cyclic hemiacetal groups, an investigation of the effect of silver carbonate on celite on such compounds seemed interesting, and has now been undertaken. The present paper describes the oxidation of some tri- and tetra-*O*-methyl aldoses to aldonolactones. As far as the author is aware, silver carbonate on celite had not been applied as an oxidant in carbohydrate chemistry at the outset of this work. Recently, however, its selective oxidation of the allylic hydroxyl group of D-glucal was reported.⁴

2,3,4-Tri-*O*-methyl-D-xylose and 2,3,4,6-tetra-*O*-methyl-D-glucose were oxidized to the corresponding aldono-1,5-lactones, while the 2,3,6-tri-*O*-methyl derivatives of D-glucose and D-galactose gave the aldono-1,4-lactones on reflux with the oxidant in benzene. The yields were from 85 to 100 % within 45 min. The resistance to oxidation of the unsubstituted 5-hydroxyl group of the two last mentioned lactones, indicates a possible applicability of the oxidant for the preparation of aldonolactones also of some lower methylated aldoses. Preliminary investigations have, however, shown that a 2-*O*-substituent is necessary to prevent degradation.⁵

For the characterization of *O*-methyl sugars obtained during methylation studies of polysaccharides, the corresponding aldonolactones or, if the lactones are not crystalline, their easily derived phenyl hydrazides or amides are useful derivatives. Although it is not expected to replace the usually applied oxidation with bromine as a general method, the oxidation with silver carbonate on celite has been shown in the present work to offer a new, more rapid way to the lactones of some highly methylated, 2-*O*-substituted aldoses. Further research on the applicability of the method is in progress.

Experimental. Thin layer chromatography was performed on silica gel G plates in benzene-ethanol 20:3, 10:1, and 20:1 (v/v). As spray reagents were used diphenyl amine-aniline-phosphoric acid⁶ for the reducing sugar derivatives, and hydroxyl amine-ferric chloride⁷ for the lactones. Phenyl hydrazides were prepared by heating equimolar amounts of the aldonolactones and phenyl hydrazine on a water bath for 2 h; they were recrystallized from benzene.