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Abstract

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APPLICATION OF ORGANOZINC COMPOUNDS FOR THE SYNTHESIS OF CARBON-CARBON DERIVATIVES OF SUGARS

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As shown earlier ([1,4]), the most convenient method for the synthesis of C–C derivatives of carbohydrates proved to be the organomagnesium method, based on the interaction of acetohalogenoses with the Grignard reagent. This method is simple and gives high yields of the final products. However, a significant drawback is the need to introduce a large excess of the organomagnesium compound into the reaction, since the acetyl groups, and not only the halide of the acetohalogenose, react with it.

Attempts were made to circumvent this obstacle both by using methylated sugars instead of acetylated ones ([5]), and by replacing active organomagnesium compounds with more passive organocadmium compounds ([6]). The use of this approach encountered difficulties associated with purification of the final products, and the yields of C–C derivatives were low. Our attempt to obtain allyltetraacetylglucose by the interaction of acetochloroglucose with allylaluminum bromide likewise ended unsuccessfully.

In view of the fact that organozinc compounds have only a slight tendency to react with carbonyl groups and esters, it seemed interesting to apply them to the synthesis of carbon-carbon derivatives of carbohydrates.

As a result of heating acetochloroglucose with double quantities of phenylzinc chloride and *p*-anisylzinc chloride in toluene solution, noncrystallizing syrupy substances were obtained, from which phenyl-tetraacetylglucose and *p*-anisyltetraacetylglucose could be isolated in yields of up to 11 and 5%, respectively.

Table 1

Experiment no.	Molar ratio of acetochloroglucose and phenylzinc chloride	Heating time, h	Yield of phenyltetraacetylglucose, %	Unreacted acetochloroglucose, %	Amount of diphenylmethylcarbinol, g
1	1 : 9	10	2.5	7.3	4.02
2	1 : 2	10	4	17.8	3.18
3	1 : 2	6	8.5	18.5	2.51
4	1 : 2	4	11	27	1.8
5	1 : 2	3	5	65	1

Study of the by-products showed that incompletely substituted organozinc compounds partially react with the acetyl groups of acetochloroglucose, forming considerable amounts of carbinols. In all experiments, the presence of unreacted acetochloroglucose and of an unsaturated hydrocarbon compound was established, probably natural in this case.

tetraacetyl-2-oxyglucal. The yield of C—C derivatives and the amount of by-products varied depending on the ratio of the components and the duration of the reaction, as illustrated by the data in Table 1 (in all cases 10 g of α-acetochloroglucose was introduced into the reaction).

Fully substituted organozinc compounds, on interaction with acetohalogenoses, also form C—C derivatives of monosaccharides. By this method phenyltetraacetylglucose was obtained in yields of up to 15%, as well as phenyltriacetylarabinose.

Thus, we have shown the fundamental possibility of obtaining carbon–carbon derivatives of carbohydrates by the organozinc method; however, the yields of the final products here are lower than when organomagnesium compounds are used.

Experimental section

Synthesis of phenyltetraacetylglucose with the aid of phenylzinc chloride. In a three-necked flask equipped with a reflux condenser, a dropping funnel, and a mechanical stirrer, a solution of phenylmagnesium bromide was prepared from 1.32 g (0.055 mole) of magnesium and 9 g of bromobenzene in 30 ml of abs. ether; to this solution, with stirring and cooling, 7.44 g (0.055 mole) of anhydrous zinc chloride in 12 ml of abs. ether was gradually added. When dry toluene was added to the solution, a suspension of phenylzinc chloride formed. To the suspension, dropwise with stirring, was added a solution of 10 g (0.027 mole) of acetochloroglucose in 25 ml of toluene.

The mixture was heated on a boiling water bath in a stream of dry nitrogen; the optimum yield of phenyltetraacetylglucose was obtained on boiling for 4 hours.

After decomposition of the reaction mixture with water and dilute acetic acid, the ether-toluene layer was separated from the aqueous layer, washed with water and with a saturated solution of sodium bicarbonate, and dried over anhydrous sodium sulfate. After removal of the solvent in vacuo, 7.7 g of a light-yellow syrup was obtained.

Quantitative analysis of the syrup for chlorine (lime method) showed that it contained 27% of unreacted acetochloroglucose. The syrup readily adds bromine and decolorizes a permanganate solution, which indicates the presence in it of an unsaturated carbohydrate compound.

To separate phenyltetraacetylglucose from the accompanying carbinols, deacetylation was used. For this purpose a strongly cooled solution of the syrup in 30 ml of chloroform was added, with stirring and cooling, to a solution of 2 g of sodium in 50 ml of abs. methanol. After stirring for 5 min, the solution was left for half an hour in a cooling mixture and was then acidified with dilute acetic acid to a weakly acidic reaction of the medium. The resulting solution was extracted three times with chloroform. From the chloroform layer, after removal of the solvent, pure diphenylmethylcarbinol (m.p. 77–78°) was obtained in an amount of 1.8 g.

The aqueous layer was evaporated to a syrup and acetylated by heating for 3 hours with 50 ml of acetic anhydride and 5 g of anhydrous sodium acetate. The subsequent treatment was carried out as in the usual organomagnesium synthesis. As a result, 1.7 g of a thick syrup was obtained, from which, by recrystallization from isopropyl alcohol, 1.1 g (11% of theory) of phenyltetraacetylglucose was isolated, with m.p. after repeated recrystallization 153-154°. A mixed sample of the product obtained with an authentic phenyltetraacetylglucose melted within the same limits. Destructive oxidation with alkaline permanganate led to the formation of benzoic acid.

In order to avoid the stage of deacetylation and repeated acetylation, an experiment was carried out in which phenyltetraacetylglucose was separated from by-products by chromatography. For this purpose the ether-toluene layer obtained after the interaction of phenylzinc chloride with acetochlor-

with glucose, was chromatographed on a column with ignited aluminum oxide. The aluminum oxide was washed with 175 ml of benzene. After removal of the solvent in vacuo, a light-yellow syrup was obtained, which crystallized upon dissolution in cold isopropyl alcohol. As a result, 0.45 g (5% of theory) of phenyltetraacetylglucose was obtained, m.p. 153-154°. A mixed sample gave no depression. On oxidation, benzoic acid was obtained.

Preparation of anisyl tetraacetylglucose. *p*-Anisylzinc chloride was obtained by the method described above from 1.32 g of magnesium, 10.7 g of *p*-bromoanisole, and 7.44 g of anhydrous zinc chloride. An ethereal solution of 10 g of acetochloroglucose was added to the organozinc compound, and the mixture was heated for 4 hr. After deacetylation and the usual work-up, 0.5 g

(5% of theory) of anisyl tetraacetylglucose was obtained, m.p. 102°. A mixed sample gave no depression. On oxidation, *p*-methoxybenzoic acid was isolated.

Synthesis of phenyltetraacetylglucose with the aid of diphenylzinc. The diphenylmercury required for the synthesis of diphenylzinc was obtained by the diazo method of A. N. Nesmeyanov (7). Diphenylzinc was synthesized by boiling diphenylmercury with zinc powder in a xylene solution (8). A xylene suspension of diphenylzinc, obtained from 6 g (0.017 mole) of diphenylmercury and 4.8 g of zinc dust, was heated with 3 g (0.008 mole) of acetochloroglucose in 15 ml of benzene on a boiling water bath for 1.5 hr.

The reaction mixture was decomposed with dilute acetic acid. The xylene solution was separated, washed with water, dried, after which the solvent was removed in vacuo. The viscous syrup obtained was acetylated with acetic anhydride in the presence of anhydrous sodium acetate. The reaction mixture was poured into water. The aqueous solution was extracted with ether; after removal of the latter, 2.8 g of a yellow syrup was obtained. The syrup was dissolved in a minimal amount of hot isopropyl alcohol. On prolonged standing in a refrigerator, 0.46 g (14% of theory) of phenyltetraacetylglucose crystallized from the solution, m.p. 151–152°. A mixed sample gave no depression. On oxidation of the substance, benzoic acid was obtained.

Preparation of phenyltriacetylarabinose. The reaction of diphenylzinc with acetochloroarabinose was carried out by the indicated procedure. Ultimately a yellowish syrup was obtained, from which, upon prolonged crystallization from isopropanol, a small amount of phenyltriacetylarabinose was isolated, m.p. 91–92°. A mixed sample with authentic phenyltriacetylarabinose gave no depression of the m.p.

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Note: Figure translations are in progress. See original paper for figures.