Anal. Calcd. for $C_{13}H_{12}N_2O_4$: N, 10.77. Found: N, 10.64.

1-Methyl-4-carbostyrilacetonitrile (VI).—Fourteen grams (0.054 mole) of V was warmed with 100 ml. of acetic anhydride in a 500-ml. round-bottomed flask. Evolution of carbon dioxide started at 30–35° and had ceased at 75–80°. After removal of the acetic anhydride in vacuum, the residual solid was crystallized as fine white needles from a solution of 100 ml. of acetone in 200 ml. of benzene; yield 7.2 g. (67.3%), m. p. 186.5–187.5°.

Anal. Calcd. for $C_{12}H_{10}N_2O$: N, 14.14. Found: N, 14.66.

1-Methyl-4-carbostyrilacetic Acid (VII).—Five grams (0.025 mole) of VI was refluxed with a mixture of 95% ethyl alcohol (45 ml.) and concentrated hydrochloric acid (45 ml.) for eight hours. After removal of most of the alcohol by evaporation on a steam-bath and cooling the residual solution in ice, a white granular solid separated. The solid was dissolved in 10% sodium carbonate solution and reprecipitated by neutralization with 6*N* hydrochloric acid; yield 4.2 g. (79%). The acid (VII) was recrystallized from a benzene–ether (3:2) solution; m. p. 185.5–186.5° (dec.).

Anal. Calcd. for $C_{12}H_{11}NO_3$: N, 6.45. Found: N, 6.35.

Ethyl 1-Methyl-4-carbostyrilacetate (VIII).—A solution of 2 g. (0.01 mole) of VI in 50 ml. of absolute ethyl alcohol was heated to reflux temperature and dry hydrogen chloride passed into the solution for three hours. The alcohol was removed by evaporation on a steam-bath then the solid residue was treated with 100 ml. of water, neutralized with sodium carbonate and extracted with ether. After drying, the ether was evaporated and the residue extracted with 100 ml. of a boiling mixture (1:1) of benzene and ligroin (b. p. 70–80°). The insoluble portion (1.2 g.) proved to be VI. Concentration of the solution gave a 0.6 g. yield of the ester (VIII); white needles, m. p. 94–95°.

Anal. Calcd. for $C_{14}H_{15}NO_3$: N, 5.71. Found: N, 6.26.

1-Methyl-4-(α-cyanostyryl)-carbostyril (IX).—A mixture of 1 g. (0.005 mole) of VI, 1 g. (0.01 mole) of benzaldehyde and 5 ml. of acetic anhydride was heated in an oil-bath at 140–150° for twelve hours. The solution was poured into 50 ml. of water, neutralized with sodium hydroxide and the solid which precipitated was crystallized from 10 ml. of 95% ethyl alcohol giving a white flocculent solid; yield 0.2 g. (14%). Two recrystallizations from alcohol gave a product which melted at 231.5–232.5°.

Anal. Calcd. for $C_{19}H_{14}N_2O$: N, 9.79. Found: N, 9.70.

Nitration of 1,4-Dimethylcarbostyril (I).—Fifteen grams (0.087 mole) of I was dissolved in 36 ml. of concentrated sulfuric acid contained in a 500-ml. three-necked round-bottomed flask fitted with a mechanical stirrer and a dropping funnel. The solution was cooled to 5° and 15 g. (0.23 mole) of fuming nitric acid (sp. gr. 1.5) in 10 g. of concentrated sulfuric acid added dropwise while the solution was stirred. The temperature was maintained at 5–10°. After addition of the mixed acids, the solution was allowed to stand for two hours at 10° and finally at room temperature for twelve hours. The nitration mixture was poured onto 300 g. of chipped ice; yield 13 g.

(a) **Isolation of the Mononitro Derivative.**—Nine and one-half grams of the crude nitro compound was extracted with 150 ml. of a hot benzene–acetone solution (1:1), filtered and the filtrate cooled in an ice-bath; yield 3.7 g. (39%), m. p. 218–220°. Pale yellow needles were obtained after two recrystallizations of the nitro compound from the benzene–acetone solution; m. p. 228.5–229°.

Anal. Calcd. for $C_{11}H_{10}N_2O_3$: N, 12.84. Found: N, 13.1, 12.94.

(b) **Isolation of the Trinitro Derivative.**—The benzene–acetone filtrate from (a) was evaporated to dryness, then the residue extracted with 100 ml. of boiling 95% ethyl alcohol and filtered. The alcohol-insoluble solid (2.5 g.) was crystallized from 100 ml. of boiling xylene as a finely divided yellow solid; m. p. 204–205°. Recrystallization from 20 ml. of an acetone–ethyl alcohol (1:1) solution gave bright yellow platelets; m. p. 207–208.5°.

Anal. Calcd. for $C_{11}H_8N_4O_7$: C, 42.86; H, 2.6; N, 18.18. Found: C, 43.0, 43.0; H, 2.87, 3.24; N, 18.3.

Summary

1. Satisfactory methods have been described for the use of diketene and a secondary alkyl aromatic amine in the preparation of N-alkylacetoacetanilides and conversion of the latter substances to 1-alkyl-4-methylcarbostyrils.

2. The condensation of 1,4-dimethylcarbostyril with ethyl oxalate has been described and the synthesis of several compounds from ethyl 1-methyl-4-carbostyrilpyruvate has been given.

3. The nitration of 1,4-dimethylcarbostyril has been described.

BLOOMINGTON, INDIANA RECEIVED AUGUST 23, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Glycosylation of Hydrocarbons by Means of the Grignard Reagent

BY CHARLES D. HURD AND WILLIAM A. BONNER[1]

In previous communications[2] it has been demonstrated that reaction may be brought about between sugar derivatives and aromatic hydrocarbons in the presence of aluminum chloride. Reaction of benzene, for example, with either glucose pentaacetate or tetraacetylglucosyl chloride gives rise to tetraacetylglucosylbenzene and 1,1-diphenyl-1-desoxyglucitol. It was assumed that the glucose type of configuration was retained in the reaction products. Proof of this assumption is now presented by synthesizing one of these same compounds by means of the Grignard reagent under such conditions that isomerization could not occur. As a matter of fact, it would not have been unreasonable to assume that inversion might have occurred in the presence of aluminum chloride in view of the results of Hudson and collaborators[3] on the synthesis of heptaacetylneolactosyl chloride from lactose octaacetate and a mixture of aluminum chloride and phosphorus pentachloride. The glucose portion of lactose rearranges to an altrose unit during this process.

The basis for assuming that tetraacetylglucosyl

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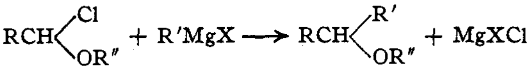
[1] Corn Products Co. Research Fellow, 1941–1944.

[2] Hurd and Bonner, THIS JOURNAL, **67**, 1664, 1759 (1945).

[3] Hudson, *ibid.*, **48**, 2002 (1926); Kunz and Hudson, *ibid.*, **48**, 1978, 2435 (1926); Richtmyer and Hudson, *ibid.*, **57**, 1716 (1935); Hockett and Chandler, *ibid.*, **66**, 627 (1944).

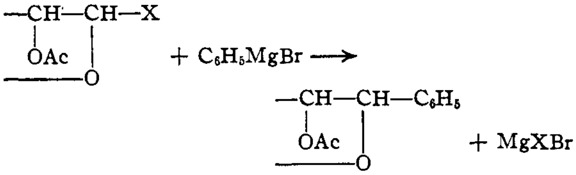
chloride should react with Grignard reagents is that it is a hemiacetal chloride and the simple chlorides of this type, namely, the α-chloro ethers, are known to react with Grignard reagents



$$RCH\begin{matrix}Cl\\OR''\end{matrix} + R'MgX \longrightarrow RCH\begin{matrix}R'\\OR''\end{matrix} + MgXCl$$

This reaction has been used in the synthesis of ethers by Houben and Führer,[4] and it also comprises one of the steps of the Boord[5] synthesis of olefins.

If tetraacetylglucosyl halide behaved analogously toward phenylmagnesium bromide (ignoring possible interaction at the ester functions) the product would be tetraacetylglycosylbenzene



Several attempts to carry out this reaction which are recorded in the literature, however, have been failures. The first such was by Paal and Hörnstein,[6] who treated tetraacetyl-α-D-glucosyl bromide with phenylmagnesium bromide. Their only isolable product was methyldiphenylcarbinol. From this it would seem that the Grignard reagent reacted at the ester functions but not at the bromide position. Glucose pentaacetate was used similarly with the Grignard reagent, the only positive finding again being that of carbinol formation. The next persons to attempt this reaction were Fischer and Hess,[7] who obtained a precipitate on mixing ether solutions of tetraacetylglucosyl bromide (1 mole) and methylmagnesium iodide (2 moles). Analysis of the precipitate corresponded to $C_{14}H_{19}O_9Br \cdot 2CH_3MgI$. The original tetraacetylglucosyl bromide was recovered on treatment of this product with dilute acid. Similar addition compounds were obtained with methylmagnesium iodide and β-D-glucose pentaacetate, β-D-glucose tetraacetate, and methyl tetraacetyl-α-D-glucoside. The same kind of addition compound was obtained in 1930 by Fröschl, Zellner and Zak[8] who employed methyl- and ethylmagnesium iodide at 0° on fructose pentaacetate, fructose tetraacetate, tetraacetylfructosyl chloride, lactose octaacetate and heptaacetyllactosyl bromide. An excess of Grignard reagent did not alter the 1:2 ratio of reactants found in the addition compound.

As would be expected, the open chain modifications of aldoses react smoothly at the aldehyde function. For example, diisopropylidene-D-arabonaldehyde reacts[9] with methylmagnesium iodide to form diisopropylidene derivatives of D-rhamnitol and 6-desoxy-L-gulitol.

After finding that aldosyl halides or acetates yielded nothing of promise with Grignard reagents, Paal and co-workers[10] turned their attention to the behavior of Grignard reagents toward acetylated glyconic lactones. Here they were successful in obtaining carbohydrate derivatives, although the yields were only 10–12%. 1,1-Diphenyl-D-glucitol was obtained, for example, by interaction of 2,3,5,6-tetraacetyl-D-gluconic lactone and a large excess of phenylmagnesium bromide.

In contrast to the negative results of previous workers we have been able to effect the interaction of Grignard reagents with the glycosyl halides. The older work suggested preferential interaction at the acetyl groups of tetraacetylglucosyl halides. Eight equivalents of Grignard reagent would, therefore, be consumed by the four acetyl groups and one equivalent by the halide group, making a total of nine.

Accordingly, an experiment was carried out using more than nine equivalents (actually, twelve) of phenylmagnesium bromide per equivalent of tetraacetyl-α-D-glucosyl chloride, both substances being dissolved in ether. The mixture was decomposed with water, and the ether and water layers investigated individually. From the ether layer was isolated methyldiphenylcarbinol in excellent yield. The water layer was evaporated to dryness, and the residue acetylated. The acetate which was obtained melted at 155–156°, $[\alpha]^{20}D$ −18.6°, hence was identical with the tetraacetyl-D-glucopyranosylbenzene obtained from the Friedel–Crafts reaction, m. p. 156.5°, $[\alpha]^{20}D$ −16.4°. A mixed melting point of the two products showed no depression. The identity was further established by oxidation of the Grignard product to benzoic acid. As was anticipated, similar results were obtained using tetraacetyl-α-D-glucosyl bromide instead of the chloride.

By evaporation of the mother liquors from the first crystallization of the acetylated Grignard product, there was obtained a sirup weighing about one-fourth as much as the crude tetraacetylglucopyranosylbenzene, and having a specific rotation of 39.9°. That this also represented a glucosylation product was shown by its ready oxidation to benzoic acid. Thus it is apparent that two products resulted from the Grignard glucosylation of benzene, a solid of negative rotation and a sirup of positive rotation. For reasons subsequently to be considered, these two products are considered to be anomers having the original glucose configuration. In accordance with terminology,[11] based on specific rotation, the crystalline, low-rotating anomer was named

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(4) Houben and Führer, *Ber.*, **40**, 4993 (1907).

(5) Swallen and Boord, THIS JOURNAL, **52**, 651 (1930).

(6) Paal and Hörnstein, *Ber.*, **39**, 1361, 2823 (1906).

(7) Fischer and Hess, *ibid.*, **45**, 912 (1912).

(8) Fröschl, Zellner and Zak, *Monatsh.*, **55**, 25 (1930).

(9) Gätzi and Reichstein, *Helv. Chim. Acta*, **21**, 914 (1938).

(10) Paal and Weidenkoff, *Ber.*, **39**, 2827 (1906); Paal and Zahn, *ibid.*, **40**, 1819 (1907); Paal and Kinscher, *ibid.*, **44**, 3543 (1911); Paal, Küster and Roth, *ibid.*, **49**, 1583 (1916).

(11) Hudson, THIS JOURNAL, **31**, 66 (1909).

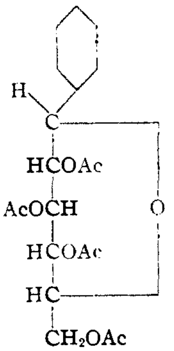
TABLE I

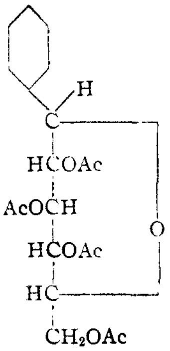
PRODUCTS FROM THE GRIGNARD GLYCOSYLATION OF HYDROCARBONS

Column 3: A, Tetraacetylglucopyranosylbenzene; B, *p*-Tetraacetylglucopyranosyltoluene; C, 1-Tetraacetylglucopyranosylnaphthalene; D, 1-Tetraacetylglucopyranosylbutane; E, Unidentified sirup mixture; F, Triacetylxylopyranosylbenzene; G, *p*-Triacetylxylopyranosyltoluene; H, Heptaacetyllactosylbenzene; I, α-D-Glucose pentaacetate; J, β-D-Glucose pentaacetate.

Polyacetylglycosyl chloride	R— in RMgX	Carbohydrate product	Crude yield, %	Anomeric composition α, %	Anomeric composition β, %	Carbinol R— in $R_2C(CH_3)OH$	Carbinol Crude yield, %
D-Glucose	Phenyl	A	82.0	28.4	71.6	Phenyl	100.0
D-Glucose	*p*-Tolyl	B	75.0	26.6	73.4	*p*-Tolyl	98.5
D-Glucose	1-Naphthyl	C	65.0	33.3	66.7	1-Naphthyl	66.0
D-Glucose	*n*-Butyl	D	59.4	...	...	*n*-Butyl	95.6
D-Glucose	*i*-Propyl	E	...	...	...	*i*-Propyl	50.8
D-Glucose	Benzyl	E	...	...	...	Benzyl	100.0
D-Xylose	Phenyl	F	86.6	25.0	75.0	Phenyl	100.0
D-Xylose	*p*-Tolyl	G	82.3	14.0	86.0	*p*-Tolyl	100.0
Lactose	Phenyl	H	69.4	41.0	59.0	Phenyl	95.4
I	Phenyl	E	...	...	...	Phenyl	97.8
J	Phenyl	E	...	...	...	Phenyl	89.3

tetraacetyl-β-D-glucopyranosylbenzene, while the sirupy, high-rotating form was called tetraacetyl-α-D-glucopyranosylbenzene. The two structures are these:





Experiments designed to determine the actual stereochemical configurations at position 1 of these compounds are in progress.

Gratifying yields in the above experiments made it imperative to test the generality of the Grignard glycosylation both with regard to the sugar and the Grignard reagent. Table I indicates that the reaction is general for polyacetylglycosyl halides with either aromatic or aliphatic Grignard reagents.

In each instance a substantial quantity of the high-rotating α-anomer was formed. The yields of methyldialkyl- or methyldiarylcarbinol obtained in most cases were almost quantitative.

Two experiments bearing on the mechanism of this reaction are of interest to record. One bears out the contention that the Grignard reagent reacts at the ester groups preferentially but the other demonstrates that reaction proceeds appreciably at the halide position before all the ester groups are consumed.

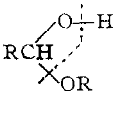
Mixing of equivalent quantities of tetraacetyl-α-D-glucosyl bromide and phenylmagnesium bromide in ether solution caused precipitation of a solid which was soluble in chloroform. The ether and chloroform solutions were mixed and the whole was decomposed with water. Optical activity was observed in both the ether and water layers, but water solubility of any of the carbohydrate material was obviously associated with removal of acetyl groups. Also, a halogen-containing sirup was obtained from the ether layer.

In the next experiment an equivalent of tetraacetylglucosyl bromide was added to 7.5 equivalents of phenylmagnesium bromide. This lacks 0.5 equiv. of the required number to consume the four acetyl groups. Then an excess of *p*-tolylmagnesium bromide was added to complete the reaction. On working up the product it was found to be a mixture containing about one-tenth *p*-tetraacetylglucosyltoluene and nine-tenths tetraacetylglucosylbenzene, as indicated by the melting point of the product and its oxidation to both benzoic and terephthalic acids. If reaction had occurred on all four acetyls before attacking the bromide position the product should have been pure tetraacetylglucosyltoluene.

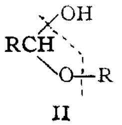
Stereochemical Considerations

The isolation of identical products (both in the case of glucose and xylose) from the Friedel–Crafts and Grignard glycosylations of benzene indicates beyond reasonable doubt that no Walden inversion of the several asymmetric centers at positions 2 and higher has accompanied the Friedel–Crafts reaction. This seems reasonable in view of the following considerations.

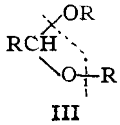
Hemiacetals must decompose in the manner of I, not II, otherwise acetals, III, should decompose as readily as hemiacetals, which is not the case. The RMgX addition product to an ester also decomposes spontaneously, hence must follow



I

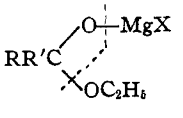


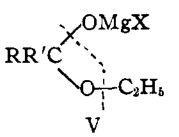
II



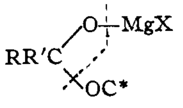
III

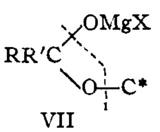
pattern IV (analogous to I) rather than V (analogous to II). Now if the alcohol part of the ester–


IV


V

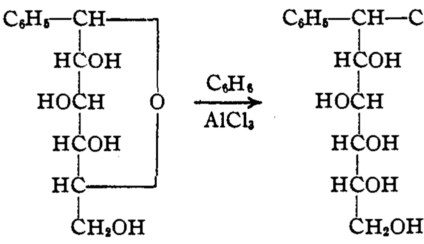
Grignard complex is replaced by an asymmetric grouping, it is obvious that decomposition of the complex VI in a manner analogous to IV should have no disturbing effect on the asymmetric center. Only the bond *beyond* the oxygen connecting to the asymmetric position is broken, hence inversion or racemization cannot occur. In contrast,


VI


VII

decomposition of the complex according to VII would involve the asymmetric center as a carbonium ion, so that non-retention of configuration would be expected. Similarly, in other mechanisms proposed[12] for the reaction of Grignard reagents with esters, it can be shown simply that the bond from oxygen to the asymmetric grouping would remain intact. Consequently it is safe to assume that no inversion or racemization accompanied the Grignard glycosylation, and hence also the Friedel–Crafts glycosylation, since the carbohydrates from both are the same. The stereochemical configurations in all the glycosylated aromatic hydrocarbons prepared in the previous catalytic studies[2] must, therefore, parallel the configurations of the parent sugars. Obviously, similar considerations argue for the same retention of configuration in the high-rotating anomeric sirups obtained as by-products in the Grignard glycosylation.

It is believed further that the same generalizations apply to the structure of the 1,1-diaryl-1-desoxyalditols previously obtained in the Friedel–Crafts process. An additional argument here is that since the substituted alditol may be formed from a stereochemically intact glycopyranosylbenzene by a rupture of the carbon–oxygen bond at the number 1 carbon rather than the number 5 carbon, Walden inversion at position 5 could not occur



Mention should be made of the fact that there is no theoretical possibility of a change in ring size during the Grignard glycosylation, thus justifying the naming of these as well as the earlier catalytic products on the basis of the ring size of the parent sugar. The experimental proof of this statement will be given in a later paper.

Lastly, it is interesting briefly to contrast the Grignard and Friedel–Crafts methods for glycosylating hydrocarbons. The yields in the Grignard reaction are so superior as to make it the ideal synthetic approach to such compounds, despite the lesser availability of the starting materials. The Grignard reaction is cleaner, quicker, and the products more readily isolated. Monosubstituted hydrocarbons are the sole products in the Grignard approach, and the complication of pyranose ring cleavage is absent. Finally the Grignard method is of far greater generality with regard both to the type of sugar and the type of hydrocarbon.

Experimental

Preparation of Glycosylated Hydrocarbons.—The general method for the synthesis of glycosylated hydrocarbons is illustrated with a specific case, namely, the preparation of tetraacetyl-D-glucopyranosylbenzene. The other reactions were conducted analogously. The quantity of Grignard reagent required for each run is roughly $2n + 4$ molecular equivalents, where n is the number of acetyl groupings in the polyacetylglycosyl halide employed.

Phenylmagnesium bromide was made in dry ether (75 ml.) from magnesium turnings (3.93 g., 0.1615 mole) and bromobenzene (17.3 ml., 0.1650 mole) using a three-necked flask equipped with stirrer, mercury seal, and a reflux condenser protected by a calcium chloride tube. The Grignard solution was stirred under reflux for an additional fifteen to thirty minutes after completion of the reaction. Heating was discontinued and a solution of tetraacetyl-α-D-glucosyl chloride (5.00 g., 0.0136 mole) in dry ether (70 ml.) was added with stirring over the course of an hour. The mixture was stirred under reflux for an additional four to five hours. The mixture was then cooled and the ether decanted into water. The gummy residue was decomposed by the cautious addition of water, and the last traces removed with a small quantity of acetic acid, combining these washings with the previous two phase system of ether and water. The two phases were shaken well, filtered (Celite) and separated. The ether layer was washed with water and the water layer with ether, combining the washings with the appropriate phases.

The ether layer was dried over anhydrous sodium sulfate and, if necessary, decolorized by filtration through a bed of Norit and Celite. Removal of the solvent at 100°, finally under diminished pressure, left 11.5 g. (slightly over the theoretical weight) of crude methyldiphenylcarbinol. This was recrystallized at 15° from a mixture of ether and petroleum ether to give crystals melting at 78–79°, and showing no mixed melting point depression with an authentic sample.

The water layer from the reaction was neutralized to litmus with sodium hydroxide solution, then concentrated to dryness *in vacuo* on the steam-bath. Acetylation of the residue was accomplished with acetic anhydride (150 ml.) and sodium acetate (5 g.) by heating and stirring at 100° for three hours. Care must be taken at the start of the acetylation to keep the vigor of the reaction under control and to avoid frothing over. The acetylation mixture was then cooled, poured into about 200 ml. of cold water and stirred for several hours to hydrolyze the excess anhydride. The precipitate which formed was extracted into ether and the extract was washed with water, saturated sodium bi-

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(12) *Cf.* Gilman, "Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 502 ff.

TABLE II

PROPERTIES OF GLYCOSYLATION PRODUCTS

	Alpha anomer			Beta anomer						
		Sp. rotation°			Sp. rotation[a]		Carbon, %[d]		Hydrogen, %[d]	
Compound	M. p., °C.	$[\alpha]^{20}\text{D}$	Concn.	M. p., °C.	$[\alpha]^{20}\text{D}$	Concn.	Calcd.	Found	Calcd.	Found
Tetraacetyl-D-glucosylbenzene	Sirup	(39.9)	1.029	155–156[b]	−18.6	2.010	...	...	...	...
p-(Tetraacetyl-D-glucosyl)-toluene	Sirup	(40.0)	1.772	138.5	−42.8	1.122	59.8	59.99	6.21	6.00
1-(Tetraacetyl-D-glucosyl)-naphthalene	Sirup	(95.4)	2.312	186.5–187	1.3	0.718	62.9	63.22	5.73	5.89
1-(Tetraacetyl-D-glucosyl)-butane	109–109.5[c]	77.2	1.050	Sirup	(3.5)	2.274	...	...	...	...
Triacetyl-D-xylosylbenzene	Sirup	(−23.0)	2.440	168.5–169[b]	−57.5	1.470	...	...	...	...
p-(Triacetyl-D-xylosyl)-toluene	Sirup	(−34.4)	3.790	126	−60.2	1.230	61.7	62.14	6.34	6.44
Heptaacetyllactosylbenzene	Sirup	(10.7)	3.595	217	− 7.5	1.140	55.2	55.27	5.80	5.70

[a] All rotations were taken in chloroform in a 2-dm. micro-tube of *ca.* 2 ml. volume. [b] These compounds have been prepared and analyzed previously. [c] *Anal.* Calcd.: C, 55.6; H, 7.27. Found: C, 55.89; H, 7.22. [d] All analyses were made by Dr. T. S. Ma.

carbonate solution (until gas evolution ceased), and again with water. It was then dried over sodium sulfate and decolorized by filtration through Norit. Removal of the solvent left 4.57 g. (82%) of the mixture of α- and β-tetraacetylglucosylbenzenes. Crystallization from the minimum quantity of 2-propanol gave 3.28 g. of the β-modification, m. p. 153–154°. By concentration of the mother liquors to dryness *in vacuo* at 100° there was obtained 0.81 g. of an amber sirup, the α-isomer. Each product was oxidized with permanganate in the previously described manner[2] to yield benzoic acid, as shown by m. p. and mixed m. p. A recrystallized sample of tetraacetyl-β-D-glucopyranosylbenzene, m. p. 155–156°, showed no mixed melting point depression (153–156.5°) with a sample of the tetraacetyl-D-glucopyranosylbenzene, m. p. 154–155°, from a Friedel-Crafts glucosylation.[2]

In Table II are listed the physical constants and analytical data for the new products obtained by the application of the Grignard glycosylation to other hydrocarbons and sugars. The sirupy α-anomers in each case were not analyzed since they could not be purified by crystallization or by other means. The lack of exact knowledge of their composition is further emphasized by placing their specific rotations in parentheses.

The Carbinols.—Results are given below for a few of the products which were obtained. The carbinols were not worked up in all cases.

Methyldiphenylcarbinol.—This product invariably melted between 78–80° after one recrystallization from ether and petroleum ether, which compares well with the values in the literature.[13]

Methyldi-*p*-tolylcarbinol.—Di-*p*-tolyl, m. p. 119–119.5°, was invariably isolated in small quantity along with the carbinol in reactions employing *p*-tolylmagnesium bromide. Previously reported melting points for di-*p*-tolyl are 121[14] and 122°. The identity was also confirmed by analysis.

Anal. Calcd. for $C_{14}H_{14}$: C, 92.25; H, 7.75. Found: C, 92.53; H, 7.79.

The crude methyldi-*p*-tolylcarbinol boiled at 134–135° (3 mm.) to give a slightly cloudy product, $n^{28}\text{D}$ 1.5822, after filtration through Norit. Repeated distillations at atmospheric pressure converted it to 1,1-di-*p*-tolylethene, m. p. 59–60°, after two recrystallizations from methanol. The m. p. of this olefin is given[15] as 61°.

Methyldi-*n*-butylcarbinol.—This consisted of a light, pleasant smelling oil, b. p. 63–64° (0.2 mm.), $n^{23}\text{D}$ 1.4333. Stadnikoff[16] reports 84–85° (10 mm.) as the boiling point.

Mechanism of the Grignard Glycosylation.—Phenylmagnesium bromide (0.0911 mole) was made in the usual manner in 150 ml. of ether. To this reagent was added with stirring over a two-hour period tetraacetyl-α-D-glucosyl bromide (0.0122 mole) in 100 ml. of dry ether. Meanwhile a second solution of *p*-tolylmagnesium bromide (0.0425 mole) in 50 ml. of ether was prepared and added, after completion of the above addition, over a ten-minute period to the partially completed reaction. The entire mixture was stirred for three and one-half hours, then separated in the usual fashion. The ether layer yielded methyldiphenylcarbinol, m. p. 76–78°. The water layer was acetylated to yield 3.38 g. of crude product, which was recrystallized from 45 ml. of 2-propanol. The first crop melted at 147–149°, and was recrystallized to give white needles, m. p. 148–150.5°. These needles melted at 150.5–152.5° when mixed with tetraacetyl-β-D-glucosylbenzene (m. p. 155–156°), and at 125–137° when mixed with *p*-(tetraacetyl-β-D-glucosyl)-toluene (m. p. 138.5°). Since one recrystallization failed to raise the m. p. of the product appreciably it was thought that mixed crystals of the two compounds were present. The presence of both the phenyl and *p*-tolyl group in the product was confirmed by oxidation. One-half gram of the product, m. p. 150.5–152.5°, was oxidized by refluxing for three hours with alkaline permanganate. The manganese dioxide was filtered off and washed with hot water. The filtrate was acidified, digested on the steam-bath for an hour, and filtered hot. The solid residue (0.02 g.) was dried, heated with an equal volume of phosphorus pentachloride, then cautiously decomposed with methanol. The ester was thrown down with water, collected, and recrystallized from dilute methanol. The ester was methyl terephthalate, m. p. and mixed m. p. 139.5–140°. The hot filtrate from above was cooled, extracted with ether, and the extract washed twice with water, dried and distilled to dryness. The residue weighed 0.13 g., m. p. 120–122° (with a small quantity of terephthalic acid not melting). The solid showed no depression when mixed with benzoic acid. From the weights of the two acids isolated it can be calculated (assuming equal oxidation yields) that the crude glycosylation product contained about 90% of tetraacetyl-D-glucopyranosylbenzene and 10% of *p*-(tetraacetyl-D-glucopyranosyl)-toluene.

Summary

The reaction between polyacetylglycosyl halides and aliphatic or aromatic Grignard reagents has been shown to be a general one yielding methyldialkyl- or methyldiarylcarbinols and glycosylated hydrocarbons. The yields of the carbinol are quantitative and the yields of glycosylated hydrocarbons are good. About three-fourths of the crude glycosylation products consist of a low-rotating, crystalline β-anomer, and one-fourth of a high-rotating, sirupy α-anomer.

The reaction apparently proceeds initially by interaction of the Grignard reagent with the carbonyl groups but before all the ester groups have reacted a metathetical reaction begins at the halide function.

It has been shown theoretically that the stereochemical configuration of the parent sugar is retained in both anomeric glycosylation products.

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[13] Klages, *Ber.*, **35**, 2616 (1902); Tiffeneau, *Ann. chim. phys.*, [8] **10**, 359 (1907).

[14] Zincke, *Ber.*, **4**, 396 (1871); Ullmann and Meyer, *Ann.*, **332**, 44 (1904).

[15] Bistrzycki and Reintke, *Ber.*, **38**, 840 (1905).

[16] Stadnikoff, *ibid.*, **47**, 2139 (1914).

It has been demonstrated that the tetraacetyl-β-D-glucopyranosylbenzene and the triacetyl-β-D-xylopyranosylbenzene prepared by the Grignard method are identical with the same compounds prepared by interaction of benzene and aluminum chloride with tetraacetyl-α-D-glucosyl chloride or triacetyl-α-D-xylosyl chloride. This indicates the absence of isomerization during the aluminum chloride process.

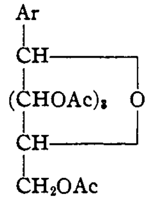
EVANSTON, ILLINOIS RECEIVED AUGUST 2, 1945

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

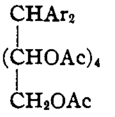
The Reaction of Aromatic Hydrocarbons with Polyacetylglycosyl Derivatives of Hydrocarbons

BY CHARLES D. HURD AND WILLIAM A. BONNER[1]

Previous reports[2] from this Laboratory have indicated that polyacetylglycosyl halides and polyacetylglycoses in the monosaccharide series react with aromatic hydrocarbons in the presence of aluminum chloride to yield, on subsequent acetylation, polyacetylglycosyl derivatives of aromatic hydrocarbons as well as 1,1-diaryl-1-desoxyalditol polyacetates. For aldohexose derivatives these two types are represented by structures I and II, respectively. The relative proportions of I and II formed depend on the reaction conditions, I being the predominant product when a molecular deficiency of catalyst is employed, and II being the sole product obtained with the theoretical quantity of catalyst.



I



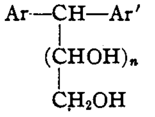
$$\begin{array}{l} \mathrm{CHAr_2} \\ | \\ \mathrm{(CHOAc)_4} \\ | \\ \mathrm{CH_2OAc} \end{array}$$

II

The fact that compounds of type I could be isolated from reactions where quantities of catalyst below the theoretical were employed, suggested that they were probably the precursors of type II, the steps intermediate being ring cleavage and arylation. Such a hypothesis could be verified readily by bringing I into reaction with the appropriate aromatic hydrocarbon. The same 1,1-diaryl-1-desoxyhexitol derivative should be obtained as was previously isolated from the over-all reaction.[2]

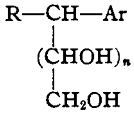
Tetraacetyl-β-D-glucosylbenzene, prepared from phenylmagnesium bromide[3] was treated with benzene and aluminum chloride. On warming, hydrogen chloride was evolved in quantity and the catalyst phase clumped together, finally dissolving to give a black, homogeneous solution. The reaction mixture was handled in the usual manner[2] to yield acetophenone and tar from the benzene layer, and 1,1-diphenyl-1-desoxy-D-glucitol pentaacetate from the water layer. In the same manner, the action of triacetyl-β-D-xyloxylbenzene upon benzene gave rise to the same 1,1-diphenyl-1-desoxy-D-xylitol tetraacetate as was obtained by the catalytic alkylation of benzene with β-D-xylose tetraacetate. It is evident, therefore, that the 1,1-diaryl-1-desoxyalditols synthesized in the earlier studies[2] arose in all probability from the intermediate glycosylbenzene and glycosyltoluene derivatives.

The discovery of this reaction makes possible the synthesis of hitherto inaccessible carbohydrate derivatives, especially the unsymmetrical 1,1-diaryl-1-desoxyalditols, such as III, and the 1-alkyl-1-aryl-1-desoxyalditols (IV).



$$\begin{array}{l} \mathrm{Ar{-}CH{-}Ar'} \\ \quad | \\ \mathrm{(CHOH)_n} \\ \quad | \\ \mathrm{CH_2OH} \end{array}$$

III



$$\begin{array}{l} \mathrm{R{-}CH{-}Ar} \\ \quad | \\ \mathrm{(CHOH)_n} \\ \quad | \\ \mathrm{CH_2OH} \end{array}$$

IV

The first extension of this synthesis to compounds such as III involved the use of *p*-(tetraacetyl-β-D-glucosyl)-toluene and benzene. The product anticipated from these reactants would be α-1-phenyl-β-1-*p*-tolyl-1-desoxy-D-glucitol. This product, a hydrate, m. p. 151.5–153.5°, $[\alpha]^{25}\mathrm{D}$ 55.8°, was readily obtained. Its structure was supported by analysis and by oxidation to *p*-benzoylbenzoic acid. The two prefixes in the above name, phenyl and tolyl, are arbitrarily designated α- and β- with "tolyl" as β- in view of the fact that β-D-glucosyl-toluene was the name assigned, on the basis of specific rotation, to the parent compound. Actually, the reaction may or may not proceed with Walden inversion, and until this fact, as well as the absolute configuration of the number 1 carbon atom in the parent compound, is established, a nomenclature based on actual configuration cannot be employed. These problems are under consideration at the present time.

To demonstrate the non-racemization of the number 1 carbon atom during the reaction, the action of tetraacetyl-β-D-glucosylbenzene on toluene was studied. A crystalline hydrate was isolated having properties different from those pre-

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(1) Corn Products Refining Company Research Fellow, 1941–1944.

(2) Hurd and Bonner, THIS JOURNAL, 67, 1664, 1759 (1945).

(3) Hurd and Bonner, *ibid.*, 67, 1972 (1945).