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Carbanilates of α- and β-Methyl-*d*-glucosides

BY W. M. HEARON, GORDON D. HIATT AND CHARLES R. FORDYCE

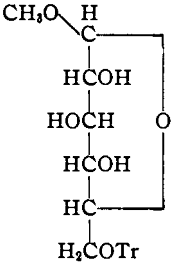
The carbanilate group imparts to its derivatives certain properties which are of considerable value for investigations in the sugar field. These include tendency toward high melting point, water insolubility, tendency to crystallize, ease of preparation under mild conditions, and stability toward mild acid and alkaline reagents.

Tessmer[1] in 1885 prepared carbanilate derivatives of certain sugar alcohols. In 1904, carbanilates of five common sugars were prepared.[2] Jolles and Botrini[3] in 1935 used the carbanilate group to prepare derivatives of four naturally occurring glucosides, and recently Wolfrom and Pletcher[4] have extended this reaction to include several of the simple methyl glucosides. The tendency for glucoside carbanilates to crystallize was utilized by Salmon and Powell.[5]

This report covers the preparation of representative mono, di, and tri carbanilates of α- and β-methyl-*d*-glucosides, and comparison of their physical properties.[5a]

α- and β-Methyl-*d*-glucoside-6-carbanilates. The tritylation[6] of α- or β-methyl-*d*-glucoside[7] gives the corresponding 6-monotrityl derivative (I). Acetylation of this gives 6-trityl methyl-*d*-glucoside 2,3,4-triacetate (II). However, both tritylation and acetylation may be carried out without isolating the intermediate.[8,9] Removal of the trityl group with complete retention of acetyl has been found by Helferich to proceed in acetic acid under the influence of dry hydrogen bromide.[10]

Methyl *d*-glucoside-2,3-4-triacetate (III) prepared by this procedure was carbanilated with phenyl isocyanate in pyridine to produce methyl *d*-glucoside-2,3,4-triacetate-6-carbanilate (IV), which upon deacetylation yielded methyl-*d*-glucoside-6-carbanilate (V). That neither mutarotation nor migration of groups had occurred during deacetylation was shown by reacetylation of the α-methyl-*d*-glucoside-6-carbanilate in good yields to a product whose melting point and mixed melting point showed no depression with that of α-methyl-*d*-glucoside-2,3,4-triacetate-6-carbanilate.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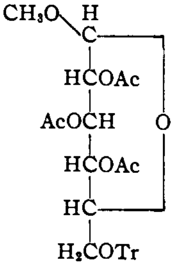
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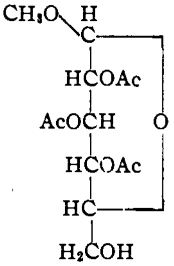
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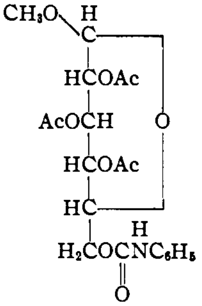
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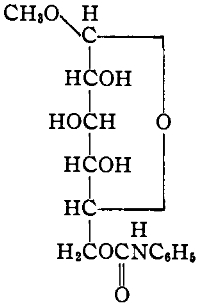
(V)

α- and β-Methyl-*d*-glucoside-2,3,4-triacetate-6-carbanilates.—After drying at 90° for two hours, 50 g. of α-methyl-glucoside-2,3,4-triacetate was dissolved in 40 cc. of dry pyridine and treated with 24 g. (1.5 theory) of phenyl isocyanate. After the initial liberation of heat, the mixture was heated under reflux at 100° for one hour, cooled, diluted with 30 cc. of methanol to remove excess isocyanate, and heated another ten minutes. After cooling, the mixture was poured into cold water, stirred until semi-solid, and the water decanted. Recrystallized twice from hot methanol, 46 g. of α-methyl-*d*-glucoside-2,3,4-triacetate-6-carbanilate (84%) was obtained melting at 147–148°; $[\alpha]^{25}\text{D}$ +145°, ($CHCl_3$, C = 1).

Anal. C, 54.62; H, 5.80; N, 3.26. Calcd. for $C_{20}H_{25}O_{10}N$: C, 54.7; H, 5.68; N, 3.19.

The crude product from 10 g. of the β-isomer was isolated by warm ligroin, then recrystallized from hot methanol–water; yield, 12 g. (87.5%); m. p. 147–148°; $[\alpha]^{25}\text{D}$ +15, ($CHCl_3$, C = 1).

Anal. C, 54.95; H, 5.84; N, 3.29.

α- and β-Methyl-*d*-glucoside-6-carbanilates.—Five grams of α-methyl-*d*-glucoside-2,3,4-triacetate-6-carbanilate was refluxed for two hours at 100° with 100 cc. of 0.5% hydrogen chloride in methanol. After cooling, 5 g. of barium carbonate was added, the mixture shaken and filtered. The neutral solution was evaporated by means of an air stream to a sirup containing a white precipitate. The sirup was dissolved in warm ethyl acetate, and filtered from the barium chloride. The solution deposited a gelatinous precipitate which was filtered off, washed with ethyl acetate, and dried. Recrystallization from ethyl acetate yielded 2.5 g. (70%), m. p. 131–133°; $[\alpha]^{25}\text{D}$ +115° (pyridine, C = 1).

Anal. Calcd. for $C_{14}H_{19}O_7N$: methoxyl, 9.9; C, 53.7; H, 6.07; N, 4.47. Found: methoxyl, 10.2; C, 53.38; H, 6.07; N, 4.46.

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(1) H. Tessmer, *Ber.*, **18**, 968 (1885).

(2) L. Maquenne and W. Goodwin, *Bull. soc. chim.*, [3] **31**, 430 (1904).

(3) E. Jolles and M. Botrini, *Gazz. chim. ital.*, **65**, 1217–1221 (1395).

(4) M. L. Wolfrom and D. E. Pletcher, THIS JOURNAL, **62**, 1151 (1940).

(5) M. R. Salmon and G. Powell, *ibid.*, **61**, 3507 (1939).

(5a) For table giving solubilities of the Compounds, order Document 1808 from the American Documentation Institute, 1719 N Street, N.W., Washington 6, D. C., remitting 50¢ for microfilm or 50¢ for photoprints.

(6) B. Helferich, *Ann.*, **440**, 8 (1924).

(7) β-Methyl-*d*-glucoside was prepared by the method of M. L. Maquenne, *Bull. soc. chim.*, [3] **33**, 469–470 (1905).

(8) Helferich, Klein and Schafer, *Ber.*, **59**, 81 (1926).

(9) Helferich and Schneidmuller, *ibid.*, **60**, 2002 (1927).

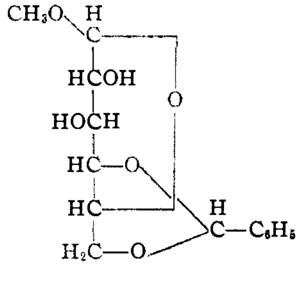
(10) Helferich, Broderich and Schneidmuller, *Ann.*, **458**, 111 (1927).

Prepared as the α-isomer, 5 g. of β-methyl-*d*-glucoside-2,3,4-triacetate-6-carbanilate with 100 cc. of 0.5% HCl in methanol gave after recrystallization from ethyl acetate, 2.7 g. (75%) melting at 144–145°. A mixed melting point with the triacetate precursor gave a 10° depression. $[\alpha]^{25}\text{D}$ −9°, (pyridine, *C* = 1).

Anal. C, 53.29; H, 6.08; N, 4.44.

α- and β-methyl-*d*-glucoside-2,3-dicarbanilates

Benzalation of α- and β-methyl-*d*-glucosides was carried out by a well-known procedure[11] to yield the 4,6-benzylidene methyl-*d*-glucosides (VI). Carbanilation in pyridine with phenyl isocyanate gave the corresponding 4,6-benzylidene methyl-*d*-glucoside-2,3-dicarbanilates (VII). Debenzalation gave the 2,3-dicarbanilates (VIII). To be sure that no mutarotation or Walden inversion had occurred, the α-methyl-*d*-glucoside-2,3-dicarbanilate was rebenzalated. The product had a melting point in agreement with that of the 4,6-benzylidene α-methyl-*d*-glucoside-2,3-dicarbanilate (VII) and a mixed melting point with that material showed no depression.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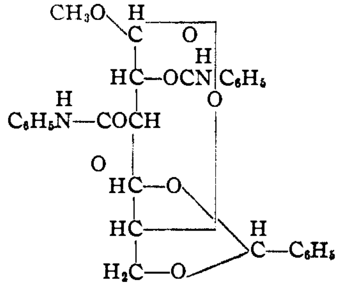
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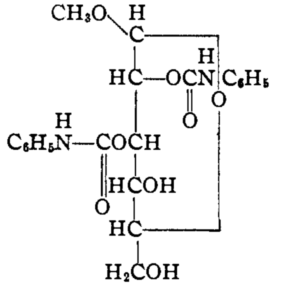
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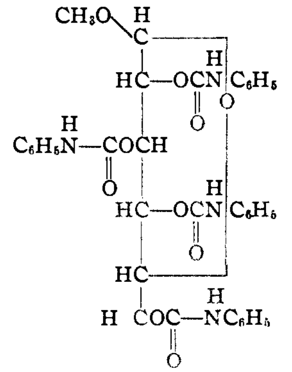
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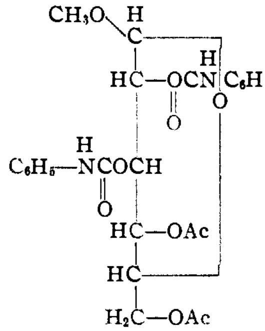
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α-Methyl-*d*-glucoside-2,3-dicarbanilate (VIII) further reacted completely with phenyl isocyanate in pyridine to give the tetracarbanilate (IX) previously prepared.[4] Both α- and β-methyl-*d*-glucoside-2,3-dicarbanilates (VIII) were acetylated in pyridine with acetic anhydride to give the corresponding 4,6-diacetates (X). These materials have somewhat better crystallizing properties than their precursors, as might be expected.

4,6-Benzylidene α- and β-Methyl-*d*-glucoside-2,3-dicarbanilates.—To 20 g. of 4,6-benzylidene α-methyl-*d*-glucoside (dried at 100° for four hours) dissolved in 40 cc. of dry pyridine was added 25 g. of phenyl isocyanate (1.5 × theoretical). After the initial evolution of heat, the mixture was heated for one hour at 100° under reflux. To the cold solution was added 10 cc. of methanol to remove excess isocyanate. After ten minutes, 700 cc. of ligroin was added and the mixture stirred on a steam-bath. The oil changed to a white solid and was removed by filtration while hot. The filtrate containing methyl carbanilate was discarded. The precipitate when dried was ground to a powder, digested with hot methanol, cooled, and filtered; yield, 30 g. (92%); m. p. 216–217°; $[\alpha]^{25}\text{D}$ +40°, ($CHCl_3$, *C* = 1).

Anal. Calcd. for $C_{28}H_{28}O_8N_2$: C, 64.6; H, 5.43; N, 5.38; CH_3O, 5.96. Found: C, 64.64; H, 5.36; N, 5.39; CH_3O, 5.91.

Nine grams of 4,6-benzylidene β-methyl-*d*-glucoside in 30 cc. of dry pyridine treated with 11.4 g. of phenyl isocyanate gave 14 g. of product from hot alcohol (85%), m. p. 247–248°; $[\alpha]^{25}\text{D}$ −50°, ($CHCl_3$, *C* = 1).

Anal. C, 64.94; H, 5.40.

α- and β-Methyl-*d*-glucoside-2,3-dicarbanilates.—Thirty grams of 4,6-benzylidene-α-methyl-*d*-glucoside-2,3-dicarbanilate was refluxed for two hours with 300 cc. of 0.75% hydrogen chloride in methanol. The hydrogen chloride was removed with 36 g. of barium carbonate, the filtrate concentrated to a sirup, and after dilution with chloroform was filtered from barium chloride and concentrated to a small volume. Seeding the solution yielded a white precipitate, which was recrystallized from a mixture of ligroin and ethyl acetate (3:1); yield 23 g. (92%); m. p. 151–153°; $[\alpha]^{25}\text{D}$ +55°, (pyridine, *C* = 1).

Anal. Calcd. for $C_{21}H_{24}O_8N_2$: C, 58.3; H, 5.60; N, 6.48. Found: C, 58.51; H, 5.53; N, 6.49.

4,6-Benzylidene β-methyl-*d*-glucoside-2,3-dicarbanilate (13.5 g.) in 135 cc. of 0.75% hydrogen chloride in methanol gave 6 g. of product from hot methanol (53%); m. p. 219–220°; $[\alpha]^{25}\text{D}$ −103°, (pyridine, *C* = 1).

Anal. C, 58.2; H, 5.54; N, 6.35.

α- and β-Methyl-*d*-glucoside-2,3-dicarbanilate-4,6-diacetates.—Acetylation of α-methyl-*d*-glucoside-2,3-dicarbanilate (6.5 g.) in 50 cc. of pyridine by 30 cc. of acetic anhydride for three hours at 100° gave, after recrystallization from methanol, 5.2 g. (67%), m. p. 189–190°; $[\alpha]^{25}\text{D}$ +124° (pyridine, *C* = 1).

Anal. Calcd. for $C_{25}H_{28}O_{10}N_2$: C, 58.2; H, 5.47; N, 5.43. Found: C, 58.31; H, 5.44.

β-Methyl-*d*-glucoside-2,3-dicarbanilate (0.44 g.) in 3 cc. of pyridine, treated with 2 cc. of acetic anhydride gave 0.4 g. from hot methanol (64%), m. p. 217–218°; $[\alpha]^{25}\text{D}$ −22° (pyridine, *C* = 1).

Anal. C, 58.2; H, 5.28; N, 5.48.

α- and β-Methyl-*d*-glucoside-2,3,4-tricarbanilates

6-Trityl methyl-*d*-glucoside (I) treated with phenyl isocyanate in pyridine gave the tricarbanilate (XI) which on detritylation produced the desired 2,3,4-tricarbanilate (XII).

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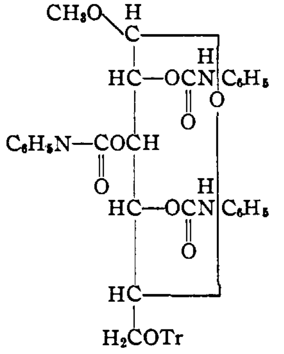
[11] Freudenberg, Toepffer and Anderson, *Ber.*, **61**, 1753 (1928).



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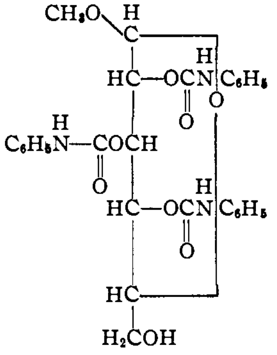

(XII)

6-Trityl α- and β-Methyl-*d*-glucoside-2,3,4-tricarbanilates.—To 10 g. of 6-trityl-α-methyl-*d*-glucoside, dried at 100°, in 25 cc. of dry pyridine was added 15.9 g. of phenyl isocyanate. After one hour at 100°, the mixture was washed with water, then with hot ligroin, after which it solidified. Recrystallization from benzene gave 12.8 g. (83%), m. p. 229–231°, $[\alpha]^{25}_{D}$ +52° ($CHCl_3$, *C* = 1).

Anal. Calcd. for $C_{47}H_{43}O_9N_3$: C, 71.2; H, 5.42; N, 5.29; trityl, 30.6. Found: C, 70.89; H, 5.35; N, 5.53; trityl, 30.1.

Prepared as the α-isomer, 10 g. of 6-trityl-β-methyl-*d*-glucoside in 15 cc. of pyridine and 15 cc. of phenyl isocyanate gave from hot benzene 7.45 g. (82%), m. p. 232–234°; $[\alpha]^{25}_{D}$ −5° ($CHCl_3$, *C* = 1).

Anal. C, 71.13; H, 5.45; N, 5.35.

α- and β-Methyl-*d*-glucoside-2,3,4-tricarbanilates.—6-Trityl α-methyl-*d*-glucoside-2,3,4-tricarbanilate (4 g.) was refluxed for two hours with 20 cc. of methanol containing 1% hydrogen chloride. After cooling, the solution was seeded with trityl methyl ether. The precipitate was filtered off and the filtrate evaporated on a steam-bath to a small volume then to dryness by means of air. The residue was dissolved in acetone diluted with benzene and the solution heated until most of the acetone had boiled off. On cooling, the product was precipitated and was filtered off. This purification was repeated twice, giving 1.5 g. (54%), m. p. 192–193°; $[\alpha]^{25}_{D}$ +84° ($CHCl_3$, *C* = 1). The product, when dissolved in concentrated sulfuric acid, gave no yellow color and on dilution with water produced no precipitate.

Anal. Calcd. for $C_{28}H_{29}O_9N_3$: C, 60.96; H, 5.27; N, 7.62. Found: C, 60.71; H, 5.20; N, 7.56.

Following the procedure for the α-isomer, 5 g. of 6-trityl-β-methyl-*d*-glucoside-2,3,4-tricarbanilate was refluxed for three hours in 40 cc. of methanol containing 1% hydrogen chloride. During this period of heating, β-methyl-*d*-glucoside-2,3,4-tricarbanilate precipitated. After cooling the precipitate was filtered, washed with methanol and dried; yield, 2.4 g. (68%), m. p. 230–232°. By repeated crystallization from ethyl acetate and acetone, the melting point could be raised to 234.5°; $[\alpha]^{25}_{D}$ +6° (pyridine, *C* = 1).

Anal. C, 60.83; H, 5.18; N, 7.59.

Acknowledgment.—The authors wish to express their appreciation for the assistance of John T. Clarke in connection with the experimental part of this paper.

Summary

Certain mono-, di- and tricarbanilates of both α- and β-methyl-*d*-glucosides have been prepared and identified.

For preparation of glucoside derivatives these carbanilates have the advantages of being high melting, stable, readily prepared, and, in general, easily crystallized.

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[CONTRIBUTION NO. 522 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

Unsaturated Synthetic Glycerides. VII. Preparation and Properties of Synthetic 1-Monoglycerides and Simple Triglycerides of Linoleic and Linolenic Acids[1]

BY B. F. DAUBERT AND A. R. BALDWIN[2]

During the investigation in this Laboratory on the preparation of synthetic glycerides containing unsaturated acids, it was determined experimentally that both linoleyl and linolenyl chlorides could be prepared, in good yields, from the respective debromination acids and oxalyl chloride.[3] The total diene conjugation in each acid chloride, when examined spectrophotometrically, was less than 1%. As a result of this work these acid chlorides were considered satisfactory for the synthesis of highly purified synthetic glycerides.

Since both 1-monolinolein and trilinolein have been reportedly prepared by other methods, a comparison of the properties of the compounds prepared by independent methods would serve to establish whether the glycerides synthesized, using acid chlorides as intermediates, exhibit any significant differences in properties.

The preparation of 1-monolinolein by heating dry potassium linoleate with 1-monochlorhydrin at 160° for one hour in an atmosphere of carbon dioxide was reported by Izar.[4] This same investigator also reported the synthesis of trilinolein from trichlorhydrin and potassium linoleate. In both instances, the compounds were reported as oily liquids but were not further characterized. More recently Black and Overley[5] reported the synthesis of 1-monolinolein and trilinolein by debromination of the respective 1-(9,10,12,13-tetrabromo)-stearin and tri-(9,10,12,13-tetrabromo)-stearin; the latter compounds were synthesized using tetrabromostearyl chloride. These investigators indicated that possible configurational changes could be avoided when de-

[1] The authors are indebted to the Buhl Foundation and to Swift and Company for grants in support of this investigation.

[2] Nutrition Foundation, Inc., Fellow.

[3] Wood, Jackson, Baldwin and Longenecker, THIS JOURNAL, **66**, 287 (1944).

[4] Izar, *Biochem. Z.*, **60**, 320 (1914).

[5] Black and Overley, THIS JOURNAL, **61**, 3051 (1939).