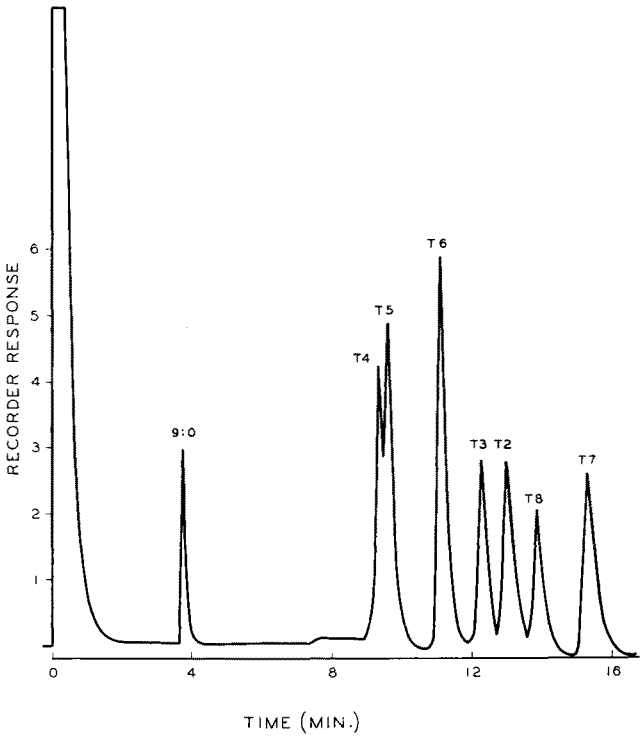

FIG. 3. Analysis of a mixture of seven isomeric nonynoic esters on an 85 ft DEGS capillary column at 136C. Reference compound is methyl nonanoate.

esters containing triple bonds at some distance from either end of the chain would be resolved only with great difficulty. This could account for the inability of Miwa et al. and Lefort et al. to resolve 18:T6 and 18:T9. The reported inability to resolve monoenoic positional isomers by GLC may be due to the fact that the compounds studied most thoroughly have also been of long chain length with the double bond near the middle of the molecule. Preliminary studies by us with the positionally isomeric *cis*-nonenoic esters have shown that they too are resolvable by GLC.

It has been reported (1–3) that 18:0 precedes 18:T9 on the polar DEGS column, but follows it on the nonpolar Apiezon L column. In the present study, the nine carbon acetylenic esters were eluted from both the DEGS and Apiezon L columns after their saturated counterpart. The observation (1–3) that the relative retention times of the acetylenic esters are greater on the polar column than on the nonpolar column was confirmed, however.

By plotting the log retention time versus carbon number of 18:T9 and 22:T13, Zeman obtained a line parallel to those for the saturated and monoenoic esters. From this he concluded that the behavior of the triple bond esters was similar to that of the other classes of esters and that log plots could be used to easily identify acetylenic esters. The two esters he chromatographed had their triple bond near the center of the molecule. From the results of the present study, it is unlikely that long chain acetylenic esters with their triple bond near either end of the molecule would fall on this line.

ACKNOWLEDGMENT

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Preparation of Some Linseed Esters of Methyl *a*-D-Glucopyranoside Using the Methoxycarbonyl Blocking Group[1]

E. J. DUFEK and W. J. DeJARLAIS, Northern Regional Research Laboratory,[2] Peoria, Illinois

Abstract

The three possible methoxycarbonyl derivatives of methyl 4,6-*O*-benzylidene-*a*-D-glucopyranoside have been prepared. The methoxycarbonyl at the C_2 position in the 2,3-di-*O*-methoxycarbonyl derivative is removed selectively in anhydrous ammonia. The ability of the methoxycarbonyl group to block selectively the C_2 hydroxyl in methyl glucoside has been utilized to synthesize some mono-, di-, and tri-linseed esters of methyl glucoside. The use of this new blocking group has permitted the first synthesis of some unsaturated esters of methyl glucoside.

RECENT WORK at the Northern Laboratory necessitated the use of some positionally distinct linseed acid esters of methyl *a*-D-glucopyranoside. Preparation of the tetralinseed ester is straightforward and unequivocal. Preparation of partial esters, such as the 2,3-di-*O*-linseed and 2,3,4-tri-*O*-linseed acyl esters, requires use of the 4,6-benzylidene and the 6-trityl groups as acid-removable blocking groups as is done in making certain acetates. Preparation of partial esters requiring blocking groups at the 2 and 3 positions or both, as well as at the 4 and 6 positions, is more difficult. Methyl 2- or 3-*O*-linseed acyl-*a*-D-glucopyranosides are examples. Blocking groups used in the 2 and 3 positions are the tosylate (10), trifluoroacetate (2,3), trichloroacetate (8), benzyl ether (5), and the benzylthiocarbonyl group (14).

The use of these groups was not feasible in this work. For example, because the tosylate group is removed by hydrogenation or alkali, it is not suitable with linseed esters. Trifluoroacetate and trichloroacetate groups are subject to migration; neither is trifluoracetate stable to aqueous acid. The benzyl

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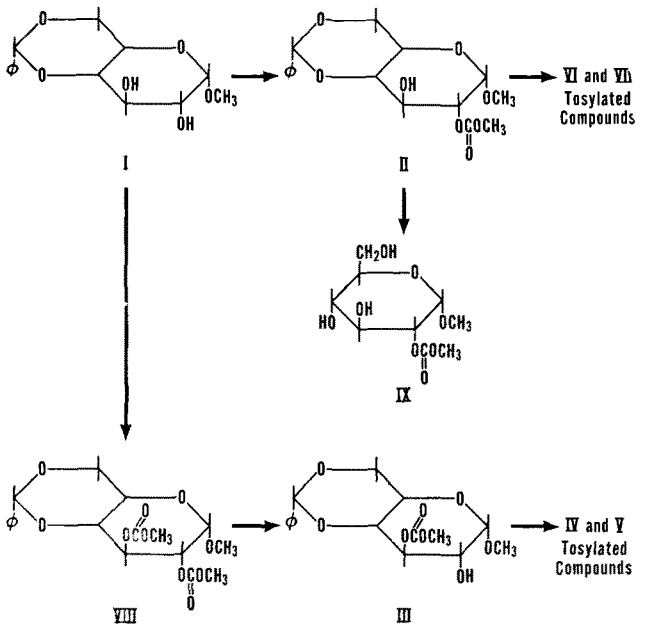
[2] A laboratory of the No. Utiliz. Res. Dev. Div., ARS, USDA.



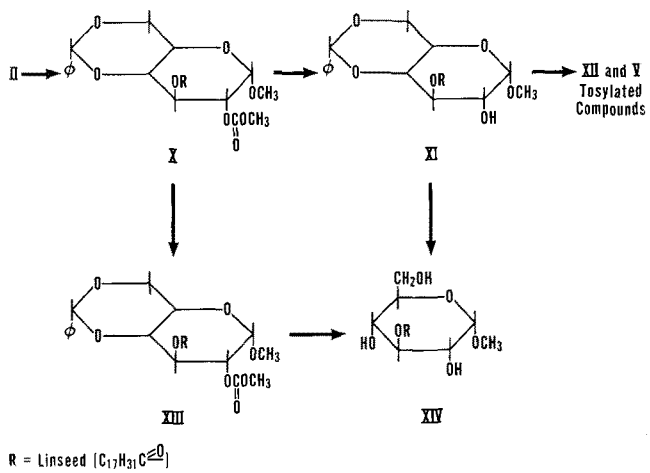
group may be removed by hydrogenation, although not always easily (14), but hydrogenation is not desirable in making unsaturated compounds. The 2-*O*-benzylthiocarbonyl 3-, 3,4-, and the 3,4,6-mono-, di-, and tri-benzoyl esters have been shown to be stable to aqueous acid and the benzylthiocarbonyl group was removed readily with hydrogen peroxide or Raney nickel. These reagents, however, are not suitable when olefinic unsaturation is present.

This paper describes the use of the *O*-methoxycarbonyl group as a new and selective blocking group in the preparation of certain unsaturated esters of methyl α-D-glucopyranoside.

Discussion

Reactivity of the 2-*O*-methoxycarbonyl blocking group in liquid ammonia is demonstrated by synthesis of methyl 3-*O*-methoxycarbonyl-4,6-*O*-benzylidene-α-D-glucopyranoside by selectively removing the 2-*O*-methoxycarbonyl group from methyl 2,3-di-*O*-methoxycarbonyl -4,6-*O*-benzylidene-α-D-glucopyranoside. Removal of the 2-*O*-methoxycarbonyl blocking group in basic media was used to synthesize three linseed esters of methyl α-D-glucopyranoside, namely: methyl 3-*O*-linseed acyl, 3,6-di-*O*-linseed acyl, and 3,4,6-tri-*O*-linseed acyl-α-D-glucopyranoside.

Treatment of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (I) in benzene and pyridine solution with methyl chloroformate yielded a mixture of the two possible mono- and the di-methoxycarbonyl derivatives from which the methyl 2-*O*-methoxycarbonyl derivative (II) was obtained by crystallization in 33% yield. Tosylation of II followed by treatment with barium hydroxide gave the known methyl 3-*O*-*p*-toluenesulfonyl-4,6-*O*-benzylidene-α-D-glucopyranoside (VII) (9), which reaction confirmed the structure of II. Also obtained in the preparation of II was a small amount of methyl 3-*O*-methoxycarbonyl-4,6-*O*-benzylidene-α-D-glucopyranoside (III) that melted at 186–187C with sublimation. Assignment of the 3-*O*-methoxycarbonyl structure to III was based on

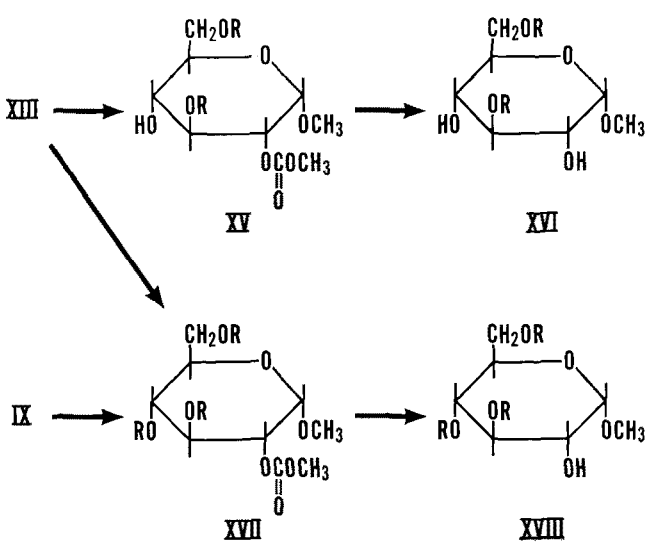


its conversion to the 2-*O*-p-toluenesulfonyl derivative (IV), followed by basic hydrolysis to the known methyl 2-*O*-toluenesulfonyl-4,6-*O*-benzylidene-α-D-glucopyranoside (V) (9).

Treatment of I with excess methyl chloroformate gave an 87% yield of methyl 2,3-di-*O*-methoxycarbonyl-4,6-*O*-benzylidene-α-D-glucopyranoside (VIII). When treated with liquid ammonia at its boiling point for 1 hr, VIII gave a 91% yield of the 3-*O*-methoxycarbonyl derivative (III). Since prolonged reaction of VII in liquid ammonia gave only the original starting material I, the 2-*O*-methoxycarbonyl group must be removed preferentially followed by removal of the 3-*O*-methoxycarbonyl group.

Removal of the benzylidene group from II with hydrochloric acid in acetone solution gave methyl 2-*O*-methoxycarbonyl-α-D-glucopyranoside (IX), which failed to crystallize. The acid hydrolysis of II demonstrates that the methoxycarbonyl group is stable to acid, thus allowing removal of acid-sensitive blocking groups (such as benzylidene and triphenylmethyl) at positions 4 and 6.

Treatment of II with linseed acid chloride in pyridine produced a 96% yield of methyl 2-*O*-methoxycarbonyl-3-*O*-linseed acyl-4,6-*O*-benzylidene-α-D-glucopyranoside (X).



R = Linseed ($C_{17}H_{31}C(=O)$)

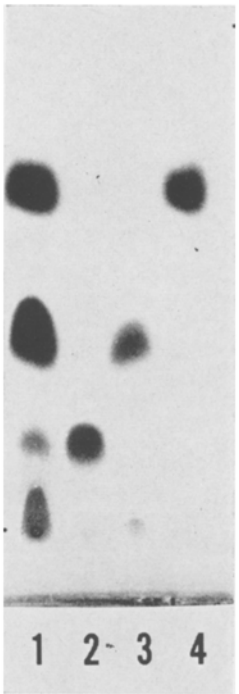


FIG. 1. Thin-layer chromatogram of linseed acylation of methyl 4,6-o-benzylidene-α-D-glucopyranoside developed in 25% ethyl acetate in hexane: (1) Crude acylation mixture; (2) compound XI; (3) compound XXI; (4) compound XIX.

When X was reacted with morpholine at room temperature for 20 hr and when the morpholine was removed under vacuum, the 2-*O*-methoxycarbonyl group was lost. Methyl 3-*O*-linseed acyl-4,6-*O*-benzylidene-α-D-glucopyranoside (XI) was obtained in a 74.5% yield. This compound had the correct carbon and hydrogen analysis; however, its iodine value (I.V.) of 82.7 was 11.1 units lower than calculated. This lowering of I.V. is attributed to some fractionation taking place during the recrystallization of XI from methanol. Because thin-layer chromatography (TLC) showed only one spot (see TLC discussion) this product was considered to be pure.

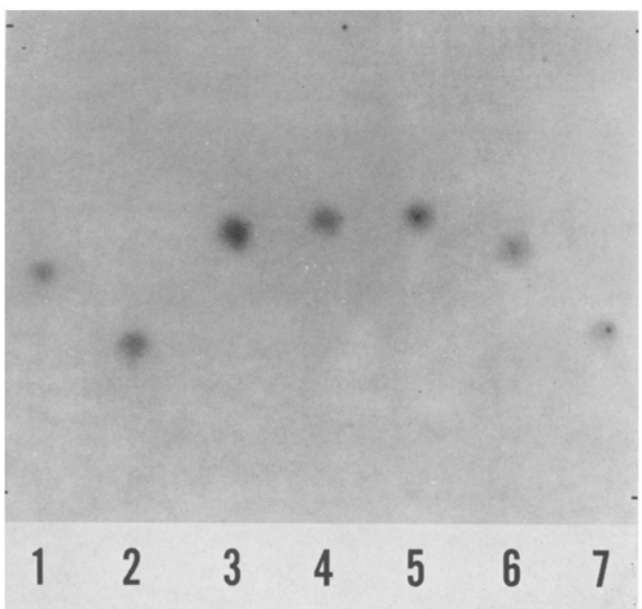


FIG. 2. Thin-layer chromatogram developed in 50% ethyl acetate in hexane: (1) compound II; (2) compound III; (3) compound VIII; (4) compound IV; (5) compound V; (6) compound VI; (7) compound VII.

Unequivocal structure proof of XI was obtained by first converting it to methyl 2-*O*-*p*-toluenesulfonyl-3-*O*-linseed acyl-4,6-*O*-benzylidene-α-D-glucopyranoside (XII) which was then hydrolyzed with barium hydroxide to the known methyl 2-*O*-*p*-toluenesulfonyl-4,6-*O*-benzylidene-α-D-glucopyranoside (V).

Compound XI was also obtained by reaction of X with liquid ammonia at the boiling point, but this procedure because of solubility problems is less convenient than that in which morpholine is used. By using diethyl amine as a solvent, a 54% yield of XI was obtained. Attempts to remove the methoxycarbonyl group from X with *n*-butylamine as the reactant and solvent for the aminolysis gave linseed acid *n*-butyl amide. Attempts to use other bases, such as sodium acetate or sodium bicarbonate in methanol, resulted in a methanolysis reaction yielding the methyl esters of linseed acids.

Removal of the benzylidene group from X by acidic hydrolysis gave methyl 2-*O*-methoxycarbonyl-3-*O*-linseed acyl-α-D-glucopyranoside (XIII). Treating XIII with morpholine at room temperature gave methyl 3-*O*-linseed acyl-α-D-glucopyranoside XIV. The acid hydrolysis of XI also gave XIV as shown by TLC.

When XIII in chloroform was treated with one molecular equivalent of linseed acid chloride following the procedure for the preparation of methyl 2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside (1), methyl 2-*O*-methoxycarbonyl-3,6-di-*O*-linseed acyl-α-D-glucopyranoside XV was obtained in a 41.1% yield. Allowing XV to stand overnight in morpholine gave methyl 3,6-di-*O*-linseed acyl-α-D-glucopyranoside (XVI) in a 68.4% yield.

Similarly, when treated with excess linseed acid chloride, XIII was converted to methyl 2-*O*-methoxycarbonyl-3,4,6-tri-*O*-linseed acyl-α-D-glucopyranoside (XVII). Compound XVII was also obtained in 67.4% yield from IX treated with excess linseed acid chloride. Compound XVII was then reacted with morpholine to yield methyl 3,4,6-tri-*O*-linseed acyl-α-D-glucopyranoside (XVIII).

During these syntheses extensive use was made of the TLC technique (Figs. 1–4). With the use of silicic acid (Stahl type, see ref. 13) on glass plates and hexane, ethyl acetate, or mixtures of these as solvents and development distances of 10 cm, no resolution of the component linseed acid esters was observed.

All reactions such as acidic hydrolysis to remove the benzylidene blocking group and as acylations with linseed acid chloride were followed by TLC in order to complete the reaction. After being passed through an alumina or silicic acid column, each compound was analyzed by TLC to determine if any migration of groups had taken place. No procedure is reported in the Experimental section when migration of a group was observed.

Based on TLC, little or no cleavage to linseed acid morpholide was observed in the reaction of the various methyl methoxycarbonyl linseed acyl glucopyranosides with morpholine. In the reaction with morpholine, and again based on TLC, little or no migration of the linseed group occurred if the reaction mixture was not heated. Trace amounts of the migration products when formed were removed successfully by passing the product through a silicic acid column.

Acylation of I with one equivalent of linseed acid chloride gave a mixture of the two possible mono- and the di-substituted linseed acyl esters (Fig. 1).

The top spot was identified as the methyl 2,3,-di-*O*-linseed acyl-4,6-*O*-benzylidene-α-D-glucopyranoside (XIX). XIX was prepared by diesterification of I with excess linseed acyl chloride. The second spot (most intense) was isolated by chromatographic separation on silicic acid. Because the C_2 hydroxyl in I is the more reactive, mono-esterification should give methyl 2-*O*-linseed acyl-4,6-*O*-benzylidene-α-D-glucopyranoside (XXI). Elemental analysis and iodine values were correct for this compound. The third spot (faint) was identified as XI by comparison with an authenic sample prepared from X by reaction with morpholine. The bottom spot (base line) was linseed acid. A similar TLC plate was obtained for the preparation of the mono- and di-methoxycarbonyl derivatives of I (Fig. 2). Again, the dimethoxycarbonyl compound (VIII) was shown to be the top spot by dimethoxycarbonylation of I. The second spot was shown to be the 2-*O*-methoxycarbonyl compound (II) by conversion to the 3-*O*-tosylate (VII), and the bottom spot was identified as the 3-*O*-methoxycarbonyl derivative (III). Compound III was identified as the 2-*O*-tosylate (V).

Among partial esters of the same degree of substitution, those in which the most exposed hydroxyl groups were esterified exhibited the largest R_f values. Such observations of the R_f values of the derivatives can provide confirmatory evidence of structure.

Some work has been carried out on the removal of the 2,3-di-*O*-methoxycarbonyl groups to prepare methyl 4- and 6-mono-, and 4,6-di-*O*-linseed acyl-α-D-glucopyranosides. Based only on TLC, these compounds can be prepared by using the methoxycarbonyl blocking groups, however, additional work must be carried out to confirm TLC results.

We believe that the methoxycarbonyl group will prove to be quite useful in the syntheses of partially acylated sugars where the requirements are for an acid-stable group removable with a mild base treatment.

Experimental

Starting Materials

All melting points were taken on a Kofler hot stage and are uncorrected. All solvent mixtures are expressed as v/v. TLC plates were prepared according to Stahl (13) with silicic acid (Brinkmann Instruments, Inc. see ref. 15). The plates were developed in ethyl acetate, hexane, or in mixtures of these solvents, and spots were detected with iodine vapor (12).

Alumina (chromatography grade F-20, 80–200 mesh, Aluminum Company of America) and silicic acid (chromatography grade, 100 mesh, Mallinckrodt Chemical Co.) were heated overnight at 110C. Morpholine (Matheson, Coleman, and Bell Co.) and methyl chloroformate (FMC Corp.) were purified by distillation before use. Pyridine (J. T. Baker Chemical Co.) was purified by distillation from sodium hydroxide. Methyl α-D-glucopyranoside (Corn Products Co.) was used as received.

Where no procedure is given, the compound was synthesized by standard procedures. Acylations were carried out in anhydrous chloroform-pyridine solutions.

Linseed acid chloride (linseed acyl chloride) was prepared from linseed acid (eq wt 279.8; I.V. 183.5) with phosphorous trichloride as the chlorinating agent (4). The linseed acid chloride was distilled through an all-glass falling film still. The yields were 85–92% and 99–100% pure as determined by hydrolysis and methanolysis reactions (bp 145–150C at 0.1 mm; I.V. 170.9).

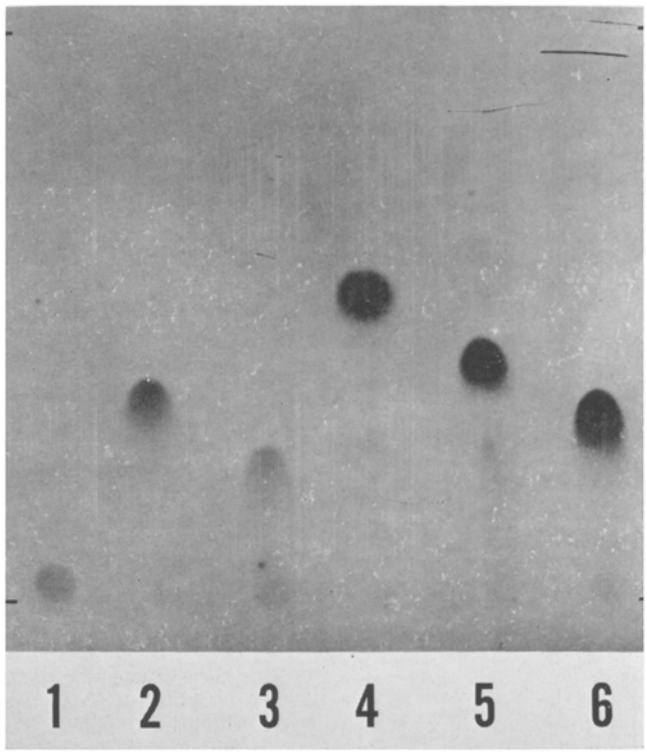


FIG. 3. Thin-layer chromatogram developed in 100% ethyl acetate: (1) Methyl α-D-glucopyranoside; (2) compound I; (3) compound IX; (4) compound XIII; (5) compound XIV; (6) compound XXII.

Linseed acid morpholide was prepared by the addition of linseed acid chloride to morpholine. After acidification and washing, the product was purified by chromatography on an alumina column. The water-white liquid had the following properties: I.V. 144.1; N_D^{25} 1.4875. Anal. Calc. for $C_{22}H_{39}NO_2$; N, 4.01. Found: N, 4.10.

Methyl 4,6-O-benzylidene-α-D-glucopyranoside (I). Compound I was prepared from methyl α-D-glucopyranoside by a standard method (6).

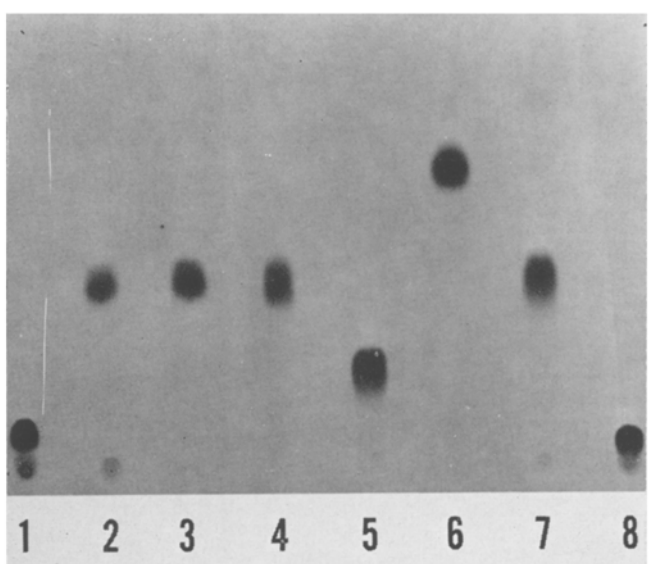


FIG. 4. Thin-layer chromatogram developed in 25% ethyl acetate in hexane: (1) Linseed acid morpholide; (2) compound X; (3) compound XII; (4) compound XV; (5) compound XVI; (6) compound XVII; (7) compound XVIII; (8) compound XX.

Methyl 2-O-methoxycarbonyl - 4,6-O-benzylidene-α-D-glucopyranoside (II). Methyl chloroformate (4.25 g in 50-ml anhydrous benzene) was added in 20 min to a rapidly stirred solution of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (14.2 g) in anhydrous benzene (100 ml) and pyridine (25 ml). The temperature was kept below 20C. After addition was complete, the solution (set overnight) was decanted from a viscous oil, washed successively with several portions of warm water, dilute hydrochloric acid until acidic, then with water till neutral to litmus, and then dried with magnesium sulfate. After removal of the solvent the residue was recrystallized from benzene (25 ml) and hexane (added to the cloud point). A second crystallization was made by adding ethyl acetate (15 ml) to the crystals and filtering rapidly to remove a small amount (< 0.5 g) of insoluble 3-*O*-methozycarbonyl isomer (see below). After the filtrate was heated, hexane was added to the cloud point. On cooling, the white needles (5.2 g, 33.5%) had mp of 125–127 C and $[\alpha]_D^{20}$ + 99.0° (c 1, $CHCl_3$). Anal. Calc. for $C_{16}H_{20}O_8$: C, 56.47; H, 5.88. Found: C, 56.54; H, 6.26.

Methyl 3-O-methoxycarbonyl-4,6-O-benzylidene-α-D-glucopyranoside (III). The small amount of insoluble material isolated in the preparation of II was recrystallized from ethyl acetate. The white crystals melted at 185–187C with sublimation taking place above 160C and $[\alpha]_D^{20}$ + 108.6° (c 1, $CHCl_3$). Anal. Calc. for $C_{16}H_{20}O_8$: C, 56.47; H, 5.88. Found: C, 56.36; H, 5.99.

Ammonolysis of Methyl 2,3-di-O-methoxycarbonyl-4,6-O-benzylidene-α-D-glucopyranoside. In a three-necked flask equipped with an anhydrous ammonia inlet tube, a solid carbon dioxide condenser capped with a sodium hydroxide drying tube, and a magnetic stirrer was placed 16 g of VIII. The flask was cooled to −40C and enough ammonia admitted rapidly to dissolve the starting material. After 1 hr the ammonia was evaporated as rapidly as possible. Ethyl acetate was added to the solid residue and stripped to dryness to remove trace amounts of ammonia.

Recrystallization from ethyl acetate gave III in 91.2% yield, mp 185–187C with sublimation. No depression in mp was observed when mixed with the byproduct obtained in the preparation of the 2-*O*-methoxycarbonyl isomer.

Ammonolysis of VIII for 6 hr as described gave a quantitative yield of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside.

Methyl 2-O-p-toluenesulfonyl-3-O-methoxycarbonyl-4,6-O-benzylidene-α-D-glucopyranoside (IV) was prepared from III. The white needles from ethanol melted at 110–111C; $[\alpha]_D^{20}$ + 45.2° (c 1, $CHCl_3$). Anal. Calc. for $C_{23}H_{26}O_{10}S$: C, 55.87; H, 5.26. Found: C, 55.94; H, 5.46.

Methyl 2-O-toluenesulfonyl-4,6-O-benzylidene-α-D-glucopyranoside (V) was prepared from IV and XII by treatment with a theoretical amount of barium hydroxide in methanol. After acidification followed by recrystallization from aqueous methanol the white needles melted at 152–154C. The mp for this compound reported in the literature is 153–154C (6,11). Anal. Calc. for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.50. Found: C, 57.71; H, 5.83.

Methyl 2-O-methoxycarbonyl-3-O-p-toluenesulfonyl-4,6-O-benzylidene-α-D-glucopyranoside (VI) was prepared from II. The white needles from methanol melted at 136–137C; $[\alpha]_D^{20}$ + 31.1° (c 1, $CHCl_3$). Anal. Calc. for $C_{23}H_{26}O_{10}S$: C, 55.87; H, 5.26. Found: C, 55.54; H, 5.15.

Methyl 3-O-p-toluenesulfonyl-4,6-O-benzylidene-α-D-glucopyranoside (VII) was prepared from VI by treatment with barium hydroxide in methanol. The white cottonlike needles melted at 165–166C. The reported melting point in the literature is 164C (9). Anal. Calc. for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.50. Found: C, 57.93; H, 5.50.

Methyl 2,3-di-O-methoxycarbonyl-4,6-O-benzylidene-α-D-glucopyranoside (VIII) was prepared by the addition of excess methyl chloroformate to I in anhydrous chloroform-pyridine solution. The white crystals (86.6% yield) from ethyl acetate-hexane melted at 97–99C and $[\alpha]_D^{20}$ + 74.5° (c 1, $CHCl_3$). Anal. Calc. for $C_{18}H_{22}O_{10}$: C, 54.27; H, 5.52. Found: C, 54.11; H, 5.56.

Methyl 2-O-methoxycarbonyl-α-D-glucopyranoside (IX). A solution of II (5 g), acetone (125 ml), and 0.2 *N* hydrochloric acid (15 ml) was refluxed for 5 hr. The acetone was removed under vacuum. The remaining water solution was extracted with two 10-ml portions of benzene. The water solution was evaporated to dryness to give 3.4 g of glassy product. Attempts to crystallize this material failed. $[\alpha]_D^{20}$ + 127.7° (c 1, $CHCl_3$). Anal. Calc. for $C_9H_{16}O_8$: C, 42.85; H, 6.31. Found: C, 42.85; H, 6.33.

Methyl 2-O-methoxycarbonyl-3-O-linseed acyl-4,6-benzylidene-α-D-glucopyranoside (X) was prepared by the addition of linseed acid chloride (10.7 g) to II (11.2 g) dissolved in pyridine (50 ml).

After washing and drying, the crude product was dissolved in hexane and passed through a column of alumina (6 × 1.9 cm) topped with carbon (2 cm). The column was eluted with 25% ethyl acetate-hexane solution (25 ml). Removal of the solvent under vacuo at 100C gave 18.3 g (96.1%) of water-white product which gave a single spot on TLC. I.V. Calc.: 84.6; obs. 82.3; N_D^{25} 1.5008; $[\alpha]_D^{20}$ + 37.0° (c 1, $CHCl_3$). Anal. Calc. for $C_{34}H_{50}O_9$: C, 67.77; H, 8.30. Found: C, 67.88; H, 8.54.

Methyl 3-O-linseed acyl-4,6-O-benzylidene-α-D-glucopyranoside (XI). a. Preparation in Morpholine: A solution of X (7.0 g) in morpholine (100 ml) was heated on a steam bath under anhydrous conditions. After 35 min the solvent was distilled rapidly under vacuum. The residue was cooled, dissolved in ethyl acetate, acidified with dilute hydrochloric acid, and washed until neutral to litmus. The solution was dried with magnesium sulfate and the solvent removed to give a colored waxy solid.

The solid was dissolved in 5% ethyl acetate in hexane and passed through a silicic acid column (7 X 4.4 cm). The column was eluted with 25% ethyl acetate in hexane (200 ml). Removal of the solvent and recrystallization from methanol gave a white-waxy product (4.7 g; 74.5%) melting at 96–99C; $[\alpha]_D^{20}$ + 60.4° (c 1, $CHCl_3$). I.V. Calc: 93.8; I.V. Found: 82.7. Anal. Calc. for $C_{32}H_{48}O_7$: C, 70.59; H, 8.82. Found: C, 70.54; H, 9.13.

b. Preparation in Anhydrous Ammonia: To a stirred solution of X (7.5 g) in diethylamine (75 ml) at −40C was added about 200 ml of anhydrous ammonia. The solution was maintained at the boiling point for 8 hr. The ammonia was allowed to boil off overnight and the diethylamine distilled under reduced pressure. Ethyl acetate was added and removed under reduced pressure to eliminate the remaining bases. The waxy material was treated as in

Part a to give 3.6 g (54% yield) of product melting at 95–99C. This product was identical with that of Part a by mixed melting point and TLC.

Methyl 2-O-p-toluenesulfonyl-3-O-linseed acyl-4,6-O-benzylidene-α-D-glucopyranoside (XII) was prepared by adding *p*-toluenesulfonyl chloride to XI dissolved in pyridine. The crude product in hexane was passed through a small alumina column. The water-white oil had the following properties: N_D^{25} 1.5171; $[\alpha]_D^{20}$ + 29.8° (c 1, $CHCl_3$). I.V. 73.1. Anal. Calc. for $C_{39}H_{54}O_9S$: C, 67.05; H, 7.73. Found: C, 67.02; H, 8.03.

Methyl 2-O-methoxycarbonyl-3-O-linseed acyl-α-D-glucopyranoside (XIII). A solution of X (10.0 g), acetone (250 ml), and 0.2 *N* hydrochloric acid (30 ml) was refluxed for 6 hr. Acetone was removed in vacuo while maintaing the temperature below 50C. The product was taken up in ethyl acetate, washed until neutral to litmus, and dried. After removal of the solvent the product was dissolved in hexane and passed through a silicic acid column (7 × 4.4 cm) and eluted with the following solvents: hexane (3 × 100 ml), ethyl acetate in hexane, 1% (100 ml), 5% (2 × 100 ml), 10% (100 ml), 25% (100 ml), and finally with ethyl acetate (3 × 100 ml). After TLC analysis the fractions containing the major product were combined and stripped to dryness. A light yellow oil (7.6 g; 89.2%) was obtained with observed I.V. of 99.4. Calc. I.V.: 99.6. N_D^{25} 1.4797; $[\alpha]_D^{20}$ + 84.4° (c 1, $CHCl_3$). Anal. Calc. for $C_{27}H_{46}O_9$: C, 63.02; H, 8.94. Found: C, 62.55; H, 8.83.

Methyl 3-O-linseed acyl-α-D-glucopyranoside (XIV). A solution of XIII (7.6 g) dissolved in morpholine (110 ml) was allowed to stand at room temperature for 20 hr. The morpholine was distilled as rapidly as possible under reduced pressure (< 5 mm). The residue was cooled, dissolved in ethyl acetate, acidified with dilute hydrochloric acid, and then washed until neutral to litmus. After drying with magnesium sulfate and removal of the solvent, the oil was dissolved in hexane and passed through a silicic acid column (7 × 1.9 cm). The column was eluted with the following solvents: (a) hexane (50 ml), (b) 25% ethyl acetate in hexane (25 ml), (c) 50% ethyl acetate in hexane (25 ml), and (d) ethyl acetate (25 ml). The hexane fraction was evaporated to give 4.6 g (68.2%) of viscous, light yellow oil which analyzed for methyl 3-*O*-linseed acyl-α-D-glucopyranoside. I.V. Calc.: 110.5. I.V. Found: 108.5 $[\alpha]_D^{20}$ + 93.0° (c 1, $CHCl_3$). Anal. Calc. for $C_{25}H_{44}O_7$: C, 65.79; H, 9.65. Found: C, 65.53; H, 9.75. Acidic hydrolysis of XI in acetone gave an oil with an identical TLC.

Removal of the solvent from Fractions b and c gave an oil which contained XIII and *N*-methoxycarbonyl morpholine. The latter was isolated by distillation and had N_D^{30} 1.4578. An authentic sample of *N*-methoxycarbonyl morpholine was prepared by the addition of methyl chloroformate to morpholine. The water-white liquid obtained boiled at 109–110C at 23 mm; N_D^{30} 1.4573. Anal. Calc. for $C_6H_{11}NO_3$: N, 9.70. Found: N, 9.67.

Methyl 2-O-methoxycarbonyl-3,6-di-O-linseed acyl-α-D-glucopyranoside (XV). Linseed acid chloride (5.7 g) in chloroform (50 ml) was added dropwise to a solution of XIII (10 g) in pyridine (25 ml) and chloroform (25 ml). After washing and drying, the product was dissolved in hexane and passed through a silicic acid column (12 × 4.4 cm). The column was eluted with 4–100 ml portions of each of the following solvents: hexane, 1%, 2%, 5%, 10% and 25% ethyl acetate in hexane. After TLC analysis the fraction containing the major product was stripped to dryness to give 6.2 g (41.1%) of a pale yellow oil with the following properties: I.V. Calc.: 130.9. I.V. Found: 129.5: N_D^{25} 1.4780; $[\alpha]_D^{20}$ + 50.3° (c 1, $CHCl_3$). Anal. Calc. for $C_{45}H_{76}O_{10}$: C, 69.58; H, 9.79. Found: C, 69.10; H, 9.90.

Methyl 3,6-di-O-linseed acyl-α-D-glucopyranoside (XVI). A solution of XV (3 g) in pyridine (50 ml) was allowed to stand for 20 hr at room temperature. The solvent was removed under reduced pressure (< 5 mm). The residue was dissolved in ethyl acetate, acidified, washed with water, and dried with magnesium sulfate.

A hexane solution of the crude product was passed through a silicic acid column (4 × 4.4 cm) and the column eluted with 2–100 ml portions of the following solvents: hexane, 1%, 2%, 5%, 10% and 25% ethyl acetate in hexane; and finally with ethyl acetate. After TLC analysis the solvent was removed from the fractions containing the product to give 1.9 g (68.4%) of a water-white oil. I.V. Calc: 141.5. I.V. Found: 137.5 N_D^{25} 1.4812. $[\alpha]_D^{20}$ + 47.2° (c 1, $CHCl_3$). Anal. Calc. for $C_{43}H_{74}O_8$: C, 71.72; H, 10.30. Found: C, 71.65; H, 10.36.

Methyl 2-O-methoxycarbonyl-3,4,6-tri-O-linseed acyl-α-D-glucopyranoside (XVII) was prepared by the addition of excess linseed acid chloride to IX in pyridine. The product was dissolved in hexane and first passed through an alumina column (6 × 4.4 cm) to remove the linseed acid then passed through a silicic acid column (12 × 4.4 cm). The second column was eluted with portions of hexane (total 1.5 l). The product was eluted with 5% ethyl acetate in hexane (4–100 ml) to give 9.4 g (68.4%) of a water-white oil. I.V. Calc.: 146.8. I.V. Found: 146.1. $[\alpha]_D^{20}$ + 44.1° (c 1, $CHCl_3$). N_D^{25} 1.4769. Anal. Calc. for $C_{63}H_{106}O_{11}$: C, 72.83; H, 10.21. Found: C, 72.87; H, 10.32.

This product was also obtained by the addition of linseed acid chloride to compound XIII.

Methyl 3,4,6-Tri-O-linseed acyl-α-D-glucopyranoside (XVIII). Compound XVII (4 g) dissolved in morpholine (50 ml) was treated according to the procedure for the preparation of XIV. The product was passed through a silicic acid column (12 × 1.9 cm). The following fractions were collected: hexane (3–50 ml), 1% ethyl acetate in hexane (3–50 ml), 5% ethyl acetate in hexane (3–50 ml), and finally with 10% ethyl acetate in hexane. After TLC analysis the fractions containing the product were combined and evaporated to give 2.6 g (67.4%) of a water-white oil. I.V. Calc: 155.6. I.V. Found: 153.9. $[\alpha]_D^{20}$ + 56.0° (c 1, $CHCl_3$). N_D^{25} 1.4802. Anal. Calc. for $C_{61}H_{104}O_9$: C, 74.69; H, 10.61. Found: C, 74.41; H, 10.99.

Methyl 2,3-di-O-linseed acyl-4,6-O-benzylidene-α-D-glucopyranoside (XIX) was prepared by the addition of excess linseed acid chloride to I (14.2 g). The crude product was dissolved in hexane and passed through a small alumina column. The column was eluted with 10% ethyl acetate in hexane solution. Evaporation of the solvent gave 21.6 g (53.6%) of water-white oil. I.V. Calc.: 126.1. I.V. Found: 126.5. N_D^{25} 1.4949. $[\alpha]_D^{25}$ + 31.2° (c 1, $CHCl_3$). Anal. Calc. for $C_{50}H_{78}O_8$: C, 74.44; H, 9.80. Found: C, 74.19; H, 9.84.

Methyl 2,3-di-O-linseed acyl-α-D-glucopyranoside (XX) was prepared from XIX (10 g) following the procedure given for XIII. The water-white oil (6.1 g, 68.1%) had the following properties: I.V. Calc.: 141.5; I.V. Found: 135.9; N_D^{25} 1.4831; $[\alpha]_D^{25}$ + 58.5° (c 1, $CHCl_3$). Anal. Calc. for $C_{43}H_{74}O_8$: C, 71.72; H, 10.30. Found: C, 71.69; H, 10.26.

Methyl 2-O-linseed acyl-4,6-O-benzylidene-α-D-glucopyranoside (XXI) was prepared by the dropwise addition of linseed acid chloride (17 g) to I (17 g) in pyridine (50 ml). After washing and drying 20 g of the crude product were passed through an alumina column (12 × 4.4 cm) and then through a silicic acid column (12 × 4.4 cm). The second column was eluted with 4–100 ml portions of hexane and with 4–100 ml portions of each of the following: 0.5, 1.0, 1.5, 2, and 10% ethyl acetate in hexane. After TLC analysis the fractions containing the product (second spot from the top, Fig. 1) were combined. Removal of the solvent gave 11.8 g of water-white oil. I.V. Calc.: 93.8. I.V. Found: 90.4. $[\alpha]_D^{25}$ + 102.3° (c 1, $CHCl_3$). N_D^{25} 1.5035. Anal. Calc. for $C_{32}H_{48}O_7$: C, 70.59; H, 8.82. Found: C, 70.17; H, 9.14.

Methyl 2-O-linseed acyl-α-D-glucopyranoside (XXII). Compound XXI (3.2 g) was dissolved in acetone (50 ml) containing 0.1 *N* hydrochloric acid (10 ml) and refluxed for 2 hr. The solvent was removed in vacuo and the residue extracted with ether. The ether solution was washed with water and dried. After removal of the ether, the residue was dissolved in hexane and passed through a silicic acid column (4 × 1.9 cm). The column was eluted with hexane (25 ml), 10% ethyl acetate in hexane (25 ml), 25% ethyl acetate in hexane (25 ml), and finally with ethyl acetate. Removal of the ethyl acetate gave a viscous yellow oil. I.V. Calc.: 110.5. I.V. Found: 109.7. $[\alpha]_D^{25}$ + 83.1° (c 1, $CHCl_3$). Anal. Calc. for $C_{25}H_{44}O_7$: C, 65.79; H, 9.65. Found: C, 65.62; H, 9.65.

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Further Observations on the Dicarbonyl Compounds Formed Via Autoxidation of Methyl Linoleate[1]

W. Y. COBB[2] and E. A. DAY

Department of Food Science and Technology, Oregon State University, Corvallis

Abstract

α-Dicarbonyls isolated from oxidized methyl linoleate and conclusively identified as DNP-osazones[3] were glyoxal, methyl glyoxal, α-keto hexanal, α-keto heptanal, and α-keto octanal.

Introduction

IN A PREVIOUS PAPER (1) tentative evidence was presented for the presence of a series of dicarbonyls occurring in oxidized methyl linoleate. Due to the small quantities of derivative isolated, conclusive identification of the compounds was not possible. The purpose of this paper is to present evidence for the identification of the dicarbonyls.

Experimental

The volume of packing used in the column chromatographic procedures (2–4) was increased and 2 in. diameter columns were employed to accommodate the rather large quantities of sample. Following complete resolution of the crude DNP-osazone mixture, pooled fractions were rechromatographed on partition columns (4); the column size was determined by the quantity of derivative isolated. Carbonyl-free solvents (5) were used throughout the experiment for column development and extraction purposes.

Methyl linoleate (19.62 g) was oxidized under a stream of oxygen in the manner described previously (1). The oxidized ester was passed over alumina 2,4 DNP-hydrazine reaction columns (2) containing about 60 g of packing. The DNP-hydrazones of monocarbonyls and the unaltered ester were eluted with 500 ml of benzene. The amount of 300 ml of acetic acid-chloroform (3:2) was then percolated through the columns to remove all remaining material. The eluate from 20 columns was pooled and the chloroform was removed by evaporation. Excess DNP-hydrazine reagent was added and the mixture was refluxed for 16 hr. Water was added, and the cooled mixture was extracted with chloroform. This extract was chromatographed on magnesia adsorption columns (3), and the DNP-osazone fraction recovered (1) was rechromatographed on Celite-ethanolamine columns (4). Columns for resolution of more polar derivatives (e.g., glyoxal, methyl glyoxal) consisted of 30 g Celite, 14 ml ethanolamine, and 4.5 g water. For the derivatives of longer chain dicarbonyls, columns consisting of 60 g Celite, 28 ml ethanolamine, and 2.0 g water were employed. All the columns were developed until adequate resolution of bands was obtained. The column packing was then extruded, and the individual

[1] Technical Paper No. 2012, Oregon Agricultural Experiment Station.
[2] Present address: Department of Food Science, North Carolina State of the University of North Carolina, Raleigh.
[3] DNP = 2,4,-dinitrophenyl.