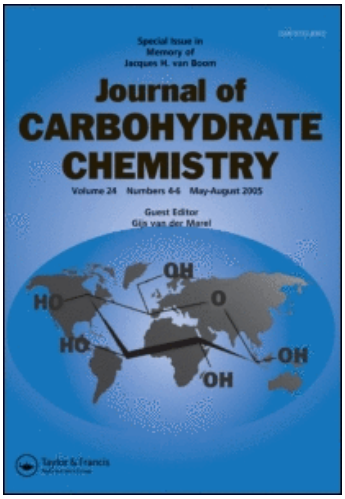

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A SIMPLE SYNTHESIS OF 2-DEOXY-3-O-METHYL-D-ARABINO-HEXOSE VIA PHOTODEOXYGENATION[1]

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ABSTRACT

2-Deoxy-3-O-methyl-D-arabino-hexose (2) was synthesized by photodeoxygenation in hexamethyl-phosphor-triamide/water with light of 254 nm. The isopropylidene-protecting group was photochemically resistent, whilst the benzylidene group was cleaved.

INTRODUCTION

The synthesis of deoxy sugars has been an important field of research for years.[3] Many laborious multi-step procedures for the regioselective deoxygenation of particu-

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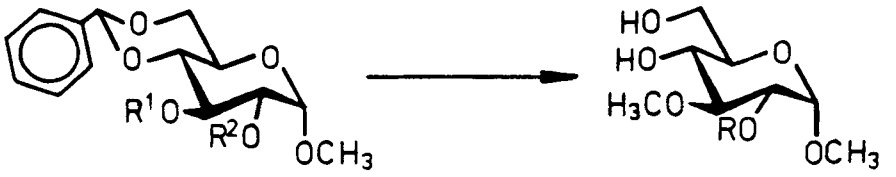
lar hydroxylfunctions have been developed.[4] The reduction of regioselectively prepared esters[5-10] with solvated electrons, which are prepared by irradiation in hexamethyl phosphortriamide (HMPT)/water (97/3, v/v)[2,4,10-16], works well.

This method shortens long reaction paths as we recently described for the synthesis of D-oleandrose 1.[2] Pivaloates yield more deoxygenated products than acetates.[13,16] Furthermore, the pivaloyl group can be regioselectively introduced into carbohydrates.[5,10,17] Other bulky esters such as benzoates and p-toluolsulfonates are not suitable for photodeoxygenation, because these esters are saponified.[4,16] The isopropylidene-protecting group[13,14b,17] and the tert-butyldimethylsilyl group[2,17,19] proved to be stable under the experimental conditions of the photodeoxygenation. The reaction of the ultraviolet light adsorbing benzylidene function, which is frequently used in carbohydrate chemistry, with photochemically generated solvated electrons has not yet been investigated. Irradiation under oxidative conditions (acetone, air) cleaves the benzylidene ketal to a mixture of the benzoates.[20] The present study investigates the suitability of this protecting group for the photodeoxygenation process illustrated by the synthesis of 2-deoxy-3-O-methyl-D-arabino-hexose 2, a constituent of Pteris inaequalis Baker var. aequata (MiQ) Tagawa.[21]

RESULTS AND DISCUSSION

The described[5,6] regioselective acylation of the readily available methyl 4,6-O-benzylidene-α-D-glucopy-

ranoside (3)[23] with pivaloyl chloride in pyridine could be improved and resulted in the 2-monopivaloate 4, isolated after crystallisation, (schema 1). Methylation of 4 with sodium hydride/methyl iodide in N,N-dimethyl formamide only gives the methyl ether 5 in 14 % yield (20 % turnover) due to the steric covering of the 3-hydroxyl group by the adjacent bulky O-substituents 2-O-pivaloyl and 4,6-O-benzylidene. Thus 4 was treated with the more reactive reagent methyl trifluoromethane sulfonate/2,6-di-tert-butyl pyridine/$Hg(CN)_2$ yielding 89 % of the methyl ether 5. Irradiation of 5 in HMPT/H_2O (97/3, v/v) does not lead to the deoxygenated product but cleaves the benzylidene-protecting group. After 48 h of irradiation the educt 5 is completely converted to 6. Extension of the reaction time to 24 h does not convert 6 but decomposes it. For characterisation 6 was converted by



	R^1	R^2
3	H	H
4	H	Piv
5	CH_3	Piv

	R
6	Piv
7	H

Scheme 1

Zemplén-cleavage to the known methyl 3-O-methyl-α-D-glucopyranoside 7,[25] which has recently been isolated from the holotoxines.[26]

Thus, the benzylidene-protection group is not only photochemically labile under oxidative conditions,[10] but also reacts in the photoreduction.

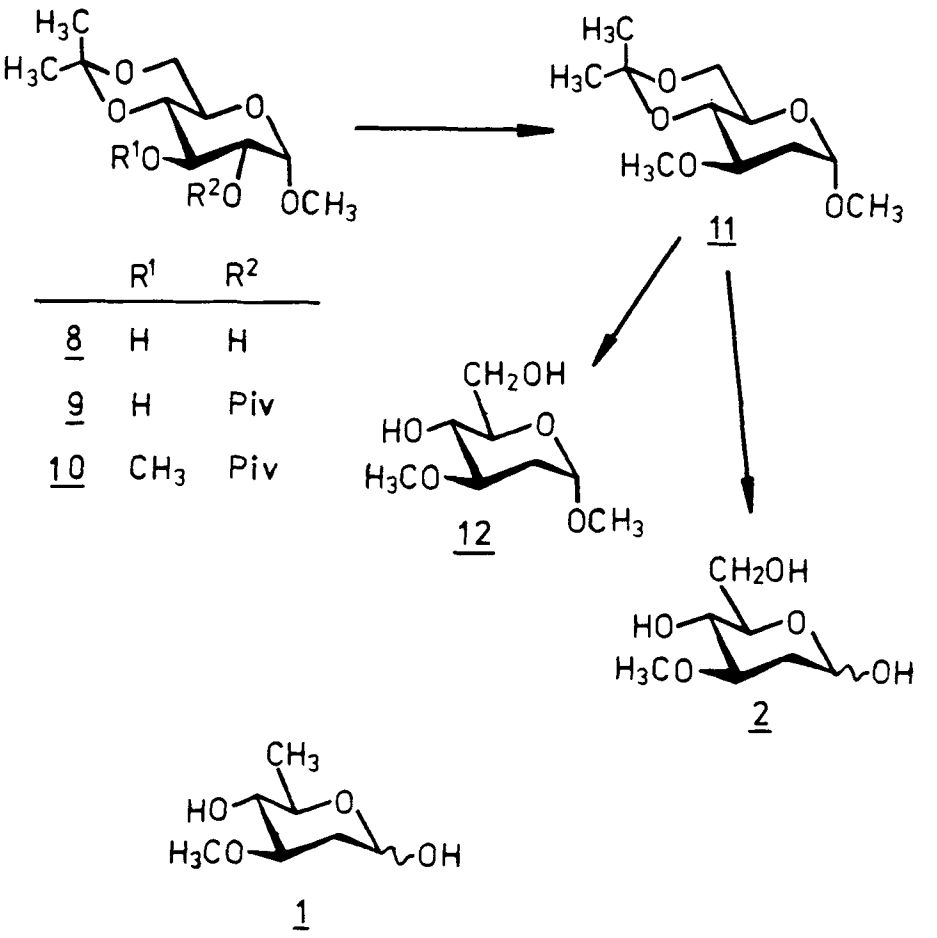
So the isopropylidene group was used, which proved to be stable under the experimental conditions.[13,14b,17] Methyl 4,6-O-isopropylidene-2-O-pivaloyl-α-D-glucopyranoside 9, which is easily accessible from 8,[17] was successfully methylated with methyl iodide/silver oxide to 10 (schema 2). In the subsequent photodeoxygenation of ester 10 the protecting group does not interfer, giving the 2-deoxy sugar 11 in high yields. Acidic hydrolysis of 11 or of 12, which is obtained by deprotection of 11 using the mild method of J. Thiem et al.,[12] gives the title compound 2.

This photochemical procedure shortens the conventional synthesis of 2-deoxy-3-O-methyl-D-arabino-hexose 2, which involves eight steps from D-glucose, to six steps, showing the synthetic power of the photodeoxygenation process.

EXPERIMENTAL

For general remarks and procedures see lit.[10]

Methyl 4,6-O-benzylidene-2-O-pivaloyl-α-D-glucopyranoside (4).[5] This compound was prepared according to



	R^1	R^2
8	H	H
9	H	Piv
10	CH_3	Piv

Scheme 2

the procedure for methyl 3,6-di-O-pivaloyl-α-D-mannopyranoside.[10,17]

Methyl 4,6-O-benzylidene-3-O-methyl-2-O-pivaloyl-α-D-glucopyranoside (5). a) To a solution of 4 (25.65 g, 70.0 mmol), 2,6-di-tert-butyl pyridine (35 ml, 160.0 mmol) and $Hg(CN)_2$ (0.42 g) in abs. CH_2Cl_2 (300 ml) was added methyl

trifluoromethane sulfonate (16.7 ml, 153.0 mmol) The solution was refluxed for 26 h, then cooled to 0°C and after addition of methanol (10 ml) to destroy the reagent the solvent was removed in vacuo and the resulting syrup chromatographed on silica gel with ethyl acetate/n-hexane (1:10) to give 23.7 g (89 %).

b) Methylation of 4 (19.5 g, 53.2 mmol) with sodium hydride/methyl iodide in tetrahydrofuran as usual[2] gave after chromatographic separation on silica gel with ethyl acetate/n-hexane (1:10) 2.86 g (14 %) 5 and 15.6 g (80 %) of the educt 4. Compd. 5: m.p. 40-43°C, $[\alpha]_D^{25}$ + 58.0° (c = 1.06, $CHCl_3$), ^{1}H-NMR ($CDCl_3$): δ = 1.23 (s, 9H, C-CH_3), 3.55 (s, 3H, 3-OCH_3), 3.6-4.3 and 4.6-4.8 (m, 6H, 2-H, 3-H, 4-H, 5-H, 6-H), 4.87 (d, 1H, 1-H), 5.50 (s, 1H, H-benzylidene), 7.2-7.5 (m, 5H, ArH), $J_{1,2}$= 4.5 Hz.

Anal. Calcd for $C_{20}H_{28}O_7$ (380.4):C, 63.14; H, 7.42. Found: C, 63.07; H, 7.56.

Photodeoxygenation of methyl 4,6-O-benzylidene-3-O-methyl-3-O-pivaloyl-α-D-glucopyranoside (5). A solution of 5 (8.00 g, 21.0 mmol) in HMPT/H_2O (240 ml, 97/3, v/v) was irradiated for 48 h as described in ref.[2,10,11] Additional 24 h of irradiation led to total decompositon. The reaction mixture was worked up as usual[2,10,11] and chromatographed on silica gel with ethyl acetate to give 2.11 g (34 %) of a syrup (6), $[\alpha]_D^{25}$ + 123.3 (c= 1.33, $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 1.25 (s, 9H, C-CH_3), 3.37 (s, 3H, 1-OCH_3), 3.60 (s, 3H, 3-OCH_3), 3.7-4.7 (m, 8H, 2-H,

3-H, 4-H, 5-H, 6-H, OH), 4.90 (1H, d, 1-H), $J_{1,2}$= 4.5 Hz; ^{13}C-NMR ($CDCl_3$): δ = 27.10 (C-$\underline{C}H_3$), 38.77 ($\underline{C}$-CH_3), 55.38, 61.12 (OCH_3), 61.89 (C-6), 70.06, 71.16, 73.72, 81.39 (C-2, C-3, C-4, C-5), 97.23, 178.05 ($\underline{C}$=O).

Anal. Calcd for $C_{13}H_{24}O_7$ (292): C, 53.41; H, 8.28.
Found: C, 53.20; H, 8.39.

Methyl 3-O-methyl-α-D-glucopyranoside (7). A solution of 6 (1.96 g, 6.7 mmol) and sodium methylate (120 mg) in abs. methanol (120 ml) was stirred at room temperature for 72 h. After neutralisation with acidic ion exchanger, the reaction mixture was filtered, the solvent removed and the residue chromatographed on silica gel with ethyl acetate to give 7 1.14 g (82 %): m.p. 102-105° C (lit. 80-81°C,[25a] 80-82°C,[27] 103-106°C[25b]), $[\alpha]_D^{25}$ + 158.4 (c= 1.01, acetone) (lit. $[\alpha]_D^{24}$ + 157.0±1 (c= 1.95, acetone),[25b] $[\alpha]_D^{21}$ + 164±2 (c= 0.86, H_2O),[25a] $[\alpha]_D^{25}$ + + 161(c= 1.4, acetone)[27]); ^{1}H-NMR (d_5-pyridine): δ = 3.43 (s, 3H, 1-OCH_3), 3.80 (s, 3H, 3-OCH_3), 3.7-4.3 (m, 6H, 2-H, 3-H, 4-H, 5-H, 6-H), 4.98 (s, 1H, 1-H), 5.7-7.7 (bs, 3H, OH); ^{13}C-NMR (d_5-pyridine): δ = 54.98 (3-OCH_3), 60.80 (1-OCH_3), 62.44 (C-6), 70.94, 73.14, 73.68, 85.35 (C-2, C-3, C-4, C-5), 101.13 (C-1).

Anal. Calcd for $C_8H_{16}O_6$ (208.2): C, 46.15; H, 7.75.
Found: C, 46,32; H, 7.81.

Methyl 4,6-O-isopropylidene-2-O-pivaloyl-α-D-glucopyranoside (9). This compound was prepared according to

literature[17] using a general procedure as described in ref.[10] to give 9 (75 %); m.p. 134°C (lit. 134°C[17]); $[\alpha]_D^{25}$ + 122.3 (c= 1.00, $CHCl_3$) (lit. $[\alpha]_D^{20}$ + 122.6 (c= 1.00, $CHCl_3$)[17]); ^{1}H-MMR ($CDCl_3$): δ = 1.24 (s, 9H, C-CH_3), 1.44 (s, 3H, CH_3-isopropylidene), 1.52 (s, 3H, CH_3-isopropylidene), 3.26 (bs, 1H, OH), 3.35 (s, 3H, OCH_3), 3.4-4.2 (m, 5H, 3-H, 4-H, 5-H, 6-H), 4.69 (dd, 1H, 2-H), 4.89 (d, 1H, 1-H); $J_{1,2}$= 3.9, $J_{2,3}$= 9.4 Hz; ^{13}C-NMR ($CDCl_3$): δ = 19.10, 29.09 (CH_3-isopropylidene), 27.02 (C-$\underline{C}H_3$), 38.85 ($\underline{C}$-CH_3), 55.44 (OCH_3), 62.32 (C-6), 62.98, 69.02, 73.54, 74.23 (C-2, C-3, C-4, C-5), 97.71 (C-1), 99.88 (C-isopropylidene), 178.24 ($\underline{C}$=O).

Anal. Calcd for $C_{15}H_{26}O_7$ (318.4): C, 56.59; H, 8.23. Found: C, 56.73; H, 8.08.

Methyl 4,6-O-isopropylidene-3-O-methyl-3-O-pivaloyl-α-D-glucopyranoside (10). A solution of 9 (10.0 g, 31.4 mmol) in methyl iodide (300 ml) was refluxed with silver oxide (90.0g) for 120 h. After filtration, the solvent was removed in vacuo and the remainig residue was chromatographed on silica gel with ethyl acetate/n-hexane (1:10) to give a syrup (10) 6.38 (65 %); $[\alpha]_D^{25}$ + 119.3 (c= 1.21, $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 1.22 (s, 9H, C-CH_3), 1.30 (s, 3H, CH_3-isopropylidene), 1.50 (s, 3H, CH_3-isopropylidene), 3.32 (s, 3H, 1-OCH_3), 3.48 (s, 3H, 3-OCH_3), 3.5-3.9 (m, 5H, 3-H, 4-H, 5-H, 6-H), 4.6-4.7 (m, 1H, 2-H), 4.82 (d, 1H, 1-H), $J_{1,2}$= 4.0 Hz.

Anal. Calcd for $C_{16}H_{28}O_7$ (332.4): C, 57.82; H, 8.49. Found: C, 57.73; H, 8.61.

Methyl 2-deoxy-4,6-O-isopropylidene-3-O-methyl-α-D-arabino-hexopyranoside (11). A solution of 10 (6.60 g, 19.9 mmol) in HMPT/H_2O (240 ml, 97/3, v/v) was irradiated for 48 h as described for 5 and worked up as usual [2,10,11] to give 11 2.76 g (60 %), colourless syrup, $[\alpha]_D^{25}$ + 93.8 (c= 1.13, $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ = 1.30 (s, 3H, CH_3-isopropylidene), 1.51 (s, 3H, CH_3-isopropylidene), 1.5-1.8 (m, 1H, 2a-H), 2.24 (ddd, 1H, 2e-H), 3.30 (s, 3H, 1-OCH_3), 3.40 (s, 3H, 3-OCH_3), 3.5-3.9 (m, 5H, 3-H, 4-H, 5-H, 6-H), 4.75 (d, 1H, 1-H); $J_{1,2}$= 4.2, $J_{2a,2e}$= 13.5, $J_{2e,3}$= 3.0 Hz; ^{13}C-NMR ($CDCl_3$): δ = 19.19, 29.34 (CH_3-isopropylidene), 35.55 (C-2), 54.61, 57.66 (OCH_3), 62.57 (C-6), 63.77 (C-5), 74.82, 75.83 (C-3, C-4), 99.07 (C-1), 99.61 (C-isopropylidene).
Anal. Calcd for $C_{11}H_{20}O_5$ (232.3): C, 56.88; H, 8.68. Found: C, 56.73; H, 8.95.

Methyl 2-deoxy-3-O-methyl-α-D-arabino-hexopyranoside (12). To a solution of 11 (1.86 g, 8.0 mmol) in abs. methanol (20 ml) was added dropwise trifluoroacetic acid anhydride (0.3 ml) and stirred for 3h at 20°C. The solvent was removed in vacuo and the remaining syrup dissolved in abs. methanol (10 ml) and again concentrated in vacuo. This procedure was repeated twice. The remaining syrup was chromatographed on silica gel with

ethyl acetate/n-hexane (1:5) to give 12 1.06 g (69 %), colourless syrup, $[\alpha]_D^{25}$ + 83.61, $[\alpha]_{546}^{25}$ + 99.1, $[\alpha]_{436}^{25}$ + 163.6, $[\alpha]_{235}^{25}$ + 245.8 (c= 1.10, $CHCl_3$).

Anal. Calcd for $C_8H_{16}O_5$ (192.2): C, 49.99; H, 8.39.
Found: C, 50.10; H, 8.27.

2-Deoxy-3-O-methyl-D-arabino-hexose (2). A solution of 11 (602 mg, 2.6 mmol) in acetic acid/water (20 ml, 1/3, v/v) was stirred at 100°C for 1 h and worked up as usual[2] to give 2 425 mg (99 %); m.p. 110-112°C (lit. 110-111°C,[2] 110-112°C[22]); $[\alpha]_D^{25}$ + 14.1 (c= 1.00, H_2O) (lit. $[\alpha]_D^{25}$ + 18.5 (c= 1.84, H_2O),[2] + 14.7 (c= 1.56, H_2O),[21] + 5.1 (5 min) → + 13.9 (30 min) (c= 1.37, H_2O).[22]

Anal. Calcd for $C_7H_{14}O_5$ (178.2): C, 47.19; H, 7.92.
Found: C, 47.31; H, 8.11.

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LITERATURE

1a. Reactions of partial acylated aldohexopyranosides, Part V; for Part IV see ref.[2]
b. Part of J. Dornhagen, Dissertation RWTH Aachen, 1985.

2. J. Dornhagen, A. Klausener, J. Runsink and H.-D. Scharf, Liebigs Ann. Chem., 1838 (1985).

3. N. R. Williams and J. D. Wander in: "The Carbohydrates", Vol. IB; W. Pigman and D. Horton, Eds., Academic Press, New York, NY, 1980, p. 761.

4. W. Hartwig, Tetrahedron, 39, 2609 (1983).

5. S. Tomić-Kulvenović, Carbohydr. Res., 85, 302 (1980).

6. A. H. Haines, Adv. Carbohydr. Chem. Biochem., 33, 11 (1976).

7. B. Matsuhiro and A. B. Zanhingo, Carbohydr. Res., 81, 330 (1980).

8. S. David and S. Hanessian, Tetrahedron, 41, 643 (1985).

9. Y. Kondo, Carbohydr. Res., 107, 303 (1982).

10. A. Klausener, E. Müller, J. Runsink and H.-D. Scharf, Carbohydr. Res., 116, 295 (1983).

11. A. Klausenr, J. Runsink and H.-D. Scharf, Liebigs Ann. Chem., 783 (1984).

12. J. Thiem and B. Meyer, Chem. Ber., 113, 3058 (1980).

13. P. M. Collins and V. R. Z. Munasinghe, J. Chem. Soc., Chem. Commun., 927 (1977).

14a. C. Portella and J.-D. Pete, Tetrahedron Lett., 26, 211 (1985).
b. J. P. Pete, C. Portella and D. Scholler, J. Photochem., 27, 128 (1984).

15. J. P. Pete and C. Portella, Bull. Soc. Chim. France, 195 (1985), and cited references.

16. G. Beyer, Dissertation RWTH Aachen 1984.

17. A. Klausener, Dissertation RWTH Aachen 1983.

18. D. M. Clode, D. McHall, J. B. Steridan, G. G. Birch and E. B. Rathbone, Carbohydr. Res., 139, 141 (1985).

19. W. C. Still and M.-Y. Tsai, J. Am. Chem. Soc., 102, 3654 (1980).

20a. R. W. Binkley, Adv. Carbohydr. Chem. Biochem., 38, 165 (1980).

b. J.Gelas, Adv. Carbohydr. Chem. Biochem., 39, 71 (1981) and cited references.

21. T. Murokami, N. Tanaka, T. Tezuka and C.-M. Chen, Chem. Pharm. Bull., 23, 1634 (1975).

22. H. R. Bollinger and D. A. Prins, Helv. Chim. Acta, 24, 1121 (1946).

23a. M. E. Evans, Carbohydr. Res., 21, 473 (1972).
b. D. M. Hall, Carbohydr. Red., 86, 158 (1980).

24. P. J. Stang, M. Hanack and L. R. Subramanian, Synthesis, 85 (1982) and cited references.

25a. R. W. Jeanloz and M. Gut, J. Am. Chem. Soc., 76, 5793 (1954).
b. A. P. Krasso, E. Weiss and T. Reichstein, Helv. Chim. Acta, 46, 2539 (1963).

26. I. Kitagana, Chem. Pharm. Bull., 24, 266 (1976).

27. H. Umezawa, T. Tsuchiya, R. Muto and S. Umezawa, Bull. Chem. Soc. Jpn., 45, 2842 (1972).