Acta Chemica Scandinavica B 31 (1977) 475—478

Decomposition of the *p*-Chlorophenyltriazene and *N*-Nitrosoacetamide of Glucosylamine. Formation of Cyclohexyl and Methyl Glucopyranosides

OLLE LARM, KJELL LARSSON and MONICA WANNONG

Department of Chemistry Div. II, Agricultural College of Sweden, S-750 07 Uppsala 7, Sweden

N-Acetyl-2,3,4,5-tetra-*O*-acetyl-*N*-nitroso-β-D-glucopyranosylamine and 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-*p*-chlorophenyltriazene, have been synthesized and their reactions in dichloromethane, methanol and cyclohexanol have been studied. In dichloromethane, penta-*O*-acetyl-β-D-glucopyranose and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine are formed. When the degradations are performed in methanol or cyclohexanol, the corresponding α- and β-glucosides are obtained with the former predominating. The best yields of glucosides are obtained from the triazene derivatives.

Decomposition of *N*-acetyl-2,3,4,6-tetra-*O*-acetyl-*N*-nitroso-β-D-glucopyranosylamine (*1*) in dichloromethane yields penta-*O*-acetyl-β-D-glucopyranose. When, however, the *N*-nitroso derivative is refluxed in methanol, a mixture of methyl tetra-*O*-acetyl-α- and β-D-glucopyranosides (3:1) is obtained.[1] This was suggested as an alternative way of preparing glycosides; especially α-linked glycosides. In the present work, the study has been extended to include the reaction of the *N*-nitroso derivatives in cyclohexanol and the reactions of the triazene derivative of glucosylamine in dichloromethane, methanol, and cyclohexanol.

RESULTS

The synthesis of *N*-acetyl-2,3,4,6-tetra-*O*-acetyl-*N*-nitroso-β-D-glucopyranosylamine (*1*) is described in Ref. 1.

When 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (*2*)[3] is reacted with *p*-chlorobenzenediazonium tetrafluoroborate in *N*,*N*-dimethylformamide, crystalline 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-*p*-chlorophenyltriazene (*4*) is obtained. Unlike *1*, compound *4* is stable at room temperature.

When heated in various solvents, the *N*-nitroso and triazene derivatives decompose with evolution of molecular nitrogen. The resulting mixtures were analysed by GLC-MS. When authentic samples were not available, a part of each reaction mixture was separated by column chromatography and the components were identified.

Decomposition of *1* in dichloromethane gives mainly penta-*O*-acetyl-β-D-glucopyranose (*7*), as reported earlier[1] (Table 1). When refluxed in dichloromethane in the presence of an acidic catalyst (boron trifluoride), *4* yields *2* and not 2,3,4,6-tetra-*O*-acetyl-*N*-*p*-chlorophenyl-β-D-glucopyranosylamine (*8*) as might have been expected.

When *1* is refluxed in methanol/pyridine (1:1)[1] or cyclohexanol/pyridine (1:1) the methyl- and cyclohexyl glucopyranosides *9*, *10*, *11*, and *12*, respectively, are formed. The ratio between α- and β-linked glucopyranosides is about 3:1 in both reactions, but the cyclohexyl glucopyranosides are obtained in lower yields (Table 1). In each of the above solvents, *N*-acetyl-2,3,4-tri-*O*-acetyl-*N*-nitroso-α-L-arabinopyranosylamine reacts similarly to *1*, giving the α- and β-anomers in similar yields and ratios. Refluxing *4* in methanol and cyclohexanol, respectively, in the presence of boron trifluoride yields the corresponding glucopyranosides, *9*,

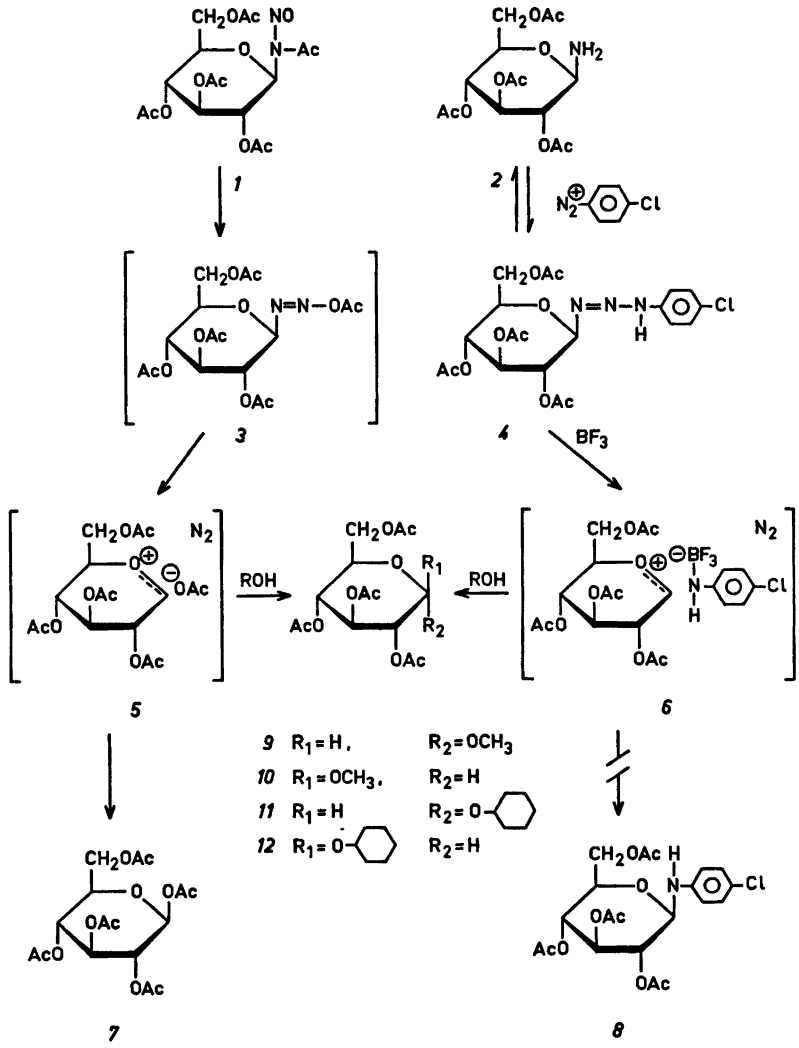

Table 1. The decomposition products and their yields [a] as estimated by GLC.

Decomposition of	Product (yield %)
1 in CH_2Cl_2/pyridine	*7*(65)
1 in CH_3OH/pyridine	*9*(75), *10*(25)
1 in $C_6H_{11}OH$/pyridine	*7*(29), *11*(31), *12*(11)
4 in $CH_2Cl_2BF_3$	*2*(15)
4 in CH_3OH/BF_3	*9*(85), *10*(15)
4 in $C_6H_{11}OH/BF_3$	*11*(60), *12*(15)

[a] The yields are calculated against *myo*-inositol, which is added as an internal standard.

10, *11* and *12*. The α-anomer is formed in higher yield in these reactions (Table 1). The yields of glucosides in most reactions were not quantitative. Other products, not accounted for, must have been formed.

DISCUSSION

Mechanisms for the decomposition of aliphatic *N*-nitrosamides and 1,3-di-substituted triazenes have been reviewed.[5] Thus, *N*-nitrosamides are believed to rearrange to a diazoester (*3*), which loses molecular nitrogen and an ion pair (*5*) is formed. When the reaction

is performed in an inert solvent, the ion pair collapses to yield the ester or possibly an alkene. When a large cation is involved in the ion pair, the reaction proceeds essentially with retention of configuration.[5] It has also been shown that neighbouring group participation is not important in these reactions.[5] In accordance with these findings, decomposition of *1* in inert solvents should give predominantly the β-anomer, which was also found.

Solvolysis of aliphatic *N*-nitrosoamides in protic solvents leads to products with retained or inverted configuration.[5]

If we assume that a solvent-separated ion pair is formed in the solvolysis reaction of *1*, this ion pair should react with the solvent giving both α- and β-linked glycosides. However, α-linked glycosides are formed preferentially.

The mechanism for the decomposition of triazenes (*4*) is similar to that for nitrosamide decomposition, but the reaction is catalyzed by acids.[5] As in the nitrosamide decomposition, loss of nitrogen leads presumably to the formation of the ion pair *6*. The ion pairs *5* and *6* have identical cations but different anions and should behave analogously on solvolysis. The triazene derivatives are more stable than the *N*-nitroso derivatives and give higher yields of glycosides in reactions with alcohols.

EXPERIMENTAL

General methods. Melting points are corrected. Optical rotations were measured with a Perkin-Elmer Model 141 polarimeter. NMR spectra were recorded at 100 MHz and ca. 30 °C on a Varian HA-100 D spectrometer, IR spectra with a Perkin-Elmer 337 spectrometer. TLC was performed on Silica Gel F_{254} (Merck) and column chromatography on Silica Gel 60 (Merck). GLC was conducted at 190–220 °C with a Varian model 2700 instrument fitted with a glass column containing 3 % of OV-225 on Gas-Chrom Q (100–120 mesh). For quantitative evaluations of the results, obtained by GLC, an Autolab, minigrator was used. GLC-MS was performed with a Varian CH 7 mass spectrometer.

Decomposition reactions of 1. The reactions in dichloromethane/pyridine and methanol/pyridine are already described.[1] Decomposition of *1* in cyclohexanol/pyridine (1:1) was performed and the reaction mixture was processed and analysed as described for the reaction of *1* in methanol/pyridine. Cyclohexyl glucosides were obtained in 40 % yield and the ratio between α and β-anomers was 3:1 (Table 1) as analysed by GLC and the products identified by GLC-MS.

The detector responses and relative retention times of acetylated cyclohexyl α- and β-D-glucopyranosides were determined by reference to a constant amount of *myo*-inositol.

In a preparative experiment, *N*-acetyl-tetra-*O*-acetyl-β-D-glucopyranosylamine (3 g) was dissolved in pyridine (30 ml) at 0 °C, dinitrogen tetraoxide (3 g) in dichloromethane (25 ml) was then added. After 30 min, the mixture was purged with nitrogen for 1 h at 0 °C. Cyclohexanol (30 ml) was added and the reaction mixture was heated for 1 h at 50 °C. The solution was concentrated and the residue was fractionated on a Silica Gel column (3 × 50 cm), which was irrigated with light petroleum–ethyl acetate (1:1 v/v). The separation was followed polarimetrically and by TLC. Three main products, *7* (0.8), *11* (0.94 g) and *12* (0.33 g) were obtained. Compound *7* had m.p. 135 °C, $[\alpha]_{578}$ +4° (*c* 1, chloroform); lit.[8] m.p. 132–134 °C, $[\alpha]_D$ +4°. Compound *11* had m.p. 38–39 °C, $[\alpha]_{578}$ +115° (*c* 1.8, chloroform); lit.[9] m.p. 40 °C, $[\alpha]_D^{20}$ +112°. Compound *12* had m.p. 121 °C, $[\alpha]_{578}$ −21°, lit.[9] m.p. 121–122 °C, $[\alpha]_D^{20}$ −23.8°.

*Synthesis of 1-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-3-*p*-chlorophenyltriazene (5).* To a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (*3*) (1 g) in *N*,*N*-dimethylformamide (5 ml) was added Na_2CO_3 (0.30 g) at 0 °C followed by a solution of *p*-chlorobenzenediazonium tetrafluoroborate (0.65 g) in *N*,*N*-dimethylformamide (10 ml).[4] After stirring at 0 °C for 5 min, chloroform (50 ml) was added and the reaction mixture was washed with ice-water (2 × 25 ml). The organic phase was dried ($MgSO_4$), filtered and evaporated to dryness. After recrystallisation (dichloromethane, light petroleum) 1.2 g of *5* was obtained as yellowish crystals and had m.p. 189–191 °C, $[\alpha]_{578}$ +2.5 (*c* 1.5, chloroform); λ_{max} ($CHCl_3$) 5.7 (C=O) 6.8 (C=C) and 7.2 (O–$COCH_3$) μm. ^{1}H NMR ($CDCl_3$): δ 7.35 (s, 4 H, phenyl), 5.54–5.10 (m, 3 H, H-1, H-2, H-2, H-3), 5.15 (q, 1 H, $J_{4,3}$ 7.5, $J_{4,5}$ 9.5, H-4), 4.3 (q, 2 H, $J_{5,6'}$ 4.5, $J_{6,6'}$ 12.5, H-6), 4.1 (q, 2 H, $J_{5,6}$ 2.5, $J_{6,6'}$ 12.5, H-6), 3.9 (m, 1 H, H-5), 2.06, 2.04, 2.03, 2.01 (4 s, 4 OAc). *Anal.* Calc. for $C_{20}H_{24}O_9N_3Cl$: C 49.4; H 4.9; N 8.7; Cl 7.3. Found: C 49.4, H 5.2, N 8.2, Cl 7.0.

Decompositions reactions of 4. (a) To a stirred solution of *4* (0.34 g) and a drying agent ($MgSO_4$, 1 g) in dichloromethane was added 45 % boron trifluoride–ethyl ether complex (0.4 ml). The colour changed from yellow to dark brown within 3 min at room temperature and TLC revealed that no starting material was left. Another 50 ml of dichloromethane was added and the reaction mixture was extracted with an aqueous solution of sodium hydrogen carbonate (2 %, 500 ml) and water (2 × 100 ml).

The organic layer was dried ($MgSO_4$), filtered and evaporated to dryness. Recrystallisation from dichloromethane/light petroleum yielded *2* (50 mg). The compound, 2,3,4,6-tetra-*O*-acetyl-*N*-*p*-chlorophenyl-β-D-glucopyranosylamine (*8*) could not be detected in the reaction mixture.

(b) The reaction was performed as described in (a), except that methanol (50 ml) instead of dichloromethane was added. Evolution of nitrogen was observed and after the reaction had gone to completion (20 min), pyridine (10 ml) was added together with an internal standard (*myo*-inositol). The reaction mixture was evaporated to dryness and acetylated. GLC revealed that the methyl glucosides [1] had been obtained in quantitative yield with an α/β ratio of 6/1 (Table 1).

(c) The reaction was performed as described in (b), using cyclohexanol (50 ml) instead of methanol. The reaction mixture was heated for 15 min at 95 °C. Cyclohexyl glucopyranosides were formed in 80 % yield and the α/β ratio was 4:1. The analyses were performed as described above.

Acknowledgements. We are indebted to Professor Olof Theander and to Docent Kjell Olsson for valuable discussions and to Professor Tore Timell for a sample of cyclohexyl α-D-glucopyranoside. Mr. Rolf Andersson is thanked for recording the NMR spectra. This work was supported by a grant from the Swedish Natural Science Research Council.

REFERENCES

1. Larm, O. *Carbohydr. Res. 43* (1975) 192.
2. Isbell, H. S. and Frush, H. L. *J. Org. Chem. 23* (1958) 1309.
3. Bertho, A. and Aures, D. *Justus Liebigs Ann. Chem. 592* (1955) 54.
4. Kuhn, R. and Krüger, G. *Justus Liebigs Ann. Chem. 628* (1959) 240.
5. White E. H. and Woodcock, D. J. In Patai, S., Ed., *The Chemistry of the Amino Group*, Wiley, New York 1968, Vol. 4, Chapter 8, and references therein.
6. Kawanisi, M., Otani, I. and Nozaki, H. *Tetrahedron Lett. 53* (1968) 5575.
7. Bayne, S. and Holms, W. H. *J. Chem. Soc. 621* (1952) 3247.
8. Allen, P. Z. *Methods Carbohydr. Chem. 1* (1962) 372.
9. Lindberg, B. *Acta Chem. Scand. 3* (1949) 151.

Received February 18, 1977.