4.3 g (16%) of 1-methyl-5-phenyltetrazole, m.p. 101–103°; lit. m.p. 101–102° (2). Evaporation of the filtrate and recrystallization of the residue from warm petroleum ether (b.p. 30–60°) gave 15.0 g (55%) of 2-methyl-5-phenyltetrazole, m.p. 50–51°; lit. m.p. 50–51° (2).

Methylation of 5-p-Nitrophenyltetrazole

Methylation of 7.2 g of 5-*p*-nitrophenyltetrazole by the procedure of Henry (2) gave a crude mixture which was separated into ether-soluble and ether-insoluble fractions. Recrystallization of the ether-soluble fraction from 85% isopropyl alcohol gave 0.42 g (6%) of 1-methyl-5-*p*-nitrophenyltetrazole, m.p. 121–123°; lit. m.p. 123–126° (16).

Recrystallization of the ether-insoluble fraction from 85% isopropyl alcohol gave 6.5 g (88%) of 2-methyl-5-*p*-nitrophenyltetrazole, m.p. 171–172°.

Anal. Calcd. for $C_8H_7N_5O_2$: C, 46.93; H, 3.44; N, 34.12. Found: C, 47.23; H, 3.74; N, 34.30.

Preparation of ^{15}N-Labelled Tetrazoles

The procedure of Roberts and co-workers (17) was used to prepare benzonitrile-^{15}N from benzoyl chloride and NH_4Cl-^{15}N (Merck, Sharp and Dohme of Canada, 95%-^{15}N). The benzonitrile-^{15}N was then converted into the methylated tetrazoles by the same procedures used above.

Acknowledgment

The authors are indebted to the National Research Council of Canada for financial support of this research.

1. W. G. FINNEGAN, R. A. HENRY, and R. LOFTQUIST. J. Am. Chem. Soc. **80**, 3908 (1958).
2. R. A. HENRY. J. Am. Chem. Soc. **73**, 4470 (1951).
3. J. VON BRAUN and W. RUDOLPH. Chem. Ber. **74**, 264 (1941).
4. H. G. MARKGRAF, W. T. BUCHMANN, and D. P. HOLLIS. J. Org. Chem. **30**, 3472 (1965).
5. G. B. BARLIN and T. J. BATTERHAM. J. Chem. Soc. B, 516 (1967).
6. B. M. LYNCH and Y. Y. HUNG. Can. J. Chem. **42**, 1605 (1964).
7. L. G. TENSMEYER and C. AINSWORTH. J. Org. Chem. **31**, 1878 (1966).
8. I. CROSSLAND. Acta Chem. Scand. **20**, 258 (1966).
9. (*a*) S. CASTELLANO, H. GUNTHER, and S. EBERSOLE. J. Phys. Chem. **69**, 4166 (1965); (*b*) T. M. SPOTSWOOD and C. I. TANZER. Australian J. Chem. **20**, 1227 (1967).
10. H. GUNTHER and S. CASTELLANO. Ber. Bunsenges. Physik. Chem. **70**, 913 (1966).
11. H. SPIESECKE and W. G. SCHNEIDER. J. Chem. Phys. **35**, 731 (1961).
12. R. E. MAYO and J. H. GOLDSTEIN. Mol. Phys. **10**, 301 (1966).
13. P. DIEHL. Helv. Chim. Acta, **44**, 829 (1961).
14. G. BINSCH, J. B. LAMBERT, B. W. ROBERTS, and J. D. ROBERTS. J. Am. Chem. Soc. **86**, 5564 (1964).
15. R. M. HERBST and J. M. MCMANUS. J. Org. Chem. **24**, 1044 (1959).
16. E. K. HARVILL, R. M. HERBST, C. W. ROBERTS, and H. T. F. GIVENS. J. Org. Chem. **17**, 262 (1952).
17. J. B. LAMBERT, W. L. OLIVER, and J. D. ROBERTS. J. Am. Chem. Soc. **87**, 5085 (1965).

Synthesis of 2-amino-2-deoxy-D-allose, 2-amino-2-deoxy-D-altrose, and 2-deoxy-D-*ribo*-hexose from 3,4,5,6-tetraacetoxy-D-*ribo*-1-nitro-1-hexene[1]

M. B. PERRY AND JANA FURDOVÁ

Division of Biosciences, National Research Council of Canada, Ottawa, Canada

Received April 11, 1968

3,4,5,6-Tetraacetoxy-D-*ribo*-1-nitro-1-hexene with methanolic ammonia afforded a mixture of 2-acetamido-1,2-dideoxy-1-nitro-D-allitol and 2-acetamido-1,2-dideoxy-1-nitro-D-altritol, which were converted *via* the Nef reaction to 2-acetamido-2-deoxy-D-allose and 2-acetamido-2-deoxy-D-altrose. 2-Amino-2-deoxy-D-allose hydrochloride and 2-amino-2-deoxy-D-altrose hydrochloride were obtained from the 2-acetamido-2-deoxy-glycoses.

Reduction of 3,4,5,6-tetraacetoxy-D-*ribo*-1-nitro-1-hexene afforded 3,4,5,6-tetra-*O*-acetyl-1,2-dideoxy-1-nitro-D-*ribo*-hexitol which was converted *via* the Nef reaction to 2-deoxy-D-*ribo*-hexose.

Canadian Journal of Chemistry, **46**, 2859 (1968)

2-Amino-2-deoxy-D-allose and 2-amino-2-deoxy-D-altrose were prepared in 34% and 28% yield respectively from 3,4,5,6-tetraacetoxy-D-*ribo*-1-nitro-1-hexene (1) by the general procedure in which polyacetoxy-1-nitro-1-alkenes are treated with ammonia to yield epimeric 2-acetamido-1,2-dideoxy-1-nitroglycitols which may be converted *via* a modified (2) Nef (3) reaction to the corresponding 2-acetamido-2-deoxy-glycoses (4–7).

2-Amino-2-deoxy-D-allose and 2-amino-2-deoxy-D-altrose have previously been synthesized from D-ribose in 7% and 28% yield respectively by the addition of hydrogen cyanide

[1]Issued as NRCC No. 10180.

to a substituted D-ribosylamine, followed by hemihydrogenation and subsequent hydrolysis of the α-amino nitriles (8). 2-Amino-2-deoxy-D-allose has been synthesized from methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside by an inversion at C-3 of its 3-*O*-methylsulfonyl derivative (9, 10), from the oxazoline derived from 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-D-glucofuranose (11), and by intramolecular rearrangement of D-*ribo*-hexulosylamine (12).

3,4,5,6-Tetraacetoxy-D-*ribo*-1-nitro-1-hexene with saturated methanolic ammonia solution gave a mixture of 2-acetamido-1,2-dideoxy-1-nitro-D-allitol and 2-acetamido-1,2-dideoxy-1-nitro-D-altritol which could not be separated by fractional crystallization. The mixed 2-acetamido-1,2-dideoxy-1-nitroglycitols on treatment with dilute sulfuric acid afforded a mixture of 2-acetamido-2-deoxy-D-allose and 2-acetamido-2-deoxy-D-altrose, contaminated with a small quantity of the corresponding aminoglycoses. The product after treatment with aqueous acetic anhydride, was shown by paper chromatography, to contain only the 2-acetamido-2-deoxyglycoses and pure crystalline 2-acetamido-2-deoxy-D-allose was obtained from ethanol solution of the reaction mixture. The residue remaining after the removal of the 2-acetamido-2-deoxy-D-allose was fractionated by cellulose column chromatography to yield chromatographically pure 2-acetamido-2-deoxy-D-allose and 2-acetamido-2-deoxy-D-altrose. The two 2-acetamido-2-deoxyglycoses, on hydrolysis with hot dilute hydrochloric acid, afforded chromatographically pure 2-amino-2-deoxy-D-allose hydrochloride and 2-amino-2-deoxy-D-altrose hydrochloride. The acetamidoglycoses and aminoglycoses had chemical and physical properties in close agreement with those previously recorded for these compounds. This preparative procedure gives a simple and direct route to the aminoglycoses and should be of practical value.

2-Deoxy-D-*ribo*-hexose was prepared in 88% yield from 3,4,5,6-tetraacetoxy-D-*ribo*-1-nitro-1-hexene by reduction with hydrogen to give 3,4,5,6-tetra-*O*-acetyl-1,2-dideoxy-1-nitro-D-*ribo*-hexitol which underwent the Nef reaction to yield 2-deoxy-D-*ribo*-hexose. 2-Deoxy-D-*ribo*-hexose has been prepared from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (13, 14) which with sodium thiomethoxide gave methyl 4,6-*O*-benzylidene-2-*S*-methyl-2-thio-α-D-altroside which on hydrogenation afforded methyl 2-deoxy-α-D-*ribo*-hexopyranoside. It is of interest that 2-deoxy-D-*ribo*-hexose shows inhibition of glycolysis of human leucocytes, human leukemic cells, and a number of animal tumors (15).

The method described in this note for the synthesis of 2-deoxy-D-*ribo*-hexose provides a practical route to the glycose. The physical and chemical properties of the 2-deoxy-D-*ribo*-hexose agree with those recorded by other workers and its identification was further established by its reduction with sodium borohydride to the known crystalline 2-deoxy-D-*ribo*-hexitol.

Experimental

Paper chromatography was performed by the descending method (16) on Whatman No. 1 filter paper using pyridine – ethyl acetate – water (2:5:5 v/v, top layer). The glycoses were detected with (*a*) 2% silver nitrate in acetone followed by 2% sodium hydroxide in ethanol (17), (*b*) 2% *p*-anisidine hydrochloride in ethanol (18), or (*c*) 0.02 *M* aqueous sodium metaperiodate followed by ethylene glycol – acetone – sulfuric acid (50:50:0.3 v/v) and 6% aqueous sodium 2-thiobarbiturate (19). The rates of movement of the glycoses on the chromatograms are quoted relative to D-galactose (R_{Gal}).

Gas–liquid partition chromatography was carried out using a Hewlett–Packard model 402 chromatograph with a hydrogen flame detector and fitted with glass U tubes (4 ft × 6 mm × 3 mm internal diameter) packed with 10% neopentylglycol sebacate polyester on 80–100 mesh acid washed Chromosorb W, maintained at 210°. Dry helium was used as the carrier gas and retention times of the compounds are quoted relative to 2-acetamido-2-deoxy-1,3,4,5,6-penta-*O*-(trimethylsilyl)-D-glucitol (T_{GN}).

Melting points were determined on a Fisher–Johns apparatus and are corrected. Solutions were concentrated under reduced pressure below 40°. Optical rotations were determined at 20° using a Perkin–Elmer 141 polarimeter.

*2-Amino-2-deoxy-*D*-allose and 2-Amino-2-deoxy-*D*-altrose*

A solution of 3,4,5,6-tetraacetoxy-D-*ribo*-1-nitro-1-hexene (18.5 g) in absolute methanol (160 ml) cooled to 0° was saturated with dry ammonia gas (about 1 h) and the mixture was then allowed to stand at room temperature for 18 h. The reaction mixture was concentrated to a syrup which was triturated with warm chloroform solution (3 × 100 ml) to remove acetamide. The residual syrup (12 g) was then dissolved in a solution of $Ba(OH)_2 \cdot 8H_2O$ (14.6 g) in water (220 ml) and this solution was added dropwise with vigorous stirring to a cold mixture of sulfuric acid (12.5 ml) and water (100 ml). After stirring at 10° for 2 h the mixture was left at 20° for 18 h. The solution was neutralized with barium carbonate and the filtered solution after concentration to about 100 ml was

treated with Dowex-1($CO_3^=$) ion-exchange resin (30 ml), methanol (15 ml), and acetic anhydride (0.5 ml); the mixture was then shaken at room temperature for 30 min. The filtered solution was concentrated to a syrup (10 g) and paper chromatographic examination of the product showed two spots having R_{Gal} 1.58 and 1.84 in the visual ratio of 2:1, which corresponded in rates of movement with authentic 2-acetamido-2-deoxy-D-allose and 2-acetamido-2-deoxy-D-altrose respectively.

The syrup was dissolved in hot ethanol (50 ml) and, on cooling to 5°, crystalline 2-acetamido-2-deoxy-D-allose (3.08 g) was obtained and the concentrated mother liquor, which failed to yield further crystalline material, was shown by paper chromatography to contain 2-acetamido-2-deoxyallose and 2-acetamido-2-deoxyaltrose. This mixture was fractionated on a cellulose column (4.5 × 70 cm) using butan-1-ol half-saturated with water as the mobile phase. 2-Acetamido-2-deoxy-D-altrose (3.5 g) was eluted first and was followed by the 2-acetamido-2-deoxy-D-allose (1.1 g).

2-Acetamido-2-deoxy-D-altrose

The product obtained from the cellulose column gave crystalline 2-acetamido-2-deoxy-D-altrose from its solution in ethanol and after one recrystallization from ethanol the glycose (3 g) showed a single spot on paper chromatograms (R_{Gal} 1.84) and had m.p. 99–100° and $[\alpha]_D$ −2.4° → +5° (*c*, 1 in water) (lit. m.p. 95–97° and $[\alpha]_D$ −2.7° → +4.8°(8)).

Anal. Calcd. for $C_8H_{15}O_6N$: C, 43.43; H, 6.84; N, 6.33. Found: C, 43.4; H, 6.9; N, 6.3.

The fully trimethylsilylated crystalline 2-acetamido-2-deoxy-D-altrose on gas–liquid partition chromatography gave a single peak having T_{GN} 0.76 and the glycose after equilibration in water gave trimethylsilylated derivatives having T_{GN} 0.76 (34%), 1.30 (25%), and 1.44 (41%).

2-Amino-2-deoxy-D-altrose Hydrochloride

2-Acetamido-2-deoxy-D-altrose (0.3 g) in 2 *N* hydrochloric acid (10 ml) was heated on a boiling water bath for 2 h and after treatment with charcoal, the filtered solution was concentrated to a syrup. This was then co-distilled with ethanol and benzene to yield an amorphous product (0.26 g) which was dried under vacuum over phosphorus pentoxide. The 2-amino-2-deoxy-D-altrose hydrochloride, which gave a single spot on paper chromatography, (R_{Gal} 0.47) had $[\alpha]_D$ −17.3° (*c*, 2.2 in water) (lit. $[\alpha]_D$ −14° (8)).

2-Acetamido-2-deoxy-D-allose

The 2-acetamido-2-deoxy-D-allose fraction obtained from the cellulose column gave crystalline 2-acetamido-2-deoxy-D-allose (0.9 g) from ethanol and had m.p. 200° undepressed on admixture with the 2-acetamido-2-deoxy-D-allose obtained before preparative chromatography, and the two fractions were combined (4.4 g). Two recrystallizations from ethanol afforded pure 2-acetamido-2-deoxy-D-allose (3.8 g) which gave a single spot (R_{Gal} 1.58) on paper chromatography and had m.p. 207° (lit. m.p. 197° (8), 201–203° (9), 207–208° (11)) and $[\alpha]_D$ −88° → −55° (*c*, 0.2 in water) (lit. $[\alpha]_D$ −53° (8), −48° (9), −47° (11)).

Anal. Calcd. for $C_8H_{15}O_6N$: C, 43.43; H, 6.84; N, 6.33. Found: C, 43.2; H, 6.9; N, 6.3.

The trimethylsilylated crystalline 2-acetamido-2-deoxy-D-allose on gas chromatography gave a single peak (T_{GN} 1.32) and the trimethylsilylated glycose equilibrate in water showed four peaks having T_{GN} 0.92 (9.5%), 1.32 (54%), 1.38 (30%), and 1.64 (7%).

2-Amino-2-deoxy-D-allose Hydrochloride

2-Acetamido-2-deoxy-D-allose (0.3 g) was hydrolyzed with 2 *N* hydrochloric acid in the way described for the preparation of 2-amino-2-deoxy-D-altrose hydrochloride to yield 2-amino-2-deoxy-D-allose hydrochloride (0.25 g) as an amorphous powder. This gave a single spot on paper chromatography (R_{Gal} 0.39) and had $[\alpha]_D$ +16.6° (*c*, 0.5 in water) (lit. $[\alpha]_D$ +17° (8), +29° (9), +17° (11)).

2-Deoxy-D-ribo-hexose

3,4,5,6-Tetraacetoxy-D-*ribo*-1-nitro-1-hexene (10 g) in ethanol (400 ml), was shaken with hydrogen at room temperature and pressure in the presence of palladium black (0.6 g). One mole equivalent of hydrogen was absorbed in 20 min, and the rate of reduction then became very slow. At this point the mixture was filtered and the filtrate was concentrated to a syrup (9.9 g). The 3,4,5,6-tetra-*O*-acetyl-1,2-dideoxy-1-nitro-D-*ribo*-hexitol which could not be induced to crystallize had $[\alpha]_D$ −7.2° (*c*, 7 in chloroform).

Anal. Calcd. for $C_{14}H_{21}O_{10}N$: C, 46.28; H, 5.83; N, 3.86. Found: C, 46.37; H, 5.9; N, 3.8.

3,4,5,6-Tetra-*O*-acetyl-1,2-dideoxy-1-nitro-D-*ribo*-hexitol (9 g) was dissolved at 40° in *N* sodium hydroxide solution (135 ml) and the mixture, after being kept at 20° for 1 h , was added dropwise to a cooled, stirred solution of concentrated sulfuric acid (18.9 ml) in water (27 ml). The reaction mixture was adjusted in the cold to pH 5.5 by the addition of saturated barium hydroxide solution and then finally neutralized by the addition of barium carbonate. After centrifugation and filtration the solution was treated with acetic acid (1 ml) and then passed down columns of Rexyn 101(H^+) (150 ml) and Rexyn RG6(OH^-) (30 ml) ion-exchange resins, and the eluate and washing were concentrated to a syrup (4.3 g). The syrup was dissolved in hot ethanol and on cooling the solution crystalline 2-deoxy-D-*ribo*-hexose (4.0 g) having m.p. 138° was obtained which after three recrystallizations from ethanol had m.p. 138–139° (lit. m.p. 135–136° (20)) and $[\alpha]_D$ +50° → +55.2° (*c*, 0.5 in water) (lit. $[\alpha]_D$ +58° (20)).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 43.8; H, 7.4.

On paper chromatography the 2-deoxy-D-*ribo*-hexose had R_{Gal} 3.02 and gave a characteristic red spot with the periodate–thiobarbiturate spray reagents (19).

2-Deoxy-D-ribo-hexitol

2-Deoxy-D-*ribo*-hexose (120 mg) in water (5 ml) was reduced by the addition of sodium borohydride (50 mg) and after 2 h the excess borohydride was destroyed by acidification with acetic acid. The reaction mixture was passed down a column of Rexyn 101(H^+) ion-exchange resin (10 ml) and the eluate and washings after concentration to dryness were distilled with absolute methanol (5 × 20 ml) to remove boric acid and the residue was dissolved in hot ethanol (ca. 2 ml). Crystalline 2-deoxy-D-*ribo*-hexitol (95 mg) was obtained from the cooled ethanol solution and after two further recrystallizations

from ethanol it had m.p. 90° and $[\alpha]_D$ −19° (*c*, 0.8 in methanol) (lit. m.p. 90–91° and $[\alpha]_D$ −19° (*c*, 2 in methanol) (20)).

Anal. Calcd. for $C_6H_{14}O_5$: C, 43.37; H, 8.49. Found: C, 43.4; H, 8.5.

Acknowledgment

We thank Mr. A. E. Castagne for the microanalyses.

1. J. C. Sowden and H. O. L. Fischer. J. Am. Chem. Soc. **69**, 1048 (1947).
2. C. Satoh and A. Kiyomoto. Chem. Pharm. Bull. (Tokyo), **12**, 615 (1964).
3. J. U. Nef. Ann. **280**, 263 (1894).
4. A. N. O'Neill. Can. J. Chem. **37**, 1747 (1959).
5. J. C. Sowden and M. L. Oftedahl. J. Am. Chem. Soc. **82**, 2303 (1960).
6. S. D. Gero and J. Defaye. Compt. Rend. Acad. Sci. (Paris). **261**, 1555 (1965).
7. J. C. Sowden and M. L. Oftedahl. J. Org. Chem. **26**, 2153 (1961).
8. R. Kuhn and H. Fischer. Ann. **617**, 88 (1958).
9. R. W. Jeanloz. J. Am. Chem. Soc. **79**, 2591 (1957).
10. R. W. Jeanloz. Methods in carbohydrate chemistry. Vol. 1. Academic Press, New York. 1962. p. 213.
11. R. Gigg and C. D. Warren. J. Chem. Soc. 1351 (1965).
12. K. Heyns, H. Paulsen, R. Eichstedt, and M. Rolle. Chem. Ber. **90**, 2039 (1957).
13. R. W. Jeanloz, D. A. Prins, and T. Reichstein. Experientia, **1**, 336 (1945).
14. R. W. Jeanloz, D. A. Prins, and T. Reichstein. Helv. Chim. Acta, **29**, 371 (1946).
15. J. Laszlo, B. Landau, K. Wight, and D. Burk. J. Natl. Cancer Inst. **21**, 475 (1958).
16. S. M. Partridge. Biochem. J. **42**, 238 (1948).
17. W. E. Trevelyan, D. P. Procter, and J. S. Harrison. Nature, **166**, 444 (1950).
18. L. Hough, J. K. N. Jones, and W. H. Wadman. J. Chem. Soc. 1702 (1950).
19. L. Warren. Nature, **186**, 237 (1960).
20. M. Gut and D. A. Prins. Helv. Chim. Acta, **30**, 1223 (1947).

Mass-spectral rearrangements of acyloxysilanes and -germanes

A. G. Brook, A. G. Harrison, and Peter F. Jones[1]

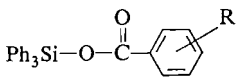
Department of Chemistry, University of Toronto, Toronto 5, Ontario

Received March 19, 1968

The mass spectra of some acyloxytriphenylmethanes, -silanes, and -germanes have been studied. The latter two classes show unusual fragmentation–rearrangement processes.

Canadian Journal of Chemistry, **46**, 2862 (1968)

During the course of some investigations into the Baeyer–Villiger oxidation of acylsilanes it became necessary to obtain the mass spectrum of benzoyloxytriphenylsilane (triphenylsilyl benzoate), **1***a*. The major ion (*m/e* 303), formed by loss



(*a*) R = H
(*b*) R = *m*-Cl
(*c*) R = *p*-*t*-Bu

1

of a phenyl group from the parent ion (*m/e* 380), further lost carbon dioxide to give the $Ph_3Si^{\oplus}$ ion (*m/e* 259) as confirmed by a metastable peak at *m/e* 221.4 for the transition 303 → 259.

$$M^{\oplus} \xrightarrow{-77} [M-Ph]^{\oplus} \xrightarrow[*]{-44} Ph_3Si^{\oplus}$$

Since this behavior differs markedly from that normally found for esters (1) we have extended our investigation to the substituted benzoyloxy compounds **1***b* and **1***c*, in order to identify the phenyl group initially lost. Neither compound showed a peak for loss of substituted-phenyl, the base peak for both being the (M−77) ion which subsequently lost CO_2. A metastable peak was observed for the loss of CO_2 in **1***c*. Thus the fragmentation path must involve loss of a phenyl group from silicon followed by migration of an aryl group to the positive silicon center, accompanied by loss of carbon dioxide.

For all these compounds the peak intensities for both the molecule-ions (<3%) and for $Ph_3Si^{\oplus}$ (<5%) were low. Major peaks for the compounds are shown in Table I. A similar rearrangement has been reported (2) for trimethylsilyl esters.

Migration to silicon is not limited to aryl groups as is shown by the mass spectrum of the acetoxy compound **2***a* for which the following pathway is the major process, (M − 77) being the

[1]Dow–Corning Fellow in Chemistry, 1967–1968.