1. D. L. BALL, M. M. CRUTCHFIELD, and J. O. EDWARDS. J. Org. Chem. **25**, 1599 (1960).
2. K. B. WIBERG. J. Am. Chem. Soc. **81**, 252 (1959).
3. L. S. LEVITT, B. W. LEVITT, and E. R. MALINOWSKI. J. Org. Chem. **27**, 2917 (1962).
4. I. M. KOLTHOFF, E. J. MEEHAN, and E. M. CARR. J. Am. Chem. Soc. **75**, 1439 (1953).
5. L. S. LEVITT. Can. J. Chem. **31**, 915 (1953).
6. E. R. MALINOWSKI and L. S. LEVITT. J. Am. Chem. Soc. **80**, 5334 (1958).
7. F. H. WESTHEIMER *et al.* J. Chem. Phys. **11**, 506 (1943); J. Am. Chem. Soc. **73**, 65 (1951); Chem. Rev. **45**, 419 (1949).
8. H. KWART and P. S. FRANCIS. J. Am. Chem. Soc. **77**, 4907 (1955).
9. L. S. LEVITT and D. Z. DENNEY. Unpublished observations.
10. M. COHEN and F. H. WESTHEIMER. J. Am. Chem. Soc. **74**, 4387 (1952).
11. E. HOWARD, JR. and L. S. LEVITT. J. Am. Chem. Soc. **75**, 6170 (1953).
12. L. S. LEVITT and E. R. MALINOWSKI. J. Am. Chem. Soc. **77**, 4517 (1955).
13. A. KAILEN and L. OLBRICH. Monatsh. **47**, 449 (1926).
14. F. P. GREENSPAN and H. M. WOODBURN. J. Am. Chem. Soc. **76**, 6345 (1954).
15. P. D. BARTLETT and J. COTMAN. J. Am. Chem. Soc. **71**, 1419 (1949).
16. I. M. KOLTHOFF and I. K. MILLER. J. Am. Chem. Soc. **73**, 3055 (1951).
17. R. L. EAGER and C. A. WINKLER. Can. J. Res. B, **26**, 527 (1948).
18. B. W. LEVITT and L. S. LEVITT. Abstracts of Papers, Chicago Meeting, American Chemical Society, September, 1958. p. 5P.
19. B. W. LEVITT and L. S. LEVITT. Abstract of Papers, Cleveland Meeting, American Chemical Society, April 5, 1960. p. 94-O.
20. L. S. LEVITT. J. Org. Chem. **20**, 1297 (1955).

RECEIVED IN ORIGINAL FORM JULY 27, 1961;
AS REVISED JULY 24, 1962.
CHEMISTRY DEPARTMENTS,
SETON HALL UNIVERSITY,
SOUTH ORANGE, N.J.,
AND
STEVENS INSTITUTE OF TECHNOLOGY,
HOBOKEN, N.J.

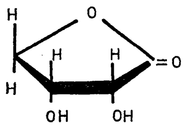
DEGRADATION OF D-RIBONO-1 → 4-LACTONE TO D-ERYTHRONO-1 → 4-LACTONE

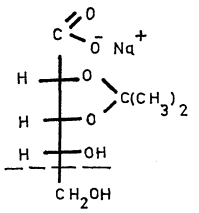
D. L. MITCHELL

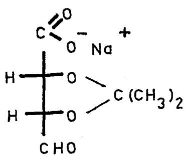
D-Erythrono-1 → 4-lactone (I) can be readily prepared by the alkaline bromine oxidation of D-erythrose. A convenient source of the D-erythro-alcohol grouping occurs at carbons 4 and 5 of D-glucose, and various procedures which employ glycol cleaving reagents have been described for the selective degradation of D-glucose (1), 4,6-*O*-ethylidene-D-glucose (2), and starch (3) to D-erythrose. An analogous degradation of L-rhamnose to L-erythrono-1 → 4-lactone has also been described (4). Most other preparations which have been described are manipulatively more difficult and give less satisfactory yields (see refs. 1 and 5 for a summary of methods).

Sodium 2,3-*O*-isopropylidene-D-ribonate (II), conveniently obtained from 2,3-*O*-isopropylidene-D-ribono-1 → 4-lactone (6), was selectively cleaved between carbons 4 and 5, by sodium metaperiodate, to form sodium 2,3-*O*-isopropylidene-L-erythruronate (III) *in situ*. After selective sodium borohydride reduction of the newly formed aldehyde group at carbon 4, D-erythrono-1 → 4-lactone was obtained in 76% yield with loss of the *O*-isopropylidene group occurring during the lactonization. In this sequence of reactions, the four carbon atoms of D-erythrono-1 → 4-lactone have originated from carbons 1 to 4 of D-ribono-1 → 4-lactone, and, therefore, subsequently from carbons 1 to 4 of D-ribose. Application of this reaction to C^{14}-labelled D-ribose could be useful in obtaining a partial degradation of this pentose.

D-Erythrono-1 → 4-lactone readily forms the derived 2,3-*O*-isopropylidene-D-erythrono-1 → 4-lactone with the reaction being easily followed polarimetrically. The molecular


I


II


III

rotational difference between the product and the reactant is large ([ΔM]$_D$ ca. 100). This observation is in agreement with the optical rotational differences previously recorded between 2,3-*O*-isopropylidene-D-ribono-1 → 4-lactone and D-ribono-1 → 4-lactone (6) and for other 2,3-*O*-isopropylidene-1 → 4-lactones prepared in this laboratory (7).

The following new derivatives were also prepared: (i) 2,3-*O*-isopropylidene-D-ribonamide, (ii) 2,3-*O*-isopropylidene-D-erythronamide, (iii) a mono-*O*-toluene-*p*-sulphonyl-D-erythrono-1 → 4-lactone, and (iv) a di-*O*-toluene-*p*-sulphonyl-D-ribono-1 → 4-lactone.

EXPERIMENTAL

Solutions were concentrated under reduced pressure (ca. 15 mm). Melting points were uncorrected and optical rotations were determined in water, unless otherwise stated. Paper chromatography was carried out by the descending method on Whatman No. 1 filter paper using the solvent system (v:v) ethyl acetate – acetic acid – formic acid – water (18:3:1:4). Unsubstituted 1 → 4-lactones were detected on paper chromatograms with an alkaline silver nitrate spray reagent (8).

Conversion of D-*Ribono-1 → 4-lactone to* D-*Erythrono-1 → 4-lactone*

2,3-*O*-Isopropylidene-D-ribono-1 → 4-lactone (5.20 g, 0.028 mole) was hydrolyzed with 1 molar equivalent of 0.1 N sodium hydroxide at room temperature. The optical rotation, $[\alpha]_D^{20}$ 56°, did not change appreciably over a period of 15 hours. The solution was adjusted to pH 7 with acetic acid, diluted to 2 liters with water, and finely powdered potassium metaperiodate (7.01 g, 0.029 mole) was added and the solution was stored in the dark for 2 hours.* A solution of lead acetate (15.3 g) in water (100 ml) was added with stirring and the insoluble lead salts were separated by filtration and washed thoroughly with cold water (50 ml). The combined filtrates were added dropwise, with stirring, to an excess of sodium borohydride (3 g). The solution was filtered free from a small deposit of metallic lead, and the filtrate was acidified with dilute acetic acid and passed down a column of Amberlite IR-120 (H) resin. The eluate was concentrated to dryness and the syrupy acid was lactonized by repeated additions of acetic acid and ethanol and reconcentration to dryness. The residue was extracted with boiling acetone and the solution concentrated to a crystalline mass (3.28 g, 76%) of m.p. 102° (from ethanol), ν_{max} 1753 cm^{-1} (nujol) and $[\alpha]_D^{20}$ −74° (c, 1.1). Lit. m.p. 103° C and $[\alpha]_D^{20}$ −73.3° (H_2O) (9). The rates of movement on paper chromatograms for D-erythrono-1 → 4-lactone and D-ribono-1 → 4-lactone were R_{Rh} 1.7 and R_{Rh} 1.4 respectively. Anal. Calc. for $C_4H_6O_4$: C, 40.7; H, 5.1. Found: C, 40.9; H, 5.2.

*2,3-O-Isopropylidene-*D-*erythrono-1 → 4-lactone*

A solution of D-erythrono-1 → 4-lactone (0.105 g) in acetone (5 ml) containing concentrated hydrochloric acid (3 drops) was observed polarimetrically (Table I). After 4 hours, the neutralized solution (silver carbonate) was filtered from inorganic salts and the filtrate was concentrated. The product spontaneously crystallized and was purified twice by sublimation (1–3 mm, 55–60° C) to yield a product (0.105 g, 74%) of m.p. 68–68.5° C, $[\alpha]_D^{20}$ −112° (c, 1.5) (Table I) and ν_{max} 1740 cm^{-1} (nujol). Lit. m.p. 65–67.5° C and $[\alpha]_D^{22}$ −116° (10). No hydroxyl absorption was detected. Anal. Calc. for $C_7H_{10}O_4$: C, 53.2; H, 6.4. Found: C, 53.4; H, 6.4.

*2,3-O-Isopropylidene-*D-*erythronamide*

A solution of 2,3-*O*-isopropylidene-D-erythrono-1 → 4-lactone (0.031 g) in liquid ammonia (2 ml) was stored in a sealed ampoule at room temperature for 48 hours (11). After the ampoule was chilled to −80° C, it was opened and stored in a desiccator over evaporating dishes containing concentrated sulphuric acid and solid sodium hydroxide. The solid had m.p. 107–109° C and ν_{max} 3300, 3250, 3150, 1670, and 1630 cm^{-1} (nujol). No lactone carbonyl absorption was detected. Anal. Calc. for $C_7H_{13}NO_4$: C, 48.0; H, 7.5; N, 8.0. Found: C, 47.8; H, 7.6; N, 8.2.

**Sodium metaperiodate was used for some preparations.*

TABLE I

Optical rotations of 1 → 4-lactones

D-Erythrono-1 → 4-lactone*								
Hours	0	0.25	0.5	0.74	1.0	1.5	3.25	4.0
$[\alpha]_D^{20}$ (deg)	−19	−53	−74	−82.5	−92	−102	−114	−115
2,3-*O*-Isopropylidene-D-erythrono-1 → 4-lactone†								
Hours	0	0.4	1.0	1.45	2.25			
$[\alpha]_D^{20}$ (deg)	−112	−87	−62.5	−52	−37.5			

*Acidified acetone (*c*, 2.1).
†Water (*c*, 1.5).

*2,3-O-Isopropylidene-*D*-ribonamide*

2,3-*O*-Isopropylidene-D-ribono-1 → 4-lactone (0.26 g) was dissolved in liquid ammonia and stored at room temperature in a sealed ampoule for 3 days. The ammonia-free syrup solidified on trituration with ethanol and was recrystallized from acetone–ether, m.p. 108–110° C. $[\alpha]_D^{21}$ 58° (*c*, 0.5, ethanol), ν_{max} 3250, 3150 (broad peak), 1650, and 1630 cm^{-1} (nujol). No lactone carbonyl absorption was detected. Anal. Calc. for $C_8H_{15}NO_5$: C, 46.8; H, 7.4; N, 6.8. Found: C, 47.1; H, 7.5; N, 6.6.

Periodate oxidation (unbuffered) indicated a periodate uptake of 0.54 mole/mole (5 minutes) and 0.70 mole/mole (8 hours). The solution after 8 hours' oxidation gave a positive test for formaldehyde with the chromotropic acid reagent.

*Mono-O-toluene-p-sulphonyl-*D*-erythrono-1 → 4-lactone*

Solid toluene-*p*-sulphonyl chloride (0.650 g) was added in one portion to a cold (0° C) solution of D-erythrono-1 → 4-lactone (0.095 g) in dry pyridine. After storage for 0.5 hour, excess sulphonyl chloride was decomposed by the addition of water (0.3 ml), and the solution poured into a slurry of chipped ice and water (75 ml). The solid was collected, dried (0.105 g, 85%), and recrystallized from methanol (4 ml) to yield fine needles first melting at 172–173° C, then solidifying at ca. 178° C in strongly birefringent prismatic flakes, and remelting at 183–184° C. ν_{max} 3300 cm^{-1} and ν_{max} 1760 cm^{-1} (nujol). Anal. Calc. for $C_{11}H_{12}SO_6$: C, 48.2; H, 4.4; S, 11.8. Found: C, 48.6; H, 4.5; S, 11.7. Attempts to prepare the di-*O*-toluene-*p*-sulphonyl derivative were unsuccessful.

*Di-O-toluene-p-sulphonyl-*D*-ribono-1 → 4-lactone*

D-Ribono-1 → 4-lactone (2.53 g) and toluene-*p*-sulphonyl chloride (16.6 g) in pyridine (20 ml) were stored in the refrigerator for 1.5 hours. Water (0.5 ml) was added to the solution to decompose the excess sulphonyl chloride, and after standing for 0.5 hours, the dark red solution was poured into a slurry of chipped ice and water (1.5 liters). The precipitated gum was extracted with chloroform and the chloroform extracts were washed successively with dilute mineral acid, dilute sodium bicarbonate solution, and finally with water. The crude tarry product was dissolved in methanol, warmed, treated with charcoal and the solution filtered through a pad of cellulose. The filtrate, upon dilution with a small volume of light petroleum, deposited crystals (3.36 g, 43%). A specimen, which was recrystallized from methanol – light petroleum (b.p. 60–80° C), melted at 123–125° C and had $[\alpha]_D^{25}$ 9° (*c*, 2.1, ethanol). ν_{max} 3350 cm^{-1} and ν_{max} 1780 cm^{-1} (nujol). Anal. Calc. for $C_{19}H_{20}O_9S_2$: C, 50.0; H, 4.4; S, 14.1. Found: C, 50.2; H, 4.5; S, 14.3.

A sample (61 mg) was dissolved in acetone (10 ml) and 0.01 *N* sodium hydroxide (50 ml). At intervals, aliquots (5 ml) were withdrawn and the remaining alkali was titrated with 0.01 *N* sulphuric acid using phenolphthalein as the indicator.

Time (minutes)	1	5	10	180	24 hr
Moles of alkali consumed/mole of compound	1.2	1.3	1.8	1.9	2.0

Attempts to prepare mono-*O*-toluene-*p*-sulphonyl-D-ribono-1 → 4-lactone by using equimolar quantities of reactants according to the method described above resulted in producing the di-*O*-toluene-*p*-sulphonyl derivative, m.p. 124–125° C, $[\alpha]_D^{25}$ 9° (*c*, 1.13, ethanol), in very low yield (9%). Found: C, 50.2; H, 4.6; S, 14.3.

Attempts to prepare the tri-*O*-toluene-*p*-sulphonyl-D-ribono-1 → 4-lactone by using a large excess of toluene-*p*-sulphonyl chloride and a warmer reaction temperature (one experiment at 37° C, a second experiment at room temperature) yielded a black tarry product that could not be crystallized.

ACKNOWLEDGMENTS

The author wishes to thank the Central Research Grants Committee, Makerere University College, for a maintenance grant and also the Royal Military College of Canada, Kingston, Ontario, for a gift of chemicals.

1. A. S. PERLIN and C. BRICE. Can. J. Chem. **33**, 1216 (1955).
2. R. BARKER and D. L. MACDONALD. J. Am. Chem. Soc. **82**, 2301 (1960).
3. A. JEANES and C. S. HUDSON. J. Org. Chem. **20**, 1565 (1955).
4. J. N. BAXTER and A. S. PERLIN. Can. J. Chem. **38**, 2217 (1960).
5. W. G. OVEREND, M. STACEY, and L. F. WIGGINS. J. Chem. Soc. 1358 (1949).
6. L. HOUGH, J. K. N. JONES, and D. L. MITCHELL. Can. J. Chem. **36**, 1720 (1958).
7. D. L. MITCHELL. Unpublished experiments.
8. W. E. TREVELYAN, D. P. PROCTOR, and J. S. HARRISON. Nature, **166**, 444 (1950).
9. O. RUFF. Ber. **32**, 3672 (1899).
10. R. SCHAFFER. J. Res. Natl. Bur. Stand. A, **65**, 507 (1961).
11. V. C. JELINEK and F. W. UPSON. J. Am. Chem. Soc. **60**, 355 (1938).

RECEIVED AUGUST 7, 1962.

DEPARTMENT OF CHEMISTRY,
MAKERERE UNIVERSITY COLLEGE,
THE UNIVERSITY COLLEGE OF EAST AFRICA,
KAMPALA, UGANDA.