*Carbohydrate Research*, 37 (1974) 384–389
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## Note

# Reactions of 2,3-diamino-2,3-dideoxy-L-ascorbic acid

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(Received July 16th, 1974; accepted July 29th, 1974)

When a saccharide osazone is chemically reduced, or catalytically hydrogenated with palladium on charcoal, the product is usually the 1-amino-1-deoxyketose[1–3],

TABLE I

PROPERTIES OF IMIDAZOLINES 3

| *R* | *M.p.* (°*C*) | *Yield* (%) | *Formula* | | *Analyses* | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | *C* | *H* | *Cl* | *N* |
| H | 220–1 | 85 | $C_{13}H_{14}N_2O_4$ | Calc. | 59.54 | 5.35 | — | 10.68 |
| | | | | Found | 59.19 | 5.47 | — | 10.63 |
| *o*-Methoxy- | 220–1 | 91 | $C_{14}H_{16}N_2O_5$ | Calc. | 55.62 | 5.29 | — | 9.27 |
| | | | | Found | 55.91 | 5.53 | — | 9.53 |
| 2,4-Dimethoxy- | 192–3 | 80 | $C_{15}H_{18}N_2O_6$ | Calc. | 55.90 | 5.59 | — | 8.69 |
| | | | | Found | 55.70 | 5.80 | — | 9.01 |
| *p*-Nitro- | 253–4 | 90 | $C_{13}H_{13}N_3O_6$ | Calc. | 50.81 | 4.23 | — | 13.68 |
| | | | | Found | 50.82 | 4.30 | — | 13.59 |
| *p*-Dimethylamino- | 237–9 | 85 | $C_{15}H_{19}N_3O_4$ | Calc. | 59.01 | 6.23 | — | 13.77 |
| | | | | Found | 58.58 | 6.40 | — | 13.89 |
| *o*-Chloro- | 228–9 | 79 | $C_{13}H_{13}ClN_2O_4$ | Calc. | 52.74 | 4.38 | 12.00 | 9.44 |
| | | | | Found | 52.63 | 4.31 | 11.74 | 9.36 |
| *p*-Chloro- | 231–2 | 80 | $C_{13}H_{13}ClN_2O_4$ | Calc. | 52.74 | 4.38 | 12.00 | 9.44 |
| | | | | Found | 52.69 | 4.17 | 11.92 | 9.52 |
| 2,6-Dichloro- | 218–9 | 78 | $C_{13}H_{12}Cl_2N_2O_4$ | Calc. | 47.13 | 3.62 | 21.45 | 8.46 |
| | | | | Found | 47.42 | 3.80 | 21.60 | 8.60 |

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which is sometimes accompanied by the 2-amino-2-deoxyaldose[4,5]. The formation of mono- or di-amino alditols requires more vigorous conditions, such as the use of Raney nickel in alcoholic potassium hydroxide, to break the chelated ring of the osazone[6,7].

Dehydro-L-ascorbic acid bis(phenylhydrazone) [L-*threo*-2,3-hexodiulos-1-ono-1,4-lactone bis(phenylhydrazone)] (**1**) has been shown to yield various reduction products. Thus, with lithium aluminum hydride, it affords a substituted tetraazaindene, and, with zinc and acetic acid, it gives a rubiazonic acid derivative[8].

Catalytic hydrogenation of **1** with palladium on charcoal has been found to yield 2,3-diamino-2,3-dideoxy-L-ascorbic acid[9] (**2**). The structure of this compound was confirmed spectroscopically; its infrared (i.r.) spectrum showed the lactone band at 1720 $cm^{-1}$ and the OH and NH bands at 3300 and 3160 $cm^{-1}$, respectively, and its mass spectrum (see Fig. 1) showed a strong molecular peak at *m/e* 174, followed by an $M - 18$ peak resulting from the loss of water, and a strong peak at *m/e* 114 due to the loss of the hydroxyalkyl chain.

Upon mild acetylation with boiling acetic acid, diamine **2** did not afford an imidazole, but gave, instead, a mono-*N*-acetyl derivative (**5**) which showed i.r. bands at 1730 (lactone) and 1650 $cm^{-1}$ (amide). The n.m.r. spectrum of this acetyl deriv-

| *λ (nm)* | | | | | *log ε* | | | | *ν ($cm^{-1}$)* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *CO* | *NH* | *OH* |
| max | 212, | 238, | 278, | 337 | 3.83, | 4.02, | 4.16, | 4.26 | 1700 | 3160 | 3400 |
| min | 220, | 248, | 305 | | 3.82, | 3.96, | 4.06 | | | | |
| max | 218, | 238, | 278, | 348 | 4,00. | 4.00, | 4.18, | 4.28 | 1760 | 3220 | 3400 |
| min | 225, | 243, | 308 | | 3.97, | 4.00, | 4.00 | | | | |
| max | 217, | 247, | 278, | 352 | 3.97, | 4.11, | 4.26, | 4.31 | 1700 | 3200 | 3400 |
| min | 227, | 255, | 313 | | 3.93, | 4.08, | 4.04 | | | | |
| max | 233, | 272, | 343 | | 4.16, | 4.32, | 4.30 | | 1740 | 3200 | 3400 |
| min | 243, | 305 | | | 4.12, | 4.08 | | | | | |
| max | 212, | 243, | 280, | 358 | 4.09, | 4.00, | 4.07, | 4.43 | 1720 | 3210 | 3420 |
| min | 225, | 257, | 303 | | 3.88, | 3.95, | 3.99 | | | | |
| max | 216, | 247, | 278, | 246 | 3.89, | 3.89, | 4.03, | 4.15 | 1720 | 3200 | 3420 |
| min | 227, | 258, | 303 | | 3.77, | 3.94, | 3.92 | | | | |
| max | 216, | 243, | 278, | 343 | 3.79, | 4.01, | 4.01, | 4.11 | 1700 | 3180 | 3420 |
| min | 227, | 250, | 305 | | 3.72, | 3.97, | 3.99 | | | | |
| max | 217, | 267, | 320 | | 4.08, | 4.19, | 4.12 | | 1730 | 3200 | 3440 |
| min | 233, | 295 | | | 3.97, | 3.99 | | | | | |

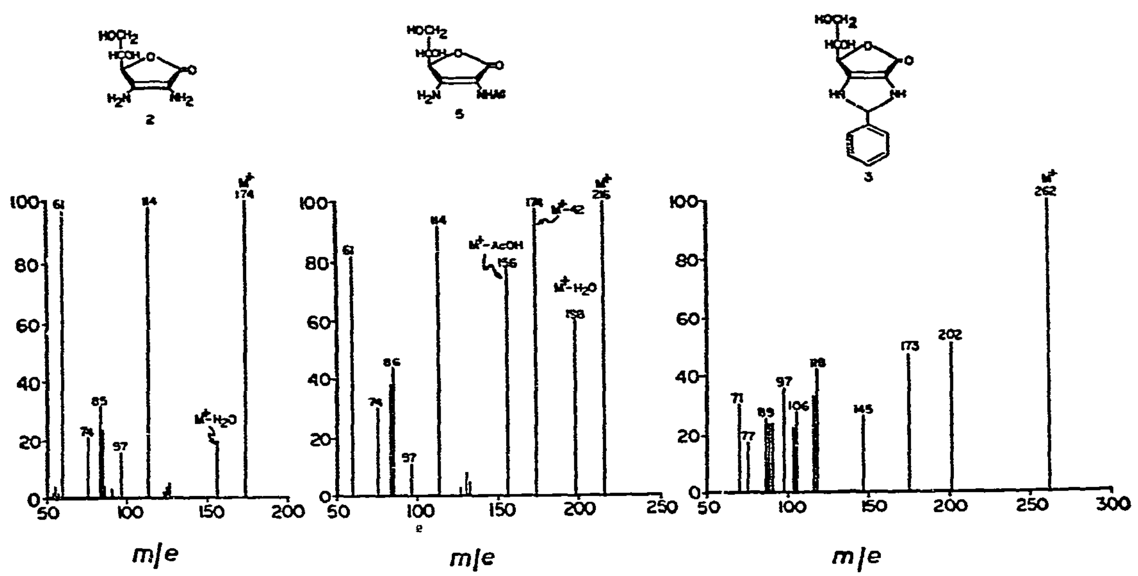
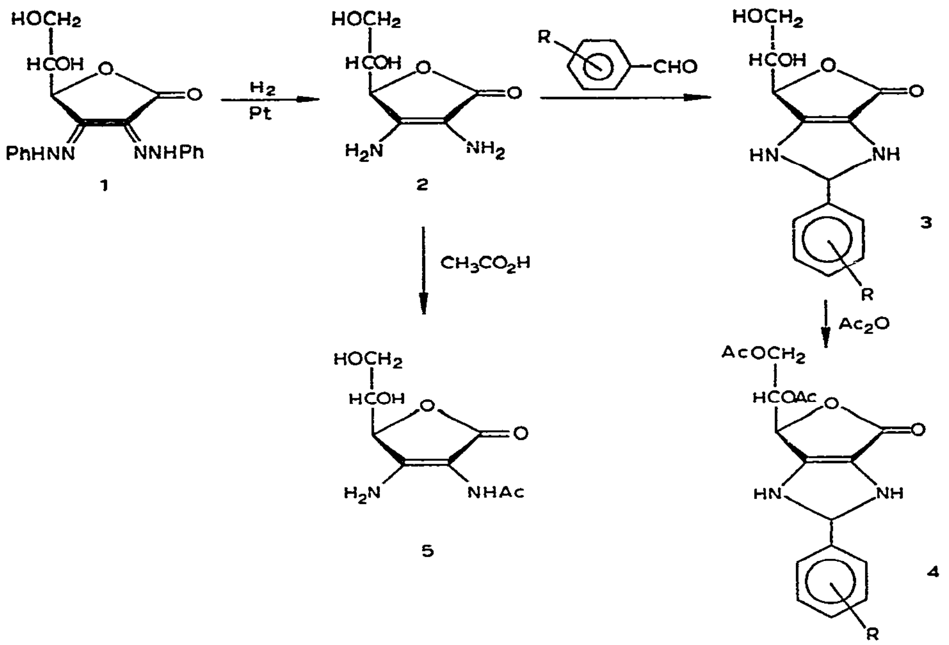


Fig. 1. Mass spectra of compounds **2**, **3**, and **5**.

ative showed the methyl proton at δ 2.60 p.p.m. characteristic of *N*-acetyl derivatives; the methylene proton on C-6 appeared at δ 4.2, and the methine proton on C-5, as a multiplet at δ 4.60. The ring-hydrogen atom on C-4 appeared at δ 5.6 as a doublet having a coupling constant $J_{4,5}$ 2 Hz. The mass spectrum of this compound was quite similar to that of diamine **2** (see Fig. 1); it showed a strong molecular peak at *m/e* 216, followed by a peak at 198 due to the loss of water. The base peak appeared at 174 and resulted from the loss of ketene, a loss characteristic of the fragmentation of acetamides *via* a McLafferty rearrangement. The base peak was followed by one that was 18 mass units lower, due to the loss of acetic acid from the molecular ion. Peaks at 114, 97, 85, and 67 present in the mass spectrum of the parent compound were also present in that of the acetate. Although no proof is available for assigning the acetyl group to the NH on C-2, it is presumed that the amino group on C-3 (being the least deactivated by the carbonyl group) is, probably, completely protonated in acetic acid, leaving the $NH_2$ group on C-2 as the nucleophile. It should, however, be stressed that structure **5** is only tentative.

Reaction of diamine **2** with benzaldehyde and with substituted benzaldehydes afforded crystalline, bicyclic 2-arylimidazolines of the general formula **3**. The i.r. spectra of these compounds (see Table I) showed the OH band at 3560–3400 $cm^{-1}$, the NH band at 3200–3160 $cm^{-1}$, and the lactone band at 1760–1700 $cm^{-1}$. Their mass spectra (see Fig. 1) showed strong molecular peaks, followed by a strong M−60 peak resulting from the loss of the hydroxyalkyl side chain by a McLafferty type of rearrangement. On vigorous acetylation with boiling acetic anhydride, compounds **3** afforded *N*-acetyl-di-*O*-acetyl derivatives (**4**) that failed to crystallize, but which gave



correct elemental analyses after purification by preparative t.l.c. In the n.m.r. spectrum, the acetates showed two distinct *O*-acetyl groups between $\delta$ 2.05 and 2.21, in addition to an *N*-acetyl methyl group between $\delta$ 2.34 and 2.40 p.p.m. (see Table II).

TABLE II

PROPERTIES OF ACETATES 4

| *R* | *Yield* (%) | *Formula* | *Analyses* | | | | $\delta$ (*p.p.m.*) | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | *C* | *H* | *N* | O-*Acetyls* | N-*Acetyl* | *NH* |
| H | 70 | $C_{19}H_{20}N_2O_7$ | Calc. | 58.76 | 5.14 | 7.22 | 2.09, 2.18 | 2.40 | 10.38 |
| | | | Found | 58.51 | 5.22 | 7.30 | | | |
| 2,4-Dimethoxy | 86 | $C_{21}H_{24}N_2O_9$ | Calc. | 56.25 | 5.35 | 6.25 | 2.05, 2.12 | 2.34 | 10.64 |
| | | | Found | 56.04 | 5.25 | 6.39 | | | |
| *p*-Nitro | 78 | $C_{19}H_{19}N_3O_9$ | Calc. | 51.47 | 4.29 | 9.49 | 2.12, 2.21 | 2.36 | 10.51 |
| | | | Found | 51.58 | 4.42 | 9.17 | | | |

## EXPERIMENTAL

*General methods.* — Melting points were determined on a Kofler block. Microanalyses were made in the Chemistry Departments of the University of Paris and of the Michigan Technological University. I.r. spectra were recorded with a Perkin–Elmer 457 spectrophotometer, and ultraviolet and visible absorption spectra with a Unicam SP800 instrument. The n.m.r. and mass spectra were respectively recorded with a Varian A60 and an M66 spectrometer.

*2,3-Diamino-2,3-dideoxy-*L*-ascorbic acid*[9] (2). — L-*threo*-2,3-Hexodiulos-1-ono-1,4-lactone 2,3-bis(phenylhydrazone)[10–12] (3.54 g, 0.01 mole) was dissolved in absolute ethanol (300 ml) and hydrogenated in the presence of 10% platinum-on-charcoal catalyst (1 g) until no more hydrogen was absorbed. The red color of the solution completely vanished, and three moles of hydrogen were absorbed per mole of the bis(phenylhydrazone). The suspension was filtered in an atmosphere of carbon dioxide, and the filtrate (which quickly acquired a violet tint) was evaporated to dryness under diminished pressure. Water (100 ml) was added, the solution was washed with ether (3 × 40 ml) to remove aniline, and the aqueous solution was evaporated under diminished pressure to a thin syrup which was dissolved in ethanol (5 ml), treated with 1:1 dry ether–petroleum ether (100 ml), and kept overnight at 0°. The rose-colored solid that separated was filtered off, washed with ethanol, and dried (yield 1.6 g, 90%). It crystallized from ethanol in faintly colored prisms, m.p. 138–140°; $\nu_{max}^{KBr}$ 3300 (broad OH and NH) and 1720 $cm^{-1}$ (lactone); $\lambda_{max}^{EtOH}$ 273 nm (log ε, 4.26); it was soluble in water, sparingly soluble in ethanol or methanol, and insoluble in ether or petroleum ether.

*Anal.* Calc. for $C_6H_{10}N_2O_4$: C, 41.37; H, 5.74; N, 16.09. Found: C, 41.05; H, 5.96; N, 16.31.

*2-Acetamido-3-amino-2,3-dideoxy-*L*-ascorbic acid* (5). — A solution of compound 2 (175 mg, 1 mmole) in glacial acetic acid (6 ml) was heated for 3 h at 100°, and evaporated under diminished pressure to a thin syrup that crystallized upon adding ethanol. The solid that separated was filtered off, washed with ethanol and ether, and dried (yield 150 mg, 75%). Compound 5 crystallized from ethanol in colorless prisms, m.p. 208–209°; $\nu_{max}^{KBr}$ 3380 (OH), 3180 (NH), and 1730 $cm^{-1}$ (lactone); $\lambda_{max}^{EtOH}$ 234 nm (log ε, 4.11); n.m.r. data (in $D_2O$): δ 2.60 (singlet, N-Ac), 4.25 (multiplet, H-6,6′, 4.52 (multiplet, H-5), and 5.6 (doublet, *J* 2 Hz, H-4).

*Anal.* Calc. for $C_8H_{12}N_2O_5$: C, 44.45; H, 5.59; N, 12.96. Found: C, 44.14; H, 5.72; N, 12.92.

*Imidazolines* (3). — A solution of compound 2 (0.05 mole) and the substituted benzaldehyde (0.05 mole) in 1:1 ethanol–water containing a few drops of acetic acid was boiled for 1 h on a steam bath. The solid that separated on cooling was filtered off, washed successively with water, ethanol, and ether, and dried; it was recrystallized from ethanol in pale-yellow needles (except for the product from 2,4-dinitrobenzaldehyde, which was red). Melting points, yields, formulas, and analyses are listed in Table I, together with the u.v. and i.r. data.

*Acetylation of the imidazoline derivatives.* — A solution of each imidazoline (3, 5 mmoles) in acetic anhydride (10 ml) was boiled under reflux for 1 h and then poured onto crushed ice. The resulting solution was evaporated under diminished pressure to a thin syrup, which was dissolved in chloroform (50 ml), and the solution washed with a dilute solution of sodium hydrogen carbonate (to eliminate traces of acetic acid), dried, and evaporated. Samples of the acetates (4) for analysis were obtained as syrups by preparative t.l.c. on silica gel with 7:3 ethyl acetate–methanol as the eluant. The yields, molecular formulas, and microanalyses are listed in Table II, together with the n.m.r.-spectral data.

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