

Photochemical Addition of 1, 3-Dioxolane to D-Ribal Triacetate and Subsequent Hydrolysis of the Adduct.

* Saadon A.Aowda ** Emad A.Jaffer * Mouhannad M.AL-Hachamii

* Dep.of chemistry, college of science, Babylon University

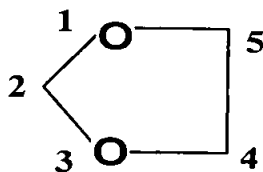
** Dep.of chemistry, college of science, Kofa University

Abstract:

The addition of 1, 3-dioxolane to the endocyclic double bond of 2, 3, 5-tri-O-acetyl-D-ribose (1) enhanced by photochemical radiation using either sunlight or a U-V. lamp. Subsequent acid hydrolysis of the adduct was carried out yielding a product with clear indication of the presence of free carbonyl group. All compounds identified by I.R; C.H.N and N.M.R spectra and T.L.C techniques.

Introduction:

Light induced addition of 1, 3-dioxolane and similar compounds to olefins have been demonstrated by Rosenthal and Elad[1]. Addition of 1, 3-dioxolane to unsaturated carbohydrates was reported later [2]. Photochemical reaction products showed that 1, 3-dioxolane favours addition at position (2) and less likely at position (4) [3]. A mixture of products is usually obtained indicating the most probable free radical mechanism of addition.



1, 3 -Dioxolane molecule

Hydrolysis of the 1:2 adduct was the important next step as the expected 2,5-anhydrofuranose to be produced would have a free aldehyde group at C₁ which is an attractive functional group for elaboration of C-nucleosides and their analogous[4].

Experimental:

Photolysis work:

1. Under Ultraviolet Light:

A) By using 1, 3-dioxolane and aqueous acetone:

A mixture of 1, 3-dioxolane (15 ml.), aqueous acetone (2 ml, 2%), and the D-ribose derivative (1 g.) was irradiated for 24 hrs.

A solution of D-ribose derivative (1) (0.5g.) in acetone (4 ml.) was then added in four equal portions at (12) hrs intervals and the mixture was further irradiated until there was no change in reaction mixture (96) hrs.

T.L.C (benzene: methanol 8:2) indicated the presence of three components after 36 hrs. which possessed identical R_f values to the reagents. After further 24 hours two more compounds were developed. The reaction mixture was dried over anhydrous sodium sulphate, filtered, and then evaporated to dryness. The residue (1.3 g.) was adsorbed on silica gel (150 g.) Elution with benzene

afforded a fraction (0.39 g. 20% yield) which was attributed to the starting material (1) followed by a second fraction (0.8g. 47.6% yield) which was identified as 1:2 adduct of 1,3-dioxolane ribofuranoside derivative whose I.R. spectrum showed a strong absorption for (OH) group at absorption band at 1645 cm^{-1} for olefinic bond ($\text{HC}=\text{C}$).

Anal. Calc.: for $\text{C}_{12}\text{H}_{18}\text{O}_8$ C = 49.65%, H = 6.20%
Found: C = 49.14%, H = 6.79%

N.M.R data: at ppm, (δ) 3.7 (A-protons, singlet, ethylene)
 4.7 (1-proton, singlet, acetal H)
 5-5.7 (1-proton, multiplet, H_3)
 4.2 (4-protons, multiplet, $\text{H}_1, \text{H}_4, 2\text{H}_3$)
 4.7 (2-protons, indistinct doublet, superimposed acetal H, and H_2).
 2.45 (1-proton, broad multiplet, OH).
 3 (9-protons, singlets, 3 OAc).
 2.03, 0.5-1.5 belonged to reagent.

Elution with benzene: methanol 8:2 gave third fraction (0.23 g.) (13.6%) whose I.R. spectrum was identical with that of the second fraction of 1:2 adduct of 1, 3-dioxolane derivative.

Anal, calc.: for $\text{C}_{10}\text{H}_{16}\text{O}_7$ C = 48.22%, H = 6.45%
Found: C = 47.38%, H = 6.96%

While the last fraction was obtained in (6% yield) whose elemental analysis indicated, that it was not a carbohydrate compound.

B) By using 1, 3-dioxolane and dry acetone:

A mixture of 1, 3-dioxolane (15 ml), dry acetone (2 ml) and D-ribose derivative (1) (1 g.) was irradiated for (24) hrs.

A solution of D-ribose derivative (1) (0.5 g.) in acetone (4 ml) was then added in four portions at (24) hrs. intervals and the mixture were further irradiated until there was no change in reaction mixture (144) hrs.

T.L.C indicated the presence of three components after (72) hrs. this was attributed to the starting material and reagents respectively. The fourth, fifth, and the sixth components were developed after (96), (120), and (156) hrs. respectively.

Excess reagents were removed under reduced pressure and the residue (1.3 g.) was chromatographed on silica gel (50 g.) Elution with benzene gave D-ribose derivative (1) (0.4 g., 26.6% yield), followed by 1:2 adduct of 1,3-dioxolane ribofuranose derivative (0.7 g., 41.6% yield) as a syrup product whose I.R. and N.M.R. spectra were identical with the ones obtained from photolysis in the presence of aqueous acetone.

Elution with benzene: methanol 8:2 afforded a third fraction (0.25 g., 14.8% yield) whose I.R. spectrum was identical with that of the second fraction of 1:2 adduct, while the last fraction was obtained in (5%) yield as a side product.

2. In direct sunlight:

The method of Rosenthal and Elad was followed [1]. A mixture of 1, 3-dioxolane (10 ml), dry acetone (2 ml) and D-ribose derivative (1) (0.5g.) was left in direct sunlight for one day.

A solution of olefinic sugar (1) (0.25 g.) in acetone (3 ml) was then added in seven equal portions at one day intervals and the mixture was left in sunlight for another (8) days.

T.L.C indicated the presence of three components after (3) days while the fourth and the fifth components were developed after (5) and (10) days respectively. Excess reagent was removed under reduced pressure and the residue (0.6 g.) was chromatographed on a silica gel (40 g.).

Benzene eluted a fraction (0.19 g., 26% yield) which was identified as the starting material. Elution with benzene: methanol 8:2 afforded a second, fraction (0.35 g., 41.66% yield) which was identified as 1:2 adduct of 1, 3-dioxolane derivative followed by a third fraction (0.12 g., 16.5% yield) which was identified as the deacetylated product of 1:2 adduct of 1, 3-dioxolane derivative, while the last fraction was also obtained in (6%) yield as in the previous experiment.

Acid hydrolysis of the 1, 3-dioxolane adduct to generate the free aldehyde compound:-

A stirred solution of 2-(2, 3, 5-tri-O-acetyl- β -D-ribo-furanosyl) -1, 3-dioxolane (2) (0.25 g.) in acetic acid-water 1:1 (8 ml) was continued for over (24) hrs.

T.L.C showed a slight change in R_f value and a yellow spot appeared on treatment with alcoholic 2, 4-dinitrophenyl hydrazine spray. The product was isolated using chloroform yielding a syrup product (0.1 g.).

I.R. data: film v max. No absorption for (OH) group.
1745 cm^{-1} due to (O=C) of Ac group,
1720 cm^{-1} due to aldehydic group (-CO)
2880 cm^{-1} due to aldehydic proton.

N.M.R data: at ppm (δ) 8.15 (integrated area was not clear presence of aldehydic H)

5.1 (1-proton, multiplet, H_3)
4.3 (4-protons, doublet, $\text{H}_1, \text{H}_4, 2\text{H}_5$)
3.9 (1-proton, triplet, H_2).
2.1 (9-protons, singlet, 3 OAc.)

Base-hydrolysis of 1:2 adduct:-

A solution of 1:2 adduct (2, 3) (0.089 g.) in dry ethanol (1 ml) was treated with a solution of sodium ethoxide (2 ml, 0.02 N). The reaction mixture was shaken for (5) hrs. T. L.C in benzene: Methanol 8:2 indicated the presence of two components.

BIO - RAD (Dowex 50 - W - X) resin (H^+) was added to stop the reaction, filtered, evaporated to dryness, yielded a syrup product.

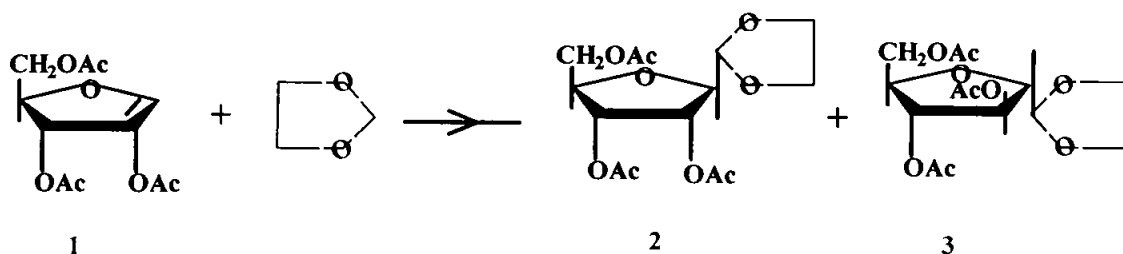
I.R. data: Film v max. 3400 cm^{-1} for (OH) groups
1745 cm^{-1} for carbonyl group

N.M.R data at ppm (δ) 4.7 (1-proton, singlet, acetal)
3.7 (4-protons, multiplet, methylene protons).

Results and discussion:

2, 3, 5-tri-O-acetyl-D-ribose (1) was radiated, under direct sunlight in dry acetone using quartz cell. The products were identical to the one obtained under radiation with U.V. light using a high pressure mercury lamp. When aqueous acetone was used, the reaction was found to be faster with better yields.

The photochemical addition of the 1,3-dioxolane-2-yl-radical to (1) would take place at C_1 mainly [3] from both α - and β sides of the 1-enofuranyl ring thus giving (2) and (3) in a relative ratio of 1:1.

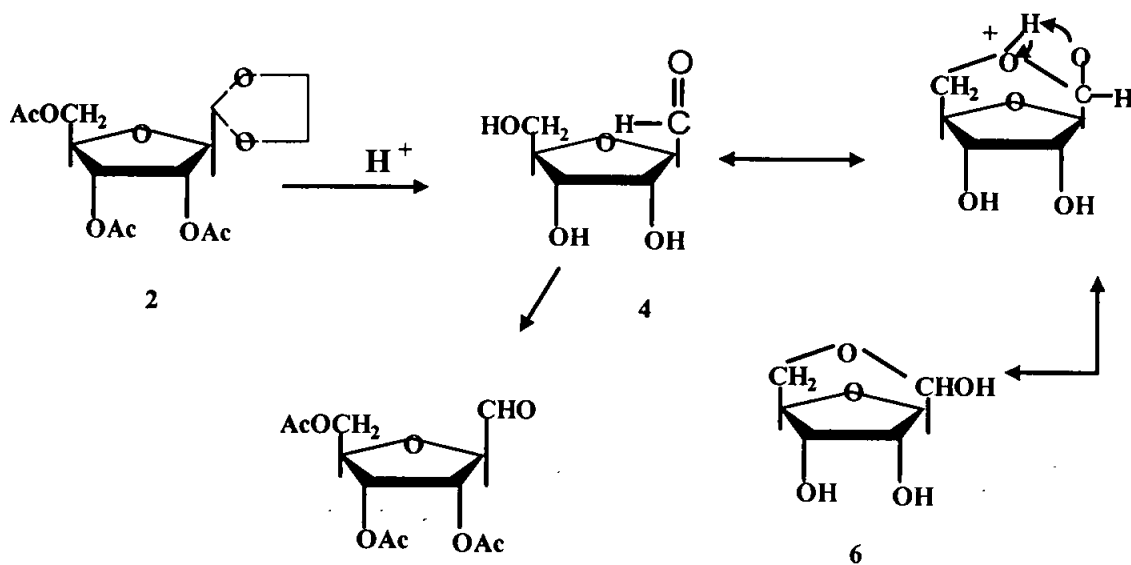


T.L.C indicated the presence of mainly two spots attributed to compounds (2) and (3) and some of the starting material. Prolonged treatment would result in the formation of deacetylated products.

Elution of the products by 1 column chromatography afforded reasonable yields of the expected products which were identified by C, H analysis and both. I. R. and N.M.R spectroscopy.

I.R. spectroscopy indicated the absence of C =C stretching in the products. N.M.R spectroscopy indicated the absence of the chemical shift of the olefinic proton with the presence of a lower shift for aldehydic proton plus other shifts for ethylenic Protons.

Acid treatment of compound (2) as an attempt to produce compound (5) was not successful due to the apparent rearrangement of (5) after deacetylation in the acidic medium [4] to give the 1, 4 anhydro allose (6) which was indicated clearly by elemental analysis on the isolated, products from such treatment.



Therefore, it was important to reacetylate (4) in the reaction mixture to protect C₅ from attack using acetic anhydride and pyridine then the product after isolation was treated with aqueous acetic acid (50%) [5-8]. T.L.C indicated the presence of two components. The more polar component gave positive test with 2, 4-dinitrophenyl hydrazine.

I.R. spectrum of the expected aldehydic product showed the presence of acetate groups at 1745 cm⁻¹, and H-C=O stretching at 2880 cm⁻¹, while the N.M.R. data showed the presence of an indistinct doublet at δ 8.81 corresponding to aldehydic proton.

Further proof of the structure of the 1:2 adduct was achieved by its hydrolysis in sodium ethoxide to give the free alcohol, 2- β -ribofuranosyl-1,3-dioxolane which showed two significant signals at δ 4.7 and δ 3.7 for the acetal and methylene protons respectively by N.M.R spectroscopy.

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