Synthesis of new di-1, 2, 3-Triazoline derivatives for D-3-deoxy-Ribohexulose sugar derivative

Ezat H. Zmam*, A.J.A. Kadir, Mufid J. Awadh*****

Chem. Dep., College of Science, University of Kufa* Chem. Dep., College of Education, University of Baghdad** Chem. Dep., College of Medicine, Babylon Universit y ***

الخلاصـــة

حضر مثيل- د- فركتوبايرانوسايد أولا من مفاعلة الفركتوز مع الميثانول في وسط حامضي تحت ظروف مسيطر عليها حرارياً لضمان الحصول على الحلقة السداسية . حجبت مجاميع الهيدروكسيل في المواقع C_4 و C_5 من خلال تحويلها إلى مجاميع الايزوبروبالدين بمفاعلة (١) مع الأسيتون في وسط حامضي وكذلك حولت المجاميع الهيدروكسيلية في المواقع C_1 و C_3 إلى مجاميع مسيل بمفاعلة (٢) مع كلوريد المسيل في درجة الصفر المئوي. المركب الرئيسي في هذا البحث هو مركب (٤) حضر بمفاعلة (٣) مع مكافئين من أزيد الصوديوم ورباعي بيوتيل امونيوم برومايد. مفاعلة (٤) مع كل من انهيدريد الماليك ، بارا- بنزوكوينون ، كحول السينناميل ، اكريل امايد ، بنزال اسيتوفينون واسيتات الفاينيل للحصول على المركبات (٥) ، (٦) ، (٧) ، (٨) ، (٩) و (١٠) . شخصت جميع المركبات المحضرة باستخدام تقنية TLC والأشعة تحت الحمراء وتحاليل العناصر وكذلك طيف الرنين النووي المغناطيسي.

Abstract

To achieve this work, Methyl- D- fructpyranoside (1) was synthesized first by treating D-Fructose with Methanol in acidic medium under thermodynamically controlled conditions to make sure that the fructopyranoside are the predominant product. The hydroxyl group at C_4 and C_5 were converted into Isopropylidine (2) by treating (1) with Acetone in acidic medium, and hydroxyl group on C_1 and C_3 were converted into mesylester (3) by treated (2) with two equivalents of mesylchloride at $0C^{\circ}$. The vital compound in this synthesis compound (4) was obtained by treatment of (3) with two moles of sodiumazide in presence of TBAB. Reaction (4) with unsaturated compound like maleicanhydride, p-benzoquinone, cinnamylalcohol, acrylamide, benzalacetophenone and vinylacetate formed compounds (5), (6), (7), (8), (9) and (10) respectively. The course of the reactions as well as the purity of products were monitored by means of T.L.C. Identification of products were achieved by elemental analysis (C.H.N), I.R. spectroscopy and ^{1}HN.M.R.

Introduction

D-Fructose is a monosaccharide that was employed to make new derivatives especially in its furanose form [1,2].In this paper, some new fructopyranoside where the introduce 1,2,3-triazoline ring at $C_1$and C_3 position , these 1,2,3-triazole system has widespread uses, and it has been considered as an interesting component in terms of biological activity [3-7]. The application of 1, 2, 3-triazoles in the field of conformational studies has occurred only recently [8-14]. The Huisgen 1,3-dipolar cycloaddition of azides and alkynes resulting in 1,2,3-triazoles is one of the most powerful click reactions [15-19] . In general, 1, 2, 3-triazole formation requires harsh conditions, that is, high temperature and longer reaction times. In the original description, the explored examples showed that although these were relatively clean processes, they could take from 12 to 48 hours at high temperatures (~110 C^{o}) [20].

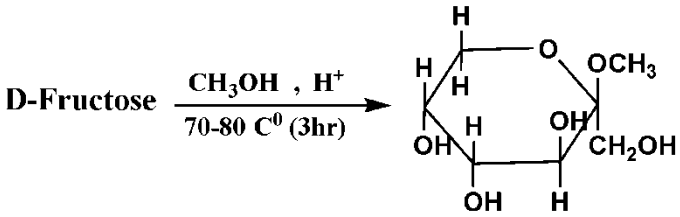
Experimental

All solvents used were redistilled. I.R spectra were recorded on Schimadzu I.R- 408 spectrophotometer. Elemental analysis was preformed using a Perkin- Elmer 204E Instrument. . ^{1}HNMR spectrum were recorded on AVarian A 80MHz . Thin layer chromatography (T.L.C) were performed on a silica- gel SG- 40 (Merck) and developed with the solvents mentioned, spots were visualized with Iodine vapor.

Methyl – D – Fructopyranoside (1): (7.5 gm, 31.63 mmole) D- Fructose is dissolved in 0.5% HCl (generated by dissolving 1ml Acetyl Chloride in 106ml absolute Methanol). Reflex under(70 – 80) C for 3hrs. then poured evaporated under vacuum gives (syrup) (5.2 gm, 97%) T.L.C (Benzene : Methanol) (8:2) (R_f, 0.32) I.R spectra (- OH) (3000 – 3500)cm^{-1}, (C-O-C) glycoside (1000 – 1100)cm^{-1}.

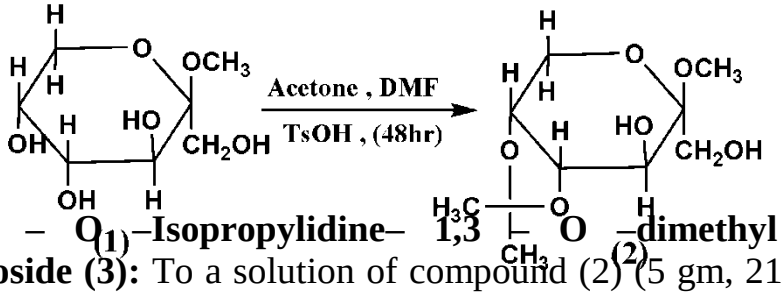
Anal. Calc. for $C_7H_{14}O_6$ C% 43.2 H% 7.21

Found C% 42.82 H% 7.6



Methyl – 4,5 – O – Isopropylidine – D – Fructopyranoside (2): (4 gm, 24.39 mmole) of compound (1) dissolved in (10)ml DMF, then a few drops of solution (Toluene sulfonic acid in Aceton) was added to make acidic. The mixture at room temperature was stirred for 48hr. few drops of solution of Na_2 CO_3 was added, then evaporated solvent under vacuum to give syrup (3 gm, 75%) T.L.C (Benzene: Methanol) (8:2) (R_f , 0.5) I.R spectra (C – H) for Isopropylidine (2700 – 2900) cm^{-1}, (C – O – C) glycoside (1000 – 1110) cm^{-1} and disappear (- OH)band .

Anal. Calc. for $C_{10}H_{18}O_6$ C % 51.28 H% 7.69
Found C% 50.87 H % 7.32

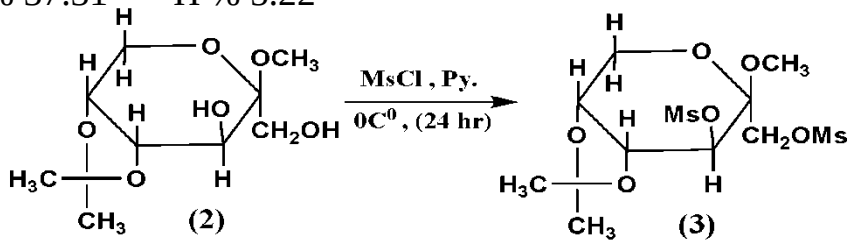


Methyl– 4,5 – O –Isopropylidine– 1,3 – O –dimethyl sulphonyl– D – Fructopyranoside (3): To a solution of compound (2) (5 gm, 21.36 mmole) in 20ml pyridine Mesylchloride was added drop wise Mesylchloride (3.21ml, 3.48mmole). At 0C the reaction mixture was left overnight, then poured in to Ice – Cold water and then extracted with chloroform, evaporated under vacuum to give syrup (4.1 gm, 60.9%) T.L.C (Benzene : Methanol) (8:2) (R_f, 0.6)

I.R spectra (- SO_2) (1180, 1350) cm^{-1}

Anal. Calc. for $C_{12}H_{22}O_{10}S_2$ C % 36.92 H% 5.64

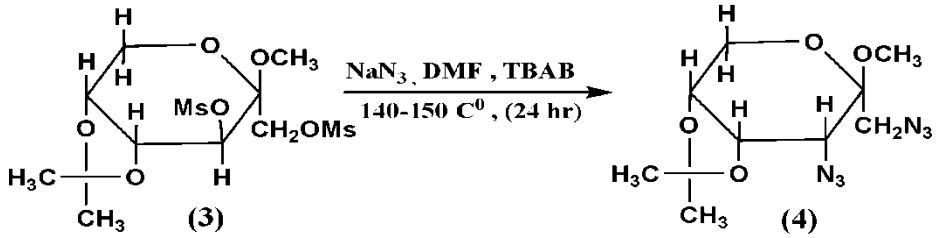
Found C % 37.31 H % 5.22



Methyl– 4,5 – O –Isopropylidine– 1,3 –diAzido– D – 3 –deoxy– Ribohexulopyranoside(4): (4 gm, 8.36 mmole) of compound (3) dissolved in (20)ml DMF, then (1.095, 20.66 mmole) sodium Azide with (0.4 gm, 1.24 mmole) TBAB were added. Reflex under 140 – 150 C for 24hr. poured in to Ice – Cold water and then extracted with chloroform, evaporated under vacuum to give syrup (2.6 gm, 47.3%) T.L.C (Benzene : Methanol) (8:2) (R_f, 0.76)

I.R spectra (C – H) for Isopropylidine (2700 – 2900) cm^{-1}, (C – O – C) glycoside (1000 – 1100) cm^{-1} and disappear ($–SO_2$) band.

Anal. Calc. for $C_{10}H_{16}O_4N_6$ C % 42.25 H % 5.63 N % 29.57
Found C % 42.16 H% 5.23 N % 28.98



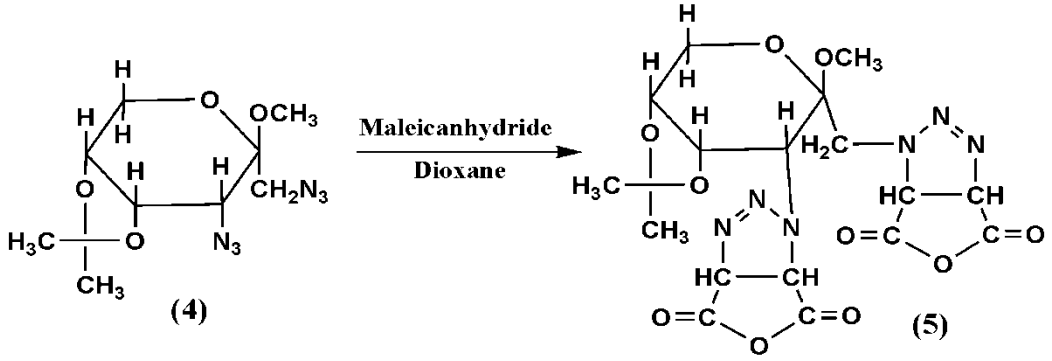
General procedure for prepare Triazoline derivatives: (0.4 gm, 1.4 mmole) of compound (4) dissolved in (20ml) Dioxan, then (20mmole) of saturated compounds was added. Reflex at (50-60)C for (72-96)hrs, poured in to Ice-Cold water, extracted with chloroform, evaporated under vacuum to give syrup.

The last unsaturated compound are Maleicanhydride, p-benzocinnamyl alcohol, acrylamide, Benzal acetophenone and vinyl acetate to form (5), (6), (7), (8), (9) and (10) respectively.

Methyl – 4,5 – O – Isopropylidine – 1,3 – di (4,5 – dicarboxilic anhydride 1,2,3 – triazolinyl) – D – 3 – deoxy – Ribohexulopyranoside (5): T.L.C. (B:M) (8:2) (R_f, 0.7) I.R spectra(C – O – C)glycoside (1000-1100)cm^{-1}, (C – H)Isoprpoylidine (2750-2950)cm^{-1}, (C=O) (1680)cm^{-1} and disappear ($-N_3$)

Anal. Calc. for $C_{18}H_{20}O_{10}N_6$ C % 45.00 H % 4.16 N % 17.50

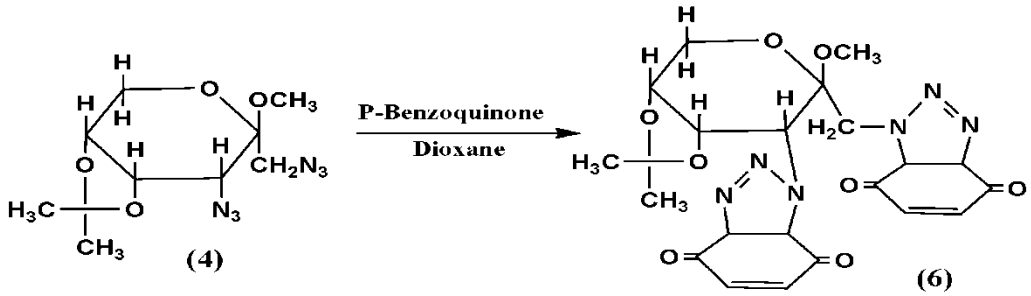
Found C % 45.43 H% 3.82 N% 17.17



Methyl – 4,5 – O – Isopropylidine – 1,3 – di [(7,8,9) – triaza – 2,5 – dione – bicycle [4:3:0]non – 3 – ene] – D – 3 – deoxy – Ribohexulopyranoside (6): T.L.C. (B: M) (8:2) (R_f, 0.6) I.R spectra (C – O – C) glycoside (1000-1100)cm^{-1}, (C – H) Isoprpoylidine (2750-2950)cm^{-1}, (C=O) (1620)cm^{-1} and (1680)cm^{-1}

Anal. Calc. for $C_{22}H_{24}O_8N_6$ C % 52.80 H % 4.80 N % 16.80

Found C % 52.17 H %5.26 N % 16.31

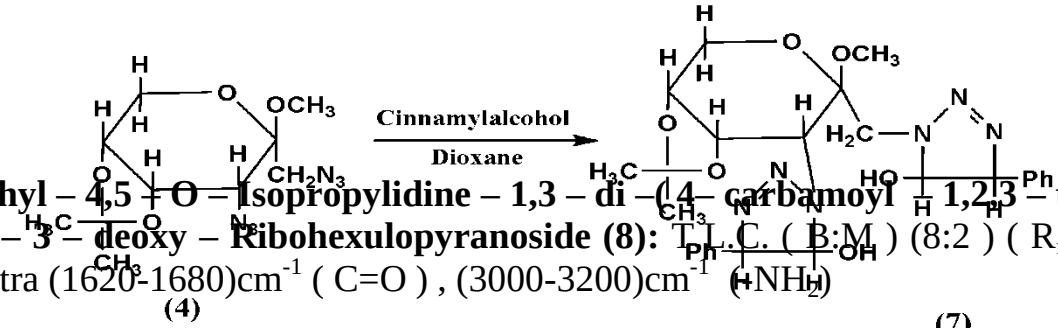


(4) (6)

Methyl – 4,5 – O – Isopropylidine – 1,3 – di –(4– hydroxymethyl – 5 – phenyl – 1,2,3 – triazolinyl) – D – 3 – deoxy – Ribohexulopyranoside (7): T.L.C. (B:M) (8:2) (R_f, 0.62) I.R spectra (-OH) (3000-3400)cm^{-1}, Aromtic (1660-1600)cm^{-1},

Anal. Calc. for $C_{26}H_{32}O_6N_6$ C % 59.54 H % 6.10 N %16.03

Found C % 58.87 H % 16.72 N %15.83

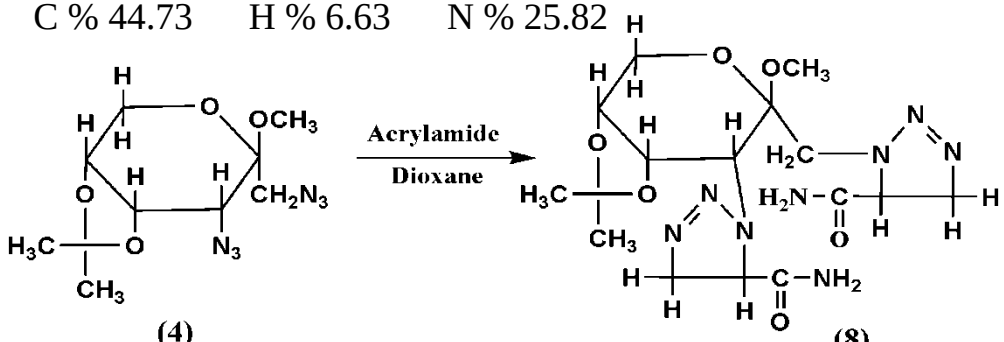


Methyl – 4,5 – O – Isopropylidine – 1,3 – di –(4– carbamoyl – 1,2,3 – triazolinyl) – D – 3 – deoxy – Ribohexulopyranoside (8): T.L.C. (B:M) (8:2) (R_f, 0.68) I.R spectra (1620-1680)cm^{-1} (C=O) , (3000-3200)cm^{-1} (NH_2)

(4) (7)

Anal. Calc. for $C_{16}H_{26}O_6N_8$ C % 45.07 H %6.10 N %26.29

Found C % 44.73 H % 6.63 N % 25.82



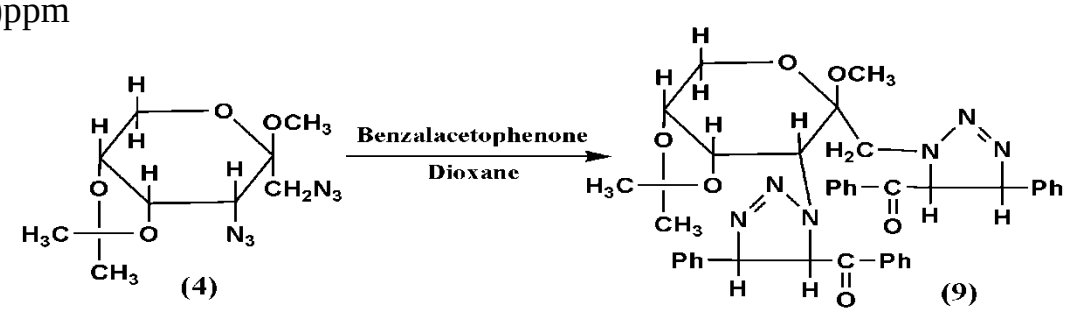
(4) (8)

Methyl – 4,5 – O – Isopropylidine – 1,3 – di (4– benzoyl – 5 – phenyl – 1,2,3 – triazolinyl) – D – 3 – deoxy – Ribohexulopyranoside (9): T.L.C. (B:M) (8:2) (R_f, 0.56) I.R spectra (C=O) (1680-1700)cm^{-1}, Aromatic (1400-1620) cm^{-1}

Anal. Calc. for $C_{40}H_{40}O_6N_6$ C % 68.57 H %5.71 N %12.00

Found C % 69.03 H % 6.22 N %11.72

HNMR spectrum: CH_3 for isopropylidine and glycoside at δ(3.3)ppm , (C-H) of triazoline ring δ(4.5)ppm , (C-H) of sugar ring δ(3.2-3.6)ppm , aromatic ring δ(7.3-7.6)ppm



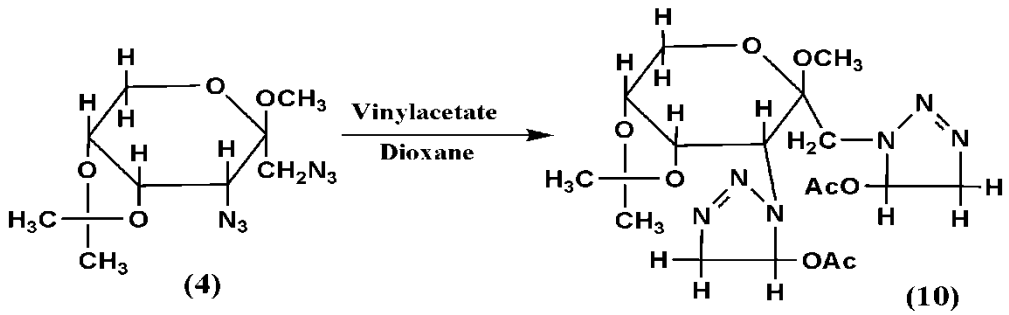
(4) (9)

Methyl – 4,5 – O – Isopropylidine – 1,3 – di (4– O– Acetyl – 1,2,3 – triazolinyl) – D – 3 – deoxy – Ribohexulopyranoside (10): T.L.C. (B:M) (8:2) (R_f, 0.81) I.R spectra (C=O) (1750)cm^{-1}

Anal. Calc. for ***$C_{18}H_{28}O_8N_6$*** C 47.36% H 6.14% N 18.42%

Found C 48.12% H 6.63% N 18.11%

HNMR spectrum: CH_3 for isopropylidine and glycoside at δ(3.3)ppm , CH_2 of triazoline ring δ(1.6-1.8)ppm , (C-H) of sugar ring δ(3.2-3.6)ppm , (CH_3) acetate δ(5.1)ppm , CH_2 δ(2.6-2.9)ppm



(4) (10)

Result and Discussion

The objective of this work is the synthesis of some new (D-3-deoxy-ribohexulopyranosyl) derivatives containing di (1, 2, 3-triazoline ring) in their structures. These compounds may have biological effects beside being prepared for the first time.

First compound was synthesized by treating D- fructose with methanol in presence of acid under thermodynamically controlled conditions to form fructopyranoside as a predominant product [21] . The structure of which was assigned from the I.R spectrum which showed strong absorption for (C-O) glycoside at (1000-1100) cm^{-1} and (-OH) at (3000-3500) cm^{-1}. Elementary analysis showed good agreement of the calculated and found percentages.

Isopropylidine derivatives compound (2) was synthesized by treating compound (1) with acetone in acidic medium, I.R spectra showed weak band of hydroxyl, as well as

Isopropylidine band at (2700-2900) cm^{-1}. C.H.N analysis (the percentages of found agreement with calculated)

Reaction compound (2) with methane sulfonyl chloride in pyridine at room temperature went smoothly (T.L.C) to give di mesylate derivative (3). I.R showed (-SO_2) bands at (1180-1350) cm^{-1} and elementary analysis showed good agreement of the calculated and found percentages. Treatment compound (4) with sodiumazid in DMF at (90-110)C° gave 1,3-diAzido compound (5), the structure of which was assigned from I.R spectrum which showed a strong absorption at (2100-2150)cm^{-1} of (-N_3) and disappear bands of (-SO_2).

The (1,3) dipolar cycloaddition reaction of compound (5) with maleic anhydride, p-benzoquinone, cinnamyl alcohol, acrylamide, benzal acetophenone and vinyl acetate leads to form compounds (5), (6), (7), (8), (9) and (10) respectively.

I.R spectrum showed disappear (-N_3) band and strong absorption of (C=O) at (1680) cm^{-1} for compound (5) and (6). (-OH) at (3000-3500) cm^{-1} and aromatic ring at (1400-1450) cm^{-1} for compound (7). (-NH_2) at (3000-3200) cm^{-1} for compound (8). Carbonyl group and aromatic at compound (9) and finally band of acetate at (1750)cm^{-1} for compound (10).

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