

Synthesis of New type of tetrazoles starting from D-ribose

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Abstract:

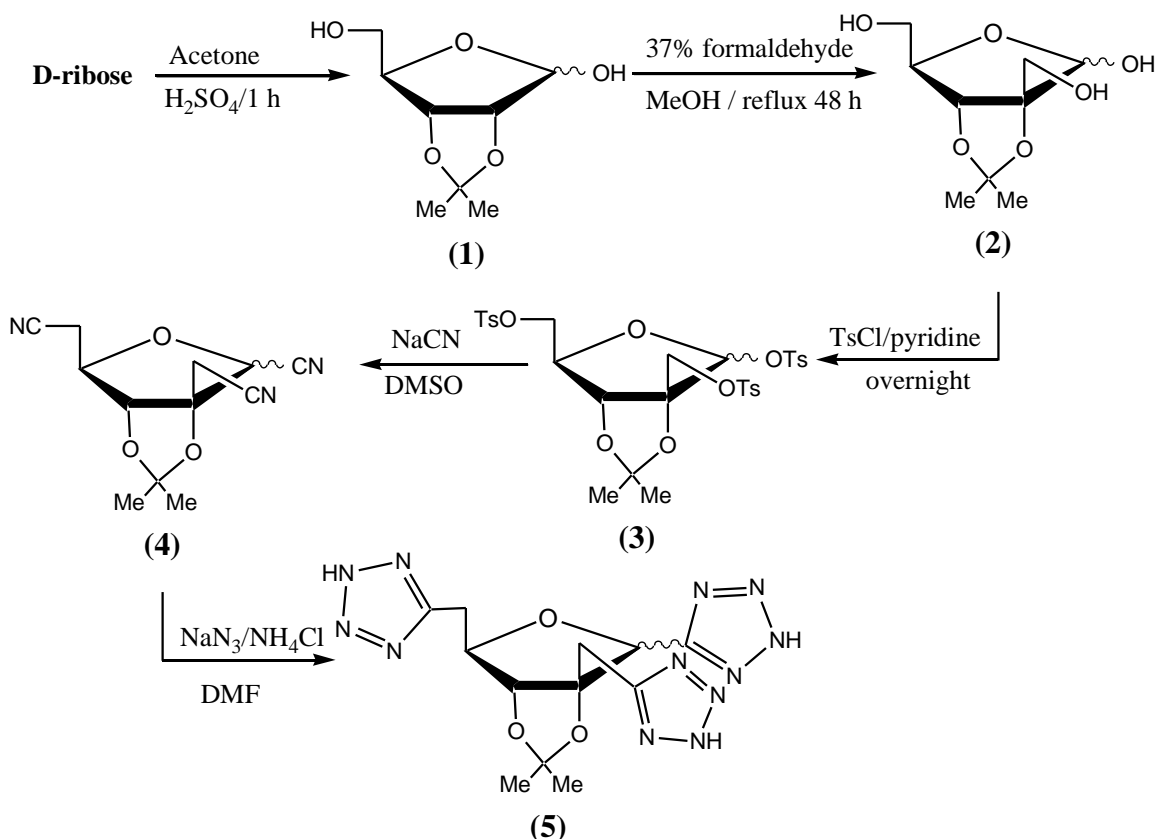
This work includes synthesis of sugar tetrazole derivative, D-ribose reacted with acetone in the presence of sulfuric acid H_2SO_4 to give 2,3-O-isopropylidene-D-ribose (1). The Aldol condensation of (1) with formaldehyde in methanolic K_2CO_3 solution gave 2-hydroxymethyl(2,3-O-isopropylidene-D-ribose) (2). Which was tosylated by Tosyl chloride in pyridine to yield compound (3), S_{N2} reaction of (3) with sodium cyanide in DMSO afforded compound (4). The [2+3] cycloaddition reaction of (4) with sodium azide gave the targeted compound (5). All prepared compounds have been characterized by: TLC, Specific rotation, Microelemental analysis and [FT-IR and 1H NMR spectroscopy]

الخلاصة:

تضمن هذا العمل تحضير مشتق سكر ثلاثي الهيدروكيل حيث تمت مفاعلة acetinatio D-ribose مع الاسيتون بوجود حامض الكبريتيك ليعطيان المركب (1) 2,3-O-isopopylidene-D-ribose، وعند اجراء تكاثف الالدول للمركب (1) مع الفورمالدهايد في محلول كاربونات البوتاسيوم في الميثانول تكون المركب (2) 2-C-hydroxymethyl(2,3-O-isopropylidene-D-ribose) الذي اضيف اليه كلورايد التوسايل كمجموعة مغادرة سهلة لينتج المركب (3)، كما ان تفاعل التعويض النيوكلوفيلي ثنائي الجزئية S_{N2} للمركب (3) مع سيانيد الصوديوم في مذيب ثنائي مثيل سلفوكسيد قد اعطى المركب (4) وعند استخدام ازيد الصوديوم مع المركب (4) بتفاعل الغلق اعطى المركب المطلوب (5). شخصت جميع المركبات المحضرة بواسطة تقنية كروموتوغرافيا الطبقة الرقيقة و الدوران النوعي والتحليل الدقيق للعناصر اضافة الى طيف الاشعة تحت الحمراء وطيف الرنين النووي المغناطيسي.

Introduction:

Tetrazoles are a class of heterocycles with a wide range of applications, receiving considerable attention⁽¹⁾. Tetrazole derivatives have shown valuable properties as precursors of a variety of nitrogen-containing heterocycles⁽²⁾, and have found use in various fields⁽³⁾. 5-Substituted 1H-tetrazoles are usually obtained by the addition of azide ion to organic nitriles, and many methods are reported in the literature^(4,5). Unfortunately, each of those procedures suffers from some disadvantages. Recently, Sharpless and co-workers have reported an innovative and safe procedure for the preparation of 5-substituted 1H-tetrazoles, starting from the corresponding nitriles, using NaN_3 and stoichiometric amounts of zinc(II) salts in water⁽⁶⁾. The preparation of metal-organic coordination polymers from hydrothermal reactions involving in situ tetrazole ligand synthesis has been carried out by Xiong *et al.*⁽⁷⁾. We report here the preparation and structure determination of a sugar tetrazole derived from D-ribose (scheme 1).



Scheme (1) The Synthesis Route

Experimental section

General methods

Fluka AG and Aldrich supplied all chemicals used, reaction were monitored by TLC (F₂₅₀ μm). Infrared were recorded using Testean Sheimadzo FT-IR 8000 series. NMR 300 MHz Bruker had been used to determine the ¹H NMR spectra

Synthesis of 2,3-O-isopropylidene-D-ribose (1)

The titled compound had been synthesised according to literature ⁽⁸⁾
 R_f = 0.57 (1:1 benzene + ether), [α]_D = + 47 (C 1.0, CH₃Cl), FT-IR :- 3445 and 3366 cm⁻¹ (ν O-H) stretching, 2972 cm⁻¹ (ν C-H, CH₃) stretching, 1145 cm⁻¹ (δ_H CH₃) bending, and 1057 cm⁻¹ (ν C-O) stretching. ¹H NMR: - δ =5.10 ppm (d, 1H, H-1), δ =4.13 ppm (m, 1H, H-2), δ =4.10 ppm (m, 2H, H-5), δ =3.66 ppm (d, 1H, H-4), δ =2.99 ppm (m, 1H, H-3) and δ =1.41 ppm (d, 6H, isopropylidene)

Tosylation of compound (2)

Tosyl chloride (3.2 mmole, 0.6g) in small amount of dry pyridine was added dropwise to the solution of compound (2) [(1 mmole, 0.22g) in (15 mL dry pyridine)] at 0 °C. The solution was left to stirring overnight, the product was separated in usual manner to obtain compound (3) as a needle crystals (0.61g, 89%), R_f = 0.41 (2:1 hexane -EtoAc), [α]_D = + 13.5 (C. 1, CH₃Cl), FT-IR :- 3080 cm⁻¹ (ν C-H aromatic) stretching, 2927 cm⁻¹ (ν C-H, CH₃) stretching, 1620 and 1550 cm⁻¹ (ν C=C aromatic) stretching, and 820 cm⁻¹ (δ C-H_{OOP}) bending. ¹H-NMR :- δ =7.87 ppm (m, H aromatic,12H), δ =5.65 ppm (d, 1H, H-1), δ =2.95-4.87 ppm (other sugar ring signals) and δ =1.33-1.57 ppm (m, 15H, isopropylidene and CH₃ of ring)

Cyanation of compound (3)

Sodium cyanide (3.5 mmole, 0.16g) was added to solution of the compound (3) (1 mmole, 0.68g) in DMSO (25 mL) the solution was kept at 50 °C for 5 h. The solution was cooled and concentrated to a residues which was taken up in EtoAc (100 mL) and washed with brine (30 mL) and with water (2 X 30 mL), the organic layer was separated, dried over MgSO₄ and evaporated to dryness to give compound (4) as a white crystals (0.24g , 81.3%), R_f= 0.51 (3:1 hexane –EtoAc), [α]_D - 22.2 (c. 1, CH₃Cl₂), FT-IR : 2926 cm⁻¹ (v C-H_{CH3}) , 2245 cm⁻¹ (v C≡N), 1057 (v C-O) , ¹H NMR :- δ =6.01 ppm (s, 1H ,H-1), δ =4.81 ppm (m, 1H, H-2), δ =3.76 (m,3H, H_{4,s}), δ =3.12 ppm (d, 1H, H-3) and other signals of 1.53 ppm for (6H isopropylidene).

Synthesis of tetrazole

Ammonium chloride (0.16g, 3mmol) was added to the solution of NaN₃ (3.5mmol, 0.22g) and compound (4) (1mmol, 0.295g) in DMF (25mL), the solution was kept at (70 °C) for (48 h) after which time the solution was cooled and concentrated to a residue which was taken up in CHCl₃ , (150mL) and washed with water (3x40mL), the organic layer was separated , dried over MgSO₄ and concentrated to a white solid compound (5) (0.29g, 68.7 %), R_f= 0.61 (6:4 Benzene- ether), [α]_D = - 13.5 (C. 1, CHCl₃), FT-IR :- 3335 cm⁻¹ (v C-H tetrazole), 2928 cm⁻¹ (v C-H_{CH3}), 1667 cm⁻¹ (v C=N tetrazole) . ¹H NMR: - δ =8.01 ppm (s, 3H, H tetrazole), δ =6.02 ppm (s, 1H, H-1), δ =4.79 ppm (m,1H, H-2) δ =3.69 ppm (m, 3H, H-4) , δ =3.09 (m,1H, H-3).

Result and discussion

The first step of this synthesis approach is finding out suitable sugar derivative. The a condensation of 2,3-O- isopropylidene -D- ribose with 37 % formaldehyde in methanol at PH= 9 gave compound (1), we indicate this conversion from the FT-IR by the increasing the intensity and broadening of (OH) band at 3450 cm⁻¹ . Also ¹H NMR spectrum introduced good indicator, the singlet at 2.33 ppm points to the branched (CH₂) the CHN data table (1) enhance our results. Introduction of Tosyl groups to sugar molecule facilitates the subsequent cyanation step, tosylation was carried out in dry pyridine using tosyl chloride, the absence of (O-H) bands around 3400 cm⁻¹ and over is excellent indicator for the tosylation process. The apperace of the aromatic signals at 7.87 ppm in ¹H NMR spectrum supports the success of tosylation. Cyanation occurred via SN₂ mechanism by sodium cyanide in DMSO. FT-IR spectrum showed a new band at 2245 cm⁻¹ which attributed to (C ≡ N) group. The disappearance of aromatic single at 7.87 ppm and the signal of (CH₃) protons around 1.30 ppm reinforced our synthesis route. [2+3] thermal cycloaddition reaction has been utilized to synthesis of tetrazole. The band at 2245 cm⁻¹ had been disappeared in the FT-IR spectrum, also the appearance of the signal at 8.01 ppm in the ¹H NMR spectrum provide the evidence of tetrazole formation.

Table (1) Microelemental analysis of the prepared compounds

Compound	MWt	Formula	C%	H%	N%
1	190.19	C ₈ H ₁₄ O ₅	50.52	7.42	-
			(50.49)	(7.33)	-
2	220.22	C ₉ H ₁₆ O ₆	49.09	7.03	-
			(49.05)	(6.98)	-
3	682.78	C ₃₀ H ₃₄ O ₁₂ S ₃	52.77	5.02	-
			(52.68)	(4.97)	-
4	247.00	C ₁₂ H ₁₃ N ₃ O ₃	58.29	5.30	17.00
			(58.26)	(5.16)	(17.09)
5	376.33	C ₁₂ H ₁₆ N ₁₂ O ₃	38.30	4.29	44.66
			(38.26)	(3.22)	(44.71)

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