Reaction of D-glycals derivatives with Carbohydrate azides derivatives Via 1,3- dipolarcycloaddition reaction

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Abstract

The compounds of the present study are synthesized of disaccharides where the link between the two carbohydrate groups via a 1,2,3,-triazole or triazoline groups one type of sugars is unsaturated sugar which contained carbon carbon double bond inside the ring , like 3,4,6 – tri acetyl glucal and 1,3,4,6,-tetra benzoyl fructal.Addition of seven azido sugars derivatives to seven tri-O-acetyl-D-glucal and 1,3,4,6,-tetra benzoyl fructal and their derivatives, by applied 1,3-dipolarcycloaddition reaction seven Triazolylsaccharides were obtained .The structures of all the products obtained have been identified by spectral (IR , H^1 – NMR) , elemental(C,H,N) analyses and by some physical properties .These compounds are expected to show an importance in organic synthesis and expected to be more stable to enzymatic and chemical hydrolysis . They may find utility as enzyme inhibitor agents and potentially as pharmaceuticals.

الخلاصة

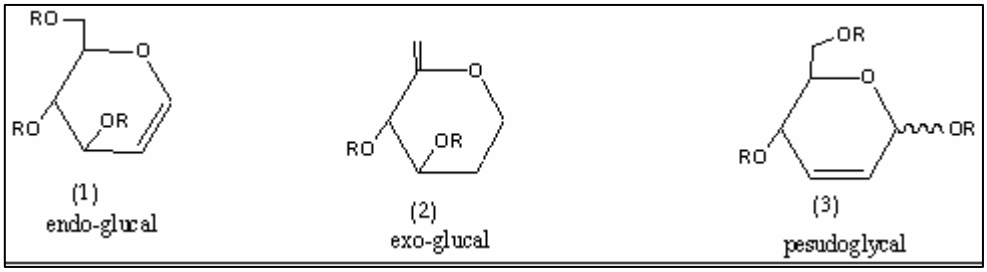
يتضمن البحث تحضير مشتقات كاربوهيدراتية جديدة تتميز بارتباط سكريين أحاديين بواسطة حلقة غير متجانسة أرومانية أو غير أرومانية حيث يرتبط السكر الأول بـ نتروجين الحلقة و يرتبط الـسكر الثـاني بـذرة كربون C-5 أو C-4 لنفس الحلقة.و للحصول على هذه الأنواع من المركبات تطلب الأمر وضع إسـتراتيجية تسهل الوصول إلى الهدف ، حيث قسمت إلى اتجاهين ، الاتجاه الأول هو تحضير مشتقات سكرية غيـر المـشبعة تحتوي في تركيبها على آصرة كربون – كربون مزدوجة فقد تم تحضير ثلاثي اسنينات كلوكال, و رباعي بنزويل فروكتال المرحلة الثانية هي تحضير مشتقات سكرية تحتوي على مجموعة أزيد أيضاً في مواقع مختلفة من السكر باستخدام طرق عمل مختلفة للحصول على المشتقات الإزيدية . المرحلة الأخيرة من الدراسة فبعد حصولنا علـى متطلبات تفاعلات الإضافة ثنائية القطب فقد اختيرت ظروف تفاعل مختلفة منها الطريقة الحراريـة الاعتياديـة حيث تطلب الآمر وقت أطول و حرارة مرتفعة . أيضاً أجريت بعض التفاعلات باستخدام تقنية الأنبوب المغلق

ولغرض التقليل من وقت التفاعل ودرجة الحرارة فقد اختيرت تقنية المايكروويف في إجـراء هـذا النـوع مـن التفاعلات .

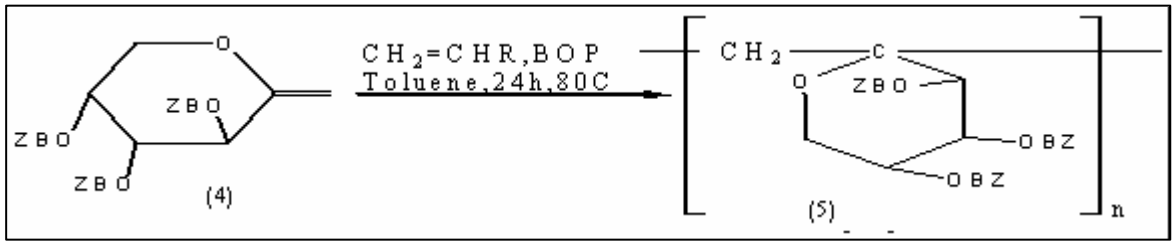
تم الحصول عل المشتقات (ترايزو سكريات ثنائية) جديدة تمتاز بكونها ذات فعاليه حياتيه حيث أن هذه المركبات هي سكريات ثنائية مرتبطة بحلقة ترايزولينيل او ترايزونليل و ليس أرتباط كلايكوسـيدي اوكـسجيني وهذا ما يجعلها مقاومة في بعض الأحيان للتحال الكيميائي و الأنزيمي و تستخدم ايضا كعوامل مثبطات انزيمية و فعالية صيدلانية .شخصت جميع المركبات أعلاه باستخدام الطرق الطيفية (طيف الأشعة تحت الحمراء و كـذلك طيف الرنين النووي المغناطيسي و كذلك تحاليل العناصر بالإضافة لدراسة بعض الخواص الفيزيائيـة للمـشتقات المحضرة) .

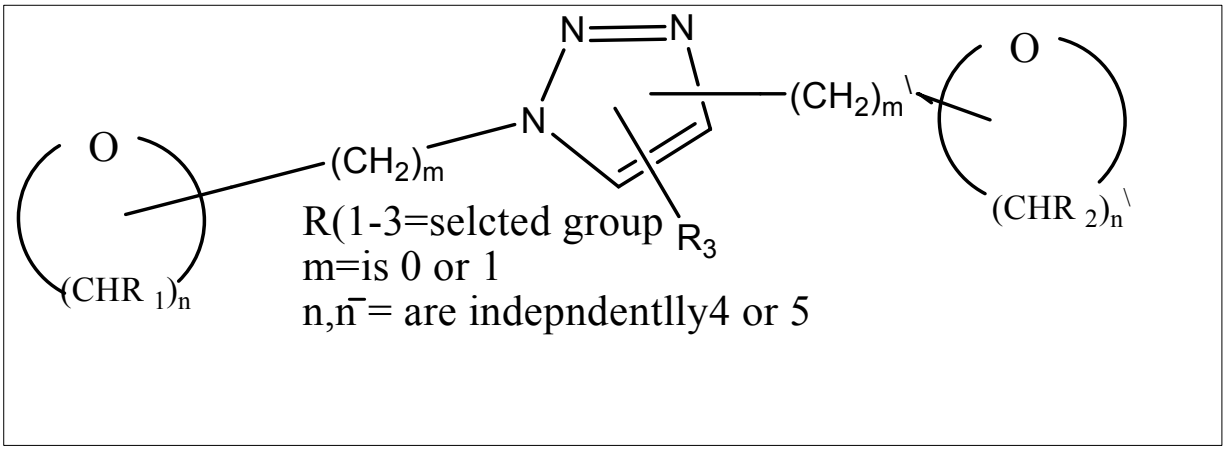
Introduction

One of the most abundant classes of organic and biological molecules found in nature is carbohydrate.Many stable discrete carbohydrate derivatives, possessing a double bond in the carbon skeleton are now known .The double bond can be produced by the dehydration of a monosaccharide. This olefin double bond can be in *endo* (inside the sugars ring)[1] or *exo* (outside the sugar ring)[2],Cyclic position of the pyranoid six – member ether ring or furanoid five member ether ring structure of the monosaccharide derivatives involving several positions of the sugars ring[1,2]



Unsaturated sugar monomers are useful building blocks for the synthesis copolymers with special properties like biocompatibility, biodegradability copolymers with special properties like biocompatibility, biodegradability hydrophilicity hydrophobic balance and skin compatibility [3]Unsaturated sugar monomers have been prepared on the basis of monosaccharide such as: D- Ribose[4], D-glucose and D-fructose[5]. The polymerization group can be *exo*- or *endo*- cyclic involving several positions of the sugar ring. Different saccharide polymers [5] based on unsaturated protected sugars have been synthesized[6]





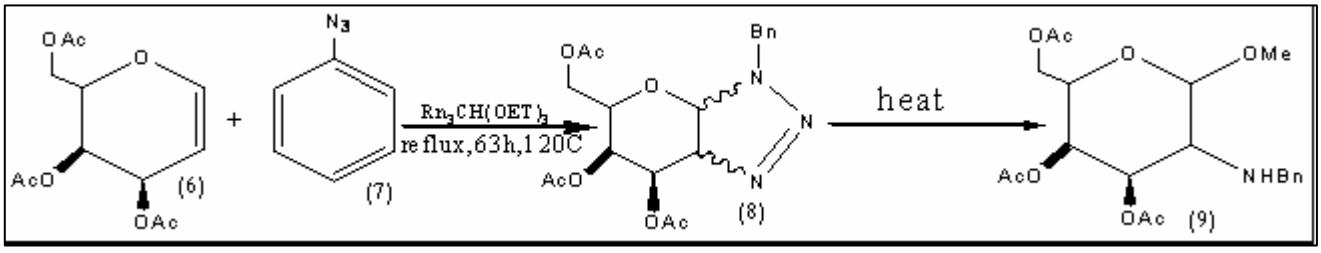
Glycals are cyclic compounds having a double bond between C-1 (anomeric carbon) and C-2

(the adjaceement carbon atom); they are vinyl ethers and consequently can take part in a wide variety of selective addition reactions because they have highly electron – rich position. Pyranoid and furanoid members are known and the esters of each also undergo rearrangement to give 2,3-unsaturated

product [7] .

Ness and Fletcher[8] noted that in view the wealth of synthetic uses which have been found for the ordinary aldopyranose related glycals,it is somewhat surprising that more attention has not been paid to ketoses related glycals [9]

The addition of a 1,3- dipole to a carbon- carbon double and triple bond leads to the synthesis of both aromatic and non- aromatic five- membered ring heterocyclic[10] is a classic reaction in organic chemistry.. 1, 2, 3- Triazoles are an important class of compounds because of their wide rang of applications [11]; they have biological activity and are seen in many drugs[12, 13] , also have broad use in industrial applications[14] such as: - dyes and brighteners for fibres; corrosion inhibitors for many metals and alloys; light stabilizers for organic materials and polymers, and agrochemicals as herbicides, fungicides, and antibacterial agent. Tri-*O*-acetyl-D-galactal [8] reacts with benzyl azide [7] to form triazoline [8] subsequent photolysis and ring opening efficiently provides the corresponding methyl glycoside [15]. [9]



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The 1, 3-DC reactions are an efficient and highly versatile tool for the construction of multivalent structures such as sugars heterodimers, glycoclusters, calyx-sugars and glycocyclodextrins.
Triazolyldisaccharides are compounds having monosaccharide where the link between them is via a 1,2,3- triazole group; where theN-1of the triazole ring is linked to the first sugar and the C-4 or C-5 of the same ring linked other sugar [16]

Triazolyldisaccharides are expected to be synthesized by more general methods which use 1, 3-DC reactions where the glycosyl azides and the alkynes are prepared by different method.

Experimental

General

Melting points (mp) were determined by Electro thermal 1A 9000 Digital – series , and uncorrected . Infrared (IR) spectra were recorded using a NICOLET 410 FT-IR spectrometer and Perkin -Elmer L110- 0627 , 2001 . (in cm^{-1}) (H-NMR) spectral were registered at Perkin –Elmer 200 MH2 and Topsin 1-2 /BRVKER 400 MH2.((Jordain and France) Using tetramethyl silane (TMS) as an internal standard, and $CDCl_3$ DMSO as solvents. Microwave reactions were preformed on apparatus Discover system CEM,2455 MHZ) , and some reaction on Domestic microwave oven in a ascre-cap close

(simith tube).(France). Evaporating of solvent by using Buch vacuum rotary evaporator type 160 TLC was performed on pre-coated sheets with 0.25 mm layer of silica Gel G/UV 254 , the detection was followed by UV-lamp or through coloring with iodine vapor or H_2SO_4 in ethanol 60% , followed by heating. The Elemental analyses were performed in the analytical Laboratory of AL-al – bayt University. The chromatography separation carried out using Merck silica gel (60-230 mesh) .The rations of the solvents and mixed mobile phase were given in volume ratios .All materials , unless otherwise noted , were obtained from commercial suppliers and used as provided .Dichloromethane and Chloroform were dried and distilled over anhydrous calcium chloride. Ethanol and methanol were dried and distilled over magnesium . Acetone was dried and distilled prior to use from phosphorus pentoxide (P_2O_5) . Pyridine was distilled from calcium hydride under nitrogen . Dimethyl formamide dried and distillation after that stored over molecular sieves. Dry CH_3CN is distilled from CaH.

Synthesis of *O*-glycoside of glucal sugar

1-*O*-Propargyl- 4, 6- di-*O*-acetyl glucal [17, 18] [10]

Method A

Tri – *O* –acetyl – D – glucal (2.5 g , 9.1 mmo1) was dissolved in (25 ml) toluene containing propargyl alcohol (0.598 ml ,10.2 mm01) under nitrogen . Anhydrous zinc chloride (1.79 g, 13.1 mmo1) was added in one portion to the mechanically stirred solution.

A purple color developed after 25 mints , the supernatant was decanted from the gelatinous solid , neutralized with solid sodium bicarbonate , filtered and concentrated to give the product[10] as a yellow syrup

(1.66g , 69% yield) *Rf* = 0.25 (CH_2Cl_2 : MeOH) (8 : 2) (v:v)IR (film)

(3277 , 2920 , 2118 , 1740 , 1370 , 1270 , 1237 , 1060 , 912 , 733)cm^{-1} , Fig (10)

calculated for $C_{13}H_{16}O_6$, C, 58.20 ; H, 5.97found C,58.00 ; H, 5.22

Method B

To a stirred solution of 3,4,6 tri-D-glucal [12a] (2.5g ,9.1mmo1) in dry toluene (25 ml) were added propargyl alcohol (0.5ml ,0.2mmo1) and a catalytic amount of $BF_3.Et_2O$ (0.4ml , 3.25 mmo1) . the mixture was allowed to react for 1 h and then neutralized by addition of Na_2CO_3 2g . After the solution had been stirred for 30 min , the solids were filtered off and the filtrate was successively washed with a saturated aqueous solution of $NaHCO_3$ and dist. water . After drying with anhydrous Na_2SO_4 , the solvent was evaporated on a rotary evaporator under vacuum affording a syrup. The residue was purified by dry flash chromatography petroleum ether : ethylacetate) (2 : 1) (v:v)

(0.87 g , 37 % yield) .

Method C:

A mixture of 3,4,6-tri –D– acetyl – D–glucal (1.36 g , 5 mmol) , propargyl alcohol (0,408ml , 7 mmol) and ceric ammonium nitrate (0.274 g , 0.5 mmol) in acetonitrile (15 ml) was stirring under reflux for 6 hr . After completion of the reaction as indicated by TLC, the reaction mixture was quenched with water (10 ml) and extracted with ethyl acetate(3 ×10ml) .The combined layers were dried over anhydrous $NaSO_4$, concentrated in vacuo and purified by column chromatography on silica-gel (petroleum ether : ethyl acetate 8 : 2) to produced [10] (1.074 g, 78 %)

***O*-Allyl- 4,6- di-*O*-acetyl glucal**

Similar procedure was followed which was used in preparation compound [10] but using allyl alcohol (0.478 ml , 7 mmo1) instead of propargyl alcohol ,to produce [11] as a syrup(1.57 g 63 % yield) . *Rf* = 0.24 (CH_2Cl_2: MeOH) (8 : 2) (v:v)IR (film) 1760 cm^{-1} (C=O) , 1651 cm^{-1} (C = CH_2) ,1044 cm^{-1} (C-O-C) Fig (11)Calculated for $C_{13}H_{18}O_6$: C,57.77 ; H , 6.66C,57.01 ; H , 6.13

Synthesis of 1,2-unsaturated sugars

Synthesis of 3 , 4, 6-Tri-acetyl glucal[19]

Part : 1

D–Glucose (5.5 g, 30.5 mmol) was added to a mixture of acetic anhydride (20ml)and 0.15 ml , 62 % perchloric acid at 40ºC during 1 hours. After the addition of red- phosphorus (1.5 g, 48.4 mmo1). The round bottom flask was cooled in ice-salt mixture, and bromine (2.9 ml, 39.03mmo1) was added drop wise with continued stirring at such a rate as to keep the internal temp. Below 20ºC (1 hours). In the same way, 5 ml of water was added during a course of 30 min with careful control of temp. The vessel was closed by stopper and kept 3 hr at room tempt. The mixture was filtered and the filter paper washed with little acetic acid. The filtrate contained tetra –*O*– acetyl-D - glycopyranosyl bromide.

Part: 2.

A solution of sodium acetate (20 g, 243mmo1) in water (29 ml) and glacial acetic acid (20ml) was prepared. After the solution was cooled in an ice-salt mixture , zinc dust (11g, 168mmo1)

and cupric sulfate(1.1 g , 6.9mmo1) in water (4 ml) were added to this solution When the blue color had disappeared ,the solution of above mentioned bromide was added gradually during 1 hr ,keeping the temperature between(–10 and–20º C).Efficient stirring was necessary and was continued for 3 hr at 0 ºC the mixture was filtered , and the filter paper was washed with 50% acetic acid . Water (50ml) was added to the combined filtrates at 0 ºC and the solution was extracted with chloroform (5×100ml). The combined chloroform extracts were washed with iced-water, saturated sodium carbonate solution, and again with cold water. The solution was dried by addition of calcium chloride, decanted, and evaporated under reduced pressure. The resulting syrup was dissolved in diethyl ether and petroleum ether was added to solution to opalescence. After a few hours with the aid of seeding crystallization provided pure [12a] . (5g , 60 % yield m.p 53-54 ºC lit[18] : 54-55 ºCIR(KBr) 1744 cm^{-1} (C=O), 1650 cm^{-1} (C=C) Fig (14)

Synthesis of glucal [12b]

To a stride solution of tri – *O*-acetyl-D- glucal[12a] , (2 g) in dry methanol (32) ml was added methanolic solution of sodium methoxide (prepared by dissolving 0.250 mg of sodium in 2 ml methanol) and the solution was left at room temp. for 2 days . Evaporation of the solution gave crystaline [12b] (1 g , 50%) m.p 56-58 ºC lit.[20] m.p 57-59 ºCIR(KBr) 3370 cm^{-1} (OH) , 1653 cm^{-1} (C=C) Fig(15)

Synthesis of Fructal[21] [13]
Tri (benzoyloxy) –1-benzoyloxymehyl –3,4- dihydro-2H-pyran (*endo* –fructal)

To a stirred solution of fructosyl bromide (2.0 g , 3 mmol) and freshly desiccated molecular sieves (4A º) in anhydrous acetone (50 ml) ,sodium iodide (0.7 g 4.7 mmol) was added and the mixture kept at ambient temp . for (10 h) .The resulting suspension was filtered through a layer of silica gel , followed by the removal of the solvent in vacuo at a bath temp. not exceeding 25 ºC .The syrup thus obtained was taken up in boiling Xylene (50 ml) and the solution stirred at 140 º C for 2 hr .The mixture was then allowed to return to room temp. where after water (20ml) was added (to hydrolyze residual fructosyl iodide) , followed by filtration of the brown solution through a layer of silica gel and removal of the solvent in vacuo .The resulting residue was dissolved in $CHCl_3$ (50ml) and the solution successively washed with water $NaHCO_3$ solution and again with water (25 ml each) . Drying over $MgSO_4$, and concentration in vacuo gave a syrup consisting mixture of *exo*- and *endo*-fructal separation has an effected on a silica gel column volume (4 × 40 ml) by elution with 10:1 toluene :EtOAc . Removal at the solvents from the fraction eluted as an syrup (0.9 g) (33 %) *Rf* = 0.31(CH_2Cl_2: MeOH)(8 : 2) (v:v) IR spectrum showed 1750 cm^{-1} for (C=O) and 1620 cm^{-1} For (C=C), fig(13).

***O*-Acetyl-4-azido2,3,4-trideoxy-α–D-erythro –hex-2-ene pyranoside [14]**

The catalytic system was prepared by stirring for 1h in a schlenk tube under argon the palladium complex $Pd(PPh_3)_4$ (3 %) in (3ml) tetrahydrfuran . This solution was added under argon to a schlenk tube containing the (1.088gm , 1mmol) Tri-acetyl glucal , and sodium azid (0.286g , 1.1mmol) in a mixture (THF: water) (3ml :2ml). The mixture was stirred at 50C for 1h , and then extracted with ether (3×10ml) and the combined extracts were washed

successively with 1M HCl (30ml), saturated $NaHCO_3$ (30ml) and brine (30ml). The organic layer was dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a residue that was submitted to column chromatography on silica gel using petroleum ether : EtOAc as the eluent to afford the product as a syrup(0.41 g 62 % yield), *Rf* = 0.56 (CH_2Cl_2: MeOH) (8 : 2) (v:v) IR(film) 2106 cm^{-1} ($-N_3$) Fig (14b)

General Methods For Synthesis of Triazoyl linked Carbohydrate (Triazoyldisaccahride).

Heating with solvent . To a solution of azid derivative (3 mmol) in toluene (10ml) was added dropwise with stirring the solution of alkynes or alkenes derivatives (3mmol) .The reaction mixture was stirred under reflux at tempt.110 ºC for the specified time (as in table 3),until the TLC or the IR- spectra of the reaction showed the end of reaction, then cooled, concentration under vacuum ,to gave the product which is isolated by flash chromatography eluting with petroleum ether: EtOAc (6:3) to yield the triazol or triazoline derivative.

Sealed tube method.

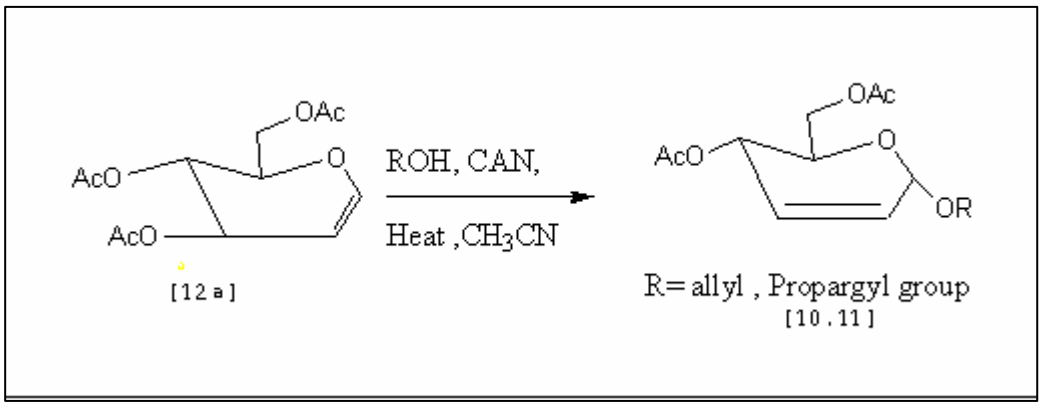
Tri -*O*- acetyl -D- glucal (200mg , 0.73 mmol) or fructal and azide derivative

(126 mg ,0.95 mmol) were heated at 120ºC in 3 ml trimethylorthoformate (sealed tube) for (54 hr.) . Evaporation and chromatography on silica gel (hexanes , ethyl acetate) (2 :1) (v:v) gave the product .

Results and Discussion

Glycosylation of glucal

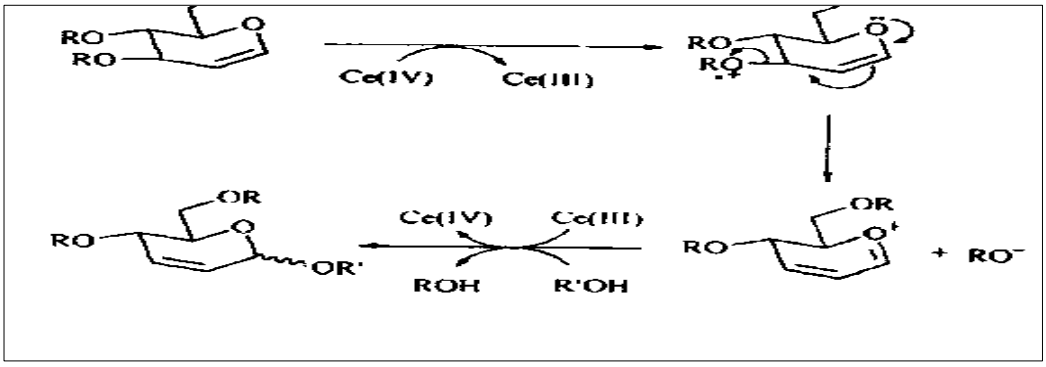
2, 3- Unsaturated glycosides are versatile chiral building blocks in the synthesis of several natural products. Ferrier rearrangement was used to prepare glycoside from the glucal using a variety of Lewis acid reagent in the presence of alcohos[22] such as ($BF_3.Et_2O$, $SnCl_4$, $AlCl_3$,$InCl_3$, $NbCl_5$) .In this work Ceric(IV) ammonium nitrate (CAN) has been used , which is mild and efficient reagent for the glycosidation .



Treatment of 3,4,6-tri-*O*-acetyl-D-glucal [12] with allyl and propargyl alcohol in the presence of

10 mol % ceric ammonium nitrate (CAN) in refluxing acetonitrile gave the corresponding *O*-allyl and

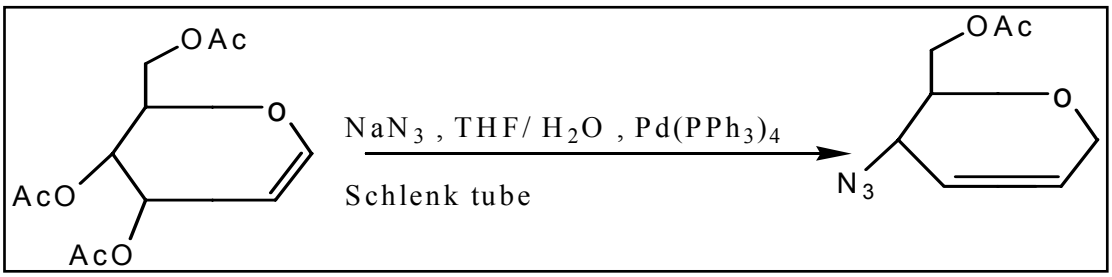
O-propargyl 2,3- unsaturated glycoside in 63% and 74% respectively. The SN_2 mechanism of the reaction illustrated below[23].



Pure 2,3 - unsaturated glycoside was afforded by purifing in column chromatography on silica- gel (ethylacelate – petroleum ether 2:8)to produce the product [10]in 74% yield , IR spectrum for compound[133] showed stretching band which were identical as described in (Ref 17,18) (3277, 2920 , 2118 ,1740, 1370 , 1270 , 1237 , 1237, 104 , 1912 , 733) cm^{-1} Fig (3-25) ,And product [11] allyl derivatives showed stretching band at(1760, 1651 , 1372 , 1231 , 1044) cm^{-1} , Fig (11)

Synthesis of glucal azide

The azidation of 3,4,6 – Triacetyl glucal was first examined by using $Pd(PPh_3)_4$ (prepared as describe in Ref 24)as the catalyst and sodium azide as the nucleophile, the reaction being preformed in a THF/H_2O mixture at 50ºC, the azidation occurred in 62% yield



The IR spectrum clearly showed Fig (3-37) stretching band at 2106 cm^{-1} for (N_3) and 1760 $cm^{-1}$for C=O of acetyl group.

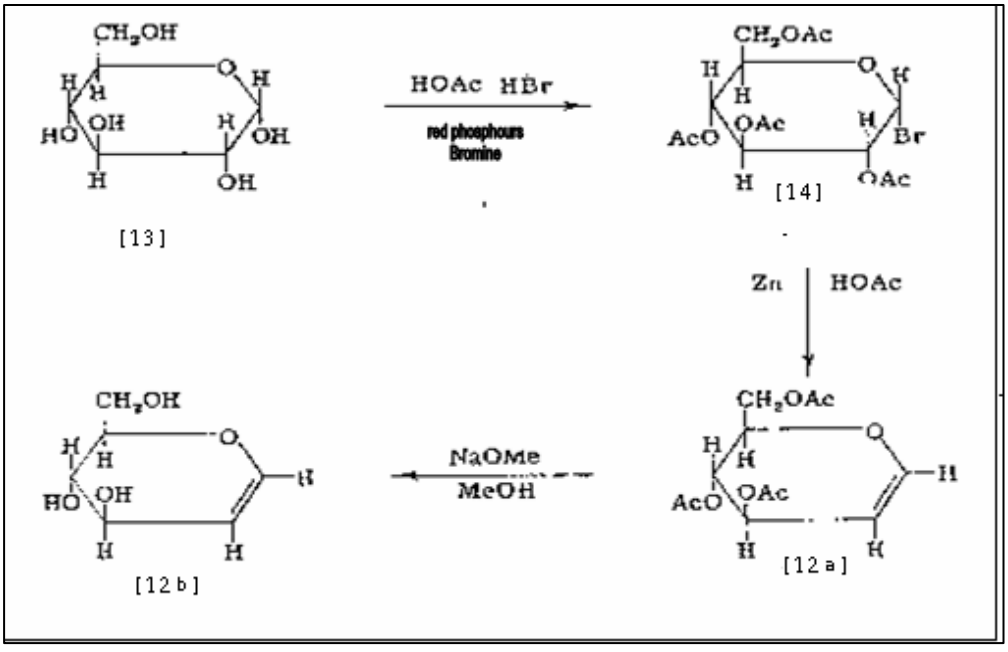
Synthesis of unsaturated sugars

The double bond can be introduced by dehydration of monosacharide to give the so-called unsaturated sugars .Those unsaturated sugars have different structures from the well-known vinyl sugar monomers. Fischer [25] reported the preparation of glycal by reduction of theper -*O*-acylglycopyranosyl halides using zinc and acetic acid to the corresponding acetylated glycols when prepared from glycosyl halide can give products in good yield and in high purity without the need for purification and has been applied to

different sugars protected with a variety of esters

Synthesis of 3,4,6- triacetyl glucal

The best studied of the glycals is the D-glucal [12a] derived from D-glucose. The strategy used for the synthesis of glucal [146a] was started with D-Glucose in a series of reaction shown in order to obtain the targeted compound1,2,3,4,5-penta-*O*-acetayl-β-D-glucopyranose [14] was prepared from D-glucose. The second reaction sequence was the bromination of [14] with red phosphorus and bromine for 4hrs at room temperature after filtration ,the filtrate contains tetra-O-acetylα-D-gucopyranosyl bromide [14b] .W.Lichtenthaler [18] preferred to use the HBr/CH_2Cl_2 in place of HBr/HOAc since acetic acid was extremely difficult to remove and severely interferes with ensuing reaction by concomitant formation at the anomerric acetate [26,27]The final step was a reductive elimination of the derivative [14] with zinc dust to affordedthe *endo*-glucal [12 a]. By different trying with the aid of seeding the residual syrup crystallizes. By recrystallization from petroleum ether and ether, the pure compound can be produced yield is 60% .m.p 55-56 ºC, lit[17]: 54-55 ºC



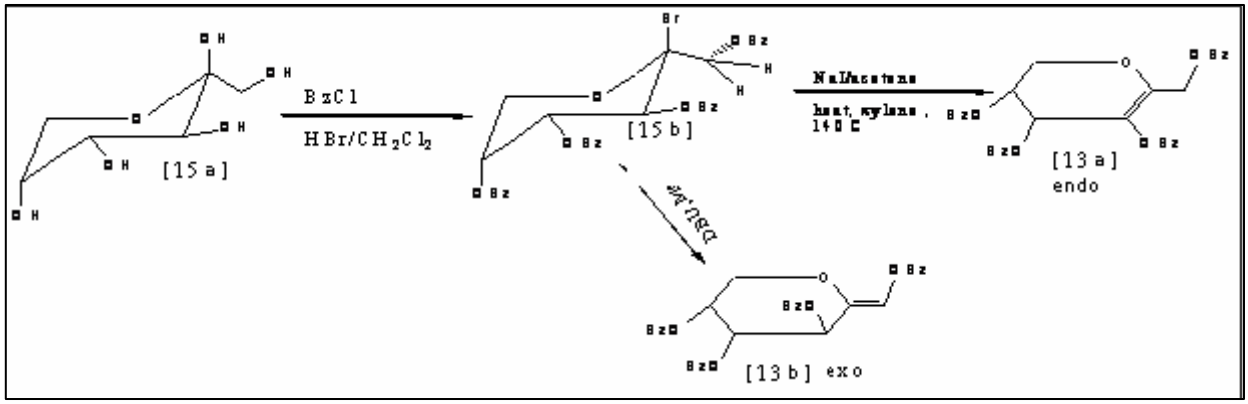
The 3,4,6-tri acetyl –glucal could be converted easily to glucal [12 b] by deactylation process with a methanolic solution containing catalytic amounts of sodium. The 3,4,6-Tri-O-acetyl glucal was characterized by IR spectrum and m.p which was identical with the literatures . The FT .IR spectrum Fig(3-38) showed band at 1740 cm^{-1} for (C=O) .And for glucal [12b] , band of OH group appeared clearly at 3475cm^{-1} Fig 15).

Synthesis of *endo*-fructal

A proper substrate to study the reductive elimination was tetra-*O*-benzoyl- β-D-fructpyronosyl bromide [130 b] readily accessible from D-fructose by benzoylation to the tetrabenzoate [15a] subsequent treatment with HBr / CH_2Cl_2 .The primary 1-*O*-Bz is more readily expelled than the secondary 3-*O*-Bz the leaving group capacityThe practical

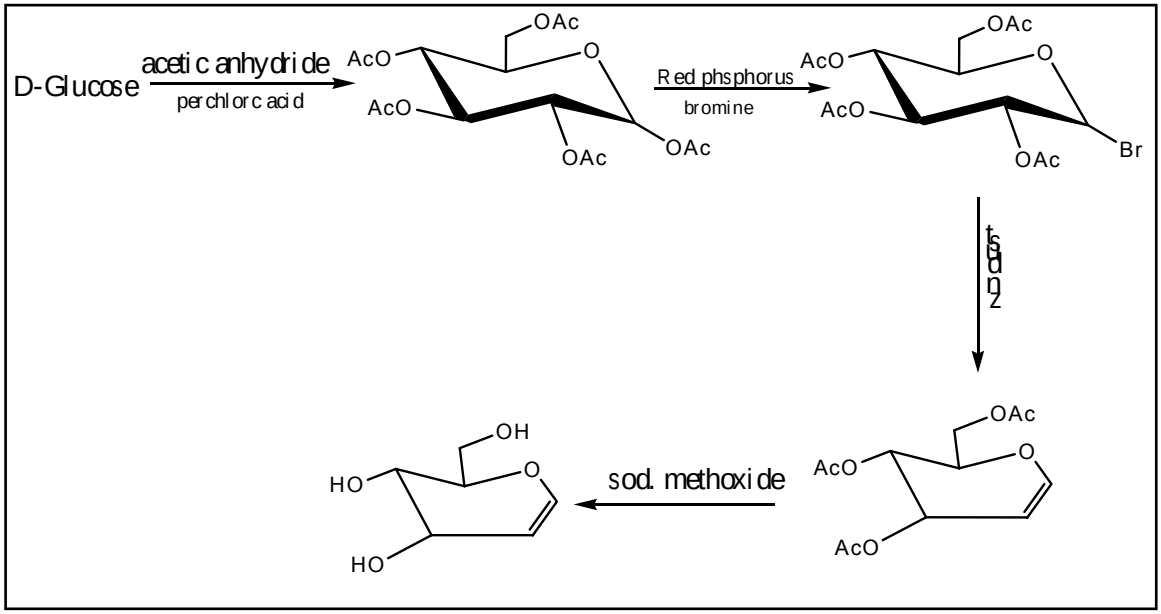
protocols have been developed to a stirred solution of fructosyl bromide [130b] in anhydrous acetone and sodium iodide The syrup was taken up in boiling Xylene (140ºC) for 2hr. to produce sugar consisting of three compounds [15b]

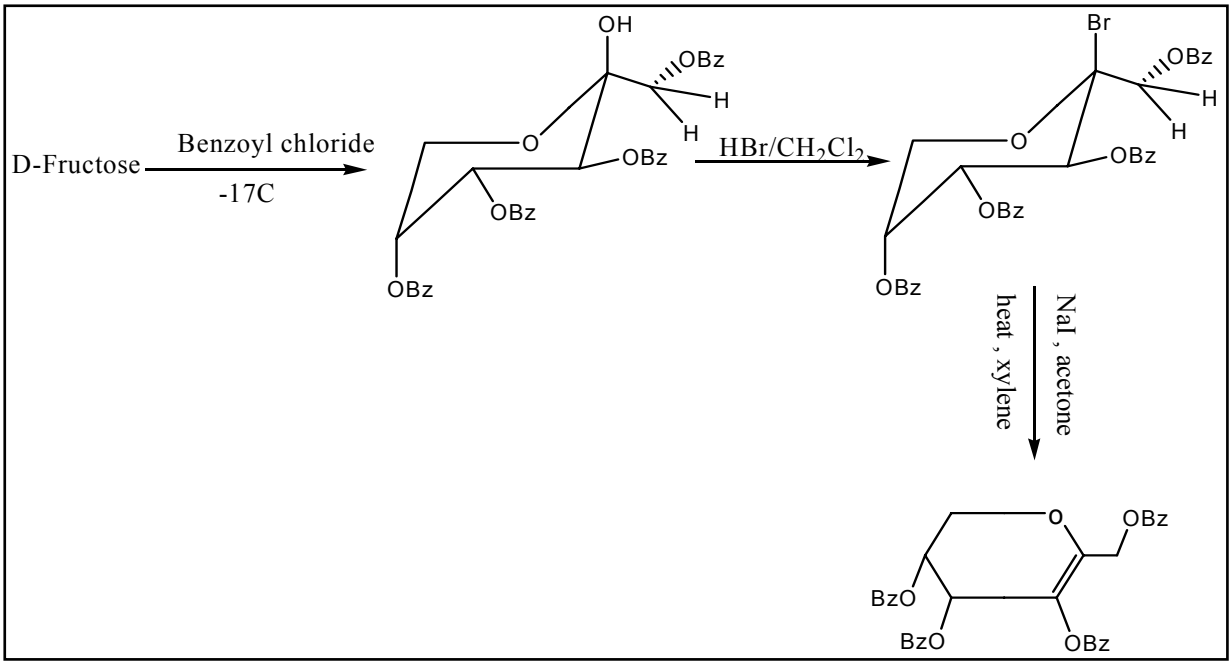
[13a][13b]Separation was effected on a silica gel column by elution with toluene : EtOAc (10: 1) to yield *endo*-hydroxy fructal ester [13b] as an syrup .32% yield which was characterized by IR spectrum,

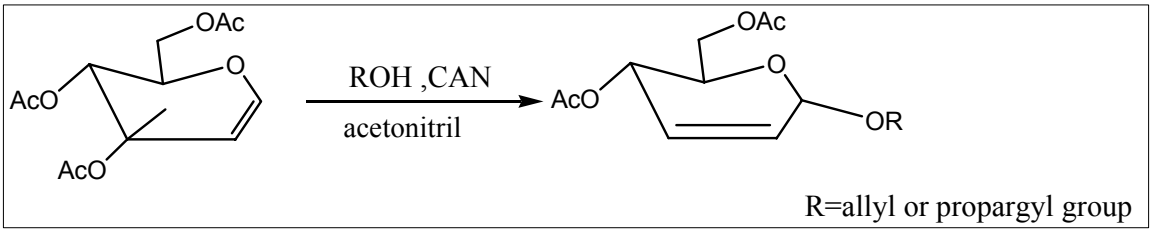


CHN – analyses ,m.p and some other physical properties which was identical with literature ,The IR spectrum showed stretching band at 1750 cm^{-1} for (C=O) ,1620 cm^{-1} for (C=C) aromatic.

Reaction Scheme (1) Synthesis of unsaturated sugars







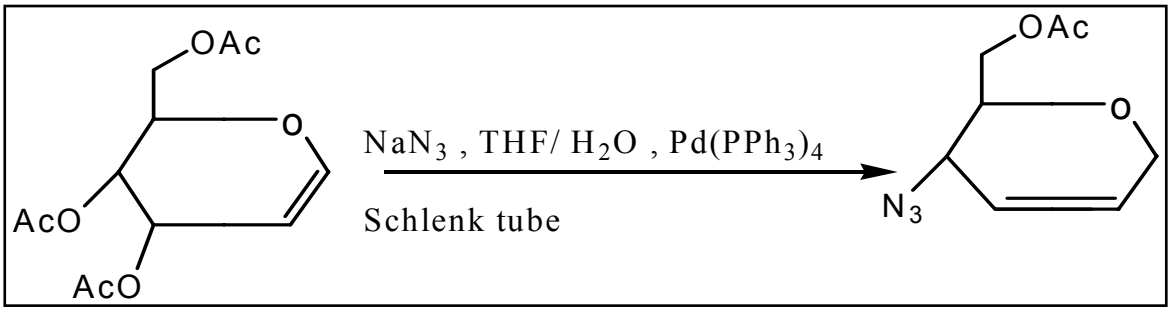


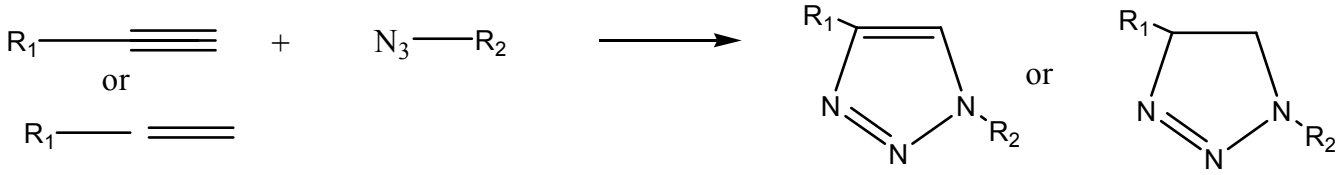
Table (1) Some Physical properties for Unsaturated sugars

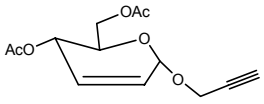
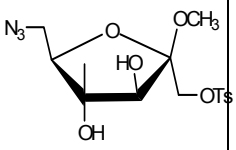
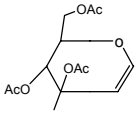
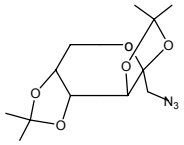
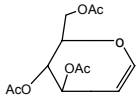
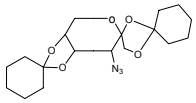
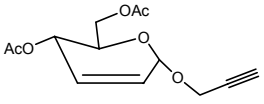
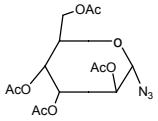
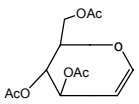
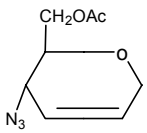
No.	Number of compound	Name of Compound	State of Compound	Percentage % Yield	molecular formula	The C.H.N analysis		
						C%	H%	N%
1	12 a	3,4,5-Tri acetyl glucal	Solid m.p55-56C	60 %	$C_{12}H_{16}O_7$	52.94 51.94	5.88 5.81	
2	13a	Endo-fructal	Syrup	33 %	$C_{34}H_{26}O_4$	70.58 70.1	4.49 4.61	

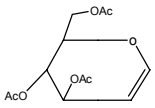
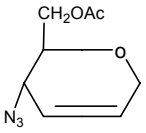
Table (2) IR and NMR Spectral data for Unsaturated sugars

No.	Number of compound	Name of Compound	Remarks of IR, cm^{-1}	Remarks of NMR
1	13 a	3,4,5-Tri acetyl glucal	IR (KBr) 1744 (C=O) 1650 (C=C)	
2	12 b	Glucal	IR (KBr) 3370 (OH) , 1653(C=C)	
3	13 a	Endo- fructal	IR (film) 1750 (C=O) 1620 (C=C)	4.10 dd(1H , H-2a) 4.16 dd (1H,H-2b) 4.59 ,5.33(two, CH_2- OBZ 5.9 (1H , H-3) , 6.33 (dd,H,H4) 7.15 – 7.99 = m 20H , $4C_6H_5$

Table (3) Conditions for preparation of triazole and triazoline derivatives



Entry	R^1	R^2	Product	Conditions	Time (min)	Yield %
1			Cop1	Thermal condition	192	60
2			Cop2	seald tube trimethylortho formte,120C°	96	40
3			Cop3	seald tube trimethylortho formed,120C°	48	60
4			Cop4	1.Schlenk tube tirmethlortho fromate 2.$CuBr(PPh_3)_3$	36	66
5			Cop5	Schlenk tube trimethylortho formte	120	68

Entry	R^1	R^2	Product	Conditions	Time (h/min)	Yield %
6			Cop6	Schlenk tube trimethyl ortho formate $CUBr.(PPh_3)_3$	96	60

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Supporting information Available:
Full characterization and spectra data for compound can found in
Ph.D thesis, Nabeel A.A Al- Rathda

References

1 - K.Bucholz ; S.Warn ; B. Skeries ; S.Wick and E.J. Yaacoub, "Carbohydrates as Organic Raw Materials", Fons verlag , Netherlands , 1994 , p.155 .

2- E.J.Yaacoub , ***Res. Adv .Macromolecules*** . 2000 ,**1,**169

3 - H. . Kim ; H.Meu and C.Lee **,** ***J.Am.Chem.Soc*** ., 2004, **126**,1336.

4- E.J.Yaacoub ; S.Wick and K.Buchhols , ***Macromol. Chem. Phys***,1995, **196** , 3155.

5- E.J Yaacoub; B.Skervies & K, Buchhols **,*Macromol. Chem. Phys*** 1990 , **198** , 879

6- S.Wick , E.J Yaacoub ; ***Macromol. Chem.Phys*** .2000, 201 ,

7.- W.-B Yang , C.- Yi Wu ; C.C.Change , S.H.Wang ***Tetrahedron Lett,*** 2001, **42** , 6907.

8- R-K.Ness and H.G.Fletcher **,** ***J.Org.Chem.***1968,**33**,181.

9- F.W.Lichtenthaler; S.Hahn and F.J Flath , ***Liebigs Ann.*** 1995, 2081.

10-M. Moore and P.Norris , ***Tetrahedron Lett*** .1998 , **39**, 7027

11- S.T.Abu-Orabi .; M.A Atfah ; I.Jibril ; F.M.Marili and A.A.Ali , ***J.Heterocycl. Chem***.1989**,26**,1461.

12- M.J.Genin ; D.A.Allwine ; D.J Anderson , ***J.Med.Chem*** . 2000,**43** , 953 .

13- C.Peto ; G.Batta ; Z,Gyorgydeak ; F.Sztaricskai , ***J.Carbohydr. Chem***. 1996 , **15** , 465.

14- F.Louerat ; K.Bougrin ; A.Loupy ; A.M.de Retana ; J.Pagaldy and F.Palacios **.** ***Heterocycles*** , 1988, **48** ,1.

15- J.E Gestwick ; C.W.Cairo; L.E.Strong ; K,A.Detjen and L.L. Kiessling ***J. Am.Chem .Soc***. 2002 , **124** , 14922

16-P.-B.Francisco ; O.-M.Mavian ; M.-S.Julia and H.-M. Fernand ***Organic Lett.*** , 2003, **5(11)**, 1915.

17- F.W.Lchtenthaler and F.Hoyer , ***Carbohydr. Res.***, 994, **253**, 141.

18- S.Konstantinovic , J.Predojevic , S.Gojkovic and V.Pavloic , ***J.Serb. Chem. Soc***. 2001 , **66(2)** , 73

19- A.Glumer , E. J Yaacoub , ***Macromol. Chem.Phys.*** 2000, **201** , 1521.

20- S . Hanessian , "Preparative Carbohydrate Chemistry" , Marcel dekker inc. , New York , 1997 , p 389 .

21- A.Boettcher and F.W Lichtenthaler , ***Tetrahedron Asymmtry***, 2004 , **15** , 2693.

22- R.J.Ferrier and P.Prasad , ***J.Am.Chem.Soc.,*** 1969, 570 .

23- J.S.Yadav ; B.V. Reddy and S.K. Pandey , ***New J. Chem.*** 2001 ,**25** , 538.

24- J.Tsuji , Palladium Reagent and Catalysit ,Wiley, Japan,1998,13.

25- E.Fischer ; M.Bergman and H.Schotte , ***Bere*** ., 1920 , **53** , 510

26--S. Caddick ,***Tetrahedron*** , 1955,51 ,**38** ,10432 .

27- C.L.Arasappan and P.L Fuchs , ***Tetrahedron Lett*** ., 1993,**34** , 3535