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Synthesis of New Carbohydrate Phenyl- and Nitro-Aryl Ethers Derived from Simple Sugars

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Methyl 2-*O*-tosyl-β-L-arabinopyranoside (14), methyl 4-*O*-tosyl-α-D-lyxopyranoside (15) and methyl 4-*O*-tosyl-α-L-rhamnopyranoside (16) were prepared from their corresponding isopropylidene-tosyl derivatives (11–13), from which upon epoxidation with sodium methoxide in methanol, their corresponding anhydro compounds (17), (19) and (20) were obtained. Reaction of anhydro compounds (17), (19) and (20) with sodium phenolate in refluxing DMF afforded methyl 3-*O*-phenyl-β-L-xylopyranoside (21), methyl 4-*O*-phenyl-α-D-lyxopyranoside (23) and methyl 3-*O*-phenyl-α-L-idopyranoside (24), respectively.

Periodata cleavage of methyl-β-D-glycopyranoside (31), methyl β-D-galactopyranoside (32) and methyl β-D-mannopyranoside (33), all gave "dialdehyde" (34). Cyclization, with nitromethane and sodium methoxide, of the dialdehyde (34) led to an aci-nitrocondensation product, from which methyl 3-nitro-3-deoxy-β-D-glucopyranoside (36) was obtained. The 4,6-*O*-benzylidene derivative (37) was obtained from (36) and converted to its 2-*O*-acetate (38). The Schmidt-Rutz reaction of (38) afforded methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-erythrohexose-2-enide (39). Reaction of hydrogen peroxide in a weakly alkaline medium with nitroolefinic sugar (39) led to methyl 2,3-anhydro-4,6-*O*-benzylidene-3-C-α-D-allopyranoside (40). Reaction of anhydro compound (40) with phenoxide, α-naphthoxide and β-naphthoxide ions gave methyl 4,6-*O*-benzylidene-3-nitro-2-*O*-phenyl-β-D-mannopyranoside (41), methyl 4,6-*O*-benzylidene-3-nitro-2-*O*-α-naphthyl-β-D-mannopyranoside and methyl 4,6-*O*-benzylidene-3-nitro-β-naphthyl-β-D-mannopyranoside (43), respectively.

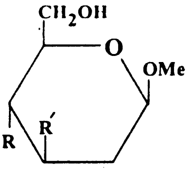
INTRODUCTION

One of the largest and most diverse of naturally occurring organic compounds is that of the phenolic compounds present in the tissues of higher plants. These compounds range from the polymers of high molecular weight, such as lignin, to relatively simple benzene derivatives[1].

Phenyl ethers of carbohydrates (as distinct from phenyl glycosides) seem to be a little known of compounds. The review by Pridham[1] on phenyl-carbohydrate derivatives, the up to date book of Stick[2] on "Carbohydrates" and a considerable survey of literature contains no mention of phenyl ethers.

A variety of aryl glycosides are prepared by the classical and by several other procedures[3]. McSweeney, Wiggins and Wood[4] have described the action of some phenols on acyclic carbohydrate epoxides. Nucleophilic attack on the epoxide ring occurred at the least hindered position and afforded in each case the corresponding aryl ether. The formation of 4-nitrophenyl ethers has been observed during alkaline hydrolysis of 4-nitrophenyl-α-D-glucopyranoside[5]. A novel type of aryl ether of carbohydrates (*i.e.*, pentafluorophenyl derivatives) has been described by Haines and Symes[6]. Bittner and Assaf[7] have described the preparation of carbohydrate phenyl ethers by reaction of phenol; an alcohol and diethyl azodicarboxylate in the presence of triphenyl phosphine. Certain aryl ethers of glycerol, particularly the 3-methyl phenyl ether show muscle relaxing activity. Aryl ethers of glycerol are also known to have some bacterio-static and fungicidal activities.

More than a dozen of aminodeoxy sugars, usually referred to as just the "amino sugars", have been characterized as components of antibiotics. These amino sugars are crucial to the well being of many organisms, including humans, because they play pivotal roles in the structure and function of biologically important oligosaccharides, polysaccharides and glyco-proteins[8]. Baer and Neilson[9] have described the synthesis of some aminodideoxy derivatives, **(2–4)**, from methyl-3-nitro-2,3-dideoxy-β-D-arabino-hexopyranoside **(1)**.



(1) R=H, $R'=NO_2$
(2) R=OH, R'=NHAc
(3) R=R'=NHAc
(4) R=OMs, R=NHAc

Synthesis of methyl 3-amino-3-deoxy-α-D-mannopyranoside hydrochloride from methyl 3-nitro-3-deoxy-α-D-mannopyranoside has also been reported[10].

A common amino sugar found in glycoproteins is N-acetylneuraminic acid. This amino sugar has received much attention of late, especially in the light of its potential to act as a precursor of the drug to combat infection by the influenza virus[11]. Consequently, efficient methods for large scale production of N-acetylneuraminic acid have been devised[12]. Some derivatives of N-acetyl-D-glucosamine[13] and N-acetyl-D-galactosamine[14], as intermediates in the synthesis of oligosaccharides, are also reported.

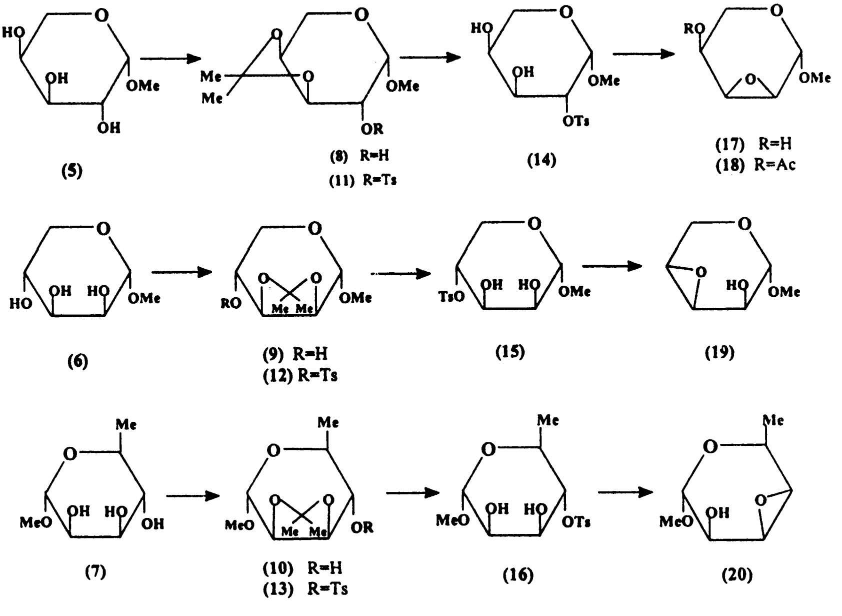
Baer and Rank[15] have synthesized a series of α-nitroepoxides in excellent yields by the reaction of nitro-olefinic sugar derivatives with hydrogen peroxide in a weakly alkaline medium. In all cases epoxidation occurred preferentially from the side of the ring opposite to the glycosidic methoxy group.

By keeping the biological activities of phenyl ethers and aminodeoxy sugars in mind, if one combines two functionalities together, it might be possible to get compounds with highest level of activity.

In the present paper, the synthesis of carbohydrate phenyl ethers and nitrodeoxy-aryl ethers which are believed to hold much promise for a considerable number of synthetic and biological purposes is reported.

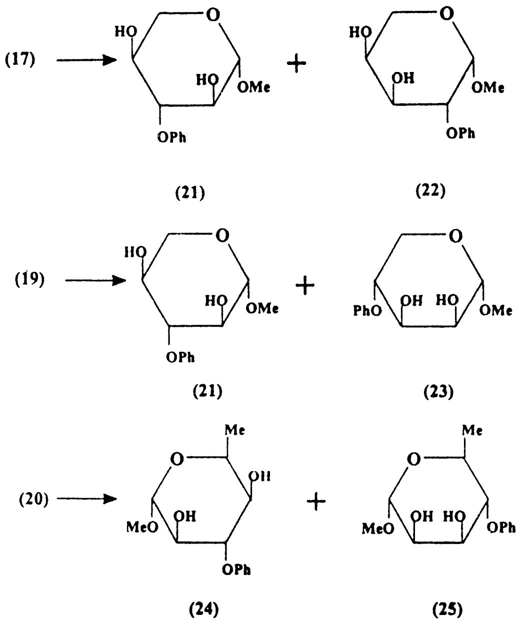
RESULTS AND DISCUSSION

Methyl β-L-arabinopyranoside **(5)**, methyl α-D-lyxopyranoside **(6)**, and methyl α-L-rhamnopyranoside **(7)** on reaction with acetone and conc. sulfuric acid, using anhydrous cupric sulphate as catalyst, afforded methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside **(8)**, methyl 2,3-*O*-isopropylidene-α-D-lyxopyranoside **(9)**, and methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside **(10)**, respectively. Tosylation of ketals **(8–10)** with tosyl choride and pyridine yielded methyl 3,4-*O*-isopropylidene-2-*O*-tosyl-β-L-arabinopyranoside **(11)**, methyl 2,3-isopropylidene-4-*O*-tosyl-α-D-lyxopranoside **(12)** and methyl 2,3-*O*-isopropylidene-4-*O*-tosyl-α-L-rhamnopyranoside **(13)**, respectively. Acid hydrolysis of esters **(11–13)** gave methyl 2-*O*-tosyl-β-L-arabinopyranoside **(14)**, methyl 4-*O*-tosyl-α-D-lyxopyranoside **(15)** and methyl 4-*O*-tosyl-α-L-rhamnopyranoside **(16)**, respectively. Treatment of esters **(14–16)** with one molar equivalent sodium methoxide in methanol yielded methyl 2,3-anhydro-β-L-ribopyranoside **(17)**, methyl 3,4-anhydro-β-L-ribopranoside **(19)**, and methyl 3,4-anhydro-6-deoxy-α-L-talopyranoside **(20)** **(Scheme-I)**. In all cases, epoxidation occurred preferentially from the side of the ring opposite to the glycosidic methoxy group[15]. Acetylation of anhydro compound **(17)** with acetic anhydride in pyridine at room temperature afforded crystalline methyl 4-*O*-acetyl-2,3-anhydro-β-L-ribopyranoside **(18)** **(Scheme-I)**.



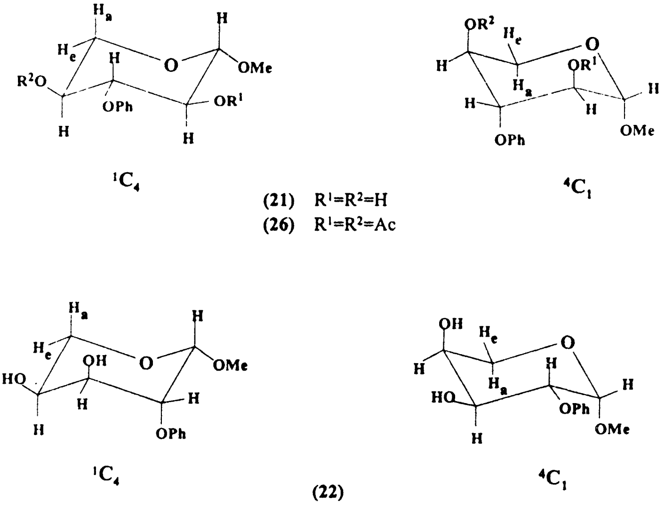
Scheme-I

It was expected that an anion generated from a phenol would attack the epoxide ring (**17**, **19** and **20**) in an analogous manner to other nucleophiles and the products would be predominantly those having a *trans*-orientation of substituents at the carbon atoms which were formerly part of the epoxide ring **(Scheme-II)**.



Scheme-II

Reaction of **(17)** with sodium phenolate in refluxing with DMF for *ca.* 2 h afforded almost exclusively (TLC) one product, $R_F = 0.16$; only a trace of a second minor product was present, $R_F = 0.2$. The major product was obtained crystalline, m.p. 137–138°C in 36% yield and was identified as methyl 3-*O*-phenyl-β-L-xylopyranoside **(21)** on the basis of a detailed analysis of NMR spectrum of its di-acetate **(26)** **(Scheme-III)**.



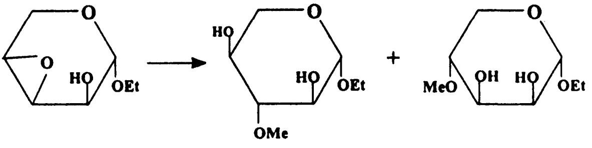
Scheme-III

The ^{1}H NMR data obtained from the first order analysis are noted in Table-1.

TABLE-1
^{1}H NMR SPECTRAL DATA FOR **(26)**

δ	H-1	H-2	H-3	H-4	H-5$_e$	H-5$_a$
(ppm)	4.42	5.05	4.43	5.07	4.18	3.39
J	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{5e,5a}$
(Hz)	7.00	8.00	8.00	4.50	8.00	-12.00

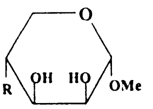
The values of the coupling constant reported in Table-1 are in full accord with compound being **(26)** in the $^1C_4$ conformation **(Scheme-III)**. In particular, the large coupling constants typical of an axial-axial disposition of vicinal protons are to be noted for $J_{1,2}$; $J_{2,3}$; $J_{3,4}$ and $J_{4,5a}$. Finally, the mechanistically feasible alternative for the structure of compound obtained on reaction of epoxide **(17)** would be methyl 2-*O*-phenyl-β-D-arabinopyranoside **(22)**. A consideration of both chair conformations available to this compound **(Scheme-III)**, enable it to be ruled out. Thus for the $^1C_4$ chair form, $J_{1,2}$, $J_{2,3}$ and $J_{3,4}$ should all be 3 Hz. In the $^4C_1$ chair form, $J_{1,2}$ and $J_{3,4}$ should both be *ca.* 3 Hz and in addition $J_{4,5e}$ and $J_{4,5a}$ should both have similar small values associated with equatorial-equatorial and equatorial-axial coupling respectively. Thus the product of the reaction is a result of attack at C-3 of the epoxide rather than at C-2. Reaction of **(19)** with sodium phenolate in DMF afforded a major product (TLC), $R_F = 0.33$, together with a minor product, $R_F = 0.37$. Isolation of the products gave the major product, m.p. 130–131°C, identified as methyl 4-*O*-phenyl-α-D-lyxopyranoside **(23)**, based on its non-identity with the other possible products of *trans*-opening of anhydro compound **(19)**, that is compound **(21)** **(Scheme-II)**. Piotrovsky and co-workers[16] have shown that the preferential product of opening of the epoxide ring in ethyl 3,4-anhydro-β-L-ribopyranoside **(27)** with sodium methoxide in methanol afforded ethyl 4-*O*-methyl-α-D-lyxopyranoside **(29)**, but not ethyl 3-*O*-methyl-β-L-xylopyranoside **(28)** **(Scheme-IV)**. This supports our own indication of the preferential ring opening of **(19)** by attack at C-4.



(27) **(28)** **(29)**

Scheme-IV

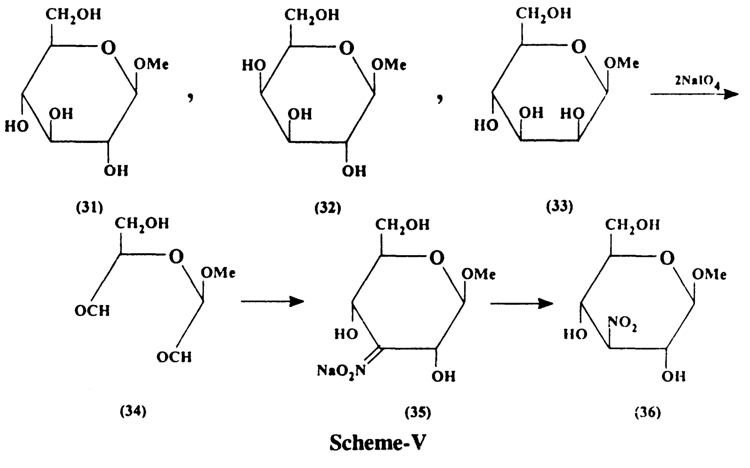
Kent *et al.*[17] and Ovrend *et al.*[18] have also shown that the cleavage of the epoxide in **(19)** by a variety of reagents give a 4-substituted derivative of methyl α-D-lyxopyranoside **(30)**.



(30) R=NH_2, NHMe,
NMe_2, NHPh, Br

Reaction of **(20)** with sodium phenolate in refluxing DMF afforded (TLC) a major product, $R_F = 0.45$; and a minor product, $R_F = 0.38$. Crystallization of the reaction product from ethyl acetate-light petroleum yielded the major product (*i.e.*, the *ido*-isomer), presumed to be methyl 3-*O*-phenyl-α-L-idopyranoside **(24)**, m.p. 75–77°C in 25% yield. The minor product was isolated by PLC from the residue obtained by concentration of the mother liquor of compound **(24)**. Recrystallization from ethyl acetate—light petroleum—gave a compound presumed to be methyl 4-*O*-phenyl-α-L-rhamnopyranoside **(25)**, m.p. 110–113°C in 5% yield which was the other possible product of *trans* ring opening of epoxide **(Scheme-II)**. Our presumption is supported by the large number of ring opening reactions on epoxide **(20)** that the major product is the *ido*-isomer, which has been reported to lead to 3-substituted *ido*-derivatives[19, 20]. For example, reaction of **(20)** with H, —OMe, —NH_2 and —NMe_2 all lead predominantly to nucleophilic attack at C-3 and thus products of the *ido*-configuration.

Periodate cleavage of methyl β-D-glucopyranoside **(31)**, methyl β-D-galactopyranoside **(32)** and methyl β-D-mannopyranoside **(33)**, all gave "dialdehyde" **(34)**[19, 21, 22]. In this reaction, C-3 of these sugars separated as formic acid and the configuration of C-1, C-5 and C-6 remains unchanged **(Scheme-V)**. Reaction of dialdehyde **(34)** with nitromethane and alkali in a two-fold condensation involving *one* molecule of nitromethane with *both* aldehyde groups. The glucoside thus reconstituted then bears an *aci*-nitro group on C-3 and is obtained as the sodium salt **(35)** which can be acidified to a mixture of epimeric methyl 3-nitro-glycosides. Conformational considerations have pointed out[10] that a selective principle as to what configuration will be favoured is the tendency of the arising new hydroxyls (on C-2 and C-4) to enter into *trans*- arrangements with respect to the adjacent substituents (on C-1 and C-5). Thus the three glycosides **(31–33)** all would have the same nitro-deoxy compound, *i.e.*, methyl 3-nitro-3-deoxy-β-D-glucopyranoside **(36)** **(Scheme-V)**.

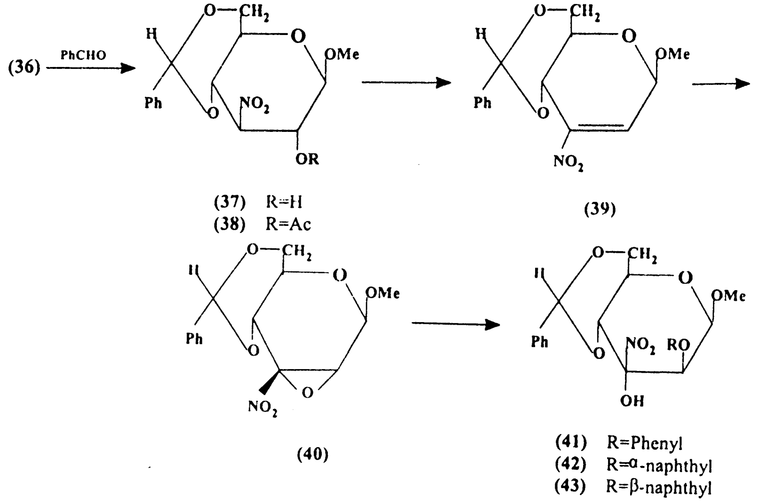


Scheme-V

The treatment of a carbohydrate diol with benzaldehyde under a variety of acidic conditions, typically utilizing fused zinc chloride, furnishes the benzylidene acetals[9, 23, 24]. Thus in this condition, the nitro compound **(36)** was converted into methyl 4,6-*O*-benzylidene-3-nitro-3-deoxy-β-D-glucopyranoside **(37)**. Acetylation of **(37)** with acetic anhydride in pyridine gave methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-nitro-deoxy-β-D-glucopyranoside **(38)**.

The generation of 3,4- or 2,3-alkene derived from carbohydrates can conveniently occur from the appropriate diol, using older or an extension method[9, 25–29]. Thus, treatment of acetate **(38)** with solid sodium bicarbonate in refluxing benzene (Schmidt-Rutz reaction) afforded methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*erythro*-hexos-2-enide **(39)**[9].

Formation of epoxide in carbohydrates can be afforded by the oxidation of an unsaturated sugar with some sort of peracid or from an internal nucleophilic displacement[15, 30–33]. Epoxidation of **(39)** with aqueous 30% hydrogen peroxide (in alkaline ethanolic solution) gave highly stereoselectively a single epoxide having the β-D-*allo* configuration: methyl 2,3-anhydro-4,6-*O*-benzylidene-3-*C*-nitro-α-D-allopyranoside **(40)**[15] **(Schme-VI)**.



Scheme-VI

Reaction of anhydro compound **(40)** with phenoxide, α-naphthoxide and β-naphthoxide ions gave methyl 4,6,-*O*-benzylidene-3-*C*-nitro-2-*O*-phenyl-β-D-mannopyranoside **(41)**, methyl 4,6-*O*-benzylidene-3-*C*-nitro-2-*O*-α-naphthyl-β-D-mannopyranoside **(42)**, and methyl 4,6-*O*-benzylidene-3-*C*-nitro-2-*O*-β-naphthyl-β-D-mannopyranoside **(43)**, respectively **(Scheme-VI)**.

In contrast to epoxides **(17)**, **(19)** and **(20)**, the attack of nucleophiles also is in *trans-* orientation and only at one position, *i.e.*, at C-2, due to electron withdrawing character of NO_2 group at C-3 and also the less hindered C-2 position of the epoxide.

EXPERIMENTAL

Melting points were measured on a Reichert hot-stage or electrothermal melting point apparatus. TLC and PLC (preparative LC) were performed on Kieselgel PG_{254} and Kieselgel PF_{254}, respectively, with 1 : 49 (v/v) methanol-chloroform (solvent A) or 1 : 19 (v/v) methanol-chloroform (solvent B), and spots were made visible by 50% aqueous sulfuric acid and heating. The ^1H NMR spectra were obtained by using 80, 100, 220 MHz Fourier transform spectrometers. Chemical shifts are reported in ppm (δ) downfield from TMS as an internal standard. IR spectra were recorded on a Perkin-Elmer 257 or with a Shimadzu Fourier transform infrared spectrometer model 4300. Optical rotations were measured for solutions in chloroform in 1 decimeter cells, at ambient temperatures and at sodium D line (589 Å) with a Perkin-Elmer 141 polarimeter.

The starting compounds, namely methyl-β-L-arabinopyranoside **(5)**[34], methyl-α-D-lyxopyranoside **(6)**[17, 35], methyl-α-L-rhamnopyranoside **(7)**[36], methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside **(8)**[37], methyl 2,3-*O*-isopropylidene-α-D-lyxopyranoside **(9)**[37], methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside **(10)**[37], methyl 3,4-*O*-isopropylidene-2-*O*-tosyl-β-L-arabinopyranoside **(11)**[37], methyl 2,3-*O*-isopropylidene-4-*O*-tosyl-α-D-lyxopyranoside **(12)**[17, 37, 38], methyl 2,3-isopropylidene-4-*O*-tosyl-α-L-rhamnopyranoside **(13)**[17, 37], methyl 2-*O*-tosyl-β-L-arabinopyranoside **(14)**[38], methyl 4-*O*-tosyl-α-D-lyxopyranoside **(15)**[38], methyl 4-*O*-tosyl-α-L-rhamnopyranoside **(16)**[38], methyl 2,3-anhydro-β-L-ribopyranoside **(17)**[40], methyl 3,4-anhydro-β-L-ribopyranoside **(19)**[17, 40], methyl 3,4-anhydro-6-deoxy-α-L-talopyranoside **(20)**[19, 20], methyl 4-*O*-acetyl-2,3-anhydro-β-L-ribopyranoside **(18)**[37, 41] were prepared according to the references cited, or by improved modifications of the original procedures.

Periodate oxidation of methyl β-D-glucopyranoside **(31)**, methyl β-D-galactopyranoside **(32)**, methyl β-D-mannopyranoside **(33)** and condensation of the corresponding dialdehyde **(34)** so obtained, with nitromethane to afford 3-nitro-3-deoxy-β-D-glucopyranoside **(36)**, was accomplished by Baer and Fischer[10] procedure. Methyl 4,6-*O*-benzylidene-3-nitro-3-deoxy-β-D-glucopyranoside **(37)**, methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-nitro-3-deoxy-β-D-glucopyranoside **(38)**, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*erythro*-hexose-2-enide **(39)** were prepared by Baer and Neilson[9] method. Baer and Rank[15] general procedure for epoxidation was used to obtain methyl 2,3-anhydro-4,6-*O*-benzylidene-3-*C*-nitro-α-D-allopyranoside **(40)**. All the above compounds showed satisfactory m.p., $[\alpha]_D$, IR and ^1H NMR spectral data and analytical analysis.

Methyl 3-*O*-phenyl-β-L-xylopyranoside (21): To a solution of phenol (3.5 g) in DMF (24 mL) was added sodium hydride (0.72 g of 80% dispersion in oil, washed with light petroleum before using). The solution of sodium phenoxide so obtained was added to a solution of anhydro-acetate **(18)** (2.26 g) in DMF (24 mL) and the mixture was heated under reflux for *ca.* 2 h during which time it turned dark brown in colour. TLC (solvent A) indicated the disappearance of starting material ($R_F = 0.54$) and the presence of a major product with $R_F = 0.16$ together with a minor product, running slightly faster ($R_F = 0.2$) than the major one. Water (135 mL) was added and the mixture was extracted with chloroform (3 × 35 mL). The combined chloroform extracts were washed with 10% aqueous sodium hydroxide (3 × 70 mL) and the alkaline aqueous extracts were back extracted with chloroform (2 × 70 mL). Concentration of the combined chloroform extracts gave a syrup (3.4 g) which was crystallized and recrystallized from ethyl acetate-light petroleum to give the phenyl ether **(21)** (1.1 g, 36%). m.p. 137–138°C, $[a]_D + 57°$ (c 0.05 in acetone). IR 3360 ν(OH), 1605, 1595 ν(C_6H_5). ^{1}H NMR [$(CD_3)_2CO$] δ 3.42 (3H, s, OMe), 3.30–4.50 (8H, m, H-1, 2, 3, 4, 5, 5′, 2 × OH), 6.70–6.90 (5H, m, Ar—H). Anal. calcd. for $C_{14}H_{16}O_5$: C, 60.0; H, 6.5; found: C, 60.2; H, 6.7.

Methyl 2,4-di-*O*-acetyl-3-*O*-phenyl-β-L-xylopyranoside (26): Ether **(21)** (0.5 g) was dissolved in pyridine (5 mL), acetic anhydride (1 mL) was added, and the reaction mixture was stored overnight, after which it was poured in ice-water containing sodium hydrogen carbonate (80 mL). The crystalline solid so obtained was collected, dried over phosphorous pentoxide and recrystallized from ethanol-light petroleum to give diacetate **(26)** (0.34 g, 50%). m.p. 113–114°C. IR 1735 ν(C=O), 1602, 1592 ν(C_6H_5). ^{1}H NMR ($CDCl_3$) 1.91, 1.96 (6H, 2 × s, MeCO), 3.39 (1H, dd, $J_{4,5a} = 8$ Hz, $J_{5e,5a} = 12$ Hz, H-5a), 3.45 (3H, s, OMe), 4.18 (1H, dd, $J_{4,5e} = 4.5$ Hz, H-5_e), 4.42 (1H, d, $J_{1,2} = 7$ Hz, H-1), 4.43 (1H, t, $J_{2,3} = 8$ Hz, $J_{3,4} = 8$ Hz, H-3), 5.0–5.14 (2H, m, H-2,4), 6.87–7.05, 7.15–7.32 (5H, m, Ar—H). Anal. calcd. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.21; found; C, 59.2; H, 6.25.

Methyl 4-*O*-phenyl-α-D-lyxopyranoside (23): To a solution of phenol (1.94 g) in DMF (14 mL) was added sodium hydride (0.42 g), followed by a solution of anhydro compound **(19)** (1.1 g) in DMF (10 mL). The mixture was heated under reflux for *ca.* 2 h under nitrogen, worked-up exactly as described for **(21)** gave the phenyl ether **(23)** (0.7 g, 39%), m.p. 130–131°C IR 3500–3100 ν(OH), 1610, 1595 ν(C_6H_5). ^{1}H NMR ($CDCl_3$) 3.16 (2H, br.s, 2 × OH), 3.42 (3H, s, OMe), 3.67–4.60 (5H, m, H-2, 3, 4, 5, 5′), 4.66 (1H, d, H-1), 6.90–7.5 (5H, m, Ar—H). Anal. calcd. for $C_{12}H_{16}O_5$: C, 60.0; H, 6.7; found: C, 60.2; H, 6.5.

Methyl 3-*O*-phenyl-α-L-idopyranoside (24): To a solution of phenol (1.6 g) in DMF (21 mL) was added sodium hydride (0.7 g), followed by a solution of anhydro compound **(20)** in DMF (15 mL). The mixture was heated under reflux for *ca.* 2 h under nitrogen. Worked-up exactly as described for solution of **(21)** yielded the phenyl ether **(24)** (1.17 g, 25%). m.p. 75–77°C IR 3530–3390 ν(OH), 1600, 1596 ν(C_6H_5). ^{1}H NMR ($CDCl_3$) 1.32 [3H, d, $J_{5,6} = 7$ Hz, C(5) Me], 2.9 (2H, br.s, 2 × OH), 3.44 (3H, s, OMe), 3.5–4.40 (4H, m, H-2, 3, 4, 5), 4.7 (1H, br.s, H-1), 6.80–7.40 (5H, m, Ar—H). Anal. calcd. for $C_{17}H_{18}O_5$: C, 61.40; H, 7.13; found; C, 61.3; H, 7.1.

The minor compound was isolated by PLC (solvent B, two development) from the residue obtained by concentration of the mother liquor of compound **(24)**. Recrystallization from ethyl acetate-light petroleum gave methyl 4-*O*-phenyl-α-L-rhamnopyranoside **(25)** (0.25 g, 5%). m.p. 102–105°C. IR 3600–3100 ν(OH), 1606, 1593 ν(C_6H_5). ^{1}H NMR ($CDCl_3$) 1.21 [3H, d, $J_{5,6} = 6$ Hz, C (5) Me], 2.74

(2H, br.s, 2 × OH), 3.34 (3H, s, OMe), 3.60–4.40 (4H, m, H-2, 3, 4, 5), 4.66 (1H, s, H-1), 6.80–7.40 (5H, m, Ar—H). Anal. calcd. for $C_{17}H_{18}O_5$: C, 61.40; H, 7.13; found: C, 61.2, H, 7.13. After further drying of compound **(25)** at 35°C for *ca.* 24 h, the m.p. increased to 110–1130°C. Anal. catcd. for $C_{17}H_{18}O_5$: C, 61.4; H, 7.13; found: C, 61.1; H, 7.0.

General procedure for the synthesis of nitro-phenyl ethers (41–43): To a stirred solution of the given aromatic alcohol (0.4–0.5 g) in 0.1 M sodium methoxide (10 mL), anhydro compound **(40)** (1.2 g) was added, and the reaction mixture was stored overnight at room temperature. After neutralization with acid, water was added and the mixture was extracted with ether (3 × 25 mL). The combined organic extracts were dried and concentrated to give chromatographically pure product.

TABLE-2
NITRO ARYL ETHERS (41–43)

Compds.	Yield	m.p		Anal. found		
				C	H	N
(41)	40	162	*	60.35	5.73	4.07
(42)	12	175	**	63.94	4.82	3.67
(43)	28	191	**	63.12	5.78	3.84

*Anal. calcd. for $C_{20}H_{21}NO_8$: C, 59.55; H, 5.25; N, 3.47.
**Anal. calcd. for $C_{24}H_{23}NO_8$: C, 63.57; H, 5.11; N, 3.09.

TABLE-3
^{1}H NMR SPECTRAL DATA FOR NITRO ARYL ETHERS (41–43)

	δ (ppm)								ν (cm^{-1})	
Compds.	OMe	Ar—H	$PhCHO_2$	Ph-	H-1	H-2	H-4	H-5	H-6,6′	OH	NO_2
(41)	3.40	^{a}6.9–7.16	5.5	7.32–7.39	5.1	4.9	4.65	4.25	4.1, 4.3	3500	1750, 1400
(42)	3.45	^{b}7.2–7.5 7.4–8.2	5.45	7.3–7.4	4.98	4.8	4.58	4.3	4.1, 4.4	3500 1400	1565,
(43)	3.40	^{c}7.3–7.6 7.4–8.0	5.4	7.3–7.4	5.0	4.85	4.6	4.3	4.1, 4.3	3500	1570, 1410

^{a} phenyl-, ^{b} α-naphthyl, ^{c} β-napthyl.

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