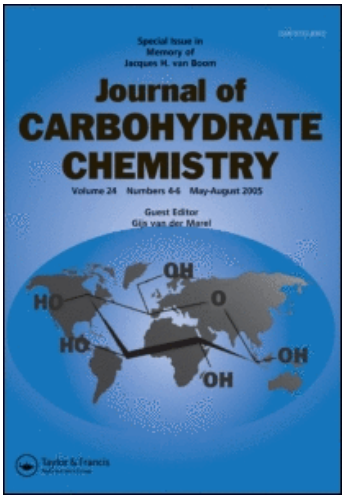

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Selective Benzoylation of 1-(β-D-Xylopyranosyl)-3,5-dimethylpyrazole

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SELECTIVE BENZOYLATION OF 1-(β-D-XYLOPYRANOSYL)-3,5-DIMETHYLPYRAZOLE [1]

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ABSTRACT

Selective benzoylation of 1-(β-D-xylopyranosyl)-3,5-dimethylpyrazole (**1**) has been performed to give 2,3,4-tri- (**2**), 3,4-di- (**3**), 2,4-di- (**4**), 3- (**5**) and 4-benzoate (**6**). The *O*-acetyl derivatives of compounds **3** and **4** (**7**, **8**), di-*O*-acetyl of **5** and **6** (**9**, **10**) and *O*-methanesulphonyl of **3** and **4** (**11**, **12**) have been obtained. The relative reactivity of the hydroxyl groups of **1** was HO-4 ≥ HO-3 >> HO-2. The analysis of ^{1}H NMR and ^{13}C NMR spectra of **1-12** is presented.

INTRODUCTION

Selective benzoylation of some *N*-acetyl-*N*-aryl-β-D-*xylo*-,[2] -β-D-*ribo*-,[3] -α-L-*arabino*-,[4] and -α-D-lyxopyranosylamines,[5] and establishment of the relative reactivity of the hydroxyl groups in these compounds have been reported.[2-5] There have been no analogous investigations of *N*-glycosides with a heterocyclic aglycon.

In this work an attempt has been made to evaluate the relative reactivity of the hydroxyl groups in the molecules of 1-(β-D-xylopyranosyl)-3,5-dimethylpyrazole (**1**) based on the selective benzoylation. This compound may be considered as a model compound suitable for studying the properties of some nucleosides. Another purpose of my work was to obtain useful yields of the di- and monobenzoate derivatives of **1** by suitable choice of reactant ratios and other

conditions of the reaction. The derivatives of the title compound containing various ester groups (*O*-benzoyl-*O*-acetyl- and *O*-benzoyl-*O*-mesyl-) in the saccharide ring have been obtained. The mesyl derivatives will be the starting material in studying S_N2 reactions in such synthetic analogs of nucleosides, in which there is no possibility of solvolysis with participation of *N*-acetyl groups, as in *N*-acetyl-*N*-aryl-*xylo*-[6] and ribopyranosylamines.[7]

RESULTS AND DISCUSSION

The synthesis of 1-(β-D-xylopyranosyl)-3,5-dimethylpyrazole (**1**) via condensation of 1-bromo-1-deoxy-2,3,4-tri-*O*-acetyl-α-D-xylopyranose with 3,5-dimethylpyrazole according to the Yamaoka, Aso and Matsuda procedure,[8] followed by the cleavage of ester linkages by means of methanolic solution of dimethylamine,[9] have been previously described.[10]

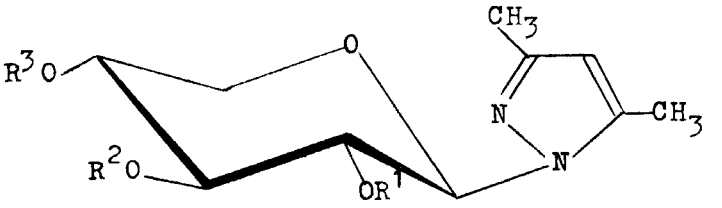
Compound **1** was treated with 3 equivalents of benzoyl chloride in dry pyridine at -10 °C to room temperature for 24 h. Under these conditions esterification of the hydroxyl groups proceeded to give five products, which were obtained as chromatographically homogeneous, after separation of crude benzoylation products by column chromatography. The product having the higher R_F values was 1-(2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**2**), the other products **3**-**6** were incompletely benzoylated 1-(β-D-xylopyranosyl)-3,5-dimethylpyrazole. Compounds **3**-**6** were converted into the acetates **7, 8** or the diacetates **9, 10** and the mesylates **11**, **12**.

Trimolar benzoylation of **1** gave the maximum yields of useful dibenzoate (**3**-23% , **4**-8%) and monobenzoate (**5**-10% , **6**-12%) together with tribenzoate (**2**-18%).

Benzoylation of **1** with 2 molar equivalents of benzoyl chloride at the same interval of temperature as in the case of trimolar benzoylation, was found to be a little more regioselective (the percentage of monobenzoate in the mixture was higher), but the yields of the products were poor. After chromatographic separation the yields of the products were: **2**-5% , **3**-6% , **4**-1% , **5**-8% and **6**-11%. For comparison: dimolar benzoylation of *N*-acetyl-*N*-*p*-chlorophenyl-β-D-xylopyranosylamine in -50 °C gave a mixture of four products with a 35% yield of the 3-benzoate and a 25% yield of the 4-benzoate.[2] Under those conditions the substrate **1** was debenzoylated.

Tri- and dimolar esterification of glycopyranosides as a rule appears to have low regioselectivity and it also may not reflect the relative reactivity of hydroxyl

groups in the unprotected carbohydrate.[11, 12] Consequently, monomolar benzoylation of the title compound was undertaken. When the title compound was treated with 1 equivalent of benzoyl chloride, benzoylation was incomplete, even when the reaction was carried out at room temperature for 3 days, and regioselectivity was low. TLC analysis showed that the 4-benzoate was the major product, accompanied by a mixture of benzoates **2**, **3** and **5**. However, most of the starting material was unreacted.



1	$R^1 = R^2 = R^3 = H$	**7**	R^1 = Ac, $R^2 = R^3$ = Bz
2	$R^1 = R^2 = R^3$ = Bz	**8**	R^2 = Ac, $R^1 = R^3$ = Bz
3	R^1 = H, $R^2 = R^3$ = Bz	**9**	$R^1 = R^3$ = Ac, R^2 = Bz
4	R^2 = H, $R^1 = R^3$ = Bz	**10**	$R^1 = R^2$ = Ac, R^3 = Bz
5	$R^1 = R^3$ = H, R^2 = Bz	**11**	R^1 = Ms, $R^2 = R^3$ = Bz
6	$R^1 = R^2$ = H, R^3 = Bz	**12**	R^2 = Ms, $R^1 = R^3$ = Bz

Identification of compounds **2–12** was based on IR, ^{1}H NMR, ^{13}C NMR, mass spectral spectroscopic data and data from elemental analyses.

Each compound **2–12** showed IR absorption for ester C=0 ν_{max} 1700–1730 cm^{-1}. In the IR spectra of compounds **3–6** there was also an ν_{max} 3200–3450 cm^{-1} band due to HO groups. This band disappeared after acetylation or mesylation and absorptions due to an *O*-acetyl carbonyl function ν_{max} 1750–1760 cm^{-1} (**7–10**) or *O*-mesyl function ν_{max} 1185 cm^{-1} (**11–12**) appeared.

The positions of the unsubstituted hydroxyl groups in **3–6** were determined by comparing their ^{1}H NMR data with those of tribenzoate **2**, *O*-acetyl (**7–10**) and *O*-mesyl derivatives (**11** and **12**). The unsubstituted hydroxyl group in **3** was located at C-2 on the basis of the downfield shift (>1 ppm) of the H-2 signal on comparing the spectrum of this compound to those of **2**, **7** and **11**. The direction of this shift displacement corresponds to the C–OH → C–OBz (1.37 ppm), C–OH → C–OAc (1.07 ppm) and C–OH → C–OMs (1.10 ppm). Positions of the remaining signals were changed only slightly. Comparison of ^{1}H NMR spectrum of **1** with

that of **3** showed downfield shifts of 2.19 and 1.60 ppm for H–3 and H–4 respectively, whereas the shifts of other signals were changed < 0.55 ppm.

Likewise, for **4**, compared with **2**, **8** and **12**, only downfield shifts (1.70, 1.46 and 1.45 ppm, respectively) were associated with H–3 signals, indicating the unsubstituted hydroxyl group to be attached to C–3. This confirms the downfield shifts 1.88 and 1.58 ppm for H–2 and H–4 respectively, comparing the spectra of **1** to **4**.

These data indicate **3** and **4** to be 1–[3,4–di–*O*–benzoyl– and 2,4–di–*O*–benzoyl–β–D–xylopyranosyl]–3,5–dimethylpyrazole, respectively.

A comparison of the ^{1}H NMR spectrum of compound **5** with the spectra of compounds **2**, **3** and **9** shows that HO groups at C–2 and C–4 in **5** are unsubstituted. This assumption is supported by the following data: the positions of the H–3 signals in the above–mentioned spectra are comparable, which suggests that the benzoyl group is at C–3. On comparing the spectra of **2** and **3** to that of **5**, the signals due to H–4 are appreciably shifted (1.53 and 1.36 ppm, respectively). Furthermore after *O*–acetylation of **5** (compound **9**), the signals for H–2 and H–4 are shifted downfield (1.13 and 1.26 ppm, respectively) thus indicating acetylation of OH groups at C–2 and C–4. Therefore, it is concluded that compound **5** is 1–(3–*O*–benzoyl–β–D–xylopyranosyl)–3,5–dimethylpyrazole. Comparing the ^{1}H NMR spectrum of **1** with that of **5**, the downfield shift of 1.64 ppm for H–3 confirms the above conclusion.

Likewise, taking into account the values of the chemical shifts of protons in the spectrum of compound **6** in comparison with those from **3**, **4** and **10**, it may be concluded that HO groups at C–2 and C–3 in **6** are unsubstituted. Since in each spectrum the position of the H–4 signal is comparable, it means that the BzO group in each compound must be at C–4. Additionally, in comparing the spectrum of **6** to those of **2** and **3**, a downfield shift (1.99 and 1.80 ppm, respectively) of the H–3 signal has been observed. A similar result was observed in comparing the shift from **6** to **2** and **4** (1.72 and 1.69 ppm, respectively) of the H–2 signal, and the shift from **6** to **10** (1.28 and 1.54 ppm) of the H–2 and H–3 signals, respectively. These data indicate **6** to be 1–(4–*O*–benzoyl–β–D–xylopyranosyl)–3,5–dimethylpyrazole. This is in accord with the downfield shift 1.36 ppm for H–4 in comparing the spectra of **1** to **6**.

Each of the compounds **1**–**12** has a β–$^4C_1$ structure, as reported for *N*–acetyl–*N*–aryl–β–D–xylopyranosylamines.[2] This structure is in accord with ^{1}H NMR data: H–1(d), H–2(dd), H–3(dd), H–5e(dd) and H–5a(dd); coupling constants $J_{1,2}= J_{2,3}= J_{3,4} = J_{4,5a}= 8.5–10$ Hz; and the magnitude

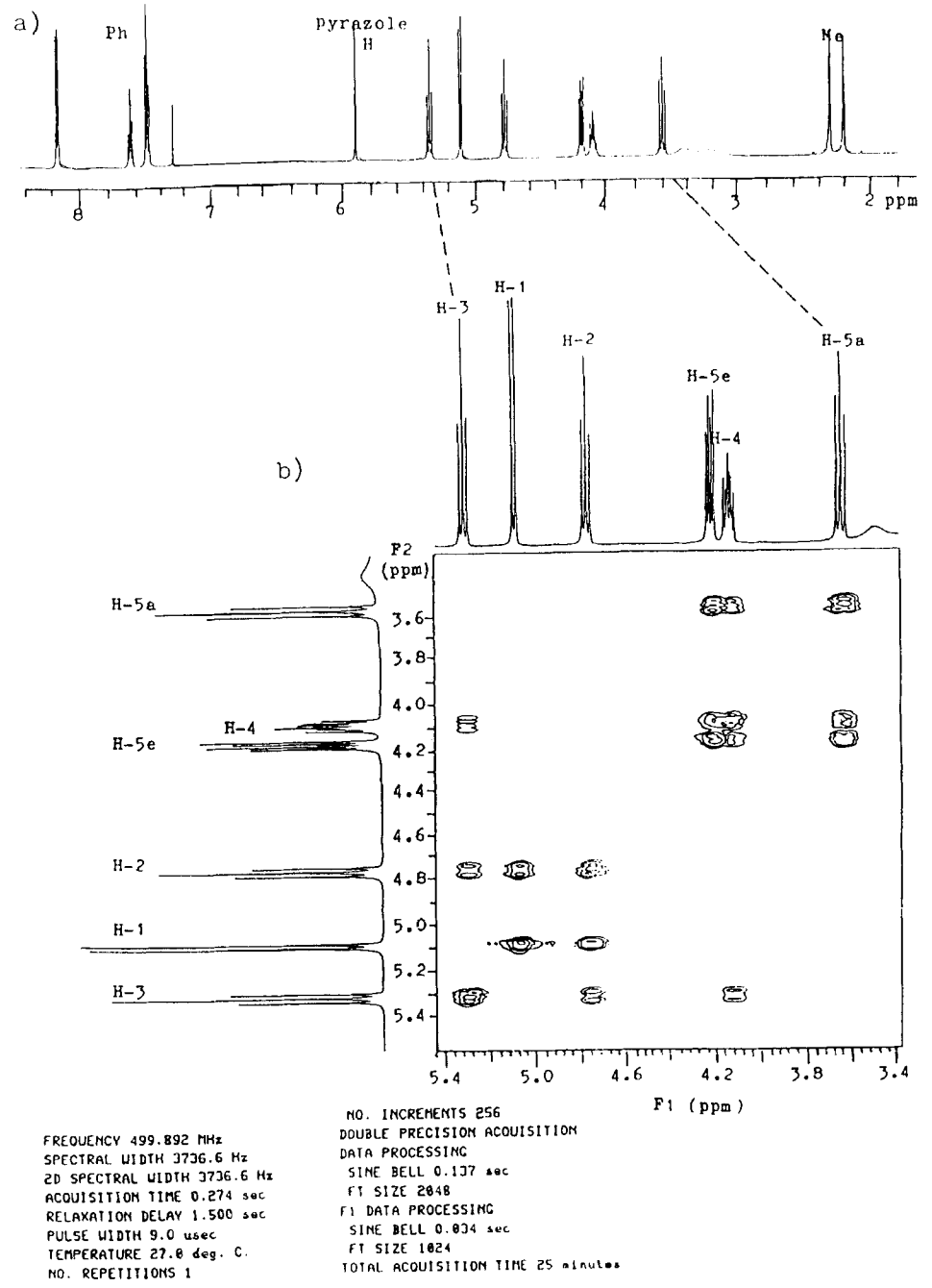


Figure 1. Homonuclear double resonance 2D ^{1}H NMR for the sugar residue of the 1-(3-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**5**)

a) the full proton spectrum of **5**

b) the sketch-plot of the 2D spectrum of **5**.

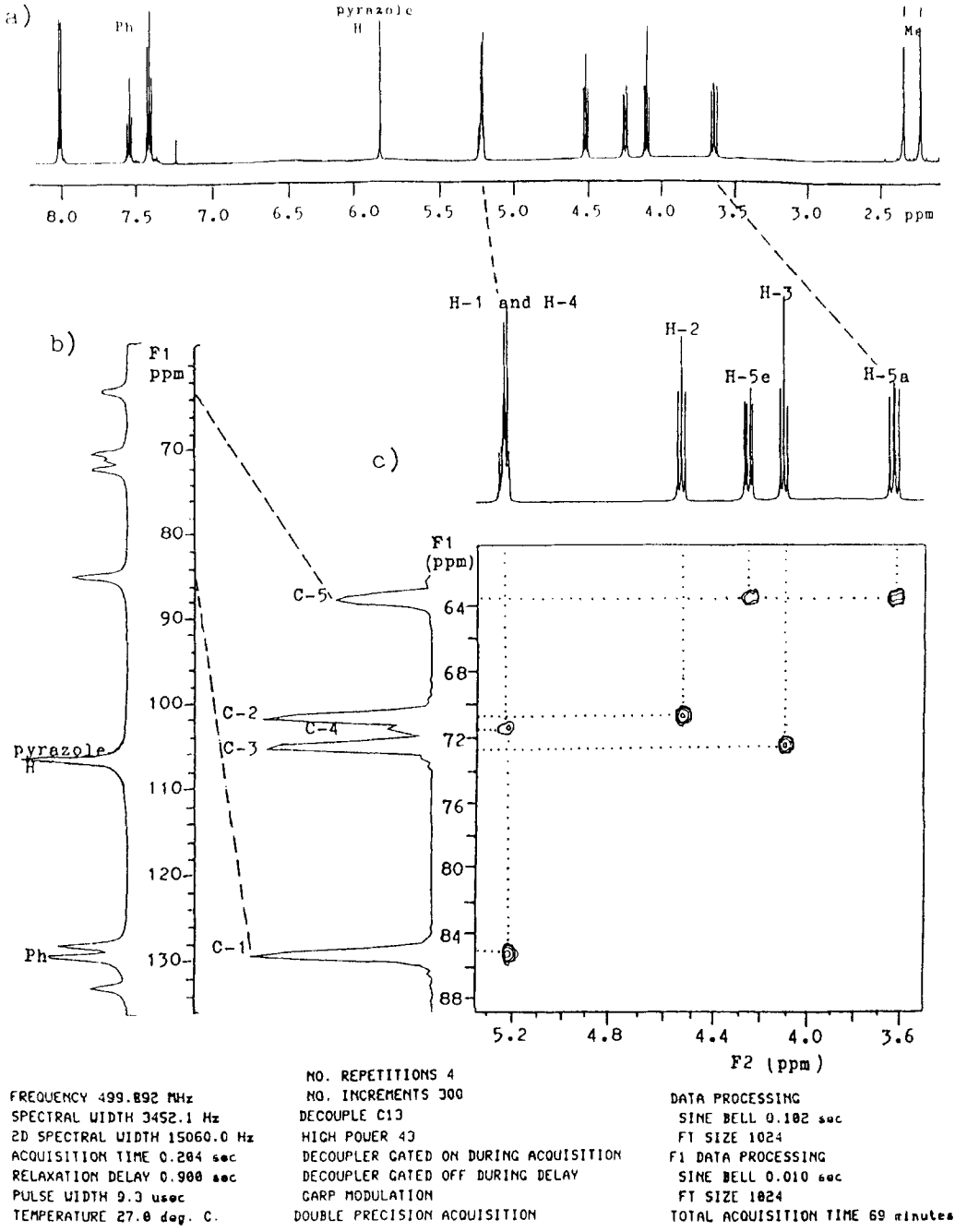


Figure 2. Heteronuclear chemical shifts correlation ^{1}H, ^{13}C 2D NMR for the sugar residue of the 1-(4-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**6**)

a) the full proton spectrum of **6**

b) the projection of the spectrum 1D ^{13}C NMR of **6**

c) the sketch-plot of the 2D spectrum of **6**.

of $\Delta\delta_{H-5e,\ H-5a}$ (0.62–0.85 ppm). Assignment of the carbohydrate proton resonances was confirmed in some cases by 2D ^{1}H NMR (for example **Fig. 1**).

^{13}C NMR spectroscopy was also used to confirm the assigned structures of the synthesized compounds. The signals were identified by application of known chemical shifts rules and by comparison to literature data on analogous compounds: β-D-xylopyranosides[13,14] and *O*-acyl derivatives β-D-gluco-[15,16] and β-D-xylopyranosides.[12,17,18] The assignments were confirmed in some cases by heteronuclear correlation of chemical shifts ^{1}H, ^{13}C 2D NMR (for example **Fig. 2**).

Anomeric carbon signals in all compounds **1–12** appeared at higher field (85.8–83.5 ppm) than were observed in β-D-xylose (97.6 ppm)[13] and in methyl β-D-xylopyranosides and their *O*-acyl derivatives (103–106 ppm),[12] but in the same range as 9-(β-D-xylopyranosyl)-adenine (84.25 ppm).[14] The electron attraction of nitrogen of heterocyclic aglycon off C-1, lesser as compared to an HO or CH_3O group, was considered to explain this fact.[14]

The acylation shifts on the introduced benzoyl groups at C-3 and C-4 of the pyranose ring in the monobenzoate of **1** were evaluated and were shown to be additive parameters for the 3,4-di-*O*-benzoyl derivative of **1**.

The ^{13}C chemical shifts (δ C-n) of the monobenzoates **5** and **6** were compared with those of **1** in calculating the acylation shift values as follows: $\Delta x = \delta^{5 \text{ or } 6}$ C-n – δ^{1}C-n, where x means effect α,β,γ,δ, and n-number of carbon atom. The resulting shift values are: for 3-benzoate (**5**): $\Delta\alpha$ +2.25 ; $\Delta\beta_{C-2}$ -1.48 ; $\Delta\beta_{C-4}$ -1.19 ; $\Delta\gamma_{C-1}$ +0.35 ; $\Delta\gamma_{C-5}$ +1.22 , and for 4-benzoate (**6**): $\Delta\alpha$ +2.28 ; $\Delta\beta_{C-3}$ -4.25 ; $\Delta\beta_{C-5}$ -3.98 ; $\Delta\gamma$ -0.07 ; $\Delta\delta$ -0.17. Although the shift values in **1** were found to differ from those in the corresponding *O*-methyl β-D-xylopyranosides,[12] the trends are the same: C_α was shifted downfield and C_β upfield, whereas C_γ and C_δ showed only small shifts (with the exception $\Delta\gamma_{C-5}$ in **5**).

I then investigated whether the acylation shift values were additive for dibenzoate (**3**) according to: $\delta_{calc.}$ C-n = δ^1 C-n +Σ α→δ , as follows:

$\delta^3_{calc.}$ C-1 = δ^1 C-1 + $\Delta\gamma^5_{C-1}$ +$\Delta\delta^6$ = 85.45+0.35-0.17=85.63 (obser. 85.86)

$\delta^3_{calc.}$ C-2 = δ^1 C-2 + $\Delta\beta^5_{C-2}$ +$\Delta\gamma^6$ = 70.78-1.48-0.07=69.23 (obser. 69.82)

$\delta^3_{calc.}$ C-3 = δ^1 C-3 + $\Delta\alpha^5$ +$\Delta\beta^6_{C-3}$= 77.14+2.25-4.25=75.14 (obser. 74.46)

$\delta^3_{calc.}$ C-4 = δ^1 C-4 + $\Delta\beta^5_{C-4}$ +$\Delta\alpha^6$ = 64.14-1.19+2.28=70.23 (obser. 69.76)

$\delta^3_{calc.}$ C-5 = δ^1 C-5 + $\Delta\gamma^5_{C-5}$ +$\Delta\beta^6_{C-5}$ = 67.76+1.22-3.98=65.00 (obser. 64.96)

The observed ^{13}C chemical shifts of the 3,4-dibenzoate (**3**) were compared with those calculated by assuming additivity of the acylation shifts. The agreement

of this set of values is satisfactory. The maximum difference between the calculated and the experimental data was $\Delta\delta_{max}$ 0.68 ppm for C-3.

The above findings concerning the position of free hydroxyl groups in *O*-benzoylated products of **1** and their yields show that the relative reactivity of the hydroxyl groups in molecules of 1-(β-D-xylopyranosyl)-3,5-dimethylpyrazole decreases in the following order: HO-4 ≥ HO-3 >> HO-2. These results for di- and monobenzoylation suggest that the HO-4 group is the most reactive, but the selectivity of the reaction as well as the total yield of monobenzoate was poor. Increasing the amount of benzoyl chloride caused an increase of the proportion of dibenzoate, but it also increased the yields of all products without considerable change in the regioselectivity of benzoylation.

The order of reactivity of the hydroxyl groups in **1** is similar to that obtained earlier during the dimolar benzoylation of *N*-acetyl-*N*-aryl-β-D-xylopyranosylamines (HO-4 ≈ HO-3 > HO-2), but no differences were observed in the reactivity of HO-4 and HO-3.[2] A more pronounced difference in the reactivities of HO-4 and HO-3 was observed for dimolar mesylation and tosylation of *N*-acetyl-*N*-aryl-β-D-xylopyranosylamines (HO-4 > HO-3 > HO-2).[6]

There are differences in the reports on the relative reactivity of the hydroxyl groups in methyl β-D-xylopyranoside.[12,19,20] In methanesulfonylation of that compound Chalk and Ball[19] established the same order of reactivity (HO-4 > HO-3 > HO-2) as in the above cases of β-D-xylopyranosylamines and found that monomolar methanesulfonylation was more regioselective than dimolar one. In contrast, Kondo[20] building on the results of di- and monobenzoylation of methyl β-D-xylopyranoside, reported a different order of reactivity (HO-2 > HO-3 > HO-4) and noticed a remarkable difference in the reactivity of HO groups in dibenzoylation compared to monobenzoylation, where no serious differences in the reactivity of HO-3 and HO-2 were observed.[21] Kondo confirmed the enhanced reactivity of the HO-2 group in comparison with the HO-4 by monobenzoylation of the 3-benzoylate, obtaining the 2,3- and 3,4-dibenzoates in the ratio of 4:1. The above changed order of reactivity of the hydroxyl groups in methyl β-D-xylopyranoside is not in accord with the reports by Tsuda and co-workers,[12] who ascertained in direct monobenzoylation and via tin intermediates that the HO-4 group in the above compound is the most reactive. Regioselective monobenzoylation by using dibutyltin oxide and bis-tributyltin oxide gave only the 4-benzoate of methyl β-D-xylopyranoside with higher yield.

Because the direct acylation of glycosides was found to occur with rather low regioselectivity and the yields of monoacyl derivatives were poor, methods based on the blocking-deblocking technique and via cyclic tin intermediates are used in regioselective acylation. Although the regioselectivity of these methods is high, they may change completely the reactivity of the HO groups in unprotected carbohydrates. Methods using Bu_2SnO and $(Bu_3Sn)_2O$ with derivatives of β-D-xylose may only enhance the reactivity of the most reactive HO-4 group.

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were determined using a Hilger-Watt polarimeter for solutions in chloroform. ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded with a Varian Gemini 200 spectrometer in $CDCl_3$ with $MeSi_4$ as an internal standard using 5 mm spinning tubes. Two-dimensional 2D ^{1} H NMR and ^{1} H, ^{13}C 2D NMR spectra were recorded with a Varian Unity Plus (500 MHz) spectrometer. IR spectra were measured as Nujol mulls with a Perkin-Elmer 257 spectrophotometer. Field desorption mass spectra were recorded on a MAT 711 mass spectrometer. TLC was performed on Merck Kieselgel 60 plates with carbon tetrachloride-acetone (3 : 1). Column chromatography was performed on Kieselgel (<0.08 mm) with carbon tetrachloride-acetone (3 : 1).

1-(β-D-Xylopyranosyl)-3,5-dimethylpyrazole (1) was prepared according to the literature method:[10] mp 125-128 °C; $[\alpha]_D^{20}$ -65° (*c*, 0.5 methanol); (lit.[10] mp 128-130 °C, $[\alpha]_D^{20}$ -68°); ^{1}H NMR δ 2.02 , 2.21 (2s, 6H, 2 Me), 3.35 (dd, 1H, $J_{4,5a}$= 9 Hz, H-5a), 3.67 (dd, 1H, $J_{3,4}$= 8.5 Hz, H-3), 3.84 (m, 1H, H-4) , 3.97 (m, 1H, H-5e) , 4.30 (dd, 1H, $J_{2,3}$= 8.5 Hz, H-2), 4.97 (d, 1H, $J_{1,2}$= 9 Hz, H-1), 5.77 (s, 1H, pyrazole H); ^{13}C NMR δ 85.45 (C-1), 70.78 (C-2), 77.14 (C-3), 69.14 (C-4), 67.76 (C-5), 106.19 (pyrazole C-4).

Selective Benzoylation of 1-(β-D-Xylopyranosyl)-3,5-dimethyl-pyrazole (1). To a solution of **1** (0.04 mol) in dry pyridine (75 mL) at -10 °C was added benzoyl chloride (0.12 or 0.08 mol) dropwise during 30 min with stirring. The mixture was kept for 1 h at ~0 °C and for 24 or 48 h at +20 °C. Maximum conversion was checked by TLC. Chloroform (200 mL) was added, and the mixture was poured into ice and water. The chloroform layer was washed with 2-3% sulfuric acid and aqueous 5% sodium hydrogen carbonate, dried

($MgSO_4$), and concentrated. Column chromatography of the syrupy residue gave, first 1-(2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**2**), crystallized from methanol: mp 172-174 °C ; $[\alpha]_D^{20}$ -11° (*c*, 0.5 chloroform); R_F 0.82 ; IR 1725 cm^{-1} (ester CO); ^1H NMR δ 2.16 , 2.36 (2s, 6H, 2 Me), 3.79 (dd, 1H, $J_{4,5a}$= 10 Hz, H-5a), 4.57 (dd, 1H, $J_{4,5e}$= 3 Hz, $J_{5e,5a}$ =11 Hz, H-5e), 5.61 (m, 1H, H-4), 5.65 (d, 1H, $J_{1,2}$= 9 Hz, H-1), 5.77 (s, 1H, pyrazole H), 6.05 (dd, 1H, $J_{3,4}$= 9.5 Hz, H-3), 6.21 (dd, 1H, $J_{2,3}$= 9 Hz, H-2), 7.27-8.00 (m, 15 H, Ph); ^{13}C NMR δ 84.77 (C-1), 70.72 (C-2), 73.09 (C-3), 69.77 (C-4), 65.37 (C-5), 106.89 (pyrazole C-4); FD-mass spectrum: *m/z* 540 $[M^+ +1]$.

Anal. Calcd for $C_{31}H_{28}N_2O_7$: C, 68.88 ; H, 5.18 ; N, 5.18. Found : C, 68.80; H, 5.05 ; N, 5.20 .

Eluted second was 1-(3,4-di-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**3**), as a syrup: $[\alpha]_D^{20}$ -70° (*c*, 0.5 chloroform); R_F 0.70 ; IR 3200 (OH), 1725 cm^{-1} (ester CO); ^1H NMR δ 2.18 , 2.30 (2s , 6H , 2 Me), 3.67 (dd, 1H, $J_{4,5a}$= 10 Hz, H-5a), 4.43 (dd, 1H, $J_{4,5e}$ = 3.5 Hz , H-5e) , 4.84 (dd , 1H, $J_{2,3}$= 9 Hz, H-2), 5.18 (d, 1H, $J_{1,2}$ = 9 Hz, H-1) , 5.44 (m , 1H , H-4) , 5.86 (m , 2H, H-3 and pyrazole H) , 7.26-8.10 (m , 10H, Ph); ^{13}C NMR δ 85.86 (C-1), 69.82 (C-2), 74.46 (C-3), 69.76 (C-4), 64.96 (C-5), 106.83 (pyrazole C-4); FD-mass spectrum : *m/z* 437 $[M^+ +1]$.

Anal. Calcd for $C_{24}H_{24}N_2O_6$: C, 66.05 ; H, 5.50 ; N, 6.42. Found: C, 66.20 ; H, 5.50; N, 6.50 .

Eluted third was 1-(2,4-di-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**4**), crystallized from carbon tetrachloride: mp 208-209 °C ; $[\alpha]_D^{20}$ +22° (*c*, 0.5 chloroform); R_F 0.36 ; IR 3400 (OH), 1725 cm^{-1} (ester CO) ; ^1H NMR δ 2.15 , 2.32 (2s , 6H , 2 Me), 3.67 (dd, 1H, $J_{4,5a}$= 9 Hz, H-5a) , 4.29 (m, 1H, H-5e) 4.35 (dd, 1H, $J_{3,4}$=9 Hz, H-3), 5.42 (m, 1H, H-4), 5.50 (d, 1H, $J_{1,2}$= 9 Hz, H-1), 5.75 (s, 1H, pyrazole H), 6.18 (dd, 1H, $J_{2,3}$= 9 Hz, H-2), 7.26-8.03 (m, 10 H, Ph); ^{13}C NMR δ 84.41 (C-1), 78.47 (C-2), 69.14 (C-3), 70.10 (C-4), 68.31 (C-5), 106.73 (pyrazole C-4); FD-mass spectrum : *m/z* 435 $[M^+ +1]$.

Anal. Calcd for $C_{24}H_{24}N_2O_6$: C, 66.05 ; H, 5.50 ; N, 6.42. Found : C, 66.15 ; H, 5.40; N, 6.55 .

Eluted fourth was 1-(3-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**5**), crystallized from carbon tetrachloride: mp 177-178 °C; $[\alpha]_D^{20}$ +8° (*c*, 0.5 chloroform); R_F 0.33; IR 3220 and 3450 (OH), 1700 cm^{-1} (ester CO);

^{1}H NMR δ 2.17, 2.28 (2s, 6H, 2 Me), 3.55 (dd, 1H, $J_{4,5a}$= 10 Hz, H-5a), 4.08 (m, 1H, H-4), 4.17 (m, 1H, H-5e), 4.73 (dd, 1H, $J_{2,3}$= 9 Hz, H-2), 5.07 (d, 1H, $J_{1,2}$= 9.5 Hz, H-1), 5.31 (dd, 1H, $J_{3,4}$ = 9 Hz, H-3), 5.86 (s, 1H, pyrazole H), 7.42-8.15 (m, 5 H, Ph); ^{13}C NMR δ 85.80 (C-1), 69.30 (C-2), 79.39 (C-3), 67.95 (C-4), 68.98 (C-5), 106.77 (pyrazole C-4); FD-mass spectrum: *m/z* 331 [M$^+$+1].

Anal. Calcd for $C_{17}H_{20}N_2O_5$: C, 61.45; H, 6.02; N, 8.43. Found: C, 61.38; H, 5.95; N, 8.45.

Eluted fifth was 1-(4-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**6**), crystallized from carbon tetrachloride: mp 160-163 °C; $[\alpha]_D^{20}$ -44° (*c*, 0.5 chloroform); R_F 0.23; IR 3400 (OH), 1720 cm^{-1} (ester CO); ^{1}H NMR δ 2.17, 2.30 (2s, 6H, 2 Me), 3.60 (dd, 1H, $J_{4,5a}$= 10 Hz, H-5a), 4.06 (dd, 1H, $J_{3,4}$ = 8 Hz, H-3), 4.23 (dd, 1H, $J_{4,5e}$= 3.5 Hz, $J_{5a,5e}$ = 11.5 Hz, H-5e), 4.49 (dd, 1H, $J_{2,3}$= 8 Hz, H-2), 5.15-5.23 (m, 2 H, H-4 and H-1), 5.89 (s, 1H, pyrazole H), 7.40-8.06 (m, 5H, Ph); ^{13}C NMR δ 85.28 (C-1), 70.71 (C-2), 72.89 (C-3), 71.42 (C-4), 63.78 (C-5), 106.75 (pyrazole C-4); FD-mass spectrum: *m/z* 333 [M$^+$+1].

Anal. Calcd for $C_{17}H_{20}N_2O_5$: C, 61.45; H, 6.02; N, 8.43. Found: C, 61.20; H, 6.10; N, 8.40.

The *O*-Acetyl Derivatives of Compounds 3-6. Conventional treatment of **3** with acetic anhydride in pyridine and crystallisation of the crude product from methanol afforded 1-(2-*O*-acetyl-3,4-di-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**7**, 84%): mp 208-210 °C; $[\alpha]_D^{20}$ -51° (*c*, 0.5 chloroform); R_F 0.76; IR 1720 and 1765 cm^{-1} (ester CO); ^{1}H NMR δ 1.80 (s, 3H, AcO), 2.22, 2.37 (2s, 6H, 2 Me), 3.68 (dd, 1H, $J_{4,5a}$= 10.5 Hz, H-5a), 4.50 (dd, 1H, $J_{4,5e}$= 3.5 Hz, $J_{5a,5e}$ = 12 Hz, H-5e), 5.46 (d, 1H, $J_{1,2}$= 9.5 Hz, H-1), 5.53 (m, 1H, H-4), 5.85 (s, 1H, pyrazole H), 5.91-6.02 (m, 2H, $J_{2,3}$= 9.5 Hz, H-2 and H-3), 7.36-8.01 (m, 10H, Ph); ^{13}C NMR δ 84.55 (C-1), 70.26 (C-2), 73.17 (C-3), 69.73 (C-4), 65.31 (C-5), 106.87 (pyrazole C-4); FD-mass spectrum: *m/z* 478 [M$^+$+1]

Anal. Calcd for $C_{26}H_{26}N_2O_7$: C, 65.27; H, 5.44; N, 5.86. Found: C, 65.18; H, 5.50; N, 5.90.

Likewise, **4** gave 1-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**8**, 82%): mp 159-161 °C; $[\alpha]_D^{20}$ +60° (*c*, 0.5 chloroform); R_F 0.68; IR 1725 and 1750 cm^{-1} (ester CO); ^{1}H NMR δ 2.00 (s, 3H, AcO), 2.13, 2.33 (2s, 6H, Me), 3.67 (dd, 1H, $J_{4,5a}$= 11 Hz, H-5a), 4.36 (dd, 1H,

$J_{4,5e}$= 3Hz, $J_{5a,5e}$ = 11 Hz, H-5e), 5.43 (m, 1H, H-4), 5.56 (d, 1H, $J_{1,2}$= 9 Hz, H-1), 5.75 (s, 1H , pyrazole H), 5.81 (dd, 1H, $J_{3,4}$= 10 Hz, H-3), 6.11 (dd, 1H, $J_{2,3}$= 9 Hz, H-2), 7.26-7.97 (m, 10 H, Ph); ^{13}C NMR δ 84.78 (C-1), 70.78 (C-2), 73.30 (C-3), 68.87 (C-4), 65.32 (C-5), 106.89 (pyrazole C-4); FD-mass spectrum : *m/z* 478 [M^{+}+1].

Anal. Calcd for $C_{26}H_{26}N_2O_7$: C, 65.27 ; H, 5.44 ; N, 5.86 . Found: C, 65.20; H, 5.56; N, 5.78 .

Likewise, **5** gave 1-(2,4-di-*O*-acetyl-3-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**9**, 68%): syrup; $[\alpha]_D^{20}$ +23° (*c*, 0.5 chloroform); R_F 0.67; IR 1725 and 1750 cm^{-1} (ester CO) ; ^{1}H NMR δ 1.75, 1.96 (2s, 6H , AcO) , 2.18, 2.32 (2s, 6H, Me), 3.58 (dd, 1H, $J_{4,5a}$= 9 Hz, H-5a), 4.29 (dd, 1H, $J_{4,5e}$= 2.8 Hz, $J_{5a,5e}$=12 Hz, H-5e), 5.34 (m, 1H, H-4), 5.39 (d, 1H, $J_{1,2}$= 9 Hz, H-1), 5.63 (dd, 1H, $J_{3,4}$= 9.5 Hz, H-3), 5.81 (s, 1H , pyrazole H), 5.86 (dd, 1H, $J_{2,3}$= 9.5 Hz, H-2), 7.39-8.02 (m, 5H, Ph); ^{13}C NMR δ 84.38 (C-1), 70.25 (C-2), 73.34 (C-3), 68.69 (C-4), 65.33 (C-5), 106.73 (pyrazole C-4); FD-mass spectrum : *m/z* 417 [M^{+}+1] .

Anal. Calcd for $C_{21}H_{24}N_2O_7$: C, 60.57 ; H, 5.77 ; N, 6.73. Found: C, 60.25 ; H, 5.82; N, 6.70.

Likewise, **6** gave 1-(2,3-di-*O*-acetyl-4-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**10**, 74%): mp 198-201 °C; $[\alpha]_D^{20}$ -55° (*c*, 0.5 chloroform); R_F 0.74; IR 1715 and 1750 cm^{-1} (ester CO); ^{1}H NMR δ 1.89, 2.01 (2s, 6H , AcO) , 2.22, 2.33 (2s, 6H, Me), 3.60 (dd, 1H, $J_{4,5a}$= 10.5 Hz, H-5a), 4.45 (dd, 1H, $J_{4,5e}$= 2.8 Hz, $J_{5a,5e}$=12 Hz, H-5e) , 5.36-5.43 (m, 2H, $J_{1,2}$= 9 Hz, H-1 and H-4), 5.60 (dd, 1H, $J_{3,4}$= 9.5 Hz, H-3), 5.77 (dd, 1H, $J_{2,3}$= 9 Hz, H-2), 5.84 (s, 1H, pyrazole H), 7.42-8.02 (m, 5H, Ph); ^{13}C NMR δ 84.64 (C-1), 70.43 (C-2), 72.70 (C-3), 69.38 (C-4), 65.26 (C-5), 106.86 (pyrazole C-4); FD-mass spectrum : *m/z* 417 [M^{+}+1].

Anal. Calcd for $C_{21}H_{24}N_2O_7$: C, 60.57 ; H, 5.77 ; N, 6.73. Found: C, 60.60 ; H, 5.65; N, 6.80.

The *O*-Methanesulphonyl Derivatives of Compounds 3 and 4. A solution of 1-(3,4-di-*O*-benzoyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (0.01 mol) in pyridine (20 mL) at 0 °C was treated with methanesulphonyl chloride (0.04 mol). The mixture was kept for 1 h at ~0 °C and then for 3 h at 20 °C. TLC then indicated complete conversion of the substrate into one product. Water (5 mL) was added and, after 20 min, the solution was poured into ice-water (250 mL). The crude sulphonate was collected, washed with water, and crystallised from methanol to afford 1-(3,4-di-*O*-benzoyl-2-*O*-methane-

sulphonyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**11**, 80%) : mp 230-233 °C; $[\alpha]_D^{20}$ -98° (*c*, 0.5 chloroform) R_F 0.67; IR 1720 (ester CO) and 1185 cm^{-1} (MsO) ; ^{1}H NMR δ 2.09, 2.20 (2s, 6H , Me) , 2.77 (s, 3H, MsO), 3.66 (dd, 1H, $J_{4,5a}$= 10 Hz, H-5a), 4.45 (dd, 1H, $J_{4,5e}$= 3.5 Hz, H-5e), 5.35 (d, 1H, $J_{1,2}$= 9 Hz, H-1), 5.44 (m, 1H, H-4), 5.71 (dd, 1H, $J_{3,4}$= 10 Hz, H-3), 5.86 (s, 1H , pyrazole H), 5.94 (dd, 1H, $J_{2,3}$= 10 Hz, H-2), 7.23-8.04 (m, 10 H, Ph) ; ^{13}C NMR δ 85.55 (C-1), 72.56 (C-2), 77.22 (C-3), 69.60 (C-4), 65.30 (C-5), 107.24 (pyrazole C-4); FD-mass spectrum: *m/z* 515 [M$^+$+1].

Anal. Calcd for $C_{25}H_{26}N_2O_8S$: C, 58.36 ; H, 5.05 ; N, 5.45. Found : C, 58.42; H, 5.10; N, 5.50.

Likewise, **4** gave 1-(2,4-di-*O*-benzoyl-3-*O*-methanesulphonyl-β-D-xylopyranosyl)-3,5-dimethylpyrazole (**12**, 60%): mp 208-210 °C; $[\alpha]_D^{20}$ +34° (*c*, 0.5 chloroform); R_F 0.42; IR 1730 (ester CO) and 1185 cm^{-1} (MsO); ^{1}H NMR δ 2.08, 2.25 (2s, 6H , Me), 2.83 (s, 3H, MsO), 3.78 (dd, 1H, $J_{4,5a}$= 9 Hz, H-5a), 4.43 (dd, 1H, $J_{4,5e}$= 3.5 Hz, $J_{5a,5e}$=11.5 Hz, H-5e), 5.04 (m, 1H, H-4), 5.50 (d, 1H, $J_{1,2}$= 9 Hz, H-1), 5.69 (s, 1H, pyrazole H), 5.80 (dd, 1H, $J_{3,4}$= 9.5 Hz, H-3), 6.07 (dd, 1H, $J_{2,3}$= 9.5 Hz, H-2), 7.24-7.94 (m, 10 H, Ph); ^{13}C NMR δ 84.15 (C-1), 72.81 (C-2), 74.44 (C-3), 70.79 (C-4), 66.05 (C-5), 106.92 (pyrazole C-4); FD-mass spectrum : *m/z* 514 [M$^+$+1].

Anal. Calcd for $C_{25}H_{26}N_2O_8S$: C, 58.36 ; H, 5.05 ; N, 5.45. Found : C, 58.28; H, 5.05; N, 5.36.

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21. Similarly these differences in reactivity of HO-2 and HO-3 groups in monoacetylation of methyl 4-*O*-benzoyl-β-D-xylopyranoside (ref.18) with acetic anhydride were not established.