Reaction of 3-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranurononitrile with Phenylmagnesium Bromide

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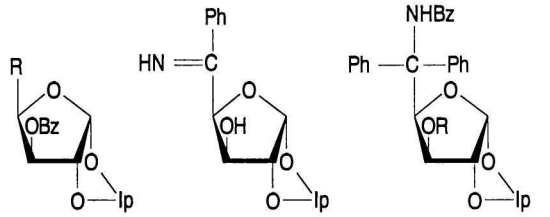
Reaction of 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranurononitrile with phenylmagnesium bromide in the mole ratio of 1 : 3 afforded 5-benzamido-5-deoxy-5,5-diphenyl-1,2-*O*-isopropylidene-α-D-xylofuranose. Its structure was proved by special NMR techniques. The imine expected from the addition reaction of Grignard reagent on the nitrile group was not isolated.

The reactions of Grignard reagents with aldehyde or ketone groups in appropriate carbohydrate derivatives have been studied extensively [1—14]. A part of these studies has been also reviewed [15, 16]. On the other hand, though the reaction of Grignard reagents with nitrile group affording ketimines or ketones is well known [17—22], there are only few mentions in the literature about such reaction with nitriles in the carbohydrate series [23—25].

Due to a possibility of several competitive reactions such as cleavage of acidic α-protons, anomerization, cleavage of protecting groups, different rearrangement and ring opening reactions, *etc.*, a great variety of reaction products can be expected in dependence on the structure of starting carbohydrate—nitrile.

In the present work, we have studied the reaction of 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranurononitrile (*I*) (prepared from the corresponding oxime and acetic anhydride) with phenylmagnesium bromide with an intention to prepare corresponding imine (*II*). Therefore, the method of *Pickard* and *Tolbert* [18] was used for decomposition of the Grignard reagent—nitrile reaction complex. Using 1 3 mole ratio of the starting nitrile and Grignard reagent, TLC revealed the presence of four compounds in the reaction mixture. After separation on a column of neutral alumina, the first two crystalline products (major) were isolated and characterized as biphenyl and 5-benzamido-5-deoxy-5,5-diphenyl-1,2-*O*-isopropylidene-α-D-xylofuranose (*III*). The other two reaction products (minor) were unidentified. However, based on the NMR spectral data (high content of aromatic protons), neither of them was expected imine *II*. When only one equivalent of Grignard reagent was used, no product *III* was obtained and mostly, starting nitrile and biphenyl were isolated. On the other hand, two equivalents of Grignard reagent afforded only negligible yields of *III*. This can be probably due to competitive reactions of Grignard reagent with acidic α-hydrogen atom at C-4 as well as with benzoyl group at C-3 atom.



I R = CN
V R = CH=O
VI R = CH=NOH

II
Bz = benzoyl
Ip = isopropylidene

III R = H
IV R = Ac

The structure of *III* was confirmed on the basis of mass and NMR spectral data. In the mass spectrum, the proving peaks corresponding to the molecular ion $[M]^+$ and to the fragments $[M - PhCONH]^+$, $[PhCONHCPh_2]^+$, $[PhCO]^+$, were registered. In the ^{13}C NMR spectrum, the carbons bearing hydrogen atom were unambiguously assigned using selective decoupling technique. The quaternary carbon atoms of three nonequivalent benzene rings were identified on the basis of semiselective INEPT experiment [26] and 1D INADEQUATE pulse sequence technique [27]. The determination of connectivities between C=O (benzamide), C-5, and quaternary carbon atoms of the benzene rings was possible on the basis of C=C coupling constants ($J_{C=O,C-140.2}$ = 58.21 Hz, $J_{C-65.4,C-143.1}$ = 59.34 Hz, $J_{C-65.4,C-135.1}$ = 61.04 Hz). Spectral data of the corresponding 3-*O*-acetyl derivative *IV* are also confirmative of the structure of *III* because the same connectivities between carbon atoms were observed.

EXPERIMENTAL

Starting 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose was prepared from 1,2:5,6-di-*O*-iso-

propylidene-α-D-glucofuranose [28] by benzoylation and partial hydrolysis according to the known method [29]. The other used chemicals were commercially available products (Merck, Darmstadt; Fluka, Buchs; Lachema, Brno).

Melting points were determined with a Boetius PHMK 05 microscope. The EI mass spectra (70 eV) were recorded on a Jeol JMS-100D spectrometer at an emission current of 300 μA, applying the direct sample-introduction technique. ^1H and ^{13}C NMR spectra were measured on a Bruker AM-300 FT spectrometer operating at 300.13 MHz or 75.46 MHz working frequencies in $CDCl_3$ solutions with TMS as an internal standard. The optimalization for $J_{C,H}$ (long-range) was 7 Hz and for $J_{C,C}$ 60 Hz. Elemental analyses were obtained on a Perkin—Elmer 240 analyzer. TLC was performed on silica gel 60 F_{254} (Merck) plates with ethyl acetate—hexane (φ_r = 3 2 (A) or φ_r = 1 1 (B)) as an eluent. Specific optical rotations were measured with Perkin—Elmer 241 polarimeter.

3-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranurononitrile (*I*)

Aldehyde *V* (4.4 g; 15 mmol) (prepared as a colourless oil from 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose by the periodate cleavage according to the procedure known for the preparation of corresponding 3-*O*-benzyl analogue [5]) in methanol (35 cm^3) was treated with a mixture of hydroxylammonium chloride (1.1 g), water (7.5 cm^3), and pyridine (7.5 cm^3) and the solution was kept overnight at room temperature. After usual work-up, the oxime *VI* (4.0 g, 86 %) was obtained as a mixture of *E* and *Z* isomers (x_r = 1 3, single spot at R_f = 0.66, eluent B): m.p. = 162—163 °C. Mass spectrum, *m/z*: 274 $[M - H_2O - CH_3]^+$, 105 $[PhCO]^+$

The above oxime *VI* (4.0 g; 13 mmol) was added dropwise into 25 cm^3 of hot acetic anhydride. The mixture was heated under reflux for 30 min, and then evaporated under diminished pressure to dryness. The residue was dissolved in ether (50 cm^3), washed with 5 % sodium hydrogencarbonate and dried with sodium sulfate. The ethereal solution was decolourized (charcoal), concentrated at reduced pressure to give crude product. One recrystallization from a mixture of ether—hexane afforded 3.1 g (82 %) of *I* in the form of white crystals (R_f = 0.85, B), m.p. = 117—118 °C, [α](D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = – 25°. EI mass spectrum, *m/z*: 274 $[M - CH_3]^+$, 231 $[M - CH_3COCH_3]^+$, 105 $[PhCO]^+$, 43 $[CH_3CO]^+$ ^1H NMR spectrum ($CDCl_3$), δ: 7.45—8.10 (m, 5H, H_{arom}), 6.27 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 5.63 (d, 1H, $J_{3,4}$ = 3.4 Hz, H-4), 5.09 (d, 1H, H-3), 4.75 (d, 1H, H-2). ^{13}C NMR spectrum ($CDCl_3$), δ: 164.8 (C=O), 133.9 (C-4′), 129.9 (C-3′ and C-5′), 128.6 (C-2′ and C-6′), 128.3 (C-1′), 113.7 (CN), 113.6 ($\underline{C}Me_2$), 105.5 (C-1), 82.5 (C-2), 76.3 (C-3), 68.5 (C-4), 26.8 and 26.1 (2 × CH_3). For $C_{15}H_{15}NO_5$ (M_r = 289.31) w_i(calc.): 62.30 % C, 5.24 % H, 4.85 % N; w_i(found): 62.24 % C, 5.28 % H, 4.81 % N.

5-Benzamido-5-deoxy-5,5-diphenyl-1,2-*O*-isopropylidene-α-D-xylofuranose (*III*)

To the Grignard reagent, prepared by the conventional procedure from magnesium turnings (0.63 g; 26 mmol) and bromobenzene (4.16 g; 26.5 mmol) in dry ether (20 cm^3), a solution of nitrile *I* (2.49 g; 8.6 mmol) in dry ether (25 cm^3) was added dropwise at room temperature and the mixture was then heated under reflux for 2 h. After cooling to room temperature, dry methanol (2 cm^3) was added, the solid filtered off, washed with ether and the solvents evaporated under diminished pressure to give a mixture of crude products. This was separated on a column of neutral alumina using the solvent B as an eluent, affording white crystals (1.2 g) of *III* (R_f = 0.59, A), m.p. = 108—109 °C, [α] (D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = – 53°. EI mass spectrum, *m/z*: 445 $[M]^+$, 430 $[M - CH_3]^+$, 325 $[M - PhCONH]^+$, 287, 286 $[PhCONHCPh_2]^+$, 196, 183, 105 $[PhCO]^+$, 43 $[CH_3CO]^+$ ^1H NMR spectrum ($CDCl_3$), δ: 7.62—7.75 and 7.15—7.45 (m, 15H, H_{arom}), 7.69 (bs, 1H, NH), 6.09 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.73 (d, 1H, $J_{3,4}$ = 2.3 Hz, H-4), 4.29 (dd, 1H, $J_{2,3}$ = 0.6 Hz, H-2), 3.70 (dd, 1H, H-3), 2.52 (d, 1H, OH), 1.41 and 1.23 (s, 6H, 2 × CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ: 166.0 (C=O), 143.1, 140.2, 135.1, 131.4, 129.3, 128.5, 128.4, 127.6, 127.4, 127.2, 127.0 (C_{arom}), 111.9 ($\underline{C}Me_2$), 105.1 (C-1), 86.0 (C-4), 83.4 (C-2), 76.2 (C-3), 65.4 (C-5), 26.9 and 26.2 (2 × CH_3). For $C_{27}H_{27}NO_6$ (M_r = 445.55) w_i(calc.): 72.78 % C, 6.12 % H, 3.14 % N; w_i(found): 72.62 % C, 6.16 % H, 3.11 % N.

3-*O*-Acetyl-5-benzamido-5-deoxy-5,5-diphenyl-1,2-*O*-isopropylidene-α-D-xylofuranose (*IV*)

A mixture of *III* (250 mg), acetic anhydride (2 cm^3), and pyridine (4 cm^3) was kept at room temperature for 24 h. After usual work-up, the crude product was dissolved in ether, decolourized with charcoal, filtered and the solvent was evaporated at diminished pressure to give a sirup which solidified upon drying in vacuum desiccator. One recrystallization from ether—hexane afforded white crystals (235 mg, 86 %) of *IV* (R_f = 0.71, A), m.p. = 77—78 °C, [α] (D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = – 36°. EI mass spectrum, *m/z*: 487 $[M]^+$, 472 $[M - CH_3]^+$, 429 $[M - CH_3COCH_3]^+$, 428 $[M - CH_3COO]^+$, 367 $[M - PhCONH]^+$, 287, 286 $[PhCONHCPh_2]^+$, 105 $[PhCO]^+$, 43 $[CH_3CO]^+$ ^1H NMR spectrum ($CDCl_3$), δ: 7.68—7.80 and 7.14—7.45 (m,

15H, H_{arom}), 7.64 (bs, 1H, NH), 6.13 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 4.93 (d, 1H, $J_{3,4}$ = 2.5 Hz, H-4), 4.50 (dd, 1H, $J_{2,3}$ = 0.7 Hz, H-3), 4.30 (dd, 1H, H-2), 1.85 (s, 3H, CH_3CO), 1.47 and 1.25 (s, 6H, 2 × CH_3). ^{13}C NMR spectrum ($CDCl_3$), δ: 168.5 ($O{=}C_{acetyl}$), 164.9 ($O{=}C_{benzoyl}$), 143.7, 138.6, 135.3, 131.3, 129.3, 128.5, 127.8, 127.5, 127.4, 126.8 (C_{arom}), 112.6 ($\underline{C}Me_2$), 105.0 (C-1), 84.1 (C-4), 81.6 (C-2), 77.4 (C-3), 64.8 (C-5), 26.7 and 26.2 (2 × CH_3), 20.8 (H_3C_{acetyl}). For $C_{29}H_{29}NO_6$ (M_r = 487.59) w_i(calc.): 71.43 % C, 6.01 % H, 2.87 % N; w_i(found): 71.32 % C, 6.05 % H, 2.89 % N.

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