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Hydrophilically functionalized pyrazoles from sugars[1]

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Abstract

An effective and convenient protocol has been developed for the conversion of D-glucose and 6-*O*-α-D-glucopyranosyl-D-fructose (palatinose®, isomaltulose) into 5-[(1′*S*)-1′,2′-dihydroxyethyl]-1-phenylpyrazole-3-carboxaldehyde (**4**) and 5-[(1*S*)-2-(α-D-glucopyranosyloxy)-1-hydroxethyl])-1-phenylpyrazole-3-carboxaldehyde (**5**), key steps being the acetic anhydride-promoted dehydrative cyclization of the respective phenylosazones, and subsequent liberation of the *N*-acetylphenylhydrazone-blocked aldehyde function. Exploitation of the ensuing chemistry of **4** and **5** led to a variety of pyrazole building blocks with a diverse level of hydrophilic substituents (hydroxymethyl, dihydroxyethyl or glucosyl residues) and useful functional groups, such as chloro, cyano, aminomethyl, vinyl and acryloyl moieties.

Keywords: Osazone→pyrazole conversions; Hydrophilic pyrazoles; Isomaltulose; Palatinose

1. Introduction

To improve the competitiveness of low molecular weight carbohydrates over petrochemical raw materials, the development of practical, large-scale adaptable *reaction channels* is required leading from cheap, ton-scale accessible sugars to building blocks with industrial application profiles [2]. Prototype of such industrially useful building blocks are the oxygen heterocycles furfural (**1**) and its 5-hydroxymethyl analog HMF (**2**), as they can be readily produced from wood- or straw-derived xylans [3], and D-fructose [4–6], respectively, in processes worked out on a pilot plant level. By contrast, technically viable reaction channels from carbohydrates to nitrogen heterocycles, which would be of similar industrial importance, have not been systematically exploited. Although the transformation of carbohydrates into N-heterocycles occurs extensively on the exposure of foodstuffs to heat (Maillard reaction [7]), the yields obtainable are so modest as to be of little if any preparative use. The same holds for various chemically induced

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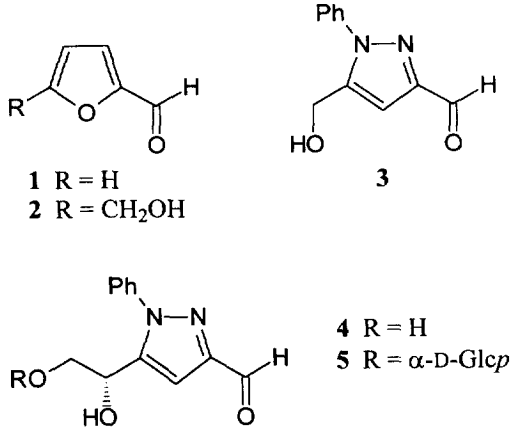
conversions sugar→N-heterocycle [8–10], as only a few short, simple, and reasonably well elaborated procedures are available that lead from inexpensive, bulk scale-accessible sugars to N-heterocyclic building blocks with potential use as industrial intermediate chemicals. Notable examples are the generation of pyrrole from galactaric acid by pyrolysis of its ammonium salt [11], the preparation of pyrrole derivatives by cyclocondensation of 2-amino-2-deoxy-D-glucose with dicarbonyl compounds [8], of 4-hydroxymethyl- [12] and 4-tetrahydroxybutyl-imidazole [13] from D-fructose by heating with formamidine acetate in ammonia, and the recently developed, practical access to pyrazolecarboxaldehyde **3** from D-xylose [1].

As pyrazoles with a variable level of hydrophilic substituents offer the prospect of serving as useful starting materials for the synthesis of a wide variety of products—bacteriostatics of the sulfaphenazol-type [14] with higher bioavailability, or more readily biodegradable agricultural chemicals—this report describes the practical elaboration of acetic anhydride-induced pyrazole cyclizations of the D-glucose- and isomaltulose-derived phenylosazones, and a first exploitation of the ensuing chemistry feasible.

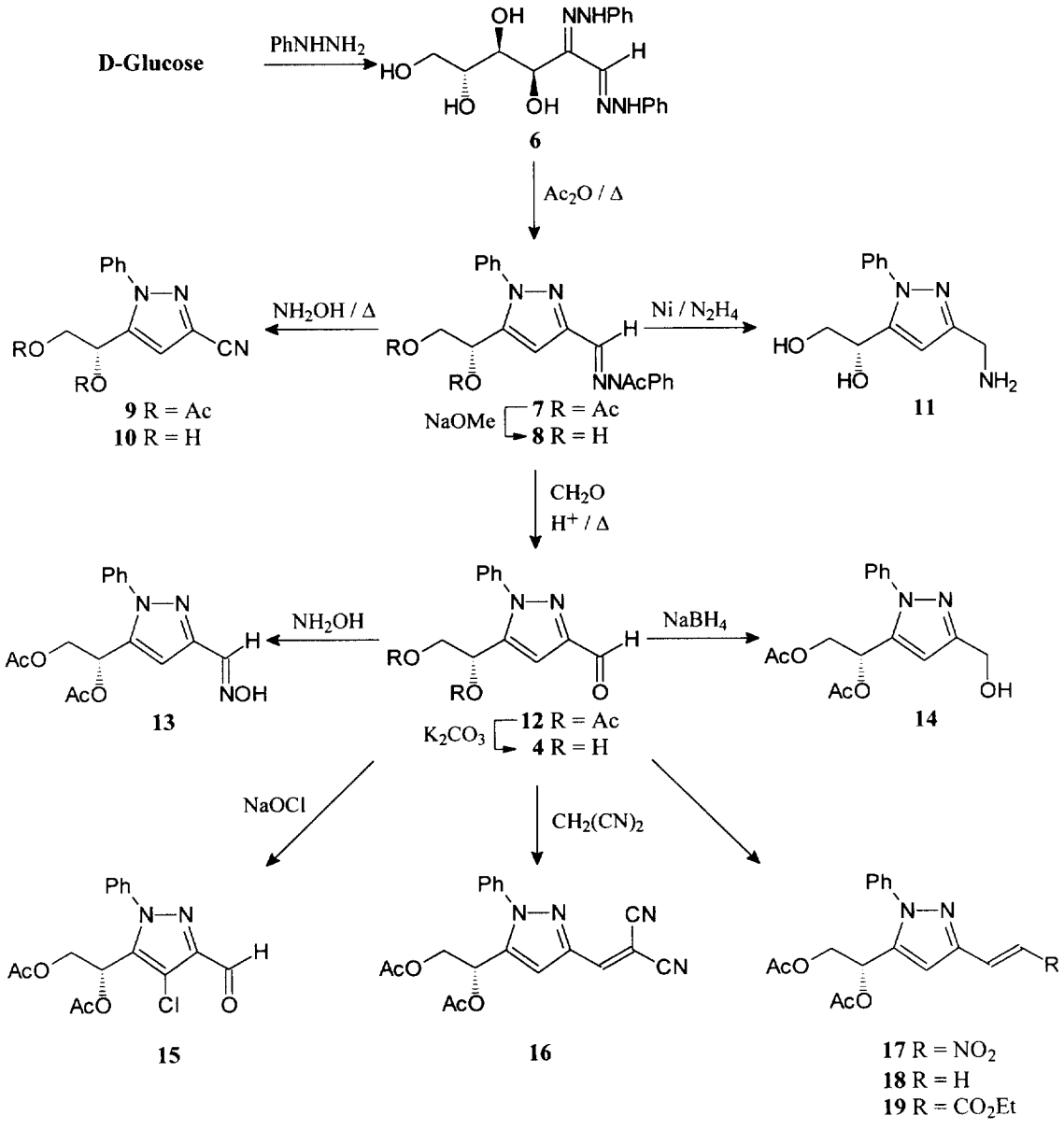
2. Results and discussion

Phenylosazones derived from various monosaccharides have been shown, upon refluxing in acetic anhydride, to elaborate the pyrazole ring by spanning C-2 and C-4 of the sugar with an N–N-bond [15,16]. Although the mechanism of this complex reaction has not been studied in detail, it conceivably involves three consecutive steps, acetylation of the OH and NH groups, displacement of the 4-acetoxy function by the 2-phenyl-hydrazono nitrogen and elimination of acetic acid from the pyrazoline thus formed. In re-addressing the conversion of D-glucose phenylosazone **6** into the respective pyrazole **7**—no yield had been reported previously [15]—it was found advantageous to add the osazone to refluxing acetic anhydride, thereby effecting quick dissolution and, hence, short reaction times (40 min), allowing the isolation of **7** in preparatively useful yield (77%). Various attempts to further improve on the conversion of **6**→**7**, e.g. by addition of zinc chloride or sodium acetate, gave inferior results.



Scheme 1.

The utility of pyrazole **7** as a potential key compound for the generation of versatile building blocks rests on the efficiency with which ensuing reactions can be performed, particularly with respect to modifications at the phenylhydrazono-blocked aldehyde group. These can be effected in several ways. Heating with hydroxylamine hydrochloride in dimethyl sulfoxide (2 h at 100 °C or 45 min at 120 °C) effectively (70%) converted pyrazole **7** or its de-*O*-acetylated derivative **8** into the respective nitrils **9** and **10**, a reaction sequence obviously initiated by exchange of the phenylhydrazone group by the hydroxylamine function, the respective aldoxime intermediate thus formed then undergoing thermal dehydration. The comparative ease with which this reaction occurred is noteworthy, as the conditions had only been applied for the conversion of aromatic aldehydes into their nitriles, e.g. of furfural into furonitrile [17] and not for the prior removal of phenylhydrazono residues which are particularly stable when *N*-acetylated [1]. Thus, **7** remained unchanged after refluxing with benzaldehyde/acetic acid, i.e. conditions that readily allow the removal of the (non-acetylated) phenylhydrazone residues in osazone **6** to yield the respective osone [18]. Employing the more reactive formaldehyde, however, i.e. refluxing **7** with 35% aqueous formaldehyde/acetic acid, efficiently liberated the *N*-acetylphenylhydrazone-blocked aldehyde function to give the acetyl derivative **12** (86%). Another means for removing the *N*-acetylphenylhydrazone moiety in **7** proved to be exposure to hydrazine in the presence of Raney nickel, which induced a smooth (2 h at 25 °C) and efficient catalytic reduction (of the intermediate hydrazone conceivably) to afford the nicely crystalline amine **11** (91%).

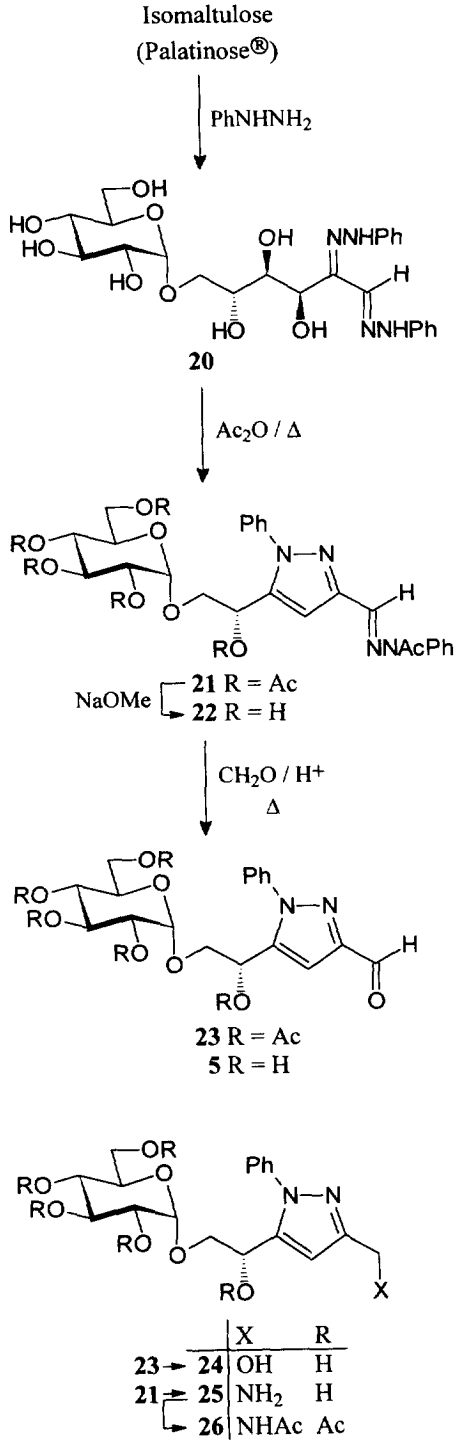


Scheme 2.

Pyrazole-aldehyde **12** and its deacetylated derivative **4**, were subjected to various further modifications: the aldoxime **13** was readily prepared from **12**, and—by its conversion into the nitrile **9** on heating in dimethyl sulfoxide—shown to be the intermediate in the generation of **9** from the phenylhydrazone **7**. Reduction of **12** with sodium borohydride smoothly afforded the respective alcohol **14**. Attempts to oxidize the aldehyde group in **12** to the carboxylic acid with a cheap oxidant, i.e. sodium hypochlorite, led to chlorination of the pyrazole ring instead, to give the 4-chloropyrazole analog **15** (88%). The pyrazole-aldehyde **12** readily underwent aldol type reaction without affecting the acetate ester functions. Thus, aluminium oxide-catalyzed [19] Knoevenagel reaction with malononitrile afforded the dicyanovinyl derivative **16** (82%), whilst butylammonium acetate-induced [20] addition of nitromethane afforded the 2-nitrovinyl analog **17** (70%). Vinyl analogs with a polymerizable double bond could be generated by Wittig-type reactions: exposure to methyltriphenylphosphonium bromide in THF in the presence of *n*-butyl lithium afforded the corresponding unsubstituted alkene **18**, whereas carbonyl olefination with ethoxycarbonylmethylene triphenylphosphorane gave the pyrazole-acrylate **19** in nearly quantitatively.

The methodology developed has been further extended to 6-*O*-α-D-glucopyranosyl-D-fructose (isomaltulose, palatinose®), a disaccharide available on an industrial scale from sucrose via *Protaminobacter rubrum*-induced $^{2}O\rightarrow{}^{6}O$-glycosyl transfer [21]. Indeed, the efficacy with which the palatinose phenylosazone **20** responded to the dehydrative cyclization, when refluxed in acetic anhydride, proved a quite attractive route (79%) to the glucosylated pyrazoles **21** and **22** (after de-*O*-acetylation). Liberation of the carbonyl function in **21** or **22** from its phenylhydrazono protection was carried out as above by heating with formaldehyde/acetic acid to give the carboxaldehydes **5** and **23**, respectively, in yields over 90%, or, upon hydride reduction, the corresponding alcohol **24**. Similarly, the acetylated phenylhydrazone **21** underwent reductive cleavage with Raney-nickel/hydrazine to deliver the amine **25** (93%), also characterized as its N-acetate **26**.

In conclusion, the varied level of hydrophilic substituents purposefully introduced into the pyrazole ring by its generation from inexpensive, bulk scale-accessible sugars, and the high degree of functional group diversity achievable by exploiting the ensuing chemistry of the key pyrazoles **7** and **21**, provides a useful array of versatile pyrazole building blocks with broad application profiles for the generation of pharmaceuticals, agrochemicals, and novel polymers.



Scheme 3.

3. Experimental

General methods.—Melting points were determined with a Bock hot-stage microscope and are not corrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Mass spectra were recorded with a Varian 311A spectrometer and NMR spectra with Bruker WM300 and AC300 instruments at 300 (^{1}H) and 75.5 MHz (^{13}C). Chemical shifts are given in ppm using Me_4Si as internal standard. TLC on Silica Gel 60 F_{254} plastic sheets (E. Merck, Darmstadt) was used to monitor the reactions and ascertain the puritiy of the products. Eluents employed: toluene-EtOAc in 1:1–5:1 ratios for acylated products, $CHCl_3$-MeOH in 2:1–5:1 ratios for the pyrazoles with free OH groups, and 6:1 EtOH–2.5% aq ammonia for amines **11** and **25**. The spots were visualized by UV light or by spraying with 50% H_2SO_4 and charring at 120 °C for 5 min. Column chromatography was performed on Silica Gel 60 (Macherey & Nagel; 63–200 nm). Evaporations were conducted under diminished pressure at bath temperatures below 45 °C.

D-arabino-*Hexose phenylosazone* (**6**).—To a solution of 18 g (0.1 mmol) of D-glucose in 150 mL of water, phenylhydrazine (35 mL, 0.35 mol) and

glacial HOAc (5 mL) were added. The mixture was stirred for 2 h at 100 °C. After cooling, finally in a refrigerator, the voluminous yellow precipitate was collected and washed with water and *n*-hexane. The product (mp 202 °C) was recrystallized from MeOH to give 31.2 g (87%) of **6** as yellow needles; mp 210 °C, $[\alpha]_D^{20}$ −88.2° (*c* 0.5, Me_2SO); Lit [22].: no yield given, mp 208–209 °C, $[\alpha]_D^{20}$ −59.5° (*c* 0.46, 2-methoxyethanol); ^1H NMR (Me_2SO-d_6): δ 3.48 (m, 2H, H-4), H-5, 3.62 (m, 2H, two H-6), 4.38 (t, 1H, 6-OH), 4.54 (dd, 1H, H-3), 4.60 (m, 2H, 4-OH, 5-OH), 5.12 (d, 1H, 3-OH), 6.83–7.38 (m, 10 H, 2 C_6H_5), 7.89 (s, 1H, H-1), 10.70, 12.19 (2 s, 1H each, 2 NH), $J_{3,4}$ 2.6, $J_{3,3\text{-OH}}$ 5.2, $J_{6,6\text{-OH}}$ 5.5 Hz; ^{13}C NMR ([D_6]DMSO): δ 63.3 (C-6), 71.3 (C-5), 72.1 (C-3), 74.5 (C-4), 111.8–129.5, 144.0, 144.4 (2 C_6H_5), 134.7 (C-1), 137.8 (C-2); MS (FD): *m*/*z* 358 (M^+).

5-[(1′S)-1′,2′-Diacetoxyethyl]-1-phenylpyrazole-3-carboxaldehyde N-*acetylphenyl-hydrazone* (**7**).—To refluxing Ac_2O (400 mL) was added in portions 28 g (78 mmol) of **6**, and the mixture was refluxed (bath temp. 140 °C) for 40 min, then poured into a mixture of ice (300 g) and satd $NaHCO_3$ solution (300 mL), and extracted with 300 mL of CH_2Cl_2. The extract was washed with satd $NaHCO_3$ solution and water. Drying ($MgSO_4$) and removal of the solvent gave a syrup, which crystallized from aq EtOH to give **7** (24.5 g, 71%) as colorless needles; mp 132–133 °C, $[\alpha]_D^{20}$ +60° (*c* 1.0, $CHCl_3$). A second crop (1.9 g) was obtained by working up the mother liquor, increasing the yield to 77%; Lit [13].: no yield given, mp 131 °C, $[\alpha]_D^{20}$ +68° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.02, 2.04 (2 s, 3H each, 2 OAc), 2.62 (s, 3-H, NAc), 4.33 (m, 2 H, two H-2′), 6.02 (t, 1H, H-1′), 6.91 (s, 1H, H-4), 7.36 (s, 1H, 3-C*H*), 7.14–7.54 (m, 10 H, 2 C_6H_5), $J_{1',2'}$ 5.9 Hz; ^{13}C NMR ($CDCl_3$): δ 20.7, 20.8 (2 OCO*Me*), 22.2 (NCO*Me*), 64.2 (C-2′), 65.4 (C-1′), 103.5 (C-4), 125.8–130.5, 149.1 (2 C_6H_5), 135.9 (3-*C*H), 138.8, 140.7 (C-3, C-5), 169.7, 170.4 (2 O*C*OMe), 172.8 (N*C*OMe); MS (FD): *m*/*z* 448 (M^+). Anal. Calcd for $C_{24}H_{24}N_4O_5$ (448.5): C, 64.28, H, 5.39, N, 12.49. Found: C, 64.25, H, 5.36, N, 12.55.

5-[(1′S)-1′,2′-Dihydroxyethyl]-1-phenylpyrazole-3-carboxaldehyde N-*acetylphenyl-hydrazone* (**8**).—To a solution of 500 mg (1.1 mmol) of pyrazole **7** in dry MeOH (50 mL) was added 20 mg of NaOMe, and the mixture was stirred at room temp. for 1.5 h. Neutralization with 500 mg of strongly acidic ion exchange resin (Amberlite IR-120, H^+ form), filtration of the mixture and removal of the solvent from the filtrate under reduced pressure yielded a syrup, which was crystallized from EtOAc to afford **8** (411 mg, quant.) as colorless needles; mp 176–178 °C, $[\alpha]_D^{20}$ +9.2° (*c* 1, MeOH); Lit [15].: no yield given, mp 185 °C, $[\alpha]_D^{20}$ +13° (*c* 1, EtOH); ^1H NMR (Me_2SO-d_6): δ 2.50 (s, 3H, NAc), 3.59, 3.65 (2 ddd, 1H each, two H-2′), 4.53 (ddd, 1H, H-1′), 4.91 (t, 1H, OH-2′), 5.60 (d, 1H, OH-1′), 6.89 (s, 1H, H-4), 7.16 (s, 1H, N=C*H*), 7.23–7.62 (m, 10 H, 2 C_6H_5), $J_{1',2'}$ 5.9 and 6.4, $J_{2',2'}$ 11.5 Hz; ^{13}C NMR ([Me_2SO-d_6): δ 21.7 (NCO*Me*), 64.9 (C-2′), 65.3 (C-1′), 102.4 (C-4), 124.8–130.1, 146.7, 147.6 (2 C_6H_5), 135.2 (3-*C*H), 135.7, 139.0 (C-3, C-5), 171.2 (*C*OMe); MS (FD): *m*/*z* 364 (M^+).

5-[(1′S)-1′,2′-Diacetoxyethyl]-3-cyano-1-phenylpyrazole (**9**).—Hydroxylamine hydrochloride (210 mg, 3 mmol) was added to a solution of pyrazole **7** (898 mg, 2 mmol) in dry Me_2SO (10 mL), and the mixture was heated to 100 °C for 2 h. After cooling to ambient temp., the mixture was poured into ice cold, satd. $NaHCO_3$ solution (50 mL), then extracted with EtOAc (3×100 mL), washed with water (2×100 mL), and dried ($NaSO_4$). The residue remaining after removal of the solvent in vacuo was purified by column (2×20 cm) chromatography (1:1 *n*-hexane-EtOAc) to give **9** (410 mg, 67%) as a syrup; $[\alpha]_D^{20}$ +53.3 (*c* 1.5, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 2.01, 2.02 (2 s, 3H each, 2 Ac), 4.26, 4.33 (2 dd, 1H each, two H-2′), 5.99 (dd, 1H, H-1′), 6.90 (s, 1H, H-4), 7.45–7.59 (m, 5 H, C_6H_5), $J_{1',2'}$ 6.4 and 4.6, $J_{2',2'}$ 11.9 Hz; ^{13}C NMR ($CDCl_3$): δ 20.7 (2 CO*Me*), 63.6 (C-2′), 65.0 (C-1′), 111.4 (C-4), 113.6 (CN), 125.8, 125.9, 129.7, 130.2 (C_6H_5), 138.0, 141.1 (C-3, C-5), 169.6, 170.2 (2 *C*OMe). MS (FD): *m*/*z* 313 (M^+). Anal. Calcd for $C_{16}H_{15}N_3O_4$ (313.3): C, 61.33; H, 4.83; N, 13.41. Found: C, 61.30; H, 4.76; N, 13.47.

3-Cyano-5-[(1′S)-1′,2′-dihydroxyethyl]-1-phenylpyrazole (**10**).—Hydroxylamine hydrochloride (230 mg, 3.3 mol) was added to a solution of **8** (1.0 g, 2.7 mmol) in Me_2SO (10 mL), and the mixture was kept for 45 min at 120 °C. Processing of the mixture in a manner analogous to the conversion of **7**→**9** gave **10** (440 mg, 70%) as an amorphous powder; $[\alpha]_D^{20}$ +19.5° (*c* 1.1, MeOH); ^1H NMR ($CDCl_3$): δ 2.75, 3.40 (2 bs, each 1H, 2 OH), 3.73 (d, 2H, two H-2′), 4.73 (t, 1H, H-1′), 6.87 (s, 1H, H-4), 7.42–7.57 (m, 5H, C_6H_5), $J_{1',2'}$ 5.0 Hz; ^{13}C NMR ($CDCl_3$): δ 65.2 (C-2′), 65.7 (C-1′), 110.9 (C-4), 114.0 (CN), 125.4, 125.6, 129.7, 139.9 (C_6H_5),

138.2, 144.6 (C-3, C-5); MS (FD): *m/z* 229 (M^+). Anal. Calcd for $C_{12}H_{11}N_3O_2$ (229.23): C, 62.87; H, 4.84; N, 18.33. Found: C, 62.80; H, 4.78; N, 18.28.

3-Aminomethyl-5-[(1'S)-1',2'-dihydroxyethyl]-1-phenylpyrazole (**11**).—To a solution of pyrazole **7** (5.0 g, 11.1 mmol) in 50 mL of MeOH was added liquid hydrazine hydrate (50 mL, equivalent to 64 % N_2H_4), and the mixture was stirred for 2 h at ambient temperature. Raney-nickel (1 g) was then added, and stirring was continued until evolution of gas had ceased (ca. 5 h). Subsequently, the catalyst was filtered off, the solvent was removed uder reduced pressure from the filtrate, and the residue was purified by crystallization from CH_3CN to give **11** (2.4 g, 91%) as colorless prisms; mp 122 °C; $[\alpha]_D^{20}$ +14° (*c* 1.1, MeOH); ^1H NMR (Me_2SO-d_6): δ 3.53, 3.62 (2 dd, 1H each, two H-2'), 3.70 (s, 2H, 3-NCH_2), 4.51 (t, 1H, 1'-H), 6.43 (s, 1H, H-4), 7.38–7.60 (m, 5H, C_6H_5), $J_{1',2'}$ 6.4, $J_{2',2'}$ 10.8 Hz; ^{13}C NMR (Me_2SO-d_6): δ 39.7 (3-CH_2), 65.2 (C-2'), 65.4 (C-1'), 103.4 (C-4), 124.7, 127.3, 128.9, 139.6 (C_6H_5), 145.1, 154.7 (C-3, C-5); MS (FD): *m/z* 233 (M^+). Anal. Calcd for $C_{12}H_{15}N_3O_2$ (233.3): C, 61.79; H, 6.48; N, 18.01. Found: C, 61.72; H, 6.45; N, 18.11.

5-[(1'S)-1',2'-Diacetoxyethyl]-1-phenylpyrazole-3-carboxaldehyde (**12**).—To a solution of **7** (10 g, 22 mmol) in 100 mL of EtOH was added 35% aqueous solution of formaldehyde (120 mL) and HOAc (5 mL). After stirring the mixture for 5 h at 100 °C, it was made slightly basic by the addition of ice cold, satd. $NaHCO_3$ solution. Several extractions with ether (4×100 mL), washing with water (3×50 mL), drying (Na_2SO_4), and evaporation of the solvent left a residue, which was purified by column (4×30 cm) chromatography (5:1 toluene–EtOAc) to afford **12** (6.1 g, 86%) as a syrup; $[\alpha]_D^{20}$ + 52.6° (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.02, 2.03 (2 s, 3H each, 2 Ac), 4.27, 4.34 (2 dd, 1H each, two H-2'), 6.01 (dd, 1H, H-1'), 7.01 (s, 1H, H-4), 7.50–7.59 (m, 5H, C_6H_5), 10.01 (s, 1H, CHO), $J_{1',2'}$ 6.4 and 5.4, $J_{2',2'}$ 11.9 Hz; ^{13}C NMR ($CDCl_3$): δ 20.7 (2 CO*Me*), 63.9 (C-2'), 65.3 (C-1'), 105.6 (C-4), 125.9, 129.7, 130.0, 151.6 (C_6H_5), 138.6, 141.7 (C-3, C-5), 169.7, 170.3 (2 *C*OMe), 186.6 (*C*HO); MS (FD): *m/z* 316 (M^+). Anal. Calcd for $C_{16}H_{16}N_2N_5$ (316.3): C, 60.75; H, 5.10; N, 8.86. Found: C, 60.61; H, 5.04; N, 8.80.

5-[(1'S)-1',2'-Dihydroxyethyl]-1-phenylpyrazole-3-carboxaldehyde (**4**).—To a solution of pyrazole **12** (700 mg, 2.2 mmol) in 1:1 MeOH–water (60 mL), was added K_2CO_3 (1 g, 7.2 mmol) and the mixture was stirred for 3 h at ambient temperature. After removal of MeOH under reduced pressure, water (50 mL) was added, followed by extraction with EtOAc (3×50 mL). Drying of the organic phases ($MgSO_4$), and concentration left a residue, which was purified by column (3×25 cm) chromatography (1:1 toluene-EtOAc) to yield syrupy **4** (510 mg, quant.); $[\alpha]_D^{20}$ + 20.3° (*c* 1.2, MeOH); ^1H NMR (Me_2SO-d_6): δ 3.60 (m, 2H, two H-2'), 4.54 (t, 1H, H-1'), 4.92 (t, 1H, 2'-OH), 5.65 (d, 1H, 1'-OH), 6.97 (s, 1H, H-4), 7.53–7.70 (m, 5H, C_6H_5), 9.96 (s, 1H, CHO), $J_{1',2'}$ 6.3; ^{13}C NMR (Me_2SO-d_6): δ 65.1 (C-2'), 65.6 (C-1'), 104.9 (C-4), 125.7, 129.4, 129.7, 151.1 (C_6H_5), 139.2, 148.2 (C-3, C-5), 187.3 (CHO); MS (FD): *m/z* 232 (M^+). Anal. Calcd for $C_{12}H_{12}N_2O_3$ (232.2): C, 62.06; H, 5.21; N, 12.06. Found: C, 62.09; H, 5.18; N, 12.00.

5-[(1'S)-1',2'-Diacetoxyethyl]-1-phenylpyrazole-3-carboxaldehyde oxime (**13**).—Aldehyde **12** (316 mg, 1 mmol) in MeOH (40 mL) was added to a solution of 2.2 g (31 mmol) of $NH_2OH{\cdot}HCl$ and 2.1 g (25 mmol) of NaOAc in 10 mL of water, and the mixture was stirred for 1 h at ambient temp. The solvent was removed in vacuo, and the residue was purified by elution from a silica gel column (2×22 cm) with 4:1 *n*-hexane-EtOAc to afford **13** (280 mg, 84%) as an amorphous powder; ^1H NMR ($CDCl_3$): δ 2.02 (2 s, 3H each, 2 Ac), 4.30, 4.36 (2 dd, 1H each, two H-2'), 6.06 (dd, 1H, H-1'), 6.88 (s, 1H, H-4), 7.45–7.54 (m, 5 H, C_6H_5), 8.29 (s, 1H, 3-CH), 9.40 (bs, 1H, OH), $J_{1',2'}$ 7.1 and 4.4, $J_{2',2'}$ 11.8 Hz; ^{13}C NMR ($CDCl_3$): δ 22.3 (2 CO*Me*), 65.7 (C-2'), 66.9 (C-1'), 105.6 (C-4), 127.5, 130.9, 131.2, 148.2 (C_6H_5), 140.3, 142.0 (C-3, C-5), 145.6 (3-CH), 171.5, 172.2 (2 *C*OMe); MS (FD): *m/z* 331 (M^+). Anal. Calcd for $C_{16}H_{17}N_3O_5$ (331.3): C, 58.00; H, 5.17; N, 12.68. Found: C, 57.86; H, 5.10; N, 12.70.

5-[(1'S)-1',2'-Diacetoxyethyl]-3-hydroxymethyl-1-phenylpyrazole (**14**).—To a cooled (0 °C) solution of aldehyde **12** (158 mg, 0.5 mmol) in MeOH (10 mL) was added $NaBH_4$ (90 mg, 2.4 mmol) and the mixture was stirred 0 °C for 45 min, followed by decomposition of excessive $NaBH_4$ with few drops of HOAc. Removal of the solvent under reduced pressure left a syrup which was purified by column (2×22 cm) chromatography (1:1 toluene-EtOAc) to give **14** (145 mg, 91%) as a colorless syrup; ^1H NMR ($CDCl_3$): δ 1.99 (2 s, 3H each, 2 Ac), 3.25 (bs, 1H, OH), 4.25, 4.33 (2 dd, 1H each, two H-2'), 4.66 (s, 2H, 3-CH_2), 6.03 (dd, 1H, H-1'), 6.49 (s, 1H, H-4), 7.43–7.51 (m, 5 H, C_6H_5), $J_{1',2'}$ 7.2 and 4.5, $J_{2',2'}$ 11.8 Hz; ^{13}C NMR ($CDCl_3$): δ 20.6 (CO*Me*), 58.5 (3-CH_2), 64.1 (C-2'), 65.3 (C-1'),

104.8 (C-4), 125.8, 128.4, 128.9, 153.0 (C_6H_5), 138.9, 139.8 (C-3, C-5), 169.7, 170.4 (*C*OMe); MS (FD): *m/z* 318 (M^+). Anal. Calcd for $C_{16}H_{18}O_5N_2$ (318.3): C, 60.37; H, 5.70; N, 8.80. Found: C, 60.34; H, 5.75; N, 8.70.

4-Chloro-[(1'S)-1',2'-diacetoxyethyl]-1-phenylpyrazole-3-carboxaldehyde (**15**).—To a cooled (0 °C) solution of aldehyde **12** (316 mg, 1 mmol) in MeOH (4 mL) was added HOAc (0.2 mL) and, subsequently, a 14% aq NaOCl solution (1 mL, dropwise), and the mixture was stirred for 1 h at 0 °C. After addition of 20 mL of ice water, the mixture was extracted with $CHCl_3$ (3×50 mL). The combined organic phases were washed with sat. $NaHCO_3$ solution, and water (50 mL each), followed by drying (Na_2SO_4), and removal of the solvent under reduced pressure. Purification of the residue by elution from a silica gel column (2×25 cm) with 4:1 toluene–EtOAc and evaporation of the solvents yielded syrupy **15** (310 mg, 88%). ^1H NMR ($CDCl_3$): δ 1.97, 2.03 (2 s, 3H each, 2 Ac), 4.39, 4.46 (2 dd, 1H each, two H-2'), 5.87 (dd, 1H, H-1'), 7.42–7.54 (m, 5 H, C_6H_5), 10.00 (s, 1H, CHO), $J_{1',2'}$ 7.5 and 4.4, $J_{2',2'}$ 11.7 Hz; ^{13}C NMR ($CDCl_3$): δ 20.4, 20.7 (2 CO*M*e), 62.4 (C-2'), 67.0 (C-1'), 105.6 (C-4), 126.3, 129.7, 130.4, 145.9 (C_6H_5), 137.4, 138.5 (C-3, C-5), 169.8, 170.2 (2 *C*OMe), 184.8 (CHO); MS (FD): *m/z* 350, 352 ($M[^{35}Cl]^+$, $M[^{37}Cl]^+$). Anal. Calcd for $C_{16}H_{15}N_2O_5Cl$ (350.7): C, 54.79; H, 4.31; N, 7.99. Found: C, 54.69; H, 4.33; N, 7.86.

5-[(1'S)-1',2'-Diacetoxyethyl]-3-[2,2-dicyanovinyl)-1-phenylpyrazole (**16**).—To a solution of aldehyde **12** (316 mg, 1 mmol), and malono-nitrile (90 mg, 1.4 mmol) in dry MeOH (50 mL) was added freshly dried Al_2O_3 (400 mg) and the mixture was stirred for 18 h at room temp. The solution was filtered through celite, the filter washed thoroughly with MeOH, and the entire filtrate taken to dryness under reduced pressure. Purification of the resulting syrup by column chromatography (4:1 toluene–EtOAc) gave **16** (300 mg, 82%) as an amorphous product; ^1H NMR ($CDCl_3$): δ 2.03, 2.05 (2 s, 3H each, 2 Ac), 4.30, 4.35 (2 dd, 1H each, two H-2'), 5.99 (dd, 1H, H-1'), 7.41 (s, 1H, H-4), 7.48–7.59 (m, 5H, C_6H_5), 7.91 (s, 1H, H-1''), $J_{1',2'}$ 6.1 and 4.1, $J_{2',2'}$ 11.9 Hz; ^{13}C NMR ($CDCl_3$): δ 20.7 (2 CO*M*e), 63.9 (C-2'), 65.2 (C-1'), 83.0 (C-2''), 108.4 (C-4), 112.5, 113.4 (2 CN), 125.7, 129.8, 130.2, 145.0 (C_6H_5), 138.1, 142.5 (C-3, C-5), 152.2 (C-1''), 169.7, 170.3 (2 *C*OMe); MS (FD): *m/z* 364 (M^+). Anal. Calcd for $C_{19}H_{16}O_4N_4$ (364.3): C, 62.63; H, 4.43; N, 15.38. Found: C, 62.43; H, 4.38; N, 15.40.

5-[(1'S)-1',2'-Diacetoxyethyl]-3-[(E)-2''-nitro-1''-vinyl)]-1-phenylpyrazole (**17**).—To a solution of aldehyde **12** (500 mg, 1.6 mmol) in CH_3NO_2 (5 mL) over freshly desiccated molecular sieve (3 Å) was added *n*-butylamine and AcOH (one drop each) and the mixture was stirred for 18 h at ambient temperature. Evaporation and silica gel column (2×22 cm) chromatography (9:1 toluene-EtOAc) afforded **17** (400 mg, 70%) as a yellowish syrup; ^1H NMR ($CDCl_3$): δ 2.02, 2.04 (s, 3H each, 2 Ac), 4.27, 4.34 (2 dd, 1H each, two H-2'), 6.02 (dd, 1H, H-1'), 6.76 (s, 1H, H-4), 7.48–7.59 (m, 5 H, C_6H_5), 7.68 (d, 1H, H-1''), 7.98 (d, 1H, H-2''), $J_{1',2'}$ 6.8 and 4.6, $J_{2',2'}$ 11.8, $J_{1'',2''}$ 13.7 Hz; ^{13}C NMR ($CDCl_3$): δ 20.7 (CO*M*e), 63.9 (C-2'), 65.2 (C-1'), 107.2 (C-4), 125.8, 129.7, 129.8, 143.9 (C_6H_5), 130.5 (C-1''), 138.4, 141.6 (C-3, C-5), 138.5 (C-2''), 169.7, 170.3 (2 *C*OMe); MS (FD): *m/z* 359 (M^+). Anal. Calcd for $C_6H_{17}N_3O_6$ (359.3): C, 56,82; H, 4.77; N, 11.70. Found: C, 56.87; H, 4.70; N, 11.67.

5-[(1S)-1',2'-Diacetoxyethyl]-3-vinyl-1-phenylpyrazole (**18**).—A suspension of methyltriphenylphosphonium bromide (450 mg, 1.3 mmol) and 0.8 mL (1.3 mmol) of a commercial 1.6 M *n*-hexane solution of BuLi in 5 mL of dry THF was cooled at −40 °C and a solution of aldehyde **12** (200 mg, 0.7 mmol) in THF (1 mL) was added. The mixture was stirred under N_2 for 1 h, then poured into an ice-cooled 2 N $NaHSO_4$ solution (30 mL), and extracted with Et_2O (2×50 mL). The combined organic phases were washed with satd. $NaHCO_3$, and water (30 mL each), dried, and evaporated to dryness. The residue was purified by elution from silica gel (2×20 cm column) with 4:1 toluene–EtOAc to yield **18** (133 mg, 67%) as a colorless, amorphous solid; ^1H NMR ($CDCl_3$): δ 2.01 (2 s, 3H each, 2 Ac), 4.27, 4.33 (2 dd, 1H each, two H-2'), 5.36 (dd, 1H, H-2''$_{trans}$), 5.78 (dd, 1H, H-2''$_{cis}$), 6.05 (dd, 1H, H-1'), 6.62 (s, 1H, H-4), 6.75 (dd, 1H, H-1'), 7.42–7.50 (m, 5 H, C_6H_5); $J_{1',2'}$ 7.2 and 4.6, $J_{1',2'}$ 11.8, $J_{1'',2''trans}$ 11.0 and 7.8, $J_{2'',2''}$ 1.2 Hz; ^{13}C NMR ($CDCl_3$): δ 20.6, 20.7 (2 CO*M*e), 64.1 (C-2'), 65.3 (C-1'), 103.0 (C-4), 116.2 (C-2''), 125.8, 128.7, 129.3, 151.3 (C_6H_5), 128.8 (C-1''), 139.0 (C-5), 139.8 (C-3), 169.6, 170.3 (2 *C*OMe); MS (FD): *m/z* 314 (M^+).

5-[(1'S)-1',2'-Diacetoxyethyl]-3-[(E)-2-ethoxycarbonyl-1-vinyl]-1-phenylpyrazole (**19**).—To a solution of aldehyde **12** (1.0 g, 3.1 mmol) in THF (30 mL) was added commercial ethoxycarbonylmethylene triphenylphosphorane (1.3 g, 3.4 mmol)

and the mixture was stirred for 6 h at room temp. Concentration under reduced pressure, elution of the residue from a silica gel column (3×27 cm) with 4:1 toluene–EtOAc and drying under vacuum (finally at 0.1 Torr) gave **19** (1.20 g, 98%) as a syrup; ^{1}H NMR ($CDCl_3$): δ 1.27 (t, 3H, CH_2CH_3), 1.96, 1.97 (2 s, 3H each, 2 Ac), 4.20 (q, 2H, CH_2CH_3), 4.22, 4.29 (2 dd, 1H each, two H-2′), 6.00 (dd, 1H, H-1′), 6.44 (d, 1H, H-2″), 6.68 (s, 1H, H-4), 7.42–7.50 (m, 5 H, C_6H_5), 7.64 (d, 1H, H-1″), $J_{1',2'}$ 7.0 and 4.5, $J_{2',2'}$ 11.8, $J_{1'',2''}$ 16.1 Hz; MS (FD): *m/z* 386 (M^+). Anal. Calcd for $C_{20}H_{22}N_2O_6$ (386.4): C, 62.16; H, 5.74; N, 7.25. Found: C, 62.08; H, 5.80; N, 7.21.

6-O-(α-D-Glucopyranosyl)-D-arabino-hexose phenylosazone (**20**).—A solution of 30 mL (0.35 mmol) of phenylhydrazine in 100 mL of water was made slightly acidic by adding 16 mL of AcOH. A solution of 30.0 g (84 mmol) of isomaltulose monohydrate in 100 mL of water was then added, and the mixture was stirred for 2 h at 100 °C. After addition of water (300 mL) to the hot solution, it was allowed to come to room temperature and subsequently placed in a refrigerator overnight. The voluminous precipitate was filtered off, and washed with water and *n*-hexane to give 40.2 g (92%) of crude osazone **20** as yellow needles of mp 180–181 °C, which was used for the subsequent conversion into pyrazole **21**. Recrystallization from water or MeOH raised the mp to 192–194 °C; $[\alpha]_D^{20}$ +30→47° (24 h, *c* 1, 2-methoxyethanol); Lit [23].: mp 177–179 °C and $[\alpha]_D^{20}$ +3346° (24 h, *c* 2, 2-methoxyethanol) for a sample prepared from isomaltose; ^{1}H NMR (Me_2SO-d_6): δ 3.10–3.22 (m, 2H, two H-6′), 3.43–3.63 (m, 6 H, H-4, H-5, H-2′, H-3′, H-4′, H-5′), 3.70–3.80 (m, 2H, two H-6), 4.42 (t, 1H, OH-6′), 4.58 (s, 1H, H-1′), 4.69 (d, 1H, H-3), 4.59, 4.60, 4.70, 4.81, 4.88, 5.20 (6 d, 1H each, 6 OH), 6.84–7.34 (m, 10H, 2 C_6H_5), 7.91 (s, 1H, H-1), 10.71, 12.27 (s, 1H each, 2 NH); $J_{3,4}$ 3.5, $J_{6',6'\text{-OH}}$ 5.6 Hz; ^{13}C NMR (Me_2SO-d_6): δ 60.7 (C-6′), 69.3 (C-6), 69.1, 70.0, 71.9, 72.2, 72.4, 73.5, 74.3 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 98.7 (C-1′), 111.8–129.5, 144.0, 144.4 (2 C_6H_5), 134.9 (C-1), 138.0 (C-2); MS (FD): *m/z* 520 (M^+). Anal. Calcd. for $C_{24}H_{32}N_4O_9$ (520.5): C, 55.38; H, 6.20; N, 10.76. Found: C, 55.31; H, 6.25; N, 10.75.

5-[(1′S)-1-Acetoxy-2-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyloxy)ethyl]-1-phenylpyrazole-3-carboxaldehyde N-*acetylphenylhydrazone* (**21**).—A suspension of osazone **20** (22.2 g, 43 mmol) in Ac_2O (250 mL) was heated for 3 h to 140 °C. After cooling to ambient temperature, the mixture was poured into ice-cold satd. $NaHCO_3$ (300 mL) with vigorous stirring, and was then made slightly basic by the addition of solid $NaHCO_3$. Extraction with CH_2Cl_2 (4×200 mL), washing with satd. $NaHCO_3$ (2×100 mL), and drying ($MgSO_4$) yielded a solid residue which was recrystallized from EtOH to afford **21** (25.2 g, 79%) in two crops as colorless needles; mp 190 °C; $[\alpha]_D^{20}$ 118° (*c* 0.9, $CHCl_3$); Lit. [24]: 60%, mp 190 °C, $[\alpha]_D^{20}$ +118° (*c* 0.55, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.86, 2.01, 2.03, 2.04, 2.09 (5 s, 3H each, 5 OAc) 2.63 (s, 3H, NAc), 3.72, 4.01 (2 dd, 1H each, two H-2′), 3.95 (ddd, 1H, H-5″) 4.08, 4.23 (2 dd, 1H each, two H-6″), 4.82 (dd, 1H, H-2″), 5.05 (d, 1H, H-1″), 5.06 (t, 1H, H-4″), 5.48 (t, 1H, H-3″), 5.99 (t, 1H, H-1′), 6.93 (s, 1H, 3-CH), 7.36 (s, 1H, H-4), 7.12–7.56 (m, 10 H, 2 C_6H_5), $J_{1',2'}$ 6.2, $J_{2',2'}$ 10.6, $J_{1'',2''}$ 3.7, $J_{2'',3''}$ 10.3, $J_{3'',4''}$ 9.8, $J_{4'',5''}$ 10.0, $J_{5'',6''}$ 4.3 and 2.2, $J_{6'',6''}$ 12.4 Hz; ^{13}C NMR ($CDCl_3$): δ 20.5–20.8 (5 OCO*Me*), 22.2 (NCO*Me*), 61.7 (C-6″), 65.5 (C-1′), 67.9 (C-5″), 68.3 (C-4″), 69.8 (C-3″), 68.9 (C-2′), 70.6 (C-2″), 96.3 (C-1″), 103.1 (C-4), 126.1–130.5, 144.7, 149.1 (2 C_6H_5), 135.8, 138.8 (C-3, C-5), 135.9 (3-*C*H), 169.5–170.7 (6 *C*OMe); MS (FD): *m/z* 736 (M^+). Anal. Calcd. for $C_{36}H_{40}N_4O_{13}$ (736.7): C, 58.69; H, 5.47; N, 7.60. Found: C, 58.60; H, 5.34; N, 7.53.

5-[(1S)-2-(α-D-Glucopyranosyloxy)-1-hydroxyethyl]-1-phenylpyrazole-3-carboxaldehyde N-*acetylphenylhydrazone* (**22**).—To a solution of 10 g (1.3 mmol) of pyrazole **21** in dry MeOH (250 mL) was added NaOMe (0.5 g, 9.2 mmol), and the mixture was kept for 4 h at room temp. Subsequently, the solution was neutralized with a strongly acidic ion exchange resin (Amberlite IR-120, H^+ form), filtered and the filtrate was taken to dryness under reduced pressure. The residue was crystallized on trituration with aqueous *i*PrOH (90%) and was recrystallized from MeOH to give **22** (6.7 g, 96%) as colorless needles; mp 207 °C; $[\alpha]_D^{20}$ +71° (*c* 0.9, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 2.51 (s, 3H, NAc), 3.10 (dt, 1H, H-4″), 3.17 (ddd, 1H, H-2″), 3.32 (ddd, 1H, H-5″), 3.40 (m, 1H, H-3″), 3.43, 3.51 (m, dd, 1H each, two H-6″), 3.64, 3.89 (2 dd, 1H each, two H-2′), 4.45 (t, 1H, OH-6″), 4.63 (d, 1H, OH-2″), 4.67 (d, 1H, H-1″), 4.68 (m, 1H, H-1′), 4.81 (d, 1H, OH-3″), 4.93 (d, 1H, OH-4″), 5.71 (d, 1H, OH-1′), 6.97 (s, 1H, N=C*H*), 7.16 (s, 1H, H-4), 7.24–7.63 (m, 10H, 2 C_6H_5), $J_{1',2'}$ 5.7, $J_{2',2'}$ 10.3, $J_{1'',2''}$ 3.5, $J_{2'',3''}$ 9.5, $J_{3'',4''}$ 9.2, $J_{4'',5''}$ 9.8, $J_{5'',6''}$ 4.6 and < 1.0, $J_{6'',6''}$ 10.5, $J_{1',1'\text{-OH}}$ 6.6, $J_{2'',2''\text{-OH}}$ 7.2,

$J_{3'',3''\text{-OH}}$ 4.7, $J_{4'',4''\text{-OH}}$ 4.9, $J_{6'',6''\text{-OH}}$ 5.7 Hz; ^{13}C NMR (Me_2SO-d_6): δ 22.2 (NCO*Me*), 60.6 (C-6″), 63.0 (C-1′), 69.8 (C-4″), 70.7 (C-2′), 71.9 (C-2″), 72.9 (C-3″), 73.3 (C-5″), 99.1 (C-1″), 102.7 (C-4), 124.0-130.1, 145.9, 147.6 (2 C_6H_5), 135.0 (3-CH), 135.7, 138.8 (C-3, C-5), 171.3 (*C*OMe); MS (FD): *m/z* 526 (M^+). Anal. Calcd for $C_{26}H_{30}N_4O_8$ (526.6): C, 59.31; H, 5.74; N, 10.64. Found: C, 59.28; H, 5.69; N, 10.58.

5-[(1S)-2-(α-D-Glucopyranosyloxy)-1-hydroxyethyl])-1-phenylpyrazole-3-carboxaldehyde (**5**).—To a suspension of pyrazole **22** (3.40 g, 6.5 mmol) in 80 mL of MeOH and 80 mL of a 35% aqueous formaldehyde solution was added 2.5 mL of HOAc, and the mixture was refluxed for 4 h. Subsequently, the solution was taken to dryness under reduced pressure and the residue was purified by column (4×35 cm) chromatography (5:1 $CHCl_3$–MeOH) to afford **5** (2.35 g, 92%) as a solid foam; $[\alpha]_D^{20}$ +100° (*c* 1, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 3.06 (t, 1H, H-4″), 3.15 (m, 1H, H-2″), 3.26 (m, 1H, H-5″), 3.31–3.57 (m, 3H, H-3″, two H-6″), 3.63, 3.85 (2 dd, 1H each, two H-2′), 4.42 (bs, 1H, OH-6″), 4.63 (bs, 1H, OH-2″), 4.65 (d, 1H, H-1″), 4.71 (m, 1H, H-1′), 4.81 (bs, 1H, OH-3″), 4.88 (bs, 1H, OH-4″), 5.73 (d, 1H, OH-1′), 7.03 (s, 1H, H-4), 7.55–7.72 (m, 5 H, C_6H_5), 9.95 (s, 1H, CHO), $J_{1',2'}$ 6.1 and 5.6, $J_{2',2'}$ 10.4, $J_{1'',2''}$ 3.6, $J_{3'',4''}$ 9.2, $J_{4'',5''}$ 9.2, $J_{1',1'\text{-OH}}$ 5.1 Hz; ^{13}C NMR (Me_2SO-d_6): δ 61.1 (C-6″), 63.4 (C-1′), 70.3 (C-4″), 70.8 (C-2′), 72.2 (C-2″), 73.3 (C-5″), 73.6 (C-3″), 99.6 (C-1″), 105.2 (C-4), 125.9, 129.5, 129.7, 151.0 (C_6H_5), 139.2, 147.5 (C-3, C-5), 187.3 (CHO); MS (FD): *m/z* 394 (M^+). Anal. Calcd for $C_{18}H_{22}N_2O_8$ (394.37): C, 54.82; H, 5.62; N, 7.10. Found: C, 54.76; H, 5.58; N, 7.01.

5-[(1′S)-Acetoxy-2-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyloxy)ethyl]-1-phenylpyrazole-3-carboxaldehyde (**23**).—To a solution of 1 g (1.4 mmol) of pyrazole **21** in EtOH (6 mL) was added 6 mL of a 35% aq formaldehyde solution and 0.3 mL of HOAc, and the mixture was stirred for 6 h at 100 °C. After concentration under reduced pressure to a few mL, 20 mL of an ice-cold satd. $NaHCO_3$ solution was added, followed by extraction with CH_2Cl_2 (4×30 mL), washing with water (3×30 mL), drying (Na_2SO_4). Purification by column (2×20 cm) chromatography (2:3 *n*-hexane–EtOAc) gave **23** (600 mg, 73%) of **23** as an amorphous powder; ^{1}H NMR ($CDCl_3$): δ 1.88, 2.01–2.08 (5 s, 3H each, 5 Ac), 3.69, 3.99 (2 dd, 1H each, two H-2′), 3.90 (ddd, 1H, H-5″), 4.06, 4.22 (2 dd, 1H each, two H-6″), 4.81 (dd, 1H, H-2″), 5.02 (d, 1H, H-1″), 5.03 (t, 1H, H-4″), 5.44 (t, 1H, H-3″), 5.89 (t, 1H, H-1′), 7.00 (s, 1H, H-4), 7.13–7.65 (m, 5H, C_6H_5), 10.01 (s, 1H, CHO) $J_{1',2'}$ 7.0, $J_{2',2'}$ 10.4, $J_{1'',2''}$ 3.7, $J_{2'',3''}$ 10.3, $J_{3'',4''}$ 9.8, $J_{4'',5''}$ 10.0, $J_{5'',6''}$ 4.3 and 2.2, $J_{6'',6''}$ 12.4 Hz; ^{13}C NMR ($CDCl_3$): δ 20.5–20.7 (5 CO*Me*), 61.7 (C-6″), 65.3 (C-1′), 67.9 (C-5″), 68.3 (C-4″), 68.6 (C-2′), 69.8 (C-3″), 70.5 (C-2″), 96.3 (C-1″), 105.1 (C-4), 126.1–130.5, 151.6 (C_6H_5), 138.6, 142.7 (C-3, C-5), 169.5–170.7 (5 *C*OMe), 186.4 (CHO); MS (FD): *m/z* 603 (M^+). Anal. Calcd for $C_{28}H_{32}N_2O_{13}$ (604.56): C, 55.63; H, 5.34; N, 4.63. Found: C, 55.57; H, 5.24; N, 4.60.

5-[(1′S)-2-(α-D-Glucopyranosyloxy)-1-hydroxyethyl]-3-hydroxymethyl-1-phenylpyrazole (**24**).—To a stirred solution of **23** (3.65 g, 6.0 mmol) in MeOH (150 mL) was added $NaBH_4$ (1.3 g, 34 mmol), and stirring was continued for 16 h at ambient temperature. Decomposition of excessive $NaBH_4$ by a few drops of HOAc and removal of the solvent under reduced pressure left a residue which was purified by column (5×39 cm) chromatography (2:1 $CHCl_3$–MeOH) to give **24** (2.06 g, 87%) as a solid foam. $[\alpha]_D^{20}$ +100° (*c* 1, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 3.07 (t, 1H, H-4″), 3.15 (dd, 1H, H-2″), 3.32 (m, 1H, H-5″), 3.40, 3.51 (2 dd, 1H each, two H-6″), 3.43 (m, 1H, H-3″), 3.58, 3.83 (2 dd, 1H each, two H-2′), 4.46 (s, 2H, 3-CH_2), 4.65 (d, 1H, H-1″), 4.68 (m, 1H, H-1′), 4.9 (bs, 6 H, 6 OH), 6.49 (s, 1H, H-4), 7.40–7.62 (m, 5H, C_6H_5), $J_{1',2'}$ 6.4 and 5.2, $J_{2',2'}$ 10.3, $J_{1'',2''}$ 3.6, $J_{2'',3''}$ 9.6, $J_{3'',4''}$ 9.2, $J_{4'',5''}$ 9.2, $J_{5'',6''}$ 5.0 and 1.9, $J_{6'',6''}$ 11.7 Hz; ^{13}C NMR (Me_2SO-d_6): δ 57.2 (3-CH_2), 60.6 (C-6″), 63.0 (C-1′), 69.9 (C-4″), 70.7 (C-2′), 71.9 (C-2″), 72.8 (C-5″), 73.1 (C-3″), 98.9 (C-1″), 104.3 (C-4), 124.8, 127.5, 129.0, 153.2 (C_6H_5), 139.4, 144.4 (C-3, C-5); MS (FD): *m/z* 419 ($M+Na^+$), 396 (M^+). Anal. Calcd for $C_{18}H_{24}N_2O_8$ (396.39): C, 54.54; H, 6.10; N, 7.07. Found: C, 54.55; H, 6.00; N, 7.02.

3-Aminomethyl-5-[(1′S)-2-(α-D-glucopyranosyloxy)-1-hydroxyethyl]-1-phenylpyrazole (**25**).—Acetylated phenylhydrazone **21** (1 g, 1.4 mmol) was added to hydrazine hydrate (80% 50 mL), and the mixture was heated for 1 h at 100 °C. After cooling to ambient temperature, 500 mg of Raney-nickel was added and the mixture was kept at room temperature for about 30 h. Filtration of the catalyst, washing with water and MeOH, and evaporation of the filtrate to dryness gave a residue, which was purified by column (3.5×17 cm) chromatography (6:1 *i*PrOH-2.5% aq NH_3) to yield **25** (0.52 g, 93%) as a solid foam; $[\alpha]_D^{20}$ +103° (*c* 1.0, MeOH); ^{1}H NMR (Me_2SO-d_6): δ 3.11 (t, 1H, H-4″), 3.19 (dd,

1H, H-2″), 3.28 (ddd, 1H, H-5″), 3.41–3.52 (m, 3H, H-3″, two H-6″), 3.57, 3.81 (2 dd, 1H each, two H-2′), 3.82 (s, 2H, NCH_2), 4.60 (bs, 2H, 2 OH), 4.66 (d, 1H, H-1″), 4.72 (m, 1H, H-1′), 4.94, 5.10, 5.87 (3 bs, 1H each, 3 OH), 6.73 (s, 1H, H-4), 7.46–7.65 (m, 5H, C_6H_5), 7.70 (s, 2H, NH_2); $J_{1',2'}$ 6.3 and 5.5, $J_{2',2'}$ 10.6, $J_{1'',2''}$ 3.5, $J_{2'',3''}$ 9.6, $J_{3'',4''}$ 9.3, $J_{4'',5''}$ 9.8, $J_{5'',6''}$ 4.5 and 2.0 Hz; ^{13}C NMR (Me_2SO-d_6): δ 36.3 (3-CH_2), 60.6 (C-6″), 63.0 (C-1′), 69.9 (C-4″), 70.5 (C-2′), 71.8 (C-2″), 72.8 (C-3″), 73.2 (C-5″), 98.9 (C-1″), 104.7 (C-4), 125.1, 128.3, 129.2, 138.9 (C_6H_5), 145.4, 145.6 (C-3, C-5); MS (FD): *m/z* 395 (M^+).

3-Acetamidomethyl-5-[1′S-acetoxy-2-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyloxy)ethyl]-1-phenylpyrazole (**26**).—To a stirred and cooled (0 °C) solution of **25** (513 mg, 1.3 mmol) in 20 mL of dry pyridine were added dropwise 5 ml of Ac_2O. After 30 min the ice bath was removed and the solution was stirred for an additional 15 h at ambient temp. The resulting mixture was hydrolyzed by the addition of ice-water (5 mL), then concentrated under reduced pressure to a syrup, which was extracted with CH_2Cl_2 (100 mL). The extract was washed successively with 2 N HCl (3×50 mL), NaCl solution (30 mL), satd. $NaHCO_3$ solution (3×30 mL), and again with NaCl solution (30 mL). Column (4×25 cm) chromatography (EtOAc) furnished **26** (698 mg, 83%) as a solid foam; $[\alpha]_D^{20}$ +109° (*c* 1, $CHCl_3$); 1H NMR ($CDCl_3$): δ 1.88–2.08 (6 s, 3H each, 6 Ac), 3.68, 3.96 (2 dd, 1H each, two H-2′), 3.90 (ddd, 1H, H-5″), 4.06, 4.22 (2 dd, 1H each, two H-6″), 4.43, 4.55 (2 dd, 1H each, NCH_2), 4.74 (dd, 1H, H-2″), 5.02 (d, 1H, H-1″), 5.03 (t, 1H, H-4″), 5.46 (t, 1H, H-3″), 5.90 (t, 1H, H-1′), 6.33 (m, 1H, NH), 6.44 (s, 1H, H-4), 7.47–7.57 (m, 5H, C_6H_5); $J_{gem(3\text{-}CH_2)}$ 5.3, $J_{3\text{-}CH_2,NH}$ 5.0 and 5.6, $J_{1',2'}$ 6.6 and 5.9, $J_{2',2'}$ 10.8, $J_{1'',2''}$ 3.6, $J_{2'',3''}$ 10.3, $J_{3'',4''}$ 9.9, $J_{4'',5''}$ 10.2, $J_{5'',6''}$ 4.4 and 2.0, $J_{6'',6''}$ 12.4 Hz; ^{13}C NMR ($CDCl_3$): δ 20.5–23.1 (6 CO*Me*), 37.6 (NCH_2), 61.7 (C-6″), 65.4 (C-1′), 67.9 (C-5″), 68.2 (C-4″), 68.6 (C-2′), 69.7 (C-3″), 70.9 (C-2″), 96.2 (C-1″), 104.8 (C-4), 126.1-129.5, 150.0 (C_6H_5), 139.0, 141.0, (C-3, C-5), 169.5-170.5 (6 O*C*OMe); MS (FD): *m/z* 647 (M^+). Anal. Calcd for $C_{30}H_{37}N_3O_{13}$ (647.6): C, 55.64; H, 5.76; N, 6.49. Found: C, 55.58; H, 5.73; N, 6.54.

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