Carbohydrate Research, 171 (1987) 329–341
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

SYNTHESIS OF *C*-PENTO, -HEXO-, AND -HEPTULO-PYRANOSYL COMPOUNDS *VIA* RADICAL C–C BOND-FORMATION REACTIONS

BERND GIESE*, JACQUES DUPUIS, MICHAEL LEISING, MARIANNE NIX, AND HANS JÖRG LINDNER
Institut für Organische Chemie und Biochemie, TH Darmstadt, Petersenstraße 22, D-6100 Darmstadt, Federal Republik of Germany.

(Received January 20th, 1986; accepted for publication in revised form, July 11th, 1986)

ABSTRACT

C-Glycosyl compounds were synthesized by addition of pyranosyl radicals to acrylonitrile, fumarodinitrile, or methacrylonitrile in the presence of tributyltin hydride in 34–75% yields. The pyranosyl radicals were generated by abstraction of a bromine atom or a nitro group by tributyltin radicals. The stereoselectivity of the C–C bond to the pyranosyl radicals was, in most cases, remarkably high, but hexopyranosyl and pentopyranosyl radicals showed different selectivity. Whereas the tetra-*O*-acetylglucosyl radical reacted with acrylonitrile preponderantly to give a *C*-glycosyl compound having the newly formed C–C bond in an axial position, the tri-*O*-acetylxylosyl radical gave a *C*-glycosyl compound having an equatorial C–C bond. In the tetra-*O*-acetylmannosyl radical, the axial acetoxy substituent, adjacent to the radical center, led exclusively to a compound having a *trans* C–C bond, whereas the tri-*O*-acetyllyxosyl radical showed *trans*- and *cis*-addition to acrylonitrile in a 7:3 ratio.

INTRODUCTION

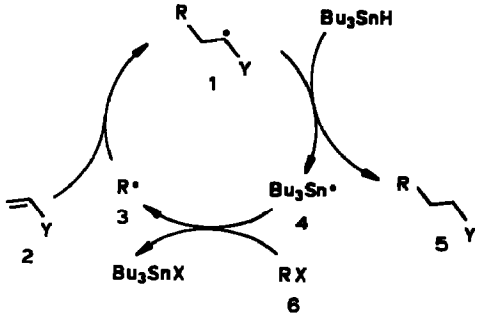
The formation of C–C bonds *via* addition of an alkyl radical **3** to an alkene (**2**) has proved to be a very versatile method for the synthesis of target molecules under mild conditions[1]. For a successful application of this reaction, the adduct radical **1** is converted into compounds before these can then further react with alkenes to give polymers. Several methods have been developed to intercept this unwanted polymerization side-reaction, for example, by trapping with atom donors[1] or by radical-fragmentation reactions[2]. A useful trap is tributyltin hydride that reacts with the adduct radical **1** to give **5** and the tin radical **4**. With a suitably substituted educt **6**, *e.g.*, halides, selenides, or xanthates, the tributyltin radical regenerates the alkyl radical **3**.

We have previously used this tin method for the selective generation and the C–C bond-formation reactions of carbohydrate radicals[3]. We describe herein the

*To whom correspondence should be addressed.

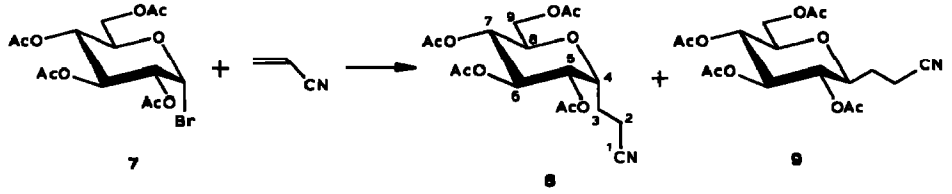
0008-6215/87/$ 03.50

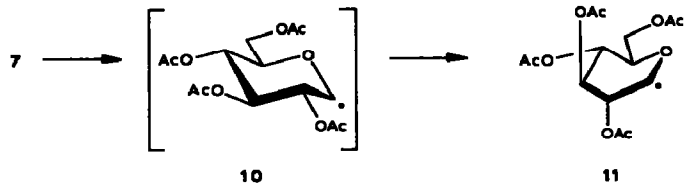
synthesis of *C*-hexopyranosyl, -heptulopyranosyl, and -pentopyranosyl derivatives.



RESULTS AND DISCUSSION

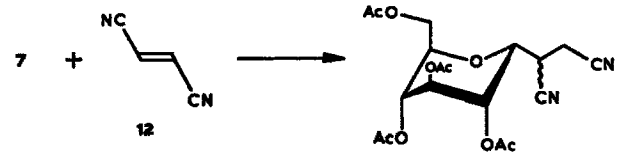
The reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**7**) with tributyltin hydride and acrylonitrile gave the *C*-α-D- (**8**) and -β-D-glucopyranoside **9** in 75% yield and a 93:7 ratio. With photolytical initiation of the radical-chain reaction in ether, most of the product **8** precipitated directly from the solution. The axial orientation of the cyanoethyl group was deduced from the ^{1}H-n.m.r. coupling $J_{4,5}$ 5.2 Hz, whereas the equatorial acetoxy and acetoxymethyl groups led to diaxial-coupling constants $J_{5,6} = J_{6,7} = J_{7,8}$ 8.3 Hz. The minor anomer **9**, which was isolated by column chromatography, only exhibited the diaxial-coupling constants $J_{4,5} = J_{5,6}$ 9.6, $J_{6,7}$ 9.4, and $J_{7,8}$ 9.8 Hz at the pyranosyl ring. As a side-product, tetra-*O*-acetyl-1,5-anhydro-D-glucitol was formed, in 5% yield, by reduction of **7**.

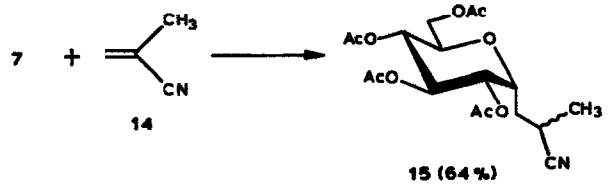


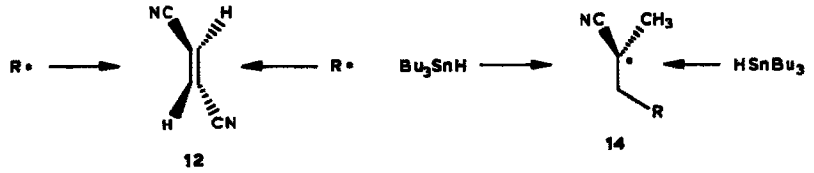


The high selectivity of formation of the axially substituted *C*-glucopyranosyl compound **8** was surprising because equatorially substituted glycopyranosyl radi-

cals having radical centers at C-2, C-3, and C-4 are attacked by alkenes preponderantly from the equatorial side[4]. The reason for the opposite selectivity of the reaction with **7** may be explained by a slightly twisted boat conformation **11** for the intermediate radical instead of the chair conformation **10**. This was shown by the small β-coupling constant in the e.s.r. spectrum[5]. The twist-boat conformation **11** is stabilized by the interaction between the SOMO (single-occupied molecular orbital) of the radical center and the LUMO (lowest-unoccupied molecular orbital) of the adjacent axial C–OAc bond. This interaction is very effective in radical **11** because the neighboring oxygen atom increases the SOMO and, therefore, decreases the SOMO–LUMO energy difference. The preponderant formation of the axially substituted compound **8** resulted from a quasi-equatorial attack at radical **11**. Conversion from the twist-boat to the chair form then led to **8**. The formation of compounds having an axial substituent *via* radical **11** is analogous to cationic reactions. Lemieux *et al.*[6] and Lewis *et al.*[7] explained the rates and stereochemical relations of ionic reactions at the anomeric carbon atom of D-glucose derivatives *via* a cationic intermediate having a conformation that resembles that of radical **11**.

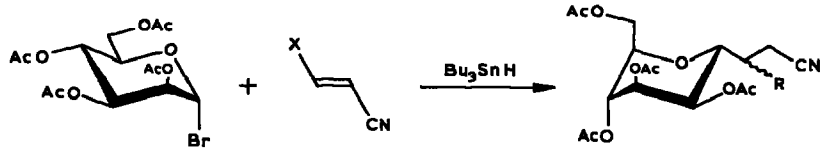






Reactions with 1,2- or 1,1-disubstituted alkenes induce a new chiral center at the side-chain of the oxolane system. Thus, in reactions with fumarodinitrile (**12**) and methacrylonitrile (**14**) in which only axially-substituted products could be isolated, two diastereomers were obtained in 33:17 and 61:39 ratios, respectively. The

small ratio of the compounds obtained shows that the asymmetric induction, caused by the chiral pyranosyl ring, on the diastereoface selectivity in the side chain is low. However, it was not possible to deduce from the n.m.r. data the side-chain chirality of the minor and the major diastereomer. The coupling constants $J_{5,6}$, $J_{6,7}$, and $J_{7,8}$ of **13** (3.4–4.7 Hz) were too far from diaxial couplings. Therefore, we concluded that the $^4C_1$ (D) chair of **7** had been converted into a $^1C_4$ (D)-like conformation in **(13)**.



16 (X = H or CN) **17** R = H (68 %) **18** R = CN (34 %)

19

Similarly to the D-glucosyl system, 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (**16**) reacted with a high selectivity at the pyranosyl ring and a low selectivity at the side chain. The mannosyl radical was attacked by alkenes with an even higher stereoselectivity than the glucosyl radical and only isomers **17** and **18** were detected. In view of the diaxial coupling constant $J_{4,5}$ 9.4 Hz and the diequatorial or axial–equatorial couplings $J_{5,6}$, $J_{6,7}$, and $J_{7,8'}$ which are between 1.8 and 3.6 Hz, the $^1C_4$ (D) chair conformation was attributed to the fumarodinitrile adduct **18**. For the acrylonitrile aduct **17**, the coupling constants $J_{4,5}$ 6.1 Hz and $J_{5,6}$, $J_{6,7}$, and $J_{7,8}$ 3.4–6.3 Hz suggested a conformation that is between a $^1C_4$ (D) chair and a twist-boat conformation. The selective formation of **17** and **18** may be explained by the intermediate mannosyl radical **19** for which the e.s.r. analysis indicated a $^4C_1$ (D) conformation[5]. In the mannosyl radical **19**, the SOMO of the radical and the LUMO of the adjacent, axial C–OAc bond are already in one plane and may, therefore, lead to a stabilizing interaction without change of the $^4C_1$ (D) conformation. The axial acetoxy group directs the attack of the alkene to the axial side. Ring inversion then gives the isomers **17** and **18** having the $^1C_4$ (D) conformation.

The reaction of the D-*gluco*-heptulopyranose derivative **20** (synthesized according to the procedure of Baumberger and Vasella[8]) with tributyltin hydride and acrylonitrile gave **21** as the only isolable compound. Its structure, determined by X-ray crystallography (Fig. 1), showed that an axial C–C bond is formed. Thus, the

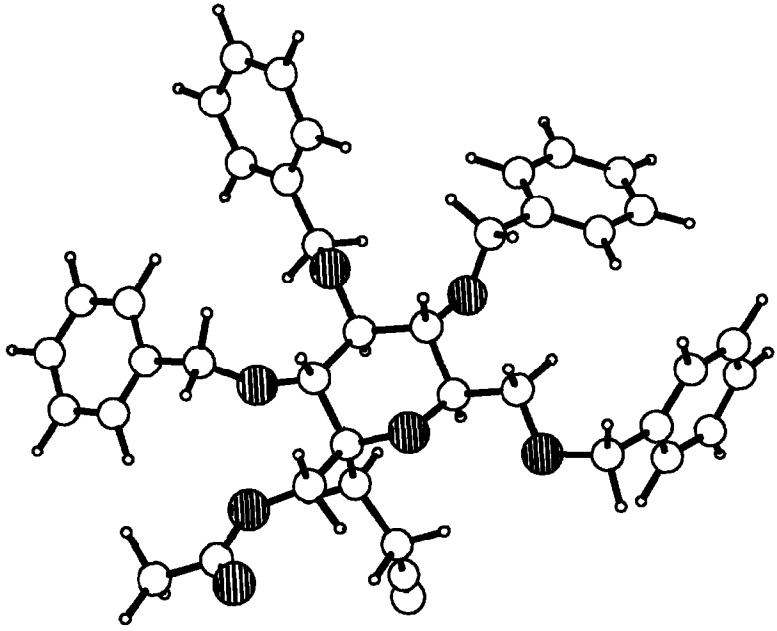
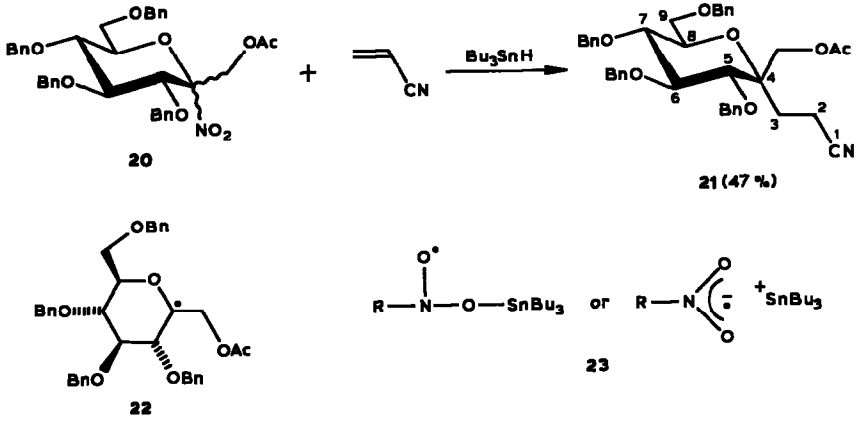
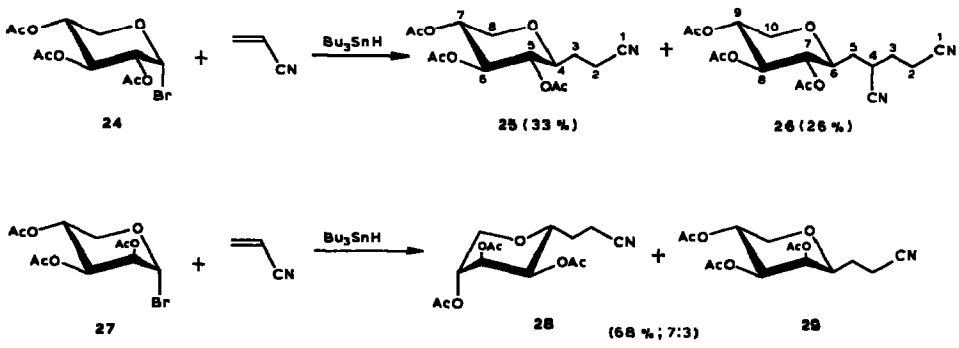


Fig. 1. Crystal structure of **21**. The oxygen atoms are hatched.



stereochemical outcome of the reaction of the D-*gluco*-heptulopyranosyl radical **22** is similar to that of the D-glucopyranosyl radical **11**. The conformation of the tertiary radical **22** could not be determined because the e.s.r. spectrum showed only signals of radical **23**, generated by the attack of the tin radical on the nitro compound[9].

2,3,4-Tri-*O*-acetyl-α-D-xylopyranosyl bromide (**24**) and 2,3,4-tri-*O*-acetyl-α-D-lyxopyranosyl bromide (**27**) gave **25** and **26**, and **28** and **29**, respectively, in the



radical-chain reaction with acrylonitrile. All products have conformations in which the newly formed C–C bonds are in equatorial position. This was shown by the large diaxial coupling-constants $J_{4,5}$ 9.6, 9.5, and 9.9 Hz for **25**, **26**, and **28**, respectively, and the small coupling $J_{4,5}$ 1.1 Hz for **29**. The reason for the relatively large amount of the 2:1 addition product in the reaction with **24** is not known. Although the e.s.r. spectra of the pentopyranosyl radicals are not much different from those of the hexopyranosyl radicals[10], the stereochemical relations differ considerably from each other. The D-xylosyl bromide **24** reacted with a selectivity that is opposite to that of the D-glucosyl bromide **7**, and the D-lyxosyl bromide **27** gave 30% of the *cis* isomer **29**, although the D-mannosyl bromide **16** gave exclusively the *trans* compound **17**.

Thus, the reactions with pentopyranosyl rings led, to a larger extent, to the more stable diastereomers, in which less substituents are axial, than did the reactions with hexopyranosyl rings. Maybe the intermediate pentopyranosyl radicals are so flexible, owing to the absence of an acetoxymethyl substituent at C-5, that the stability of the compounds formed already plays a role in the transition states of the C–C bond-forming reactions.

EXPERIMENTAL

General methods. — Melting points were determined with a Büchi apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. I.r. spectra (KBr discs) were recorded with a Perkin-Elmer 297 spectrometer and ^{1}H-n.m.r. spectra with a Bruker WM-300 spectrometer (300 MHz) for solutions in $CDCl_3$. Analyses were performed with a Perkin-Elmer Sigma 3 gas chromatograph; column chromatography used silica gel (Machery and Nagel, 40–63 μm).

*5,6,7,9-Tetra-*O*-acetyl-4,8-anhydro-2,3-dideoxy-*D-glycero-D-ido-*nonononitrile* (**8**) *and 5,6,7,9-tetra-*O*-acetyl-4,8-anhydro-2,3-dideoxy-*D-glycero-D-gulo-*nononitrile* (**9**). (*Photolytic initiation*). — To a a solution of compound **7** (ref. 11; 50 mmol, 20.6 g) in anhydrous ether (100 mL) at reflux were added, under N_2, acrylonitrile (250 mmol, 13.5 g) and tributyltin hydride (55 mmol, 16.0 g). After a 4-h

irradiation with a sun lamp or a high-pressure mercury lamp, the precipitate was filtered off, further acrylonitrile (120 mmol, 6.6 g) and tributyltin hydride (20 mmol, 5.8 g) were added, and the filtrate was again irradiated. When the starting bromide **7** had completely reacted, the cold mixture was filtered, and the combined precipitates gave **8** (8.6 g, 45%) after crystallization from ether. The filtrates were evaporated, the residue was dissolved in acetonitrile (50 mL), and the solution extracted three times with pentane (50 mL each). The acetonitrile solution was evaporated and the resulting sirup flash-chromatographed on silica gel (1:1 ethyl acetate–hexane). The first fraction contained tetra-*O*-acetyl-1,5-anhydro-D-glucitol (3.5 g, 21%), the second pure **9** (950 mg, 5%), and the third additional **8** (2.5 g, 13%). The ratio of **8** to **9** of the mixture before work up was 93:7 (g.l.p.c.). In a synthesis with **7** (2.0 g) in boiling oxolane (50 mL), **8** (75%) was isolated in 75% yield (1.4 g) by flash-chromatography.

Compound **8**. Colorless crystals (from ether), m.p. 121–123°, $[\alpha]_D^{20}$ + 66.2° (*c* 0.7, chloroform); ν_{max}^{KBr} 2240 (C≡N) and 1745 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 1.84–1.95 (m, 1 H, H-3a), 2.05 (s, 6 H, OAc), 2.09 (s, 3 H, OAc), 2.11 (s, 3 H, OAc), 2.05–2.24 (m, 1 H, H-3b), 3.46 (m, 2 H, H_2-2), 3.88 (ddd, 1 H, $J_{7,8}$ 8.3, $J_{8,9a}$ 2.9, $J_{8,9b}$ 5.8 Hz, H-8), 4.12 (dd, 1 H, $J_{8,9b}$ 5.8, $J_{9a,9b}$ 12.2 hz, H-9b), 4.23 (m, 1 H, H-4), 4.32 (dd, 1 H, $J_{8,9a}$ 5.8, $J_{9,9b}$ 12.2 Hz, H-9a), 4.98 (t, 1 H, $J_{6,7} = J_{7,8}$ 8.3, H-7), 5.09 (dd, 1 H, $J_{4,5}$ 5.2, $J_{5,6}$ 8.3 Hz, H-5), and 5.23 (t, 1 H, $J_{5,6} = J_{6,7}$ 8.3, H-6).

Anal. Calc. for $C_{17}H_{23}NO_9$: C, 52.98; H, 6.02; N, 3.63. Found: C, 52.80; H, 6.01; N, 3.63.

Compound **9**. Colorless crystals, m.p. 117–119°, $[\alpha]_D^{25}$ −19.6° (*c* 1.0, chloroform); ν_{max}^{KBr} 2240 (C≡N) and 1745 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 1.79 (m, 1 H, H-3a), 1.92 (m, 1 H, H-3b), 2.00 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 2.07 (s, 3 H, OAc), 2.09 (s, 3 H, OAc), 2.52 (m, 2 H, H_2-2), 3.56 (dt, 1 H, $J_{3,4}$ 2.6, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 3.58 (ddd, 1 H, $J_{7,8}$ 9.9, $J_{8,9a}$ 5.0, $J_{8,9a}$ 2.1 Hz, H-8), 4.11 (dd, 1 H, $H_{8,9a}$ 5.0, $H_{9a,9b}$ 12.2 Hz, H-9a), 4.88 (t, 1 H, $J_{4,5} = J_{5,6}$ 9.6 Hz, H-5), 5.05 (t, 1 H, $J_{6,7} = J_{7,8}$ 9.4 Hz, H-7), and 5.20 (dd, 1 H, $J_{5,6}$ 9.6, $J_{6,7}$ 9.4 Hz, H-6).

Anal. Calc. for $C_{17}H_{23}NO_9$: C, 52.98; H, 6.02; N, 3.63. Found: C, 52.85; H, 6.09; N, 3.70.

(3RS)-*5,6,7,9-Tetra*-O-*acetyl-4,8-anhydro-3-cyano-2,3-dideoxy*-D-glycero-D-ido-*nonononitrile* (**13**). — To a solution of **7** (7.3 mmol, 3.0 g) and fumarodinitrile **12** (73 mmol, 5.7 g) in toluene (180 mL) were added, at 100° under N_2 within 5 h, a solution of tributyltin hydride (7.9 mmol, 2.3 g) and azoisobutyronitrile (300 mg) in toluene (20 mL). The toluene was destilled off, and the residue dissolved in acetonitrile (300 mL) and extracted three times with pentane (50 mL each). The acetonitrile solution was evaporated, and the residue dissolved in ethyl acetate (20 mL) and chromatographed on silica gel (1:1 ethyl acetate–pentane). The two isomers **13** were isolated in 890 and 490 mg amounts (47%). From the ^{1}H-n.m.r. spectra, it could not be concluded which of these was the [(3*R*)-3-cyano or the (3*S*)-3-cyano]nononononitrile derivative.

Major isomer. Colorless crystals (from ether), m.p. 137–138°, $[\alpha]_D^{20}$ +24.2° (*c*

0.43, chloroform); ν_{max}^{KBr} 2260 (C≡N) and 1740 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 2.11 (s, 3 H, OAc), 2.12 (s, 6 H, OAc), 2.21 (s, 3 H, OAc), 2.87 (m, 2 H, H_2-2), 3.11 (dt, 1 H, $J_{2,3}$ 7.0, $J_{3,4}$ 3.4 Hz, H-3), 4.08 (dd, 1 H, $J_{8,9b}$ 3.4 $J_{9,9'}$ 12.3 Hz, H-9b), 4.29 (t, 1 H, $J_{3,4} = J_{4,5}$ 3.4 Hz, H-4), 4.34 (m, 1 H, H-8), 4.59 (dd, 1 H, $J_{8,9a}$ 7.7, $J_{9a,9b}$ 12.3 Hz, H-9), 4.88 (t, 1 H, $J_{6,7} = J_{7,8}$ 4.7 Hz, H-7), 5.05 (t, 1 H, $J_{4,5} = J_{5,6}$ 3.4 Hz, H-5), and 5.19 (dd, 1 H, $J_{5,6}$ 3.4, $J_{6,7}$ 4.7 Hz, H-6).

Anal. Calc. for $C_{18}H_{22}N_2O_9$: C, 52.68; H, 5.40; N, 6.83. Found: C, 52.62; H, 5.32; N, 6.69.

Minor isomer. Colorless crystals (from ether), m.p. 134–135°, $[\alpha]_D^{20}$ +21.9° (*c* 0.48, chloroform); ν_{max}^{KBr} 2260 (C≡N) and 1740 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 2.09 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.15 (s, 3 H, OAc), 2.18 (s, 3 H, OAc), 2.87 (m, 2 H, H_2-2), 3.30 (ddd, 1 H, $J_{2,3}$ 5.4, $J_{2b,3}$ 6.5, $J_{3,4}$ 10.1 Hz, H-3), 4.07 (m, 2 H, H-8,9b), 4.36 (dd, 1 H, $J_{3,4}$ 10.1, $J_{4,5}$ 3.1 Hz, H-4), 4.52 (dd, 1 H, $J_{8,9a}$ 8.6, $J_{9a,9b}$ 13.0 Hz, H-9a), 4.86 (t, 1 H, $J_{6,7} = J_{7,8}$ 4.7 Hz, H-7), 5.08 (dd, 1 H, $J_{4,5}$ 3.1, $J_{5,6}$ 4.7 Hz, H-5), and 5.24 (t, 1 H, $J_{5,6} = J_{6,7}$ 4.7 Hz, H-6).

Anal. Calc. for $C_{18}H_{22}N_2O_9$: C, 52.68; H, 5.40; N, 6.83. Found: C, 52.46; H, 5.37; N, 6.81.

(2RS)-*5,6,7,9-Tetra*-O-*acetyl-4,8-anhydro-2,3-dideoxy-2-methyl*-D-glycero-D-ido-*nonononitrile* (15). — To a solution of 7 (2.4 mmol, 1.0 g) and methacrylonitrile (48.7 mmol, 3.3 g) in boiling oxolane (40 mL) were added slowly, under N_2 and irradiation with a high-pressure mercury lamp, a solution of tributyltin hydride (2.9 mmol, 850 mg) in oxolane (30 mL). After 1 h, the solution was evaporated *in vacuo*, the residue dissolved in ether (100 mL), and the solution treated with KF (4.0 g) in water (3 mL). After filtration and column chromatography on silica gel (ether), a mixture of isomers (15; 620 mg, 64%) was isolated as crystals in a 61:39 ratio (^{1}H-n.m.r.). The isomers could not be separated and were analyzed as a mixture.

Major isomer. ^{1}H-n.m.r.: δ 1.41 (d, 3 H, J_{2,CH_3} 5.8 Hz, CH_3), 1.62–1.84 (m, 1 H, H-3a), 2.05 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.11 (s, 3 H, OAc), 2.20–2.34 (m, 1 H, H-3b), 2.80–2.90 (m, 1 H, H-2), 3.87 (ddd, 1 H, $J_{7,8}$ 8.0, $J_{8,9a}$ 5.7, $J_{8,9a}$ 3.5 Hz, H-8), 4.15 (dd, 1 H, $J_{8,9a}$ 3.5, $J_{9a,9b}$ 12.3 Hz, H-9b), 4.24–4.30 (m, 2 H, H-4,9a), 4.98 (t, 1 H, $J_{6,7} = J_{7,8}$ 8.0 Hz, H-7), 5.10 (dd, 1 H, $J_{4,5}$ 5.0, $J_{5,6}$ 8.0 Hz, H-5), and 5.20 (t, 1 H, $J_{5,6} = J_{6,7}$ 8.0 Hz, H-6).

Minor isomer. ^{1}H-n.m.r.: δ 1.39 (d, 3 H, J_{2,CH_3} 6.0 Hz, CH_3), 1.62–1.84 (m, 1 H, H-3a), 2.04 (s, 9 H, 3 OAc), 2.08 (s, 3 H, OAc), 2.20–2.34 (m, 1 H, H-3b), 2.66–2.78 (m, 1 H, H-2), 3.93 (ddd, 1 H, $J_{7,8}$ 8.5, $J_{8,9a}$ 4.8, $J_{8,9a}$ 2.5 Hz, H-8), 4.12 (dd, 1 H, $J_{8,9a}$ 2.5, $J_{9a,9b}$ 12.5 Hz, H-9b), 4.24–4.30 (m, 2 H, H-4,9a), 5.00 (t, 1 H, $J_{6,7} = J_{7,8}$ 8.5 Hz, H-7), 5.08 (dd, 1 H, $J_{4,5}$ 5.7, $J_{5,6}$ 8.5 Hz, H-5), and 5.26 (t, 1 H, $J_{5,6} = J_{6,7}$ 8.5 Hz).

Anal. Calc. for $C_{18}H_{25}NO_9$: C, 54.14; H, 6.27; N, 3.51. Found: C, 53.80; H, 6.51; N, 3.28.

5,6,7,9-Tetra-O-*acetyl-4,8-anhydro-2,3-dideoxy*-D-glycero-D-talo-*nonononitrile* (17). — A boiling solution of **16** (ref. 11; 12.0 mmol, 4.9 g), acrylonitrile (120 mmol, 6.4 g), and tributyltin hydride (13.7 mmol, 4.0 g) in ether (200 mL) was

irradiated with a mercury high-pressure lamp. After 9 h, the mixture was filtered, further acrylonitrile (56.6 mmol, 3.0 g) and tributyltin hydride (6.9 mmol, 2.0 g) were added to the filtrate which was again irradiated for 15 h. The solution was treated with KF (3.0 g) in water (2 mL), filtered and evaporated. Column chromatography on silica gel (5:1 ether–pentane) of the residue gave **17** (3.1 g, 68%), colorless oil, $[\alpha]_D^{20}$ +20.3° (*c* 4.3, chloroform); ν_{max}^{KBr} 2240 (C≡N) and 1750 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 1.92–2.04 (m, 1 H, H-3a), 2.04–2.15 (m, 1 H, H-3b), 2.09 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.11 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.49 (t, 2 H, $J_{2,3a} = J_{2,3b}$ 7.3 Hz, H_2-2), 3.97 (ddd, 1 H, $J_{7,8}$ 6.5, $J_{8,9}$ 7.7, $J_{8,9a}$ 3.6 Hz, H-8), 4.04 (ddd, 1 H, $J_{3,4}$ 5.8, $J_{3b,4}$ 9.5, $J_{4,5}$ 6.1 Hz, H-4), 4.10 (dd, 1 H, $J_{8,9b}$ 3.6, $J_{9a,9b}$ 12.3 Hz, H-9b), 4.58 (dd, 1 H, $J_{8,9a}$ 7.7, $J_{9a,9b}$ 12.3 Hz, H-9a), 5.07 (dd, 1 H, $J_{4,5}$ 6.1, $J_{5,6}$ 3.5 Hz, H-5), 5.08 (dd, 1 H, $J_{6,7}$ 5.1, $J_{7,8}$ 6.5 Hz, H-7), and 5.26 (dd, 1 H, $J_{5,6}$ 3.5, $J_{6,7}$ 5.1 Hz, H-6).

Anal. Calc. for $C_{17}H_{23}NO_9$: C, 52.99; H, 5.97; N, 3.64. Found: C, 52.95; H, 6.16; N, 3.46.

*(3*RS*)-5,6,7,9-Tetra-*O*-acetyl-4,8-anhydro-3-cyano-2,3-dideoxy-*D*-glycero-*D*-talo-nonononitrile* (**18**). — To a boiling solution of **16** (3.6 mmol, 1.5 g) and fumarodinitrile (36 mmol, 2.8 g) in toluene (80 mL) was added, under N_2 within 2 h, a solution of tributyltin hydride (7.2 mmol, 2.1 g) and azoisobutyronitrile (240 mg) in toluene (20 mL). After further 30 min, the solution was evaporated, the residue dissolved in acetonitrile (300 mL), and the solution extracted three times with pentane (50 mL each). The acetonitrile solution was treated at reflux with charcoal, filtered, and evaporated. Two column chromatographies of the resulting residue on silica gel (5:4 pentane–ethyl acetate) gave a mixture of isomers (**18**; 510 mg, 34%) in a 69:31 ratio, but it could not be concluded from the ^{1}H-n.m.r. spectra which of the isomers was the (3*R*)-cyano or the (3*S*)-cyano-nonononitrile. The isomers could not be separated and were analyzed as a mixture.

Major isomer. ^{1}H-n.m.r.: δ 2.10 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.14 (s, 3 H, OAc), 2.20 (s, 3 H, OAc), 2.86 (m, 2 H, H_2-2), 3.11 (m, 1 H, H-3), 4.05 (dd, 1 H, $J_{8,9b}$ 4.1, $J_{9a,9b}$ 12.2 Hz, H-9b), 4.17 (m, 1 H, H-8), 4.28 (dd, 1 H, $J_{3,4}$ 7.2, $J_{4,5}$ 9.4 Hz, H-4), 4.83 (dd, $J_{8,9a}$ 9.4, $J_{9a,9b}$ 12.2 Hz, H-9a), 4.91 (dd, 1 H, $J_{6,7}$ 3.6, $J_{7,8}$ 1.8 Hz, H-7), 5.16 (dd, 1 H, $J_{4,5}$ 9.4, $J_{5,6}$ 3.6 Hz, H-5), and 5.34 (t, 1 H, $J_{5,6} = J_{6,7}$ 3.6 Hz, H-6).

Minor isomer. ^{1}H-n.m.r.: δ 2.06 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.18 (s, 3 H, OAc), 2.19 (s, 3 H, OAc), 2.86 (m, 2 H, H_2-2), 3.25 (m, 1 H, H-3), 3.94 (dd, 1 H, $J_{8,9a}$ 3.5, $J_{9a,9b}$ 12.4, H-9b), 4.17 (m, 1 H, H-8), 4.23 (dd, 1 H, $J_{3,4}$ 2.4, $J_{4,5}$ 7.4 Hz, H-4), 4.90 (m, 1 H, H-7), 4.95 (dd, 1 H, $J_{8,9}$ 10.0, $J_{9a,9b}$ 12.4 Hz, H-9a), 5.22 (dd, 1 H, $J_{4,5}$ 7.4, $J_{5,6}$ 3.2 Hz, H-5), and 5.47 (t, 1 H, $J_{5,6} = J_{6,7}$ 3.2 Hz, H-6).

Anal. Calc. for $C_{18}H_{22}O_9N_2$: C, 52.68; H, 5.40; N, 6.83. Found: C, 52.48; H, 5.39; N, 6.70.

*4-C-Acetoxymethyl-4,8-anhydro-5,6,7,9-tetra-*O*-benzyl-2,3-dideoxy-*D*-glycero-*D*-ido-nononitrile* (**21**). — To a boiling solution of acrylonitrile (27.0 mmol, 1.43 g) in benzene (60 mL) was added, under N_2 within 3 h, a solution of **20** (ref. 8;

0.90 mmol, 575 mg), tributyltin hydride (1.2 mmol, 350 mg), and azoisobutyronitrile (0.96 mmol, 160 mg) in benzene (90 mL). After 1 h, the solution was evaporated, the residue dissolved in acetonitrile (50 mL), and the solution extracted three times with pentane (30 mL each). The acetonitrile solution was evaporated and the residue chromatographed on silica gel (3:1 hexane–ethyl acetate) to give **21** (274 mg, 47%) after crystallization from ethanol, m.p. 103–105°, $[\alpha]_D^{20}$ +22.4° (*c* 1.2, dichloromethane); ^{1}H-n.m.r.: δ 1.97 (s, 3 H, OAc), 2.10–2.36 (m, 2 H, H_2-3), 2.38–2.48 (m, 2 H, H_2-2), 3.55–3.68 (m, 4 H, H-7,8,9a,9b), 3.73 (d, 1 H, $J_{5,6}$ 9.5 Hz, H-5), 3.85 (dd, 1 H, $J_{5,6}$ 9.5, $J_{6,7}$ 8.5 Hz, H-6), 4.20 (d, 1 H, *J* 11.7 Hz, CH_2OAc), 4.50–4.65 (m, 4 H, 2 benzylic CH_2), 4.86–4.98 (m, 4 H, 2 benzylic CH_2), and 7.20–7.40 (m, 20 H, 4 OBn).

Anal. Calc. for $C_{40}H_{43}NO_7$: C, 73.92; H, 6.67; N, 2.15. Found: C, 73.57; H, 6.74; N, 2.27.

X-Ray crystallographic determination of the structure of **21**. — Space group $P3_2$; *a* 24.083(3), *c* 5.409(1) Å, *V* 2716.9 Å^3, *z* = 3, $D_{calc.}$ 1.191 g·cm^{-1}, and $\mu_{CuK\alpha}$ 5.77 cm^{-1}.

Data collection. A needle (0.15·0.08·2.4 mm) was mounted along *c* on a STE SIADI 4 diffractometer using graphite, monochromated CuKα radiation. The cell constants were determined by measuring the positions of 33 reflections with 15.3 < 2ϑ < 50.3°. From 3009 measured reflections (3 < 2ϑ < 120°), 2579 with $F_0 \geqq 3\,\sigma(F_0)'$ were used for structure determination and refinement after correction for background and geometrical factors.

Structure determination and refinement. The structure was solved by use of the MULTAN 80[12] and difference-density syntheses. The hydrogen atoms were placed in calculated positions, 1.08 Å away from their respective carbon atoms (U 0.18 Å^2). Anisotropic refinement of the non-hydrogen atoms led[13] to R 0.058. The positional parameters and U_{eq} for the non-hydrogen atoms are presented in Table I.

*5,6,7-Tri-*O*-acetyl-4,8-anhydro-2,3-dideoxy-*D*-gulo-octononitrile* (**25**) *and (4*RS*)-7,8,9-tri-*O*-acetyl-6,10-anhydro-4-cyano-2,3,4,5-tetradeoxy-*D*-gulo-decanonitrile* (**26**). — To a boiling solution of **24** (ref. 74; 2.95 mmol, 1.0 g) and acrylonitrile (29.5 mmol, 1.6 g) in toluene (50 mL) was added, under N_2, a solution of tributyltin hydride (6.0 mmol, 1.75 g) and azoisobutyronitrile (150 mg) in toluene (30 mL). After 2 h, the solution was evaporated, the residue dissolved in acetonitrile (50 mL), and the solution extracted three times with pentane (30 mL each). The acetonitrile solution was evaporated and the residue chromatographed on silica gel (diethyl ether) to give the 1:1 adduct **25** (301 mg, 33%) and the 2:1 adduct **26** (283 mg, 26%).

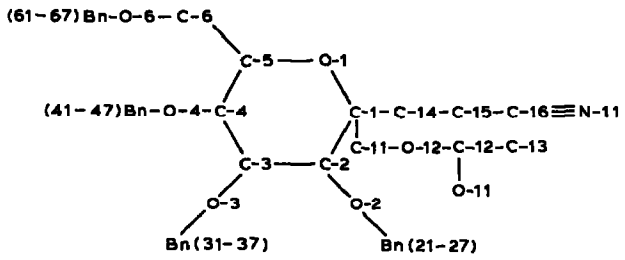
Compound **25**. Colorless crystals, m.p. 94–95° (ether), $[\alpha]_D^{20}$ −36.9° (*c* 0.5, chloroform); ν_{max}^{KBr} 2250 (C≡N) and 1740 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 1.70–1.78 (m, 1 H, H-3b), 1.84–1.93 (m, 1 H, H-3a), 2.03 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.52 (dd, 2 H, $J_{2,3a}$ 6.3, $J_{2,3a}$ 8.2 Hz, H_2-2), 3.29 (t, 1 H, $J_{7,8a} = J_{8a,8b}$ 10.8 Hz, H-8a), 3.46 (dt, 1 H, $J_{3a,4} = J_{4,5}$ 9.6, $J_{3a,4}$ 2.8 Hz, H-4), 4.81 (t, 1 H, $J_{4,5} = J_{5,6}$ 9.6 Hz, H-5), 4.96 (ddd, 1 H, $J_{6,7}$ 9.6, $J_{7,8}$ 5.6, $J_{7,8a}$ 5.6, $J_{7,8b}$ 10.8 Hz, H-7), and

TABLE I

FINAL ATOMIC COORDINATES AND THERMAL PARAMETERS FOR COMPOUND[a] 21

Atom	*x/A*	*y/B*	*z/C*	U(eq)
C-1	0.0203(3)	−0.7176(3)	0.0619(10)	0.063(3)
C-2	−0.0481(2)	−0.7383(2)	−0.0220(0)	0.056(3)
C-3	−0.0534(2)	−0.6831(2)	−0.1378(10)	0.060(3)
C-4	−0.0220(3)	−0.6226(3)	0.0197(11)	0.065(3)
C-5	0.0447(3)	−0.6078(2)	0.0975(12)	0.069(3)
C-6	0.0717(3)	−0.5534(3)	0.2934(13)	0.088(4)
C-11	0.0225(3)	−0.7654(3)	0.2443(11)	0.073(3)
C-12	0.0243(4)	−0.8619(3)	0.2223(15)	0.098(5)
C-13	0.0076(5)	−0.9193(4)	0.0701(18)	0.160(7)
C-14	0.0655(3)	−0.7049(3)	−0.1569(11)	0.065(3)
C-15	0.1363(3)	−0.6734(4)	−0.0815(13)	0.086(4)
C-16	0.1756(3)	−0.6606(4)	−0.2994(16)	0.089(4)
C-21	−0.1269(3)	−0.8457(3)	−0.1138(13)	0.080(4)
C-22	−0.1552(3)	−0.8927(3)	−0.3266(13)	0.072(4)
C-23	−0.2080(4)	−0.8986(5)	−0.4419(18)	0.137(7)
C-24	−0.2357(5)	−0.9425(8)	−0.6288(23)	0.162(9)
C-25	−0.2122(9)	−0.9802(6)	−0.6904(26)	0.160(11)
C-26	−0.1601(10)	−0.9748(7)	−0.5772(28)	0.241(15)
C-27	−0.1308(6)	−0.9290(5)	−0.3983(18)	0.181(9)
C-31	−0.1399(3)	−0.7026(3)	−0.4057(12)	0.083(4)
C-32	−0.2116(3)	−0.7264(3)	−0.4069(12)	0.072(3)
C-33	−0.2496(4)	−0.7646(4)	−0.5918(16)	0.116(6)
C-34	−0.3163(4)	−0.7841(5)	−0.5906(21)	0.125(7)
C-35	−0.3392(4)	−0.7626(5)	−0.4059(23)	0.128(7)
C-36	−0.3019(4)	−0.7263(5)	−0.2268(19)	0.123(6)
C-37	−0.2381(3)	−0.7078(3)	−0.2268(15)	0.097(5)
C-41	−0.0539(3)	−0.5442(3)	−0.0306(14)	0.103(4)
C-42	−0.0369(3)	−0.4846(3)	−0.1744(12)	0.080(4)
C-43	0.0150(3)	−0.4272(3)	−0.1065(14)	0.094(4)
C-44	0.0290(4)	−0.3718(3)	−0.2430(19)	0.112(5)
C-45	−0.0074(5)	−0.3756(5)	−0.4437(19)	0.147(8)
C-46	−0.0609(5)	−0.4341(5)	−0.5068(17)	0.142(7)
C-47	−0.0741(3)	−0.4876(4)	−0.3721(14)	0.100(5)
C-61	0.1656(5)	−0.4857(4)	0.5086(20)	0.154(7)
C-62	0.1813(4)	−0.4244(3)	0.3724(17)	0.095(5)
C-63	0.1546(4)	−0.3885(5)	0.4364(20)	0.133(7)
C-64	0.1682(5)	−0.3328(5)	0.3151(29)	0.165(6)
C-65	0.2059(5)	−0.3159(5)	0.1244(33)	0.174(10)
C-66	0.2370(5)	−0.3474(6)	0.0520(24)	0.152(9)
C-67	0.2235(5)	−0.4039(5)	0.1730(23)	0.135(7)
N-11	0.2052(3)	−0.6509(3)	−0.4752(15)	0.119(5)
O-1	0.0417(2)	−0.6624(2)	0.2184(7)	0.066(2)
O-2	−0.0718(2)	−0.7892(2)	−0.1986(7)	0.058(2)
O-3	−0.1201(2)	−0.7035(2)	−0.1621(7)	0.067(2)
O-4	−0.0163(2)	−0.5700(2)	−0.1199(6)	0.070(2)
O-6	0.1341(2)	−0.5395(2)	0.3463(13)	0.140(4)
O-11	0.0101(2)	−0.8219(2)	0.1114(8)	0.090(3)
O-12	0.0433(3)	−0.8540(3)	0.4319(12)	0.142(4)

[a]For numbering scheme, see 30.



30

5.19 (t, 1 H, $J_{5,6} = J_{6,7}$ 9.6 Hz, H-6).

Anal. Calc. for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.07; N, 4.47. Found: C, 53.56; H, 6.21; N, 4.51.

Compound **26**. Mixture of diasteromers, only from the ^{1}H-n.m.r. data of the main isomer could all lines be identified; ^{1}H-n.m.r.: δ 1.85–1.95 (m, 2 H, H_2-5), 1.97–2.17 (m, 2 H, H_2-3), 2.03 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.52–2.66 (m, 2 H, H_2-2), 2.94–2.99 (m, 1 H, H-4), 3.28 (t, 1 H, $J_{9,10} = J_{10a,10b}$ 9.5 Hz, H-10a), 3.52 (dt, 1 H, $J_{5a,6}$ 3.9, $J_{5b,6} = J_{6,7}$ 9.5 Hz, H-6), 4.14 (dd, 1 H, $J_{9,10b}$ 5.5, $J_{10a,10b}$ 9.5 Hz, H-10b), 4.84 (t, 1 H, $J_{6,7} = J_{7,8}$ 9.5 Hz, H-7), 4.79 (dt, 1 H, $J_{8,9} = J_{9,10b}$ 9.5, $J_{9,10a}$ 5.5 Hz, H-9), and 5.18 (t, 1 H, $J_{7,8} = J_{8,9}$ 9.5 Hz, H-8).

Anal. Calc. for $C_{17}H_{22}N_2O_7$ (mixture): C, 55.73; H, 6.05; N, 7.65. Found: C, 55.91; H, 5.81; N, 7.41.

*5,6,7-Tri-*O*-acetyl-4,8-anhydro-2,3-dideoxy-*D*-talo-octononitrile* (**28**) *and 5,6,7-tri-*O*-acetyl-4,8-anhydro-2,3-dideoxy-*D*-galacto-octononitrile* (**29**). — To a boiling solution of **27** (ref. 15, 5.9 mmol, 2.0 g) and acrylonitrile (59.0 mmol, 3.0 g) in toluene (60 mL) was added, under N_2, a solution of tributyltin hydride (9.0 mmol, 2.55 g) and azoisobutyronitrile (200 mg) in toluene (40 mL). After 3 h, the solution was evaporated, the residue dissolved in acetonitrile (50 mL), and the solution extracted three times with pentane (50 mL each). The acetonitrile solution was evaporated and the residue chromatographed on silica gel (diethyl ether) to give **28** (870 mg, 47%) and **29** (401 mg, 21%) as colorless oils.

Compounds **28**. $[\alpha]_D^{20}$ −13.6° (*c* 4.2, chloroform); ν_{max}^{KBr} 2250 (C≡N) and 1745 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 1.99–2.02 (m, 1 H, H-3b), 2.02 (s, 3 H, OAc), 2.10–2.20 (m, 1 H, H-3a), 2.15 (s, 6 H, OAc), 2.50–2.56 (m, 2 H, H_2-2), 3.77 (dt, 1 H, $J_{3a,4}$ 2.6, $J_{3a,4} = J_{4,5}$ 9.9 Hz, H-4), 3.82–3.95 (m, 2 H, H_2-8), 4.84 (dt, 1 H, $J_{6,7} = J_{7,8}$ 9.0, $J_{7,8}$ 1.8 Hz, H-7), 4.92 (dd, 1 H, $J_{4,5}$ 9.9, $J_{5,6}$ 9.0 Hz, H-5), and 5.34 (t, 1 H, $J_{5,6} = J_{6,7}$ 9.0 Hz, H-6).

Anal. Calc. for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.07; N, 4.47. Found: C, 53.41; H, 5.98; N, 4.21.

Compounds **28**. $[\alpha]_D^{20}$ −39.5° (*c* 2.2, chloroform); ν_{max}^{KBr} 2260 (C≡N) and 1745 (C=O) cm^{-1}; ^{1}H-n.m.r.: δ 1.60–1.80 (m, 1 H, H-3a), 1.80–2.00 (m, 1 H, H-3b), 2.01 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 2.17 (s, 3 H, OAc), 2.46–2.56 (m, 2 H, H_2-2), 3.29 (dd, 1 H, $J_{7,8a}$ 10.3, $J_{8a,8b}$ 11.2 Hz, H-8a), 3.69 (ddd, 1 H, $J_{3a,4}$ 3.4, $J_{3b,4}$ 10.0,

$J_{4,5}$ 1.1 Hz, H-4), 4.17 (dd, 1 H, $J_{7,8b}$ 5.5, $J_{8a,8b}$ 11.2 Hz, H-8b), 5.06 (dd, 1 H, $J_{5,6}$ 3.4, $J_{6,7}$ 10.3 Hz, H-6), 5.20 (dt, 1 H, $J_{6,7} = J_{7,8a}$ 10.3, $J_{7,8a}$ 5.5 Hz, H-7), and 5.34 (dd, 1 H, $J_{4,5}$ 1.1, $J_{5,6}$ 3.4 Hz, H-5).

Anal. Calc. for $C_{14}H_{19}NO_7$: C, 53.67; H, 6.07; N, 4.47. Found: C, 53.61; H, 6.12; N, 4.35.

ACKNOWLEDGMENT

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

REFERENCES

1 D. J. Hart, *Science*, 223 (1984) 883–887; B. Giese, *Angew. Chem.*, 97 (1985) 555–567; *Angew. Chem., Int. Ed. Engl.*, 24 (1985) 553–565.
2 G. E. Keck, E. J. Enholm, J. B. Yates, and M. R. Wiley, *Tetrahedron*, 41 (1985) 4079–4094.
3 B. Giese and J. Dupuis, *Angew. Chem.*, 95 (1983) 633–634; *Angew. Chem., Int. Ed. Engl.*, 22 (1983) 622–623; see also, R. M. Adlington, J. E. Baldwin, A. Basak, and R. P. Kozyrod, *J. Chem. Soc., Chem. Commun.*, (1983) 944–945.
4 B. Giese and K. Gröninger, *Tetrahedron Lett.*, 25 (1984) 2743–2746; B. Giese, J. A. González-Gómez, and T. Witzel, *Angew. Chem.*, 96 (1984) 51; *Angew. Chem. Int. Ed. Engl.*, 23 (1984) 69.
5 J. Dupuis, B. Giese, D. Rüegge, H. Fischer, H.-G. Korth, and R. Sustmann, *Angew. Chem.*, 96 (1984) 887–888; *Angew. Chem. Int. Ed. Engl.*, 23 (1984) 896–898.
6 R. U. Lemieux, K. B. Hendriks, R. U. Stick, and K. James, *J. Am. Chem. Soc.*, 97 (1975) 4056–4062.
7 M. D. Lewis, J. K. Cha, and Y. Kishi, *J. Am. Chem. Soc.*, 104 (1982) 4976–4978.
8 F. Baumberger and A. Vasella, *Helv. Chim. Acta*, 66 (1983) 2210–2222.
9 J. Dupuis, B. Giese, J. Hartung, and M. Leising, *J. Am. Chem. Soc.*, 107 (1985) 4332–4333.
10 H.-G. Korth, R. Sustmann, J. Dupuis, and B. Giese, *J. Chem. Soc., Perkin Trans. 2*, (1986) 1453–1459.
11 R. U. Lemieux, *Methods Carbohydr. Chem.*, 2 (1963) 221–222.
12 P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J.-P. Declereq, and M. M. Woolfson, *MULTAN 80, a System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data*, University of York, York, England, 1980.
13 G. W. Sheldrick, *SHECK-76, a Program for Crystal Structure Determination*, University of Cambridge, Cambridge, England, 1976.
14 F. Weygand, *Methods Carbohydr. Chem.*, 1 (1962) 182–185.
15 P. L. Durette and D. Horton, *Carbohydr. Res.*, 18 (1971) 57–80.