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STEREOCHEMISTRY OF NUCLEOPHILIC ADDITION REACTIONS—13†

KINETICALLY CONTROLLED NUCLEOPHILIC ADDITION REACTIONS TO METHYL 4,6-*O*-BENZYLIDENE-2,3-DIDEOXY-2-NITRO-β-D-*ERYTHRO*-HEX-2-ENOPYRANOSIDE: AN IMPORTANT ROLE OF $A^{(1,3)}$ STRAIN‡

TOHRU SAKAKIBARA*, YOSHIFUSA TACHIMORI and the late ROKURO SUDOH
Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152 Japan

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Abstract—An improved synthesis of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-nitro-β-D-*erythro*-hex-2-enopyranoside and its reactions with various nucleophiles are described; all the nucleophiles were found to approach exclusively or predominantly from the equatorial side of the molecule, giving the β-D-glucopyranoside derivatives as the major or exclusive product. The stereochemical course of approach of a nucleophile observed in the present reactions and in the literature are discussed.

Stereochemistry of nucleophilic addition reactions to six-membered ring systems including sugar derivatives is extensively studied and the results are generally accounted for on the basis of two factors,[2-4] viz (i) axial attack predominates over equatorial attack, because the former leads to a thermodynamically more stable chair-like transition state, whereas the latter a less stable boat-like transition state for stereoelectronic control,[5] and (ii) steric hindrance between an approaching nucleophile and the substituent(s) around the reactive site. However, several examples are difficult to explain by these two factors only. For example, Collins *et al.*[6] reported that methoxide, deuteride, and azide ions attacked from the equatorial side of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-phenylazo-β-D-*erythro*-hex-2-enopyranoside (**1**). Except the reduction of **1** with sodium borodeuteride, the possibility that the reactions of **1** with the nucleophiles proceeded under thermodynamic control may not be excluded, since the *arabino* isomer isolated should be thermodynamically more stable, but equilibration tests were not performed. However, we found that a cyanide ion of almost the same bulkiness as an azide ion, approached exclusively from the axial side of methyl 4,6-*O*-benzylidene-2-cyano-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside (**2**).[8] These conflicting results may be attributable to the nature of the electron-withdrawing groups at chair-like transition state derived by axial attack of a nucleophile. In contrast with the linear cyano group, the nonlinear phenylazo group should suffer electrostatic or steric repulsion from the anomeric methoxyl group. If this is true, nucleophiles may approach from the equatorial side of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-nitro-β-D-*erythro*-hex-2-enopyranoside (**3**) with high selectivity, since such a repulsion between the *aci*-nitro group and the anomeric methoxyl group in a chair-like transition state should be more serious than that between the phenylazo and methoxyl groups. Then we have investigated the addition reaction of **3** with various nucleophiles. Part of this work was reported in preliminary form.[9]

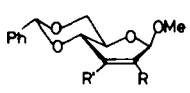
RESULTS AND DISCUSSION

The 2-nitro alcohol **4** was previously prepared by treatment of the 3-nitro acetate **6** with sodium nitrite in around 20% yield.[10] Similar reaction of the α-anomer **7** resulted in the recovery of **7**, but treatment of the nitro alkene **8** with sodium nitrite afforded the 2-nitro alkene **9** (47%) or 2,3-dinitro compound **10** (58%), depending on the absence or presence of acetic acid.[11] We, therefore, have applied this method to the β-anomer **5**.

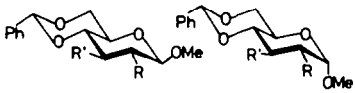
Treatment of **5** with sodium nitrite in benzene-water in the presence of 1.3 equivalent amounts of acetic acid and tributylhexadecylphosphonium bromide as a phase-transfer catalyst yielded a complex mixture, from which the intended dinitro compound was not isolated. Similar heterogeneous reaction, except in the absence of acetic acid, afforded a mixture containing the 2-nitro **3** and 3-nitro alkene **5**, together with small amounts of 2-nitro **4** and 3-nitro alcohol **11**, as judged from TLC and ^{1}H-NMR spectroscopy. Attempts at isolation of **3** by crystallization or column chromatography on silica gel failed. The intended 2-nitro sugar was isolated as the nitro alcohol **4** (57%), together with the 3-nitro alcohol **11** (12%), by treatment of the crude product with pyridine-water. Although the 2-nitro-alkene **3** had been synthesized by the elimination of acetic acid from the acetate **12** in 83% yield,[10] more convenient

†For Part 12, see Ref. 30[b].

‡Original definition of $A^{(1,3)}$ strain[1] is based on steric hindrance, however, in this paper it is modified to involve electrostatic repulsion.

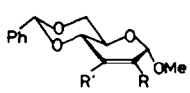


1, R = N=N-Ar, R'=H
2; R = CN, R'=H
3; R = NO_2, R'=H
5; R=H, R'=NO_2
21, R=H, R'=CN

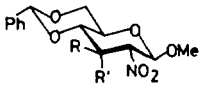


4, R=NO_2, R=OH
6, R=OAc, R'=NO_2
11, R=OH, R'=NO_2
12, R=NO_2, R'=OAc

7; R=OAc, R'=NO_2
10, R=R'=NO_2



8; R=H, R'=NO_2
9; R=NO_2, R'=H



13; R=$CHAc_2$, R'=H
14, R=OMe, R'=H
15; R=H, R'=OMe
16, R=R'=H
17; R=H, R'=D
18; R=D, R'=H
19, R=CN, R'=H
20; R=H, R'=CN

direct method[12] for converting a nitro alcohol into the corresponding nitro-alkene was examined. The desired nitro alkene **3** was isolated in 85% yield by addition of methanesulfonyl chloride to a solution of **4** in THF containing triethylamine. The acetate **12**[10] was obtained in 86% yield by the acetylation of **4** with acetic anhydride–pyridine in dichloromethane.

Treatment of the nitro-alkene **3** with 2,4-pentanedione in THF in the presence of 0.1 M aqueous sodium hydroxide for 30 min at 0° afforded only one spot in TLC, giving the glucopyranoside **13** in 87% isolated yield. The *gluco* configuration in the $^4C_1$ conformation was assigned by the coupling constants; $J_{1,2} = 8.3$ and $J_{2,3} = J_{3,4} = 11.3$ Hz. This reaction, contrary to similar reaction of the α-anomer **9**,[13] did not exhibit solvent effects (DMSO, 1,4-dioxane, and benzene). The reaction seems to be controlled kinetically, because the elimination of the anomeric methoxyl group would predominate over the retro–Michael reaction as indicated in the reaction of **9** with dimethyl malonate.[13]

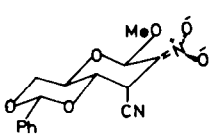
When compound **3** was heated in refluxing methanol for 1 h, the glucopyranoside **14** with the $^4C_1$ conformation ($J_{1,2} = 8.0$, $J_{2,3} = 9.8$ and $J_{3,4} = 8.3$ Hz) was exclusively formed (71% isolated yield). The fact, that the elimination of the methoxyl group at C–1 occurred more easily than that at C–3 in methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-2-nitro-α-D-allopyranoside,[14] suggests that the present reaction also proceeded under kinetic control. In fact, under the same conditions, the *allo* isomer **15**, the 3-epimer of **14**, prepared from **9**,[14] was recovered completely. Furthermore, in contrast with the situation of the α-anomer,[9,14] the reaction of **3** with refluxing methanol–DMSO, refluxing methanol-1,4-dioxane, methanol-sodium methoxide, and sodium methoxide-1,4-dioxane gave almost exclusively the glucopyranoside **14**.

Reduction of **3** with sodium borohydride in acetonitrile provided the *ribo* isomer **16** in 74% yield. The *ribo* configuration having $^4C_1$ conformation was determined on the basis of the coupling constants; $J_{1,2} = 7.5$, $J_{2,3a} = 12$, and $J_{2,3e} = 4.7$ Hz. Reduction of **3** with sodium borodeuteride gave a mixture of **17** and **18**, having the axial and equatorial deuterium atom at C-3, respectively, in the ratio of 1:2, as estimated from the areas of signals at δ 2.70 (H–3e) and 2.32 (H–3a).

Reaction of **3** with hydrogen cyanide in acetonitrile in the presence of a catalytic amount of potassium cyanide (under the conditions employed for the reaction of the cyano-alkene **2**[8]) yielded a mixture of the gluco **19**, allopyranoside **20**, and 3-cyanoalkene **21** in the ratio of *ca* 2.5:1:2, as calculated from ^{1}H-NMR spectroscopy. When the reaction was performed in 1,4-dioxane for 6.75 h (monitored by TLC), the formation of 3-cyano alkene **21** was almost suppressed and the ratio of **19** and **20** became 4.5:1 (by ^{1}H-NMR spectroscopy). However, when the reaction time was extended to 24 h, the 3-cyano alkene **21** became the major product. The *gluco* and *manno* configuration with $^4C_1$ conformation of **19** and **20**, respectively, was again determined from the coupling constants; $J_{1,2} = 7.5$ and $J_{2,3} = 10.5$ Hz for **19**, $J_{1,2} = 8.3$ and $J_{2,3} = 4.9$ Hz for **20**. Assignment of the cyano alkene structure to **21** was based on its ^{1}H-NMR (alkenic proton at δ 6.45) and IR spectra (no absorption for a nitro group, absorption for a cyano group at 2230 cm^{-1}) as well as elemental analysis. Treatment of the allopyranoside **20** in 1,4-dioxane, under similar conditions used for the preparation of **19** and **20**, resulted in the recovery of **20**, together with a trace of **21**, indicating that attack of a cyanide ion to **3** proceeded, at least mostly, under the kinetic control.

These results, showing that the nucleophiles predominantly or almost exclusively approached from the equatorial side of nitro alkene **3**, are in good agreement with those derived in the reactions of the phenylazo derivative **1**, but contrary to those of the cyano alkene **2**.

Now our argument is focussed on the reaction of **2** and **3** with hydrogen cyanide. A linear, less bulky cyanide ion suffers less steric hindrance from the oxygen atom at C-4 as compared to the other nucleophile; this may be the reason why the stereoselectivity of hydrogen cyanide was lower than that of methanol or 2,4-pentanedione. The boat-like intermediates II and IV derived by equatorial attack are destabilized by intrinsic eclipse interaction,[15] however, they are free from bowspirit–flagpole interaction, because the bowspirit (or flagpole) position (C-2) should be planar (sp^2-hybridized).[6] The fact that a cyanide ion exclusively approached from the axial side of **2** suggests that the chair-like intermediate III is more stable than the boat-like intermediate IV; this agrees with general predominance of a chair conformation over a boat conformation. The substantial difference between the chair-like intermediate I and III is the presence of $A^{(1,3)}$ strain, which, as already mentioned at footnote, is modified to involve electrostatic repulsion besides steric repulsion, in the former, but the absence in the latter. Baer and Kovář reported that $A^{(1,3)}$ strain between the *aci*-nitro group and the hydroxyl group becomes *ca* 2.5 kcal mol^{-1} on the basis of the data obtained by the nitronate equilibration.[3,16] Assuming that $A^{(1,3)}$ strain plays an im-



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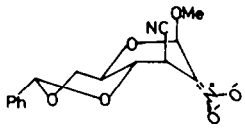

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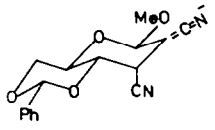
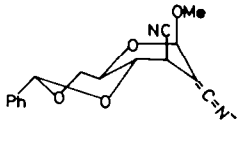


III



IV

portant role, a cyanide ion should enter from the equatorial side of the nitro alkene **3** leading to the boat-like intermediate II, whereas it would approach from the axial side of the cyano alkene **2** to yield the chair-like intermediate III; both the intermediates are free from $A^{(1,3)}$ strain.

The present investigation showed that the course of nucleophilic attack may also be governed by $A^{(1,3)}$ strain generated in an intermediary *aci*-nitronate [factor (iii)]. This factor, hitherto not considered for the Michael type reaction, of course, competes with the two factors (i) and (ii). From practical viewpoints, these three factors may be rewritten as follows on the basis of the substituent(s) around the reactive site. The approach of a nucleophile under kinetically controlled conditions is presumably determined by three factors, viz (i) regardless of the substituent(s), axial attack preponderates over equatorial attack for stereoelectronic control; (ii) concerned with the substituent at the γ-position, trans addition predominates over cis addition; and (iii) concerned with the substituent at the β'-position, cis addition prevails over trans addition, if there is $A^{(1,3)}$ strain in a transition state. For the α, β and γ definition, α' instead of β' is adopted in the enone system, as illustrated in the figure (Class l, m, and o). In this expression, however, factor (ii) is too simplified in some cases; for example, not only the γ-substituent but also the β'-substituent plays a role for determining the direction of an approaching nucleophile,[9,14] and electrostatic attraction between a nucleophile and the substituent(s) around the reactive site may operate, as shown in the reactions of 3-nitro-hex-2-enopyranosides with diazomethane[17] and Simmons–Smith reaction of ethyl 6 - *O* - acetyl-2,3 - dideoxy - α - D - *glycero* - hex - 2 - enopyranosid-4 - ulose.[18] Furthermore, quantitative analysis of these factors is undoubtedly very difficult, because their relative importance should depend on many factors. For example, if a nucleophile is bulky and/or negatively charged, the factor (ii) becomes important, and if a transition state resembles to an intermediary anion or reactant, the factors (i) and (iii) or factor (ii) should have a strong influence. In spite of these situations, most data reported in the literature may be explained in terms of these factors [(i)–(ii)] as shown in Table 2 and consideration of these factors is probably useful in predicting a kinetically favorable product. As an example for constructing Table 2, the reaction of the 3-nitro alkene **5** with a nucleophile is

Table 1. ^{1}H-NMR data[a]

Comp.	H-1	H-2	H-3	H-4	H-5	H-6a	H-6e	PhCH	OMe
13[b]	4.91	4.66	3.16	4.25	3.55	3.81	4.36	5.46	3.52
	$J_{1,2}$=8.3,	$J_{2,3}$=11.3,		$J_{3,4}$=11.3,		$J_{4,5}$=9.0,	$J_{5,6a}$=9.8,	$J_{5,6e}$=4.5,	$J_{6a,6e}$=9.8
14	4.80	4.43	4.09	3.66	3.63	3.80	4.38	5.55	3.54 and 3.51
	$J_{1,2}$=8.0,	$J_{2,3}$=9.8,		$J_{3,4}$=8.3,		$J_{4,5}$=8.3,	$J_{5,6a}$=9.8,	$J_{5,6e}$=3.8,	$J_{6a,6e}$=9.8
16	4.88	4.51	c	3.4-3.7		3.78	4.34	5.52	3.53
	$J_{1,2}$=7.5			c			$J_{5,6a}$=9.0,	$J_{5,6e}$=3.0,	$J_{6a,6e}$=10
19	4.84	4.66		3.5-3.9			4.40	5.62	3.55
	$J_{1,2}$=7.5,	$J_{2,3}$=10.5						$J_{5,6e}$=3.8,	$J_{6a,6e}$=9.9
20	5.21	4.52		3.5-4.1			4.43	5.58	3.63
	$J_{1,2}$=8.3,	$J_{2,3}$=4.9						$J_{5,6e}$=3.8,	$J_{6a,6e}$=9.8
21	5.31	6.45	-	4.18	3.73	3.90	4.18	5.64	3.48
	$J_{1,2}$=1.8[d]	-		-		$J_{4,5}$=6.0,	$J_{5,6a}$=10,	$J_{5,6e}$=4.1,	$J_{6a,6e}$=10

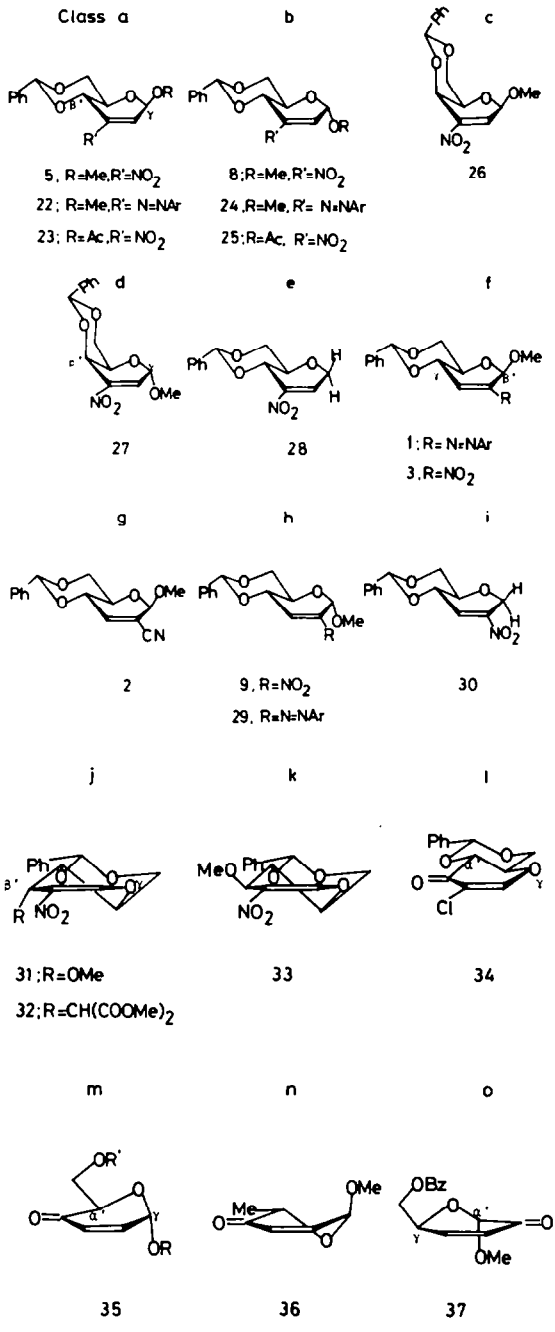
[a] First-order analysis at 100 MHz in $CDCl_3$ with Me_4Si as the internal standard: δ and Hz. [b] Signals of diacetylmethyl group: C-H δ3.62 and Ac 2.13, $J_{3,CH}$=4.5 Hz. [c] δ 2.32 (H-3a) and 2.70 (H-3e); $J_{2,3a}$=$J_{3a,3e}$=12, $J_{2,3e}$=4.7, $J_{3a,4}$=10.5, and $J_{3e,4}$=4.5 Hz. [d] $J_{1,4}$=3.0 and $J_{2,4}$=1.5 Hz.

Table 2. Prediction and observation of an approaching direction of nucleophiles to various Michael acceptors†

	Class of Compounds													
	a	b*	c	d	e*	f	g	h*	i*	j	k	l	m	n	o
Factor (i)	↓	↓	↓	↓	↓	↑	↑	↑	↑	↑	↑	↑	↓	↑	↓
Factor (ii)	↑	↓	↑	↓	–	↓	↓	↓	↓	–	–	–	↓	↑	↑
Factor (iii)	↑	↑	↓	↓	↑	↓	–	↑	–	↑	↓	–	–	–	–
Prediction	↓↑	↓↑	↓↑	↓	↓↑	↓↑	↓↑	↓↑	↓↑	↑	↓↑	↑	↓	↑	↓↑
Observation	↓↑	↓↑	↓↑*	↓	↓↑	↓↑	↑	↓↑*	↓↑	↑	↓↑	↓↑	↓	↑	↓*

†The arrow means the favorable direction of an approaching nucleophile; ↓ coming from the upside (the β-site of the D-series compounds), ↑ from the downside (the α-site) of the molecule and the longer, the more important. * Solvent effects were observed in one, at least, reaction. - means negligible. *If hindrance due to the quasi-axial substituent is taken into consideration, prediction is not inconsistent with observation.

illustrated. Axial attack (↓) predominates by the factor (i), and trans addition (↑, equatorial attack) to the γ-substituent (the anomeric methoxyl group) and cis addition (↑, equatorial attack) to the β′-substituent (the oxygen atom at C-4) are favorable by the factors (ii) and (iii), respectively. Consequently, equatorial attack should preponderate over axial attack; this prediction agrees with the observation. The prediction is based on that the compounds **35**, **36** and **37**, which are not so rigid compared with the other compounds, occupy the S°, S_0 and $^{\circ}S$ conformation, respectively, from conformational analysis (favorable equatorial orientation of the substituent at C-5 and anomeric effect).[40] Furthermore, molecular model investigation strongly suggests that, in the compound **37**, steric and electrostatic repulsion due to the anomeric methoxyl group is more serious than those due to the benzoyloxymethyl group at C-5. The data included in Table 2 are as follows: (a) Almost exclusive equatorial attack to **5** was observed in the Michael reaction,[20] epoxidation,[21] amidation with N-bromoacetamide (NBA),[22] or the addition of hydrogen cyanide,[4,23] S-ylides,[24] a deuteride ion,[25] and organo copper reagents.[26] Anthranilic acid exceptionally approached from the axial side of **5**;[19] one possible explanation of this result is presented.[4]. A similar trend was found in the reaction of **22** with sodium borodeuteride, methylmagnesium iodide, acetic acid, and hydrazoic acid,[2] as well as in the reaction of **23** with hydrazoic acid.[27] (b) Axial attack predominated over equatorial attack in the reactions of **8** with hydrazoic acid, hydrogen cyanide, and 2,6-dichloropurine,[28] active methylene compounds,[29,30] hydrogen peroxide,[21a] S-ylides,[31] sodium borodeuteride,[25] NBA,[22] and organo copper reagents.[26] Similar findings were reported in the reactions of **24** with methanol, acetic acid, 2-methoxyethanol, and sodium borodeuteride[2] and in the reactions of **25** with hydrazoic acid and hydrogen cyanide.[27] (c) Equatorial attack exclusively occurred in amidation of **26** with NBA[22] and the addition of hydrogen cyanide[4] and organo copper reagents,[26] while in epoxidation equatorial and axial attacks were observed in the ratio of 5:1.[21a] (d) Exclusive axial attack was observed in amidation with NBA,[22] epoxidation,[21a] and reduction with sodium borodeuteride of **27**.[32] (e) Highly selective axial attack was detected in the reaction of **28** with hydrogen cyanide, whereas equatorial and axial attacks almost equally occurred in reduction with sodium borodeuteride.[25] (f) As had been described in this paper, nucleophiles almost exclusively attacked from the equatorial side of **3** in the reactions with methanol and 2,4-pentanedione, while the selectivity decreased in the reactions with hydrogen cyanide and sodium borodeuteride. Equatorial attack took place in the reactions of **1** with methoxide, azide, and deuteride ions.[6] (g) A cyanide ion attacked from the axial side of **2**.[8] (h) Almost exclusive equatorial attack was found in the reactions of **9** with active methylene compounds,[13] t-butyl peroxide, and methoxide ions, whereas methanol, sodium borodeuteride, and hy-



drogen cyanide exclusively approached from the axial side of **9**.[9,14] Axial attack also occurred in reduction of **29** with sodium borodeuteride.[2] (i) Peroxide and deuteride ions added from the axial and equatorial sides of **30** in the ratio of *ca* 3:1, whereas t-butyl peroxide and 2,4-pentanedione ions exclusively came from the equatorial side.[33] (j) Methanol almost exclusively added from the axial side of **31**[9] and **32**.[13] (k) Methanol almost equally attacked from the axial and equatorial sides of **33**.[9] (l) Predominant addition of methanol from the axial side of **34** was observed.[34] (m) Axial attack exclusively occurred in the reactions of **35** with hydrazoic acid,[35,36] hydrogen peroxide,[35] and diazomethane.[37] (n) Profound attack from the antiparallel direction of the methoxyl group was observed in the reaction of **36** with ethoxycarbonyl-2-lithio-1,3-dithiolane.[38] Since the conformation of product has some ambiguity, the terms axial and equatorial attack are not suitable. (o) Hydrazoic acid exclusively came from the axial side of **37**.[39]

EXPERIMENTAL

All the m.ps were determined with a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 polarimeter. Solutions were dried over $MgSO_4$ and evaporated under diminished pressure. Column chromatography was conducted on silica gel (Wakogel C-300). Tlc was performed with Merck (Darmstadt) silica gel GF 254. The catalyst used refers to tributylhexadecylphosphonium bromide. IR spectra were recorded for potassium bromide pellets, and ^{1}H-NMR spectra were recorded with a JNM PS-100 (JEOL) spectrometer.

Methyl 4,6-O-*benzylidene*-2-*deoxy*-2-*nitro*-β-D-*glucopyranoside* (**4**). A mixture of 3-nitro alkene **5**[41] (1.03 g, 3.53 mmol), $NaNO_2$ (1.10 g, 16 mmol), the catalyst (70 mg), benzene (70 ml), and H_2O (7 ml) was stirred for 2 h at room temp. The organic layer was separated and the aqueous layer was extracted with benzene. The combined organic layers were washed with H_2O, dried, and evaporated. To the residue was added pyridine (14 ml) and H_2O (4.5 ml) and the resulting mixture was stirred for 4 h at room temp. After evaporation of the mixture *in vacuo* (*ca* 1 mmHg), CH_2Cl_2 was added to the residue and the solution was successively washed with dil aq HCl and H_2O, dried, and evaporated to a solid. Recrystallization from EtOH–Me_2CO afforded 460 mg (42%) of **4**. The mother liquor was evaporated and the resulting residue was chromatographed eluting successively with benzene and benzene–ethyl acetate (50:1, 20:1, and 10:1, v/v). The fast-moving component gave 131 mg (12%) of the 3-nitro alcohol **11**.[41] The slow-moving component afforded 168 mg (total yield, 57%) of the 2-nitro alcohol **4**.[10] These compounds were identical (tlc and IR and ^{1}H-NMR spectroscopy) with the corresponding authentic samples, respectively.

Methyl 4,6-O-*benzylidene*-2,3-*dideoxy*-2-*nitro*-β-D-erythro *hex*-2-*enopyranoside* (**3**). To a stirred soln of **4** (2.04 g 6.55 mmol) and Et_3N (2.28 ml, 16.3 mmol) in THF (170 ml) was added dropwise $MeSO_2Cl$ (980 mg, 8.56 mmol) at room temp. After stirring for 30 min, Et_3N (1.14 ml, 8.2 mmol) and $MeSO_2Cl$ (490 mg, 4.28 mmol) were again added to the mixture. After stirring for 15 min, the mixture was diluted with benzene (50 ml) and the organic layer was washed with sat aq NaCl, dried, and evaporated. Recrystallization from Et_2O yielded 1.63 g (85%) of **3**, identical with an authentic sample.[10]

Similar treatment of **5** (586 mg, 2 mmol) with $NaNO_2$(623 mg, 9 mmol) in benzene (40 ml)-D_2O (4 ml), followed by hydration with pyridine–H_2O, and subsequent dehydration with $MeSO_2Cl$ and Et_3N gave the C-3 partially deuterated derivative of **3** (238 mg, 38%). Acetylation of the partially deuterated derivative of **4** (62 mg, 0.2 mmol) with acetic anhydride (0.15 ml)-pyridine (0.12 ml) in CH_2Cl_2 (1 ml) for 2.5 h at room temperature afforded the acetate **12** (60.5 mg, 68%), ^{1}H-NMR spectrum of which showed that *ca* 40% of **12** was deuterated at C-3.

Methyl 4,6 - O - *benzylidene* - 2,3 - *dideoxy* - 3 - C - *diacetylmethyl* - 2 - *nitro* - β - D - *glucopyranoside* (**13**). To an ice-cooled soln of **3** (145 mg, 0.5 mmol) in THF (10 ml) was added 0.1 M aq NaOH (1 ml) with stirring. After stirring for 30 min at ambient temperature, the mixture was de-ionized with Amberlite IR-120 (H^+) cation-exchange resin, the resin was filtered off, and the filtrate evaporated to a solid, which was recrystallized from EtOH to provide 169 mg (87%) of **13**; m.p. 111–112°, $[\alpha]_D^{22}$ – 60.3°(*c* 0.54, $CHCl_3$); IR: 1730, 1700 (CO), and 1555 cm^{-1} (NO_2). (Found:C, 57.94; H, 5.80; N,

3.83. Calc for $C_{19}H_{23}NO_8$: C, 58.01; H, 5.89; N, 3.56%.)

Methyl 4,6-O-*benzylidene*-2-*deoxy*-3-O-*methyl*-2-*nitro*-β-D-*glucopyranoside* (**14**). A soln of the nitro-alcohol **3** (89 mg, 0.3 mmol) in MeOH (6 ml) was heated for 1 h under reflux. The mixture was cooled and evaporated to a solid, which was almost pure **14**, as judged from ^{1}H-NMR spectra. Recrystallization from EtOH–hexane gave 70 mg (71%) of **14**; m.p. 135–136°, $[\alpha]_D^{20} - 51.5°$ (*c* 0.74, $CHCl_3$); IR: 1550 cm^{-1} (NO_2). (Found: C, 55.62; H, 5.87; N, 4.27. Calc. for $C_{15}H_{19}NO_7$: C, 55.38; H, 5.89; N, 4.31%.)

A soln of methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-2-nitro-β-D-allopyranoside (**15**)[14] (23 mg, 0.07 mmol) in MeOH (1.4 ml) was heated for 1 h under reflux and evaporated to give unchanged **15** in almost quantitative yield. The IR and ^{1}H-NMR spectra were identical with those of an authentic specimen.[14]

Methyl 4,6-O-*benzylidene*-2,3-*dideoxy*-2-*nitro*-β-D-*ribo*-*hexopyranoside* (**16**). To a soln of **3** (89 mg, 0.3 mmol) in CH_3CN (6 ml) was added $NaBH_4$ (30 mg, 0.79 mmol) with stirring at room temp. After stirring for 140 min, excess reagent was decomposed with AcOH (0.3 ml) and the mixture was partitioned between H_2O (10 ml) and $CHCl_3$ (3 × 10 ml). The combined extracts were successively washed with aq $NaHCO_3$ and H_2O, dried, and evaporated to a solid. Recrystallization from EtOH yielded 66 mg (74%) of **16**; m.p. 169–169.5°, $[\alpha]_D^{22} - 55.6°$ (*c* 1, $CHCl_3$); IR: 1545 cm^{-1} (NO_2). (Found: C, 56.92; H, 5.78; N, 4.76. Calc for $C_{14}H_{17}NO_6$: C, 56.94; H, 5.80; N, 4.74%.)

Similar treatment of **3** with $NaBD_4$ afforded a mixture of **17** and **18**, which have an axial and equatorial deuterium atom at C-3, respectively, in the ratio of 1:2, as estimated from ^{1}H-NMR spectroscopy.

Methyl 4,6-O-*benzylidene*-3-*cyano*-2,3-*dideoxy*-2-*nitro*-β-D-*gluco* (**19**) *and* -D-*allopyranoside* (**20**). To a soln of **3** (85 mg, 0.29 mmol) and HCN (1.0 ml, *ca* 1.6 M in CH_3CN) in 1,4-dioxane (15 ml, chromatographed through neutral Al_2O_3 just before use) was added KCN (30 mg). The mixture was stirred at room temp. until disappearance of the spot due to **3** in tlc (*ca* 6.75 h) and then partitioned between $CHCl_3$ and H_2O. The organic layers were washed with H_2O, dried, and evaporated to give a residue (71 mg) containing **19** and **20** in the ratio of *ca* 4.5:1, as judged from the integration of ^{1}H-NMR signals of benzylidene methine and methoxyl groups. The residue was chromatographed with benzene as the eluant to give 55 mg of **19** as the fast-moving fraction and 11 mg of **20** as the slow-moving fraction. Analytical samples were obtained by recrystallization from isopropanol; compound **19** had m.p. 139.5–140.5°; $[\alpha]_D^{22} - 82.2°$ (*c* 0.72, CH_2Cl_2); IR: 2240 (CN) and 1565 cm^{-1} (NO_2). (Found: C, 56.40; H, 4.96; N, 8.56. Calc for $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.04; N, 8.75%.)

Compound **20** had m.p. 143.5–144.5°; $[\alpha]_D^{22} - 23.2°$ (*c* 1, CH_2Cl_2); IR: 2230 (CN) and 1550 cm^{-1} (NO_2). (Found: C, 56.02; H, 4.98; N, 8.57. Calc for $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.04; N, 8.75%.)

Treatment of **3** (14.5 mg) with HCN (0.05 ml, *ca* 1.6 M CH_3CN solution) in the presence of KCN (3.2 mg) in CH_3CN (0.5 ml) for 30 min at room temperature afforded a mixture of **19**, **20** and **21** in the ratio of *ca* 2.5:1:2 as estimated by ^{1}H-NMR spectroscopy.

Methyl 4,6 - O - *benzylidene* - 3 - *cyano* - 2,3 - *dideoxy* - β - D - erythro - *hex* - 2 - *enopyranoside* (**21**). A mixture of **3** (89 mg, 0.3 mmol), HCN (1 ml, *ca* 2 M in CH_3CN), KCN (30 mg), 1,4-dioxane (15 ml) or THF (15 ml) was stirred for 24 h at room temp. The mixture was partitioned between CH_2Cl_2 and H_2O and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with H_2O, dried, and evaporated to a residue, whose ^{1}H-NMR spectrum showed that it mainly consisted of **21**, together with small amounts of **19** and **20**. Recrystallization from EtOH afforded 59 mg (71%) of **21**; m.p. 164–165°, $[\alpha]_D^{22} - 25°$ (*c* 0.5, $CHCl_3$); IR: 2230 cm^{-1} (CN). (Found: C, 65.69; H, 5.62; N, 5.11. Calc for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13%.)

Attempt at epimerization of the allopyranoside **20**. The allopyranoside **20** (15 mg, 0.05 mmol) was treated with HCN (0.1 ml, *ca* 1.6 M in CH_3CN) in 1,4-dioxane (2.5 ml) in the presence of KCN (4.9 mg) for 6.75 h at room temp. Similar procedure described above gave a residue, the ^{1}H-NMR spectrum of which showed that it was almost pure **20**, together with a trace of **21**.

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