Diastereoselective Hydrocyanation of Chiral Nitrones. Synthesis of Novel α-(Hydroxyamino) Nitriles

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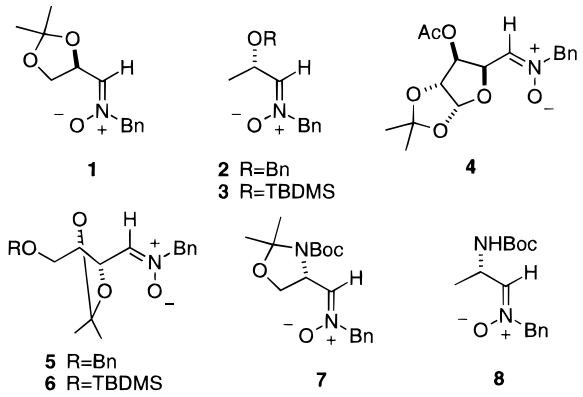
Received July 9, 1996

The asymmetric hydrocyanation of carbonyl compounds constitutes a useful transformation in organic chemistry[1] due to the utility of the resulting optically active cyanohydrins as useful precursors of many important classes of organic compounds.[2] In particular, when the reaction is conducted in the presence of either ammonium chloride or salts of amines (Strecker synthesis), α-amino nitriles, which are direct precursors of α-amino acids, are obtained.[3] In the asymmetric version of the reaction a great number of alternative approaches to the classical Strecker conditions have been described in the past,[4] the most popular being the addition of cyanide to chiral imines.[5] By contrast, other chiral nonracemic substrates bearing a carbon−nitrogen double bond have not been investigated. To our knowledge only three reports concerning the nonasymmetric addition of cyanide to oximes[6] and nitrones[7] have been described.

Nitrones are a particularly interesting class of compounds by virtue of their utility in organic synthesis. They are reactive starting materials in a large number of 1,3-dipolar cycloadditions[8] and can act as electrophiles with a variety of both carbon[9] and heteronucleophiles.[10] In this context, we and Dondoni's group have amply demonstrated the synthetic utility of nitrones (readily accessible from the parent carbonyl compounds[11]) for the preparation of several nitrogen-containing compounds of interest (i.e., aza- and aminosugars,[12] amino acids,[13] amino aldehydes,[12] allyl amines,[14] nucleoside antibiotics,[15] and (aminomethyl)thiazoles[16]). Within our continuing interest in the application of the nucleophilic addition to nitrones in organic synthesis, we have investigated the stereoselective hydrocyanation of α-alkoxy and α-amino nitrones and herein we report our results.[17]

Chart 1



Results

The results from the hydrocyanation of the various nitrones **1**−**8** (Chart 1) are summarized in Table 1. The obtained α-(hydroxyamino) nitriles **9**−**21** (Scheme 1) are collected in Chart 2.

The nitrone **1** was studied as a prototypical probe of stereoselective induction (entries 1−11, Table 1). The reaction with various cyanide reagents proceeded highly stereoselectively (entries 1, 2, 4, 7, 8, and 10, Table 1) giving a mixture of *syn*-**10a** and *anti*-**10b**. In the case of

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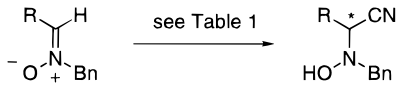
S0022-3263(96)01293-5 CCC: $12.00

Table 1. Stereoselective Addition of Cyanide Reagents to Nitrones 1−8

entry	nitrone	cyanide reagent (equiv)	additive[a]	solvent	*T* (°C)	time (h)	syn:anti	yield[b] (%)	adduct
1	**1**	Me_3SiCN (5.0)	none	CH_2Cl_2	0	48	≥95:5	84	**9**
2	**1**	Me_3SiCN (3.0)	none	MeOH	20	48	81:19	100	**10**
3	**1**	Me_3SiCN (1.1)	Et_2AlCl	CH_2Cl_2	0	4	≥95:5	68	**9**
4	**1**	Et_2AlCN (1.1)	none	CH_2Cl_2	0	2	68:32	90	**10**
5	**1**	Et_2AlCN (5.0)	none	CH_2Cl_2	0	2	44:56	65	**10**
6	**1**	Et_2AlCN (1.1)	Me_3SiCl	CH_2Cl_2	0	2	46:54	80	**9**
7	**1**	Et_2AlCN (1.1)	none	THF	0	6	86:14	91	**10**
8	**1**	Bu_4NCN (1.1)	none	CH_2Cl_2	−60	12	83:17	86	**10**
9	**1**	Bu_4NCN (1.1)	Et_2AlCl	CH_2Cl_2	−60	12	74:26	64	**10**
10	**1**	LiCN (1.1)	none	$THF-CH_2Cl_2$	−60	2	86:14	82	**10**
11	**1**	LiCN (1.1)	Et_2AlCl	$THF-CH_2Cl_2$	−60	2	80:20	80	**10**
12	**2**	Me_3SiCN (3.0)	none	CH_2Cl_2	20	48	70:30	98[c]	**11**
13	**2**	Me_3SiCN (3.0)	none	MeOH	20	48	71:29	100	**12**
14	**2**	Et_2AlCN (1.1)	none	THF	−40	6	73:27	100	**12**
15	**2**	Et_2AlCN (1.1)	none	toluene	−80	16	80:20	96	**12**
16	**2**	LiCN (1.1)	none	$THF-CH_2Cl_2$	−60	24	55:45	85	**12**
17	**3**	Me_3SiCN (3.0)	none	CH_2Cl_2	0	48	68:32	94	**13**
18	**3**	Et_2AlCN (1.1)	none	THF	−40	6	75:25	90	**14**
19	**4**	Me_3SiCN (3.0)	none	MeOH	0	48	70:30	96	**15**
20	**4**	Et_2AlCN (1.1)	none	THF	−60	6	65:35	90	**15**
21	**4**	Et_2AlCN (3.0)	none	THF	−60	6	56:44	88	**15**
22	**5**	Me_3SiCN (3.0)	none	CH_2Cl_2	0	48	80:20	96	**16**
23	**5**	Me_3SiCN (3.0)	none	MeOH	0	48	83:17	100	**17**
24	**5**	Et_2AlCN (1.1)	none	THF	0	4	86:14	93	**17**
25	**5**	Et_2AlCN (1.1)	none	THF	−60	6	90:10	95	**17**
26	**6**	Me_3SiCN (3.0)	none	MeOH	0	48	92:8	100	**18**
27	**6**	Et_2AlCN (1.1)	none	THF	−60	6	90:10	86	**18**
28	**6**	Et_2AlCN (1.1)	Et_2AlCl	THF	−60	6	59:41	89	**18**
29	**7**	Me_3SiCN (3.0)	none	CH_2Cl_2	0	48	≥95:5	98[c]	**19**
30	**7**	Me_3SiCN (3.0)	none	MeOH	0	48	≥95:5	100	**20**
31	**7**	Et_2AlCN (1.1)	none	THF	−60	6	≥95:5	96	**20**
32	**7**	Et_2AlCN (1.1)	Et_2AlCl	THF	−60	6	≥95:5	98	**20**
33	**8**	Me_3SiCN (3.0)	none	MeOH	0	48	70:30	100	**21**
34	**8**	Et_2AlCN (1.1)	none	THF	−60	6	76:24	96	**21**

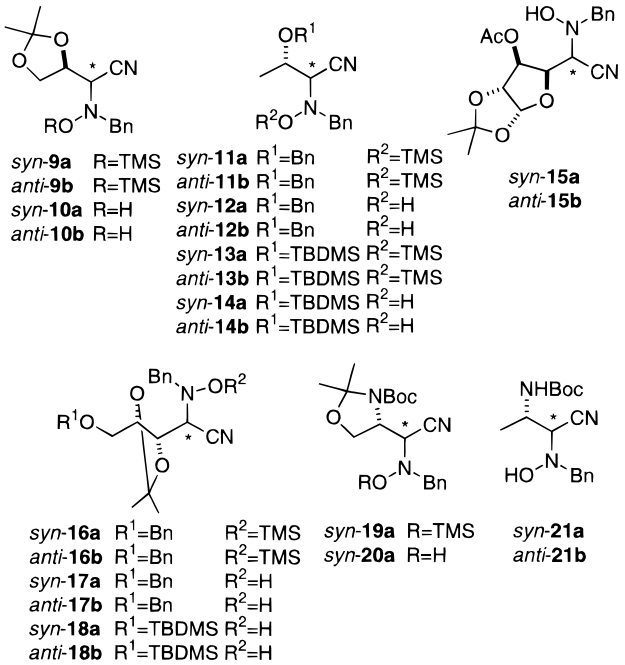
[a] 1.0 equiv was used. [b] Isolated yield of the crude mixture of diastereomers.

Scheme 1



the reaction of **1** with trimethylsilyl cyanide in dichloromethane as a solvent (entry 1, Table 1) the corresponding *O*-(trimethylsilyl) derivative *syn*-**9a** was obtained.[18] In this case only one diastereoisomer could be detected by NMR. On the other hand, the lower selectivity was observed with 1.1 equiv of diethylaluminum cyanide in dichloromethane at 0 °C (entry 4, Table 1).[19] At lower temperatures (−60 °C) and using tetrahydrofuran as a solvent, the diastereofacial selectivity was improved to a ratio of 86:14 (entry 7, Table 1). In previous reports from our laboratory we described the use of diethylaluminum chloride as an efficient precomplexing agent for inducing the reversal of selectivity in nucleophilic additions to **1**.[12a,14,20] However, when **1** was treated with diethylaluminum chloride and then trimethylsilyl cyanide (entry 3, Table 1) the same sense of diastereofacial preference was observed as that in the absence of the chelating agent. This behavior can be attributed to the competitive reaction between diethylaluminum chloride and trimethylsilyl cyanide to form diethylaluminum cyanide and trimethylsilyl chloride.[21] In fact, when nitrone **1** was added to a mixture of diethylaluminum cyanide and trimethylsilyl chloride the same stereochemical result was obtained. Surprisingly, when the nitrone

Chart 2



(18) *O*-(Trimethylsilyl) derivatives can be readily transformed into the α-(hydroxyamino) nitriles by treatment with 4% p/v methanolic citric acid at room temperature.

(19) In our previous paper (see ref 17) we reported a reversed selectivity for these conditions. After several repetitions we were unable to obtain our previously reported result.

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(21) The reaction of both reagents to give diethylaluminum cyanide has been previously described. See: Imi, K.; Yanagihara, N.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 1013−1016.

1 was previously treated with trimethylsilyl chloride and then diethylaluminum cyanide (entry 6, Table 1) a complete lack of selectivity was observed and a 46:54 mixture of *syn*-**9a** and *anti*-**9b** was obtained. A similar result was observed when the reaction was carried out with an excess of diethylaluminum cyanide (entry 5, Table 1). When the reaction was made with 1 equiv of diethylaluminum cyanide in the presence of 1 equiv of diethylaluminum chloride an identical lack of selectivity was found. These results support the possibility of diethylaluminum cyanide acting both as a cyanide equivalent and as a chelating agent (see below). Precomplexation of **1** with diethylaluminum chloride had little effect upon the addition of other cyanide reagents like tetrabutylammonium cyanide (entry 9, Table 1) or lithium cyanide (entry 11, Table 1).

Since better and more interesting results were obtained with trimethylsilyl cyanide and diethylaluminum cyanide we examined them in greater detail with other nitrones. In all the substrates tested thus far the *syn* α-(hydroxyamino) nitriles were obtained as major adducts. When trimethylsilyl cyanide was used in dichloromethane the corresponding *O*-(trimethylsilyl) derivatives were obtained[22] (entries 12, 17, 22, 29, Table 1). Again, the use of diethylaluminum chloride as additive (entry 28, Table 1) or an excess of diethylaluminum cyanide (entry 21, Table 1) led to a considerable decrease in the diastereoselectivity. For the L-serine-derived nitrone **7**, >95% diastereoselectivity toward the *syn* adduct was achieved in all cases (entries 29−32, Table 1). It is notable that, regardless of the level of the diastereofacial selectivity, excellent yields were consistently observed for all nitrones tested.

The configurational assignment of *syn* and *anti* α-(hydroxyamino) nitriles **9**−**21** was based on X-ray structural analyses of the adducts *anti*-**10b** *anti*-**12b**, *anti*-**15b**, and *syn*-**20a**, which confirmed the stereochemical outcome of the addition to nitrones **1**, **2**, **4**, and **7**, respectively.[23] The configurational assignments of the other adducts were made on the basis of analogy, since the ^{1}H and ^{13}C NMR data did not allow for general rules regarding the configurational assignment. It is noteworthy that in all cases the R_f value (TLC) of the major diastereomer (*syn* adduct) was larger than that of the minor diastereomer (*anti* adduct). Similar behavior has been previously observed by Reetz and co-workers for amino alcohols and diamines.[5d]

The observed sense of the diastereoselectivity conforms to our previously proposed model[12] **A**, similar to that invoked by Houk for asymmetric addition to double bonds.[24] This model has been further supported for α-alkoxy nitrones by semiempirical calculations made for nitrone **1**.[25] In the case of α-amino nitrones **7** and **8** both chemical and structural observations led to the same model.[26] However, as we pointed out in our preliminary paper,[17] the possibility that diethylaluminum cyanide can act like both a cyanide transfer reagent and a chelating agent, leading to internal and/or external cyanide delivery, respectively, makes the above interpretation rather speculative, and other possibilities to explain the results may exist.

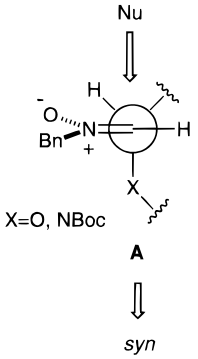

Figure 1. Proposed model for the addition of cyanide reagents to nitrones.

In conclusion, we have described a stereoselective entry to novel optically active α-(hydroxyamino) nitriles. The addition of both trimethylsilyl cyanide and diethylaluminum cyanide to chiral nitrones proceeds with good to excellent diastereoselectivity and very high yields (quantitative in some cases). Further studies on the synthetic utility of the prepared α-(hydroxyamino) nitriles for their use as starting materials in the preparation of α-amino nitriles and α-(hydroxyamino) acids are ongoing and will be published in due course.

Experimental Section

General Methods. For general experimental information see ref 27. Nitrones **1**−**8** were prepared as described.[11b] Trimethylsilyl cyanide was purchased from Aldrich (98%) and used without further purification. Diethylaluminum cyanide was prepared from diethylaluminum chloride (Aldrich) and trimethylsilyl cyanide as described,[21] and accompanying trimethylsilyl chloride was removed under reduced pressure in the absence of moisture; in one case (Table 1, entry 15), diethylaluminum cyanide was used in toluene from a 1.0 M commercial solution. Tetrabutylaluminum cyanide was prepared by treating a solution of trimethylsilyl cyanide in dichloromethane with anhydrous tetrabutylammonium fluoride. Lithium cyanide was prepared by treating a solution of trimethylsilyl cyanide in dichloromethane with a 1.6 M solution of butyllithium in hexanes.

Precomplexation of Nitrones. When trimethylsilyl chloride or diethylaluminum chloride was used as additive a solution of the nitrone (1 mmol) in the corresponding solvent (Table 1) was treated at ambient temperature with 1.0 equiv of the additive. The resulting mixture was stirred for 5 min at ambient temperature prior to the addition of the cyanide reagent.

Typical Procedure for the Addition of Cyanide Reagents to Nitrones. To a solution of nitrone (1 mmol) in the solvent (25 mL) and at the temperature indicated in Table 1 was added the corresponding cyanide reagent (see Table 1 for equivalents). The reaction was kept at the indicated temperature for the given time (see Table 1). The reaction mixture was then quenched by the addition of either 1 N NaOH (15 mL) (when diethylaluminum cyanide or diethylaluminum chloride was used) or brine (15 mL). Dichloromethane (10 mL) was added, and the organic layer was separated. The aqueous layer was extracted twice with dichloromethane (20 mL), and the

(22) Compounds **11** and **13** could not be separated, and they were isolated and characterized as the corresponding α-(hydroxyamino) nitriles **12** and **14**, respectively. In addition, compounds *anti*-**16b** and *anti*-**17b** could not be isolated as single diastereoisomers.

(23) The authors have deposited atomic coordinates, bond lengths, and angles for structures *anti*-**10b**, *anti*-**11b**, *anti*-**13b**, and *syn*-**18a** with the Cambridge Crystallographic Data Centre. The data can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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combined organic extracts were washed with brine, dried over magnesium sulfate, and evaporated under reduced pressure to yield the crude product, which was purified by column chromatography. Both the diastereoselectivities (measured from the isolated mixture of diastereomers by ^{1}H NMR) and the chemical yields are given in Table 1.

***N*-Benzyl-1-cyano-1-deoxy-1-((trimethylsiloxy)amino)-2,3-*O*-isopropylidene-D-*threo*-triitol (*syn*-9a)** (90:10 hexane−diethyl ether, R_f 0.31): oil; $[\alpha]_D$ −43.4° (*c* 1.1, $CHCl_3$); ^{1}H NMR (55 °C) δ 0.21 (s, 9H), 1.29 (s, 3H), 1.31 (s, 3H), 3.76 (d, 1H, J = 5.6 Hz), 3.96 (d, 1H, J = 12.7 Hz), 4.03 (dd, 1H, J = 9.3, 6.1 Hz), 4.10 (dd, 1H, J = 9.3, 6.1 Hz), 4.20 (d, 1H, J = 12.7 Hz), 4.25 (pseudo q, 1H, J = 6.1 Hz), 7.29−7.38 (m, 5H); ^{13}C NMR (55 °C) δ −0.2, 25.2, 26.4, 61.4, 63.6, 67.2, 74.2, 109.7, 114.7, 128.4, 128.8, 129.4, 134.7. Anal. Calcd for $C_{17}H_{26}N_2O_3Si$: C, 61.04; H, 7.84; N, 8.37. Found: C, 60.82; H, 8.09; N, 8.40.

***N*-Benzyl-1-cyano-1-deoxy-1-((trimethylsiloxy)amino)-2,3-*O*-isopropylidene-D-*erythro*-triitol (*anti*-9b)** (90:10 hexane−diethyl ether, R_f 0.22): oil; $[\alpha]_D$ +35.9° (*c* 0.76, $CHCl_3$); ^{1}H NMR (55 °C) δ 0.09 (s, 9H), 1.30 (s, 3H), 1.34 (s, 3H), 3.55 (d, 1H, J = 8.1 Hz), 3.78 (dd, 1H, J = 8.9, 4.2 Hz), 3.94 (d, 1H, J = 12.7 Hz), 3.95 (dd, 1H, 8.9, 5.9 Hz), 4.14 (d, 1H, J = 12.7 Hz), 4.21 (ddd, 1H, J = 8.1, 5.9, 4.2 Hz), 7.29−7.36 (m, 5H); ^{13}C NMR (55 °C) δ −0.4, 25.0, 26.9, 61.3, 64.0, 67.0, 72.5, 110.5, 115.2, 128.4, 128.8, 129.6, 134.8. Anal. Calcd for $C_{17}H_{26}N_2O_3Si$: C, 61.043; H, 7.84; N, 8.37. Found: C, 61.23; H, 7.95; N, 8.70.

***N*-Benzyl-1-cyano-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-D-*threo*-triitol (*syn*-10a)** (60:40 hexane−diethyl ether, R_f 0.33): white solid; mp 116 °C; $[\alpha]_D$ −34.8° (*c* 0.87, $CHCl_3$); ^{1}H NMR δ 1.30 (s, 3H), 1.32 (s, 3H), 3.75 (d, 1H, J = 7.1 Hz), 3.91 (d, 1H, J = 12.5 Hz), 4.02 (dd, 1H, J = 9.5, 4.6 Hz), 4.12 (dd, 1H, J = 9.5, 6.1 Hz), 4.19 (d, 1H, J = 12.5 Hz), 4.42 (ddd, 1H, J = 7.1, 6.1, 4.6 Hz), 6.26 (bs, 1H, ex. D_2O), 7.33−7.36 (m, 5H); ^{13}C NMR δ 25.4, 26.5, 61.0, 63.3, 67.0, 74.0, 110.3, 114.4, 128.4, 128.8, 129.6, 134.7. Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.11; H, 6.92; N, 10.68. Found: C, 64.34; H, 6.80; N, 10.42.

***N*-Benzyl-1-cyano-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-D-*erythro*-triitol (*anti*-10b)** (60:40 hexane−diethyl ether, R_f 0.26): transparent plates; mp 139 °C; $[\alpha]_D$ +8.6° (*c* 0.80, $CHCl_3$); ^{1}H NMR δ 1.33 (s, 3H), 1.43 (s, 3H), 3.58 (d, 1H, J = 7.9 Hz), 3.84 (d, 1H, J = 12.6 Hz), 3.94 (dd, 1H, J = 9.2, 4.0 Hz), 4.04 (dd, 1H, J = 9.2, 5.9 Hz), 4.14 (d, 1H, J = 12.6 Hz), 4.42 (ddd, 1H, J = 7.9, 5.9, 4.0 Hz), 5.39 (bs, 1H, ex. D_2O), 7.33 (bs, 5H); ^{13}C NMR δ 25.1, 26.8, 61.9, 63.1, 67.0, 74.2, 110.8, 115.0, 128.2, 128.7, 129.5, 135.3. Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.11; H, 6.92; N, 10.68. Found: C, 63.84; H, 7.11; N, 10.91.

***N*-Benzyl-2-*O*-benzyl-1-cyano-1,3-dideoxy-1-(hydroxyamino)-L-*threo*-triitol (*syn*-12a)** (90:10 hexane−diethyl ether, R_f 0.18): oil; $[\alpha]_D$ +5.3° (*c* 0.9, $CHCl_3$); ^{1}H NMR δ 1.37 (d, 3H, J = 6.3 Hz), 3.69 (d, 1H, J = 6.5 Hz), 3.84 (d, 1H, J = 12.8 Hz), 3.91 (pseudo quintuplet, 1H, J = 6.4 Hz), 4.15 (d, 1H, J = 12.8 Hz), 4.56 (d, 1H, J = 11.7 Hz), 4.64 (d, 1H, J = 11.7 Hz), 5.04 (bs, 1H, ex. D_2O), 7.26−7.39 (m, 10H); ^{13}C NMR δ 17.5, 62.7, 63.8, 71.7, 73.2, 115.2, 127.9, 127.9, 128.4, 128.6, 128.6, 129.3, 135.7, 137.6. Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.78; H, 6.68; N, 9.80.

***N*-Benzyl-2-*O*-benzyl-1-cyano-1,3-dideoxy-1-(hydroxyamino)-L-*erythro*-triitol (*anti*-12b)** (90:10 hexane−diethyl ether, R_f 0.12): white crystals; mp 95 °C; $[\alpha]_D$ −16.8° (*c* 1.10, $CHCl_3$); ^{1}H NMR δ 1.29 (d, 3H, J = 6.2 Hz), 3.53 (d, 1H, J = 8.4 Hz), 3.89 (d, 1H, J = 12.7 Hz), 3.95 (dq, 1H, J = 8.4, 6.2), 4.19 (d, 1H, J = 12.7 Hz), 4.60 (d, 1H, J = 11.2 Hz), 4.65 (d, 1H, J = 11.2 Hz), 4.99 (s, 1H, ex. D_2O), 7.26−7.39 (m, 10H); ^{13}C NMR δ 17.4, 63.1, 64.0, 72.1, 74.3, 115.7, 127.9, 128.0, 128.1, 128.5, 128.7, 129.4, 135.5, 137.5. Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 73.08; H, 7.08; N, 9.57.

***N*-Benzyl-2-*O*-(*tert*-butyldimethylsilyl)-1-cyano-1,3-dideoxy-1-(hydroxyamino)-L-*threo*-triitol (*syn*-14a)** (95:5 hexane−diethyl ether, R_f 0.21): oil; $[\alpha]_D$ +4.1° (*c* 0.21, $CHCl_3$); ^{1}H NMR δ 0.07 (s, 3H), 0.11 (s, 3H), 0.88 (s, 9H), 1.31 (d, 3H, J = 6.3 Hz), 3.54 (d, 1H, J = 5.2 Hz), 3.82 (d, 1H, J = 12.7 Hz), 4.15 (dq, 1H, J = 6.3, 5.2 Hz), 4.19 (d, 1H, J = 12.7 Hz), 5.50 (bs, 1H, ex. D_2O), 7.28−7.40 (m, 5H); ^{13}C NMR δ −6.5, −6.5, 20.8, 22.4, 25.5, 62.68, 54.6, 68.2, 115.7, 127.8, 128.4, 129.2, 135.5. Anal. Calcd for $C_{17}H_{28}N_2O_2Si$: C, 63.71; H, 8.81; N, 8.74. Found: C, 63.78; H, 8.54; N, 8.99.

***N*-Benzyl-2-*O*-(*tert*-butyldimethylsilyl)-1-cyano-1,3-dideoxy-1-(hydroxyamino)-L-*erythro*-triitol (*anti*-14b)** (95:5 hexane−diethyl ether, R_f 0.19): oil; $[\alpha]_D$ −12.3° (*c* 0.33, $CHCl_3$); ^{1}H NMR δ 0.10 (s, 3H), 0.15 (s, 3H), 0.90 (s, 9H), 1.24 (d, 3H, J = 6.3 Hz), 3.38 (d, 1H, J = 8.6 Hz), 3.85 (d, 1H, J = 12.7 Hz), 4.06 (dq, 1H, J = 8.6, 6.3 Hz), 4.12 (d, 1H, J = 12.7 Hz), 5.62 (bs, 1H, ex. D_2O), 7.30−7.38 (m, 5H); ^{13}C NMR δ −6.7, −6.3, 21.1, 22.4, 25.5, 62.9, 66.0, 67.6, 116.0, 127.8, 128.4, 129.2, 135.5. Anal. Calcd for $C_{17}H_{28}N_2O_2Si$: C, 63.71; H, 8.81; N, 8.74. Found: C, 63.54; H, 8.67; N, 8.65.

3-*O*-Acetyl-*N*-benzyl-5-cyano-5-deoxy-5-(hydroxyamino)-1,2-*O*-isopropylidene-β-L-*ido*-1,4-pentofuranoside (*syn*-15a) (40:60 hexane−diethyl ether, R_f 0.38): white solid; mp 94 °C; $[\alpha]_D$ −31.4° (*c* 1.60, $CHCl_3$); ^{1}H NMR δ 1.27 (s, 3H), 1.47 (s, 3H), 2.08 (s, 3H), 3.87 (d, 1H, J = 12.7 Hz), 4.02 (d, 1H, J = 8.0 Hz), 4.12 (d, 1H, J = 12.7 Hz), 4.50 (d, 1H, J = 3.7 Hz), 4.62 (dd, 1H, J = 5.9, 3.1 Hz), 5.12 (d, 1H, J = 3.1 Hz), 5.62 (bs, 1H, ex. D_2O), 5.89 (d, 1H, J = 3.7 Hz), 7.29−7.38 (m, 5H); ^{13}C NMR δ 20.4, 25.9, 26.4, 57.6, 62.9, 76.0, 76.3, 82.7, 104.6, 112.5, 113.8, 127.9, 128.4, 129.4, 135.1, 169.4. Anal. Calcd for $C_{18}H_{22}N_2O_6$: C, 59.66; H, 6.12; N, 7.63. Found: C, 59.60; H, 6.30; N, 7.94.

3-*O*-Acetyl-*N*-benzyl-5-cyano-5-deoxy-5-(hydroxyamino)-1,2-*O*-isopropylidene-α-D-*gluco*-1,4-pentofuranoside (*anti*-15b) (40:60 hexane−diethyl ether, R_f 0.31): transparent blocks; mp 136 °C; $[\alpha]_D$ −67.8° (*c* 1.8, $CHCl_3$); ^{1}H NMR δ 1.27 (s, 3H), 1.49 (s, 3H), 1.80 (s, 3H), 3.85 (d, 1H, J = 8.7 Hz), 3.90 (d, 1H, J = 12.5 Hz), 4.20 (d, 1H, J = 12.5 Hz), 4.39 (d, 1H, J = 3.6 Hz), 4.64 (dd, 1H, J = 8.7, 2.9 Hz), 5.30 (d, 1H, J = 2.9 Hz), 5.84 (bs, 1H, ex. D_2O), 5.88 (d, 1H, J = 3.6 Hz), 7.29−7.35 (m, 5H); ^{13}C NMR δ 20.6, 26.1, 26.62, 56.5, 63.1, 74.8, 77.0, 82.7, 104.9, 112.7, 114.6, 128.2, 128.8, 129.7, 134.8, 169.6. Anal. Calcd for $C_{18}H_{22}N_2O_6$: C, 59.66; H, 6.12; N, 7.63. Found: C, 59.62; H, 5.83; N, 7.89.

***N*-Benzyl-4-*O*-benzyl-1-cyano-1-deoxy-1-((trimethylsiloxy)amino)-2,3-*O*-isopropylidene-L-*xylo*-tetritol (*syn*-16a)** (80:20 hexane−diethyl ether, R_f 0.39): oil; $[\alpha]_D$ −27.6° (*c* 0.32, $CHCl_3$); ^{1}H NMR (55 °C) δ −0.22 (s, 9H), 1.54 (s, 3H), 1.57 (s, 3H), 3.69 (dd, 1H, J = 10.7, 4.8 Hz), 3.76 (dd, 1H, J = 10.7, 3.1 Hz), 3.93 (d, 1H, J = 13.1 Hz), 4.12−4.21 (m, 3H), 4.26 (d, 1H, J = 6.8 Hz), 4.61 (ABq, 2H, J = 12.7 Hz, $\Delta\delta$ = 0.042), 7.20−7.36 (m, 10H); ^{13}C NMR (55 °C) δ −0.4, 27.0, 27.5, 62.4, 63.2, 70.2, 73.6, 74.4, 78.6, 110.5, 114.6, 127.6, 127.8, 128.1, 128.3, 128.5, 129.7, 135.5, 138.1. Anal. Calcd for $C_{25}H_{34}N_2O_4Si$: C, 66.0; H, 7.54; N, 6.16. Found: C, 66.34; H, 7.19; N, 6.38.

***N*-Benzyl-4-*O*-benzyl-1-cyano-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-L-*xylo*-tetritol (*syn*-17a)** (80:20 hexane−diethyl ether, R_f 0.14): oil; $[\alpha]_D$ −14.3° (*c* 1.84, $CHCl_3$); ^{1}H NMR δ 1.36 (s, 3H), 1.40 (s, 3H), 3.58 (dd, 1H, J = 9.7, 6.9 Hz), 3.78 (dd, 1H, J = 9.7, 5.9 Hz), 3.87 (d, 1H, J = 12.7 Hz), 3.97 (d, 1H, J = 5.1 Hz), 4.20 (d, 1H, J = 12.7 Hz), 4.25 (dd, 1H, J = 6.6, 5.1 Hz), 4.48 (pseudo dt, 1H, J = 6.8, 5.9 Hz), 4.57 (s, 2H), 6.90 (bs, 1H, ex. D_2O), 7.30−7.40 (m, 10H); ^{13}C NMR δ 26.9, 27.2, 61.4, 62.9, 71.2, 73.8, 76.6, 78.8, 110.1, 114.7, 127.9, 128.1, 128.6, 128.7, 129.3, 129.5, 135.4, 136.9. Anal. Calcd for $C_{22}H_{26}N_2O_4$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.97; H, 6.65; N, 7.26.

***N*-Benzyl-4-*O*-(*tert*-butyldimethylsilyl)-1-cyano-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-L-*xylo*-tetritol (*syn*-18a)** (80:20 hexane−diethyl ether, R_f 0.22): oil; $[\alpha]_D$ −12.7° (*c* 2.10, $CHCl_3$); ^{1}H NMR δ 0.06 (s, 3H), 0.07 (s, 3H), 0.86 (s, 9H), 1.34 (s, 3H), 1.42 (s, 3H), 3.65 (dd, 1H, J = 10.0, 8.2 Hz), 3.85 (d, 1H, J = 12.6 Hz), 3.94 (dd, 1H, J = 10.0, 4.0 Hz), 4.11 (d, 1H, J = 4.6 Hz), 4.19 (d, 1H, J = 12.6 Hz), 4.21 (dd, 1H, J = 6.6, 4.6 Hz), 4.48 (ddd, 1H, J = 8.2, 6.6, 4.0 Hz), 7.09 (bs, 1H, ex. D_2O), 7.19−7.32 (m, 5H); ^{13}C NMR δ −5.8, −5.8, 22.6, 25.7, 26.9, 27.2, 61.3, 62.7, 65.3, 77.3, 79.6, 109.8, 114.7, 127.98, 128.5, 129.5, 135.3. Anal. Calcd for $C_{21}H_{34}N_2O_4Si$: C, 62.03; H, 8.43; N, 6.89. Found: C, 62.18; H, 8.24; N, 6.72.

***N*-Benzyl-4-*O*-(*tert*-butyldimethylsilyl)-1-cyano-1-deoxy-1-(hydroxyamino)-2,3-*O*-isopropylidene-L-*lyxo*-tetritol (*anti*-18b)** (80:20 hexane−diethyl ether, R_f 0.19): oil; $[\alpha]_D$ +3.7° (*c* 1.75, $CHCl_3$); ^{1}H NMR δ 0.03 (s, 3H), 0.05 (s, 3H), 0.85 (s, 9H), 1.37 (s, 3H), 1.44 (s, 3H), 3.70 (dd, 1H, J = 10.0, 3.2 Hz), 3.73 (d, 1H, J = 7.6 Hz), 3.89 (d, 1H, J = 12.6 Hz), 3.98 (dd, 1H, J = 10.0, 3.4 Hz), 4.06 (pseudo dt, 1H, J = 7.8, 3.3 Hz), 4.22 (d, 1H, J = 12.6 Hz), 4.38 (pseudo t, 1H, J = 7.7 Hz), 6.40 (bs, 1H, ex. D_2O), 7.29−7.38 (m, 5H); ^{13}C NMR δ −5.6, −5.5, 22.7, 25.8, 26.8, 27.1, 61.8, 61.9, 65.8, 78.5, 78.6, 110.4, 115.3, 128.37, 128.7, 129.4, 135.4. Anal. Calcd for $C_{21}H_{34}N_2O_4Si$: C, 62.03; H, 8.43; N, 6.89. Found: C, 61.72; H, 8.53; N, 6.83.

1,1-Dimethylethyl [*R*-(*R*)]-4-[(*N*-benzyl-*N*-(trimethylsiloxy)amino)cyanomethyl]-2,2-dimethyl-3-oxazolidinecarboxylate (*syn*-19a) (90:10 hexane−diethyl ether, R_f 0.19): white solid; mp 48 °C; $[\alpha]_D$ −8.2° (*c* 1.80, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 110 °C) δ 0.12 (s, 9H), 1.35 (s, 9H), 1.46 (s, 3H), 1.57 (s, 3H), 3.96 (d, 1H, J = 13.0 Hz), 4.07−4.19 (m, 3H), 4.16 (d, 1H, J = 13.0 Hz), 4.24 (dd, 1H, J = 8.7, 1.3 Hz), 7.28−7.35 (m, 5H); ^{13}C NMR (DMSO-d_6, 90 °C) δ −0.3, 23.3, 26.6, 27.8, 58.2, 60.8, 63.2, 65.3, 80.4, 93.6, 115.3, 128.1, 128.5, 129.8, 135.1, 151.4. Anal. Calcd for $C_{22}H_{35}N_3O_4Si$: C, 60.94; H, 8.15; N, 9.69. Found: C, 61.10; H, 8.43; N, 9.67.

1,1-Dimethylethyl [*R*-(*R*)]-4-[1-(*N*-benzyl-*N*-hydroxyamino)cyanomethyl]-2,2-dimethyl-3-oxazolidinecarboxylate (*syn*-20a) (80:20 hexane−diethyl ether, R_f 0.23): transparent blocks; mp 154 °C; $[\alpha]_D$ +20.0° (*c* 0.99, $CHCl_3$); ^{1}H NMR (55 °C) δ 1.29 (s, 3H), 1.47 (s, 3H), 1.52 (s, 9H), 3.56 (d, 1H, J = 9.8 Hz), 3.85 (d, 1H, J = 13.0 Hz), 3.92 (d, 1H, J = 10.0 Hz), 4.00 (dd, 1H, J = 10.0, 4.7 Hz), 4.25 (d, 1H, J = 13.0 Hz), 4.40 (dd, 1H, J = 9.8, 4.7 Hz), 7.25−7.39 (m, 5H), 7.69 (bs, 1H, ex. D_2O); ^{13}C NMR (55 °C) δ 24.5, 27.3, 28.3, 57.2, 61.1, 61.7, 65.2, 81.9, 95.0, 115.5, 127.8, 128.5, 129.0, 136.1, 154.2. Anal. Calcd for $C_{19}H_{27}N_3O_4$: C, 63.14; H, 7.53; N, 11.63. Found: C, 63.16; H, 7.74; N, 11.88.

(2*S*,3*S*)-2-(*N*-Benzyl-*N*-hydroxyamino)-3-((*tert*-butoxycarbonyl)amino)butanenitrile (*syn*-21a) (80:20 hexane−diethyl ether, R_f 0.12): white solid; mp 170 °C; $[\alpha]_D$ +3.3° (*c* 1.23, $CHCl_3$); ^{1}H NMR δ 1.34 (d, 3H, J = 6.8 Hz), 1.46 (s, 9H), 3.15 (d, 1H, J = 10.0 Hz), 3.84 (d, 1H, J = 13.1 Hz), 4.10 (ddq, 1H, J = 10.0, 9.3, 6.8 Hz), 4.21 (d, 1H, J = 13.1 Hz), 4.41 (d, 1H, J = 9.3 Hz), 7.28−7.35 (m, 5H), 7.38 (bs, 1H, ex. D_2O); ^{13}C NMR δ 17.6, 28.3, 46.3, 61.3, 65.0, 80.8, 115.7, 127.6, 128.4, 128.7, 136.2, 157.3. Anal. Calcd for $C_{16}H_{23}N_3O_3$: C, 62.93; H, 7.59; N, 13.76. Found: C, 62.63; H, 7.30; N, 13.73.

(2*R*,3*S*)-2-(*N*-Benzyl-*N*-hydroxyamino)-3-((*tert*-butoxycarbonyl)amino)butanenitrile (*anti*-21b) (80:20 hexane−diethyl ether, R_f 0.06): white solid; mp 187 °C; $[\alpha]_D$ −86.5° (*c* 0.33, $CHCl_3$); ^{1}H NMR δ 1.29 (d, 3H, J = 6.8 Hz), 1.43 (s, 9H), 3.54 (d, 1H, J = 3.7 Hz), 3.85 (d, 1H, J = 13.7 Hz), 4.30 (m, 1H), 4.33 (d, 1H, J = 13.7 Hz), 4.75 (d, 1H, J = 9.5 Hz), 7.01 (bs, 1H, ex. D_2O), 7.29−7.40 (m, 5H); ^{13}C NMR δ 17.7, 46.3, 61.8, 65.0, 80.9, 115.9, 127.6, 128.3, 129.0, 136.3, 156.9. Anal. Calcd for $C_{16}H_{23}N_3O_3$: C, 62.93; H, 7.59; N, 13.76. Found: C, 62.69; H, 7.53; N, 13.64.

Acknowledgment. Support from MEC (Project PB94-0598, Madrid, Spain) is gratefully acknowledged. A.L. thanks the DGA (Aragon, Spain) for a predoctoral fellowship. The authors are also indebted to Dr. J. A. Lopez (ICMA, Aragon) for his invaluable assistance in obtaining X-ray data during some of this work.

Supporting Information Available: ORTEP diagrams of *anti*-**10b**, *anti*-**12b**, *anti*-**15b**, and *syn*-**20a** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO961293A