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SYNTHESIS OF SOME 3-ALKOXYCARBONYL-3-C-CYANO-3-DEOXY-GLYCOSIDES BY THE REACTION OF 1,5-DIALDEHYDES WITH CYANOESTERS

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ABSTRACT

The reaction of α-(*R*)-methoxydiglycolaldehyde (**1**) with ethyl and *tert*-butyl cyanoacetate yielded methyl 2,4-di-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-β-D-*xylo*- (**4**) and -α-L-*xylo*-pentopyranosides (**5**) (isolated as acetyl derivatives), and methyl 3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-β-D-*xylo*- (**6**) and -α-L-*xylo*-pentopyranosides (**7**), respectively (1:1 addition products) (major products). The minor 1:2 addition products methyl 2-*O*-acetyl-3-*tert*-butoxycarbonyl-4-(1-*tert*-butoxycarbonyl-1-cyanomethyl)-3-*C*-cyano-3,4-dideoxy-α-L-*lyxo*- (**12**) and -α-L-*xylo*-pentopyranosides (**13**), and methyl 4-*O*-acetyl-3-*tert*-butoxycarbonyl-2-(1-*tert*-butoxycarbonyl-1-cyanomethyl)-3-*C*-cyano-2,3-dideoxy-β-D-*xylo*-pentopyranoside (**14**) were also isolated in the reaction of **1** with *tert*-butyl cyanoacetate followed by acetylation. Isomerizations were observed in the acetylation of **6** and **7**, yielding methyl 2,4-di-*O*-acetyl-3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-β-D-*xylo*- (**8**) and -α-L-*arabino*- (**9**), and -α-L-*lyxo*- (**10**) and -α-L-*xylo*-pentopyranosides (**11**), respectively. Methyl 2,4,6-tri-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-α-D-*gluco*- (**15**), -α-D-*manno*- (**16**), and -β-L-*gluco*-hexopyranosides (**17**) together with 3,4-dideoxyhexopyranosides (**18** and **19**) (1:2 addition products) were isolated in the reaction of α-(*S*)-methoxy-α′-(*R*)-hydroxymethyldiglycolaldehyde (**2**) with ethyl cyanoacetate after acetylation. The same reaction using α-(*R*)-methoxy-α′-(*R*)-hydroxymethyldiglycolaldehyde (**3**) gave methyl 2,4,6-tri-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-β-D-*gluco*-hexopyranoside (**20**) after acetylation. Reaction of **3** with *tert*-butyl cyanoacetate led to methyl 2,6-di-*O*-acetyl-3-*tert*-butoxycarbonyl-4-(1-*tert*-butoxycarbonyl-1-cyanomethyl)-3-*C*-cyano-3,4-dideoxy-β-D-*gluco*-hexopyranoside (**21**; 1:2 addition product) and methyl 2,4,6-tri-*O*-acetyl-3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-β-D-*gluco*-hexopyranoside (**22**; 1:1 addition product), after acetylation.

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INTRODUCTION

The present work is part of a programme on the synthesis of 3-deoxy-*C*-glycosyl derivatives and 3-deoxyglycosides, branched at C-3, by the reaction of 1,5-dialdehydes with active methylene compounds.

We have reported[1] on the reaction of thioglycolaldehyde, diglycolaldehyde, α-(*S*)-(3-ethoxycarbonyl-2-methylfur-5-yl)diglycolaldehyde, α-(*S*)-(3-acetyl-2-methylfur-5-yl)diglycolaldehyde, α-(*R*)-methoxydiglycolaldehyde (**1**), and α-(*S*)-methoxy-α'-(*R*)-hydroxymethyldiglycolaldehyde (**2**) variously with 2,4-pentanedione, ethyl cyanoacetate, malononitrile, cyanoacetamide, and ethyl and *tert*-butyl cyanoacetate. We now report the reactions of ethyl and *tert*-butyl cyanoacetate with **1**, **2**, and α-(*R*)-methoxy-α'-(*R*)-hydroxymethyldiglycolaldehyde (**3**).

RESULTS AND DISCUSSION

The reactions were carried out in aqueous 1,4-dioxane at room temperature, using piperidine (1%) as the catalyst and a 1:1 molar ratio of dialdehyde and active methylene compound. 1,5-Dialdehydes exist in equilibrium with the cyclic hydrated form[2] but, for simplicity, **1–3** have been depicted as dialdehydes.

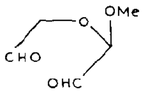
The products were isolated after acetylation of the crude product mixture (**4**, **5**, and **20**) or after acetylation of the individual components isolated by column chromatography (**8–19**, **21**, **22**, and **25**).

The reaction of **1** with ethyl cyanoacetate gave the diacetates **4** (minor) and **5** (major). When **1** reacted with *tert*-butyl cyanoacetate for 2.5 h, **6** and **7** were obtained, corresponding to 1:1 addition products, together with a small amount of a 1:2 addition product (**12**). The same reagents and longer reaction time (4 h) gave also the major products **6** and **7**, and two minor products (**13** and **14**) of 1:2 addition.

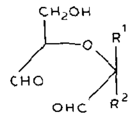
The reaction of **2** with ethyl cyanoacetate for 20 h gave a 4:1 mixture (^{1}H-n.m.r. data) of the α-D isomers **15** and **16*** and the β-L isomer **17**. When a longer reaction time (84 h) was used, a 10:1 mixture of **15** and **16** was obtained together with the 1:2 addition and de-ethoxycarbonylation products **18** and **19** (see Scheme 1). Epimerization involving the carbon atom bearing the hydroxymethyl group occurred in the formation of **17** and **18**. This effect was not observed previously in the reaction of **2** with *tert*-butyl cyanoacetate[1g]. When this reaction was re-investigated using the same conditions[1g] (96-h reaction time), **25** was isolated together with the reported compounds **23** + **24**. A similar epimerization has been reported[3] in the cyclization of **2** and **3** with nitroethane. The fact that this isomerization also occurs under the less basic conditions used here supports the view that it is unlikely to occur in the cyclized product.

Compound **20** was the only product isolated after the reaction of **3** with ethyl

*This mixture showed only one spot in t.l.c. and could not be resolved.

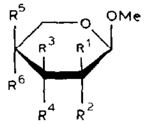


1



2 $R^1 = H, R^2 = OMe$

3 $R^1 = OMe, R^2 = H$



4 $R^1 = R^5 = H, R^2 = R^6 = OAc, R^3 = CO_2Et, R^4 = CN$

5 $R^1 = R^5 = OAc, R^2 = R^6 = H, R^3 = CN, R^4 = CO_2Et$

6 $R^1 = R^5 = H, R^2 = R^6 = OH, R^3 = Boc, R^4 = CN$

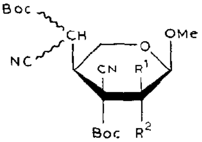
7 $R^1 = R^5 = OH, R^2 = R^6 = H, R^3 = CN, R^4 = Boc$

8 $R^1 = R^5 = H, R^2 = R^6 = OAc, R^3 = Boc, R^4 = CN$

9 $R^1 = R^6 = H, R^2 = R^5 = OAc, R^3 = Boc, R^4 = CN$

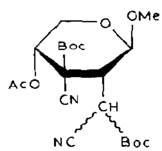
10 $R^1 = R^6 = H, R^2 = R^5 = OAc, R^3 = CN, R^4 = Boc$

11 $R^1 = R^5 = OAc, R^2 = R^6 = H, R^3 = CN, R^4 = Boc$

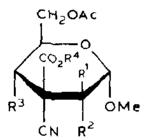


12 $R^1 = H, R^2 = OAc$

13 $R^1 = OAc, R^2 = H$



14



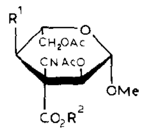
15 $R^1 = H, R^2 = R^3 = OAc, R^4 = Et$

16 $R^1 = R^3 = OAc, R^2 = H, R^4 = Et$

19 $R^1 = H, R^2 = OAc, R^3 = CH_2CN, R^4 = Et$

23 $R^1 = H, R^2 = R^3 = OH, R^4 = Bu^t$

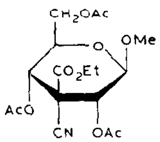
24 $R^2 = R^3 = OH, R^2 = H, R^4 = Bu^t$



17 $R^1 = OAc, R^2 = Et$

18 $R^1 = CH_2CN, R^2 = Et$

25 $R^1 = OAc, R^2 = Bu^t$



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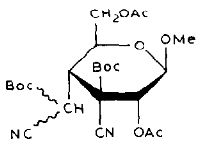

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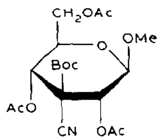
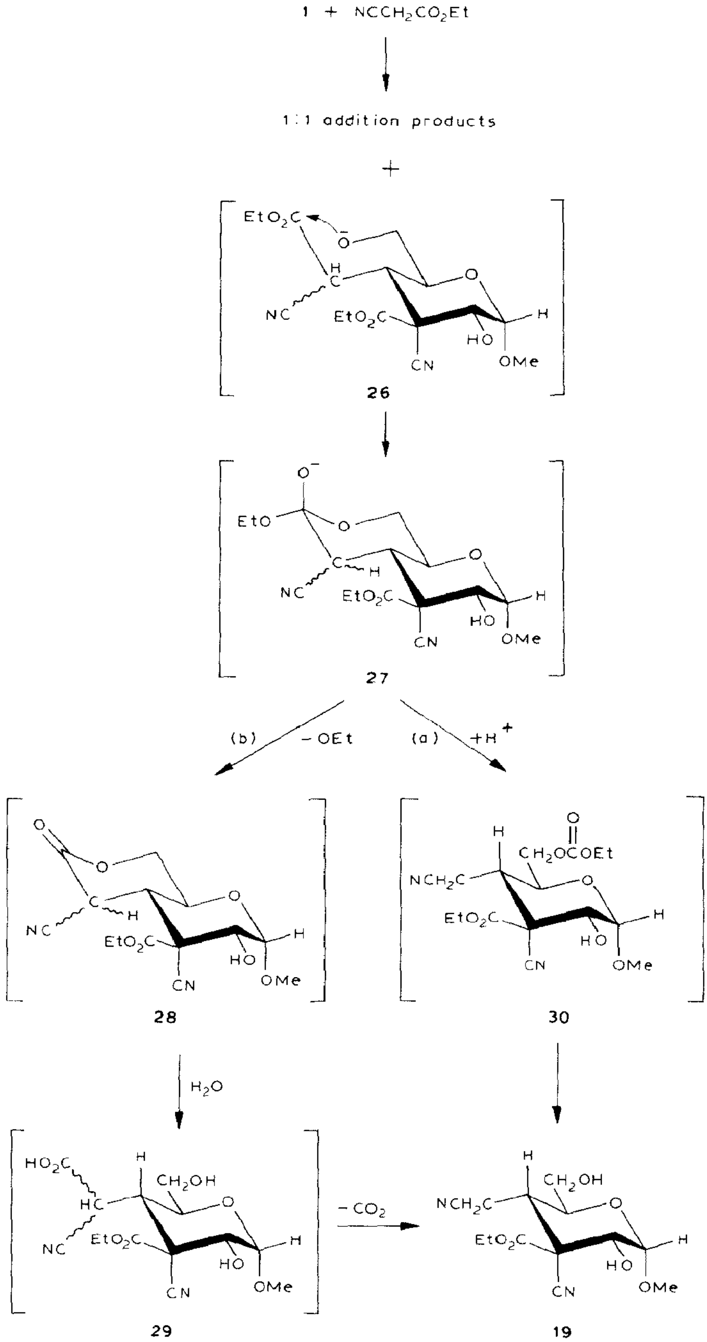


22

cyanoacetate. The reaction of **3** and *tert*-butyl cyanoacetate gave **21** (1:2 addition product) and **22** (1:1 addition product).

Conventional treatment of **6** and **7** with acetic anhydride–pyridine yielded **8** and **9**, and **10** and **11**, respectively. This fact could be explained by a ring opening–closure process. Similar isomerizations were observed[1d] in acetylations of some 3,3-diacetylpentopyranosides obtained in the reaction of **1** with 2,4-pentanedione. These observations support also the reversibility of this kind of reaction[1d].



Scheme 1. Reaction of **1** with ethyl cyanoacetate (depicted only for **19**).

TABLE I

^{1}H-N.M.R. CHEMICAL SHIFT DATA FOR **4–22** AND **25**

Compound	*H-1*	*H-2*	*H-4*	*H-5e*	*H-5a*	*H-6*	*H-6'*	*Others*
4[a,d]	4.55d	5.15d	5.32dd	4.10m	3.65dd			4.20 (q, 2 H, *J* 7.0 Hz, CH_3CH_2O), 3.42 (s, 3 H, MeO), 2.10, 2.06 (2 s, 6 H, 2 Ac), and 1.25 (t, 3 H, *J* 7.0 Hz, CH_3CH_2O)
5[a,d]	4.90d	5.20d	5.25dd	4.00–3.60m				4.25 (q, 2 H, *J* 7.0 Hz, CH_3CH_2O), 3.45 (s, 3 H, MeO), 2.12, 2.10 (2 s, 6 H, 2 Ac), and 1.25 (t, 3 H, *J* 7.0 Hz, CH_3CH_2O)
6[b,d]	4.37d	3.66dd[f]	4.05m[g]	3.81dd	3.55dd			5.21 (d, 1 H, *J* 4.7 Hz, HO-C2), 5.16 (d, 1 H, *J* 5.8 Hz, HO-C4), 3.45 (s, 3 H, MeO), and 1.48 (s, 9 H, Me_3C)
7[b,e]	4.65bd	3.94dd[h]	4.05m[i]	3.51dd	3.69d pseudo-t[j]			5.17 (d, 1 H, *J* 5.8 Hz, HO-C4), 4.58 (d, 1 H, *J* 9.4 Hz, HO-C2), 3.38 (s, 3 H, MeO), and 1.48 (s, 9 H, Me_3C)
8[a,d]	4.60d	5.25d	5.37dd	4.10dd	4.70dd			3.47 (s, 3 H, MeO), 2.15, 2.10 (2 s, 6 H, 2 Ac), and 1.47 (s, 9 H, Me_3C)
9[a,d]	4.54d	5.55d	5.40pt pseudo-t	4.05m				3.50 (s, 3 H, MeO), 2.15, 2.10 (2 s, 6 H, 2 Ac), and 1.47 (s, 9 H, Me_3C)
10[a,d]	4.60d	5.40d	5.55dd	3.75m				3.45 (s, 3 H, MeO), 2.15, 2.10 (2 s, 6 H, 2 Ac), and 1.47 (s, 9 H, Me_3C)
11[a,d]	4.85d	5.17d	5.27dd	4.00–3.60m				3.45 (s, 3 H, MeO), 2.12, 2.10 (2 s, 6 H, 2 Ac), and 1.45 (s, 9 H, Me_3C)
12[c,d]	4.62d	5.30d	3.20ddd	3.80dd	4.10 pseudo-t			3.94 (d, 1 H, *J* 2.3 Hz, NC-*CH*-Boc), 3.45 (s, 3 H, MeO), 2.06 (s, 3 H, MeCOO), 1.53, and 1.44 (2 s, 18 H, 2 Me_3C)
13[a,d]	4.90d	5.20d	3.10–2.90m	3.80dd	4.16 pseudo-t			3.62 (d, 1 H, *J* 3.2 Hz, NC-*CH*-Boc), 3.45 (s, 3 H, MeO), 2.15 (s, 3 H, MeCOO), 1.52, and 1.50 (2 s, 18 H, 2 Me_3C)
14[a,d]	4.80d	3.05dd	5.35dd	4.12dd	3.70dd			3.55 (s, 3 H, MeO), 3.45 (d, *J* 1.5 Hz, NC-*CH*-Boc), 2.12 (s, 3 H, MeCOO), and 1.50 (s, 18 H, 2 Me_3C)
15[b,d]	4.90d	5.17d	5.13d		4.10m	4.24dd	4.00m	4.10 (m, 2 H, CH_3CH_2O), 3.31 (s, 3 H, MeO), 2.05–1.90 (5 s, 9 H, 3 Ac), 1.26 and 1.24 (2 t, 3 H, CH_3CH_2O)
16[b,d]	4.57d	5.30d	5.45d			4.15–4.00m		
17 and **20**[a,d]	4.70d	5.35d	5.40d			4.35–3.90m		4.35–3.90 (m, 2 H, CH_3CH_2O), 3.50 (s, 3 H, MeO), 2.12, 2.10 (2 s, 9 H, 3 Ac), and 1.25 (t, 1 H, *J* 7.0 Hz, CH_3CH_2O)
18[a,d]	4.65d	5.14d	3.00–2.75m		3.90dt	4.50–4.20m		4.50–4.20 (m, 2 H, CH_3CH_2O), 3.50 (s, 3 H, MeO), 2.65–2.50 (m, 2 H, CH_2CN), 2.15, 2.12 (2 s, 6 H, 2 MeCOO), and 1.35 (t, 3 H, *J* 7.0 Hz, CH_3CH_2O)
19[b,d]	5.00d	5.10d	2.90–2.75m		4.05 pseudo-t	4.45–4.25m		4.45–4.25 (m, CH_3CH_2O), 3.45 (s, 3 H, MeO), 2.57 (m, 2 H, CH_2CN), 2.16, 2.15 (2 s, 6 H, 2 MeCOO), 1.36 (t, 3 H, *J* 7.3 Hz, CH_3CH_2O)
21[c,d]	4.62d	5.27d	3.18dd		4.23–4.17m		4.32dd	3.48 (s, 3 H, MeO), 3.47 (d, 1 H, *J* 0.8 Hz, NC–CH–Boc), 2.08, 2.06 (2 s, 6 H, 2 MeCOO), 1.48, and 1.44 (2 s, 18 H, 2 Me_3C)
22 and **25**[c,d]	4.57d	5.25d	5.33d		3.94ddd	4.23dd	4.04dd	3.43 (s, 3 H, MeO), 2.03, 2.01, 1.99 (3 s, 9 H, 3 Ac), and 1.34 (s, 9 H, Me_3C)

[a]80 MHz. [b]200 MHz. [c]300 MHz. [d]For solutions in $CDCl_3$ (internal Me_4Si). [e]For solutions in $(CD_3)_2CO$. [f]d, *J* 7.7 Hz, after isotopic change. [g]dd, *J* 10.3 Hz, after isotopic change. [h]d, *J* 3.8 Hz, after isotopic change. [i]dd, *J* 11.0 and 5.0 Hz, after isotopic change. [j]pseudo-t, after decoupling in the signal corresponding to H-1.

TABLE II

PROTON-PROTON COUPLING CONSTANTS (Hz) AND PREFERRED CONFORMATIONS FOR **4–22** AND **25**

Compound	$J_{1,2}$	$J_{4,5e}$	$J_{4,5a}$	$J_{5e,5a}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	*Conformation*
4	7.0	4.7	8.9	12.0				$^4C_1$(D)
5	3.4	5.8	9.7					$^1C_4$(L)
6	7.7	4.7	10.3	11.7				$^4C_1$(D)
7[a]	3.8	5.0	11.0	11.2				$^1C_4$(L)
8	7.0	4.4	8.8	11.7				$^4C_1$(D)
9	7.5	[b]	[b]					$^4C_1$(L)
10	1.5	7.0	9.0					$^1C_4$(L)
11	3.5	6.0	10.0					$^1C_4$(L)
12	1.5	4.6	11.8	11.8				$^1C_4$(L)
13	3.5	4.5	11.5	11.5				$^1C_4$(L)
14	8.5	5.0	10.0	12.0				$^4C_1$(D)
15	3.6		10.0		2.7	4.5	12.0	$^4C_1$(D)
16	1.5		10.0					$^4C_1$(D)
17 and **20**	8.0		9.7					$^1C_4$(L) and $^4C_1$(D)
18	8.0		10.0		[c]	[c]		$^1C_4$(L)
19	3.5		10.0		6.0	6.0		$^4C_1$(D)
21	8.1		9.8			5.7	13.6	$^4C_1$(D)
22 and **25**	8.1		10.0		2.6	4.3	12.3	$^4C_1$(D) and $^1C_4$(L)

[a] $^4J_{1,5a}$ ~0.6 Hz. [b] $J_{4,5} + J_{4,5'}$ ~4.0 Hz. [c] $J_{5,6} + J_{5,6'}$ ~6.0 Hz.

The structures of **4–22** and **25** were established on the basis of elemental analysis and spectroscopic data (Tables I–III).

The configurations at C-2 and C-4, and the preferred conformations were deduced from the values of $J_{1,2}$ $J_{4,5a}$, and $J_{4,5e}$ in the ^{1}H-n.m.r. spectra. Compounds **4, 6, 8, 9, 14, 17, 18, 20–22,** and **25** showed $J_{1,2}$ values of 8.5–7.0 Hz, indicating H-1,2 to be *trans*-diaxial. The same inference applies to H-4,5*a* in **4–8**, **10–22**, and **25** ($J_{4,5a}$ 11.8–8.8 Hz). The $J_{4,5a} + J_{4,5e}$ value of 4.0 Hz for **9** reflected a synclinal relationship between H-4 and H-5*a*,5*e*, the $J_{1,2}$ values of 3.4–3.8 Hz for **5, 7, 11, 13, 15,** and **19** indicated H-1,2 to be equatorial,axial, and the $J_{1,2}$ values of 1.5 Hz for **10, 12,** and **16** indicated H-1,2 to be equatorial,equatorial.

The configuraion at C-3 in each compound was assigned tentatively on the basis of the expected higher stability of equatorial alkoxycarbonyl and axial cyano groups. Supporting this assignment is the *trans*-elimination[4] of some 3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-*C*-glycosyl and 3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxyglycoside derivatives to yield 3-cyano-Δ^2- and -Δ^3-dihydropyran derivatives.

Table III includes the ^{13}C-n.m.r. data for **4–22** and **25**. The resonances of C-1 in **4, 6, 8, 9, 14, 18, 20–22,** and **25** (103.0–100.0 p.p.m.) and **5, 7, 10, 11, 12, 13, 15, 16,** and **19** (97.10–94.90 p.p.m.) accorded[5–7] with an equatorial and axial disposition respectively, of the methoxyl group.

On the basis of $J_{1,2}$ and $J_{4,5}$ values (see Table II), an isomerization at C-5 and a preferred $^1C_4$(L) conformation is assumed for **17, 18,** and **25**. This inference is

TABLE III

^{13}C-N.M.R. CHEMICAL SHIFT DATA FOR **4–22** AND **25**

Compound	C-1	C-2,C-4	C-5	C-6	C-3	MeO	CN	Others
4[a,d]	100.05	69.06, 67.81	62.18		54.10	56.73	113.63	168.91, 168.62, 163.62 (3 COO), 64.07 (OCH_2CH_3), 20.43 (*Me*COO), and 13.77 (OCH_2CH_3)
5[a,d]	94.90	69.54, 67.92	56.20		52.15	55.62	113.64	169.14, 168.86, 164.60 (3 COO), 63.95 (OCH_2CH_3), 20.32 (*Me*COO), and 13.70 (OCH_2CH_3)
6[b,e]	103.04	71.58, 69.21	66.00		60.65	56.24	115.52	165.48 (COO), 83.66 (CMe), and 27.31 (C*Me*$_3$)
7[b,e]	97.07	70.17, 68.14	59.33		[o]	55.18	[o]	84.04 (CMe$_3$), and 27.35 (C*Me*$_3$)
8[a,d]	100.16	69.02, 67.84	62.26		55.60	56.25	113.93	168.85, 168.45, 161.98 (3 COO), 85.94 (CMe$_3$), 27.46 (CMe$_3$), and 20.41 (*Me*COO)
9[a,d]	101.04	70.36, 66.73	63.74		52.38	56.82	114.08	169.14, 168.37, 161.16 (3 COO), 85.68 (CMe$_3$), 27.58 (C*Me*$_3$), and 20.67 (*Me*COO)
10[a,d]	96.84	68.96, 67.79	62.20		48.80	56.75	113.78	169.09, 168.45, 161.88 (3 COO), 85.21 (CMe$_3$), 27.41 (C*Me*$_3$), and 20.37 (*Me*COO)
11[a,d]	95.02	69.72, 68.01	56.41		53.22	55.78	114.15	169.33, 168.97, 163.17 (3 COO), 85.78 (CMe$_3$), 27.56 (C*Me*$_3$), and 20.51 (*Me*COO)
12[c,d]	96.93	68.96[f]	57.07		46.19	55.56	113.66 113.62	168.60, 163.20 (3 COO), 86.10, 85.40 (2 CMe$_3$), 27.83, 27.65 (2 C*Me*$_3$), and 20.65 (*Me*COO)
13[a,d]	95.28	70.20[g]	56.88		51.05	55.85	114.00 112.94	169.32, 163.8, 162.68 (3 COO), 86.58, 85.83 (2 CMe$_3$), 27.75, 27.67 (2 C*Me*$_3$), and 20.60 (*Me*COO)
14[a,d]	101.0	[h] 68.60	62.83		54.15	57.30	113.26	168.74, 162.62 (2 COO), 86.61 (2 CMe$_3$), 27.65, 27.53 (2 C*Me*$_3$), and 20.37 (2 *Me*COO)
15[b,d]	95.24	69.23, 67.02	65.15	61.29	52.28	55.59	113.54	170.17, 168.90, 168.53, 164.13 (4 COO), 64.04 (OCH_2CH_3), 20.66, 20.17 (2 *Me*COO), and 13.55 (OCH_2CH_3)
16[b,d]	97.10		[o]		19.40	55.11	[o]	
17 and **20**[a,d]	100.72	72.29, 69.22	67.51	61.64	56.33	57.15	113.61	{170.44, 168.41, 168.23, 163.28 (4 COO), 64.24 (OCH_2CH_3), 20.63, 20.34 (3 *Me*COO), and 13.74 (OCH_2CH_3)
18[a,d]	100.35	[i] 39.06	[i]	[j]	55.26	57.00	115.70 113.70	170.40, 168.60 (2 COOMe), 164.24 (COOEt), 20.70, 20.35 (2 MeCOO), 15.91 (CH_2CN), and 13.66 (OCH_2CH_3)
19[a,d]	95.72	[k] 29.24	[k]	[l]	51.28	55.86	116.05 114.11	170.40, 168.90 (2 COOMe), 165.50 (COOEt), 20.60, 20.10 (2 MeCOO), 16.10 (CH_2CN), and 14.10 (OCH_2CH_3)
21[c,d]	100.41	[m] [n]	[m]	63.03	56.10	57.11	113.39 112.93	170.22, 168.43 (2 COOMe), 162.92, 162.16 (2 COOMe$_3$), 87.10, 86.26 (2 CMe$_3$), 27.63, 27.46 (2 C*Me*$_3$), 20.85, and 20.50 (2 *Me*COO)
22 and **25**[c,d]	100.57	72.14, 69.10	67.24	61.45	57.36	57.06	113.79	170.36, 168.15, 168.04, 161.61 (4 COO), 86.14 (CMe$_3$), 27.19 (C*Me*$_3$), 20.54, 20.28, and 20.18 (3 *Me*COO)

[a]20 MHz. [b]50 MHz. [c]75 MHz. [d]For solution in $CDCl_3$. [e]For solution in *in* $(CD_3)_2CO$. [f]Signals at 37.30 and 32.36 correspond to C-4, NC–CH–Boc. [g]Signals at 38.79 and 37.01 correspond to C-4, NC–*CH*–Boc. [h]Signals at 43.44 and 37.38 correspond to C-2, NC–CH–Boc. [i]Signals at 72.97 and 70.11 correspond to C-2,C-5. [j]Signals at 64.64 and 63.00 correspond to C-6, -OCH_2CH_3. [k]Signals at 71.95 and 69.88 correspond to C-2,C-5. [l]Signals at 64.23 and 63.25 correspond to C-6, -OCH_2CH_3. [m]Signals at 71.95 and 69.88 correspond to C-2,C-5. [n]Signals at 40.60 and 37.20 correspond to C-4, NC–*CH*–Boc. [o]Accurate data could not be obtained.

supported by the chemical shift values (100.5 ±0.2 p.p.m.) of the resonances for C-1 in these compounds, which accord with an equatorial disposition of the methoxyl group.

In addition to the signals noted above, the 1:2 addition compounds **12–14** and **21** gave ^{13}C signals for CN (~113 p.p.m.) and CMe_3 groups (87.1–85.4 and 27.8–27.5 p.p.m.). The position of the CN–CH–Boc group was deduced from the chemical shifts of the resonances for H-2,4 and C-2,4 (see Tables I and III). However, **18** and **19** gave signals for two CN groups, but only one each for *C*OOEt and -*C*H_2CN groups, suggesting that **18** and **19** had been formed by loss of the COOEt group of the 1-ethoxycarbonyl-1-cyanomethyl moiety linked at C-4 in an initial 1:2 addition product **26**, as shown in Scheme 1. The isolation of a compound similar to the intermediate **28** in the reaction of **2** with 2,4-pentanedione[1g] supports the proposed mechanism.

In each of the preferred conformers (see Table II), the bulky substituents are generally equatorial. Only **9, 10, 12,** and **16** have an axial AcO group at C-2. These observations accord with thermodynamic control in a reversible process.

Thus, the behaviour of the dialdehyde **1** was similar to that of ethyl and *tert*-butyl cyanoacetate. However, **2** and **3** gave higher yields of products with *tert*-butyl cyanoacetate than with ethyl cyanoacetate. 1:1 Addition products with *gluco* and *manno* configurations were obtained from **2** and ethyl or *tert*-butyl cyanoacetate. However, **3** gave only *gluco* products, reflecting the Δ^2 effect[8] in *manno* isomers. Epimerization at the carbon bearing the hydroxymethyl group was observed only in the reactions of **2**.

EXPERIMENTAL

General methods. — Organic solutions were dried over anhydrous Na_2SO_4. Solvents were evaporated under diminished pressure at <40°. Column chromatography was carried out on silica gel (Merck, 70–230 mesh, ASTM). Melting points (uncorrected) were obtained with an Electrothermal apparatus. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter and i.r. spectra with a Perkin–Elmer 983 G spectrometer. N.m.r. spectra (internal Me_4Si) were obtained with a Bruker WP 80, WP 200, or AM 300 spectrometer.

Reactions of **1–3** *with ethyl and* tert-*butyl cyanoacetate.* — Ethyl or *tert*-butyl cyanoacetate and piperidine (0.2 mL) were added to a solution of the dialdehyde (**1–3**) in aqueous 1,4-dioxane (2:1, 30 mL). Each mixture was stored at room temperature and then concentrated. Water (~20 mL) was added to the residue, and the mixture was extracted with ethyl acetate (4 × 50 mL). The combined extracts were dried, filtered, and concentrated to give the crude product.

The following amounts and conditions were used.

(*a*) *Reaction of ethyl cyanoacetate with* **1**. The crude product was treated at room temperature for 16 h with acetic acid–acetic anhydride–acetyl chloride (8:4:16 mL). Column chromatography (3:1 hexane–ether) of the products

Starting compound (g)	*Active methylene compound*[a] *(g)*	*Time (h)*	*Products (g, %)*
1[b]	A (1.7)	0.5	**4** (0.96, 19.6) **5** (2.72, 27.7)
1[b]	B (2.1)	2.5	**6** (1.10, 27.2) **7** (0.53, 14.3) **12** (0.08, 1.2)
1[b]	B (2.1)	4.0	**6** (0.46, 11.3) **7** (0.27, 6.6) **13** (0.30, 4.6) **14** (0.14, 2.2)
2[c]	A (1.7)	20.0	**15** + **16** (0.30, 4.5)[d] **17** (0.30, 4.2)
2[c]	A (1.7)	84.0	**15** + **16** (0.30, 4.5)[e] **18** (0.13, 2.0) **19** (0.10, 1.5)
2[c]	B (2.1)	96.0	**23** + **24** (1.9, 42.5)[d,g] **25** (0.50, 8.0)
3[f]	A (1.7)	14.0	**20** (2.25, 37.4)
3[f]	B (2.1)	14.0	**21** (1.18, 18.3) **22** (1.10, 17.1)

[a]A, ethyl cyanoacetate; B, tert-butyl cyanoacetate. [b]Prepared from methyl β-D-xylopyranoside (2.44 g, 15 mmol)[1d]. [c]Prepared from methyl α-D-glucopyranoside (2.91 g, 15 mmol)[1e]. [d]Molar ratio ~4:1. [e]Molar ratio ~10:1. [f]Prepared from methyl β-D-glucopyranoside (2.91 g, 15 mmol)[9].

gave, first, methyl 2,4-di-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-β-D-*xylo*-pentopyranoside (**4**), m.p. 90° (from hexane), $[\alpha]_D^{25}$ −56° (*c* 1, chloroform); ν_{max}^{KBr} 1759, 1259, 1214, 1073, 1044, 978, 899, and 855 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 51.35; H, 5.50; N, 4.44. $C_{14}H_{19}NO_8$ calc.: C, 51.06; H, 5.81; N, 4.25%.)

Eluted second was methyl 2,4-di-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-α-L-*xylo*-pentopyranoside (**5**), m.p. 79–80° (from hexane–ether), $[\alpha]_D^{25}$ +113° (*c* 1, chloroform); ν_{max}^{KBr} 1744, 1285, 1265, 1218, 1140, 1049, 965, and 898 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 50.70; H, 5.82; N, 4.27. $C_{14}H_{19}NO_8$ calc.: C, 51.06; H, 5.81; N, 4.25%.)

(*b*) *Reaction of* tert-*butyl cyanoacetate with* **1**. Column chromatography (2:1 hexane–ether) of the crude product (2.5-h reaction) gave, first, a product which was treated with acetic acid–acetic anhydride–acetyl chloride (4:2:8 mL). Column chromatography (3:1 hexane–ether) gave only methyl 2-*O*-acetyl-3-*tert*-butoxycarbonyl-4-(1-*tert*-butoxycarbonyl-1-cyanomethyl)-3-*C*-cyano-3,4-dideoxy-α-L-*lyxo*-pentopyranoside (**12**), m.p. 154–156° (from hexane–ether), $[\alpha]_D^{24}$ +24° (*c* 1, chloroform); ν_{max}^{KBr} 2250, 1748, 1254, 1221, 1143, and 834 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III (Found: C, 57.70; N, 7.00; N, 6.54. $C_{21}H_{30}N_2O_8$ calc.: C, 57.52; H, 6.89; N, 6.38%). A slow-moving complex mixture (0.2 g) was obtained which was not investigated.

Eluted second was methyl 3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-β-D-

xylo-pentopyranoside (**6**), m.p. 138–141° (from hexane–ether), $[\alpha]_D^{25}$ −27° (*c* 1, methanol); ν_{max}^{KBr} 3470, 3380, 2250, 1740, 1250, 1220, 1195, 1140, 1100–1080, 1040, 930, and 838 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.03; H, 6.83; N, 5.03. $C_{12}H_{19}NO_6$: calc.: C, 52.73; H, 7.00; N, 5.12%).

Eluted third was methyl 3-*tert*-butoxycarbonyl-3-*C*-cyano-α-L-*xylo*-pentopyranoside (**7**), m.p. 151–152° (from hexane–ether), $[\alpha]_D^{25}$ −115° (*c* 1, methanol); ν_{max}^{KBr} 3529, 3445, 2258, 1721, 1292, 1065, 1016, 952, and 838 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.27; H, 7.12; N, 5.20. $C_{12}H_{19}NO_6$ calc.: C, 52.73; H, 7.00; N, 5.12%.)

The reaction of **1** with *tert*-butyl cyanoacetate at room temperature (4 h) and column chromatography (2:1 hexane–ether) gave, first, a product that was conventionally acetylated with acetic anhydride–pyridine (6:3 mL). Column chromatography (4:1 hexane–ether) gave methyl 4-*O*-acetyl-3-*tert*-butoxycarbonyl-2-(1-*tert*-butoxycarbonyl-1-cyanomethyl)-3-*C*-cyano-2,3-dideoxy-β-D-*xylo*-pentopyranoside (**14**), isolated as a syrup, $[\alpha]_{436}^{25}$ +7° (*c* 1, chloroform); ν_{max}^{film} 2253, 1750, 1744, 1280, 1258, 1214, 1096, and 839 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 57.35; H, 6.70; N, 6.65. $C_{21}H_{30}N_2O_8$ calc.: C, 57.52; H, 6.89; N, 6.38%.)

Eluted second was a product that was conventionally acetylated with acetic anhydride–pyridine (6:3 mL). Column chromatography (2:1 hexane–ether) then gave methyl 2-*O*-acetyl-3-*tert*-butoxycarbonyl-4-(1-*tert*-butoxycarbonyl-1-cyanomethyl)-3-*C*-cyano-3,4-dideoxy-α-L-*xylo*-pentopyranoside (**13**), m.p. 112–113° (from hexane–ether), $[\alpha]_D^{20}$ −36° (*c* 1, chloroform); ν_{max}^{KBr} 1740, 1299, 1224, 1160, 1140, 1058, 903, and 833 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 57.35; H, 6.70; N, 6.65. $C_{21}H_{30}N_2O_8$ calc.: C, 57.52; H, 6.89; N, 6.38%.)

Eluted third and fourth were **6** and **7**.

(*c*) *Reaction of ethyl cyanoacetate with* **2**. Column chromatography (ether) of the crude product (20-h reaction) gave, first, a product that was treated with acetic anhydride–pyridine (7:5 mL) at −10°. Column chromatography (1:1 hexane–ether) then gave methyl 2,4,6-tri-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-β-L-*gluco*-hexopyranoside (**17**), m.p. 114–115° (from hexane–ether), $[\alpha]_D^{25}$ +25.6° (*c* 1, chloroform); ν_{max}^{KBr} 2250, 1766, 1375, 1248–1200, 1161, 1101, 1046, and 909 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 50.80, H, 5.36; N, 3.37. $C_{17}H_{23}NO_{10}$ calc.: C, 50.87; H, 5.77; N, 3.48%.)

Eluted second was a product that was treated with acetic anhydride–pyridine (10:5 mL). Column chromatography (1:1 hexane–ether) gave methyl 2,4,6-tri-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-α-D-*gluco*- (**15**) and -α-D-*manno*-hexopyranosides (**16**), isolated as a syrup; ν_{max}^{film} 1751, 1224, and 1052 cm^{-1}. For ^{1}H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 51.00; H, 5.62; N, 3.65. $C_{17}H_{23}NO_{10}$ calc.: C, 50.87; H, 5.77; N, 3.49%.)

Column chromatography (ether) of the crude product (84-h reaction) gave, first, a product that was treated with acetic anhydride–pyridine (6:3 mL) at −10°.

Column chromatography (1:1 hexane–ether) then gave methyl 2,6-di-*O*-acetyl-3-*C*-cyano-4-cyanomethyl-3,4-dideoxy-3-ethoxycarbonyl-β-L-*gluco*-hexopyranoside (**18**), m.p. 112–113° (from hexane–ether), $[\alpha]_D^{25}$ +64° (*c* 1, chloroform); ν_{max}^{KBr} 2252, 1747, 1449, 1371, 1238, 1054, 894, and 854 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.60; H, 5.71; N, 7.32. $C_{17}H_{22}N_2O_8$ calc.: C, 53.39; H, 5.80; N, 7.32%.)

Eluted second was a product that was treated with acetic anhydride–pyridine (8:3 mL). Column chromatography (1:2 hexane–ether), gave methyl 2,6-di-*O*-acetyl-3-*C*-cyanomethyl-3,4-dideoxy-3-ethoxycarbonyl-α-D-*gluco*-hexopyranoside (**19**) isolated as a syrup, $[\alpha]_D^{27}$ +90° (*c* 1, chloroform); ν_{max}^{film} 2252, 1749, 1243, 1057, 961, and 854 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.22; H, 6.12; N, 7.25. $C_{17}H_{22}N_2O_8$ calc.: C, 53.39; H, 5.80; N, 7.32%.)

Eluted third was a product that was acetylated with acetic anhydride–pyridine (10:5 mL). Column chromatography (1:1 hexane–ether) then gave a mixture of **15** and **16**.

(*d*) *Reaction*[1g] *of* tert-*butyl cyanoacetate with* **2**. Column chromatography (ether) of the crude product gave, first, a product that was treated with acetic anhydride–pyridine (8:4 mL) at −10°. Column chromatography (4:1 hexane–ether) then gave a mixture of products. Crystallisation from 6:1 hexane–ether gave methyl 2,4,6-tri-*O*-acetyl-3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-β-L-*gluco*-hexopyranoside (**25**), m.p. 135–136°, $[\alpha]_D^{25}$ +28° (*c* 1, chloroform); ν_{max}^{KBr} 1758, 1740, 1216, 1157, 1121, 1056, 902, and 835 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 52.78; H, 5.96; N, 3.21. $C_{19}H_{27}NO_{10}$ calc.: C, 53.14; H, 6.33; N, 3.26%.)

Eluted second was a mixture of methyl 3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-α-D-*gluco*- (**23**) and -α-D-*manno*-hexopyranosides (**24**)[1g].

(*e*) *Reaction of ethyl cyanoacetate with* **3**. The crude product was acetylated with acetic anhydride–pyridine (10:5 mL) at −10°. Column chromatography (1:1 hexane–ether) then gave methyl 2,4,6-tri-*O*-acetyl-3-*C*-cyano-3-deoxy-3-ethoxycarbonyl-β-D-*gluco*-hexopyranoside (**20**), m.p. 114–115° (from hexane–ether), $[\alpha]_D^{25}$ −26° (*c* 1, chloroform). The i.r. and n.m.r. data were identical to those for **17**. (Found: C, 50.90; H, 5.52; N, 3.46. $C_{17}H_{23}NO_{10}$ calc.: C, 50.87; H, 5.77; N, 3.49%.)

(*f*) *Reaction of* tert-*butyl cyanoacetate with* **3**. Column chromatography (1:6 hexane–ether) of the crude product gave, first, a product that was treated with acetic anhydride–acetic acid–acetyl chloride (6:3:12 mL). Column chromatography (1:1 hexane–ether) then gave methyl 2,6-di-*O*-acetyl-3-*tert*-butoxycarbonyl-4-(1-*tert*-butoxycarbonyl-1-cyanomethyl)-3-*C*-cyano-3,4-dideoxy-β-D-*gluco*-hexopyranoside (**21**), m.p. 138–140° (from hexane–ether), $[\alpha]_D^{20}$ −57° (*c* 1, chloroform); ν_{max}^{KBr} 1746, 1210, 1136, 1065, 899, and 836 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 56.77; H, 6.82; N, 5.49. $C_{24}H_{34}N_2O_{10}$ calc.: C, 56.37; H, 6.87; N, 5.46%.)

Eluted second was a complex mixture (0.86 g) that was not investigated.

Eluted third was a product that was treated with acetic anhydride–pyridine (10:5 mL). Column chromatography of the crude product (1:1 hexane–ether) then gave methyl 2,4,6-tri-*O*-acetyl-3-*tert*-butoxycarbonyl-3-*C*-cyano-3-deoxy-β-D-*gluco*-hexopyranoside (**22**), m.p. 135–136° (from hexane–ether), $[\alpha]_D^{20}$ −27° (*c* 1, chloroform); ν_{max}^{KBr} 1757, 1218, 1156, 1052, 902, and 834 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 52.70; H, 6.02; N, 3.57. $C_{19}H_{27}NO_{10}$ calc.: C, 53.14; H, 6.33; N, 3.26%.)

Acetylation of **6** *and* **7**. — Conventional treatment of **6** and **7** with acetic anhydride–pyridine at −10° and extraction of the products into chloroform gave the following results.

Starting compound (g)	*Ac_2O–pyridine (mL)*	*Products (g, %)*
6 (0.9)	10.5	**8** (0.75, 63.7), **9** (0.20, 16.6)
7 (0.32)	6:3	**10** (0.06, 14.3), **11** (0.08, 19.1)

(*a*) *Methyl 2,4-di-O-acetyl-3-*tert*-butoxycarbonyl-3-C-cyano-3-deoxy-β-*D-xylo- (**8**) *and -α-*L-arabino-*pentopyranosides* (**9**). Column chromatography (3:1 hexane–ether) of the crude product gave, first, **8**, m.p. 89–90° (from hexane–ether), $[\alpha]_D^{25}$ −43° (*c* 1, chloroform); ν_{max}^{KBr} 2245, 1757, 1279, 1212, 1155, 1069, 1041, 981, 898, and 834 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.56; H, 6.43; N, 3.83. $C_{16}H_{23}NO_8$ calc.: C, 53.77; H, 6.48; N, 3.90%).

Eluted second was **9**, m.p. 126–128° (from hexane–ether), $[\alpha]_{4360}^{25}$ +12° (*c* 1, chloroform); ν_{max}^{KBr} 2253, 1753, 1276, 1240, 1222, 1154, 1106, 902, 833, and 747 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.40; H, 6.31; N, 3.99. $C_{16}H_{23}NO_8$ calc.: C, 53.77; H, 6.48; N, 3.90%.)

(*b*) *Methyl 2,4-di-O-acetyl-3-*tert*-butoxycarbonyl-3-C-cyano-3-deoxy-α-*L-lyxo- (**10**) *and -α-*L-xylo-*pentopyranosides* (**11**). Column chromatography (3:1 hexane–ether) of the crude product gave, first, **10**, isolated as a syrup; ν_{max}^{KBr} 2252, 1756, 1260, 1218, 1138, 1088, 1047, 1011, 896, and 837 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.85, H. 6.60; N, 3.95. $C_{16}H_{23}NO_8$ calc.: C, 53.77; H, 6.48; N, 3.90%).

Eluted second was **11**, m.p. 70–72°, $[\alpha]_D^{25}$ −87° (*c* 1, chloroform); ν_{max}^{KBr} 1757, 1280, 1218, 1140, 1054, 964, 900, and 838 cm^{-1}. For ^1H- and ^{13}C-n.m.r. data, see Tables I–III. (Found: C, 53.98; H, 6.62; N, 4.03. $C_{16}H_{23}NO_8$ calc.: C, 53.77; H, 6.48; N, 3.90%.)

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