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Preliminary communication

A facile synthesis of moenuronic acid derivatives

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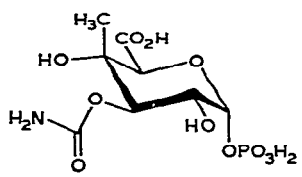
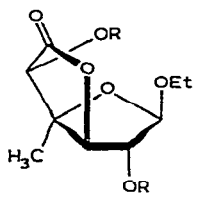
Moenomycin A is a phosphoglycolipid antibiotic that inhibits cell-wall biosynthesis[1–4]. The whole structure of moenomycin A is not yet completely determined; however, a new, branched-chain uronic acid called moenuronic acid (4-*C*-methyl-D-glucuronic acid) has been found, as its 3-*O*-carbamoyl 1-phosphate (**1**), by hydrolysis with trifluoroacetic acid and 2-propanol[5]. The uronic acid moiety afforded ethyl β-D-glucofuranosidurono-6,3-lactone (**2**) on hydrolysis with a stronger acid and subsequent glycosidation, and the structures of **2** and its diacetate (**3**) were thoroughly established[6]. This communication describes the first synthesis of moenuronic acid derivatives.

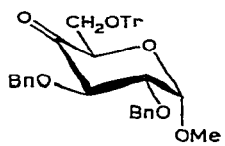
Oxidation of methyl 2,3-di-*O*-benzyl-6-*O*-trityl-α-D-glucopyranoside[7] with dimethyl sulfoxide–trifluoroacetic anhydride gave the corresponding hexosid-4-ulose (**4**)



1



2 R = H
3 R = Ac



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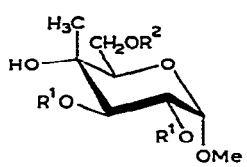
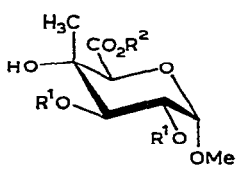


5 R^1 = Bn, R^2 = Tr
6 R^1 = Bn, R^2 = H
7 R^1 = H, R^2 = H



8 R^1 = H, R^2 = H
9 R^1 = Ac, R^2 = Et

Bn = $PhCH_2$
Tr = Ph_3C

as a syrup, $[\alpha]_D$ +47.1° (*c* 1.2, $CHCl_3$), in 72% yield. Reaction of **4** with methyllithium in ether at −78° gave, exclusively, one syrupy 4-*C*-methyl derivative (**5**) of D-*gluco* configuration {$[\alpha]_D$ +7.8° (*c* 1.5, $CHCl_3$); ^{13}C-n.m.r.: 4-Me, 14.92 p.p.m.} in 95% yield, as shown in the case of analogous glycos-4-uloses by Miljković *et al.*[8]. Partial hydrolysis of **5** with 70% aqueous acetic acid gave the corresponding *O*-detrityl derivative (**6**) as a syrup, $[\alpha]_D$ +31.4° (*c* 0.9, $CHCl_3$), in good yield. Hydrogenolysis of **6** in the presence of palladium–carbon gave methyl 4-*C*-methyl-α-D-glucopyranoside (**7**) as a syrup, $[\alpha]_D$ +100° (*c* 0.8, MeOH), quantitatively. Oxidation of **7** in slightly alkaline aqueous solution with oxygen in the presence of platinum–carbon for 40 h at 90° gave the corresponding α-D-glucosiduronic acid (**8**) as a syrup {$[\alpha]_D$ +87.0° (*c* 0.7, MeOH); ν_{max}^{film} 3400 (OH) and 1730 cm^{-1} (C=O); ^{1}H-n.m.r. data (CD_3OD): δ 4.77 (d, 1 H, *J* 4.0 Hz, H-1), 4.19 (s, 1 H, H-5), 3.74 (d, 1 H, $J_{2,3}$ 10.5 Hz, H-3), 3 43 (dd, 1 H, H-2), 3.43 (s, 3 H, OMe), and 1.18 (s, 3 H, 4-Me)}, in 86% yield. Treatment of **8** with 0.1M ethanolic hydrogen chloride for 16 h at the reflux temperature and subsequent acetylation of the products, gave syrupy **3** and ethyl (methyl 2,3-di-*O*-acetyl-4-*C*-methyl-α-D-glucopyranosid)uronate (**9**) {m.p. 99–101°; $[\alpha]_D$ +112° (*c* 0.6, $CHCl_3$); ν_{max}^{KBr} 3500 (OH) and 1730 cm^{-1} (C=O); ^{1}H-n.m.r. data ($CDCl_3$): δ 5.41 (d, 1 H, $J_{2,3}$ 10.4 Hz, H-3), 5.03 (d, 1 H, *J* 3.4 Hz, H-1), 4.77 (dd, 1 H, H-2), 4.37 (s, 1 H, H-5), 4.30 (q, 2 H, *J* 7.0 Hz, CH_2), 3.44 (s, 3 H, OMe), 2.12 and 2 07 (each s, 6 H, 2 OAc), 1.35 (t, 3 H, CH_3), and 1.30 (s, 3 H, 4-Me)} in 28 and 55% yield, respectively. Similar ethanolysis of **9** for 3 days gave syrupy **2** {$[\alpha]_D$ −47.6° (*c* 0.6, EtOH); ν_{max}^{film} 3420 (OH) and 1790 cm^{-1} (C=O); ^{1}H-n.m.r. data: δ 5.14 (s, 1 H, H-1), 4.60 (s, 1 H, H-3), 4.41 (s, 1 H, H-2), 4.16 (s, 1 H, H-5). 3.9–3.3 (m, 2 H, CH_2), 1.67 (s, 3 H, 4-Me), and 1.18 (t, *J* 7.0 Hz, CH_3)}, quantitatively. The physical data for **8**, **9**, and **2**, and comparison of the data for **3** with those reported (shown in Table I) indicated that **3** was identical with the natural compound reported (although the rotational value and the magnetic nonequivalence of the methylene protons in the 1-ethoxyl group were not given in the literature[6]).

TABLE I

COMPARISON OF PHYSICAL PROPERTIES

Compound	$[\alpha]_D$ *in* $CHCl_3$ *(degrees)*	*Chemical shifts (δ) and coupling constants (Hz)*								$\nu_{C=O}$ *(cm^{-1})*
		H-1	*H-2*	*H-3*	*H-5*	*Me-4*	*OAc*	OCH_2 *(J_{gem})*	CH_3 *(J_{CH_2,CH_3})*	
3	+55.4	5.12s	5.42s	4 62s	5.17s	1.63s	2 24s 2.13s	3.45dq 3.86dq (9.0)	1.18t (7.0)	1810 1750
3 (reported)	—	5.14s	5.42s	4.60s	5.19s	1.63s	2 25s 2.13s	3.70m	1.19t	1810 1750

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REFERENCES

1 W. A. SLUSARCHYK, *Biotechnol. Bioeng.*, 13 (1971) 399–407.
2 R. TSCHESCHE, D. LENOIR, AND H. L. WEIDENWÜLLER, *Tetrahedron Lett*, (1969) 141–144.
3 P. WELZEL, H. BUHLKE, P. MICHALKE, J. SIMONS, L. WINTERFELD, R. TSCHESCHE, H. W. FELHAKER, AND G HUBER, *Tetrahedron Lett.*, (1973) 227–230.
4 P. WELZEL, F.-J. WITTELER, AND D. MULLER, *Tetrahedron Lett.*, (1976) 1665–1668.
5 F.-J. WITTELER, P. WELZEL, H. DUDDECK, G. HÖFLE, W. RIEMER, AND H. BUDZIKIEWIC, *Tetrahedron Lett.*, (1979) 3493–3496; *cf.*, R. TSCHESCHE AND J. E MOCH, *ibid.*, (1979) 2119–2122; P. WELZEL, G. KNUPP, F -J. WITTELER, T. SCHUBERT, H. DUDDECK, AND D. MULLER, *Tetrahedron*, 37 (1981) 97–104; P. WELZEL, F -J. WITTELER, L. HERMSDORF, R. TSCHESCHE, H. BUHLKE, P. MICHALKE, J. SIMONS, H.-W. FEHLHABER, J. BLUMBACH, AND G. HUBER, *ibid*, 37 (1981) 105–112; P. WELZEL, F -J. WITTELER, L. HERMSDORF, AND W. RIEMER, *ibid*, 37 (1981) 113–118.
6 N. LANGENFELD AND P. WELZEL, *Tetrahedron Lett.*, (1978) 1833–1836.
7 R. E. WING, C. L. COLLINS, AND J. N. BEMILLER, *J. Chromatogr.*, 32 (1968) 303–310.
8 M. MILJKOVIĆ, M. GLIGORIJEVIĆ, T. SATOH, AND D. MILJKOVIĆ, *J. Org. Chem.*, 39 (1974) 1379–1384; M. MILJKOVIĆ, M. GLIGORIJEVIĆ, T. SATOH, D. GLISHIN, AND R D. PITCHER, *ibid*, 39 (1974) 3847–3850.