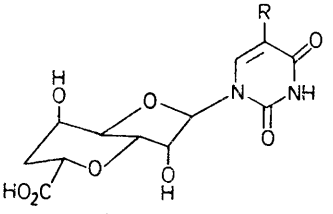
Synthesis of 3,7-Anhydro-octose Derivatives Related to Octosyl Acids

By K. ANZAI* and T. SAITA
(*The Institute of Physical and Chemical Research, Wako-shi, Saitama, Japan* 351)

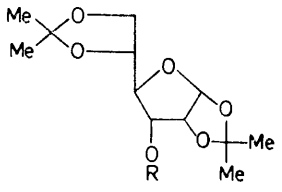
Summary Some derivatives of 3,7-anhydro-6-deoxy-D-*glycero*-D-*allo*-octofuranosyluronic acid, the sugar portion of octosyl acids A and B, have been synthesized.

As an approach to the synthesis of octosyl acids A and B (**1**) and (**2**),[1] which were isolated from the fermentation broth of the polyoxin[2]-producing micro-organism, *Streptomyces cacaoi* var. *asoensis*,[3] and were considered to be

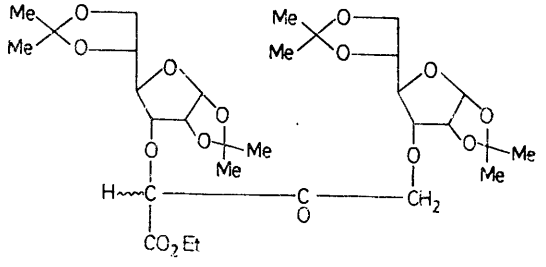
carbo-analogues of cyclic AMP,[1] the synthesis of the sugar portion of these nucleosides has been attempted. Thus, reaction of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**3**)[4] with ethyl bromoacetate in the presence of NaH afforded the ethyl ester (**4**), m.p. 89—90 °C; *m/e* 331 (M^+ — Me),† which was converted into the malonic acid derivative (**5**) by treatment in refluxing diethyl carbonate (b.p. 127 °C) with an equimolar amount of NaH; yield 80%; m.p. 50—51 °C, ν (KBr) 1740 and 1770 cm^{-1} (CO); *m/e* 403 (M^+ — Me); δ 4·78 (1H, s, EtO_2CCHCO_2Et). If (**4**) was treated with diethyl carbonate and NaH in tetrahydrofuran at 0 °C, the Claisen condensation product (**6**) (syrup) was obtained exclusively as a mixture of stereoisomers; *m/e* 631 (M^+ —Me); δ 5·68 — 5·88 (2H, m, 1- and 1'-H), and 4·72 (1H, s, EtO_2CCHCO_2Et).



(1) R = CO_2H
(2) R = CH_2OH

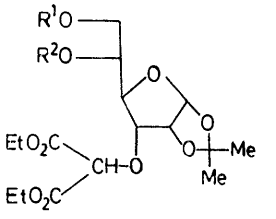


(3) R = H
(4) R = CH_2CO_2Et
(5) R = $CH(CO_2Et)_2$

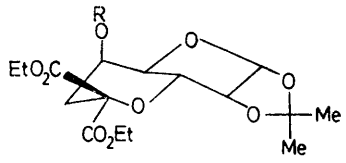


(6)

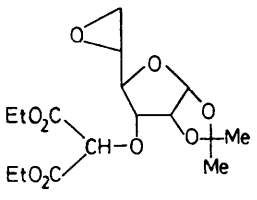
Treatment of (**5**) in 70% acetic acid at 37 °C for 3 h afforded the partially deacetonated product (**7**) (82%), m.p. 53 °C; *m/e* 363 (M^+ — Me), which was converted into the monotosylate (**8**), (syrup) *m/e* 517 (M^+ — Me), by reaction with an equimolar amount of tosyl chloride (70%). With excess of tosyl chloride the ditosylate (**9**) (syrup) was obtained. Treatment of (**8**) with NaH afforded the epoxy compound (**11**) (syrup) as well as the product of C–C bond formation (**12**) (syrup) in a ratio of 1:2—3; (**11**): *m/e* (75 eV) 345 (M^+ — Me), 302 [M^+ — Me — $CH_2CH(O)$], 169 [M^+ — Me — $EtO_2CCH(O)CO_2Et$ — H], and 127 [M^+ — Me — $EtO_2CCH(O)CO_2Et$ — $CH_2CH(O)$]; δ 4·68 (1H, s, EtO_2CCHCO_2Et); (**12**): ν (KBr) 3500 (OH), 1700sh, and 1743 (CO) cm^{-1}; δ ($CDCl_3$, Me_4Si) 2·31 and 2·77 (2H, 2 × dd, 6-H^a and -H^b, $J_{5,6a}$ 3, $J_{5,6b}$ 4, J_{gem} 15 Hz), 4·35 (1H, dd, 3-H, $J_{2,3}$, 4, $J_{3,4}$ 12 Hz), and 5·77 (1H, d, 1-H, $J_{1,2}$ 4 Hz). A large $J_{3,4}$ value in (**12**) corresponds well with the $J_{3',4'}$ value of 10·5 Hz in octosyl acid A (**1**).[1]



(7) $R^1 = R^2 = H$
(8) $R^1 = p\text{-}MeC_6H_4SO_2$, $R^2 = H$
(9) $R^1 = R^2 = p\text{-}MeC_6H_4SO_2$
(10) $R^1 = p\text{-}MeC_6H_4SO_2$, $R^2 = MeCO$



(12) R = H
(13) R = MeCO
(14) R = $p\text{-}MeC_6H_4SO_2$



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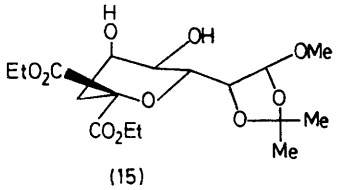

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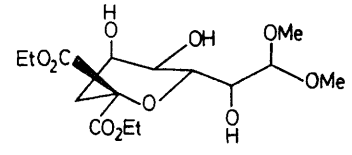

(16)

Similarly, the ditosylate (**9**) and the acetyl tosyl compound (**10**) (syrup) were converted into the tosylate (**14**), m.p. 146—147 °C, *m/e* 499 (M^+ — Me), and the acetate (**13**) (syrup), *m/e* 387 (M^+ — Me), of (**12**). Compound (**10**) was prepared by treatment of (**8**) with Ac_2O–pyridine.

Treatment of (**12**) with 0·01N HCl in methanol resulted in initial cleavage of the furanose ring prior to release of Me_2CO to give (**15**), followed by further conversion into compound (**16**); (**15**): m.p. 90 °C, *m/e* 377 (M^+ — Me), and 361 (M^+ — OMe); δ ($CDCl_3$) 1·47 and 1·49 (6H, 2 × s, $Me_2C<$), 2·23 and 2·76 (2H, 2 × dd, 6-H^a and -H^b, $J_{5,6a}$ 3, $J_{5,6b}$ 4, J_{gem} 15 Hz), 3·41 (3H, s, MeO) and 5·33 (1H, d, 1-H, $J_{1,2}$ 1 Hz); (**16**): δ ($CDCl_3$) 2·21 and 2·77 (2H, 2 × dd, 6-H^a and -H^b, $J_{5,6a}$ 3, $J_{5,6b}$ 4, J_{gem} 15 Hz), and 3·44 and 3·76 (6H, 2 × s, OMe).

This acid lability of (**12**) may explain unsuccessful attempts to convert (**12**) into octosyl acid nucleosides through a route involving acetolysis of (**12**) using H_2SO_4 as catalyst followed by reaction with trimethylsilyluracil using $SnCl_4$ as catalyst.[5]

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† All compounds were adequately characterised; only selected spectral data are reported.

[1] K. Isono, P. F. Crain, and J. A. McClosky, *J. Amer. Chem. Soc.*, 1975, **97**, 943.
[2] K. Isono, K. Asahi, and S. Suzuki, *J. Amer. Chem. Soc.*, 1969, **91**, 7940.
[3] K. Isono, J. Nagatsu, Y. Kawashima, and S. Suzuki, *Agric. Biol. Chem.*, 1965, **29**, 848.
[4] R. L. Whistler and J. N. Beniller, *Methods Carbohydrate Chem.*, 1972, **6**, 123; D. C. Baker, D. Horton, and C. G. Tindall, Jr., *Carbohydrate Res.*, 1972, **24**, 192.
[5] H. Vorbrüggen, K. Krolikiewicz, and U. Niedballa, *Ann. New York Acad. Sci.*, 1975, **255**, 82; H. Vorbrüggen and U. Niedballa, *Angew. Chem.*, 1971, **83**, 729.