Carbohydrate Research, 89 (1981) 163–165
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

The reaction of *keto*-D-fructose penta-acetate with diazomethane*

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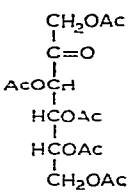
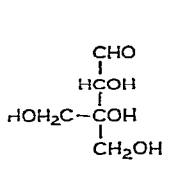
(Received April 22nd, 1980, accepted for publication June 5th, 1980)

The action of diazomethane on *keto*-D-fructose penta-acetate (**1**, 1,3,4,5,6-penta-*O*-acetyl-D-*arabino*-hexulose) dissolved in chloroform containing traces of methanol was reported[2,3] to give 75% of a crystalline epoxide {m.p. 86–87°, $[\alpha]_D^{24}$ +32° (chloroform)}, but the stereochemistry of the reaction was not elucidated. This epoxide has been used in a synthesis[4] of (+)-apiose (**2**), but the stereochemistry of the reaction was not important because the chiral C-2 became the achiral C-3 in **2**.



1



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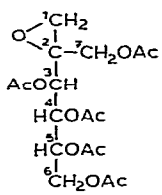

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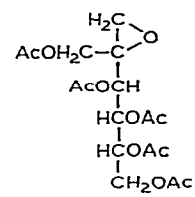
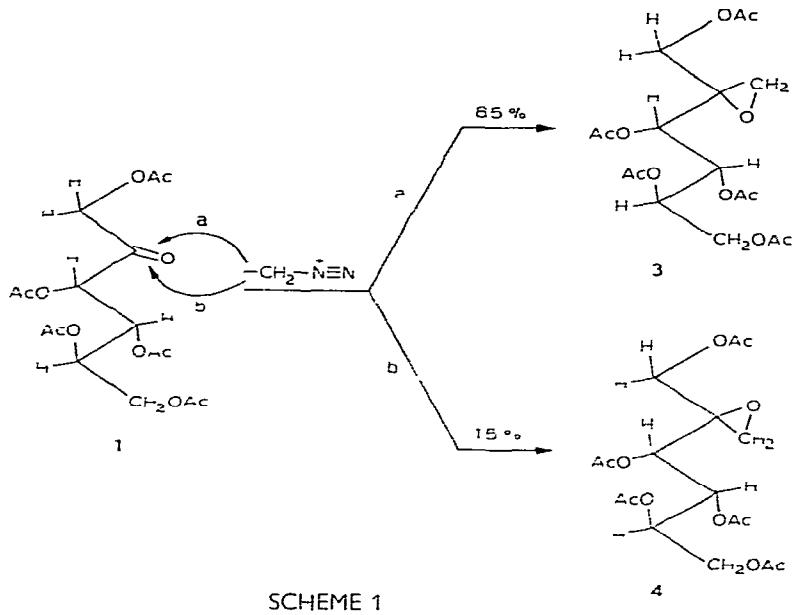


4

Much work has been done on the addition of diazomethane to glycosulose derivatives[1,5,6]. Such compounds are usually in a fixed conformation and, on this basis, the stereochemistry of the reactions has been explained.

We have studied additions to the oxo-group in acyclic derivatives of ketoses and aldoses[1,7,8]. Such compounds are conformationally mobile. Addition of sulfur ylids yields epoxides only, whereas diazomethane also gives ketones. A two-step mechanism, proposed on the basis of experiments in which the polarity of the reaction media was varied, to explain the relative yields of the epimeric epoxides and ketones, involved the so-called dipolar model for steric control of asymmetric induction[9], but also included an electrostatic interaction between the positively charged nitrogen and the oxygen function in the α-position (*cf.* ref. 6). It was suggested that the preponderant epoxide and ketone arose from a common betaine intermediate.

*Addition of Diazomethane and Sulfur Ylids to the Carbonyl Group in Derivatives of Ketoses and Aldoses, Part 4. For Part 3, see ref. 1.



SCHEME 1

On re-investigation, the reaction between *keto*-D-fructose penta-acetate (**1**) and diazomethane was found to yield two epoxides in the ratio 85 15

The predominant conformation of **1** is near to the planar zigzag structure, as inferred from ^{1}H-n m r data ($J_{3,4}$ 2 0, $J_{4,5}$ 8 8 Hz) Molecular models suggest that diazomethane will have best access to face (a) in **1**, leading to **3** as the preponderant epoxide (Scheme 1) It is also possible that interaction between the positive nitrogen atom and the oxygen function at C-3 will be important

The previous reports[2–4] on the reaction between diazomethane and **1** reported a preponderant product having the physical properties noted above We have used ^{13}C-n m r spectroscopy to monitor the reaction carried out under various conditions, since the resonances of C-1 and C-2 were suitable for this purpose The resonances for H-1 were equivalent (δ 2 77) in the ^{1}H-n m r spectrum of **3**, but appeared as an AB-quartet (δ 2 70 and 2 84 J_{AB} 4 9 Hz) in the spectrum of the epimeric epoxide **4** ^{1}H-N m r spectra of mixtures of **3** and **4** therefore show characteristic, five-line patterns which may be of analytical value The compositions of the reaction mixtures were always close to 85 15 and the preponderant epoxide had m p 68° and $[\alpha]_D$ +35° (chloroform)

Fractional crystallisation gave the minor epoxide **4** (m p 86°, $[\alpha]_D$ +33°)

EXPERIMENTAL

N m r spectra ($CDCl_3$, internal Me_4Si) were recorded with a Jeol FX-100 instrument at 25 1 MHz for ^{13}C, and 99 6 MHz for ^{1}H

Reaction of keto-D-*fructose penta-acetate* (**1**) *with diazomethane* — To a solu-

tion of **1** {8 g, 0 02 mol, m p 68°, $[\alpha]_D$ +35° (*c* 1 26, chloroform)} in methanol (50 ml) was added a solution of diazomethane (3 g, 0 07 mol) in methanol (50 ml), and ether (100 ml) was added After 24 h at room temperature, the reaction mixture was filtered and concentrated *in vacuo*, to yield a yellow syrup (8 g, 97%) which crystallised from ethanol (8 ml) and ether (8 ml), to yield 2-*C*-acetoxymethyl-3,4,5 6-tetra-*O*-acetyl-1,2-anhydro-D-mannitol (**3**, 4 8 g, 60%), m p 68°, $[\alpha]_D^{21}$ +35° (*c* 1, chloroform) Mass spectrum *m/e* 331 1026 (0 2%, $[M - CH_2OAc]^+$, calc for $C_{14}H_{19}O_9$ 331 1029) ^{1}H-N m r data δ 2 07 2 07, 2 10, 2 11, and 2 13 (5 s, 5 AcO), 2 77 (s, 2 H, H-1,1′), 4 17 and 4 49 (AB system, J_{AB} 12 7 Hz, H-7,7′), 4 20 and 4 23 (m, 2 H, H-6,6′), 5 13 (m, H-5), 5 28 (d H-3), and 5 55 (dd, H-4) $J_{3,4}$ 3 4, $J_{4,5}$ 7 8, $J_{5,6}$ 2 3 $J_{5,6}$ 5 3, and $J_{6,6}$ 12 4 Hz ^{13}C-N m r data δ 20 7 (5 CH_3CO), 48 1 (C-1, 57 1 (C-2), 61 5 (C-6) 63 2 (C-7), 68 3 and 68 4 (C-3,4,5), and 169 4 (5 CH_3CO)

The mother liquor from the above crystallisation of **3** was concentrated *in vacuo*, and the residue was recrystallised from ether, to yield 2-*C*-acetoxymethyl-3,4 5 6-tetra-*O*-acetyl-1,2-anhydro-D-glucitol (**4** 0 5 g) m p 86–87° $[\alpha]_D^{22}$ +33° (*c* 1, chloroform), lit [2] m p 86–87°, $[\alpha]_D^{24}$ +32° ^{1}H-N m r data δ 2 07 and 2 11 (2 s, 9 and 6 H 5 AcO), 2 70 and 2 84 (AB system, J_{AB} 4 9 Hz, H-1,1′), 4 08 and 4 55 (AB system, J_{AB} 12 7 Hz, H-7,7′), 4 19 and 4 27 (m, 2 H, H-6,6), 5 19 (m, H-5), 5 30 (d, H-3), and 5 52 (dd, H-4), $J_{3,4}$ 2 9 and $J_{4,5}$ 7 9 Hz ^{13}C-N m r data δ 20 4 and 20 7 (5 CH_3CO), 47 5 (C-1), 55 2 (C-2), 61 7 (C-6), 63 5 (C-7), 67 3, 68 4 68 4 (C-3, C-4, C-5), 169 5, 169 7, 170 3, and 170 6 (5 CH_3CO)

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