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Note

Acyclic sugars: the ring-opening of 2-acetamido-2-deoxyhexopyranoses in trifluoroacetic acid

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During an investigation of solvent effects on the anomeric equilibria of 2-acetamido-2-deoxyhexoses, we have observed a novel, reversible reaction of these sugars with trifluoroacetic acid that is described herein. Fig. 1 shows the ^{1}H-n.m.r. spectra of 2-acetamido-2 deoxy-D-glucopyranose (**1**) in trifluoroacetic acid, recorded at intervals after dissolution[2]. A sharp doublet (J = 5.5 Hz) at δ ~7 and a singlet at δ ~2.6 begin to appear within a few min. The increase in the intensity of these resonances is accompanied by a concomitant decrease of the H-1 peak at δ ~5.4 and the methyl resonance at δ 2.4 of **1**. The reaction is essentially complete after 3 h, and Fig. 1c shows the spectrum after 19 h. During this conversion, the specific rotation changes from an initial $[\alpha]_D$ of +49° to a final value of −54.4°. Evaporation of the trifluoroacetic acid *in vacuo* yielded an unstable oil that showed the presence of acetamido and trifluoroacetyl groups (ν_{CO} 1680 and 1795 cm^{-1}). Addition of D_2O led to rapid reversal of the reaction. Fig. 2 shows the n.m.r. spectra of the oil in D_2O, recorded at intervals. The doublet at δ 7 and the singlet at δ 2.6 disappear, whereas the resonances of **1** reappear. An interesting feature of the reverse reaction is the growth and decay of a doublet at δ ~6.5 and a methyl resonance at δ 2.15, characteristic of a short-lived intermediate. Analysis of curves of the progress of reaction suggests that consecutive first-order processes are operative.

In Scheme I we propose a reaction sequence that accounts for our results. Acid-catalysed ring opening of **1** is assisted by participation of the 2-acetamido group[1,2]. We have failed to observe similar reactions with D-glucose or 2-amino-2-deoxy-D-glucopyranose. Oxazolinium ions have been previously implicated in reactions of acetamido sugars[3,4]. The acyclic structure (**2**) proposed in Scheme I is a masked aldehyde. Fig. 1d (inset) shows the spectrum of butanal in trifluoroacetic acid after a period of 2 days. A triplet (J ~7.5 Hz) appears at δ 7, whereas the intensity of the aldehyde resonance at δ 9.7 is decreased. Similar results were obtained with hexanal.

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However, the reaction was significantly slower with the simple aldehydes. The coincidence of the chemical shifts of the species obtained from aliphatic aldehydes and the sugars is strong evidence for an acyclic structure in the latter. The lower rate of addition of trifluoroacetic acid to the carbonyl group of the model aldehydes suggests that the trifluoroacetyl derivatives of the acetamido sugars may be derived directly from the oxazolinium intermediate. The formation of geminal bis(trifluoroacetates) from aldehydes and trifluoroacetic anhydride has been reported[5]. The reported chemical-shift of the aldehydo proton on formation of the bis(trifluoroacetyl) derivatives agrees very well with the shift of the H-1 resonance of **1** in trifluoroacetic acid. We therefore assign the bis(ester) structure **2** to the species observed in trifluoroacetic acid. Preliminary studies with trifluoroacetic anhydride also show the appearance of a triplet at $\delta \sim 7$. Comparison of the ^{13}C-n.m.r. spectra of **1** in D_2O and in trifluoroacetic acid after completion of the reaction shows a downfield shift of C-1 by ~ 20 p.p.m. in trifluoroacetic acid. The large change in $[\alpha]_D$, the general downfield-shift of the H-2–H-5 protons (δ 4–4.5 to 4.2–5.2), and the observation of i.r. bands at 1795 and 1680 cm^{-1} provide supporting evidence for **2**.

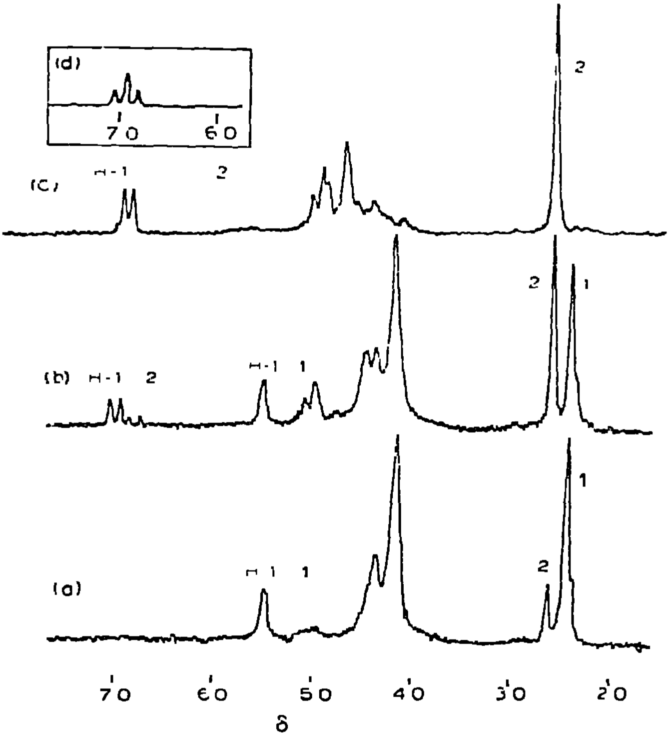


Fig. 1. 60-MHz proton n.m.r. spectra of **1** in trifluoroacetic acid: (*a*) 3 min after dissolution (scan rate, 2 Hz/sec), (*b*) after 14 min, and (*c*) after 19 h. The inset (*d*) shows the δ 6–8 region of a solution of butanol in trifluoroacetic acid, 2 days after dissolution.

Prolonged (5 days) treatment of cellulose with trifluoroacetic acid has been shown[6] to lead to trifluoroacetylation at O-6. The present studies do not provide clear evidence for trifluoroacetylation at O-6 after 16 h. The mono(trifluoroacetyl) structure for the intermediate (3) in the reverse reaction is speculative, at present, and is based only on the chemical shift of H-1. Similar reactions have been observed with the 2-acetamido-2-deoxy-derivatives of D-galactose and D-mannose. Quenching of **2** with alcohols leads to the formation of glycosides. Although glycoside formation may also proceed from the oxazolinium trifluoroacetate, the i.r. spectrum rules out this structure for the final product of the reaction in trifluoroacetic acid. The kinetics of these reactions and their probable synthetic utility are under investigation. The spectroscopic observation of open-chain structures should also prove useful in the conformational analysis of sugars. Preliminary attempts to trap the acyclic species chemically by acetylation have proved unsuccessful. In this context, the thermal lability of the geminal bis(trifluoroacetates) reported earlier[5] is noteworthy.

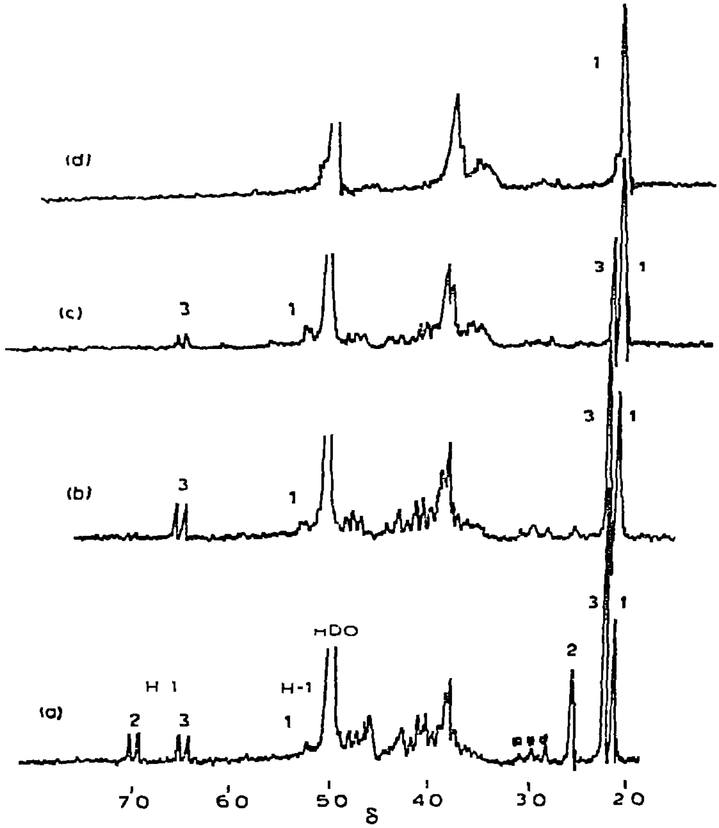
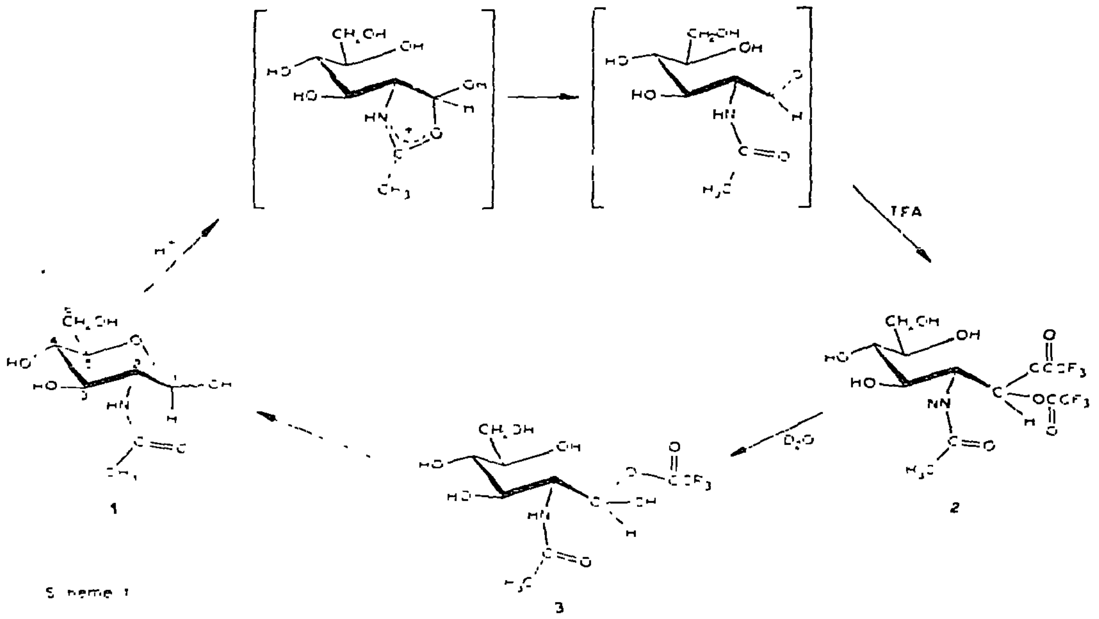


Fig. 2. 60-MHz proton spectra obtained after evaporating off the trifluoroacetic acid and redissolving the oil in D$_2$O· (*a*) 2–4 min, (*b*) 11–14 min, (*c*) 3.5 h, and (*d*) 19 h. Peaks marked with asterisks correspond to the internal standard (DSS).



Scheme 1

EXPERIMENTAL

2-Acetamido-2-deoxy-D-glucose (Sigma) was used without further purification. Trifluoroacetic acid and aldehydes were distilled before use. ^1H n.m.r. spectra were recorded on Varian T-60 and HA-100 spectrometers. Chemical shifts are expressed as δ (p.p.m.) from tetramethylsilane in trifluoroacetic acid, and 4,4-dimethyl-4-silapentane-1-sulfonate (DSS) in D_2O. ^{13}C n.m.r. spectra were recorded on a Bruker spectrometer at 22.63 MHz. Optical rotations were obtained with a Jasco J-20 spectropolarimeter and i.r. spectra of **2** were recorded neat on a Carl Zeiss UR-10 spectrometer.

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REFERENCES

1 H. Paulsen, *Adv. Carbohydr. Chem. Biochem.*, 26 (1971) 127–195.
2 L. Goodman, *Adv. Carbohydr. Chem.*, 22 (1967) 109–175.
3 H. Paulsen and C. P. Herold, *Chem. Ber.*, 104 (1971) 1311–1321.
4 F. Micheel, F.-P. van der Kamp, and H. Petersen, *Chem. Ber.*, 90 (1957) 521–526.
5 A. L. Ternay, D. Deavenport, and G. Bledsoe, *J. Org. Chem.*, 39 (1974) 3268–3271.
6 A. L. Geddes, *J. Polym. Sci.*, 22 (1956) 31–39.