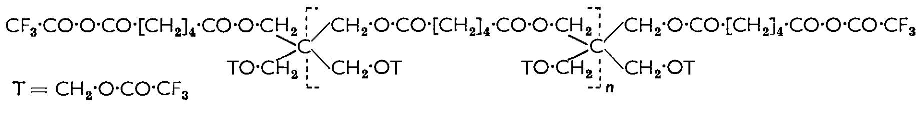
588. *Ring Scission of Cyclic Acetals. Part II.*[1] *The Reactions of Di-O-methylenepentaerythritol with Carboxylic Acids and Trifluoroacetic Anhydride.*

By T. G. Bonner, E. J. Bourne, and N. M. Saville.

The reaction of adipic acid and trifluoroacetic anhydride with di-*O*-methylenepentaerythritol appears to give a cross-linked polyester and not the expected linear product. The interpretation of this result is based on a study of the reaction using a monocarboxylic acid in place of adipic acid which shows that (i) partially esterified pentaerythritols tend to disproportionate in solutions of pH 9, and (ii) the trifluoroacetoxymethyl group is labile to an acylating reagent when linked to the oxygen atom of a primary alcohol group.

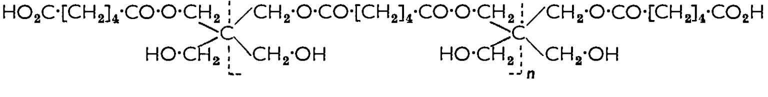
When a linear polyester was obtained from tri-*O*-methylene-D-glucitol by the action of trifluoroacetic anhydride and adipic acid,[1] the analogous reaction was studied with di-*O*-methylenepentaerythritol, which was expected to give products (A) and, after hydrolysis, (B).

(A)



T = $CH_2 \cdot O \cdot CO \cdot CF_3$

(B)



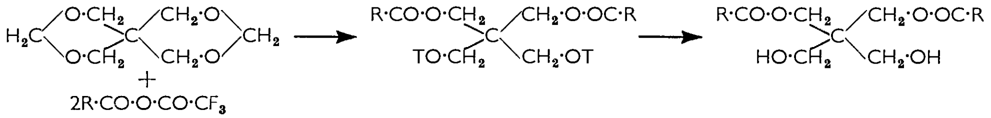
Equimolar quantities of di-*O*-methylenepentaerythritol and adipic acid were dissolved in an excess of trifluoroacetic anhydride and left at room temperature for three hours. Evaporation of volatile constituents and treatment with aqueous sodium hydrogen

---

[1] Part I, preceding paper.

carbonate solution, as before, gave a colourless, rubber-like solid which did not dissolve completely in any common organic solvent. It did not melt but charring began at *ca.* 300°. These properties were different from those of the linear polyester obtained from 1,3:2,4:5,6-tri-*O*-methylene-D-glucitol and suggested a cross-linked polymer. Alkaline hydrolysis of the polymer gave, as predicted, pentaerythritol and adipic acid in good yield. Viscosity measurements were not possible in absence of a suitable solvent; pyridine which had been in contact with the material was unchanged in viscosity. It was realised that the apparent branching of the polymer chain could be due to dipentaerythritol known to be present in technical pentaerythritol.[2] This would form di-*O*-methylenedipentaerythritol containing two free hydroxy-groups which would be readily acylated to give a product having four active acylating centres. Purification of pentaerythritol by the standard procedure [2] produced a sample of higher m. p., but its di-*O*-methylene derivative had the same m. p. as that from technical pentaerythritol, and reaction with adipic acid and trifluoroacetic anhydride gave a similar colourless, rubber-like product. It seemed that the bismethylenedioxy-derivative had been effectively purified.

Two explanations for the formation of a cross-linked polyester were considered: (i) that the acylating agent displaces trifluoroacetoxymethyl residues which thus do not serve as efficient blocking groups, and (ii) that a third or even a fourth adipate ester constituent is introduced into some of the pentaerythritol units in the chain during removal by mild hydrolysis of the trifluoroacetoxymethyl groups. To examine these possibilities simpler systems were first investigated, with a monocarboxylic acid in place of adipic acid.



With benzoic acid–trifluoroacetic anhydride the product should be the known, crystalline di-*O*-benzoylpentaerythritol.[3] It was, however, an oil, alkaline hydrolysis of which gave pentaerythritol and benzoic acid. Reaction with acetic acid and trifluoroacetic anhydride followed by the usual hydrolysis gave an oil which was shown by chromatography to contain at least two esters. The preparation of the known compound, di-*O*-acetylpentaerythritol, was then carried out for a study of its stability to alkali and its R_{F} values. This preparation was revealing: mono-*O*-isopropylidenepentaerythritol is converted into its diacetate by acetic anhydride and sodium acetate, and the isopropylidene group is then hydrolysed by N/20-hydrochloric acid, the excess of acid being finally removed with silver carbonate.[3] Chromatography showed that isopropylidenepentaerythritol diacetate contained only a trace of the tetra-acetate, but that the hydrolysis product contained three esters in addition to the tetra-acetate and some pentaerythritol, but no unchanged isopropylidene derivative. When the tetra-acetate was removed from the product, no more appeared to be generated on storage; when samples were then treated with aqueous solutions of pH <8 and the chloroform-soluble products examined by chromatography, no tetra-acetate was detected, but after treatment at pH 9—10 evidence of its presence was obtained, indicating that alkali-catalysed disproportionation of diacetate to tetra-acetate had probably occurred. Intramolecular acyl migrations in partially esterified polyols are known to be catalysed by traces of alkali; [4] while intramolecular migration in a pentaerythritol ester would not yield a different ester, intermolecular migrations could do so. The reaction of di-*O*-methylenepentaerythritol with acetic acid and trifluoroacetic anhydride was therefore repeated with the hydrolysis carried out in an aqueous solution buffered at pH 7; at this pH trifluoroacetoxymethyl groups should be removed [5] without disproportionation of diacetate. The chloroform-soluble

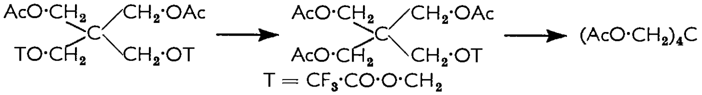
[2] Berlow, Barth, and Snow, " The Pentaerythritols," Reinhold Publ. Corp., New York, 1958

[3] Orthner and Freyss, *Annalen*, 1930, **484**, 147.

[4] Pacsu, *Adv. Carbohydrate Chem.*, 1945, **1**, 108.

[5] Moffat and Hunt, *J. Amer. Chem. Soc.*, 1957, **79**, 54.

material, however, again contained a mixture of three esters including the tetra-acetate, and the R_F values indicated the presence of the di- and tri-esters. Since our experiments indicate that these are not formed during hydrolysis at pH 7, they were presumably formed during acylation of the acetal, by displacement of trifluoroacetoxymethyl by acetyl groups after initial ring opening:



No such reaction occurs with tri-*O*-methylene-D-glucitol; but there the trifluoroacetoxymethyl groups are linked to oxygen atoms from secondary alcohol groups while in the pentaerythritol derivatives they are linked to oxygen atoms from primary alcohol groups. The preference of an acetylating agent for attack at a primary position is already established in the acetolysis of 1,3:2,5:4,6-tri-*O*-methylene-D-mannitol,[6] which gives 3,4-di-*O*-acetoxymethyl-1,6-di-*O*-acetyl-2,5-*O*-methylene-D-mannitol, and in the reaction of tri-*O*-methylene-D-glucitol with trifluoroacetic anhydride–carboxylic acid mixtures. It appears therefore that when trifluoroacetic anhydride and adipic acid are used, displacement of trifluoroacetoxymethyl groups in the initial linear polymer will lead to further reactive centres and thus to cross-linking.

We next studied some benzylidene and isopropylidene derivatives. Tri-*O*-benzylidene- and di-*O*-isopropylidene-D-mannitol are converted by acetic acid and trifluoroacetic anhydride into mannitol hexa-acetate;[7] the product from di-*O*-benzylidenepentaerythritol contained the tetra-acetate and smaller amounts of three other esters. Hydrolysis with dilute hydrochloric acid liberated benzaldehyde, suggesting that one ester was probably di-*O*-acetyl-*O*-benzylidenepentaerythritol. This compound was prepared by acetylation of mono-*O*-benzylidenepentaerythritol and had the same R_F value as one of the three esters just mentioned. Di-*O*-benzylidenepentaerythritol was also treated with trifluoroacetic anhydride and excess of acetic acid. This reagent opens methylene rings, as in acetolysis, with the formation of one acetate and one acetoxymethyl group per ring opened.[7] The product was similar to that obtained in the previous experiment but contained mostly the tetra-acetate and the di-*O*-acetyl-*O*-benzylidene derivative. Mono-*O*-benzylidenepentaerythritol under the same conditions gave a similar mixture of esters. Thus, one acetal ring in the dibenzylidene compound is readily opened but the other acetal ring is more resistant, which is unusual since under comparable conditions no products containing intact benzylidene rings have been detected with the corresponding benzylidene hexitols. Examination of Catalin models provides an explanation. There is no steric hindrance to the approach of a reagent (unless very bulky) to any of the four ring-oxygen atoms of di-*O*-benzylidenepentaerythritol, but when the first benzylidene ring is opened the acetoxymethyl groups introduced can hinder the approach of the mixed anhydride to the unopened ring. The same situation can arise in mono-*O*-benzylidenepentaerythritol since the free alcohol groups are almost certainly more rapidly attacked than the acetal ring.[7]

With equimolar proportions of acetic acid and trifluoroacetic anhydride mono-*O*-isopropylidenepentaerythritol gave a small yield of the tetra-acetate which was doubled when excess of acetic acid was used. Only traces of other esters could be detected and di-*O*-acetyl-*O*-isopropylidenepentaerythritol was not obtained. This behaviour is similar to that of isopropylidenehexitols which give low yields of the hexitol hexa-acetate under the same conditions.

EXPERIMENTAL

Detection of Products by Paper Chromatography.—The two solvents mainly employed were (*a*) water-saturated butan-1-cl, prepared by shaking the two liquids together for a few hours, cooling to 0°, and removing the organic layer, and (*b*) light petroleum (b. p. 60—80°) saturated

---

[6] Ness, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 2215.

[7] Bourne, Burdon, and Tatlow, *J.*, 1959, 1864.

with dimethyl sulphoxide,[8] the stationary phase in the paper being the sulphoxide. With the latter solvent the paper is dipped in a 20% solution of the sulphoxide in benzene, pressed between absorbent paper, and dried for 1 min. at 60°; this treatment is repeated and the paper placed between glass plates to prevent absorption of water. After elution of a reaction product with the light petroleum solvent the paper is dried at 120° for 20 min. before being sprayed. Both solvents (*a*) and (*b*) were used with Whatman No. 1 paper. The most satisfactory spray for esters of pentaerythritol is the hydroxylamine reagent [9] [a freshly prepared 1 : 1 v/v mixture of methanolic hydroxylamine hydrochloride (6·95 g./100 ml.) and potassium hydroxide (6·17 g./100 ml.)]. After spraying, the paper is dried at a temperature and for a time depending on the reactivity of the ester, *e.g.*, pentaerythritol tetra-acetate is detected only by heating to 110° for 10 min. The paper is finally sprayed with a 1 : 1 v/v mixture of aqueous ferric chloride and aqueous 0·5N-hydrochloric acid. Acetates and lactones appear as purple spots on a yellow background, but benzoates are not detected. The 2,4-dinitrophenylhydrazine spray [10] was used to detect benzylidene and isopropylidene derivatives.

*Reaction of Trifluoroacetic Anhydride–Adipic Acid with Di-*O*-methylenepentaerythritol.*—The acetal (0·5 g.) and adipic acid (0·46 g., 1 mol.) were treated with trifluoroacetic anhydride (2·6 ml., 6·3 mol.) and left for 3 hr. at room temperature. The volatile constituents were removed at 40° under reduced pressure, carbon tetrachloride was added, and the solution again evaporated. This was repeated twice to give a colourless glass. Aqueous sodium hydrogen carbonate was added and after 4 days the insoluble residue was filtered off, washed with water, and dried. The rubber-like solid obtained (0·54 g.) did not melt but darkened at 300° (Found: C, 52·9; H, 7·5%).

The product (0·13 g.) was hydrolysed with boiling 0·1N-sodium hydroxide, and the mixture evaporated to dryness. Extraction of the residue with boiling pyridine gave a soluble product, *A*, which after concentration of the pyridine solution was acetylated with sodium acetate and acetic anhydride, to give tetra-*O*-acetylpentaerythritol (0·08 g., 50%), m. p. 78—79°, mixed m. p. 79—80°. The residue from the pyridine extraction was dissolved in water, and the solution was acidified and evaporated to dryness. The residue was extracted with methanol and the solution shown to contain adipic acid [*S*-benzylisothiouronium salt (0·06 g., 68%), m. p. and mixed m. p. 161—162°].

*Di-*O*-acetylpentaerythritol.*—(i) Mono-*O*-isopropylidenepentaerythritol was prepared by stirring together for 15 min. at room temperature pentaerythritol (10 g.), hydrochloric acid (*d* 1·18; 5·0 ml.), water (53 ml.), and acetone (202 ml.) and then refluxing the whole for 30 min. After 24 hr. at room temperature, the solution was treated with aqueous 25% sodium hydroxide to obtain a pH of 8 and then concentrated under reduced pressure, first at 50° and then at 70° (sublimation of the product occurs at higher temperatures). The dry residue was ground and extracted (Soxhlet), first with light petroleum (b. p. 40—60°) for 6 hr., then with ether for 12 hr. The ether yielded colourless crystals (3·6 g., 28%), m. p. 126·5—127·5° (Rapoport [11] gave m. p. 126—127° for isopropylidenepentaerythritol) (Found: C, 54·4; H, 9·3. Calc. for $C_8H_{16}O_4$: C, 54·5; H, 9·2%).

(ii) Di-*O*-acetyl-*O*-isopropylidenepentaerythritol was obtained by refluxing the ketal (0·83 g.), sodium acetate (0·83 g., 2·1 mol.), and acetic anhydride (3·75 ml., 8·6 mol.) in chloroform (16·6 ml.) for 1 hr. and leaving the mixture overnight at room temperature. The solution was filtered and evaporated, and the residue extracted with light petroleum (b. p. 60—80°); concentration of the extract gave the diacetate (0·94 g., 77%), m. p. 45—46° (Orthner and Freyss [3] gave m. p. 48—49°) (Found: C, 55·5; H, 7·7. Calc. for $C_{12}H_{20}O_6$: C, 55·4; H, 7·7%).

(iii) " Di-*O*-acetylpentaerythritol " was obtained by shaking the ketal diacetate (0·7 g.) with 0·05N-hydrochloric acid for 15 min.; after 1 hr. silver carbonate was added; the pH did not rise above 4. The mixture was filtered, concentrated under reduced pressure, and treated with hydrogen sulphide. As no silver sulphide separated, the black solution was shaken with charcoal and filtered, then concentrated and freeze-dried. From the residue ether removed a colourless oil (0·51 g.) from which a solid later separated. Chromatography with solvent (*a*) and the hydroxylamine spray reagent revealed constituents with R_F 0·67 and 0·81—0·89 (tetra-*O*-acetylpentaerythritol, R_F 0·94). With solvent (*b*) some of the product remained on the base

---

[8] Wickberg, *Acta Chem. Scand.*, 1958, **12**, 615.

[9] Abdel-Akher and Smith, *J. Amer. Chem. Soc.*, 1951, **73**, 5859.

[10] Barker, Bourne, Foster, and Pinkard, *Chem. and Ind.*, 1959, 226.

[11] Rapoport, U.S.P. 2,441,595 (*Chem. Abstr.*, 1948, **42**, 7323d).

line; in addition, there was one constituent with R_{F} 0·27 (tetra-*O*-acetylpentaerythritol, 0·27). The tetra-acetate was separated from the product by elution on Whatman No. 3 paper with solvent (*b*). The base line was cut away and eluted with chloroform. The chloroform solution was concentrated to give an oil on which chromatograms were run after different time intervals; no disproportionation to tetra-acetate was detected in the oil itself. The oil was left in contact with aqueous solutions of different pH values (see below) for several hours, the mixtures were extracted with chloroform, and chromatograms run on the extracts, examination for tetra-acetate gave the following results: with 0·05N-hydrochloric acid or 1% sodium hydrogen carbonate (pH 7—8), none; with 10% sodium hydrogen carbonate (pH 9), a trace; with a sodium hydrogen carbonate–carbonate (pH 10), an appreciable amount.

Reactions of Trifluoroacetic Anhydride–Acetic Acid.—(i) *With di-*O*-methylenepentaerythritol.* A mixture of acetic acid (0·22 ml., 6·0 mol.), trifluoroacetic anhydride (0·55 ml., 6·3 mol.) and the acetal (0·10 g.) formed a homogeneous solution which was left at room temperature for 3 hr. Volatile constituents were removed to give an oil (0·31 g.) which was shaken for 2 hr. with an aqueous solution (80 ml.) buffered at pH 7 (phosphate) and then left at room temperature overnight. Chloroform-extraction yielded an oil *A* (0·04 g.); the aqueous layer was freeze-dried and the residue extracted with chloroform to give an oil *B* (0·09 g.); finally, the residue was extracted with pyridine to give a solution *C*. Chromatograms with solvent (*a*) showed that these three fractions contained constituents with R_{F} values: *A*, 0·79 and 0·87; *B*, 0·64 and 0·79; *C*, 0·64 and 0·76. With this solvent pentaerytritol has R_{F} 0·45 and its tetra-acetate has R_{F} 0·94; with solvent (*b*), the tetra-acetate was detected in the oil *A*. The products therefore appear to be mono-, di-, tri-, and tetra-acetate.

(ii) *With di-*O*-benzylidenepentaerythritol.* A mixture of acetic acid (0·37 ml., 20 mol.), trifluoroacetic anhydride (0·9 ml., 20 mol.), and the acetal (0·1 g.) formed a red solution. After 24 hr. at room temperature the volatile constituents were removed to give a dark oil (0·20 g.). This was hydrolysed as in (i), and extracted with chloroform to yield a yellow oil (0·13 g.), chromatography of which with solvent (*a*) revealed tetra-*O*-acetylpentaerythritol, and with solvent (*b*) three other products of R_{F} 0, 0·68, and 0·84. As one of these appeared to be *di-*O*-acetyl-*O*-benzylidenepentaerythritol* this ester was prepared by acetylation of mono-*O*-benzylidenepentaerythritol (0·10 g.) with sodium acetate and acetic anhydride (procedure as above). It was a colourless oil which on chromatography with solvent (*b*) gave two compounds with R_{F} values of 0·05 (possibly the monoacetate) and 0·66 (cf. 0·68 above). Separation on a cellulose column (length 21 cm., diameter 1·5 cm.) with solvent (*b*) gave an oil (0·1 g.), chromatographically pure and corresponding to the diacetate (Found: C, 62·2; H, 7·1. $C_{16}H_{20}O_6$ requires C, 62·3; H, 6·5%).

(iii) *With mono-*O*-isopropylidenepentaerythritol.* Acetic acid (0·37 ml., 20 mol.), trifluoroacetic anhydride (1·0 ml., 20 mol.), and the ketal (0·06 g.) gave a yellow solution which became red in 26 hr. This was treated as in (ii), to yield an oil (0·14 g.) which partly crystallised; with solvent (*b*) chromatographic examination revealed tetra-*O*-acetylpentaerythritol and a product with R_{F} 0. Crystallisation from light petroleum (b. p. 60—80°) gave the tetra-acetate (0·014 g., 14%), m. p. 78—79°, mixed m. p. 79·5—80°.

Reactions of Trifluoroacetic Anhydride and Excess of Acetic Acid.—(i) *With di-*O*-benzylidenepentaerythritol.* Acetic acid (1·90 ml., 100 mol.), trifluoroacetic anhydride (0·45 ml., 10 mol.), and the acetal (0·1 g.) formed a colourless solution which became yellow in 24 hr. Treatment with the aqueous buffer (pH 7) as above and chloroform-extraction yielded an oil (0·14 g.). With solvent (*b*) the chromatogram showed compounds with R_{F} 0, 0·51, 0·71, and 0·82 (tetra-O-acetylpentaerythritol, R_{F} 0·51; di-*O*-acetyl-*O*-benzylidenepentaerythritol, 0·71). A similar chromatogram was obtained with mono-*O*-benzylidenepentaerythritol after the same treatment.

(ii) *With mono-*O*-isopropylidenepentaerythritol.* Acetic acid (1·90 ml., 100 mol.), trifluoroacetic anhydride (0·5 ml., 11 mol.), and the ketal (0·06 g.) gave a yellow solution, from which after 17 hr. a colourless oil (0·14 g.) was obtained. The chromatogram showed compounds with R_{F} 0, 0·49 (tetra-*O*-acetylpentaerythritol, R_{F} 0·49), and 0·78 (very faint). A light petroleum (b. p. 60—80°) extract of the oil yielded crystals of tetra-*O*-acetylpentaerythritol (0·026 g., 25%), m. p. and mixed m. p. 75—77°.

The authors thank Dr. A. Lovecy and Mr. C. H. Miller for their interest.

ROYAL HOLLOWAY COLLEGE (UNIVERSITY OF LONDON),
ENGLEFIELD GREEN, EGHAM, SURREY.

[*Received, February* 10*th*, 1960.]