2.95 (8 H, m), 3.00 (3 H, s), 3.13 (3 H, s), 2.95–3.30 (1 H, m), 3.40–3.70 (1 H, m), 3.84 (3 H, s), and 7.10–7.50 (3 H, m); mass spectrum (70 eV) *m/e* (rel intensity) 371 (4), 273 (11), 231 (15), 230 (100), 100 (25), 55 (20), 46 (11), and 43 (18).

No attempt was made to isolate the minor diastereomer from the mother liquors.

Reformatsky Reaction of Bromo Ester 12b. Esters 13f and 13g.—A mixture of 6.19 g (14.2 mmol) of freshly prepared bromo ester **12b** and 23.2 g (0.35 g-atom) of activated zinc dust in 150 ml of dry benzene[32] was refluxed under nitrogen for 4 hr. The reaction mixture was cooled to room temperature, 10 ml of acetic anhydride was added, and the mixture was stirred for 1 hr under nitrogen. Work-up (*vide supra*) afforded 5.14 g (90%) of a semicrystalline solid, the thin layer chromatogram of which indicated a mixture of two components of almost identical R_f contaminated with a small amount of polar material. Trituration of the residue with ether afforded 980 mg (19%) of ester **13f**: mp 153–154° (ethanol); ir ($CHCl_3$) 1732 and 1709 cm^{-1}; nmr ($CDCl_3$) δ 1.50 (9 H, s), 2.00 (3 H, s), 1.30–2.60 (8 H, m), 2.65–3.30 (2 H, m), 3.82 (3 H, s), and 7.10–7.60 (3 H, m); mass spectrum (70 eV) *m/e* (rel intensity) 400 (17), 343 (17), 327 (12), 285 (17), 284 (46), 272 (27), 267 (14), 266 (10), 256 (11), 242 (13), 240 (37), 239 (12), 230 (63), 229 (23), 211 (12), 187 (12), 174 (16), 173 (11), 57 (100), 55 (21), 43 (38), and 41 (25). Chromatography of the mother liquors on Florisil afforded 170 mg (3%) of pure ester **13g**, mp 98–99° (methanol), upon elution with 1–2% ether–benzene: ir ($CHCl_3$) 1710 cm^{-1}; nmr ($CDCl_3$) δ 0.52 (9 H, s), 2.03 (3 H, s), 1.50–2.65 (8 H, m), 2.70–3.70 (2 H, m), 3.82 (3 H, s), and 7.10–7.60 (3 H, m); mass spectrum (70 eV) *m/e* (rel intensity) 400 (1), 343 (10), 285 (24), 284 (100), 267 (14), 266 (15), 265 (10), 240 (14), 239 (46), 238 (41), 237 (26), 211 (17), 57 (32), 55 (18), 43 (36), and 41 (19).

Lithium Aluminum Hydride Reduction of Ester 13f.—A mixture of 50 mg (0.125 mmol) of ester **13f** and 20 mg (0.53 mmol) of lithium aluminum hydride in 5 ml of tetrahydrofuran was refluxed under nitrogen for 1 hr. Work-up (*vide supra*) yielded 34 mg (94%) of triol **14a**, mp 178–180° (ethyl acetate), exhibiting no melting point depression on admixture with a sample of triol **14a** prepared by reduction of benzoate **13c**.

Lithium Aluminum Hydride Reduction of Ester 13g.—A mixture of 30 mg (0.075 mmol) of ester **13g** and 15 mg (0.39 mmol) of lithium aluminum hydride in 3 ml of tetrahydrofuran was refluxed under nitrogen for 1 hr. Work-up (*vide supra*) yielded 24 mg (92%) of triol **14b**, mp 209–210° (ethyl acetate), exhibiting no melting point depression on admixture with a sample of triol **14b** prepared by reduction of benzoate **13d**.

Registry No.—**2a**, 23673-44-1; **2b**, 31729-94-9; **2c**, 23673-45-2; **3a**, 23673-46-3; **3c**, 23673-47-4; **5a**, 23668-27-1; **5b**, 31729-99-4; **5c**, 23668-28-2; **5d**, 31730-01-5; **5e**, 31730-02-6; **5f**, 31730-03-7; **5g**, 24905-74-6; **6a**, 31730-05-9; **6b**, 31730-06-0; **7b**, 23755-91-1; **7c**, 31730-08-2; **7e**, 31730-09-3; **8b**, 31730-10-6; **8c**, 31730-11-7; **12a**, 31730-12-8; **12b**, 31790-82-6; **12c**, 31790-83-7; **12d**, 31730-13-9; **13a**, 31730-14-0; **13b**, 31730-15-1; **13c**, 31730-16-2; **13d**, 31730-17-3; **13e**, 31730-18-4; **13f**, 31730-19-5; **13g**, 31730-20-8; **13h**, 31730-21-9; **14a**, 31730-22-0; **14b**, 31730-23-1; 2-methyl-4-(*p*-methoxybenzylidene)oxazol-5-one, 31730-24-2; α-bromo-*N*,*N*-dimethylacrylamide, 31730-25-3.

Acknowledgment.—Financial support for this work was provided by the National Science Foundation (GP-5828, GP-11273) and the National Cancer Institute, National Institutes of Health (CA-08869).

(32) *Cf.* A. E. Opara and G. Read, *Chem. Commun.*, 679 (1969).

The Influence of Reaction Conditions and Stereochemistry on Some Thioacetate Displacements with Carbohydrate Sulfonates[1]

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Received April 16, 1971

The reaction of 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-apio-L-furanose (**1**) with potassium thioacetate in boiling ethanol gave bis(5-deoxy-1,2-*O*-isopropylidene-α-D-apio-L-furanose-5-yl) disulfide (**2**) in high yield. Deacetylation of the intermediate thiolacetate **6** and subsequent oxidation of the thiol to **2** evidently occurred under these conditions. In aprotic solvents (DMF or acetone), both intramolecular S → O acetyl migration and S acetylation were observed in the reaction of **1** with potassium thioacetate, and a complex mixture of products was obtained. Acid-catalyzed methanolysis of the thiol obtained by reduction of **2** led to migration of the isopropylidene group and the formation of methyl 2,3-*O*-isopropylidene-4-thio-β-D-apio-D-furanoside (**8**). The reaction of methyl 2,3-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-β-D-apio-D-furanoside (**9**) with potassium thioacetate in boiling ethanol gave a mixture of disulfide **12** and monosulfide **13**. In this case, the intermediate thiol is a sufficiently powerful nucleophile to complete with thioacetate ion for **9** and, when thes ame reaction was carried out with 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylofuranose (**14**), the monosulfide **15** was obtained in 85% yield. Displacement of the sulfonyloxy group of 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-allofuranose was readily effected with potassium thioacetate in DMF to give, in high yield, 3-*S*-acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-glucofuranose. Oxidative deacetylation of this compound gave the corresponding gluco disulfide and similar treatment of 3-*S*-acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-allofuranose gave the isomeric allo disulfide.

The use of potassium thioacetate in nucleophilic displacements of sulfonyloxy groups was reported first by Owen and coworkers in 1950.[3,4] They found that primary sulfonates reacted readily on heating with 2 equiv of potassium thioacetate in acetone or ethanol to give fairly good yields of thiolacetates. An advantage to the use of ethanol is that potassium thioacetate is very much more soluble in this solvent than it is in acetone; and the secondary mesyloxy groups of 1,4:3,6-dianhydro-2,5-di-*O*-methylsulfonyl-D-mannitol can be displaced by potassium thioacetate in ethanol at 110°[4] to give an L-iditol derivative.[5] Deacetylation was observed in this reaction and the reaction mixture was reacetylated prior to isolation of the product. In view of our results (see below), it is probable that transfer of the acetyl group from initially formed thiolacetate to solvent is a rapid reaction in boiling ethanol, catalyzed by the alkalinity of the medium.

(1) Part VI in a series of publications from this laboratory concerning the chemistry of apiose.

(2) National Academy of Sciences, National Research Council Visiting Scientist Research Associate, 1968–1970.

(3) J. H. Chapman and L. N. Owen, *J. Chem. Soc.*, 579 (1950).

(4) P. Bladon and L. N. Owen, *ibid.*, 585 (1950).

(5) A. C. Cope and T. Y. Shen, *J. Amer. Chem. Soc.*, **78**, 3177 (1956).

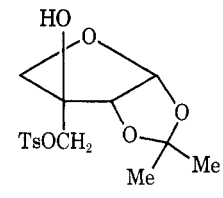
Thioacetate displacements with carbohydrates were reviewed in 1963[6] and, in the past decade, dipolar aprotic solvents, especially *N*,*N*-dimethylformamide (DMF), have been used with notable success in thioacetate displacements of primary[7-9] and secondary[10,11] sulfonyloxy groups. A most convincing demonstration of the nucleophilicity of the thioacetate ion in DMF was the high yield of D-*allo*-thiolacetate obtained with these reagents and 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-glucofuranose,[12] the classic example of a "hindered" sulfonate.

The thiobenzoate ion in DMF has also been used to displace sulfonyloxy groups in carbohydrates[13-16] and the rates of reaction of some 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-hexofuranoses with potassium thiobenzoate in DMF have been measured.[17] Although it appears that the thiobenzoate ion is a stronger nucleophile than thioacetate, the isolated yields obtained from the above displacements of the D-*gluco*- and D-*allo*-thiolbenzoates were both less than 7%,[17] whereas the corresponding thiolacetates were isolated in yields of almost 70% (ref 12 and see below). It therefore seems doubtful that there are any practical advantages to the use of potassium thiobenzoate. Competing thionoacylate formation must be considered as unlikely to occur in detectable amounts in view of the observation that alkylation of potassium thiobenzoate with methyl iodide in acetone gives less than 1% oxygen alkylation.[18]

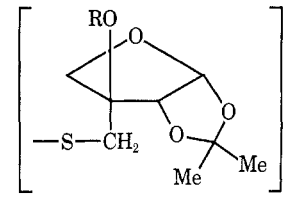
Our interest in thioacetate displacements began with syntheses of analogs of apiose in which the ring oxygen atom is replaced by sulfur, and a preliminary communication of a part of this work has appeared previously.[19] In view of extensive monosulfide formation during a thioacetate displacement with an apiose sulfonate, we have also examined a similar reaction with 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylofuranose. Displacement of the secondary sulfonyloxy group from 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-allofuranose by thioacetate ion in DMF is also described.

Results

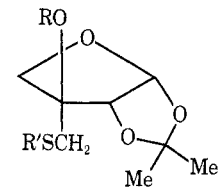
The reaction of 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-apio-L-furanose[20,21] [1,2-*O*-isopropylidene-3-*C*-(*p*-tolysulfonyloxymethyl)-β-L-threofuranose] (**1**) with 2 equiv of potassium thioacetate in boiling ethanol was monitored by thin layer chromatography (tlc). After 2 hr, **1** was absent and the major product (shown later to be the thiol **7**) was slowly converted at 0° to a slower moving, uv-absorbing compound. The thiolacetate **6**, presumed to be formed initially, was not observed. After 2 days, bis(5-deoxy-1,2-*O*-isopropylidene-α-D-apio-L-furanose-5-yl) disulfide (**2**) was obtained crystalline in high yield. It appears that the reaction mixture is sufficiently basic to effect rapid transfer of the *S*-acetyl group of **6** to solvent and to promote oxidation of **7** to **2**.



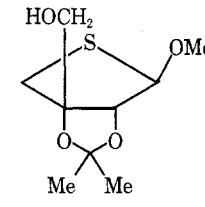
1



2, R = H
3, R = Ac



4, R = R′ = Ac
5, R = Ac; R′ = H
6, R = H; R′ = Ac
7, R = R′ = H



8

When a similar reaction was carried out in DMF at 100°, **1** was again shown by tlc to be absent after 2 hr and three products were detected and were separated by silica gel chromatography. Initial fractions yielded 3-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-α-D-apio-L-furanose (**4**) (an oil) in 25% yield. The second component was obtained crystalline and was shown to be bis(3-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-α-D-apio-L-furanose-5-yl) disulfide (**3**) (56% yield). A third fraction, which was mainly one compound, gave a positive thiol test. Treatment of an aliquot with iodine gave the disulfide **3** and S-acetylation with potassium thioacetate in DMF gave the *O*,*S*-diacetate **4**. The major component of this fraction was therefore identified as the thiol **5** and the isolated yield was 9%.

A similar reaction with acetone replacing DMF was complete in 3 days at room temperature and the same products were formed in approximately the same proportions. In an attempt to isolate and fully characterize the thiol **5**, the reaction was modified by using 1 equiv of potassium thioacetate and by rigorous exclusion of oxygen. Disulfide **3** was not detected; the major product after silica gel chromatography was the *O*,*S*-diacetate **4**. The *O*-acetate **5** and the *S*-acetate **6** were isolated as a mixture (21% yield) in an approximate ratio of 3:2, as indicated by nmr spectroscopy. Acetylation of the mixture gave a single compound identical with **4**. A minor constituent of the reaction mixture (*ca.* 10%) was identified as an unsymmetrical disulfide (**2**, with one of the tertiary hydroxyl goups acetylated).

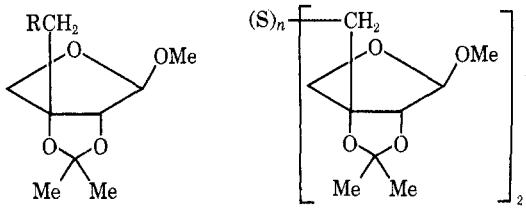
(6) D. Horton and D. H. Hutson, *Advan. Carbohyd. Chem.*, **18**, 123 (1963).
(7) T. J. Adley and L. N. Owen, *Proc. Chem. Soc.*, 418 (1961); *J. Chem. Soc. C*, 1287 (1966).
(8) C. J. Clayton and N. A. Hughes, *Chem. Ind. (London)*, 1795 (1962); *Carbohyd. Res.*, **4**, 32 (1967).
(9) J. M. Cox and L. N. Owen, *J. Chem. Soc. C*, 1121 (1967).
(10) R. L. Whistler, W. E. Dick, T. R. Ingle, R. M. Rowell, and B. Urbas, *J. Org. Chem.*, **29**, 3723 (1964).
(11) L. N. Owen and P. L. Ragg, *J. Chem. Soc. C*, 1291 (1966); L. N. Owen, *Chem. Commun.*, 526 (1967).
(12) U. G. Nayak and R. L. Whistler, *J. Org. Chem.*, **34**, 3819 (1969).
(13) M. A. Bukhari, A. B. Foster, J. Lehman, J. M. Webber, and J. H. Westwood, *J. Chem. Soc.*, 2291 (1963).
(14) E. J. Reist, D. E. Gueffroy, and L. Goodman, *J. Amer. Chem. Soc.*, **85**, 3715 (1963); *ibid.*, **86**, 5658 (1964).
(15) E. J. Reist, L. V. Fisher, D. E. Gueffroy, and L. Goodman, *J. Org. Chem.*, **31**, 1506 (1966).
(16) E. J. Reist, L. V. Fisher, and L. Goodman, *ibid.*, **33**, 189 (1968).
(17) J. M. Heap and L. N. Owen, *J. Chem. Soc. C*, 712 (1970).
(18) S. G. Smith, *Tetrahedron Lett.*, No. 21, 979 (1962).
(19) M. H. Halford, D. H. Ball, and L. Long, Jr., *Carbohyd. Res.*, **8**, 363 (1968).
(20) D. H. Ball, F. A. Carey, I. L. Klundt, and L. Long, Jr., *ibid.*, **10**, 121 (1969).
(21) To preserve the relationship with apiose of the compounds described, the nomenclature used is that suggested by Cahn; see D. J. Bell, F. A. Isherwood, N. R. Hardwick, and R. S. Cahn, *J. Chem. Soc.*, 3702 (1954).

Intramolecular acetyl migration from sulfur to oxygen has been found to occur when the intermediate is a five- or a six-membered ring[22] and is about 30 times faster in the former case.[23] The use of aprotic solvents in the above displacements therefore favors the intramolecular S → O acetyl migration (*via* a five-membered cyclic orthoacetate) to give the thiol **5** from initially formed **6**. The thiol can then be either acetylated to give **4** or oxidized to **3**. It therefore appears that, where such an intramolecular acyl migration is sterically favored, the use of aprotic solvents is likely to give complex mixtures, and the use of protic solvents may be preferable if the disulfide is a useful product. An alternative would be to block the hydroxyl group by, for example, acetylation.

Reduction of **2** with lithium aluminum hydride in ether gave a syrupy thiol which was treated with a 2% solution of hydrogen chloride in methanol. The major product was obtained crystalline after silica gel chromatography and shown to be methyl 2,3-*O*-isopropylidene-4-thio-β-D-apio-D-furanoside (**8**) as anticipated in view of the results obtained with the oxygen analog.[24,25]

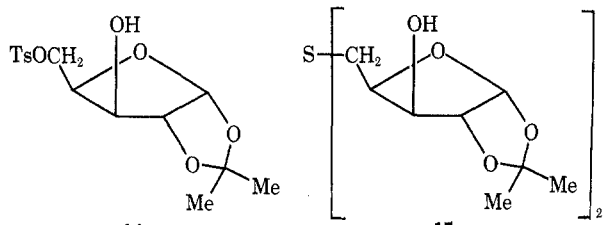
The reaction of methyl 2,3-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-β-D-apio-D-furanoside (**9**)[25] with 2 equiv of potassium thioacetate in boiling ethanol was also examined in the expectation that a disulfide would be the major product. After 2 hr, tlc indicated **9** and a faster moving product (later shown to be the thiol **10**), and these compounds slowly disappeared and were replaced by two slower moving products, one of which was uv absorbing. There was no further change after 24 hr and the mixture was fractionated by chromatography on silica gel. Each of the compounds was obtained as a chromatographically and spectroscopically (nmr) homogeneous syrup. The faster moving, uv-absorbing compound was identified by analytical and spectroscopic data as bis(methyl 5-deoxy-2,3-*O*-isopropylidene-β-D-apio-D-furanoside-5-yl) disulfide (**12**). The slower moving product was similarly characterized as the corresponding monosulfide **13** and the molar ratio of **12**:**13** was determined to be 1:1.3. In this case, it appears that the thiol **10** (formed by rapid deacetylation of the initially formed thiolacetate **11**) is a sufficiently powerful nucleophile to compete with an excess of thioacetate ion for the sulfonate **9**. The remote possibility that the monosulfide **13** could have been formed from the disulfide **12**, a reaction which takes place if the sulfur atom is attached to an active methylene group,[26] was eliminated since no trace of **13** could be detected when a solution of **12** in ethanol was boiled with potassium thioacetate.

When the reaction was repeated with only 1 equiv of potassium thioacetate, **9** and the thiol **10** were still present (together with **12** and **13**) after 48 hr. Fractionation by silica gel chromatography afforded the thiol **10** (15%), starting material (**9**) (5%), and a mixture of **12** and **13** (*ca.* 73%). Integration of the nmr spectrum of the mixture gave the ratio of **12**:**13** as 1:5; *i.e.*, a greater preponderance of monosulfide had been achieved by lowering the concentration of thioacetate ion. Thus, in thioacetate displacements carried out in protic solvents, monosulfide formation is a potential complicating factor. This could also occur in aprotic solvents if intramolecular acetyl migration is possible although the nucleophilicity of the thioacetate ion relative to that of larger thiolate ions may be much greater in these solvents.



9, R = OTs
10, R = SH
11, R = SAc

12, $n = 2$
13, $n = 1$



14 **15**

Adley and Owen[7] found that treatment of 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylofuranose (**14**) with potassium thioacetate in boiling DMF gave a mixture of 5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-α-D-xylofuranose and 3-*O*-acetyl-1,2-*O*-isopropylidene-5-thio-α-D-xylofuranose, the product of intramolecular acetyl migration. They also found a small amount of bis(3-*O*-acetyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose-5-yl) disulfide. Neither the *O*,*S*-diacetate nor a monosulfide was found.

When **14** was boiled with 2 equiv of potassium thioacetate in ethanol for 24 hr, tlc indicated the formation of one major product. After silica gel chromatography, the monosulfide **15** was obtained crystalline in 85% yield. There was evidence for the presence of a small amount of the corresponding disulfide but in this case the thiolate ion produced is apparently a more powerful nucleophile and competes very effectively with thioacetate ion for **14**.

The structure of the compound formed by thermal rearrangement of 1,2:5,6-di-*O*-isopropylidene-3-*O*-[(methylthio)thiocarbonyl]-α-D-glucofuranose[27] was shown by nmr spectroscopy to have the D-gluco configuration[28] and is 1,2:5,6-di-*O*-isopropylidene-3-*S*-[(methylthio)carbonyl]-3-thio-α-D-glucofuranose. While the present work was in progress, the spectroscopic evidence was confirmed chemically.[29] An alternative route to 3-thioglucose derivatives is by the reaction of sulfur nucleophiles on the readily available 1,2:5,6-di-*O*-ispropylidene-3-*O*-*p*-tolylsulfonyl-α-D-allofuranose.[30] Treatment of this sulfonate with 3 equiv of potassium thioacetate in DMF at 100° for 2 days gave

(22) J. S. Harding and L. N. Owen, *J. Chem. Soc.*, 1528, 1536 (1954).
(23) R. B. Martin and R. I. Hedrick, *J. Amer. Chem. Soc.*, **84**, 106 (1962).
(24) The product from acid-catalyzed methanolysis of 1,2-*O*-isopropylidene-α-D-apio-L-furanose was incorrectly designated as an α-glycoside in ref 19.
(25) D. H. Ball, F. H. Bissett, I. L. Klundt, and L. Long, Jr., *Carbohyd. Res.*, **17**, 165 (1971).
(26) R. G. Hiskey and A. J. Dennis, *J. Org. Chem.*, **33**, 563 (1968).
(27) K. Freudenberg and A. Wolf, *Ber.*, **60**, 232 (1927).
(28) D. Horton and H. S. Prihar, *Carbohyd. Res.*, **4**, 115 (1967).
(29) J. M. Heap and L. N. Owen, *J. Chem. Soc. C*, 707 (1970).
(30) K. W. Buck, A. B. Foster, R. Hems, and J. M. Webber, *Carbohyd. Res.*, **3**, 137 (1966).

a 70% yield (81% based on unrecovered sulfonate) of 3-*S*-acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-glucofuranose, a syrup previously prepared by acetylation of 1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-glucofuranose.[29] The formation of a small amount (<3%) of 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose was attributed to the presence of approximately 10% acetate ion in the potassium thioacetate used (determined by integration of the nmr spectrum). Oxidative deacetylation of the thiolacetate gave bis(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-yl) disulfide in good yield. Deacetylation–oxidation of the isomeric 3-*S*-acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-alpofuranose[12] gave crystalline bis(3-deoxy-1,2:5,6-di-*O*-isoprolylidene-α-D-allofuranose-3-yl) disulfide with physical constants very different from those of the gluco isomer.

Experimental Section

Solutions were concentrated under diminished pressure. Melting points were determined in glass capillaries with a Thomas-Hoover apparatus. Thin layer chromatography (tlc) was performed on silica gel GF and developed plates were examined under ultraviolet light and then sprayed with α-naphthol solution and sulfuric acid and heated. Column chromatography was performed on 70–325 mesh ASTM silica gel (E. Merck AG, Darmstadt, Germany; distributed by Brinkmann Instruments, Inc.). Infrared spectra were recorded with a Perkin-Elmer Model 137 spectrophotometer and optical rotations were measured with a Bendix-Ericcson ETL-NPL automatic polarimeter. Ultraviolet spectra were obtained using a Cary Model 14 spectrophotometer. Pmr spectra were recorded at 100 MHz with a Varian Associates HA-100 spectrometer, operating in the "frequency-sweep" mode, and data are for solutions in chloroform-*d* containing tetramethylsilane (τ = 10.00) as internal reference. Microanalyses were by Midwest Microlabs, Inc., Indianapolis, Ind.

Commercial potassium thioacetate (Eastman Organic Chemicals), a dark brown powder, was purified as follows. A suspension of the crude material (25 g) in water (200 ml) was filtered and the resultant orange-red solution was concentrated (bath temperature *ca.* 60°) until crystals began to form. The mixture was cooled at 0° for 30 min and the crystalline product was collected by filtration, washed with tetrahydrofuran until white, and dried *in vacuo* over P_2O_5, yield *ca.* 7 g.

Bis(5-deoxy-1,2-*O*-isopropylidene-α-D-apio-L-furanose-5-yl) Disulfide (2).—To a solution of 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-apio-L-furanose (1)[20] (2.0 g, 5.8 mmol) in ethanol (40 ml) was added potassium thioacetate (1.32 g, 11.6 mmol). The solution was boiled under reflux and the reaction was monitored by tlc (chloroform–ethyl acetate, 9:1). After 2 hr, 1 (R_f 0.2) was absent and the major product (R_f 0.3) was weakly uv absorbing; a second, minor product (R_f 0.1) was strongly uv absorbing. After 5 hr, the component with R_f 0.3 was still preponderant; the reaction flask was then stoppered and kept at 0° for 2 days, after which time the component with R_f 0.1 appeared to be the major product. Potassium *p*-toluenesulfonate was removed by filtration and washed with ethanol, and the combined filtrate and washings were concentrated to a pale yellow syrup. At this stage, only a trace of the component with R_f 0.3 could be detected and the mixture was fractionated by chromatography on silica gel (70 g) with ethyl acetate as eluent. The major product (R_f 0.1) was obtained as a syrup (1.15 g, 96%) which crystallized on standing and was shown to be the disulfide **2**. Recrystallization from ether afforded pure material with mp 128–129°: $[\alpha]^{26}D$ +182° (*c* 0.77, EtOH); uv max (EtOH) 251 mμ (ε 440); nmr ($CDCl_3$) τ 4.03 (d, 1, $J_{1,2}$ = 3.5 Hz, H_1), 5.65 (d, 1, H_2), 6.12 (s, 2, $H_{4A,4B}$), 6.52, 7.05 (AB quartet, J_{AB} = 14.5 Hz, $H_{5,5'}$), 6.63 (broad s, 1, OH), 8.47, 8.65 (3 H singlets, CMe_2).

Anal. Calcd for $C_{16}H_{26}O_8S_2$: C, 46.81; H, 6.38; S, 15.62. Found: C, 46.82; H, 6.38; S, 15.44.

To a solution of **2** in water (*ca.* 0.01%) was added an equal volume of aqueous potassium cyanide (5%). After 2 min, addition of sodium nitroprusside solution resulted in an immediate, intense purple color. No reaction occurred without pretreatment with potassium cyanide.

Reaction of 1 with Potassium Thioacetate in Aprotic Solvents. A. DMF.—A solution of 1 (0.75 g, 2.2 mmol) and potassium thioacetate (0.50 g, 4.4 mmol) in DMF (15 ml) was heated at 100° in a stoppered flask. After 2 hr, tlc (chloroform–ethyl acetate, 9:1) indicated the absence of 1 and the formation of three products with R_f 0.6 (uv absorbing), 0.4 (uv absorbing), and 0.2. The solution was concentrated to dryness (nitrogen bleed, bath temperature *ca.* 35°) and the residue was extracted with hot chloroform (three 10-ml portions). Concentration of the extracts afforded a syrup which was fractionated by chromatography on silica gel (150 g) with chloroform as eluent. Fractions were concentrated under nitrogen.

Fraction 1 (163 mg), the product with R_f 0.6, was an oil with $[\alpha]^{25}D$ +97° (*c* 0.76, $CHCl_3$): ir ($CHCl_3$) 1735 (OAc) and 1680 cm^{-1} (SAc) consistent with the structure 3-*O*-acetyl-5-*S*-acetyl-1,2-*O*-isopropylidene-5-thio-α-D-apio-L-furanose (**4**); nmr ($CDCl_3$) τ 4.11 (d, 1, $J_{1,2}$ = 4 Hz, H_1), 5.35 (broad d, 1, $J_{2,4A}$ = 1 Hz, H_2), 5.64, 6.10 (AB quartet, J_{AB} = 10.5 Hz, $H_{4A,4B}$), 6.14, 6.42 (AB quartet, J_{AB} = 15 Hz, $H_{5,5'}$), 7.64 (s, 3, SAc), 7.95 (s, 3, OAc), 8.44, 8.64 (3 H singlets, CMe_2).

Anal. Calcd for $C_{12}H_{18}O_6S$: C, 49.64; H, 6.25; S, 11.04. Found: C, 49.98; H, 6.32; S, 10.77.

Fraction 2 (306 mg), R_f 0.4, crystallized and recrystallization from ether gave the disulfide **3** as white needles: mp 151–152°; $[\alpha]^{25}D$ +170° (*c* 0.78, $CHCl_3$); ir (KBr) 1735 cm^{-1} (ester C=O); nmr ($CDCl_3$) τ 4.11 (d, 1, $J_{1,2}$ = 3.5 Hz, H_1), 5.29 (d, 1, H_2), 5.59, 6.17 (AB quartet, $J_{A,B}$ = 10.5 Hz, $H_{4A,4B}$), 6.49 (s, 2, $H_{5,5'}$), 7.93 (s, 3, OAc), 8.49, 8.66 (3 H singlets, CMe_2).

Anal. Calcd for $C_{20}H_{30}O_{10}S_2$: C, 48.57; H, 6.11; S, 12.97. Found: C, 48.57; H, 6.09; S, 12.94.

Fraction 3 (49 mg), R_f 0.2 gave a purple color with 1% sodium nitroprusside solution and treatment of an aliquot with excess potassium thioacetate in hot DMF resulted in S-acetylation and the formation of **4**. Treatment of an aliquot with iodine in aqueous acetone gave crystalline **3** and the major constituent of the fraction was therefore the thiol **5**.

B. Acetone.—Substitution of anhydrous acetone for the DMF used above led to a similar series of reactions (complete in 3 days at room temperature), giving the same products in similar proportions. In an attempt to isolate and fully characterize **5**, the conditions were modified by the use of less potassium thioacetate and by rigorous exclusion of oxygen.

A solution of 1 (1.72 g, 5.0 mmol) in anhydrous acetone (30 ml) was deoxygenated with a stream of prepurified nitrogen. Potassium thioacetate (0.68 g, 5.5 mmol) was added and the suspension was stirred at 50° under reflux in a stream of nitrogen and with exclusion of water. After 1 hr, tlc (chloroform–ethyl acetate, 9:1) indicated 1 (R_f 0.1) and two products with R_f 0.6 and 0.2; disulfide **3** was absent. After 9 hr, 1 had reacted completely to give the above two major products and small amounts of other compounds. Potassium *p*-toluenesulfonate was removed by filtration under nitrogen and washed with acetone. The combined filtrate and washings were concentrated (nitrogen bleed) to a syrup which was fractionated by chromatography on silica gel (150 g) with dichloromethane as eluent.

Fraction 1 (410 mg) was a syrup identical (ir, nmr) with **4**.

Fraction 2 (260 mg) was a syrup: ir (neat) 3450 (OH), 2570 (SH), 1730 (*O*-acetyl C=O), and 1680 cm^{-1} (*S*-acetyl C=O). These data indicate a mixture of compounds **5** and **6** and this was supported by the nmr ($CDCl_3$) which also indicated a ratio of OAc (τ 7.89):SAc (τ 7.60) (and therefore of **5**:**6**) of 3:2. A portion (150 mg) of the syrup was heated at 70° with acetic anhydride and pyridine (1:20, 4 ml). Tlc (chloroform–ethyl acetate, 9:1) indicated complete conversion to a single product after 24 hr. Concentration afforded a yellow residue which was purified by chromatography on silica gel (1.5 g) with chloroform as eluent. The product was identical (tlc, ir, nmr) with **4**.

Fraction 3 (120 mg) was a syrup: ir (neat) 3400 (OH), 1730 cm^{-1} (*O*-acetyl C=O). The nmr spectrum was consistent with an equimolar mixture of two compounds or with an unsymmetrical di- (or mono-) sulfide. A portion (45 mg) of the syrup was heated at 70° with acetic anhydride and pyridine (1:20, 0.5 ml). Tlc (dichloromethane–ethyl acetate, 9:1) indicated a slow conversion to a faster moving compound (R_f 0.4), and after 48 hr concentration afforded a syrup which was purified by chromatography on silica gel (1 g) with dichloromethane–ethyl acetate (9:1) as eluent. The crystalline product (35 mg) was identical

with **3** and the original compound was therefore an unsymmetrical disulfide (**2**, with one of the tertiary hydroxyl groups acetylated).

Methyl 2,3-*O*-Isopropylidene-4-thio-β-D-apio-D-furanoside (8).—To a solution of **2** (0.65 g) in anhydrous ether (30 ml) was added lithium aluminum hydride (*ca.* 0.15 g) and the suspension was stirred at room temperature for 3 hr. Water (30 ml) was then added cautiously, followed by acetic acid (5 ml). The solution was extracted with ether (three 50-ml portions) as rapidly as possible and the extracts were concentrated (nitrogen bleed) to a syrup. Tlc (chloroform–ethyl acetate, 1:1) showed a preponderant product (R_f 0.6, chromatographically indistinguishable from the compound initially formed in the preparation of **2**, and presumably the thiol **7**) together with a lesser amount of **2**. The syrup was dried *in vacuo* over P_2O_5 and then taken up in 2% methanolic HCl. A test for thiol (addition to an aliquot of an equal volume of 5% potassium carbonate solution followed by 1% potassium nitroferricyanide), which initially gave an intense violet color, was negative after 24 hr. Tlc (chloroform–ethyl acetate, 1:1) showed, in addition to components with R_f 0.2, a product with the same mobility as the thiol **7**. The solution was neutralized by passage down a column of Dowex 1 (OH^-) analytical grade ion-exchange resin, previously washed with methanol. Concentration of the effluent gave a syrup which was fractionated by chromatography on silica gel (100 g) with chloroform as eluent. Fractions containing the fast-moving component were combined and concentrated to a syrup (0.21 g, 31%) which crystallized on standing. Recrystallization from *n*-heptane afforded analytically pure methyl 2,3-*O*-isopropylidene-4-thio-β-D-apio-D-furanoside (**8**): mp 52.5–53°; $[\alpha]^{28}D$ −264° (*c* 0.8, EtOH); nmr ($CDCl_3$) τ 5.10 (s, 1, H_1), 5.48 (s, 1, H_2), 6.28 (s, 2, $H_{5,5'}$), 6.66 (s, 3, OMe), 6.94, 7.20 (AB quartet, J_{AB} = 12.5 Hz, $H_{4A,4B}$), 7.82 (broad s, 1, OH), 8.44, 8.59 (3 H singlets, CMe_2). Double irradiation experiments indicated small couplings between H_1 and H_2 = 0.7 Hz and H_1 and H_{4A} < 0.5 Hz.[31]

Anal. Calcd for $C_9H_{16}O_4S$: C, 49.07; H, 7.32; S, 14.56. Found: C, 49.14; H, 7.30; S, 14.30.

Reaction of Methyl 2,3-*O*-Isopropylidene-5-*O*-*p*-tolylsulfonyl-β-D-apio-D-furanoside (9) with Potassium Thioacetate in Ethanol. A. With 2 Equiv of Potassium Thioacetate.—To a solution of **9** (1.0 g, 2.8 mmol) in ethanol (20 ml) was added potassium thioacetate (0.64 g, 5.6 mmol) and the mixture was stirred and boiled under reflux with exclusion of moisture. After 2 hr, tlc (benzene–ether, 9:1) showed **9** (R_f 0.4) and a component with R_f 0.5 (not uv absorbing). After 6 hr very little **9** remained but, in addition to the spot at R_f 0.5, two more components, R_f 0.30 (strongly uv absorbing) and R_f 0.25 (not uv absorbing), were observed, and, after 24 hr, only the last two components were present. Potassium *p*-toluenesulfonate was removed by filtration and washed with ethanol, the filtrate was concentrated, and the residue was fractionated by chromatography on silica gel (50 g) with benzene–ether (9:1) as eluent.

Fraction 1 (196 mg) was a syrup, homogeneous by tlc and nmr: $[\alpha]^{25}D$ −230° (*c* 0.30, $CHCl_3$); uv max (EtOH) 251 mμ (ε 310). The nmr spectrum and analytical data indicated this compound to be the disulfide **12**: nmr ($CDCl_3$) τ 5.09 (s, 1, H_1), 5.70 (s, 1, H_2), 5.99, 6.13 (AB quartet, J_{AB} = 10 Hz, $H_{4A,4B}$), 6.67 (s, 3, OMe), 6.71 (s, 2, $H_{5,5'}$), 8.52, 8.56 (3 H singlets, CMe_2).

Anal. Calcd for $C_{18}H_{30}O_8S_2$: C, 49.29; H, 6.90; S, 14.62. Found: C, 49.01; H, 6.71; S, 14.31.

Fraction 2 (127 mg) was a mixture of the two components.

Fraction 3 (251 mg) was a syrup, homogeneous by tlc and nmr, $[\alpha]^{25}D$ −128° (*c* 1.0, $CHCl_3$). The nmr spectrum and analytical data indicated this compound to be the sulfide **13**: nmr ($CDCl_3$) τ 5.09 (s, 1, H_1), 5.75 (s, 1, H_2), 5.98, 6.14 (AB quartet, J_{AB} = 10 Hz, $H_{4A,4B}$), 6.68 (s, 3, OMe), 6.92 (s, 2, $H_{5,5'}$), 8.51, 8.55 (3 H singlets, CMe_2).

Anal. Calcd for $C_{18}H_{30}O_8S$: C, 53.18; H, 7.44; S, 7.89. Found: C, 52.96; H, 7.42; S, 7.91.

The ratio **12**:**13** in fraction 2 was determined by integration of the nmr absorptions attributable to the exocyclic methylene groups and the molar ratio of **12**:**13** in the reaction product was 1:1.3.

B. With 1 Equiv of Potassium Thioacetate.—A solution of **9** (0.75 g, 2.1 mmol) and potassium thioacetate (0.24 g, 2.1 mmol) in ethanol (15 ml) was boiled under reflux with exclusion of moisture. Tlc (benzene–ether, 9:1) indicated a reaction similar to that in A except that no change was observed after 48 hr when **9** and the component with R_f 0.5 were still present in small amounts.[32] The reaction mixture was concentrated and the residue was extracted with dry acetone. Residual, insoluble potassium *p*-toluene-sulfonate was washed well with acetone and the combined extracts were concentrated to a syrup which was fractionated by chromatography on silica gel (50 g) with benzene–ether (20:1) as eluent.

Fraction 1 (68 mg) was a syrup, homogeneous by tlc and nmr: $[\alpha]^{25}D$ −121° (*c* 1.4, $CHCl_3$); ir (neat) 2550 cm^{-1} (SH). The nmr and ir spectra and elemental analysis indicated this compound to be the thiol **10**: nmr ($CDCl_3$) τ 5.07 (s, 1, H_1), 5.75 (s, 1, H_2), 5.97, 6.14 (AB quartet, J_{AB} = 10 Hz, $H_{4A,4B}$), 6.68 (s, 3, OMe), 7.06, 7.17 (AB part of an ABX pattern, J_{AB} = 13.5, J_{AX} = 8.7, J_{BX} = 7.3 Hz, $H_{5A,5B}$), 8.28 (X part of ABX pattern, SH), 8.50, 8.56 (3 H singlets, CMe_2).

Anal. Calcd for $C_9H_{16}O_4S$: C, 49.07; H, 7.32; S, 14.56. Found: C, 49.90; H, 7.37; S, 13.75.

Fraction 2 (40 mg) was crystallized and was identical (nmr) with **9**.

Fraction 3 (315 mg) was a syrupy mixture of **12** and **13**. Integration of the nmr spectrum gave the ratio **12**:**13** = 1:5.

Bis(5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose-5-yl) Sulfide (15).—To a solution of 1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-xylofuranose (**14**)[33] (1.5 g, 4.35 mmol) in ethanol (15 ml) was added potassium thioacetate (1.0 g, 8.7 mmol) and the solution was boiled under reflux. After 24 hr, tlc (chloroform–ethyl acetate, 1:1) indicated a major product at R_f 0.25 (weakly uv absorbing). The cooled mixture was filtered to remove potassium *p*-toluenesulfonate which was washed with ethanol, and the combined filtrates were concentrated to a syrup. After chromatography on silica gel (200 g) with chloroform–ethyl acetate (3:1) as eluent, the product was obtained as an oil (0.75 g) which crystallized on standing.[34] Recrystallization from dichloromethane gave 0.69 g (85%) of analytically pure monosulfide **15**: mp 161–162°; $[\alpha]^{24}D$ −83° (*c* 1.0, EtOH); nmr ($CDCl_3$) τ 4.09 (d, 1, $J_{1,2}$ = 3.5 Hz, H_1), 5.48 (d, 1, H_2), 5.60–5.88 (m, 2, H_3 and H_4), 6.98–7.20 (m, 2, $H_{5,5'}$), 7.25 (broad d, 1, OH), 8.48, 8.67 (3 H singlets, CMe_2).

Anal. Calcd for $C_{16}H_{26}O_8S$: C, 50.78; H, 6.93; S, 8.47. Found: C, 50.77; H, 6.92; S, 8.46.

3-*S*-Acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-glucofuranose.—A solution of 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolysulfonyl)-α-D-allofuranose[30] (2.07 g, 5 mmol) and potassium thioacetate (1.71 g, 15 mmol) in DMF (25 ml) was heated at 100° in a stream of nitrogen. The reaction was monitored by tlc (ether–hexane, 1:1) and after 48 hr the solution was concentrated, the dark residue was extracted with ether, and the extract was concentrated to an oil which was fractionated on silica gel (225 g) with ether–hexane (1:1) as eluent.

Fraction 1 (1.08 g) was a chromatographically homogeneous syrup with $[\alpha]^{25}D$ −46° (*c* 1.2, $CHCl_3$); ir (CCl_4) 1700 cm^{-1} (*S*-acetyl C=O); nmr ($CDCl_3$) τ 4.21 (d, 1, $J_{1,2}$ = 3.5 Hz, H_1), 5.46 (d, 1, H_2), 5.60–6.10 (m, 5), 7.62 (s, 3, SAc), 8.47, 8.59, 8.67, 8.70 (3 H singlets, $2CMe_2$).

Anal. Calcd for $C_{14}H_{22}O_6S$: C, 52.81; H, 6.96; S, 10.07. Found: C, 52.86; H, 7.20; S, 10.35.

Fraction 2 (0.03 g) was not fully characterized but the nmr spectrum was identical with that of 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.

Fraction 3 (0.33 g) was unreacted starting material.

Bis(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose-3-yl) Disulfide.—Air was drawn through a solution of 3-*S*-acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-glucofuranose (1.0 g) in methanol (25 ml) containing 0.2% w/v sodium methoxide. Tlc (ether–hexane, 1:1) indicated rapid deacetylation followed by slow oxidation to the disulfide which began to precipitate after 1 day. After 1 week, crystalline disulfide (0.59 g) was collected by filtration, and fractionation of the mother liquors on silica gel afforded an additional 50 mg: total yield 0.64 g (74%); mp 163.5–164.5°; $[\alpha]^{25}D$ −285° (*c* 0.95, $CHCl_3$) [lit.[29] mp 165°; $[\alpha]^{21}D$ −281° (*c* 0.5, $CHCl_3$)].

(31) H_{4A} and H_{4B} designate respectively the protons "above" and "below" the plane of the furanose ring.

(32) After treatment of an aliquot of this solution with an equal volume of 5% sodium ethoxide in ethanol at the boiling point for 1 hr, tlc indicated the major product to be the sulfide **13**.

(33) P. A. Levene and A. L. Raymond, *J. Biol. Chem.*, **102**, 317 (1933).

(34) The oil gave a positive test for disulfide (purple color with 1% sodium nitroprusside solution after treatment of an aliquot with 5% potassium cyanide solution for 30 min at room temperature). This, and the weak uv absorption after tlc, indicates probable contamination of **15** with the corresponding disulfide.

Bis(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose-3-yl) Disulfide.—3-*S*-Acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-allofuranose[12] (0.25 g) was deacetylated and oxidized as above to give crystalline bis(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose-3-yl) disulfide (0.13 g, 60%). Two recrystallizations from hexane gave pure material with mp 108–109°; $[\alpha]^{25}D$ +64° (*c* 0.9, $CHCl_3$); uv max 249 mμ (ε 280); nmr ($CDCl_3$) τ 4.20 (d, 1, $J_{1,2}$ = 3.5 Hz, H_1), 5.20 (t, 1, $J_{2,3}$ = 4.5 Hz, H_2), 5.57–6.10 (m, 4, H_4, H_5, $H_{6,6'}$), 6.65 (doublet of doublets, 1, $J_{3,4}$ = 10 Hz, H_3), 8.45, 8.52, 8.62, 8.64 (3 H singlets, $2CMe_2$).

Anal. Calcd for $C_{24}H_{38}O_{10}S_2$: C, 52.35; H, 6.96; S, 11.64. Found: C, 52.48; H, 7.21; S, 11.47.

Registry No.—**2**, 24679-85-4; **3**, 24679-84-3; **4**, 24679-86-5; **5**, 24679-87-6; **6**, 31735-45-2; **8**, 25050-39-9; **10**, 31735-46-3; **12**, 31729-55-2; **13**, 31729-56-3; **15**, 31729-57-4; 3-*S*-acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-glucofuranose, 28251-80-1; bis(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose-3-yl) disulfide, 31790-92-8.

Acknowledgment.—The authors wish to thank Mr. F. H. Bissett and Dr. R. C. Chalk for the determination of nmr spectra.

Structure of Anhydro Butenandt Acid

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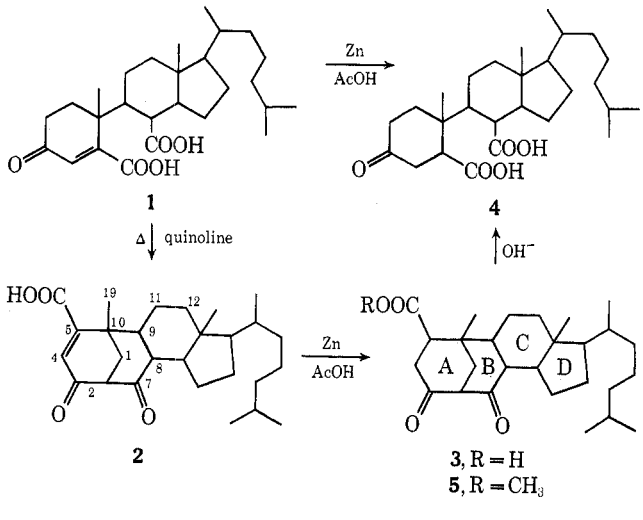
Received March 30, 1971

Chemical and spectroscopic evidence has confirmed the structure of anhydro Butenandt acid (**2**), for which an improved preparation is described. The saturated nonenolizable β-diketone **3** obtained from **2** had relatively high intensity ultraviolet absorption indicating the presence of a homoconjugated system. CD measurements on **3** and its methyl ester suggest that it exists as an equilibrium mixture of the boat–chair and twin-chair conformers at room temperature.

In 1953, Fieser,[3] in studies of the oxidation products of cholesterol, reported the preparation of a novel conversion product of Butenandt acid (**1**) for which structure **2** was suggested.



Anhydro Butenandt acid (**2**) was obtained by heating **1** with quinoline or with acetic anhydride and boron trifluoride etherate. The original evidence for structure **2** consisted of (a) the similarity of the ultraviolet spectrum to that of other enedione systems,[3,4] (b) the infrared spectrum, which showed bands assigned to an acid and six-ring ketone, an α,β-unsaturated ketone, and a double bond, and (c) mild base hydrolysis, which gave back **1**, suggesting a β-diketone system.

The nmr spectrum of the anhydro acid **2** supports the suggested structure in complete detail. The nmr spectrum had an ill-resolved triplet centered at δ 3.56 (J = 2 Hz), which was assigned to the bridgehead proton between the two carbonyl groups.[5] The low value of the coupling constant is due to the fixed orientation of the bridgehead proton with respect to the neighboring methylene bridge with an angle such that the coupling constant is near a minimum.[6] The vinyl proton gave rise to a doublet at δ 7.05 (J = 1 Hz). The splitting of this band appears due to long-range coupling with the bridgehead proton.[7] Such coupling across four single bonds appears to be at a maximum when the interacting protons are confined to a planar zigzag configuration. The C-19 methyl resonance occurred at δ 1.57.

Preparation of compound **2** could be improved by exhaustive oxidation of cholesterol,[3,8] isolation of the total acid fraction, and heating this with quinoline without purification. The yield of **2** from cholesterol was thus about 15% in a much shorter working time. Repeated attempts to prepare a 2,4-dinitrophenylhydrazone or semicarbazone of **2** were unsuccessful. However, a high-melting bisoxime could be formed.

Attempted addition of bromine to **2** in glacial acetic acid or chloroform resulted in recovery of starting material. The anhydro acid **2** rapidly took up 1 mol of hydrogen over Pd/C to give **3**. The anhydro acid **2** could also be reduced to **3** by refluxing with excess zinc dust in glacial acetic acid. This latter reaction provides chemical evidence for the presence of an enedione system in **2**. Attempted reduction of the enedione system

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(3) L. F. Fieser, *J. Amer. Chem. Soc.*, **75**, 4386 (1953).

(4) P. Yates and G. F. Fields, *ibid.*, **82**, 5764 (1960).

(5) Similar values can be found for a bridgehead proton between two carbonyl groups in "citrylidenemalonic acid:" C. E. Berkoff and L. Crombie, *J. Chem. Soc.*, 3734 (1960); see also W. Herz and G. Caple, *J. Amer. Chem. Soc.*, **84**, 3517 (1962).

(6) *Cf.* L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," 2nd ed, Pergamon Press, Oxford, 1969, p 280.

(7) Reference 6, p 334. For similar cases of long-range coupling, see C. Lehmann, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **45**, 1031 (1962); N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, p 121;. N. S. Bhacca, J. E. Gurst, and D. H. Williams, *J. Amer. Chem. Soc.*, **87**, 302 (1965).

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