

TABLE II
COMPARISON OF C-H BENDING VIBRATIONS OF HEXA-METHYL ETHERS

Hexamethyl ether of	Band maxima and intensities				
Gossypol	6.86 (385.3)				7.45 (517.7)
Apogossypol	6.82 (377.1)	7.03 (322.4)	7.32 (273.3)		7.43 (235.0)
Desapogossypol	6.67 (337.3)	6.80 (314.2)	7.33 (184.8)		7.63 (157.1)

taining compounds exhibit several strong bands in the 8μ region arising from stretching vibrations of the C-O group. Colthup²⁵ attributes bands with maxima in this region to aromatic ketones, aldehydes, alcohols, esters and ethers. These three bands exhibited in the spectra of gossypol could arise from C-OH²⁶ and Ph-C-H-O²⁵ groups as indicated by the structure of tautomeric form No. 1. Complete acetylation, and the structure of tautomeric form No. 2, would eliminate both of these sources of vibration in the spectra of the hexaacetates. The three bands observed, however, could easily be attributed to the triple C-O stretching vibrations of esters.²⁷ Similar assignments can be made for bands in this region exhibited by other derivatives of gossypol, but they are of little or no value to this study.

Bands above 9.0μ .—The infrared spectrum above 9.0μ has been called the "fingerprint" region as distinguished from the "group frequency" region below 9μ . Above 9μ the spectra begin to take on features characteristic of the particular molecule which make it particularly valuable for identification by direct comparison, but maxima characteristic of particular groupings become less well-defined.

About 9.4 – 9.5μ the C-O stretching vibration of

(26) Harris Rosenkrantz, *J. Biol. Chem.*, **173**, 439 (1948).

(27) O. D. Shreve, M. R. Heether, H. B. Knight and D. Swern, *Anal. Chem.*, **22**, 1498 (1950).

$\text{CH}_3\text{-C-OH}$ would account for the band in gossypol.^{28,29} At 9.6μ , O'Connor, *et al.*,¹⁶ showed evidence for a band due to the ester group and the C-O-C stretching vibration of aromatic ethers has been placed at about 9.5μ by Colthup.²⁰

Bands at 9.7 , 10.0 , 10.5 and 11.0μ are quite likely attributable to CH_3 bendings about various C=C groups.

Of particular interest to the study of gossypol is evidence concerning the presence of the binaphthyl grouping. The spectrum of gossypol has been compared with those of both 1,1'-binaphthyl and 2,2'-binaphthyl. The latter two compounds exhibit rather weak bands, due probably to their high degree of symmetry. 2,2'-Dihydroxy-3,3'-diacetoxy-1,1'-binaphthyl was prepared and its infrared spectrum measured. A comparison of the bands above 10.0μ is given in Table III. Considering the four bands exhibited by gossypol as its "fingerprint" it will be readily seen from the data in Table III that none of the compounds of known structure can be considered as matching it. However, none of these bands, probably, arise from the binaphthyl group. For evidence of binaphthyl it will be necessary, most likely, to study the spectra above 12μ in the potassium bromide region of the infrared.

TABLE III
COMPARISON OF BANDS IN THE "FINGERPRINT" REGION

1,1'-Binaphthyl	9.82	10.30	10.55		11.55
2,2'-Binaphthyl	9.82	10.45	10.65	11.18	11.65 12.20
2,2'-Dihydroxy-3,3'-diacetoxy-1,1'-binaphthyl	9.75		10.68	10.98	11.55
Gossypol	9.72	10.05		10.95	11.82
		10.35			

(28) F. A. Smith and E. C. Creitz, *J. Research Natl. Bur. Standards*, **46**, 145 (1951).

(29) Earle K. Plyler, *ibid.*, **46**, 281 (1952).

NEW ORLEANS, LOUISIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TORONTO]

Cyclitols. VII. Debromination of Inositol Dibromohydrins. Synthesis of New Cyclohexanetetrols^{1,2}

BY G. E. McCASLAND AND E. CLYDE HORSWILL³

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The dibromotetrol of m.p. 190° derived from inositol is shown to be 3,6-dibromocyclohexanetetrol-1,2,4,5 since on debromination it gives a 1,2,4,5-tetrol of m.p. 208° identical with one recently prepared by hydroxylation of 1,4-cyclohexadiene. The dibromocyclohexanetetrol of m.p. 216° , previously shown to have a 4,6-dibromo structure, on debromination gives a new 1,2,3,5-tetrol of m.p. 182° . Bromoviboquercitol-A can be converted into these two dibromotetrols but bromoscyloquercitol-A resists further bromination. Tentative assignments of configuration for these tetrols and for all of the known dibromo and diamino-cyclohexanetetrols are proposed.

We recently reported⁴ that two bromocyclohexanepentols derived from *myo*-inositol can be catalytically debrominated to pentols (quercitols). We now find that two dibromocyclohexanetetrols, also prepared from inositol, can be debrominated in a similar manner, giving new cyclohexanetetrols.

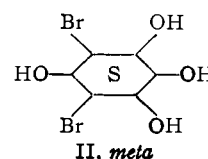
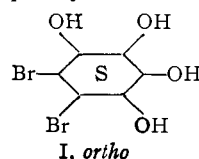
(1) For the preceding paper in this series see G. E. McCasland and E. C. Horswill, *THIS JOURNAL*, **76**, 0000 (1954).

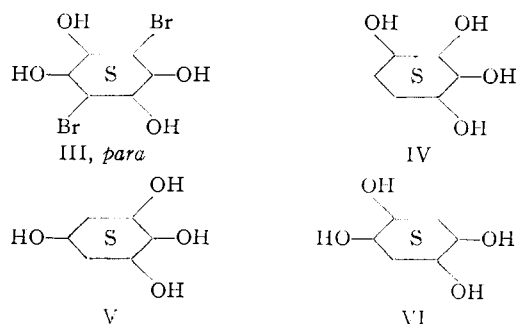
(2) From the Ph.D. Thesis of E. Clyde Horswill, 1953.

(3) Fellow of the National Research Council, 1952-1953.

(4) G. E. McCasland and E. Clyde Horswill, *THIS JOURNAL*, **75**, 4020 (1953).

Considerable progress has been made in elucidating the structure and the configuration of these compounds, which are important because of their relationship to the biologically active inositol and streptomycin.





A. The "para" Dibromocyclohexanetetrol^{5,6} of M.p. 190°

Formation of the "para" Dibromotetrol from *myo*-Inositol.—In 1912 Müller⁷ by heating *myo*-inositol hexaacetate with hydrogen bromide in acetic acid obtained a complicated mixture of products from which he isolated a dibromotetrol tetraacetate of reported m.p. 235°. This same tetraacetate was prepared by Griffin and Nelson⁸ in 1915, and by Menzel, Moore and Wintersteiner⁹ in 1949, using an improved acetyl bromide procedure. The correct m.p. was shown to be 225° (see Table I).

TABLE I

THE KNOWN DIBROMOCYCLOHEXANETETROLS ⁷⁻¹⁰ (1954)					
M.p., °C., and rotation	Structure	Probable configuration ¹⁵ (tentative)	M.p. of tetraacetate, °C.	M.p. of other derivs., °C.	M.p. of corresponding tetrol, °C.
190 (inactive)	<i>para</i> ^a	DL(1,3,4)	225	208
216 (inactive)	<i>meta</i> ^b	DL(1,3,4)	130	Diacetate 214 Triacetate 124	182

^a Six *meso* and eight active diastereomers possible.
^b Eight *meso* and twelve active diastereomers possible.

The corresponding free dibromotetrol, m.p. 190°, was first prepared by Wintersteiner, *et al.*, in 1949 by hydrolyzing the tetraacetate. It was also prepared by Carter and Flynn¹⁰ at about the same time.

Formation of the "para" Dibromotetrol from *scyllo*-Inositol and Pinitol.—It is of great interest that *scyllo*-inositol (XXXVIII) reportedly⁷ gives exactly the same bromoquercitols and dibromotetrols as does *myo*-inositol.

Pinitol also⁸ gives these products (with the possible exception of bromoviboquercitol-*A*). Preliminary experiments by us suggest that this is true also of quebrachitol, and of active or racemic inositol itself (XXXVII).

(5) By using the benzene prefixes *ortho*, *meta* and *para* convenient trivial names can be assigned to the three dibromocyclohexanetetrol structures, and by extension to the corresponding tetrols. However, numerals should be used for the systematic naming of these compounds.

(6) Our *p*-dibromotetrol (m.p. 190°) is the so-called "α" isomer of previous investigators, and our *m*-dibromotetrol (m.p. 216°) was previously called "β." Since these Greek letter prefixes often have a structural significance it would seem better not to use them for designating any such isomers of unknown structure.

(7) (a) H. Müller, *J. Chem. Soc.*, **91**, 1790 (1907); (b) **101**, 2383 (1912).

(8) E. G. Griffin and J. M. Nelson, *THIS JOURNAL*, **37**, 1552 (1915).

(9) A. E. O. Menzel, M. Moore and O. Wintersteiner, *ibid.*, **71**, 1268 (1949).

(10) E. H. Flynn, Ph.D. Thesis, University of Illinois, 1949 (with Professor H. E. Carter). We wish to thank Professor Carter for helpful information regarding this work.

These facts suggest that under the conditions of the bromination reaction *myo*-, *scyllo*- and D/L-inositol are either interconvertible or convertible to some common intermediate. It is known that *myo*-inositol is partly converted to racemic inositol when heated with hydrohalic acids in acetic acid. However, the other inositols are probably *not* converted to *scyllo*-inositol since it reacts much more slowly. Quite possibly the common intermediate for the dibromotetrols is bromoviboquercitol-*A* (see below).

Formation of the "para" Dibromotetrol from Monobromopentol.—So far as we know, no one has previously attempted to prepare the dibromotetrols by further bromination of monobromopentols (bromoquercitols). When we subjected bromo*scyllo*quercitol-*A* to the usual acetyl bromide procedure it was recovered unchanged. Apparently this isomer is resistant to further bromination. It is interesting to note that *scyllo*-inositol, which likewise has the "all-*trans*" configuration, is also difficult to brominate (see above).

Bromoviboquercitol-*A*, however, was easily brominated further, and both of the known dibromotetrols were obtained as products. It thus seems probable that bromoviboquercitol-*A* is the principal intermediate between inositols and dibromotetrols, although the evidence for this is not yet conclusive.

As shown below, plausible mechanisms for the transformation of bromoviboquercitol-*A* to dibromotetrols can be formulated. This gives us increased confidence in the DL(1,2,4) configuration XXI tentatively assigned to bromoviboquercitol-*A* in a previous communication.^{4,10a} The configuration of the bromine atom at position six was previously in doubt.

Debromination to the "para" Tetrol of M.p. 208°.—The dibromotetrol of m.p. 190° on hydrogenation with Raney nickel catalyst in the presence of Amberlite IR-4B resin gave a new tetrol of m.p. 208°, which was characterized by conversion to its tetraacetate, m.p. 148°, and the tetrabenzoate, m.p. 181°. Since the structure of this dibromotetrol was unknown, it was necessary to consider all three structures (IV, V, VI) for the tetrol itself.

Structure of the "para" Tetrol.—The new tetrol was shown not to be dihydroconduritol-*A*¹¹ (m.p. 210°) since a mixed melting point was depressed. It must differ also from Posternak and Friedli's isomer¹¹ of m.p. 216°, since the latter's tetraacetate reportedly melts at 110°. No other cyclohexanetetrol of similar m.p. is mentioned in the previous literature.

After unsuccessful attempts to employ the periodate or lead tetraacetate methods (see below), the structural problem was solved by a fortunate coincidence. In a separate series of experiments¹ we had been investigating the preparation of benzoylated enediols and tetrols by reaction of 1,4-

(10a) ADDED IN PROOF.—Very recent experiments by S. J. Angyal show that the epoxide obtained when bromoviboquercitol-*A* reacts with alkali is identical with that given by bromo*scyllo*quercitol-*A* on similar treatment. This seems to provide definite proof for the configurations XXI and XXXV previously assigned. We are indebted to Dr. Angyal (N. S. W. University of Technology, Sydney, Australia) for a personal communication describing his experiments.

(11) T. Posternak and H. Friedli, *Helv. Chim. Acta*, **36**, 251 (1953).

cyclohexadiene with silver iodine dibenzoate, but had no reason to expect that the products would correspond to those derived from inositol dibromohydrins. However, when a tetrol tetrabenzoate of m.p. 181° was obtained, it was compared to the above tetrabenzoate of the same m.p. and the two were indeed identical. Thus the new cyclohexanetetrol of m.p. 208° was shown to have the "para" structure VI.

Our tetrol of m.p. 208° showed a periodate uptake of 5.35 moles (theoretical two moles), and all attempts to isolate malonic acid (after further oxidation) were unsuccessful. This anomalous result is not surprising in view of the recent work of Huebner, *et al.*,¹² which indicates that malonic dialdehyde and similar β -dicarbonyl compounds are readily oxidized by periodic acid, so that the total moles of periodate consumed greatly exceeds the number of vicinal diol groupings in the substrate.

Abraham¹³ has reported a method by which the number of "intervening" hydroxy groups in a polyol can be determined. Under the action of lead tetraacetate each such group is reportedly oxidized to formic acid and then to carbon dioxide, which is evolved and can be measured by titration. However, our 1,2,4,5-tetrol with no intervening hydroxyls gave more than 2.5 moles of carbon dioxide. It appears that this method is also subject to the " β -dicarbonyl anomaly."

Configuration of the "para" Tetrol.—For a cyclohexanetetrol of this structure five diastereomers are possible. A table showing the known examples is given in a recent article.¹ Since each diol grouping in our 208° isomer must have the *trans* arrangement, only the configurations XXX or XXXII need be considered. Of these two possibilities the DL(1,4) configuration XXX seems more probable if our conclusions regarding the dibromotetrol itself are correct (see below).

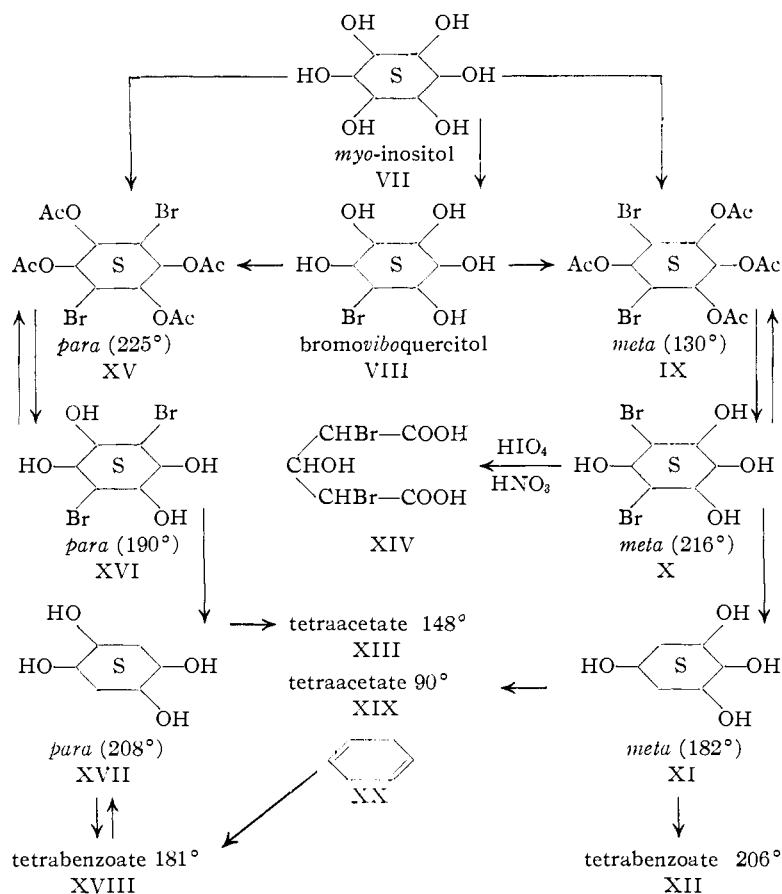
Structure of the "para" Dibromotetrol.—The first attempt to determine the structure of the dibromotetrol of m.p. 190° was made by Wintersteiner, *et al.*,⁹ in 1949, using the periodate method. One might predict a periodate consumption of three moles for an *o*-dibromotetrol (I), and two moles for the *meta* or *para* isomer (II or III). The observed uptake, however, showed a continuous shift from 1.46 moles at 46 hours to 4.01 moles at 192 hours, so that no useful conclusion could be drawn. Carter and Flynn in a similar and independent experiment¹⁰ also obtained anomalous results.

Our own debromination studies now show that

(12) C. F. Huebner, S. Ames and E. Bubl, *THIS JOURNAL*, **68**, 1621 (1946).

(13) S. Abraham, *ibid.*, **72**, 4050 (1950).

CHART I
FORMATION AND DEBROMINATION OF DIBROMOTETROLS FROM INOSITOL



the dibromotetrol of m.p. 190° must have the *para* structure III. Thus with normal behavior it should show a periodate uptake of 2.0 moles. The excess uptake is probably not due to the presence of bromine atoms, but to the fact that the initial product is a β -dicarbonyl compound subject to further oxidation (see above).

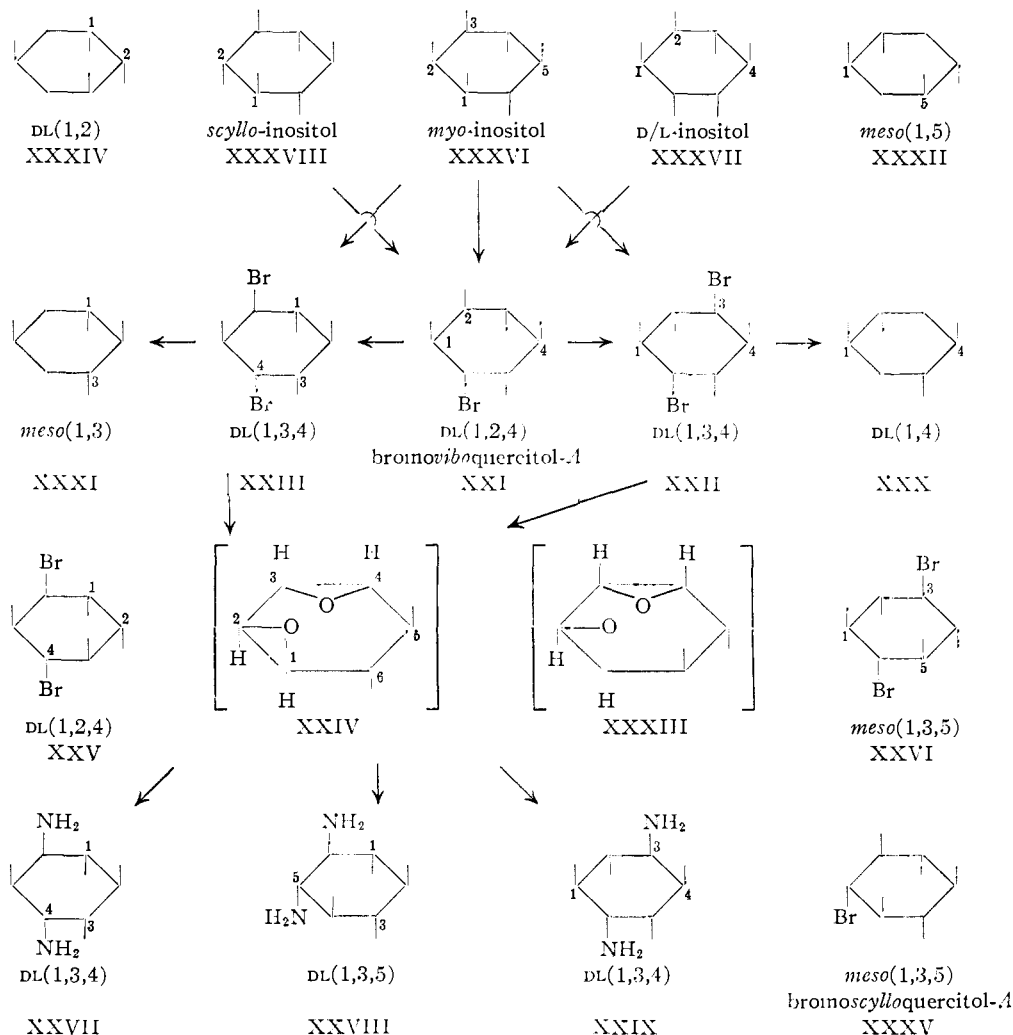
Configuration of the "para" Dibromotetrol.—Of the fourteen diastereomers possible for a dibromocyclohexanetetrol of *para* structure, only one has yet been prepared. For this diastereomer of m.p. 190°, one need only consider those five configurations which have a "*trans-trans*" arrangement of the two pairs of hydroxy groups.

The choices can be further reduced to two by considering the amination results of Wintersteiner, *et al.*⁹ They found that the *p*-dibromotetrol gives an *o*-diaminotetrol (see Chart II). This result can best be explained by invoking a diepoxydiol intermediate which could only be XXIV or XXX-III, since the two epoxy groups are necessarily *trans*, and the two hydroxy groups are also necessarily *trans*. Thus the *p*-dibromotetrol itself must be either XXII or XXVI.

It should finally be noted that configuration XXII could result easily from the bromination of bromoviboquercitol (see above), by a neighboring acetoxy group mechanism.¹⁴ On the other hand

(14) S. Winstein, *et al.*, *ibid.*, **64**, 2792, 2796 (1942).

CHART II

FORMATION, DEBROMINATION AND AMINATION⁹ OF DIBROMOCYCLOHEXANETETROLS, SHOWING PROBABLE CONFIGURATIONS

it would be difficult to explain the formation of XXVI.

On the basis of present evidence, we thus favor tentative assignment of the DL(1,3,4) configuration XXII to the *p*-dibromotetrol of melting point 190°.

B. The "meta" Dibromocyclohexanetetrol of M.p. 216°

Formation of the "meta" Dibromotetrol.—From the same bromination mixture mentioned above, Müller⁷ in 1907 isolated a second dibromotetrol tetraacetate, reported m.p. 140°. The same isomer (cor. m.p. 130°) was later prepared by Griffin and Nelson⁸ and by Wintersteiner, *et al.*⁹ (see Table I).

Müller also had isolated a free dibromotetrol of reported m.p. 210°. Griffin and Nelson in 1915 again prepared this compound (cor. m.p. 216°), and demonstrated by acetylation that it corresponds to the 130° tetraacetate. They also isolated a diacetate and a tetraacetate (m.p. 214 and 124°) which on acetylation also gave the 130° tetraacetate.

In 1949, Wintersteiner hydrolyzed the 130° tetra-

acetate to the 216° dibromotetrol, thus confirming their relationship.

This same dibromotetrol also can be prepared from *scyllo*-inositol,⁷ from pinitol⁸ or from bromoviboquercitol-A (see above).

Structure of the "meta" Dibromotetrol.—The structure of this dibromotetrol was first established by Carter and Flynn¹⁰ who found that it consumed two moles of periodate and yielded 0.9 mole of formic acid. This indicated a *meta* structure. Although another research group⁹ had reported a periodate uptake of 3.02 moles, Carter and Flynn confirmed their own result by isolating 2,4-dibromo-3-hydroxyglutaric acid (XIV) from their periodate mixture (after further oxidation with nitric acid). This shows conclusively that the dibromotetrol of m.p. 216° has the *meta* structure (II).

Configuration of the "meta" Dibromotetrol.—Although twenty diastereomeric configurations are possible for a dibromocyclohexanetetrol of *meta* structure one can show that only a very few of these need now be considered for the diastereomer of m.p. 216°.

The formation of this isomer from bromovibio-*quercitol-A* pentaacetate presumably occurs by a displacement at positions 2 or 4 (formula XXI) involving the usual type of neighboring acetoxy group mechanism.¹⁴ Thus it should have one of the four configurations¹⁵: *meso*(1,2,3), DL(1,2,4), DL(1,2,5), DL(1,3,4).

A second very significant fact is that on amination this *m*-dibromotetrol reportedly gave the *same* *o*-diaminotetrol (N,N'-diacetyl, m.p. 269°) which was given by the *p*-dibromotetrol.⁹ The intermediate here might be the diepoxydiol XXIV; however, a bromoepoxytriol is also possible. In either case the observed facts are best explained if one assigns the DL(1,3,4) configuration XXIII to the *m*-dibromotetrol of m.p. 216°.

Debromination to the "meta" Tetrol of M.p. 182°.—When the dibromotetrol of m.p. 216° was hydrogenated in the above manner, the product was a new cyclohexanetetrol of m.p. 182°. It was characterized by conversion to its tetraacetate, m.p. 92°, and its tetrabenzoate, m.p. 206°.

Structure of the "meta" Tetrol.—Since the dibromotetrol of m.p. 216° previously had been shown by Carter and Flynn¹⁰ to have the "meta" structure II, it was apparent that the tetrol must have the corresponding structure V.

TABLE II
THE KNOWN¹⁷ "Meta" OR 1,2,3,5-CYCLOHEXANETETROLS (1954)^{a,b}

M.p., °C. and rotation	Probable configuration ¹⁵ (tentative)	M.p. of tetraacetate, °C.	M.p. of other derivatives, °C.	Prepared from
151 (levo 61)	D/L(1,2,5) ^c	"Quinic triolone"
208 (levo 8)	D/L(1,2,5) ^c	"Quinic triolone"
182 (inactive)	<i>meso</i> (1,3)	92	Tetrabenzoate 206	Dibromotetrol 216°

^a Four *meso* and three active diastereomers possible.

^b For a table of the "para"-tetrols see ref. 1. For a description of the "ortho"-tetrols see ref. 11. ^c The isomers of m.p. 151° and 208° are epimeric at position 5; see ref. 16.

The new tetrol showed a periodate uptake of two moles. This could mean either a *meta* or *para* structure. The actual structure is undoubtedly *meta*.

By Abraham's method (see above) this tetrol with one intervening hydroxyl gave roughly the predicted one mole of carbon dioxide.

Configuration of the "meta" Tetrol.—Seven diastereomers are possible for a cyclohexanetetrol of "meta" structure, and two of these were previously known (see Table II). These two diastereomers were prepared by Fischer and Dangschat¹⁶ in 1939 by reducing a cyclohexanetriolone derived from *l*-quinic acid. Both diastereomers were levorotatory, and from the method of preparation they must have the epimeric configurations¹⁵ D/L(1,2) and D/L(1,2,5), although it is uncertain which compound has which configuration. Al-

(15) (a) The symbols used to designate stereoisomers in this article are explained in a pamphlet entitled "A New General System for the Naming of Stereoisomers," available from Chemical Abstracts, Ohio State University, Columbus 10, Ohio. (b) The symbol D/L signifies "D or L" configuration. "R" stands for relative and "A" for absolute configuration.

(16) G. Dangschat and H. O. I. Fischer, *Naturwissenschaften*, **27**, 756 (1939).

though our new tetrol of m.p. 182° might conceivably be the racemic form of one of Fischer's products or of betitol,¹⁷ we regard the *meso*(1,3) configuration XXXI as more probable, if our conclusions regarding the parent dibromotetrol are correct (see above).

C. The Known Diaminocyclohexanetetrols

In addition to an *o*-diaminotetrol (probably XXVIII), the above *m*-dibromotetrol on amination gave a *m*- or *p*-diaminotetrol (hexabenzoyl, m.p. 262–263°); and the *p*-dibromotetrol gave a different *m*- or *p*-diaminotetrol (hexabenzoyl, m.p. 252–255°).⁹ If our configurational assignments above are correct, one of these products would be a *m*-diaminotetrol with the DL(1,3,4) configuration XXVII, and the other would be a *p*-diaminotetrol with the DL(1,3,4) configuration XXIX. However, one cannot say which compound is which, since both might arise from the common intermediate XXIV. Carter and Flynn¹⁰ also aminated the *m*-dibromotetrol, obtaining a diaminotetrol (hexaacetyl, m.p. 293°), which may possibly be identical with Wintersteiner's *o*-diaminotetrol (hexaacetyl not prepared).

These diaminotetrols are of great interest because of their relationship to natural streptomycin, which reportedly¹⁸ is a *m*-diaminotetrol of configuration *meso*(1,3,5) and thus differs from all of the above isomers. From their synthesis of natural streptomycin Wolfrom, *et al.*, also obtained a diastereomer (hexaacetyl, m.p. 350–355°) for which they suggest the configuration DL(1,2,4,5).

Experimental

All melting and boiling points are corrected. M.p.'s taken on Kofler block. Analyses by Micro-Tech Laboratories, Skokie, Illinois. Calculated analytical values from Gysel's Tables.¹⁹ All configurational assignments¹⁵ should be regarded as tentative.

Derivatives of "para" or 1,2,4,5-Cyclohexanetetrol

DL(1,3,4)R-3,6-Dibromocyclohexanetetrol-1,2,4,5. (A) From *myo*-Inositol.—Sealed Pyrex tubes (Corning No. 8560), each containing 20 g. of finely pulverized oven-dried *myo*-inositol and 80 g. of acetyl bromide, were heated at 120° for six hours. After cooling, the contents of each tube was transferred into a flask containing 500 ml. of warm absolute alcohol with the aid of 60 ml. additional alcohol. The resulting crystals after 4 to 24 hours were collected, washed and dried giving about 10 to 12 g. of flaky, greyish crystals per tube, m.p. 196–210°.

To this material (50 g.) was added 1000 ml. of a 1 *M* solution of hydrogen chloride in 50% (v./v.) aqueous ethanol, and the mixture boiled for six hours. Darco charcoal was then added and the whole mixture boiled for 15 minutes longer. After filtration the colorless solution was vacuum-concentrated down to a sirup, which was repeatedly taken up in warm 100-ml. portions of absolute ethanol and reconcentrated. The product turned crystalline during these operations.

The crystals were collected, dried and finely pulverized, then extracted with 500 ml. of ethyl acetate (reflux 30 minutes). The mixture was filtered hot, and the filtrate diluted with 2.5 liters of warm chloroform. After several

(17) Betitol, a dextrorotatory cyclohexanetetrol from beet sugar molasses (*Ber.*, **34**, 1159 (1901)) may possibly have the 1,2,3,5-structure. It is not an enantiomer of either of Fischer and Dangschat's tetrols.

(18) M. L. Wolfrom, *et al.*, *THIS JOURNAL*, **72**, 1724 (1950).

(19) H. Gysel, "Tables of Percentage Composition of Organic Compounds," Verlag Birkhauser, Basel, Switzerland, 1951.

days the crystals which had separated were collected, washed and dried, giving 20.7 g. (8-9% based on *myo*-inositol) of the *p*-dibromotetrol, m.p. 187-189°.

In some runs a further recrystallization from 1:2 methanol-benzene (2 ml./g.) was needed.

The residue from the ethyl acetate extraction (3.6 g., m.p. 215-224°) was recrystallized from 6:1 ethanol-water (1 ml./g.) giving 2.8 g. of bromoscyloquercitol, m.p. 224.5-226.5°.

DL(1,3,4)R-3,6-Dibromocyclohexanetetrol-1,2,4,5 Tetraacetate.—This derivative can be prepared by chromatographic purification⁹ of the original bromination mixture, or by acetylating the dibromotetrol.⁸

DL(1,4)R-Cyclohexanetetrol-1,2,4,5. (A) From Dibromotetrol.—To 4.6 g. of *p*-dibromotetrol dissolved in 110 ml. of water was added 10 g. of well-washed commercial Raney nickel catalyst and 15 g. of specially washed (see below) Amberlite IR-4B resin, and the mixture hydrogenated at 3 atm./25° for five hours. The hydrogen uptake reached theoretical within three hours.

To prevent release by the Amberlite resin of a troublesome orange impurity, it should be shaken beforehand with excess one molar sodium hydroxide for 24 hours, and washed thoroughly with water.

Catalyst and resin were filtered off with the aid of Hyflo Super-cel diatomaceous earth. The clear colorless neutral filtrate was shaken with Amberlite IR-120 (H⁺) resin (2 g.) until it gave a negative dimethylglyoxime test for nickel. The filtered solution was deacidified by treatment with IR-4B resin, again filtered, and vacuum-distilled to dryness.

The resulting crystalline residue was taken up repeatedly in 25-ml. portions of absolute alcohol which were evaporated to dryness. Thus 1.93 g. of cream-colored crystals was obtained. These were recrystallized by dissolving in boiling methanol (charcoal) and adding four volumes of benzene, giving 1.52 g. (68%) of the tetrol as colorless prisms, m.p. 203-207°.

(B) From the Tetrabenzoate.—For highest purity the tetrol can be prepared from its tetrabenzoate (see below). To 4 ml. of saturated methanolic ammonia at 25° was added 100 mg. of the tetrabenzoate. After 24 hours the clear solution was vacuum distilled to dryness. The residue was washed with 9 ml. of hot dry benzene. The resulting crystalline product (22 mg.) was recrystallized from methanol-benzene, giving a small amount of the pure tetrol, m.p. 207.5-208°.

Anal. Calcd. for C₆H₁₂O₄: C, 48.64; H, 8.17. Found: C, 48.19; H, 8.12.

It was shown by mixed melting points and by X-ray powder pictures that this compound is identical with the tetrol of similar m.p. prepared¹ from 1,4-cyclohexadiene.

Preparation of the tetraacetate of this tetrol has previously¹ been described.

DL(1,4)R-Cyclohexanetetrol-1,2,4,5 Tetrabenzoate. (A) From Tetrol.—The dry pulverized tetrol (0.150 g.) was added with cooling to a solution of 0.62 g. redistilled benzoyl chloride in 1.0 ml. of dry pyridine. The mixture was left at 25° for 24 hours. Chloroform (5 ml.) was added and the solution washed with 1 *N* sulfuric acid, saturated sodium bicarbonate solution, and water, and dried with anhydrous magnesium sulfate. The solution on evaporation gave a viscous oil. Small portions of absolute ethanol were repeatedly added, and removed by vacuum distillation, giving 0.44 g. of crystalline residue, m.p. 181-183°. On recrystallization from 95% ethanol, 0.32 g. (56%) of the tetrabenzoate was obtained as colorless prisms, m.p. 181-182.5°.

For analysis a portion was again recrystallized, m.p. 182.5-183.5°.

Anal. Calcd. for C₃₄H₂₈O₈: C, 72.33; H, 5.02. Found: C, 72.79; H, 5.28.

Identity of this compound with the tetrol tetrabenzoate of similar m.p. prepared from 1,4-cyclohexadiene was demonstrated by mixed m.p., fusion analysis,²⁰ and X-ray powder pictures.

(B).—Preparation of the tetrabenzoate from 1,4-cyclohexadiene has been described previously.¹

Derivatives of "meta" or 1,2,3,5-Cyclohexanetetrol

meso(1,3)A-4,6-Dibromocyclohexanetetrol-1,2,3,5 Tetraacetate.—The bromination was carried out as described

by Griffin and Nelson⁸ and by Wintersteiner, *et al.*⁹ To improve the yield, the crude (partially deacetylated) second crop from the original ethanolic mother liquor was reacylated with acetic anhydride before purification, as suggested by Carter and Flynn.¹⁰

meso(1,3)A-4,6-Dibromocyclohexanetetrol-1,2,3,5.—The tetraacetate was hydrolyzed with aqueous ethanolic hydrogen chloride as described by Wintersteiner.⁹ The product is best crystallized from water, as recommended by Müller.⁷

meso(1,3)A-Cyclohexanetetrol-1,2,3,5.—To 20 g. of Raney nickel and 20 g. of specially washed (see above) Amberlite IR-4B resin was added a solution of 6.1 g. of the *m*-dibromotetrol in 200 ml. of warm water. The mixture was cooled and immediately hydrogenated at 3 atm./25°. The reaction mixture after hydrogenation was treated by the above procedure, giving 2.33 g. of the tetrol, m.p. 171-180°.

This material (2.04 g.) was dissolved in boiling methanol and eight volumes of hot benzene added, giving 1.70 g. (57%) of colorless crystals, m.p. 181.5-182.5°.

For analysis the tetrol was recrystallized from 95% ethanol, m.p. unchanged.

Anal. Calcd. for C₆H₁₂O₄: C, 48.64; H, 8.17. Found: C, 48.50; H, 8.41.

meso(1,3)A-Cyclohexanetetrol-1,2,3,5 Tetraacetate.—To 300 mg. of the tetrol was added 1.60 ml. of acetic anhydride and 3 mg. of freshly fused zinc chloride. The mixture was boiled 2 minutes, then vacuum-distilled down to a thick sirup, which crystallized on addition of 4 ml. of absolute ethanol. Thus 0.29 g. of the tetraacetate, colorless crystals, m.p. 91-92°, was obtained. The second crop melted at 88-89° and weighed 0.26 g., making the total yield 87%.

For analysis the sample was recrystallized from dilute methanol.

Anal. Calcd. for C₁₄H₂₀O₈: C, 53.16; H, 6.37. Found: C, 53.01; H, 6.70.

meso(1,3)A-Cyclohexanetetrol-1,2,3,5 Tetrabenzoate.—A 74-mg. portion of tetrol when benzoylated in the above described manner gave 210 mg. (75%) of product, m.p. 205-206.5°. Recrystallization from absolute ethanol gave 170 mg. of m.p. 205.5-207°.

A sample recrystallized again for analysis melted at 207-208°.

Anal. Calcd. for C₃₄H₂₈O₈: C, 72.33; H, 5.02. Found: C, 72.79, 72.21; H, 5.28, 5.02.

Dibromotetrols from Monobromopentols

Attempted Bromination of Bromoscyloquercitol.—To 611 mg. (2.5 mmoles) of 6-bromoscyloquercitol (m.p. 223°) was added 2.00 ml. (24.8 mmoles) of acetyl bromide and the mixture heated in a sealed Pyrex tube at 120° for six hours. The cold mixture was poured into 15 ml. of absolute ethanol. Crystals separated at once. These were collected and dried, giving 1.02 g. (90% recovery) of the acetylated starting material, melting sharply at 241.5°.

In another run using a fivefold molar ratio of acetyl bromide, 78% of the acetylated starting material was recovered.

Conversion of Bromoviboquercitol to *m*- and *p*-Dibromotetrols.—A 1.13-g. portion of 6-bromoviboquercitol (m.p. 171°) was treated in the above manner with 2.00 ml. (5.3 moles per mole) of acetyl bromide. After cooling to 0° the tube was opened (*Caution*) and its contents transferred into 10 ml. of absolute ethanol. The crystals which separated were found to consist of 0.31 g. (14%) of the *p*-dibromotetrol tetraacetate, tiny colorless flakes, m.p. 223-225°.

The mother liquor was concentrated to one third volume and left at 4° for several days, giving 0.23 g. (16%) of the free *m*-dibromotetrol as microscopic prisms, m.p. 213-217°. This product was recrystallized from water giving 0.16 g. of colorless prisms, m.p. 219.5-220.5°. The ethanolic mother liquor gave a third crop of crystals on standing, consisting of 0.28 g. of the free *m*-dibromotetrol, m.p. 214-217°, making the total yield 0.51 g. (36%).

Bromination of Quebrachitol

A sealed tube containing 5.0 g. of 1,2,4,5R-inositol 2-methyl ether ("quebrachitol") and 19 g. of acetyl bromide was heated at 120° for six hours. The mixture after cooling was poured into 50 ml. of absolute alcohol. Colorless crystals (0.31 g., 2.7%) of 6-bromoscyloquercitol pentaacetate,

²⁰ W. C. McCrone, *Anal. Chem.*, **21**, 436 (1949).

m.p. 243–244°, separated. The identity was confirmed by mixed melting points.

The dark filtrate was vacuum distilled down to one fourth volume. After five days 1.79 g. of *m*-dibromotetrol, greyish crystals, m.p. 205–213°, was obtained.

Oxidation of Tetrols

Cyclohexanetetrol-1,2,3,5 with Periodate.—To 0.0362 g. of the tetrol dissolved in a little water was added 50 ml. of 0.0214 *M* sodium metaperiodate and water q.s. 100 ml. The solution was kept at 25.0° and 10-ml. aliquots were withdrawn at intervals for titration. Each aliquot was immediately mixed with 25 ml. of 0.01 *N* sodium arsenite, 10 ml. of saturated sodium bicarbonate and 1 ml. of 1.2 *M* potassium iodide solution. After 15 minutes standing the excess arsenite was determined iodometrically.

The 1,2,3,5-tetrol gave the following results (theoretical consumption 2.0 moles).

Time, hr.	0	0.5	1.0	2.0	5.0	22.5
Periodate consumed, moles/mole	0.00	2.07	2.07	2.11	2.12	2.18

Cyclohexanetetrol-1,2,4,5 with Periodate.—The above procedure was used and the following anomalous results obtained (theoretical consumption 2.0 moles).

Time, hr.	0	1.25	6.1	8.1	20.5	29.3	49.6
Periodate consumed, moles/mole	0.0	1.50	2.04	2.32	3.46	4.14	5.35

Oxidation with Lead Tetraacetate (Abraham's Carbon Dioxide Method).—In a control experiment L-arabinose when oxidized with lead tetraacetate using Abraham's procedure¹³ gave only 75–87% of the theoretical carbon dioxide (reported¹³ 99%).

The procedure was modified by using a brom thymol blue-brom cresol purple mixed indicator,²¹ and a sintered glass bubbler in the carbon dioxide absorption tube. This made the procedure more convenient but did not improve the above result.

Several runs on the 1,2,3,5-tetrol gave 75–76% of the theoretical one mole of carbon dioxide.

The 1,2,4,5-tetrol which one might expect to give no carbon dioxide, gave 2.52 moles in four hours, when the experiment was discontinued.

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TORONTO, CANADA

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, GENERAL MILLS, INC.]

The Reaction of Methyl Linoleate and Methyl Linolelaidate with Di-*t*-butyl Peroxide^{1,2}

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The reaction of methyl linoleate and methyl linolelaidate with di-*t*-butyl peroxide at 125° has been studied. It was found that the products were largely the dehydro dimers of the fatty esters. The dimer from each fatty ester was found to be a mixture of isomers differing in the number of conjugated double bonds and in the *cis*, *trans* configuration of the double bonds.

Recent reports have shown that when methyl linoleate and di-*t*-butyl peroxide are heated together at from 125–135° a dehydro methyl linoleate dimer is formed^{3,4} accompanied by a minor amount of higher molecular weight material. The dimer has four double bonds of which somewhat less than one-half are conjugated. This dehydro dimer is formed in the stoichiometric proportion of one mole of dimer for each mole of peroxide decomposed. It is considered to result from the loss of a hydrogen atom at carbon no. 11 of methyl linoleate, followed by combination of two of the three limiting resonance hybrid radicals.

The results of a more detailed study of the reaction of di-*t*-butyl peroxide and the methyl esters of linoleic and linolelaidic acids are reported in this paper.

Decomposition of Di-*t*-butyl Peroxide.—Examination of the volatile products formed when di-*t*-butyl peroxide was decomposed in the methyl esters showed that *t*-butyl alcohol was nearly the sole decomposition product of the peroxide. Ad-

vantage was taken of this fact to follow the decomposition of the peroxide. The alcohol was determined quantitatively and used as a direct measure of peroxide decomposed. In Fig. 1 the log of the per cent. di-*t*-butyl peroxide is plotted against reaction time for the decomposition of peroxide in methyl linoleate and methyl linolelaidate. It is evident that the decomposition in the two esters is first order and in agreement with the order and rates (in other media) reported by Raley, Rust and Vaughan.⁵

Dimer Formation.—When low concentrations of di-*t*-butyl peroxide are used very little ester polymer of higher molecular weight than dimer is formed. For example, when 12 mole per cent. of di-*t*-butyl peroxide is decomposed in either methyl linoleate or methyl linolelaidate about 95% of the polymeric product is dimer. The amount of dimer was determined by molecular distillation of the reaction mixture concurrently with the determination of the peroxide decomposed. The results which are plotted in Fig. 2 show that very nearly one mole of dimer is formed for each mole of di-*t*-butyl peroxide decomposed.

Structure of Dimers.—As was pointed out by Clingman and Sutton⁴ the *t*-butoxy radicals remove hydrogen atoms from carbon atom no. 11 in

(1) Paper No. 143, Journal Series, Research Laboratories, General Mills, Inc.

(2) Presented in part at the 123rd Meeting of the American Chemical Society in Los Angeles, California.

(3) S. A. Harrison and D. H. Wheeler, *Minnesota Chemist*, **4**, No. 5, 17 (1952).

(4) A. L. Clingman and D. A. Sutton, *J. Am. Oil Chemists' Soc.*, **30**, 53 (1953).

(5) J. H. Raley, F. F. Rust and W. E. Vaughan, *THIS JOURNAL*, **70**, 1336 (1948).