was poured onto ice, the ether layer separated and washed. After drying, the ether was distilled leaving 916 mg. (93%) of crude ketone which was used directly in the perbenzoic acid reaction. A small sample was converted to a 2,4-dinitrophenylhydrazone which was recrystallized from ethanol, m.p. 160.5–160.9°.

(b) *trans-trans*-1-**Ketone.**—Due to the insolubility of the lithium salt of this acid, the methyl ketone was prepared by means of the acid chloride and dimethylcadmium. Such a reaction has been shown to be stereospecific.[40] The acid (2.74 g., m.p. 99°) was dissolved in 10 ml. of dry benzene and 3 ml. of thionyl chloride was allowed to stand at room temperature for 36 hours. The solvent was removed, additional benzene added and the process repeated. The crude acid chloride was dissolved in anhydrous ether and added to a solution of dimethylcadmium prepared from methylmagnesium bromide and 1.84 g. of anhydrous cadmium chloride. The reaction was heated under reflux for 3 hours and processed in the usual manner; 0.6 g. of acid was recovered and 0.89 g. (42%) of the ketone obtained, b.p. 125–130° (11 mm.), $n^{25}D$ 1.4822.

(c) *trans-cis*-2-**Ketone.**—Using the methyllithium procedure, 7.2 g. (0.04 mole) of the *trans-cis*-2-acid (m.p. 103.5–105°) was converted to the methyl ketone and the product distilled, b.p. 132–137° (10 mm.), $n^{23}D$ 1.4815, yield 6.4 g. (90%). The yellow 2,4-dinitrophenylhydrazone melts 134–135°.

Perbenzoic Acid Oxidation of Ketones.[1] (a) *cis-cis*-1-**Decalol.**—*cis-cis*-1-Acetyldecalin (0.84 g., 4.7 mmoles) was dissolved in chloroform and allowed to react for 12 days with 935 mg. of 77% perbenzoic acid (5.2 mmoles). The solution then was diluted with ether and washed with base until neutral. The solvents were distilled and the residue saponified by refluxing with 1 *N* sodium hydroxide in methanol for 2 hours. The solution was diluted with water, extracted 2 times with ether and the crude decalol obtained upon evaporation of the ether. The product was recrystallized from pentane, m.p. 89.9–91.4° (lit.[38] 93°), yield 392 mg. (55%).

(b) *trans-trans*-1-**Decalol.**—The *trans-trans*-1-acetyldecalin (0.68 g., 3.78 mmoles) was treated with perbenzoic acid and the crude reaction mixture treated with Girard's reagent T and the non-ketonic fraction isolated. It was found that this ester was quite resistant to saponification and the reflux period was extended to 18 hours. After dilution of the saponification mixture, the decalol was isolated by ether extraction and the solvent removed. The crude decalol (490 mg., 72%) was allowed to react with 750 mg. of *p*-nitrobenzoyl chloride in 4 ml. of dry pyridine for 24 hours at room temperature. After the usual processing procedure, the ester was recrystallized, yield 347 mg. (42%), m.p. 83.5–85° (lit.[38] 86°).

(c) *trans-cis*-2-**Decalol.**—The *trans-cis*-2-acetyldecalin (6.0 g., 0.033 mole) was degraded as described for the 1-isomers and the crude decalol recrystallized from hexane, yield 2.85 g. (55%), m.p. 72.1–74.8° (lit.[39] 76°).

Acknowledgment.—The authors are most indebted to Drs. K. S. Pitzer, A. Streitwieser and S. Winstein for most helpful discussions pertaining to this work.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Stereochemistry and Reactivity of the *cis*-5-Hydrindanyl Derivatives[1]

BY WILLIAM G. DAUBEN AND JAMES JIU

RECEIVED FEBRUARY 19, 1954

The stereochemistry of the epimeric *cis*-5-hydrindanyl derivatives has been investigated and it has been found that the previously assigned steric relationships of the amines and alcohols were inverted. The steric course of the deamination of the amines has been shown to follow the general pattern developed in the *cis*-decalin series. Extension of these concepts to the epimeric *cis*-4-hydrindanyl compounds have been discussed.

The recent interest in the stereochemical aspects of the reaction of nitrous acid with alicyclic amines has brought forth certain generalizations which have been shown to be useful in elaboration of the steric configuration (and conformation) of the amines and the alcohols produced from them.[1-3] It has been found that when an amine of an equatorial conformation is deaminated with nitrous acid, the reaction yields practically a single product and this material is an alcohol of the same steric configuration as the original amine. With compounds which possess the amino grouping in an axial conformation, however, the reaction produces both olefins and alcohols, and these alcohols are composed of a predominant amount of the epimer of inverted (or equatorial) configuration. Special attention has been given to the amines derived from *cis*-decalin since in such compounds both of the epimeric amines can exist in an equatorial conformation. In such a series, Hückel[4] had reported the interesting results that deamination of the *cis*-1-decalylamines proceeded with retention while the *cis*-2-decalylamines gave rise to inverted products. Dauben and Hoerger[5] reinvestigated this anomaly to the above generalizations and found that the relationship between *cis*-2-decalylamines and *cis*-2-decalols had been incorrectly assigned and by correcting such steric configurations, a consistent pathway of reaction in the deamination was followed.

Hückel[4,6] also has reported a detailed investigation of the aminohydrindanes substituted on either the 5- or 6-membered ring. In the latter series, direct analogy to the previous work in the decalin field was to be found and it was noted that here again, the *cis*-4-hydrindanylamines underwent deamination with retention of configuration and the *cis*-5-hydrindanylamines followed the inversion pathway. In order to ascertain whether such results were due to incorrect configurational assignments or whether a true anomaly existed from the conformational concepts of deamination, the steric relationship between the *cis*-5-hydrindanyl derivatives was investigated as previously described[5] for the *cis*-2-decalin compounds.

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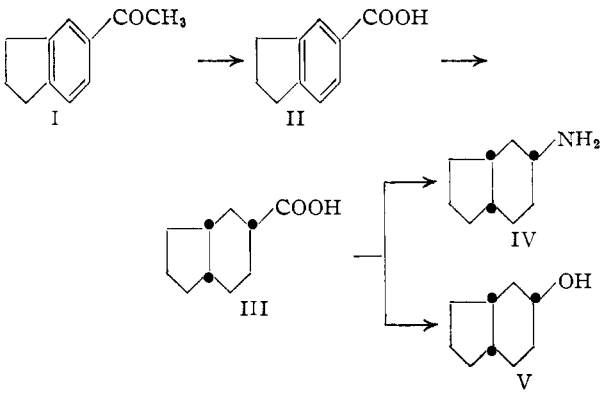
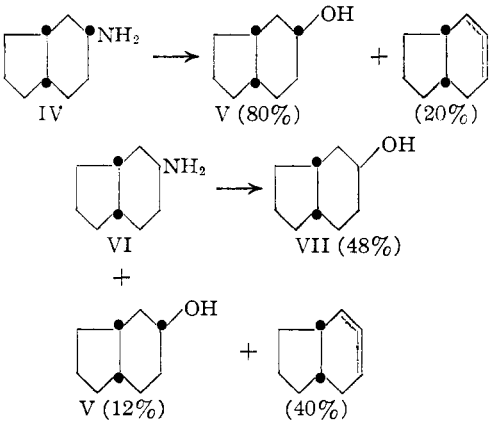
(6) W. Hückel, R. Schlüter, W. Doll and F. Reimer, *Ann.*, **530**, 166 (1937).



5-Acetylindane (I),[7-9] prepared by a Friedel–Crafts reaction between acetyl chloride and indane, was converted to 5-indanecarboxylic acid (II)[10] by sodium hypobromite oxidation. The acid when hydrogenated in acetic acid over platinum gave rise to a mixture of perhydro isomers which could be separated into one pure compound (III) in a yield of 20–25% by fractional crystallization or by isolation of the piperazine salt. The acid was degraded to 5-hydrindanylamine (IV) by a Schmidt reaction and the amine isolated as the benzamide. This amide corresponded to the *cis*-5-amine of series II of Hückel.[11] The acid also was converted to the methyl ketone which in turn was cleaved with perbenzoic acid to a *cis*-5-hydrindanol. The product obtained corresponded to the *cis*-5-alcohol of series I.[11] Since previous work[5] has demonstrated that all the reactions employed in these degradations proceed with stereochemical retention, the results show that the correlation of amine and alcohol given by Hückel is incorrect. Using the corrected series relationships, the reaction of the amines with nitrous acid can be summarized as shown below to illustrate that retention of configuration is the usual reaction.



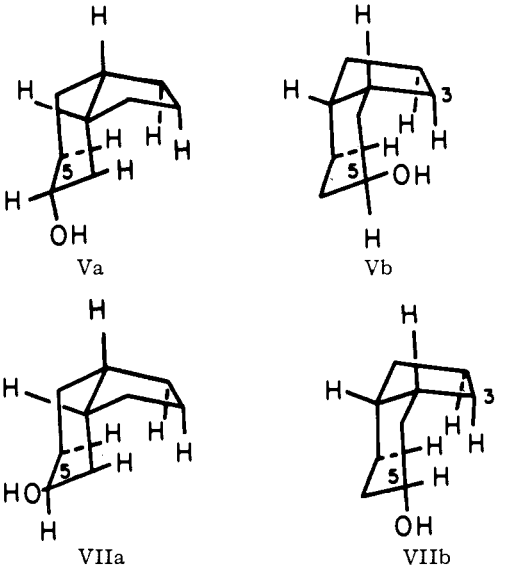
The assignment of the steric configuration of the substituent with respect to the ring juncture could not be given, with certainty, from the results of the catalytic hydrogenation since such a small yield of a pure isomer was obtained. However, the amine related to the acid prepared in this work followed the deamination pattern (pure retention) which is characteristic of the *cis–cis*-decalylamines and accordingly this same structure[12] has been assigned the acid III, the amine IV and the alcohol V. On the basis of such an assignment, the physical properties of the epimeric 5-hydrindanyl derivatives are listed in Table I.

TABLE I

MELTING POINTS OF THE EPIMERIC 5-HYDRINDANYL DERIVATIVES

Configuration C_8, C_9	C_9, C_5	Acid		Alcohol		Amine	
		acid	amide	ol	phenylurethan	amine	benzamide
cis	*cis*	53	197	43	125	⩽20	145
cis	*trans*			20	74	−19	166

Further confirmation of these configurational assignments can be gained by examination of the work of Hückel[4] on the relative stability of the epimeric *cis*-5-hydrindanols. It was found that when either alcohol was heated under reflux with sodium in xylene or when *cis*-5-hydrindanone was reduced with sodium and ethanol,[13] a mixture composed of 80% of VII (m.p. 20°) and 20% of V (m.p. 43°) was obtained. As with the *cis*-decalin derivatives,[1,2] the flexibility of the *cis*-hydrindane system allows a substituent of any relative configuration to occupy either an equatorial or axial conformation (Va or Vb and VIIa or VIIb) by simple interconversion of all equatorial to axial bonds and *vice versa*. Assuming that the 5-membered ring of hydrindane behaves as a cyclopentane, then from the



(7) J. v. Braun, G. Kirschbaum and H. Schuhman, *Ber.*, **53**, 1155 (1920).

(8) W. Borsche and M. Pommer, *ibid.*, **54**, 102 (1921).

(9) L. F. Fieser and E. B. Hershberg, THIS JOURNAL, **62**, 49 (1940).

(10) J. Lindner, F. Schmitt and B. Zaunbauer, *Monatsh.*, **72**, 216 (1939).

(11) Series I and II refer to the epimeric compounds of the hydrindanylamines and alcohols. The compounds of the same series were believed to possess the same configuration.

(12) All configurational assignments are in terms of the relative positions of the hydrogen atoms at C_8, C_9 and C_9, C_5. The positions of the hydrogen atoms are represented in the formulas by black dots, a dot indicating that a hydrogen atom is above the plane of the molecule. A dot is always placed at C_9.

(13) It is well established in other cases[4] that sodium and ethanol reduction affords a mixture of alcohols of the same composition as is obtained by direct equilibration and can be employed to measure the relative stability of alcohols.

work of Pitzer[14] one must keep 4 of the 5 carbon atoms in a single plane. Accordingly, the structures of the alcohols can be viewed as Va–VIIb. It is seen that the *cis–cis* isomer Vb displays a steric interaction between the C_5-hydroxyl and the C_3-hydrogen atom when the hydroxyl group is placed in an axial conformation. Such an interference is absent in both conformations of the *cis–trans* isomer (VIIa and VIIb). Since states Va and VIIb are of equal energy and Vb is of higher energy than VIIa, it would be expected that the isomer VII would be the more stable thermodynamically. If the *cis–trans* structure is assigned to the more stable alcohol (m.p. 20°) it is seen that it is the same configurational assignment arrived at by consideration of the nitrous acid reaction. It is also to be noted that Hückel[4,6] has reported that the sodium and ethanol reduction[13] of *cis*-5-hydrindanone oxime gives rise to the amine which has been assigned the *cis–trans* or the more stable configuration.

In contrast to the equilibration studies, the catalytic hydrogenation of the ketone and the oxime gave rise to products of a configuration opposite to that which would be predicted by the concepts of the effect of the media on the steric course of hydrogenation. Recently Barton[15] reviewed such concepts and from his work it can be assumed that hydrogenation under acidic conditions gives rise to the unstable isomer and under neutral condition to the stable isomer. Hückel[4] has reported, however, that the hydrogenation of the ketone in ether formed only the unstable *cis–cis*-alcohol V while the ketoxime in acid produced the stable *cis–trans*-amine VI. Before such results can be evaluated, it will be necessary to ascertain if the steric course of these hydrogenations are, indeed, dependent upon the media.

Using the concepts of the stereospecificity of the deamination reaction, relative stability of the alcohols and the role of the media in catalytic hydrogenation discussed above, the configuration of the isomeric *cis*-4-hydrindane derivatives can be assigned. Table II lists the physical properties of these epimers.

TABLE II

MELTING POINTS OF THE EPIMERIC 4-HYDRINDANYL DERIVATIVES

Configuration C_8, C_9	C_9, C_4	Hydrindanols ol	phthalate	succinate	Hydrindanylamines amine	acetamide	benzamide
cis	*cis*	16(31)	131	47	−14	131	177
cis	*trans*	liq.	146	37	liq.	93	163

It is to be noted that Hückel[4,6] has shown that the alcohol, m.p. 16(31°), is converted to the more stable liquid isomer (phthalate 146°) on treatment with sodium in xylene and that the reduction of *cis*-4-hydrindanone oxime gives rise to the liquid amine (benzoate 163°). These latter two compounds have been assigned the more stable *cis–trans* configuration. In addition, it is of interest that in this series it has been found that hydrogenation of the oxime under acid conditions produces the expected unstable *cis–cis*-amine in contrast to the *cis–trans*-isomer produced in the 5-series.

The reaction of the *cis*-4-hydrindanylamines with nitrous acid also follows the sequence shown for the 5-series, the *cis–cis*-isomer giving rise only to alcohol of retained configuration while the *cis–trans* compound yields a mixture of alcohols consisting of 80% of retained and 20% of inverted product.

Experimental[16]

5-Acetylindane (I).—The methyl ketone was prepared following the procedure employed by Newman and Zahm[17] for 6-acetyltetralin. To a solution of 44.4 g. (0.376 mole) of indane[18] and 29.5 g. (0.376 mole) of redistilled acetyl chloride in 225 ml. of dry thiophene-free benzene, there was added, with stirring, 50.50 g. of anhydrous aluminum chloride in portions over a period of 40 minutes. The entire reaction was conducted at 0–5°. The mixture was allowed to stand for an additional 16 hours and then poured onto a mixture of ice and concentrated hydrochloric acid. After separation of the benzene layer, the solvent was removed and the product distilled, b.p. 162–165° (25 mm.), yield 52 g. (88%); the reported[7,8,9] value is 134–135° (11 mm.).

5-Indanecarboxylic Acid (II).—A solution of potassium hypobromite was prepared at 0° by dissolving 443 g. of potassium hydroxide in 1600 ml. of water and adding 121 ml. of bromine. There was added to this solution, with stirring, 83.7 g. (0.52 mole) of 5-acetylindane at such a rate so that the temperature was maintained below 40°. After completion of the addition, the reaction mixture was heated to 40° for one hour, then cooled, ether added and the layers separated.

The aqueous solution was tested for hypohalite with starch–iodide paper moistened with acetic acid. If a positive reaction was obtained, methanol was added until the test was negative and then the aqueous solution was acidified. The crude acid so obtained melts from 175–178° and was recrystallized several times from benzene, yield 63 g. (73.5%), m.p. 183–185° (lit.[10] m.p. 183–184°).

***cis–cis*-5-Hydrindanecarboxylic Acid** (III).—A solution of 13.2 g. (0.082 mole) of 5-indanecarboxylic acid in 200 ml. of acetic acid and 0.5 g. of platinum oxide was hydrogenated at low pressure. After the theoretical amount of hydrogen had been absorbed, the catalyst was filtered, the solvent removed and the product distilled, b.p. 126–128° (0.6 mm.), yield 10.43 g. (76.2%). The distillate partially solidified on standing.

Recrystallization of the material 7–8 times from hexane yielded a pure isomer, m.p. 52–53°, yield 1.7 g. (12.8% based upon starting aromatic acid).

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 71.39; H, 9.59. Found: C, 71.54; H, 9.65.

The amide was prepared by allowing 0.107 g. (0.637 mmole) of the acid to react with 1 ml. of thionyl chloride in the presence of 1 ml. of benzene and one drop of pyridine at 40° for 30 minutes. The excess reagent and solvent were removed under reduced pressure and the crude acid chloride added dropwise to 2 ml. of cold concentrated ammonia. The amide was recrystallized from aqueous ethanol, m.p. 196.5–197.5°, yield 54 mg. (50.5%).

Anal. Calcd. for $C_{10}H_{17}ON$: C, 71.81; H, 10.25; N, 8.38. Found: C, 71.67; H, 10.10; N, 8.25.

The piperazine salt was prepared by allowing 0.083 g. (0.495 mmole) of the acid to react with 0.022 g. (0.256 mmole) of anhydrous piperazine in 3.5 ml. of dry acetone. The mixture was heated to boiling, allowed to cool and the product filtered, yield 97 mg. (93.5%), m.p. 157.7–159.0°. The salt was recrystallized from acetone–chloroform, m.p. 157.7–159.0°, yield 80 mg. (77.0%).

Anal. Calcd. for $C_{24}H_{42}O_4N_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 68.29; H, 10.28; N, 6.57.

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(16) Analyses by the Microanalytical Laboratory of the Department of Chemistry, University of California. All melting points are corrected.

(17) M. S. Newman and H. V. Zahm, THIS JOURNAL, **65**, 1097 (1943).

(18) The indane was prepared by hydrogenation of distilled commercial indene using platinum oxide as the catalyst and ethyl acetate as the solvent. The material boils from 176–177°.

When the acid obtained directly from the hydrogenation (m.p. 40–44°) was allowed to react with 0.161 g. of piperazine as described above and the crude material recrystallized 7 times from chloroform or chloroform–acetone, 0.204 g. (28.5%) of pure salt was obtained, m.p. 156.5–158.5°. The acid was regenerated and recrystallized from hexane, m.p. 51.5–53.0°, yield 145 mg. (23%).

Also, when 8 g. of the crude acid was converted directly to the amide, the 7.75 g. (m.p. 180–187°) was recrystallized 11 times from aqueous ethanol, m.p. 194–196°, yield 1.65 g. (20.8%).

cis–cis-5-Hydrindanylamine (IV).—Powdered sodium azide (100 mg., 1.5 mmoles) was added in small portions with stirring over a period of 30 minutes to a solution of 172 mg. (1.02 mmoles) of *cis–cis*-hydrindanecarboxylic acid in 5 ml. of chloroform and 2 ml. of concentrated sulfuric acid at 40°. After completion of the addition the temperature was maintained at 50° for an additional 30 minutes and then poured over ice. The chloroform layer was separated and the aqueous layer made alkaline and extracted three times with ether. The crude amine remaining after removal of the ether was benzoylated with 0.3 ml. of benzoyl chloride in 3 ml. of 1 *N* sodium hydroxide. The N-(*cis–cis*-5-hydrindanyl)-benzamide was recrystallized from aqueous ethanol, m.p. 142–143.5° (lit.[4,6] m.p. 145°), yield 63 mg. (25.7%).

Anal. Calcd. for $C_{16}H_{21}ON$: C, 78.97; H, 8.70; N, 5.76. Found: C, 79.24; H, 8.81; N, 5.67.

cis–cis-5-Hydrindanol (V).—A solution of 1.00 g. (5.95 mmoles) of *cis–cis*-5-hydrindanecarboxylic acid in 20 ml. of dry ether was added dropwise with stirring to 32 ml. of a 0.6 *M* solution of methyllithium in ether. Following the addition, the mixture was stirred for an additional 15 minutes and then poured onto ice and the ether layer separated. The ethereal layer was washed with sodium bicarbonate, dried and the ether evaporated.

The crude ketone was allowed to react with 22 ml. of a 0.36 *M* solution of perbenzoic acid in chloroform at room temperature for 7 days. After dilution with ether, the solution was washed with dilute sodium bicarbonate solution, dried and the solvent removed under reduced pressure.

The acetate ester was saponified with 10 ml. of 2 *N* sodium hydroxide in 15 ml. of methanol by refluxing for 2 hours. The reaction mixture was diluted with water, extracted with ether, the ethereal layer separated, dried and the solvent removed. The crude hydrindanol was dissolved in hexane and chromatographed on 40 g. of alumina. By elution with hexane, 20 mg. of starting ketone was obtained. After removal of the ketone, the alcohol was removed by elution of the column with ethyl ether to yield 708 mg. (85.8% based on starting acid) of *cis–cis*-5-hydrindanol. The product was characterized by allowing 0.175 g. (1.26 mmoles) to react with 0.15 ml. of phenyl isocyanate at 100° for 5 minutes. The phenylurethan was recrystallized from ligroin, yield 116 mg. (29.8% based on starting acid, 35.8% based on starting alcohol), m.p. 120.5–121.5° (lit.[4,6] 125°).

Anal. Calcd. for $C_{16}H_{21}O_2N$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.40; H, 8.34; N, 5.55.

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[CONTRIBUTION FROM THE NORTHERN UTILIZATION RESEARCH BRANCH[1]]

Determination of Dextran Structure by Periodate Oxidation Techniques

BY JOHN W. SLOAN, B. H. ALEXANDER, R. L. LOHMAR, I. A. WOLFF AND C. E. RIST

RECEIVED JANUARY 21, 1954

Dextrans produced by six strains of *Leuconostoc mesenteroides* were oxidized with sodium metaperiodate and the proportions of the various glucosidic linkages estimated by separation and quantitative determination of structural fragments of the oxidized dextrans. Dextran from *L. mesenteroides* NRRL B-512 was shown to contain 5% 1,3-linked anhydroglucose units in addition to the previously recognized 95% 1,6-linked units. Likewise, dextran from NRRL B-1064 yielded glucose indicating 3% 1,3-linked units where none were expected from titrimetric periodate analyses. Evaluation of the fragments obtained from NRRL B-1355 dextran disclosed no evidence of 1,4-linkage. A new technique for isolating periodate-oxidized dextrans has proved successful in producing the polymeric dialdehydes in high yields.

Bacterial dextrans are formulated as polymers of α-glucopyranosyl units linked in various ways. The kinds and proportions of these linkages may be inferred from the consumption of oxidant and the production of acid when the dextrans are subjected to periodate analysis.[2,3,4] In this analysis, by periodic acid or its salts, it is assumed that for every mole of acid produced in the oxidation, one anhydroglucose unit linked *only* in the 1- and 6-positions, or a non-reducing end group (linked at position 1) has been oxidized and its carbon 3 split out as formic acid. Because this requires the reduction of two moles of periodate, any additional periodate consumed is presumed to have been used in the opening between carbons 2 and 3 of 1,4-linked anhydroglucose rings, or in the opening between carbons 3 and 4 of 1,2-linked rings. If these possibilities do not account for all the dextran, the difference is represented by anhydroglucose units not oxidized by periodate. Such units are those linked in the 1- and 3-positions. Oxidation would also not occur in units to which a branch is linked if *both* positions 2 and 4 of a single unit were involved. However, it seems unlikely that the high proportions of unoxidized units found in some of the dextrans can be accounted for solely by the presence of units involved in multiple linkage. Generally, in dealing with periodate analysis of high molecular weight dextrans no separate allowance is made for the behavior of reducing end groups.

In order to demonstrate the presence of 1,3-linked units in dextrans and to provide more concrete evidence of other structural characteristics as well, it was desired to examine fragments of the molecule, other than formic acid, obtained from the oxidation by periodate. Methods that have been used to obtain fragments from periodate-oxidized polymers include hydrolysis and treatment with aldehyde reagents,[5] oxidation of the hydrolytic products with bromine to yield characteristic acids,[6] oxidation of the polymer with bromine water followed by hydrolysis and characterization of the acids,[7] hydrolysis and identification of

(1) One of the Branches of the Agricultural Research Service, U. S. Department of Agriculture. Article not copyrighted.

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