

Direct Hydroxylation of Fats and Derivatives with a Hydrogen Peroxide Tungstic Acid System¹

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Abstract

The direct preparation of *threo*-1,2-glycols without isolation of intermediates from oleic acid, methyl oleate, and oleyl alcohol by oxidation with a hydrogen peroxide (70%)-tungstic acid system at pH 0–1 and 45–55°C without solvent has now been shown to be an efficient, high-yield reaction. The *threo*-isomers are formed from intermediate epoxides by in situ hydration with accompanying inversion. Preincorporation of about 2% of the glycol reaction product into oleic acid or methyl oleate speeds up the oxidation reactions markedly and adds to their control and reproducibility. With oleyl alcohol, addition of reaction product is not necessary.

Castor and olive oils are also readily oxidized to almost complete elimination of unsaturation, but the products are only 50–60% 1,2-glycols, owing to intra- and intermolecular polyether information. Addition of reaction product is unnecessary with castor oil, but with olive oil the reaction rate is greatly accelerated by incorporation of 2% of reaction product. Preconditioning (5 hr) of the hydrogen peroxide with the tungstic acid permits slightly faster oxidation rates. Emulsions are also rapidly oxidized under appropriate conditions, but these systems are more complicated to prepare and work up than oxidation of the substrates directly. Tentative reaction mechanisms are proposed in which an inorganic polyperoxytungstic acid is the effective oxidizing agent and hydroxyl-containing species are important interfacial or complexing agents between the substrate and oxidant system.

Introduction

THE CONTROLLED OXIDATION of unsaturated compounds with hydrogen peroxide to obtain epoxides (oxiranes) and 1,2-glycols has interested research workers for a long time. No attempt will be made however to survey the vast literature (1,2).

In 1949 Mugdan and Young (3) examined a variety of methods for the direct hydroxylation of unsaturated compounds with hydrogen peroxide by using various inorganic catalysts. Tungstic acid at 50–70°C was found to be the best catalyst, but the hydroxylation reaction was shown to be efficient only when aqueous solutions could be employed, that is, with water-soluble unsaturated compounds, such as allyl alcohol and maleic acid. Attempts to prepare 1,2-glycols from water-insoluble unsaturated compounds, such as 1-octene and cyclohexene, in aqueous suspension or even in an organic solvent were unsuccessful except when acetic acid was used, in which case peroxyacetic acid was the oxidizing agent. When the present work was initiated, the direct hydroxylation in good yield

of water-insoluble unsaturated compounds with hydrogen peroxide, catalyzed by inorganic substances, had not been successfully accomplished. Possible exceptions were cyclohexene and norbornene, which can be converted to diols in about 50–70% yields by using 90% hydrogen peroxide, *t*-butyl alcohol, and tungstic acid catalysis (4).

This paper reports an efficient, high-yield method for the preparation of 1,2-glycols from certain water-insoluble monounsaturated fatty acid derivatives (oleic acid, methyl oleate, oleyl alcohol) and fats (olive and castor oils) by means of a hydrogen peroxide-tungstic acid system at pH 0–1, which does not require the isolation of any intermediate reaction products. We have also tried the hydroxylation of methyl elaidate, 10-undecenoic acid, and 1-hexadecene to obtain information pertaining to the reaction mechanisms involved.

Results and Discussion

In 1958 Coleman and Swern (5) showed that mono-unsaturated fatty acids could be rapidly and efficiently oxidized with potassium permanganate in an emulsion system. In initial studies therefore the emulsion oxidation technique was repeated, but a hydrogen peroxide-tungstic acid oxidant system (1–3) was used instead of potassium permanganate.

Considerable experimental work was done to try to develop a reproducible, easily controlled oxidation reaction by using oleic acid as the model water-insoluble unsaturated compound. However, when concentrated hydrogen peroxide (70%) and tungstic acid were added to a stirred aqueous emulsion of oleic acid at 55°C, the oxidation reaction proceeded extremely slowly at first (7–9 hr), as shown by thin-layer chromatography (TLC). Then it often became very exothermic and uncontrollable even on a small-scale (10 g of oleic acid). Nevertheless we were encouraged to continue since yields of *threo*-9,10-dihydroxystearic acid ranged from 70–90%. On the other hand, when dilute hydrogen peroxide was employed, oxidation was exceedingly slow throughout at 55°C; decomposition of hydrogen peroxide was the major reaction. A significant observation however was that the addition of a second portion of dilute hydrogen peroxide, after the first had completely decomposed, resulted in immediate and rapid oxidation. Good yields of *threo*-9,10-dihydroxystearic acid were again obtained.

Although neither emulsion oxidation technique was satisfactory, they suggested two hypotheses which were amenable to experimental verification to account for the time lags. In the first hypothesis it was proposed that tungstic acid requires a period of preconditioning with aqueous hydrogen peroxide before it can function as a catalyst. It is well known that the degree of aggregation of tungstate systems in solution increases as the pH is lowered (6). Therefore hydrogen peroxide (70%) and tungstic acid were slowly stirred at room temperature for 20 min, 2 and 5 hr respectively, before adding the preconditioned oxidant systems to oleic acid emulsions. In the second case the reaction

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time was 7 to 9 hr at 55C, but the reactions were more readily controlled. Yields of *threo*-9,10-dihydroxystearic acid ranged from 70–90%. With the 5 hr of preconditioning however reaction was complete in 2 to 4 hr, and yields of dihydroxystearic acid were in excess of 90%. It was observed that, during the preconditioning, the color of the tungstic acid changed from lemon yellow to almost no color and that its x-ray diffraction pattern underwent a significant change from the pattern of a highly crystalline material to one that was amorphous. Also, after about 3 hr of preconditioning, hydrogen peroxide began to decompose slowly.

The second hypothesis proposed that a reaction product was forming which altered the interfacial characteristics of the emulsion and permitted a facile interaction between oleic acid, hydrogen peroxide and catalyst. This idea proved to be even more promising and permitted elimination not only of the preconditioning period but of the emulsion system as well.

In the preliminary stages of this investigation when reactions were proceeding extremely slowly, the extent of reaction was monitored by TLC on silica gel, by using 0.005-ml samples of emulsion which were removed periodically. R_f values were first obtained on a variety of known, pure compounds the presence of which might be anticipated in the oxidation reaction mixture. These consisted of *cis*- and *trans*-9,10-epoxystearic acids, *threo*- and *erythro*-9,10-dihydroxystearic acids, and 9(10),10(9)-ketohydroxystearic acids as well as the oleic acid starting-material.

From the R_f value of the products slowly being formed in the emulsion oxidation systems, it appeared that the initial product was *cis*-9,10-epoxystearic acid, which was then being converted to *threo*-9,10-dihydroxystearic acid. Since the rate of oxidation did not accelerate until several per cent of 9,10-dihydroxystearic acid had accumulated, it was postulated that the dihydroxy acid was the key interfacial agent in the oleic acid oxidation. If this were so, there should be no need to preemulsify the oleic acid.

These conclusions were verified by dissolving 2% by weight of *threo*-9,10-dihydroxystearic acid in oleic acid and then conducting the oxidation at 55C with both preconditioned and nonpreconditioned hydrogen peroxide-tungstic acid reagent. In the former case oxidation was slightly more rapid, but in both cases oxidation was smooth and started almost immediately; the exotherm was readily controlled and conversion to dihydroxystearic acid was complete within a few hours. As the oxidation proceeded however, the system became pasty (emulsified?) and then hardened as the ratio of hydroxy to unsaturated acid increased. It was therefore usually necessary to add a small quantity of water at that time to permit stirring to continue until the oxidation was complete. The crude reaction product was then dried under vacuum; it consisted almost exclusively of *threo*-9,10-dihydroxystearic acid, with small quantities of cleavage products and other minor impurities (catalyst, <5% unsaturated acids, and saturated fatty acids originally present in the oleic acid). Recrystallization from ethyl acetate provided good quality *threo*-9,10-dihydroxystearic acid in 70–80% yields. In view of these results, preparation of emulsions and preconditioning were abandoned.

The pH of a tungstic acid-hydrogen peroxide (70%) mixture is 0–1. No attempt was made to study the

effect of pH on the product obtained or its rate of formation. This is now under investigation.

A key question was whether peroxyoleic acid was being formed at the low pH values from oleic acid and hydrogen peroxide, catalyzed by tungstic acid, with the organic peroxy acid as the effective oxidizing agent. To resolve this point, methyl oleate containing 2% of methyl-*threo*-9,10-dihydroxystearate was similarly oxidized at 55C with hydrogen peroxide-tungstic acid. Excellent yields of methyl *threo*-9,10-dihydroxystearate were obtained under the same conditions as were used with oleic acid. Thus it can be concluded that some oxidizing agent other than peroxyoleic acid is effective.

If the tungstic acid is omitted, no oxidation occurs in the emulsion or nonemulsion systems. Likewise, if the dihydroxy products are left out of the nonpreconditioned systems, no oxidation of oleic acid or methyl oleate is observed at 55C. The reaction mixtures do not become pasty, and the only reaction observed is decomposition of hydrogen peroxide. When the stirring is stopped at the end of the reaction period, two layers form and starting materials are recovered.

To ascertain whether *threo*-9,10-dihydroxystearic acid (or its methyl ester) is unique, oleyl alcohol and castor oil, both of which already contain one hydroxyl function per alkyl chain, were similarly oxidized with hydrogen peroxide-tungstic acid, but no glycol additive was present in the unsaturated compounds. In both cases oxidation began immediately, and the reactions were quite exothermic. Oleyl alcohol was oxidized at 45C and castor oil at 25C. Higher initial temperatures made the reactions difficult to control; in both cases oxidation proceeded to almost complete elimination of the unsaturation. At temperatures in excess of about 25C the castor oil oxidation was usually so rapid and uncontrollable that rubberlike polymers were obtained.

Oleyl alcohol was converted to *threo*-9,10-octadecanol in about 75% yield after recrystallization. Castor oil yielded a product consisting of only about 50–60% of 1,2-glycols; the remainder was inter- and intramolecular ethers.

Olive oil was also hydroxylated, and it confirmed the need for about 2% of the oxidation product to obtain an immediate reaction in the absence of already existing hydroxyl groups, as in castor oil. With the hydroxylation product present, oxidation of olive oil proceeded rapidly to almost complete disappearance of unsaturation but, as in the case of castor oil, only about 50–60% of the products were 1,2-glycols.

If the reactions were conducted at higher temperatures than those specified or for considerably longer periods of time, cleavage products began to build up at the expense of glycol.

The catalytic efficiency of tungstic oxide and tungstic acid were compared, using oleyl alcohol as the model compound. With the oxide, oleyl alcohol required a reaction time of 8 hr at 55C for 96% conversion; with the acid 94% conversion was obtained in less than 2 hr at 45C. In all of the work described in this paper, tungstic acid was the catalyst of choice.

To assess the role of the geometry of the double bond on the reaction, the oxidation of methyl elaidate was also examined. Its oxidation was slow, and a complex mixture of reaction products was obtained. Thus, with preconditioned hydrogen peroxide-tungstic acid (5 hr), it required 19 hr at 55C to obtain only

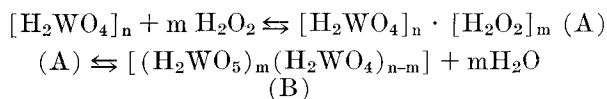
a 45% reduction in unsaturation. With 2% of methyl *erythro*-9,10-dihydrostearate predissolved in the methyl elaidate, an 80% reduction in unsaturation was noted under the same reaction conditions, but the glycol yield was only 7% and considerable cleavage was obtained. With 2% of methyl *threo*-9,10-dihydroxystearate in solution, reaction was more rapid (complete elimination of unsaturation), but conversion to glycol was about 3% and even more extensive cleavage occurred than in the preceding experiment. Elaidic acid oxidized even more slowly. There were some inconsistencies in the results with these systems however, and further studies are in progress to clarify the situation.

Unsaturated compounds with terminal double bonds (10-undecenoic acid and 1-hexadecene) are oxidized substantially more slowly than those with internal double bonds. No extensive effort was made to try to speed up these reactions.

Hydroxylation of the water-insoluble monounsaturated fatty acid derivatives described in this paper has several of the characteristics of a typical peroxy acid oxidation reaction: a) oxiranes are the primary products, b) internal double bonds are oxidized more rapidly than terminal double bonds, c) a *cis* double bond is oxidized more rapidly than a *trans*, and d) *threo*-glycols are obtained from *cis* double bonds. The mechanism of oxidation however is clearly more complicated than has been proposed by earlier investigators, who studied the tungstic acid catalyzed epoxidation of allylic alcohols (7-9).

Although monomeric peroxytungstic acid, H_2WO_5 , may play a role in the reaction, it must be a minor one for several reasons. Cotton and Wilkinson indicate (6) that tungstic acid is polymeric $(H_4WO_2)_n$. The reaction conditions employed should not depolymerize this species; at the low pH values employed more aggregation would be expected, and this is suggested by the change in the x-ray diffraction pattern noted earlier. If monomeric peroxytungstic acid were the oxidant, the large differences noted in rate between methyl oleate and elaidate would not be expected. With the usual organic peroxy acids, the ratio of oxidation rates *cis/trans* is of the order of 1.5-2.

Although we cannot propose a definite mechanism at this time, the behavior of tungstic acid (its change from crystalline to amorphous and color change) on preconditioning with hydrogen peroxide suggests that a complex (A) is forming between hydrogen peroxide and tungstic acid and that this may undergo an oxygen transfer to form a polyperoxytungstic acid (B):



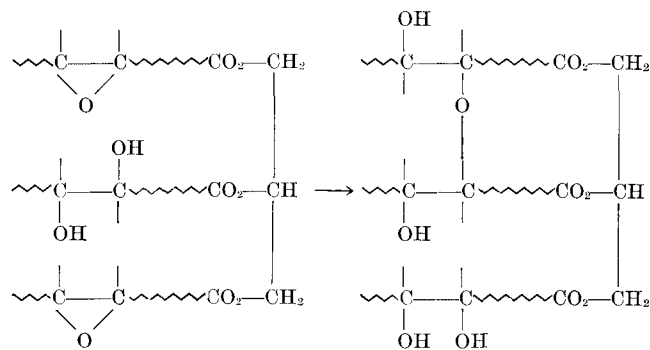
Whether polyperoxytungstic acid (B) or some entirely unknown species is the effective oxidizing agent cannot be deduced from the evidence at hand. Clearly some effective "peroxy acid" oxygen transfer agent is being produced.

Two separate mechanisms can now be considered, depending on the system. When hydroxyl-containing species are present and preconditioning is not employed, the complex (A) is formed, and the hydroxyl-containing species facilitate transfer of oxygen from hydrogen peroxide to the polytungstic moiety and then to the double bond, perhaps by way of B. The steady state concentration of B must be small at all times. When preconditioning is used and hydroxyl species

are absent, the polyperoxy acid (B) is formed, and it is the primary oxidant. After a small amount of oxidation has occurred, however, hydroxyl-containing species are now present and the oxidation may then be completed by the first mechanism suggested in which B can never build up its concentration. This duality of mechanism places major emphasis on the importance of hydroxyl-containing species and accounts for the fact that the use of preconditioned hydrogen peroxide-tungstic acid is slightly slower than the cases in which hydroxyl species are present (either by solution or as the actual substrates). The fastest rates however are observed with preconditioning and with hydroxyl species present at the start.

The function of hydroxyl species in accelerating the reactions may be that of a surfactant or, as seems more likely, as a preferential complexing agent for the polyperoxy acid oxidant, thus permitting interaction between the hydrophobic substrate and the oxidant. The change in overall appearance of the oxidation reaction system with time from one that readily separates into two layers at the start to one that has a pasty, emulsified appearance during and after the reaction strongly supports the idea that the hydroxyl species is the bridge between substrate and oxidant.

The oxidation of triglycerides is more complex than that of oleic acid, methyl oleate, and oleyl alcohol. Although it is believed that the primary oxidation step is the same, namely, oxirane formation, the epoxide groups that are formed can react with neighboring hydroxyl groups, either already present (as in castor oil) or formed by oxidation (as in olive oil). The formation of polyethers is shown in Scheme I.



Epoxide groups can also be hydrated to 1,2-glycols, as shown. Analysis of the hydroxylation products obtained from castor and olive oils by periodic acid oxidation suggests that they consist of 50-60% 1,2-glycols (approximately 1.5 glycol functions per triglyceride molecule).

Tungstic acid and tungstic oxide appear to have special catalytic properties. Sulfuric and methanesulfonic acids have been substituted for tungstic acid; under identical reaction conditions little or no hydroxylation was observed. Chromic acid was also studied. It caused extensive and vigorous decomposition of hydrogen peroxide.

Experimental

Starting Materials. Hydrogen peroxide (70%) was obtained from the Solvay Process Division, Allied Chemical Corporation. Tungstic acid was Baker's Analyzed Reagent Grade. Oleic acid was 92% pure and essentially free of polyunsaturates; it was ade-

quate for the purposes of this investigation. Methyl oleate was prepared from it in the usual way. Oleyl alcohol was a good commercial grade, Adol 90, from the Archer-Daniels-Midland Co. It contained about 90–95% of octadecenols. Olive oil was the best edible grade. Castor oil, cold pressed grade, was obtained from the Baker Castor Oil Company, and periodic acid from the G. Frederick Smith Chemical Company. Solvents and other reagents were the best quality available. Tween 20 emulsifier was obtained from Atlas Chemical Corporation.

Hydroxylation of Oleic Acid in Emulsion. Typical Procedures: 1a). Oleic acid (10 g, 0.03 mole), water (5 ml), and Tween 20 (0.2 g) were mixed and passed through a laboratory hand-homogenizer four times to ensure uniform emulsification, as shown by examination under the microscope. Hydrogen peroxide (70%) (5 ml, 0.1 mole) containing tungstic acid (0.2 g) was conditioned for 20 min at room temperature and then added dropwise to the stirred emulsion at 55C. The pH of the system was 0–1. Periodically 0.005 ml of reaction mixture was removed and spotted on TLC plates coated with silica gel. The system was developed with a mixture of petroleum ether: diethyl ether: glacial acetic acid (90:10:1) and sprayed with 2,7-dichlorofluorescein (0.2% in methanol). The plates were then observed under ultraviolet light. The R_f values of the starting material, *cis*- and *trans*-9,10-epoxystearic acids, *threo*- and *erythro*-9,10-dihydroxystearic acids, and 9(10), 10(9)-keto-hydroxystearic acids were obtained in the same way. In general, little or no oxidation occurred for 7–9 hr but speeded up after that time, and the reaction usually became uncontrollable and reached the boiling point of the system. Disappearance of unsaturation was about 70–90% of that calculated; *threo*-9,10-dihydroxystearic acid, mp 91–93C, was isolated in good yield by the procedure described below under the neat oxidations.

1b). Preconditioning the hydrogen peroxide-tungstic acid for 2 hr at room temperature prior to its addition to the emulsion gave a 90% conversion to *threo*-9,10-dihydroxystearic acid in 7–9 hr. No problem was experienced in controlling the reaction.

1c). Preconditioning for 5 hr gave between 90–100% conversion to the dihydroxy acid in about 2–3 hr. The reaction was almost immediately exothermic but was readily controlled with a cooling bath.

Hydroxylation of Oleic Acid Neat. 2a). *With Preconditioning of Reagent.* Oleic acid (10 g, 0.03 mole) was placed in a beaker and warmed to 55C in a water bath. To the magnetically stirred system, hydrogen peroxide (70%) (2.5 ml, 0.05 mole) and tungstic acid (0.1 g, 4% by weight of hydrogen peroxide) that had been preconditioned for 5 hr was added dropwise. Cooling was provided at this point. Unreacted oleic acid and oxidation products were determined periodically on 0.005-ml samples by TLC, as described above. *cis*-9,10-Epoxystearic acid was the primary oxidation product; it never exceeded 10–30% of the products. The pH of the system was 0–1 throughout. Within 1½–2½ hr the reaction mixture thickened, and magnetic stirring was no longer possible. Water (2.5 ml) was then added, and magnetic stirring was continued until the hydrogen peroxide had disappeared (about 1½ hr additional). The reaction mixture was then dried to constant weight in a vacuum oven; yield of crude product was 11 g. Its iodine number was usually 0–5.

The crude reaction product was stirred for 30 min

at room temperature with hexane (50 ml) and filtered. The residue (9–10 g) was moderately pure *threo*-9,10-dihydroxystearic acid, mp 90C. Two recrystallizations from 95% ethanol or ethyl acetate at 0C gave the pure compound, mp 94C. The yield was 7–8 g (70–80%).

To facilitate stirring of the reaction system throughout and to obviate the need for adding water, it is convenient to use 3–3.5 ml of 70% hydrogen peroxide containing 4% by weight of tungstic acid for each 10 g of oleic acid. Yields are essentially the same as described above.

2b). *Without Preconditioning of Reagent.* *threo*-9,10-Dihydroxystearic acid (0.2 g) was dissolved in oleic acid (10 g, 0.03 mole), and the oxidation was then conducted as described above at 55C with hydrogen peroxide (70%) (3.0 ml, 0.06 mole) containing tungstic acid (0.12 g) but without preconditioning. After about 5 min the reaction became strongly exothermic and required efficient cooling. The reaction mixture thickened within about 30 min, and reaction was continued for an additional 1½ hr. The workup and results were the same as in 2a). When a reaction four times this size was run, the initial temperature was 50C. This permitted better control of temperature.

Hydroxylation of Methyl Oleate. As described under 2a) above, methyl oleate (10 g, 0.03 mole) was hydroxylated at 55C with hydrogen peroxide (70%) (3 ml, 0.06 mole) and tungstic acid (0.12 g) that had been preconditioned for 5 hr. The reaction was stirred for 3½ hr at 55C, then allowed to stand overnight, during which it separated into two phases. The lower aqueous phase was decanted and discarded; the solid upper phase was dried to constant weight under vacuum. It weighed 11.5 g and had an iodine number of 3 and mp 59–63C. It was dissolved in ethyl acetate and filtered to separate catalyst; the filtrate was cooled to 0C. Moderately pure methyl *threo*-9,10-dihydroxystearate, mp 67–69C, crystallized out (yield 6–8 g; 70%).

With 2% of methyl *threo*-9,10-dihydroxystearate dissolved in the methyl oleate, only 2 hr were required for complete reaction with the 5-hr preconditioned reagent.

Hydroxylation of Oleyl Alcohol. 3a). Oleyl alcohol (40 g, 0.14 mole) was hydroxylated at 45C with 5-hr preconditioned hydrogen peroxide (70%) (10 ml, 0.21 mole) and tungstic acid (0.4 g). After 1½ hr the crude reaction mixture was evaporated to dryness; the crude triol product weighed 45 g; mp 63–68C and iodine number, <5. It was dissolved in ethyl acetate and filtered to remove catalyst; the filtrate was cooled to 0C. The white precipitate was filtered and dried (26 g, 67% yield); it was moderately pure *threo*-9,10-octadecanol-1, mp 74–6C. It is important that initial reaction temperatures not exceed 45C otherwise control is very difficult.

3b). Experiment 3a) was repeated, but 2% of *threo*-9,10-octadecanol-1 was predissolved in the oleyl alcohol. The reaction became exothermic within 5 min but was readily controlled. Yield and melting point of triol were the same as in 3a).

3c). Experiment 3a) was again repeated, but the preconditioning step was omitted. The same results were obtained as in 3a) and 3b). (This is the preferred oxidation procedure with oleyl alcohol.)

3d). Experiment 3b) was repeated, using tungstic oxide (0.4 g) instead of tungstic acid. No exotherm was observed, and eight hours reaction at 55C (not

45C) were required. The same results were obtained as in 3a), b) and c).

Hydroxylation of Olive Oil 4a). Olive oil (20 g, iodine number 84) was hydroxylated at 55C with five-hour preconditioned hydrogen peroxide (70%) (10 ml, 0.21 mole) and tungstic acid (0.4 g). After 20 hr the reaction mixture was evaporated to dryness to provide a white solid (22.6 g) mp 42–48C, iodine number 7, and acid number 28.

4b). Experiment 4a) was repeated, but 2% of hydroxylated glyceride was predissolved in the olive oil and only 6 ml of hydrogen peroxide were used. After 1½ hr reaction at 55C the mixture was allowed to stand overnight at room temperature. The crude reaction product, obtained after evaporation to dryness (22.3 g), had a melting point of 49–53C and an iodine number of 3. Slightly less cleavage had occurred (acid number 16) than in 4a). Periodic acid analysis indicated only 55% 1,2-glycol content. The product was not examined further.

Hydroxylation of Castor Oil. Castor oil (30 g, iodine number 86) was hydroxylated at 25C with 5-hr preconditioned hydrogen peroxide (70%) (7.5 ml, 0.15 mole) and tungstic acid (0.3 g). After 18 hr the reaction mixture was evaporated to dryness.

The yield of crude product was 34 g (iodine number 3 and acid number 10). The *a*-glycol content of the product was 52%.

Reaction of castor oil at 55C in the above system was violently exothermic. Within 2 min reaction temperature was 150C, and the final product was a rubber, insoluble in organic solvents.

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