[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

Improved Preparation of 9(10),10(9)-Ketohydroxystearic Acids by Oxidation of Oleic Acid with Potassium Permanganate in Neutral Solution[2]

BY JOSEPH E. COLEMAN, C. RICCIUTI AND DANIEL SWERN

RECEIVED MARCH 19, 1956

The mild oxidation of oleic acid, as the potassium soap, with dilute aqueous potassium permanganate has been reinvestigated and the marked effect of *p*H in determining the course of the reaction has been interpreted. When the *p*H is maintained in the range of 9.0–9.5 by neutralizing the liberated alkali as it is formed (equation 1), 65–75% conversions to 9(10),10(9)-ketohydroxystearic acids are obtained. If excess alkali is added before oxidation or is permitted to accumulate (*p*H 12), yields of ketol are reduced to 0–30% and yields of 9,10-dihydroxystearic acid jump to 60–96%. It has been concluded that the "neutral" oxidation of potassium oleate by potassium permanganate was never actually studied by previous investigators. A mechanism based on stepwise (*p*H controlled) or complete (*p*H not controlled) hydrolysis of the intermediate cyclic complex between oleic acid and potassium permanganate is proposed to account for this striking reversal of products. Also, with *p*H control the concentration of the reaction mixture is increased 20-fold over the best values reported in the literature. The oxidation of elaidic acid, however, is only slightly *p*H-dependent; this is not understood. Octadecadienoic acids are converted predominantly to polymeric products.

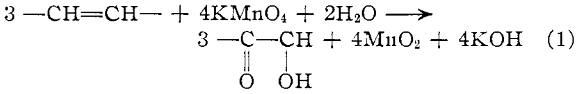
To obtain a substantial quantity of 9(10),10(9)-ketohydroxystearic acids for study, two preparative methods seemed to offer the most promise. The first involved the sequence of steps[3,4]

$$\text{oleic acid} \xrightarrow{\text{Br}_2} \text{9,10-dibromostearic acid} \xrightarrow[\text{NH}_3]{\text{NaNH}_2} $$

$$\text{stearolic acid} \xrightarrow{\text{KMnO}_4} \text{9,10-diketostearic acid} \xrightarrow{\text{Zn}} \text{9(10),10(9)-ketohydroxystearic acids}$$

The second was the so-called "neutral" oxidation of oleic acid with dilute potassium permanganate, first reported by Holde and Marcusson[5] and reinvestigated by later workers.[6-8] Both methods leave much to be desired, the first because of the number of steps and the second because of the poor yields (usually below 30%) and the high dilution (one gram of acid per liter of reaction mixture[7]) required to attain even these yields.

The second method was selected for study for several reasons. First, the direct, single-step preparation of α-ketols in good yield from oleic acid, and other unsaturated compounds, was a desirable objective and had not yet been accomplished.[9] Second, the mode of formation of α-ketols from oleic acid had not been explained. 9,10-Dihydroxystearic acid is not an intermediate since it is unaffected by potassium permanganate under the conditions of the ketol-forming reaction.[7] Third, the striking effect of alkali on the products obtained warranted further study and was, indeed, easily amenable to experimental attack. Thus, it was well known that if one mole or more of potassium hydroxide is present in excess per mole of potassium oleate, no ketohydroxystearic acids are formed but an almost quantitative yield of high-melting 9,10-dihydroxystearic acid, m.p. 131°, is obtained.[10] Fourth, if the following balanced equation for the ketol-forming reaction is correct, it is evident that although the system may have been neutral at the start it should rapidly become strongly alkaline because of the formation of potassium hydroxide



$$3\ \text{—CH=CH—} + 4\text{KMnO}_4 + 2\text{H}_2\text{O} \longrightarrow 3\ \text{—}\underset{\overset{\|}{\text{O}}}{\text{C}}\text{—}\underset{\overset{|}{\text{OH}}}{\text{CH}} + 4\text{MnO}_2 + 4\text{KOH} \qquad (1)$$

In our first experiment we observed that the *p*H of a neutral aqueous solution of potassium oleate, which is about 10 at 15°, rose rapidly to a maximum value of almost 12 by the time only 25% of the calculated amount of potassium permanganate had been added. In view of this result, it can be concluded that except for the initial stages of the reaction, a truly neutral oxidation of potassium oleate by aqueous potassium permanganate has never been carried out. After about 25% of the calculated quantity of potassium permanganate has been added, conditions are ideal for the formation of 9,10-dihydroxystearic acid. We have shown also that in the absence of *p*H control the bulk of the ketol is formed in the initial stages of the reaction as we had anticipated.

Without *p*H control during the reaction, it is evident why extremely high dilutions are required for best yields of ketohydroxystearic acids. At high dilutions the concentration of hydroxide ions is reduced and their undesirable effect, as far as formation of ketols is concerned, is diminished.

The reaction of potassium permanganate with oleate, being too rapid for a kinetic study, was investigated by product analysis. The content of unoxidized oleic acid in the crude oxidation product can be estimated from the iodine number. 9,10-Diketostearic acid can be determined polarographically,[11] using the pure compound, m.p. 85°, as a reference standard. Ketohydroxystearic acids are not reducible under these conditions. Determination of carbonyl and hydroxyl oxygen permits calculation of the content of 9(10),10(9)-keto-

---

[1] A laboratory of the Eastern Utilization Research Branch, Agricultural Research Service, U. S. Department of Agriculture. Article not copyrighted.

[2] Presented at the Fall Meeting of the American Chemical Society, Atlantic City, N. J., September 16–21, 1956.

[3] J. F. McGhie, *Chemistry & Industry*, 131 (1954).

[4] N. A. Khan, F. E. Deatherage and J. B. Brown, *J. Am. Oil Chemists' Soc.*, **28**, 27 (1951).

[5] D. Holde and J. Marcusson, *Ber.*, **36**, 2657 (1903).

[6] R. S. Morrell and E. O. Phillips, *J. Soc. Chem. Ind.*, **57**, 245 (1938).

[7] G. King, *J. Chem. Soc.*, 1788 (1936).

[8] T. P. Hilditch and H. Plimmer, *ibid.*, 204 (1942).

[9] S. M. McElvain, The Acyloins in "Organic Reactions," Vol. 4, Chapter 4, John Wiley and Sons, Inc., New York, N. Y., 1948.

[10] A. Lapworth and E. N. Mottram, *J. Chem. Soc.*, **127**, 1628 (1925).

[11] C. O. Willits, C. Ricciuti, H. B. Knight and D. Swern, *Anal. Chem.*, **24**, 785 (1952).

TABLE I

RESULTS OF OXIDATION OF OLEIC ACID WITH POTASSIUM PERMANGANATE

	A	B	C	D
Potassium oleate				
Oleic acid, moles	0.02			
Potassium hydroxide, moles	0.02			
Water, ml.	60			
Potassium permanganate solution				
Potassium permanganate, mole	0.0300	0.0300	0.0300	0.0266
Water, ml.	75	75	200	200
Reaction solution				
*p*H (after addition of $KMnO_4$)	11.8	9.0–9.5	9.0–9.5	9.0–9.5
Concn. of oleic acid, g./l.	40	40	20	20
Crude oxidation product				
Weight g.	5	5.4	5.1	
Analysis				
Neutralization equiv.	280	268	288	298
Iodine number	2	10	4	10
Hydroxyl oxygen, %	6.90	3.75	4.43	3.89
Carbonyl oxygen, %	1.31	3.08	4.09	4.16
Diketostearic acid, %	3	7	7	6
Approximate composition, %				
Ketohydroxystearic acids	20	55	70	75
Dihydroxystearic acid	60	10	10	4
Diketostearic acid	3	7	7	6
Saturated acids and unoxidized oleic acid	5	14	7	14
Unaccounted for	12	14	6	1

hydroxystearic and 9,10-dihydroxystearic acids, after correction is made for the diketostearic acid present.

Experimental

Starting Materials.—Purified oleic acid (iodine number, 87.2; oleic acid content 97% and saturated acids 3%) was isolated from olive oil fatty acids as previously reported.[12] Elaidic acid (m.p. 43°; iodine number, 84.5; elaidic acid content 94% and saturated acids 6%) was prepared from oleic acid by isomerization with selenium.[13] All other reagents were the purest available grades.

Oxidation of Oleic Acid.—In a crystallizing dish equipped with a stirrer, a thermometer and electrodes attached to a continuous-reading *p*H meter, an aqueous solution of potassium oleate was prepared from 5.64 g. (0.02 mole) of oleic acid, 1.27 g. (0.02 mole) of 89% potassium hydroxide and 60 ml. of water. After cooling to 10°, a potassium permanganate solution (see below) was added as rapidly as possible with efficient stirring. The reaction was exothermic and the temperature was maintained at 10–15° by means of an ice-bath. After stirring for an additional 15 minutes, the reaction mixture was decolorized by the addition of an aqueous sodium bisulfite solution, followed by acidification with approximately 6 *N* hydrochloric acid to *p*H 1–2. The white precipitated solid was filtered off, washed several times with cold water and dried. It was pale yellow when dried.

The above experiment was conducted in four different ways. First (experiment A), no effort was made to control the *p*H, which rose from 10.0 at the start to 11.8, reaching this point when about 25% of the potassium permanganate solution had been added and remaining there until the addition was completed. In experiments B, C and D, 1.5 *N* sulfuric acid was added from a buret as needed to maintain the *p*H at 9.0–9.5. In experiments A and B, a 12.5% excess of potassium permanganate (0.03 mole) in 75 ml. of water was used. In experiments C and D, more desirable conditions were approached as first the potassium permanganate was more highly diluted (in 200 ml. of water, experiment C), and then as the quantity of potassium permanganate was reduced to the calculated requirement (0.0266 mole, experiment D). The data for these experiments, showing the increasing yields of ketohydroxystearic acids and the decreasing yields of dihydroxystearic acid obtained in succeeding experiments, are given in Table I.

Oxidation of Elaidic Acid.—Elaidic acid was oxidized as in experiment C above, both with and without control of the *p*H. The approximate percentage compositions of the crude oxidation products are

	*p*H Uncontrolled	*p*H Controlled
Ketohydroxystearic acids	45	45
Dihydroxystearic acid	30	20
Diketostearic acid	2	5
Saturated acids and unoxidized elaidic acid	13	14
Unaccounted for	10	16

Product Separation. Method I.—One hundred grams of reaction product (composition by analysis: ketohydroxystearic acids, 65%; diketostearic acid, 7%; dihydroxystearic acid, 6%; saturated acids and oleic acid, 17%; unaccounted for, 5%), obtained from oleic acid by oxidation with the calculated quantity of potassium permanganate (*p*H controlled) was dissolved in 800 ml. of hot benzene and the solution was cooled to room temperature. The precipitate was filtered off and dried. It weighed 13 g. and consisted of impure 9,10-dihydroxystearic acid, m.p. 120–122°. It was refluxed with 100 ml. of benzene (complete solution not obtained) and the mixture was cooled to room temperature and filtered. The white precipitate weighed 9 g. and consisted of moderately pure high-melting 9,10-dihydroxystearic acid, m.p. 127.5–128.5° (lit.[14] 131°) and neutralization equivalent 322 (calcd. 316.5). The melting point of a mixture with an authentic sample was not depressed.

---

(12) H. B. Knight, E. F. Jordan, Jr., E. T. Roe and D. Swern, in "Biochemical Preparations," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1952, p. 100.

(13) D. Swern and J. T. Scanlan, in "Biochemical Preparations," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1953, p. 118.

(14) D. Swern, THIS JOURNAL, **70**, 1235 (1948).

The benzene filtrates were combined and evaporated to dryness, yielding 91 g. of pale yellow solid. This was dissolved in 730 ml. of 95% ethanol and the solution was cooled to 5° overnight. The precipitate (12 g.) was filtered off and recrystallized from 60 ml. of 95% ethanol at room temperature. The bright yellow crystalline solid weighed 5 g. and consisted of moderately pure 9,10-diketostearic acid, m.p. 82.5–83.5° (lit.[3,15] 85°); polarographic analysis, 93.5% diketostearic acid. Recrystallization from 95% ethanol at room temperature gave an analytically pure product.

The combined alcohol filtrates were cooled to −25° and the copious precipitate was filtered off and dried. It weighed 55 g. and consisted of moderately pure 9(10),10(9)-ketohydroxystearic acids, m.p. 59.5–61.5° and neutralization equivalent 313 (composition: ketohydroxystearic acids, 90%; diketostearic acid, 5%; dihydroxystearic acid, 5%).

The alcohol filtrate was evaporated and the semi-solid residue (30 g.) was crystallized at −20° from 150 ml. of petroleum naphtha, boiling range 63–70°. The white precipitate, m.p. 53–54° and neutralization equivalent 308, weighed 9 g. and had the following composition: ketohydroxystearic acids, 81%; diketostearic acid, 3%; dihydroxystearic acid, 10%; unaccounted for, 6%.

Evaporation of the solvent from the final filtrate yielded 21 g. of an oily odoriferous residue which contained the saturated acids and unoxidized oleic acid in the crude product, cleavage products, and small amounts of all the other substances originally present.

Anal. iodine no. 43; neut. equiv., 239; hydroxyl oxygen, 1.31; carbonyl oxygen, 0.64.

Method II.—Alternatively, after separation of the bulk of the 9,10-dihydroxystearic acid by crystallization of the crude reaction product from benzene, the acids obtained by evaporation of the benzene filtrates were crystallized from petroleum naphtha, boiling range 63–70° (5 ml./g. of solute) at room temperature. Fifty grams of moderately pure 9(10),10(9)-ketohydroxystearic acids, m.p. 64–66° and neutralization equivalent 315, were obtained (composition: ketohydroxystearic acids, 90%; diketostearic acid, 7%; dihydroxystearic acid, 3%).

When the filtrate was cooled to 0° an additional 7 g. of white solid, m.p. 55–57°, was obtained with the following composition: ketohydroxystearic acids, 65%; diketostearic acid, 7%; dihydroxystearic acid, 22%; unaccounted for, 6% (probably all cleavage products).

Attempted Oxidation of 9(10),10(9)-Ketohydroxystearic Acids to 9,10-Diketostearic Acid.—A soap solution was prepared from 6.3 g. of 9(10),10(9)-ketohydroxystearic acids, m.p. 59.5–61.5°, 1.27 g. of 89% potassium hydroxide and 55 ml. of water. This was cooled to 10° and a solution of 2.10 g. of potassium permanganate in 85 ml. of water was added. The temperature was maintained at 10° and the *p*H was controlled at 9.0–9.5. After a reaction time of 1.5 hours the solution was decolorized with saturated aqueous sodium bisulfite solution and then acidified with 6 *N* hydrochloric acid. The pale yellow precipitate was filtered off and dried. It weighed 6.0 g.; composition: 9,10-diketostearic acid, 25%; ketohydroxystearic acids, 70%; 9,10-dihydroxystearic acid, 5%.

Attempted Oxidation of 10-Hydroxystearic Acid.—A soap solution was prepared by warming 12.0 g. (0.04 mole) of 10-hydroxystearic acid[16] with 150 ml. of water containing 2.52 g. of 89% potassium hydroxide. To the well stirred soap solution, cooled to 10–15°, 2.05 g. (0.0132 mole, 50% of calculated amount) of potassium permanganate in 150 ml. of water was added. No decolorization or *p*H change occurred. The solution was stirred for 45 minutes and then worked up as described earlier under the oleic acid oxidations. Unchanged 10-hydroxystearic acid was isolated in 100% yield.

Discussion

It has been established beyond doubt that the low-temperature oxidation of olefins with aqueous alkaline potassium permanganate yields 1,2-glycols mainly by *cis*-hydroxylation.[17-20] The generally accepted mechanism for the reaction is that a cyclic ester intermediate, formed from the olefin and permanganate ion,[17,20,21] is hydrolyzed without inversion.[14,17,22] The cyclic complex is an unstable ester and in the presence of excess hydroxide ions it should be rapidly hydrolyzed at both C–O–Mn bonds, more or less simultaneously, to yield 1,2-glycol.

With *p*H control, on the other hand, hydroxide ions are neutralized as they are formed and the rate of hydrolysis of the cyclic ester is reduced. Presumably hydrolysis can proceed stepwise to yield an intermediate containing one hydroxyl group and one ester group.

In view of the rapidity with which ketol is formed and the high oxidative stability of free hydroxyl groups,[7,23] it follows that further oxidation of the partially hydrolyzed intermediate must occur on the carbon atom which is still connected to manganese. The concept of stepwise hydrolysis explains the marked difference in the products obtained from oleic acid with and without *p*H control.

With *p*H control (9.0–9.5), 65–75% conversions to 9(10),10(9)-ketohydroxystearic acids are consistently obtained at a final soap concentration of 1 g. in 50 ml. of total reaction solution. If the final soap concentration is 1 g. in 25 ml. of solution (*p*H 9–9.5) the conversion to ketol drops only slightly to 55%. At the higher concentration but without *p*H control, the conversion to ketol drops dramatically to 15–20% and the conversion to 9,10-dihydroxystearic acid jumps correspondingly to 60% from 10% with *p*H control.

In contrast, the effect of *p*H control on the oxidation of elaidic acid is not so spectacular and the reasons for this are not clear. With *p*H control, elaidic acid gives only slightly lower conversions to dihydroxystearic acid and slightly higher conversions to diketostearic acid and cleavage products than without *p*H control, but the conversion to ketohydroxystearic acids (45%) remains unchanged.

Even with *p*H control small amounts (5–10%) of 9,10-diketostearic and 9,10-dihydroxystearic acids are obtained from oleic acid. The former is presumably obtained by oxidative attack on both carbon atoms of the unhydrolyzed complex. The latter is formed because some complete hydrolysis of the complex to free α-glycol must take place, and this product is known to be unreactive under these conditions.

Analysis of mixed reaction products or purified ketohydroxystearic acids for carbonyl and hydroxyl oxygen only is not sufficient to determine composition or purity, as earlier investigators assumed. An equimolar mixture of 9,10-dihydroxystearic and 9,10-diketostearic acids analyzes as pure ketol. To determine composition accurately, independent determination of diketostearic acid must be made.

---

(15) G. King, *J. Chem. Soc.*, 2114 (1954).

(16) H. B. Knight, R. E. Koos and D. Swern, THIS JOURNAL, **75**, 6212 (1953).

(17) J. Böeseken, *Rec. trav. chim.*, **41**, 199 (1922); **47**, 683, 839 (1928).

(18) R. Kuhn and F. Ebel, *Ber.*, **58**, 919 (1925).

(19) D. Swern, L. P. Witnauer and H. B. Knight, THIS JOURNAL, **74**, 1655 (1952).

(20) N. A. Milas, in B. T. Brooks, "The Chemistry of Petroleum Hydrocarbons," Vol. II, Reinhold Publ. Corp., New York, N. Y., 1955, p. 417.

(21) G. Wagner, *J. Russ. Phys. Chem. Soc.*, **27**, 219 (1895).

(22) A. Y. Drummond and W. A. Waters, *J. Chem. Soc.*, 435 (1953).

(23) P. Levesley and W. A. Waters, *ibid.*, 217 (1955).

Polarographic analysis[11] is most convenient, but determination of absorptivity at 420–430 mμ using pure 9,10-diketostearic acid as the reference standard can also be employed.[24] Absorption at about 270–280 mμ may be unreliable because of interference from ketohydroxy- and dihydroxystearic acids.[24]

In ketol-forming experiments in which a small excess (12.5%) of potassium permanganate is used, 5–15% of the reaction products cannot be accounted for analytically as ketohydroxy-, dihydroxy- and diketostearic acids or as unoxidized or saturated acids. Separation of products yields a small fraction with a high acid number (270–300) and the characteristic odor of pelargonic acid. A minor amount of chain cleavage must also be occurring during the reaction. On the other hand, when exactly equivalent amounts of oleic acid and potassium permanganate are used the yield of cleavage products is negligible but about 10% of the oleic acid remains unoxidized.

Application of the ketol reaction with *p*H control to linoleic acid (*cis,cis*-9,12-octadecadienoic acid) yields a reaction product in which 90% of the unsaturation has disappeared. The combined hydroxyl and carbonyl oxygen content (5.7%) of the product, however, indicates that on the average only one oxygen atom has been introduced into the chain, whereas a total of four would be anticipated. The reaction product is a viscous liquid and, since the carboxyl function is still present, it is assumed that a substantial amount of polymerization involving the unsaturation must have occurred. *trans,trans*-9,11-Octadecadienoic acid gives similar results.

Acknowledgment.—We wish to thank George C. Nutting and Ann M. Smith for ultraviolet absorption measurements, and Howard Teeter for a sample of *trans,trans*-9,11-octadecadienoic acid.

PHILADELPHIA 18, PENNA.

---

(24) R. T. Holman, W. O. Lundberg, W. M. Lauer and G. O. Burr, THIS JOURNAL, **67**, 1285 (1945).

[CONTRIBUTION FROM THE ORGANIC CHEMICALS DIVISION, NITRO RESERACH DEPARTMENT, MONSANTO CHEMICAL CO.]

Derivatives of 4,5-Dihydronaphtho[1,2]thiazole-2-thiol and -*s*-Triazines

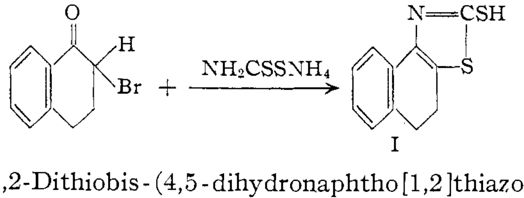
BY JOHN J. D'AMICO AND MARION W. HARMAN

RECEIVED APRIL 20, 1956

Ammonium dithiocarbamate and 2-bromo-1-tetralone reacted to give 4,5-dihydronaphtho[1,2]thiazole-2-thiol. Seventeen derivatives of this thiazolethiol were prepared. Three interesting results encountered were: (1) the reaction of cyanuric chloride with sodium dimethyldithiocarbamate or dimethylammonium dimethyldithiocarbamate gave 2-dimethylamino-4,6-bis-(dimethylthiocarbamoylthio)-*S*-triazine and 2-dimethylamino-4,6-bis-(dimethylthiocarbamoyl)-*S*-triazine, respectively; (2) potassium diethyl- or diisopropyldithiocarbamate and cyanuric chloride reacted to give 2,4,6-tris-(diethyl- or diisopropylthiocarbamoylthio)-*S*-triazine; and (3) the reaction of diethylammonium diethyldithiocarbamate or diisopropylammonium diisopropyldithiocarbamate with cyanuric chloride gave 2-diethylamino-4,6-bis-(diethylthiocarbamoylthio)-*S*-triazine and 2-diisopropylamino-4,6-bis-(diisopropylthiocarbamoylthio)-*S*-triazine, respectively.

Since 2-mercaptobenzothiazole and some of its derivatives have long been established as important accelerators for the vulcanization of rubber with sulfur, it was desirable to prepare the unknown 4,5-dihydronaphtho[1,2]thiazole-2-thiol (I) and its derivatives, and to compare their accelerator activity with that of 2-mercaptobenzothiazole and its corresponding derivatives. This evaluation will be reported elsewhere. A second objective was the preparation of cyanuryl derivatives of dialkyldithiocarbamic acids.

Ammonium dithiocarbamate reacts with 2-bromo-1-tetralone to form I. The reaction may be represented as



I

2,2-Dithiobis-(4,5-dihydronaphtho[1,2]thiazole) was prepared by the reaction of I with a 30% aqueous solution of ammonium persulfate.

The potassium salt of I reacted with N,N-diethylthiocarbamoyl chloride to give 4,5-dihydronaphtho[1,2]thiazol-2-yl diethyldithiocarbamate.

N-Cyclohexyl-4,5-dihydronaphtho[1,2]-2-thiazolesulfenamide was prepared by the oxidative condensation of I with cyclohexylamine.

Employing the elegant procedure described by Newby,[1] 4,5-(dihydronaphtho[1,2]thiazol-2-ylthio)-hydroquinone was prepared by the reaction of I with *p*-benzoquinone.

The reaction of the potassium salt of I with cyanuric chloride furnished the desired 2,4,6-tris-(4,5-dihydronaphtho)[1,2]thiazol-2-ylthio-*S*-triazine.

The zinc salt of I was obtained by treating the sodium salt of I with zinc chloride.

An acetone solution of the potassium salt of I reacted with 2,4-dinitrochlorobenzene to form 2-(2,4-dinitrophenylthio)-4,5-dihydronaphtho[1,2]-thiazole.

The reaction of an aqueous solution of the sodium salt of I with β-dimethylaminoethyl chloride gave the desired 4,5-dihydro-2-(2-dimethylaminoethylthio)-naphtho[1,2]thiazole.

2,2′-(2-Butynylenedithio)-bis-(4,5-dihydronaphtho[1,2] thiazole and 2,2′-(2-butenylenedithio)-bis-(4,5-dihydronaphtho[1,2]thiazole were prepared by the reaction of the potassium salt of I with 1,4-dichloro-2-butyne and 1,4-dichloro-2-butene, respectively.

3-(4,5-Dihydronaphtho[1,2]thiazol-2-ylthio)-pro-

---

[1] T. H. Newby, U. S. Patent 2,616,871.