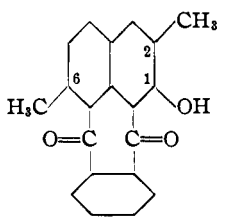
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Some Further Derivatives of Pleiadene[1]

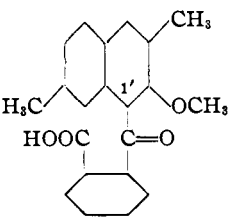
BY LOUIS F. FIESER

This paper includes an account of the preparation of certain compounds required in connection with the study of the action of hydroxylamine and of diazomethane on phthaloylnaphthol,[2] and describes also some synthetical experiments carried out in an attempt to extend the observations already recorded.

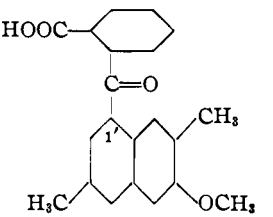
The diketone I was prepared partly in order to determine if it forms a hydroxylamine addition product, which it does, and partly with the idea that the methyl group at position 2 might block a possible addition of



I



II



III

diazomethane to the double bond of the quinonoid form. While this indeed may be the case, the compound proved to be of little use because it does not even form an ether on treatment with the reagent in question. The hydroxyl group appears to be masked, for the compound, unlike phthaloylnaphthol, does not dissolve in aqueous alkali. The same inert character is shown by a compound of similar structural type obtained by the condensation of phthalic anhydride with 2-phenanthrol (No. 2, Table I, below), and it would thus appear that this line of attack is not profitable.

The dimethyl derivative I was prepared by heating a mixture of phthalic anhydride, 2,6-dimethyl-7-naphthol[3] and aluminum chloride to a temperature of 200°, and yet the product was obtained in so excellent a yield and in such a high state of purity that it does not appear likely that there was any wandering of methyl groups in the course of the reaction. We sought to establish the point by the stepwise synthesis of the diketone, but unforeseen difficulties were encountered. In the first place the Friedel and Crafts reaction of phthalic anhydride with 2,6-dimethyl-7-methoxynaphthalene proceeded very poorly, a large proportion of the ether being recovered unchanged. More serious, however, was the fact that the chief reaction product was not the expected keto acid, II, desired for the synthesis, but an isomeric acid probably having the structure of III. The acid forms an anthraquinone on treatment with sulfuric acid and hence the keto group

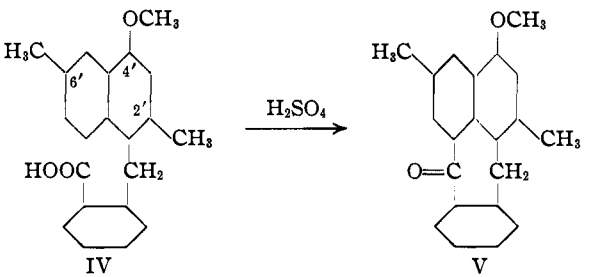
(1) Eighth paper in the series, "Condensations and Ring Closures in the Naphthalene Series."

(2) Seventh paper, THIS JOURNAL, **55**, 4963 (1933).

(3) Weissgerber and Kruber, *Ber.*, **52**, 346 (1919).

must be situated at either the 1′ (α) position, as here pictured, or at the 2′ (β) position. A keto acid which is incapable of undergoing ring closure to form an anthraquinone, and which probably has the structure of II, was also found in the reaction mixture but in quantity too small for the purpose at hand.

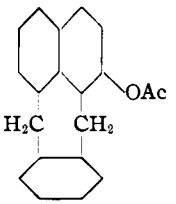
In another series of experiments an attempt was made to synthesize a substance similar to phthaloylnaphthol but having the hydroxyl group in the para rather than the ortho position with respect to a carbonyl group, for such a compound should prove an interesting subject for study. 2,6-Dimethyl-8-methoxynaphthalene was chosen as the most accessible starting material, and it was found to condense with phthalic anhydride in the



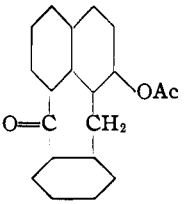
4-position as expected, though in poor yield. The keto acid failed to undergo cyclization on treatment with sulfuric acid, while its reduction product, IV, was easily converted into the ketone, V. These facts are sufficient to establish the structures of the compounds in question. It is worth noting that the cyclization of IV can be accomplished by heating the substance with sulfuric acid. The yield is quantitative and the closing of the 7-membered ring occurs just as easily as the closing of an anthrone 6-ring from an acid in which such a reaction is not blocked by a substituent group. The pleiadone derivative, however, although obtainable without great difficulty, could not be converted by oxidation into a pleiadenedione. Though disappointing, the failure of this attempted synthesis was not a great surprise, for the presence of a methoxyl group has been found to introduce complications in other oxidations of the same type.[4]

The theoretical significance of obtaining for study a pleiadone derivative in which the carbonyl group is adjacent to a hydroxyl group has been discussed in the preceding paper.[2] In a first attempt to prepare such a compound, phthaloylnaphthol was reduced by high pressure hydrogenation, and the reduction product, in the form of the acetate (VI), was subjected to partial oxidation. The oxidation product, however, was the known ketone, VII,[4] rather than the desired isomer. This method failing, we obtained a compound of the desired type from the acid VIII, which was prepared by the usual synthesis, starting with 2,7-dimethoxynaphthalene.

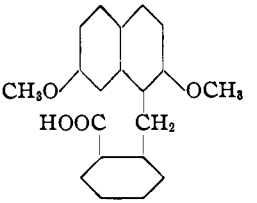
(4) L. F. and M. Fieser, THIS JOURNAL, **55**, 3010 (1933).



VI



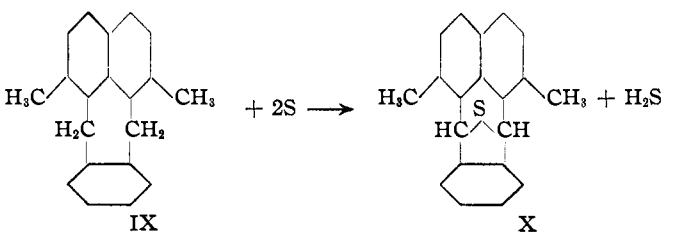
VII



VIII

The closing of the 7-ring was again brought about in a very satisfactory manner by the action of sulfuric acid on VIII, and the resulting ketone on demethylation yielded 1,6-dihydroxypleiadone.

In connection with this miscellany of compounds and experiments, we may report the results of a brief study of the possibility of producing a true pleiadene by the dehydrogenation of the corresponding dihydropleiadene. The dimethyl compound IX gave no clean products on reaction with selenium, but was converted by the action of sulfur into a quite stable and a nicely crystalline compound containing sulfur and having two atoms of hydrogen less than the starting material. Without being able at this time to present any but analytical evidence in support of the view, we may offer the following equation as representing the most probable course of the reaction



IX X

The production of the sulfur bridge may be preceded by the formation of the unsaturated hydrocarbon by dehydrogenation, and if this is the case the pleiadene is distinctly more reactive than the similarly constituted hydrocarbon anthracene.

The possibility of dehydrogenating the hydrocarbon IX with bromine was also studied and with equally surprising results. In glacial acetic acid solution the hydrocarbon combines with bromine according to the equation: $C_{20}H_{18} + CH_3COOH + Br_2 = C_{20}H_{17}Br \cdot CH_3COOH + HBr$. The reaction product is crystalline, but unstable to heat, and when treated with cold pyridine it is converted into a stable bromo compound, $C_{20}H_{17}Br$. The first product is not a molecular compound derived from the second substance, for the latter crystallizes from glacial acetic acid without solvation. The primary reaction product loses some hydrogen bromide on heating, along with acetic acid, whereas the second substance is not attacked by alcoholic alkali. From these facts it is concluded that bromine first attacks

a methylene or a methyl group to form a substance which combines, probably with the formation of a molecular compound, with acetic acid. Pyridine causes both the elimination of the acetic acid and the rearrangement to a nuclear bromo derivative.

Experimental Part[5]

1. Pleiadenediones

The compounds listed in Table I as Nos. 1, 2 and 4 were prepared by adding 1 part of 2,3-dihydroxynaphthalene, 2-phenanthrol or 2,6-dimethyl-7-naphthol,[3] respectively, to a melt from 10 parts of phthalic anhydride and 2 parts of aluminum chloride at a

TABLE I

DERIVATIVES OF 7,12-PLEIADENEDIONE

No.	Substituents	Description	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
1	1,2-Dihydroxy	Yellow needles	233	74.47	74.09	3.47	3.84
2	1-Hydroxy-4,5-benz	Yellow needles	240	81.47	81.54	3.73	3.86
3	Acetate of No. 2	Pale yellow	227	78.67	78.17	3.85	3.85
4 (I)[6]	2,6-Dimethyl-1-hydroxy	Yellow needles	209	79.45	79.41	4.67	4.54
5	Acetate of No. 4	Pale yellow	205	76.72	76.52	4.69	4.73

temperature of 160–170°. The temperature was raised to 200° and held there, with good stirring, for one-half hour, when the melt was poured into boiling water. The yellow precipitate was digested with boiling water, crystallized from glacial acetic acid, distilled, and again crystallized. The yield in the first case was only 32% of the theoretical amount; the other two compounds were obtained in yields of 85–90%. As would be expected, Compound 1 dissolves easily in cold alkali; the other two compounds are not appreciably soluble in boiling aqueous sodium hydroxide solution but dissolve easily in alcoholic alkali. These solutions in alkali or alcoholic alkali are deep orange-yellow in color and the addition of hydroxylamine hydrochloride causes first a striking change to a nearly colorless solution and then the separation of a colorless product having all the characteristics of the addition product of phthaloylnaphthol. The action of diazomethane in tetrachloroethane solution on the two alkali-insoluble compounds, Nos. 2 and 4, was studied repeatedly, but no product other than the unchanged starting material could be isolated.

In an attempt to establish by synthesis the structure of the hydroxydimethyl diketone, No. 4, phthalic anhydride was condensed with 2,6-dimethyl-7-methoxynaphthalene in tetrachloroethane solution in the presence of aluminum chloride. The mixture was cooled in a salt-ice bath and stirred intermittently for three days. In spite of the long period allowed for reaction, about half of the ether was recovered unchanged.

The soda-soluble portion consisted in predominant amount of a keto acid melting at 212° and convertible into an anthraquinone, and there was only a very small amount of the keto acid (m. p. 223°) desired for the synthesis indicated. The lower-melting isomer was isolated by crystallization from toluene and further purified by recrystallization from alcohol, in which, however, it is quite soluble. The other isomer is considerably less soluble in this solvent, and it was obtained in a pure condition by extracting the residue recovered from the toluene solution with alcohol to remove the needles of the isomer, m. p. 212°, and crystallizing the residue from the same solvent.

The conversion of the lower-melting keto acid into a quinone was accomplished by

(5) I am indebted to Dr. C. Harold Fisher for the analyses here reported and to Mrs. Louis F. Fieser for assistance in the preparative work.

(6) The Roman numeral refers to the formula given above.

heating the material (1 g.) with 82% sulfuric acid (10 cc.) for one-half hour on the steam-bath. The quinone began to separate from the red solution even before all of the acid had dissolved. The anthraquinone derivative was recognized as such from the characteristic red vat which is formed. The compounds here mentioned are described in Table II.

TABLE II

COMPOUNDS OBTAINED FROM 2,6-DIMETHYL-7-HYDROXYNAPHTHALENE

Name	Description	Color in H_2SO_4	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
2,6-Dimethyl-7-methoxy-naphthalene	Plates	None	82	83.82	84.33	7.58	7.43
3′,7-Dimethyl-6′-methoxy-1′ (or 2′)-naphthoyl-2-benzoic acid (III?)	Colorless needles	Red-purple	212	75.42	75.22	5.43	5.52
2′,4-Dimethyl-3′-methoxy-1,2-benzanthraquinone	Yellow needles	Purple	235	79.72	79.66	5.10	5.13
3′,7′-Dimethyl-2′-methoxy-1′-naphthoyl-2-benzoic acid (II?)	Yellow prisms	Blue-green	223	75.42	75.41	5.43	5.64

2. Pleiadones

The starting materials required for the synthesis of the cyclic monoketones were 2,7-dimethoxynaphthalene and 2,6-dimethyl-8-methoxynaphthalene. Two acids may be obtained by the sulfonation of 2,6-dimethylnaphthalene under suitable conditions[3] and these yield on fusion with alkali the naphthol desired and that utilized in experiments described in Section 1. In separating the acids and determining their purity it was found useful to know the melting points of the *p*-toluidine salts. These are as follows: 2,6-dimethylnaphthalene-8-sulfonate, 279°; 2,6-dimethylnaphthalene-7-sulfonate, 286°.

2,6-Dimethyl-8-methoxynaphthalene was prepared from the naphthol by methylation with dimethyl sulfate in a hot, alkaline solution. The product was distilled and then crystallized from methyl alcohol; colorless plates, m. p. 58°.

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.82; H, 7.59. Found: C, 83.66; H, 7.53.

The compounds obtained from the condensation of this ether and of the dimethoxynaphthalene with phthalic anhydride and in the subsequent reductions and ring closures are listed in Table III.

TABLE III

PROPERTIES AND ANALYSES OF COMPOUNDS

No.	Substituents	Description	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
		1′-Naphthoyl-2-benzoic acids					
6	2′,7′-$(OCH_3)_2$	Colorless plates	201	71.41	71.37	4.80	4.79
7	2′,6′-$(CH_3)_2$-4′-(OCH_3)	Yellow needles	261	75.42	75.38	5.43	5.47
		1′-Naphthoyl-2-benzoic acid methyl ester					
8	2′,7′-$(OCH_3)_2$	Prisms	114	71.98	71.95	5.18	5.33
		1′-Naphthylmethyl-2-benzoic acids					
9(VIII)	2′,7′-$(OCH_3)_2$	Fibrous needles	161	74.51	73.98	5.63	5.52
10(IV)	2′,6′-$(CH_3)_2$-4′-(OCH_3)	Colorless needles	236	78.72	78.37	6.30	6.39
		12-Pleiadones					
11	1,6-$(OCH_3)_2$	Yellow needles	201	78.92	78.99	5.30	5.13
12	1,6-$(OH)_2$	Yellow needles	233	78.24	78.09	4.38	4.26
13	1,6-$(OAc)_2$	Colorless plates	220	73.31	72.76	4.48	4.39
14(V)	2,6-$(CH_3)_2$-4-(OCH_3)	Bright yel. needles	241	83.41	82.98	6.00	6.14
15	2,6-$(CH_3)_2$-4-(OH)	Bright yel. needles	286	83.30	83.17	5.60	5.55

The Friedel and Crafts reaction with 2,7-dimethoxynaphthalene was carried out at −15° in tetrachloroethane solution for twenty hours, and about one-third of the ether was recovered unchanged. The keto acid, No. 6, was purified through the methyl ester and then by crystallization of the sodium salt. This salt crystallizes well from water, but not in the presence of alcohol. The keto acid (20 g.) was reduced with zinc dust (35 g.) in alkaline solution (25 g. of sodium hydroxide in 300 cc. of water), the mixture being boiled for two hours and heated overnight on the steam-bath. The acid, Compound No. 9, was precipitated twice as the sodium salt with alkali and sodium chloride and then crystallized from benzene–ligroin; yield, 17.5 g.

The closure of the 7-membered ring to give the pleiadone, No. 11, was accomplished most easily by the action of sulfuric acid. The product was cleaner and the yield just as good as when the acid chloride was treated with aluminum chloride in nitrobenzene solution. Thus 1 g. of the acid was stirred into 10 cc. of 82% sulfuric acid (green-yellow fluorescence) and the mixture was heated on the steam-bath for twenty minutes, when a deep red solution was obtained. The reaction product, precipitated by water and digested with soda solution, was practically pure; yield, 0.9 g. The substance crystallizes well from alcohol.

Demethylation was accomplished by boiling for three hours a solution of 4 g. of the ether in benzene with 10 g. of aluminum chloride. The benzene was removed by steam distillation and the dihydroxypleiadone (No. 12) was obtained in a nearly pure condition and in quantitative yield after being precipitated from a solution in alkali. The compound crystallizes well from alcohol. The yellow solution in alkali does not change in color on the addition of hydroxylamine and there is thus no indication of the formation of an addition product.

The condensation of phthalic anhydride with 2,6-dimethyl-8-methoxynaphthalene did not proceed well under any of the conditions tried. Both tetrachloroethane and nitrobenzene were used as solvent and the reaction was run at −15° and at room temperature and for varying periods of time (up to three days). In every case a considerable quantity of the starting material was recovered unchanged. The reaction mixture, however, appeared to contain only one keto acid, No. 7. To isolate this the oily solid left as a residue after steam distillation of the solvent was digested with alcohol. This dissolved the ether and left a solid residue of the acid, which was easily purified by crystallization from glacial acetic acid (moderately soluble). The acid forms a very sparingly soluble sodium salt. On this account it was found advisable to carry out the reduction with zinc and alkali in an alcoholic rather than an aqueous solution. Thus a mixture of 10 g. of the keto acid, 25 cc. of 6 *N* sodium hydroxide, 125 cc. of alcohol and 25 g. of zinc dust was boiled under the reflux condenser for two days, with the addition of 50 cc. of alkali solution and 25 g. of zinc at intervals. An equal volume of water was added, the bulk of the alcohol was removed by distillation and the solution was filtered and acidified. After precipitating the acid (No. 10) from a soda solution and digesting the material at the boiling point, there was obtained 9.3 g. of the nearly pure acid which required a single crystallization from alcohol.

The ring closure to the monoketone (No. 14) was again accomplished with the use of sulfuric acid, 1 g. of the acid being warmed for ten minutes on the steam-bath with 1 cc. of water and 8 cc. of concd. sulfuric acid. The solution became green for a moment and soon changed in color to an intense blue. The ketone, precipitated with water and digested with a small amount of alcohol, in which it is sparingly soluble, was obtained directly in a nearly pure condition; yield, 0.9 g. The compound crystallizes well from glacial acetic acid; the solution in concd. sulfuric acid is purple. Demethylation with aluminum chloride proceeded smoothly and the hydroxy compound, No. 15, crystallized well from glacial acetic acid. The compound dissolves in hot alkali to give a red solution; when in a finely divided condition it dissolves slowly in the cold. Hydroxylamine

forms no additive compound in alkaline solution. Attempts to oxidize the methylene group of the ether, No. 14, with either chromic acid or selenious acid were unsuccessful.

3. Dihydropleiadenes

1-Hydroxy-7,12-dihydropleiadene.—This compound was prepared by the hydrogenation of phthaloylnaphthol in the pressure apparatus described by Adkins and Connor.[7] Using 15 g. of material suspended in 150 cc. of alcohol and 3 g. of copper chromite catalyst,[8] the reaction proceeded rapidly at a moderate pressure and at a temperature of 155°; yield, 7.3 g. The substance is very soluble in alcohol or benzene and crystallizes well from benzene–ligroin as clusters of colorless, fibrous needles melting at 179°. It dissolves easily in cold alkali and the solution exhibits a distinct violet fluorescence.

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 87.77; H, 5.73. Found: C, 87.69; H, 5.71.

The acetate (VI), crystallized from alcohol, forms long, fine needles melting at 136°.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.30; H, 5.60. Found: C, 83.76; H, 5.71.

The acetate was converted by oxidation with chromic acid in glacial acetic acid solution to a substance, m. p. 195°, identified as 1-acetoxy-7-pleiadone;[4] yield, 30%.

1,6-Dimethyl-7,12-dihydropleiadene (IX).—1,6-Dimethylpleiadone[4] was hydrogenated easily in the pressure bomb under the conditions described above; yield, 60%. The compound is moderately soluble in alcohol and crystallizes from this solvent in colorless needles which may grow to a length of 10–12 cm. The solution has a purple fluorescence. On warming the compound with concd. sulfuric acid a cherry-red coloration is produced. The melting point is 133°.

Anal. Calcd. for $C_{20}H_{18}$: C, 92.98; H, 7.02. Found: C, 92.74: H, 7.05.

Attempts to nitrate the hydrocarbon led only to oily, yellow mixtures largely soluble in alcoholic alkali. Selenium had little effect on the hydrocarbon at 350° and at higher temperatures hard, insoluble solids were produced.

The Action of Sulfur (X?).—A mixture of 3 g. of the hydrocarbon and 1 g. of sulfur was heated in a small distilling flask in a metal bath and the temperature was raised rapidly. The evolution of hydrogen sulfide began at 200° and became very rapid at 260°. After heating at this temperature for eight minutes, the product was distilled *in vacuo*, a considerable black residue being left in the flask. The distillate solidified on rubbing it with alcohol. It was redistilled and then crystallized from glacial acetic acid until pure; yield, 1 g. The compound is very readily soluble in benzene, moderately soluble in glacial acetic acid or ligroin, sparingly soluble in alcohol. From glacial acetic acid it separates very slowly in the form of large, rectangular, pale orange prisms melting at 217°. It forms a deep red solution in concd. sulfuric acid. The compound contains sulfur.

Anal. Calcd. for $C_{20}H_{16}S$: C, 83.28; H, 5.60. Found: C, 83.17; H, 5.84.

The Action of Bromine.—A solution of 2.6 g. of the hydrocarbon in 40 cc. of glacial acetic acid was cooled to 80° and treated with a solution of 1.8 g. of bromine in a little glacial acetic acid. The bromine was taken up at once and hydrogen bromide was evolved. The solution on cooling deposited 2.5 g. of thick, dull yellow needles. No good product was obtained from the mother liquor. The material collected decomposes on heating at 150–160°, and it darkens when heated in glacial acetic acid solution. No solvent was found suitable for a crystallization. The crude material, however, being stable at room temperature, appeared suitable for analysis.

(7) Adkins and Connor, THIS JOURNAL, **53**, 1091 (1931).

(8) Catalyst "37 K A F" of Connor, Folkers and Adkins, *ibid.*, **54**, 1140 (1932).

Anal. Calcd. for $C_{22}H_{21}O_2Br$: C, 66.49; H, 5.33. Found: C, 66.46, 66.67; H, 4.76, 4.66.

The second compound, **a bromo-1,6-dimethyldihydropleiadene**, was best prepared as follows: 1 g. of the primary bromination product was shaken in the cold with 4 cc. of pyridine for one-half hour. The needles gradually disappeared and when dissolution was nearly complete a colorless powder began to separate. Enough alcohol was added to bring this material into solution at the boiling point and the solution was set aside to crystallize. The bromo compound separated in a very pure condition in the form of long, slender needles (0.8 g.). The substance distils without decomposition and may be recovered unchanged after prolonged boiling with alcoholic alkali. No coloration is produced with cold concd. sulfuric acid, but on heating the solution acquires an intense red color. The melting point is 179°.

Anal. Calcd. for $C_{20}H_{17}Br$: C, 71.21; H, 5.08. Found: C, 71.22; H, 5.15.

Summary

In extending earlier investigations various new pleiadenediones, pleiadones and dihydropleiadenes have been prepared and characterized.

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Preparation of *l*-Tartaric Acid by the Oxidation of *d*-Gulonic Lactone

BY J. K. DALE AND W. F. RICE, JR.

Fischer and Crossley[1] obtained a 5% yield of potassium acid *d*-tartrate by the oxidation of potassium acid *d*-saccharate with alkaline permanganate. In a patented process Odell[2] claimed a substantial yield of *d*-tartaric acid together with *d*-saccharic acid by the oxidation of *d*-glucose with nitric acid in which was dissolved a small amount of sodium vanadate. It seemed probable that the formation of *d*-tartaric acid in the Odell process might be due, at least in part, to a secondary oxidation of the saccharic acid formed in the early stages of the reaction. This view was substantiated by the fact that the authors obtained *d*-tartaric acid in appreciable yields from both *d*-gulonic and *d*-saccharic lactones by their oxidation with nitric acid containing a trace of a vanadate.

Since *d*-gulonic lactone gives *l*-saccharic[3] acid on oxidation with nitric acid alone, it should give *l*-tartaric acid in addition when oxidized with nitric acid containing a trace of the vanadate catalyst. Moreover the process involves no difficulties and, thanks to the researches[4] that have taken xylose out of the category of rare sugars, *d*-gulonic lactone may be readily obtained.

(1) Fischer and Crossley, *Ber.*, **27**, 394 (1894).
(2) Odell, U. S. Patent 1,425,605.
(3) Fischer, *Ber.*, **23**, 2611 (1890); Fischer and Stahel, *ibid.*, **24**, 534 (1891).
(4) Hudson and Harding, THIS JOURNAL, **40**, 1601–1602 (1918); Monroe, *ibid.*, **41**, 1002–1003 (1919); Schreiber, Geib, Wingfield and Acree, *Ind. Eng. Chem.*, **32**, 497–501 (1930).