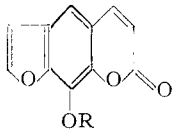
dide in the presence of potassium carbonate and obtained the secondary and isobutyl ethers, respectively (m.p. 62 and 59°). These two ethers, as well as the normal ether previously prepared, were dealkylated easily by the magnesium iodide method[4] to xanthotoxol (Ib); this establishes their constitution beyond doubt.



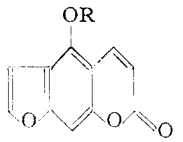
Ia, R = C_4H_9
b, R = H
c, R = $CH_2CH{=}C(CH_3)_2$

An analogous experiment carried out with *t*-butyl iodide did not lead to the isolation of *t*-butyl ether of xanthotoxol; *t*-butyl ethers are unlikely to be obtained by the action of *t*-butyl iodide on phenols.[5]

From the foregoing we conclude that provided there is no case of dimorphism, prangenin is neither the normal, the iso, nor the *sec*-butyl ether of xanthotoxol. It may, however, be the *t*-butyl ether. *t*-Butyl ethers of phenols are, however, very rare in nature.

Attention is drawn to the great similarity between prangenin (m.p. 97°) and imperatorin[6] (Ic). Both are colorless substances, insoluble in alkali, giving xanthotoxol on acid hydrolysis. The analytical values, apart from the values for carbon, show the similarity. Prangenin: Found: C, 70.00, 70.24; H, 5.28, 5.38, mol. wt., 244, 265. Calcd. for imperatorin: C, 71.1; H, 5.2; mol. wt., 270.

In this connection it should be mentioned that the authors succeeded in demethylating bergapten (IIa) to bergaptol (IIb) by the magnesium iodide method.[4] This substance seems not to have been prepared previously from this source. The identity of the bergaptol so obtained was proved by reconverting it into bergapten (methyl iodide–potassium method).



IIa, R = CH_3
b, R = H

Experimental

Butylation of Xanthoxol (Ib). *sec*-Butyl Ether.—A mixture of 1 g. of Ib, in 150 cc. of dry acetone, 3 cc. of *sec*-butyl iodide and 5 g. of potassium carbonate was refluxed for 36 hours and filtered while hot; the acetone was distilled off in a vacuum and the residue was crystallized from light petroleum (b.p. 50–70°) in colorless needles, m.p. 62°, insoluble in 10% sodium hydroxide, easily soluble in methyl alcohol; yield 0.42 g. *Anal.* Calcd. for $C_{15}H_{14}O_4$: C, 69.8; H, 5.5. Found: C, 69.6; H, 5.5.

The isobutyl ether was similarly prepared using isobutyl iodide; colorless needles, m.p. 59°, were obtained from light petroleum (b.p. 50–70°); the substance gave a strong depression in m.p. with the *sec*-butyl ether and was insoluble in 10% sodium hydroxide solution. *Anal.* Calcd. for $C_{15}H_{14}O_4$: C, 69.8; H, 5.4. Found: C, 69.6; H, 5.2.

Dealkylation of the *n*-Butyl Ether of Xanthotoxol (Ib).—0.4 g. of the ether was dissolved in 5 cc. of benzene (anhydrous), and magnesium iodide (prepared from 0.8 g. of iodine and 0.1 g. of magnesium) in 15 cc. of dry ether was added. The organic solvents were driven off in a vacuum and the residue was heated in an oil-bath at 160–170° (bath temperature) in a stream of dry carbon dioxide for 2 hours, allowed to cool and then decomposed with dilute sulfuric acid. The deposit was washed with water and then with aqueous sodium bisulfite. After crystallization from dioxane colorless crystals soluble in aqueous 10% sodium hydroxide were obtained; m.p. 246° not depressed by the addition of an authentic sample of xanthotoxol; yield 70–80%.

Dealkylation of the secondary and the isobutyl ethers was carried out in a similar manner yielding xanthotoxol in both cases (identified as previously).

Demethylation of Bergapten (IIa).—0.75 g. of bergapten was dissolved in 60 cc. of dry benzene and added to a solution of magnesium iodide (prepared from 2 g. of iodine and 0.25 g. of magnesium) in 20 cc. of dry ether; the solvents were distilled off in a vacuum and the residue dried at 120° for 15 minutes, after which the bath temperature was raised to 160–165°. After heating for 90 minutes, the reaction product was decomposed with dilute sulfuric acid and the deposit washed as in the case of the dealkylation of the *n*-butyl ether of xanthotoxol. The reaction product was crystallized from acetone–ether (1:1 by volume) and sublimed in vacuum (oil-pump) at 240–260° (bath temperature). Light yellow crystals were obtained, m.p. 276°.[7] IIb dissolves in 10% alkali with a yellow color. *Anal.* Calcd. for $C_{11}H_6O_4$: C, 65.3; H, 3.0. Found: C, 64.8; H, 3.1.

Bergapten from Bergaptol.—For further identification, bergaptol was transformed into bergapten. To 0.5 g. of bergaptol dissolved in 50 cc. of dry hot acetone, 4 g. of methyl iodide and 3 g. of potassium carbonate was added. After 32 hours refluxing, acetone was distilled off in vacuum and the residue purified by sublimation in vacuum (bath temperature 160°). Colorless needles insoluble in 10% sodium hydroxide were obtained; m.p. and mixed m.p. with an authentic sample 188°.

(4) A. Schönberg and R. Moubasher, *J. Chem. Soc.*, 462 (1944).

(5) E. W. Lewis, *ibid.*, **83**, 329 (1903).

(6) The m.p. of imperatorin (102°) is not quite definite in consequence of the thermal rearrangement into alloimperatorin (E. Späth and H. Holzen, *Ber.*, **68**, 1123 (1935)).

(7) E. Späth and L. Kahovec (*ibid.*, **66**, 1149 (1933)) gave m.p. 277°.

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The Preparation of *dl*-Alloisocitric Lactone

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The preparation of *dl*-isocitric lactone has been thoroughly studied.[1] This is the racemic lactone corresponding to the dextrorotatory isomer of isocitric acid which is found in plant tissues.[2] The diastereoisomeric racemate, *dl*-alloisocitric lactone, has not previously been prepared in a pure form, although Pucher and Vickery[1b] isolated a fraction rich in this material from the mother liquors of a preparation of *dl*-isocitric lactone by the method of Fittig and Miller.[1a]

A supply of *dl*-alloisocitric lactone was desired for stereochemical studies and for investigations of the biochemical activities of compounds related to the Krebs cycle. Attempts to isolate a pure substance from the impure material described by Pucher and Vickery were unsuccessful. Preparation of this pure racemate in a reasonable yield from *dl*-isocitric lactone proved feasible when the conditions used by Fisher[3] for epimerization of α-hydroxy acids of the sugar series were tried. An attempt to decide, through anhydride formation, which of these race-

(1) (a) R. Fittig and H. Miller, *Ann.*, **255**, 43 (1889); (b) G. W. Pucher and H. B. Vickery, *J. Biol. Chem.*, **163**, 169 (1946); (c) H. A. Krebs and L. V. Eggleston, *Biochem. J.*, **38**, 431 (1944); (d) H. P. Kato and S. R. Dickman in "Biochemical Preparations," Vol. 3, E. E. Snell, Ed., John Wiley and Sons, Inc., New York, N. Y., 1953, p. 52.

(2) G. W. Pucher and H. B. Vickery, *J. Biol. Chem.*, **145**, 525 (1942).

(3) E. Fisher, *Ber.*, **23**, 799 (1890).

mates corresponds to a *cis* configuration of the two carboxyl groups relative to the lactone ring was unsuccessful.

Experimental[4-6]

Monopyridine Salt of *dl*-Alloisocitric Lactone.—Ten grams of *dl*-isocitric lactone[1c] was dissolved in 20 ml. of redistilled pyridine and 10 ml. of water and heated at 140–150° in a sealed tube for three hours. One hundred ml. of 95% ethanol was added. Upon standing and seeding, 7.00 g. of crystals, m.p. 138–140° formed. Recrystallization from 50 ml. of 95% ethanol and treatment with Norite yielded 5.42 g. of colorless crystals, m.p. 139.6–141.8°.

Anal. Calcd. for $C_{11}H_{11}O_6N$: C, 52.17; H, 4.38. Found: C, 52.59; H, 4.46.

***dl*-Alloisocitric Lactone.**—A solution of the recrystallized pyridine salt in 50 ml. of 1.5 *N* sodium hydroxide was boiled to dryness *in vacuo*. Eight ml. of 12 *N* hydrochloric acid was added and the mixture was boiled to dryness and heated for one-half hour at 100° *in vacuo* to close the lactone ring.[1b] The residue was extracted with five 20-ml. portions of hot ethyl acetate. After treatment with Norite the combined extracts were evaporated to dryness *in vacuo* leaving an oil which crystallized on scratching. After drying on a porous plate the product weighed 3.18 g. and melted at 146–155°. Recrystallization from 25 ml. of ethyl acetate and 20 ml. of 60–70° petroleum ether yielded 1.98 g. of *dl*-alloisocitric lactone, m.p. 157–158.5°. A m.p. of 135–141° was observed when this material was mixed with *dl*-isocitric lactone, m.p. 161–163°. A second crop of 0.54 g., m.p. 155–158°, was obtained from the mother liquors, a total yield of 68% from the pyridine salt.

An analytical sample crystallized from the same solvents melted at 158.2–159.4°.

Anal. Calcd. for $C_6H_6O_6$: C, 41.39; H, 3.48. Found: C, 41.08; H, 3.62.

By direct titration a neutralization equivalent of 86.8 was observed, calculated 87.1. At the end-point excess alkali was added and the solution boiled to open the lactone ring. Back titration indicated an equivalent weight of 175.3 for the lactone, calculated 174.1.

The mother liquors from the original isolation of the pyridine salt contained additional quantities of *dl*-alloisocitric acid. Lactone prepared from them resembled the impure fractions described by Pucher and Vickery[1b] although it was possible by fractional crystallization to isolate small additional quantities of *dl*-alloisocitric lactone relatively free of *dl*-isocitric lactone.

Di-(*p*-bromophenacyl) Ester of *dl*-Alloisocitric Lactone.—By the method of Pucher and Vickery[1b] 292 mg., 45%, of an ester, m.p. 163–165.5°, was prepared from 200 mg. of *dl*-alloisocitric lactone. An analytical sample from absolute ethanol melted at 166.8–167.2°.[7]

Anal. Calcd. for $C_{22}H_{16}O_8Br_2$: C, 46.50; H, 2.84. Found: C, 46.92; H, 2.91.

(4) A grant from the Research Committee, Santa Barbara College, is gratefully acknowledged.

(5) Corrected melting points were taken in an electrically heated copper block.

(6) Microanalyses for carbon and hydrogen by Elek Microanalytical Laboratories, Los Angeles, California.

(7) Pucher and Vickery prepared an ester, m.p. 153–154°, from their impure fraction containing *dl*-alloisocitric lactone. Melting points as low as this were observed in the present work when highly impure *dl*-alloisocitric lactone was used; however, in such cases the melting point could be raised to 166°.

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New Disaccharide from the Acid Reversion of D-Galactose

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RECEIVED NOVEMBER 26, 1954

Recently, considerable attention has been focused on condensation polymerization[1] and acid reversion products of sugars[2] and in the case of the acid treatment of D-glucose, the disaccharides produced have been largely characterized.[3,4] In the present study the effect of hydrochloric acid on D-galactose has been examined, and preliminary experiments indicated that optimum polymerization, as measured by fall in reducing power, occurred in a 1.0 *M* solution of D-glactose in 37% hydrochloric acid (Fig. 1). Under these conditions equilibrium was reached after 24 hr. when the reducing power had fallen to 67% of its original value and paper chromatographic examination revealed the presence of two disaccharides, a trisaccharide and a smaller proportion of higher saccharides in addition to D-galactose. The disaccharide having the lower R_f value (referred to as "disaccharide A") was present in greater amount than the other disaccharide (disaccharide B). The mixture of disaccharides was freed from D-galactose and higher saccharides by chromatography on charcoal.[5] Repeated fractionation of this mixture on charcoal progressively reduced the proportion of disaccharide B present until it could no longer be detected by paper chromatography. The pure disaccharide A was obtained as an amorphous, slightly deliquescent powder which had $[\alpha]^{20}D$ +149° (*c* 0.725, water). Attempts at crystallization failed.

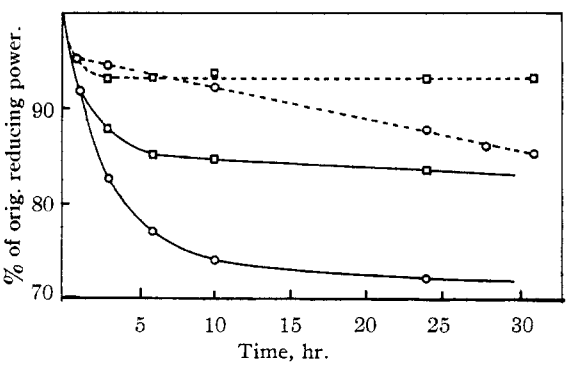

Fig. 1.—Polymerization of D-galactose by hydrochloric acid; □, 0.5 *M* D-galactose; O, 1.0 *M* D-galactose, ------ 25% hydrochloric acid and — 37% hydrochloric acid.

Disaccharide A showed reducing power and the sole product of its acid hydrolysis was D-galactose which was characterized as the phenylosazone. Methylation of the sugar followed by hydrolysis of the methylated product yielded 2,3,4,6-tetra-*O*-methyl-D-galactose and 2,3,4-tri-*O*-methyl-D-galactose which were separated by large-scale paper chromatography and characterized as their anilides. Oxidation of the biose with bromine water yielded a stable lactone which was methylated to give the octa-*O*-methyl methyl ester of the bionic acid. Hydrolysis of this ester gave 2,3,4,6-tetra-*O*-methyl-D-galactose, which was again characterized as the anilide, and a tetra-*O*-methyl acid (I) which was oxidized with nitric acid. The product of this

(1) E. Pacsu and P. T. Mora, THIS JOURNAL, **72**, 1045 (1950).

(2) W. R. Fetzer, E. K. Crosby, C. E. Engel and L. C. Kirst, *Ind. Eng. Chem.*, **45**, 1075 (1953).

(3) A. Thompson, M. L. Wolfrom and E. J. Quinn, THIS JOURNAL, **75**, 3003 (1953).

(4) A. Thompson, K. Anno, M. L. Wolfrom and M. Inatome, *ibid.*, **76**, 1309 (1954).

(5) R. L. Whistler and D. F. Durso, *ibid.*, **72**, 677 (1950).