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Oxygen Heterocycles. A New Isoflavanone from *Sophora japonica*, L.

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From *Sophora japonica*, L. there has been isolated a new isoflavanone, $C_{16}H_{12}O_6$, which has been named sophorol. By spectroscopic and degradative experiments it was shown that sophorol is either 2′,7-dihydroxy-4′,5′-methylenedioxyisoflavanone or 2′,7-dihydroxy-5′,6′-isoflavanone. The former is preferred on the basis of phytochemical ground. Attention is called to the structural similarity with known naturally occurring isoflavanone, ferreirin, and homoferreirin. Sophorol is unique in that it is first example of optically active isoflavanone.

Since the structure of chrysin was elucidated by Kostanecki in 1893 numerous flavone and isoflavone coloring matters in various oxidation states have been found in nature.[1] It is, however, only recently that some simple isoflavanones have been discovered in the vegetable kingdom. Padmakstein[2] from *Prunus puddum* and ferreirin as well as homoferreirin[3] from *Ferreirea spectabilis* are first examples of isoflavanone.

In the present studies examination of the coloring principle of the heartwood of *Sophora japonica*, L.[4] led to the isolation of a new phenolic ketone. The writer wishes now to record that this compound is a new member of this class. It was obtained in pale yellow needles approximately in 0.02–0.5% yields from dry heartwood by ethanol extraction, followed by petroleum ether treatment. In reference to the source of this new compound, the name "sophorol" is suggested for this phenolic ketone.

Analyses of sophorol and molecular weight determination of its *O*-dimethyl derivative agree most closely with the molecular formula $C_{16}H_{12}O_6$. It is optically active, giving a value of $[\alpha]_D^{15}$ 9.5 in dry acetone and $[\alpha]_D^{16}$ -13.6 in absolute ethanol. The phenolic character of sophorol was suggested by its solubility in aqueous sodium carbonate and hydroxide and insolubility in aqueous sodium hydrogen carbonate, to yield yellow orange solutions. Alcoholic solution of sophorol gives no color with ferric chloride.[6] The presence of two phenolic hydroxyl groups was shown by the preparation of the *O*-dimethyl ether with methyl iodide–potassium carbonate in acetone or methylsulfate-caustic alkali. The same ether was also produced with ethereal diazomethane. On acetylation under various conditions sophorol gave an uncrystallizable product. On the other hand, sophorol oxime readily afforded a crystalline triacetate. Thus, it might be inferred that acetylation of sophorol was accompanied, in addition to the acetylation, by a side reaction in which carbonyl group participated (*vide infra.*) Indication of a reactive carbonyl group in sophorol was afforded by the formation of an oxime. *O*-dimethylsophorol also forms an oxime and 2,4,-dinitrophenylhydrazone. By the positive color tests[7] for a methylenedioxyl group the indication for two further oxygen atoms was added. Beroza's modified procedure[8] of a spectrophotometric method[9] for the determination of combined formaldehyde with chromotropic-sulfuric acids gave 0.58 and 0.63 mole of combined formaldehyde for the sophorol and *O*-dimethylsophorol respectively, showing the presence of one methylenedioxyl group.[10] Above mentioned methylenedioxyl

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[1] (a) F. Mayer and A. H. Cook, *The Chemistry of Natural Coloring Matters*, Reinhold, 2nd Printing, New York, 1947.

(b) T. R. Seshadri, *Annual Review of Biochemistry*, **20**, 487 (1951).

(c) H. Erdtman, *Progress in Organic Chemistry*, Butterworths, London, 1952, J. W. Cook, ed., Vol. I, pp. 31, 37.

(d) T. A. Geissman and Hinreiner, *Botan. Rev.*, **18**, 77 (1952).

(e) W. K. Warburton, *Quart. Revs.*, **8**, 67 (1954).

[2] N. Narasimhachari and T. R. Seshadri, *Proc. Indian Acad. Sci.*, 202 (1952).

[3] F. E. King and K. G. Neill, *J. Chem. Soc.* 4752 (1952).

[4] Order Leguminocea. *Sophora japonica*, L. is chiefly known by the existence of many anthoxanthins[5] in its flower buds and fruits. Its heartwood has a dark brown appearance.

[5] Ref. (2) (b) pp. 183, 188, 196. Also see J. F. Couch, J. Naghiski, and C. F. Krewson, *J. Am. Chem. Soc.*, **74**, 424 (1952), (for Rutin); J. Rabate, *Bull. soc. chim. biol.*, **22**, 565 (1940). K. Freudenberg, H. Knauber, and F. Cramer, *Ber.*, **84**, 44 (1951), (for Sophoraflavonoloside); G. Zemplen, R. Bognar, *Chem. & Ind. (London)*, 518 (1954), (for Sophoricoside); G. Zemplen and R. Bognar, *Ber.*, **75**, 482 (1942); R. Bognar, *Magyar Kem. Lapja*, **4**, 519 (1949), *Chem. Abstr.* 8104 (1952), (for Sophorabioside).

[6] It has been observed that in general 6.7. or 4′ hydroxyls in flavones are lacking in a ferric chloride color reaction. L. H. Briggs and R. H. Locker, *J. Chem. Soc.*, 3136 (1951).

[7] A. Labat, *Bull. soc. chim. France*, **5**, 745 (1909); K. Weber and B. Tollens, *Ann.*, **299**, 318 (1898); G. O. Gaebel, *Arch. Pharm.*, **248**, 225 (1910).

[8] M. Beroza, *Anal. Chem.*, **26**, 1970 (1954).

[9] C. E. Bricker and H. R. Johnson, *Ind. Eng. Chem. Anal. Ed.*, **17**, 400 (1945).

[10] Beroza has shown that pinoresinol acetate which contained no methylenedioxyl groups gave 0.79 equiv. of formaldehyde, probably being due to the formation of primary alcohol groups which upon hydrolytic scission produce formaldehyde (see Ref. 8). However, in present experiments it was verified that the γ-pyranone nucleus in the isoflavanone gives no noticeable formaldehyde, under Beroza's condition, using 7,2′,4′-trimethoxyisoflavanone.

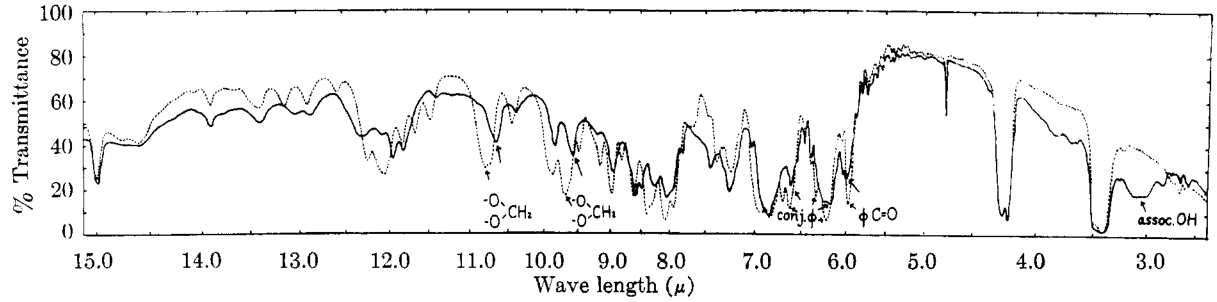
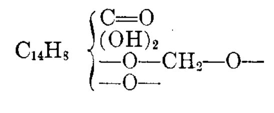


Fig. 1. Infrared spectra of sophorol (———) and *O*-dimethylsophorol (•———); Nujol paste

group was also detected by infrared spectra. According to L. H. Briggs *et al.*,[11] —C—O—C—O—C— group attached to the aromatic ring exhibits 12 major bands associated with this group. Among them, particularly those within the range from 1047 to 1025 cm.$^{-1}$ and from 938 to 919 cm.$^{-1}$ are diagnostic for the methylenedioxyl group.

The spectra of sophorol, *O*-dimethylsophorol and its hydrolyzed product (VII) show the corresponding strong bands for the methylenedioxyl group in 1044 (sophorol) 1032 (*O*-dimethyl) 1032 (hydrolyzed product VII) 939 (sophorol) 925 (*O*-dimethyl) 929 cm.$^{-1}$ (hydrolyzed product VII). Thus, the one remaining inert oxygen atom is probably present in the ether system. On the basis of above evidences the functional groups of sophorol can be symbolized as follows.



$$C_{14}H_8\left\{\begin{array}{l}C{=}O\\(OH)_2\\-O-CH_2-O-\\-O-\end{array}\right.$$

Infrared[12] *and ultraviolet spectra.* The infrared spectra of sophorol and *O*-dimethylsophorol in Nujol mull are shown in Fig. 1.

The maxima are as follows (cm.$^{-1}$): (a) Sophorol 3333~3195 (associated phenolic hydroxyl) 1661 (carbonyl conjugated with phenyl) 1618, 1575, 1508 (conjugated phenyl) 1340, 1239, 1163, 1116, 1044, 1015, 948, 843, 675.

(b) *O*-dimethylsophorol (cm.$^{-1}$): 1672, 1575, (CO—C = C— in a six membered ring) 1603, 1506 (conjugated phenyl) 1353, 1258, 1236, 1190, 1160, 1114, 1092, 1044, 1032, 1013, 966, 927, 836, 822, 675.

The absence of absorption near 3 μ in *O*-dimethylsophorol shows the lack of any alcoholic hydroxyl in sophorol.

The examination of the ultraviolet absorption spectra of sophorol and *O*-dimethylsophorol in ethanol and aqueous caustic solution gave valuable information. The absorption curves are shown in Fig. 2.

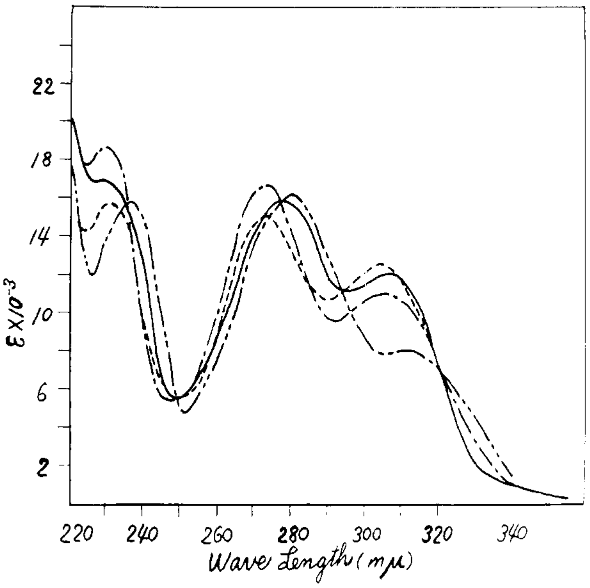
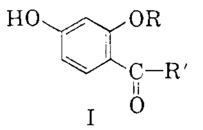


Fig. 2. Ultraviolet spectra of sophorol (———), *O*-dimethylsophorol (—•—•—), 2′,7-dimethoxy-3′,4′-methylenedioxyisoflavanone (- - - -), and 7′-hydroxy-3′,4′-methylenedioxyflavanone (—— — ——); solvent ethanol

It was found that the spectra of these two compounds were strikingly similar to those of 7-hydroxy (methoxy) 2- or 3-phenyl chromanone derivatives.[13,14] Furthermore, the ultraviolet absorption spectrum of sophorol showed a marked red shift in aqueous 0.1*N* sodium hydroxide solution (Fig. 3). These characteristic spectral properties are those[15] of resacetphenone chromophore, as exactly to be shown in Fig. 3.

Consequently it seemed reasonably certain that sophorol contains a partial formula (I).



I

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[11] L. H. Briggs, L. D. Colebrook, H. M. Fales, and W. C. Wildman, *Anal. Chem.*, **29**, 904 (1957).

[12] The writer is indebted to Mr. A. Fujino and Mr. M. Yamaguchi of Osaka City University for these spectra.

[13] B. Skarzynski, *Biochem. Zeit.*, **301**, 150 (1939). The ultraviolet spectra of 7-hydroxyisoflavanone and specimen of 7-hydroxy-3′,4′-methylenedioxyflavanone were kindly supplied by Dr. S. Hishida and Dr. N. Inoue of Tohoku University.

[14] R. B. Bradbury and D. E. White, *J. Chem. Soc.*, 871 (1953).

[15] R. A. Morton and Z. Sawires, *J. Chem. Soc.*, 1052 (1940).

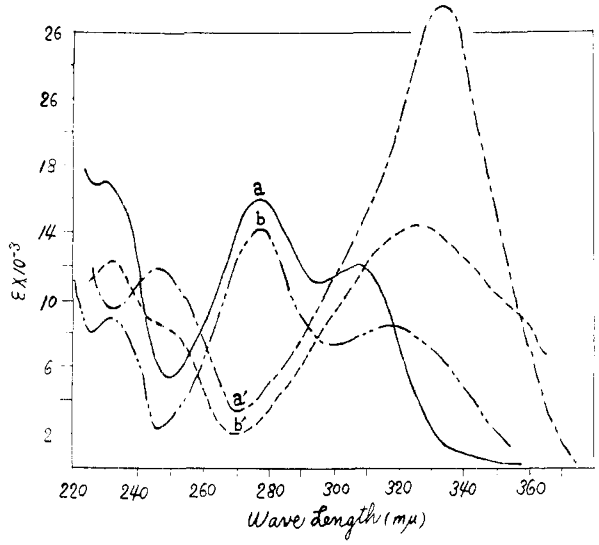
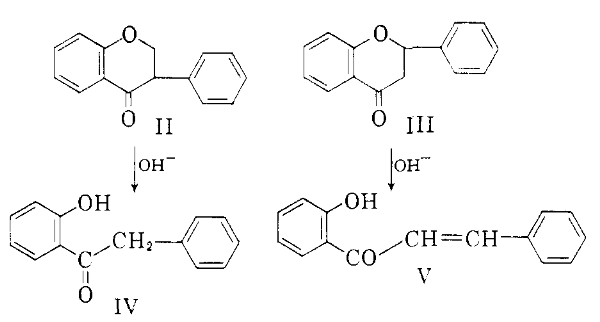


Fig. 3. Ultraviolet spectra: (a) sophorol. (b) resacetophenone (solvent ethanol). (a') sophorol (solvent 0.12*N* aqueous NaOH). (b') resacetophenone (solvent 0.1*N* aqueous NaOH).

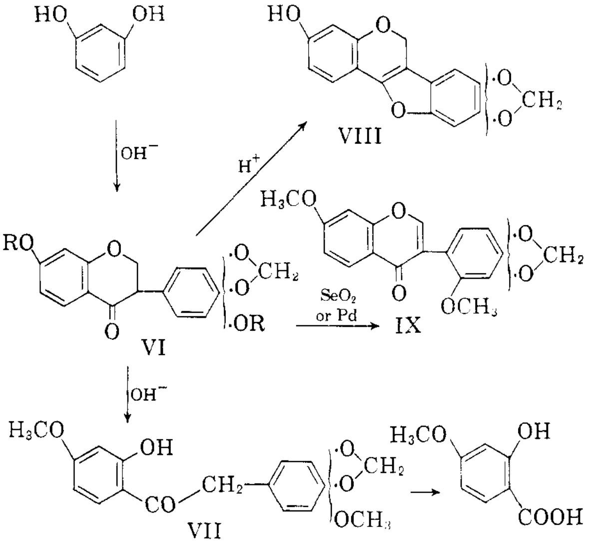
On the basis of above spectroscopic and analytical proof isoflavanone or flavanone structure for sophorol may be reasonably considered. In consistency with these facts sophorol contains no aliphatic double bonds since *O*-dimethylsophorol resists oxidation by potassium permanganate in acetone even when heated to boiling for several hours.

It is well known that flavones, flavonols, flavanones, 3-methoxyflavones, and isoflavones each show the characteristic color reactions,[16,31] by sodium amalgam or magnesium-hydrochloric reduction. Further, it has been shown that isoflavanone ferreirin also gave characteristic color on reduction by sodium amalgam.[3] Although sophorol did not give the characteristic color by sodium amalgam reduction, *O*-dimethylsophorol afforded a feeble pink color by treatment with same reagent. The Wilson boric acid test[17] for both compounds gives no color reaction. These color reactions suggest that sophorol is an isoflavanone, but not a flavanone.

The simplest method of differentiation between an isoflavanone (II) and flavanone (III) is the examination of the products of mild alkaline degradation, since the former furnishes an *O*-hydroxydesoxybenzoin (IV)[3] with loss of carbon probably as formaldehyde, while a flavanone leads to an *O*-hydroxychalcone (V).[18]



The schema of degradation concerning sophorol and *O*-dimethylsophorol is revealed to be as indicated in VII–IX.



On being fused with alkali in a nitrogen atmosphere, dimethylsophorol undergoes extensive degradation of the molecule and gives rise to resorcinol which fact is presumably due to the part structure (I). With prolonged treatment by hot 20% alcoholic potassium hydroxide in a nitrogen stream, *O*-dimethylsophorol yielded a saturated phenolic ketone $C_{17}H_{16}O_6$ (VII) which was isolated from neutral fraction as sole product. This compound exhibited an intense ferric reaction in alcohol and still kept two methoxyl groups as well as a positive methylenedioxyl color test. The ketone was evidently stable to the further action of alcoholic caustic potash. The ultraviolet absorption curve of this ketone closely resembles that of *O*-dimethylsophorol and it is clear that the main chromophoric system of the latter is unaffected by the alkaline degradation (Fig. 4).

This ketone gives a green color with nitric acid. This is property of certain hydroxyacetophenone derivatives and its methyl ethers.[19] The Zimmermann test[20] for active methylene and Weygand

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(16) L. H. Briggs and R. H. Locker, *J. Chem. Soc.*, 2157 (1949). Wolfrom, Benton, Gregory, Hess, Mohan, and Morgan, *J. Am. Chem. Soc.*, **61**, 2832 (1939). M. Shimizu, *J. pharm. chem. Japan*, 1329 (1951).

(17) C. W. Wilson, *J. Am. Chem. Soc.*, **61**, 2303 (1939).

(18) S. Fujise, *J. Chem. Soc. Japan.*, 497 (1929).

(19) Rao and Seshadri, *Proc. Ind. Acad. Sci.*, **A 30**, 30 (1949).

(20) W. Zimmermann, *Zeit. physiol. chem.*, **233**, 257 (1935).

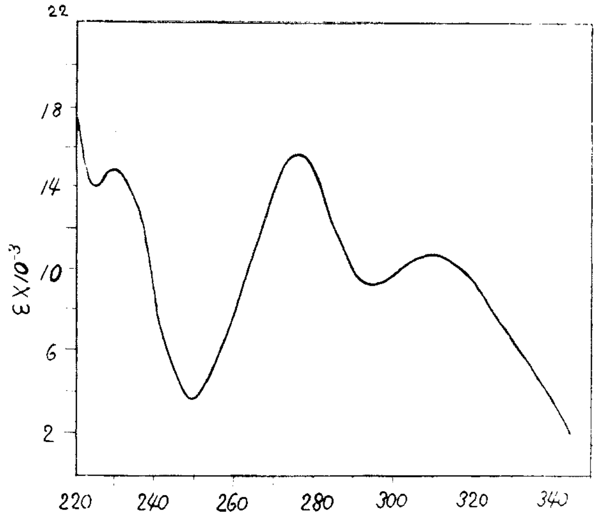

Fig. 4. Ultraviolet spectrum of hydrolyzed product (VII) of *O*-dimethylsophorol; solvent ethanol

test[21] for endiol also were positive. Further, this ketone formed the precipitation of 2,4-dinitrophenylhydrazone and showed a strong infrared band, being due to a hydrogen-bonded carbonyl of *O*-hydroxyacetophenone,[22] at 1639 cm.$^{-1}$ (Fig. 5).

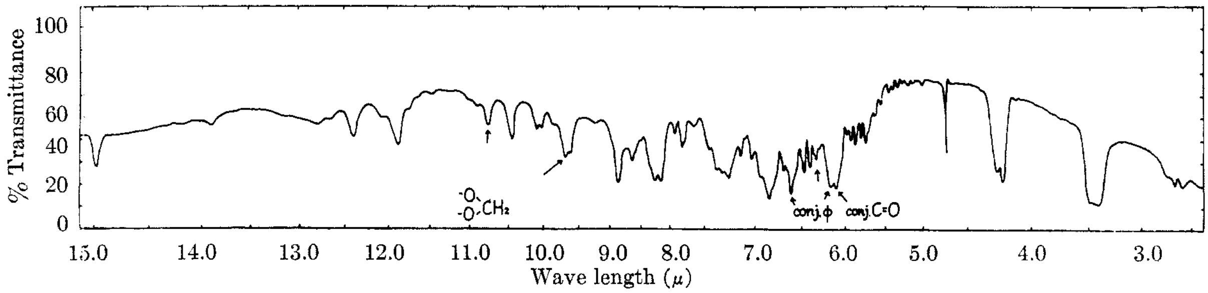

Fig. 5. The infrared spectrum of hydrolyzed product (VII) of *O*-dimethylsophorol; Nujol paste

These facts may be explained by giving partial formula (VII) for this ketone.[23] By the isolation of this desoxybenzoin derivative from the alkaline degradation product, flavanone structure for sophorol was excluded entirely and parent *O*-dimethylsophorol and sophorol are formulated as in (VI) R = CH_3, R = H, respectively.

Attempts to clarify the relative positions of the substituents in the side phenyl group of above ketone (VII), by oxidation with permanganate under various conditions were unsuccessful. Thus, the oxidation of this ketone with aqueous permanganate in boiling acetone gave only a phenolic acid as the product. It was identified as 4-methoxysalicylic acid by comparison with authentic specimen, thus only confirming the presence of the chromophoric group (I) in the molecule.

When treated with boiling diluted sulfuric acid for 2 hours sophorol was converted to form a compound which is designated "anhydrosophorol" and was indifferent to carbonyl reagents. The lack of carbonyl group in this substance was confirmed by the disappearance of infrared absorption band at 1661 cm.$^{-1}$ in original material. Analytical data are in agreement with a molecular formula $C_{16}H_{10}O_5$, showing the elimination of one molecule of water. The ultraviolet absorption spectrum of anhydrosophorol in ethanol is markedly different from that of sophorol. The change of the spectra of sophorol into anhydrosophorol is similar to that observed on the conversion of rotenone into the corresponding enol acetate.[24] (Fig. 6).

Similar example is found in the change of spectra of isoflavanone to isoflav-3-en[14] (Fig. 7). Consequently, it is probable that the change of spectrum which occurred with dehydration of sophorol is due to acid-catalyzed cyclodehydration giving a coumarone ring system. In fact, the disappearance of carbonyl band in infrared spectrum of anhydrosophorol will support the above conversion. It is therefore almost certain that phenolic hydroxyl in the side phenyl nucleus of sophorol occupies position 2′. Apparently similar examples of this reaction have been recorded by Spetz[25] and Laforge,[26] who found that 2′-hydroxydesoxybenzoins were

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(21) F. Weygand and E. Csendes, *Ber.* **85**, 45 (1952).

(22) H. L. Hergert and E. F. Kurth, *J. Amer. Chem. Soc.*, **76**, 1622 (1953).

(23) In early degradative experiments, somewhat impure material was submitted to alkaline degradation. In this case the ketone $C_{17}H_{16}O_5$ was isolated in place of ketone $C_{17}H_{16}O_6$, and the former was identified as 2′,4′,4-trimethoxy-2-hydroxydesoxybenzoin. This result led to the suspicion that the dimethylsophorol might be identical with 2′,4′,7-trimethoxyisoflavanone which had already been derived in optically active form from homopetrocarpin, one of the minor constituents of *Pterocarpus santalinus*, by Robertson, (see Ref. 31). Thus, the DL-2′,4′,4-trimethoxyisoflavanone was synthesized through the catalytic hydrogenation of the corresponding isoflavone with Adams' catalyst; it showed the melting point 128° ∼ 131°. The melting point of *O*-dimethylsophorol was depressed by mixing with a synthetic product. Therefore, 2′,4′,7-trimethoxyisoflavanone formula for the dimethylsophorol was excluded. By above mentioned results, though it might be supposed that the above isoflavanone existed in crude sophorol, unfortunately attempts for isolation of this substance were unsuccessful.

(24) R. S. Cahn, R. F. Phipers, and J. J. Boam, *J. Chem. Soc.*, 513, 734 (1938).

(25) Åke Spetz, *Acta. Chem. Scand.*, **10**, 1422 (1956).

(26) F. B. Laforge, *J. Am. Chem. Soc.*, **55**, 3040 (1933).

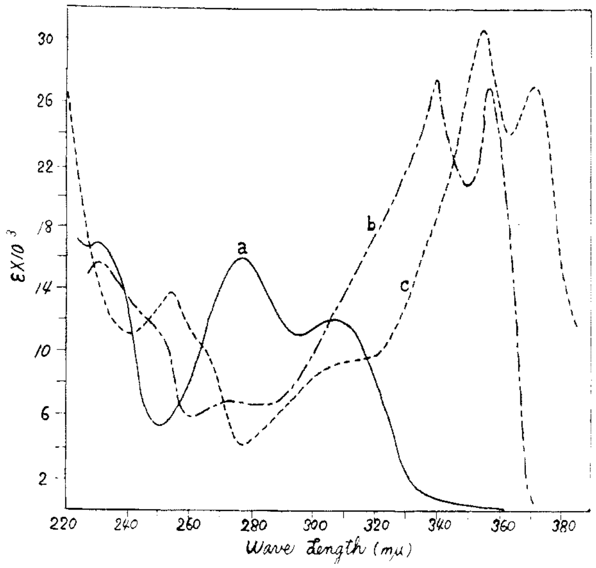


Fig. 6. Ultraviolet spectra of sophorol (curve a), anhydrosophorol (VIII) (curve b), and acetylrotenone (curve c); solvent ethanol

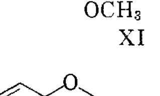
readily dehydrated to the corresponding coumarones when treated with strong acids. On the basis of these results three formulas (X), (XI), (XII), and (XIII), (XIV), (XV), may be considered for a ketone (VII) and the parent dimethylsophorol respectively.

The isoflavone which corresponds to formula (XIII) has already been synthesized by Robertson and Whalley in the course of the elucidation of the structure of pterocarpin.[27] Furthermore, the active form of the corresponding isoflavanone has been derived from pterocarpin by hydrogenolysis followed by methylation of hydroxyl and oxidation[28] (ultraviolet spectrum, Fig. 2). Thus, the conversion of *O*-dimethylsophorol to the corresponding isoflavone was attempted. When *O*-dimethylsophorol was treated with palladized charcoal and cinnamic acid as hydrogen accepter[29] at about 200° in nitrogen stream, a new ketone, $C_{18}H_{14}O_6$, (IX) was obtained. The same substance was obtained also by selenium dioxide oxidation[30] in amyl alcohol. The isoflavone structure of the new ketone was evident from the appearance of a red color upon reduction with sodium amalgam followed by acidification. The same color reaction was not shown with magnesium and HCl.[31] Further, the new ketone had melting point 203–5°, being very similar to that of synthetic 2′, 7-dimethoxy-3′, 4′-methylenedioxyisoflavone, (m.p. 203°). However, the melting point of synthetic isoflavone,[27] kindly provided by Dr. W. B. Whalley through the courtesy of Professor A. Robertson, depressed on admixture with the ketone $C_{18}H_{14}O_6$. The ultraviolet absorption spectra of both isoflavone and 2′,4′,7-trimethoxyisoflavone is shown in Fig. 8.

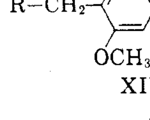
Therefore, formula XIII is definitely excluded, and dimethylsophorol must be either XIV or XV.

R=

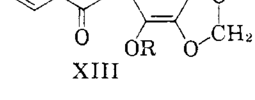

X



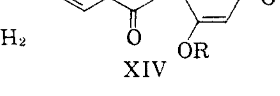
XI



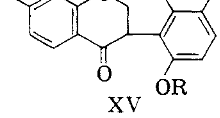
XII



XIII



XIV



XV

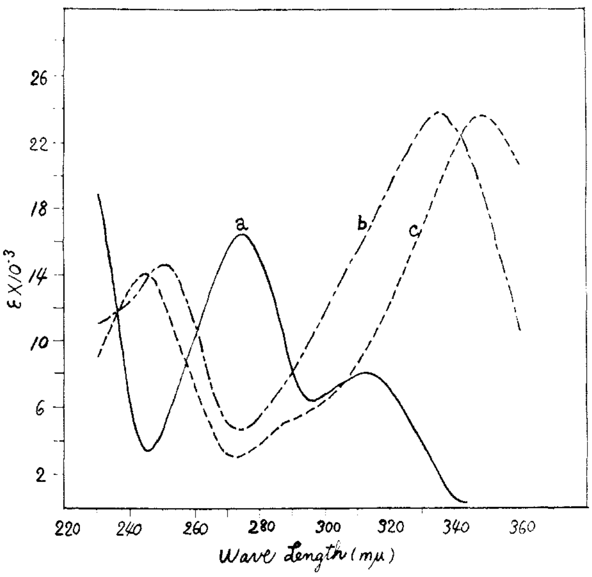


Fig. 7. Ultraviolet spectra of 4′,7-dimethoxyisoflavanone (curve a), 4′,7-dimethoxyisoflav-3-en (curve b), and 7-methoxy-3-*p*-methoxyphenylcoumarin (curve c) (from a paper of R. B. Bradbury and D. E. White)

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[27] A. Robertson and W. B. Whalley, *J. Chem. Soc.*, 1440 (1954). The ultraviolet absorption maximum of 2′,7-dimethoxy-3′,4′-methylenedioxyisoflavone (Fig. 8) are as follows. λ_{max} (alcohol) 247, 295, inflection 304 mμ (ε; 25680, 11610, and 10870).

[28] A. McGookin, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 787 (1940). Precious specimen of 2′,7-dimethoxy-3′,4′-methylenedioxyisoflavanone which was derived from pterocarpine was provided by Dr. W. B. Whalley. The ultraviolet spectrum; λ_{max} (ethanol) 231, 273, and 304 mμ (ε; 15850, 15120, and 12640).

[29] T. Kubota, *J. Chem. Soc. Japan*, 604 (1939).

[30] N. Narasimhachari and T. R. Seshadri, *Proc. Ind. Acad. Science*, **35**, Sec A. 202, (1952).

[31] S. H. Harper, *J. Chem. Soc.*, 595 (1942). Wolfrom, *J. Am. Chem. Soc.*, **63**, 1248 (1941).

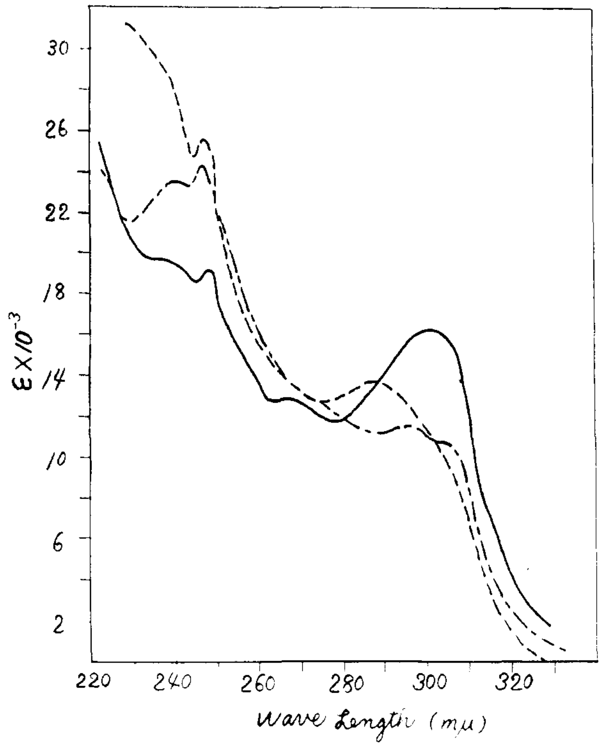

Fig. 8. Ultraviolet spectra of 2′,7-dimethoxy-3′,4′-methylendioxyisoflavone (– – – –), 2′,4′,7-trimethoxyisoflavone (—·—·—) and selenium oxidation product $C_{18}H_{14}O_6$ (IX) (———); solvent ethanol

Though no definite proof can be given so far for the constitution of the new ketone the phytochemical evidence, the nonexistence of any naturally occurring 2′,5′,6′-trisubstituted flavone, favors the formula XIV. Furthermore, it is of interest to note that formula XIV contains the essential core of rotenoide.[32] By analogy with rotenone and pachyrhizon,[32b] of the remaining alternatives, the present writer prefers formula XIV R′ = OCH_3 for dimethylsophorol. Therefore, sophorol should be considered to be formulated as formula XIV, R = H. The occurrence of 2′-hydroxyisoflavanones, ferreirin, homoferreirin,[3] and sophorol, in nature is of interest in connection with the biogenesis[33] of pterocarpin and homopterocarpin. It is considered that the formation of anhydrosophorol from sophorol suggests a possible synthetic route for pterocarpin and homopterocarpin. Further, sophorol is unique in that it is optically active isoflavanone. Synthetic work about sophorol and related compounds is now in progress.

EXPERIMENTAL[34]

Isolation and purification of sophorol. The ground heartwood of *Sophora japonica*, L. (3.0 kg.) was extracted with ethanol (9.1) at room temperature for 2–4 days. The deep red extract was then concentrated to about 200 ml. under diminished pressure. After the solution was shaken with petroleum ether (200 ml. × 4) brown solid (9.3 g.–33.5 g.) deposited during 1–2 weeks.

When the deposited solid was digested with boiling diluted methanol (methanol-water 1:1) hot methanolic solution separated a crude sophorol. It was treated with a small volume of warm benzene. From a soluble part in warm benzene the solvent was distilled off. Residual light brown solid (0.5–10 g.) was recrystallized repeatedly from diluted acetone, yielding colorless plates m.p. 178.5–179°. After drying under vacuum the melting point of this compound rose to 180–181°.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.12; H, 4.93. Found: C, 65.68; H, 4.69; in a sample dried at 100–110° *in vacuo:* C, 67.67, 67.33; H, 4.41, 4.58.

This material is soluble in aqueous sodium hydroxide and had the positive color tests for a methylenedioxyl group, but detailed examination for the constitution was deferred. After the part insoluble in warm benzene was crystallized repeatedly from diluted acetone a pure sophorol separated as slightly pale yellow short needles, m.p. 215° (slight decomp.) (0.6–15 g.).

Anal. Calcd. for $C_{16}H_{12}O_6$: C, 64.00; H, 4.03. Found: (sample dried at 100–110° *in vacuo*) C, 64.18, 63.96, 63.91; H, 4.40, 4.37, 4.24.

Light absorption in ethanol (Fig. 2), λ_{max} 230, 277, and 307.5 mμ (ε: 16950, 15950, and 12090); in aqueous 0.1*N* NaOH solution (Fig. 3) λ_{max} 246 and 332 mμ (ε: 11950, 27570) $[\alpha]_D^{15}$ 9.5 (acetone), $[\alpha]_D^{16}$ −13.6 (absolute ethanol). Combined formaldehyde determination[8] 0.58. Purified material from diluted acetone shown 0.6% methoxyl content by Zeizel determination, being due to the trace of impurity. However, it was difficult to remove this completely by recrystallization. Sophorol dissolved readily in acetone, ethylacetate, dioxane, and the simple alcohols, sparingly in chloroform, benzene, and did not dissolve in water. It gave neither ferric reaction in alcohol nor precipitate with alcoholic lead tetraacetate. It did not give characteristic color reaction with magnesium-hydrochloric acid or on sodium amalgam reduction. Alkaline solution of sophorol developed red color by application of *p*-diazobenzenesulfonic acid. Sophorol gave a yellow orange solution in concentrated sulfuric acid. The solution became a green color with a drop of 5% alcoholic gallic acid but the color reaction with phloroglucin-sulfuric acid for combined formaldehyde was very sluggish. It dissolved to yellow in aqueous 2*N* sodium hydroxide and darkened in air. Sophorol reduced an ammoniac silver nitrate and Fehling's solution with heating on the water bath.

Sophorol O-dimethyl ether. (a) *With diazomethane.* Sophorol (2 g.) in acetone (20 cc.) was treated with an ethereal solution of diazomethane (from nitrosomethylurea 3.2 g.) and set aside overnight. Evaporation under diminished pressure and recrystallization of the crystalline residue from diluted acetone yielded *O*-dimethylsophorol (0.7 g.) as optically inactive colorless short needles, m.p. 136–138°.

Anal. Calcd. for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91; Mol. wt., 328; $2OCH_3$, 18.9. Found: in a sample dried *in vacuo* at 100–110°: C, 65.25, 65.66; H, 4.73, 4.85; $2OCH_3$, 22.24; Mol. wt., 326 (Rast).

Light absorption (Fig. 2) λ_{max} (alcohol) 230, 273, and 306 mμ (ε: 18830, 16650, and 11030). *O*-dimethylsophorol dissolved readily in acetone, dioxane, and the simple alco-

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(32) (a) A. A. Morton, *The Chemistry of Heterocyclic Compounds*, McGraw-Hill, New York, 1946, p. 172.

(b) H. Bickel and H. Schmid, *Helv. Chim. Acta*, **36**, 664 (1953). Also see Sir. R. Robinson, *The Structural Relations of Natural Products*, Oxford University Press, 1955, p. 43.

(33) J. A. Ballantine and W. B. Whalley, *J. Chem. Soc.*, 3225 (1956).

(34) Melting points uncorrected. The ultraviolet absorption spectra were measured on either a Beckman Model D.U. spectrophotometer or on a Shimazu spectrophotometer in alcohol.

hol, moderately in benzene, and did not dissolve in water. It dissolved in concentrated sulfuric acid to yellow and gave a blue color with one drop of 5% alcoholic gallic acid solution indicative of a methylenedioxyl group. Combined formaldehyde determination[8,9] 0.63. When alcoholic solution of *O*-dimethylsophorol was reduced by sodium amalgam, pink color was gradually developed. Magnesium-hydrochloric acid reduction did not give the same color. *O*-dimethylsophorol was insoluble in 2*N* alkali and did not react with acetylating agents. It can be distilled at 260–270° (bath temp.) under 0.5 mm. The 2,4-dinitrophenylhydrazone slowly deposited from sulfuric alcoholic 2,4-dinitrophenylhydrazine solution. On recrystallization from diluted alcohol and acetic acid it formed red orange crystals, m.p. 180–181° (decomp.).

Anal. Calcd. for $C_{24}H_{20}O_9N_4$: N, 11.02. Found: N, 9.62.

The isomerization of *O*-dimethylsophorol (84 mg.) was tried in 1 ml. of acetic acid with 0.3 ml. of concentrated hydrochloric acid on the steam bath for 1 hr., but the original compound was recovered unchanged.

(b) *With methyl iodide.* Sophorol (0.50 g.), in dry acetone (10 cc.), was refluxed for 6 hr. with methyl iodide (2.5 cc.) and anhydrous potassium carbonate (1.5 g.). After isolation from the acetone liquor, *O*-dimethylsophorol (0.27 g.) crystallized from diluted acetone in colorless needles m.p. 136–138° and was identical to the product isolated in procedure (a).

(c) *With methylsulfate.* Thirty per cent aqueous sodium hydroxide solution was added dropwise to a mixture of sophorol (2 g.) and methyl sulfate (20 cc.) in methanol (40 cc.). After the violent reaction took place, solution became a greenish yellow and then formed precipitation. The solution was diluted with water, then set aside overnight. Next day resultant precipitation was washed and crystallized from diluted acetone, giving a *O*-dimethylsophorol, m.p. 136–138°.

O-Dimethylsophorol oxime. Sophorol dimethyl ether (100 mg.) and hydroxylamine hydrochloride (50 mg.) were heated on the water bath for 2 hr. in anhydrous pyridine (0.5 cc.) and absolute ethanol (0.5 cc.). When the solvent was evaporated and diluted with water, the oxime (70 mg.) separated. Recrystallized from diluted methanol, it formed colorless crystals decomposing at 194–195.5°.

Anal. Calcd. for $C_{18}H_{17}O_6N$: N, 4.08. Found: N, 3.34.

Sophorol oxime. Oximation of sophorol (100 mg.) as described for the *O*-dimethyl derivative gave the oxime (80 mg.). It was recrystallized from water, decomposing at 204°.

Anal. Calcd. for $C_{16}H_{13}O_6N$: N, 4.44. Found: N, 4.00.

Sophorol oxime triacetate. Sophorol oxime (200 mg.) in pyridine (1.2 cc.) was acetylated with acetic anhydride (2 cc.) by a standard procedure. After repeated crystallizations from diluted acetone it crystallized in beautiful colorless leaflets, and melted at 163.5–165.5°, not dissolving in aqueous sodium hydroxide.

Anal. Calcd. for $C_{22}H_{19}O_9N$: C, 59.86; H, 4.34; N, 3.17. Found: C, 61.30; H, 4.69; N, 2.99.

Potash fusion of O-dimethylsophorol. O-Dimethylsophorol (2.0 g.) was thoroughly mixed with finely powdered potassium hydroxide (20 g.) and heated in a nitrogen stream from 50° to 250° for 20 min., and then in 250–270° for 30 min. (bath temp.).

After cooling, the melt was dissolved in water; the resulting solution was acidified with diluted sulfuric acid and extracted with three 100-ml. portions of ether.

The ethereal solution was extracted with three 50-ml. portions of 5% sodium hydrogen carbonate (Fraction A), and then two 50-ml. portions of 2*N* aqueous sodium hydroxide (Fraction B), successively. No noticeable residue was obtained from evaporation of mother ether liquor.

Fraction A was acidified with diluted sulfuric acid, and the resinous product (606 mg.), was extracted with three 50-ml. portions of ether; it gave no recognizable compound. Fraction B was acidified with diluted sulfuric acid and extracted with three 50-ml. portions of ether. The solution was washed with a small volume of water and the solvent distilled off. On vacuum distillation at 220–240°/10^{-2} mm., residual red brown phenolic fraction yielded resorcinol (325 mg.). On recrystallization from ether–petroleum benzine it melted at 110–111° which was identical in every way with authentic specimen.

The alkaline hydrolysis of O-dimethylsophorol. O-Dimethylsophorol (1 g.) in alcohol (20 cc.), containing potassium hydroxide (5 g.) and water (5 cc.) was boiled under reflux in an atmosphere of nitrogen for 5 hr.

After alcohol was removed in vacuum the residue was diluted with water (25 cc.) and extracted with three 100-ml. portions of ether. Evaporation of the washed and dried ethereal liquor gave a yellow oily product (738 mg.), which gradually solidified. On distillation at 205–240° (bath temp.)/0.03 mm. this product yielded pale yellow distillate (440 mg.) which solidified quickly. After repeated crystallization from diluted acetone the distillate gave a ketone (VII) in colorless silky needles, m.p. 120–123°, having an intense reddish-brown ferric reaction in alcohol and not dissolving in cold aqueous sodium hydroxide. It dissolved in nitric acid to green color. Its yellow sulfuric acid solution gave a green color with a drop of 5% alcoholic gallic acid solution. The alcoholic solution gave an orange colored precipitation with alcoholic sulfuric 2,4-dinitrophenylhydrazine solution.

Anal. Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10; $2OCH_3$, 19.6%. Found: C, 65.15; H, 5.59; OCH_3, 22.3%.

Ultraviolet spectrum, (Fig. 4); combined formaldehyde determination,[8,9] 0.64. The mother alkaline layer in ether extraction was saturated with carbon dioxide and extracted with three 50-ml. portions of ether. Evaporation of the solvent yielded residue (142 mg.) which exhibited intense ferric reaction, but no homogeneous compound could be obtained.

Oxidation of the ketone (VII). Potassium permanganate (1.25 g.) in water (50 cc.) was added under reflux dropwise during 4 hr. to the foregoing ketone (699 mg.) in acetone (30 cc.). Next day, the mixture was cleared with sulfur dioxide, and extracted with ether. The oily residue left on evaporation of the extract was redissolved in ether (50 cc.) and agitated with three successive portions of 5% sodium hydrogen carbonate (20 cc. each). Acidification of the combined sodium hydrogen carbonate extracts gave 2-hydroxy-4-methoxy benzoic acid which was isolated with ether of three 100-ml. portions and purified by crystallization from hot water, forming needles (11 mg.), m.p. and mixed m.p. 153°, identified by comparison with an authentic specimen.

Anal. Calcd. for $C_8H_8O_4$: C, 57.14; H, 4.80; OCH_3, 18.5. Found: C, 57.26; H, 4.90; OCH_3, 19.2.

Evaporation of the washed and dried ethereal mother liquor remaining after the separation of 2-hydroxy-4-methoxybenzoic acid gave a resinous product (702 mg.). After washing with ether repeated crystallization from diluted ethanol yielded a product of 20 mg. in pale brown prisms, m.p. 170–172°, having an intense reddish-brown ferric reaction in alcohol and not dissolving in aqueous cold 2*N*-sodium hydroxide. It dissolved to pink color in concentrated sulfuric acid. Further investigations on this compound were prevented by lack of material.

Dehydrogenation of O-dimethylsophorol. (a) *With selenium dioxide. O*-Dimethylsophorol (245 mg.) and selenium dioxide (300 mg.) were refluxed in amyl alcohol (10 cc.) for 12 hr. After selenium was removed and washed with ether, the filtrate and washings were collected. On being diluted with a little ether, a product (40 mg.) slowly deposited which melted at 190–198°. On repeated crystallizations from methanol the precipitate formed feeble pink-colored needles, m.p. 203–205° of dehydro-*O*-dimethylsophorol (IX). Ultraviolet absorption spectrum (Fig. 8).

Anal. Calcd. for $C_{18}H_{14}O_6$: C, 66.25; H, 4.32; $2OCH_3$, 19.0. Found: C, 66.45, 66.50; H, 4.40, 4.60; $2OCH_3$, 19.9.

Reduction with sodium amalgam and acidification produced pink coloration. It gave no precipitation by addition of Brady's reagent. Evaporation of mother liquor under diminished pressure left a residue (238 mg.).

On being purified from diluted acetone, original *O*-dimethylsophorol (57 mg.) was recovered unchanged.

(b) *With palladized charcoal and cinnamic acid. O*-Dimethylsophorol (300 mg.) and 30% palladized charcoal[35] (150 mg.) were heated in cinnamic acid (0.7 g.) under stream of carbon dioxide for 2.75 hr. at about 190–200°. The melt having intense odor of β-phenylpropionic acid was dissolved in ether. The residue insoluble in ether, containing catalyst was dissolved in acetone. After the catalyst was filtered off the removal of acetone yielded 45 mg. of residual solid. Recrystallization from diluted acetone gave the dehydro-*O*-dimethylsophorol in pale pink-colored needles m.p. 201–203°, identical with a specimen from selenium dioxide oxidation. From orange-colored ether solution the solvent was distilled off. After washing of residual solid with aqueous-2*N*-caustic alkali and water successively, residue (250 mg.) (m.p. 70–130°) was purified from diluted acetone, giving the original *O*-dimethylsophorol (50 mg.).

The synthesis of DL-*7,2′,4′-trimethoxyisoflavanone.* 7,2′,4′-Trimethoxyisoflavone (200 mg.), Adams' platinum oxide (20 mg.), and glacial acetic acid (12 cc.) were shaken under hydrogen at 1 atm. for 56 min., 1.3 moles of hydrogen being absorbed. After removal of catalyst and acetic acid (*in vacuo*), DL-7,2′,4′-trimethoxyisoflavanone was obtained as colorless needles, m.p. 128–130° (70 mg.) (from acetone-water).

Anal. Calcd. for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77; $3OCH_3$, 29.6. Found: C, 68.20; H, 5.66; OCH_3, 29.0.

Ultraviolet absorptions; (Fig. 8) (alcohol) λ_{max} 229, 272, and 306 mμ (ε, 26800, 20000, and 10420).

The presence of a carbonyl group was confirmed by the infrared absorption spectrum, which showed a strong band at 1677 cm.$^{-1}$ in Nujol mull.

Anhydrosophorol (VIII). Sophorol (500 mg.) was heated under reflux with 4% sulfuric acid (50 ml.) for 2 hr. After the solution was cooled the deposited amorphous solid was collected by filtration, and recrystallized repeatedly from diluted ethanol (alcohol:water 3:2), giving anhydrosophorol (VIII) in colorless needles, m.p. 225–226° (decomp.), which darkened in a few days and gave a faint green ferric reaction in methanol. Original sophorol (200 mg.) was recovered unchanged from the filtrate.

Anal. Calcd. for $C_{16}H_{10}O_5$: C, 68.08; H, 3.57. Found: C, 67.89; H, 3.82.

Anhydrosophorol rapidly decolorizes potassium permanganate in acetone. This compound is easily soluble in acetone, dioxane, and soluble in alcohol, glacial acetic acid, ethyl acetate, while insoluble in water, chloroform, benzene, and light petroleum. It dissolves in hot aqueous 2*N*-sodium hydroxide but not in cold solution. Further, the compound reduces Tollens-reagent, and its warm alkaline solution develops red-orange color with diazobenzenesulfonic acid. The infrared spectrum showed a band at 3420 cm.$^{-1}$ (phenolic hydroxyl).

Durham test[36] *for O-dimethylsophorol.* When the crystals of *O*-dimethylsophorol were treated with a drop of concentrated nitric acid on a porcelain plate a red color developed, which quickly changed to green. The addition of a few drops of ammonia gave a violet color. On the other hand, when acetone solution of the compound was treated by Jones' method[37] a deep violet color was produced.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT AND OCEANOGRAPHIC INSTITUTE OF THE FLORIDA STATE UNIVERSITY]

Polycondensation of Thermal Precursors of Aspartic Acid[1]

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Anhydropolyaspartic acid has been synthesized by heating unsubstituted aspartic acid. It is found that the anhydropolyaspartic acid may be prepared by heating monoammonium malate, maleamic acid, and combinations of asparagine and malic acid, maleamic acid and malic acid. Postulated pathways to form anhydropolyaspartic acid are discussed and the resulting polymers are characterized.

A century ago, aspartic acid was prepared by heating ammonium fumarate or ammonium malate.[2] Recently it has been emphasized that thermal homopolymerization accompanies these reactions.[3] On the other hand, heating unsubstituted aspartic acid also yielded a homopolymer which gave aspartic acid upon hydrolysis.[4,5] It is reported in this paper that the infrared absorption spectra of these two aspartic acid homopolymers prepared from

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