3′,4′-heptamethoxyflavone,[5,6] auranetin (3,6,7,8,4′-pentamethoxyflavone),[7] and sinensetin (5,6,7,3′,4′-pentamethoxyflavone)[8–10] have been found in peels or peel oils from tangerine,[1,3] orange,[2,4–10] and grapefruit.[5]

The present contribution is part of a continuing study of orange peel constituents that may affect the flavor of products. It is specifically concerned with the identification of a sixth fully methoxylated flavone, tetra-O-methylscutellarein (5,6,7,4′-tetramethoxyflavone). This is a known compound but, as far as the writer is aware, this is the first report of its occurrence in nature.

Since the flavone was not alkali soluble, it was considered to have no free phenolic or other acidic groups. A negative reaction to ferric chloride and alkalies substantiated this.

Failure of the demethylated flavone to give color or a precipitate with neutral lead acetate indicated no 3-OH group and the absence of *o*-di-OH groups in the B ring. A negative gossypetone test on the demethylated substance showed that either the 5- or 8-positions might be substituted but probably not both. Identification of degradation fragments of the molecule as 6-OH-2,3,4-trimethoxyacetophenone and anisic acid indicated that the flavone possessed methoxyl groups in the 5-, 6-, 7-, and 4′-positions. Final identification depended upon agreement of the infrared spectrum with that of an authentic sample[11] of tetra-O-methylscutellarein when both were run in carbon disulfide solution.

Tetra-O-methylscutellarein was found by Wessely and Moser to exist in two forms melting at 142 and 158–161°.[12] Usually, the higher melting form is obtained, but in the present study, the melting point was found to be 141.9–142.4° (cor.). Herz and Sumi recently obtained a melting point of 163–164° for this compound.[11]

Since the authentic sample was obtained from these investigators and was of the higher melting variety, a mixture melting point determination was not made.

Experimental

In a paper by Swift,[2] a procedure is given for separating the neutral constituents of an extract of orange peel juice. Briefly, this involved extraction of the filtered juice with benzene followed by treatment of the extract with dilute alkali to remove acidic substances and of the resulting extract residue in aqueous–ethanol solution with strong base to decompose lactone substances. After dilution, the neutral substances were extracted with benzene and chromatographed on a Celite column with isooctane equilibrated with acetonitrile. This procedure, with supplementary column chromatography of one fraction, made possible the separation and estimation of the amounts of tangeretin, sinensetin, nobiletin, 3,5,6,7,8,3′,4′-heptamethoxyflavone, and tetra-O-methylscutellarein. In this work, the above-named flavones were found to make up about 80% of the neutral fraction of the benzene extract, tetra-O-methylscutellarein alone amounting to about 9%.

The neutral fraction has been found to vary between 42 and 72% in benzene extracts which, in turn, have been separated from peel juices in amounts ranging from 0.31 to 0.97 g./l.

After recrystallization from ethanol, the tetra-O-methylscutellarein melted at 141.9 to 142.4° (cor.).

Anal. Calcd. for $C_{19}H_{18}O_6$: C, 66.65; H, 5.30; OCH_3, 36.36; mol. wt., 342.35. Found: C, 66.88, 67.10; H, 5.87; OCH_3, 35.90, 36.20; mol. wt. (mass spectrometer), 342.

The flavone gave negative tests with ferric chloride, Shinoda, and borohydride reagents and its absorption maxima showed no change in position or intensity when sodium acetate was added to a solution in ethanol. The ultraviolet maxima and log ϵ values in absolute ethanol are 216 mμ (log ϵ 4.69), 266 (4.33), and 318 (4.58). The carbonyl absorption band in the infrared region occurs at 1630 cm.$^{-1}$ (KBr). Demethylation was carried out by refluxing 108 mg. of the flavone with 10 ml. of dry benzene and 5 g. of aluminum chloride for 8 hr. The reaction mixture was diluted with water and extracted with ether, and the extract was treated with decolorizing carbon. After filtration, the ether was evaporated, and the residue was recrystallized from a benzene–hexane mixture. Two crops of crystals were obtained, neither of which gave color or precipitate with neutral lead acetate nor a positive gossypetone reaction.

A 34-mg. portion of the original flavone was cleaved by refluxing for 6 hr. with 6 ml. of 10% potassium hydroxide in 50% ethanol. After dilution of the reaction mixture with water, it was extracted with benzene to remove any neutral reaction product. An attempt to form a derivative from this extract was not successful. The remaining alkaline aqueous solution was saturated with carbon dioxide and extracted with benzene to remove the phenolic acetophenone fragment originating in the A-ring. This extract residue gave a 2,4-dinitrophenylhydrazone melting at 174–175°. This agrees well with the melting point of 173° found by Kirby and Sutherland for this derivative of 6-OH-2,3,4-trimethoxyacetophenone.[13] Acidification and extraction of the remaining aqueous solution gave a mixture of acids which were separated on a cellulose column to which a little methyl orange indicator had been added. The development with benzene was continued until the more rapidly moving acid had been eluted. Evaporation of the eluate and recrystallization from hexane gave an acid whose infrared spectrum agreed with that of anisic acid. The final and conclusive evidence was provided by direct comparison of the infrared spectrum in carbon disulfide solution of the isolated flavone with that of an authentic sample[11] in the same solvent.

Acknowledgment.—The author is indebted to Professor Werner Herz of Florida State University for the authentic sample of tetra-O-methylscutellarein and to W. B. Brogden, Jr., of this laboratory, for the mass spectrophotometric determination of the molecular weight. References to specific products of commercial manufacture are for illustration only and do not constitute endorsement by the U. S. Department of Agriculture.

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The Base-Catalyzed Isomerization of the Resin Acids

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The acid-catalyzed isomerization of the conjugated dienic resin acids has been studied.[2] The base-cata-

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(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) W. H. Schuller, R. N. Moore, and R. V. Lawrence, *J. Am. Chem. Soc.*, **82**, 1734 (1960); D. E. Baldwin, V. M. Loeblich, and R. V. Lawrence, *ibid.*, **78**, 2015 (1956); V. M. Loeblich, D. E. Baldwin, R. T. O'Connor, and R. V. Lawrence, *ibid.*, **77**, 6311 (1955); V. M. Loeblich and R. V. Lawrence, *ibid.*, **79**, 1497 (1957); N. M. Joye, Jr., and R. V. Lawrence, *J. Org. Chem.*, **26**, 1024 (1961).

TABLE I

G.L.C. ANALYSIS OF REACTION MIXTURES FROM TREATMENT OF RESIN ACIDS WITH BASE

Resin acids	α[a]	New acid,[b] %	Levopimaric and/or palustric acid(s),[c] %	Dehydroabietic acid,[d] %	Shoulder,[e] %	Abietic acid, %	Neoabietic acid, %	New acid,[f] %
Levopimaric acid	69	5	6	12	3	67	7	...
Neoabietic acid	68	9	6	7	6	66	5	...
Palustric acid	48	14	11	17	5	46	3	4
Abietic acid	72	7	3	7	5	73	4	2
Emergence time ratio[h]	..	1.20	1.27	1.44	1.57	1.71	1.98	2.17

[a] Specific extinction coefficient of the single peak observed at λ_{max} 241 mμ at the conclusion of each 2-min. immersion in 230° bath. [b] λ_{max} 253 mμ was observed. [c] This peak contains levopimeric and/or palustric acids.[5] [d] λ_{max} 268 and 276 mμ were observed. [e] Shoulder on dehydroabietic acid peak. [f] λ_{max} 241 mμ (α 71.3–74.8) was observed. [g] λ_{max} 290 mμ was observed. [h] Emergence time of peak divided by emergence time of methyl pimarate marker.

lyzed isomerization of polyhydronaphthalenes[3] and of an allyl ether[4] made it seem worthwhile to investigate the base-catalyzed isomerization of the resin acids.

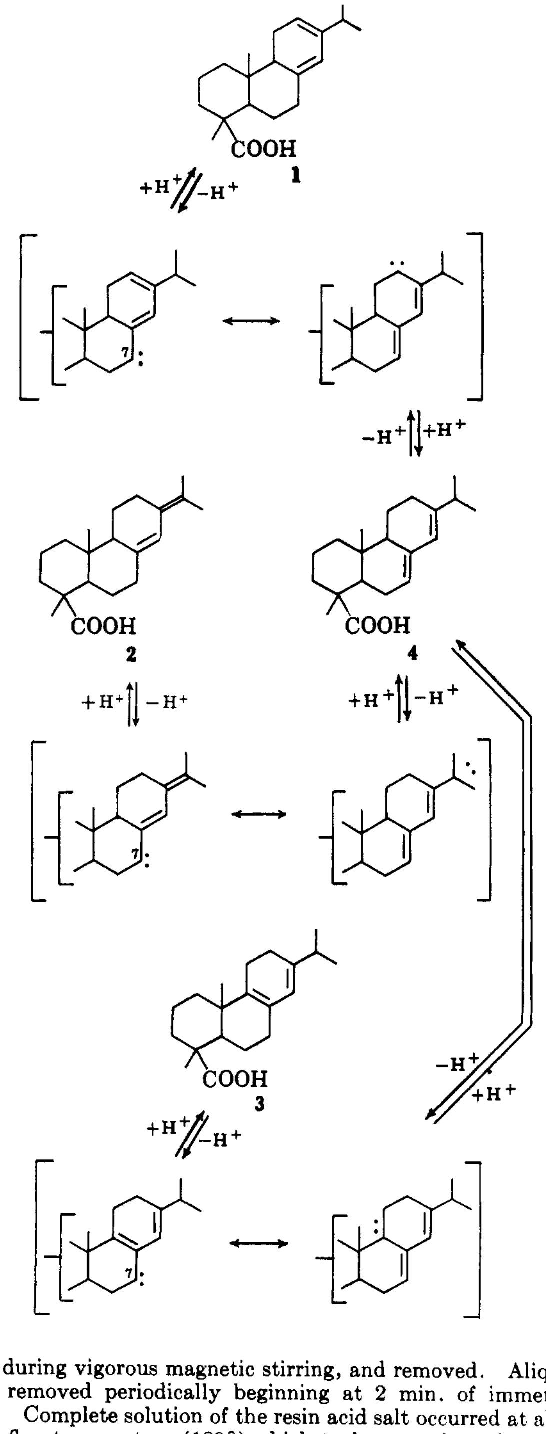
In the present work the four conjugated dienic resin acids, namely levopimaric, palustric, neoabietic, and abietic acid, were treated with an excess of potassium *t*-butoxide in dimethyl sulfoxide solution at reflux temperature (189°) for 2 min. All four solutions then exhibited a single major peak in their ultraviolet absorption spectra characteristic of abietic acid. The acids were reacted with diazomethane and the reaction mixtures were analyzed by g.l.c. (Table I).

It is apparent that the major result of the base-catalyzed reaction is the isomerization of the resin acids to abietic acid, similar to their behavior in acid solution.[2] The fact that abietic acid, on similar treatment with potassium *t*-butoxide in dimethyl sulfoxide solution, gives a spectrum of products similar to those obtained from the other three acids in about the same proportions suggests that the products are in equilibrium with one another. In contrast to acid isomerization, side reactions occurred during base isomerization which were most pronounced in the case of palustric acid (see Table I).

A possible mechanism for the base-catalyzed isomerization of the conjugated dienic resin acids is pictured in Scheme I. The allylic hydrogen at C-7 is abstracted in the case of levopimaric (**1**), neoabietic (**2**), and palustric acids (**3**), giving an anion for which a corresponding resonance form can be written identical with an allylic anion derivable from abietic acid (**4**) in each case. It is recognized that abstraction of other allylic hydrogens may also occur, particularly in the case of palustric acid, *e.g.*, from C-12 and C-18.

Treatment of levopimaric acid, the most acid-sensitive resin acid,[2] in a similar fashion in the absence of potassium *t*-butoxide did not result in any significant transformation into other products.

SCHEME I



Experimental

Reaction of Resin Acids with Base.—To a solution of 0.50 g. of resin acid in 25 ml. of dry dimethyl sulfoxide (J. T. Baker, 99.9% assay; distilled over calcium hydride) was added 0.56 g. of potassium *t*-butoxide (MSA Research Corp.) (3:1 molar ratio of base to acid). The fine white dispersion of salt was stirred magnetically in a 100-ml. round-bottom flask equipped with a gas inlet tube and a reflux condenser terminated by a drying tube filled with Drierite. After a 20-min. sweep with prepurified nitrogen, the flask was lowered into an oil bath at 230°, held there for 30 min. during vigorous magnetic stirring, and removed. Aliquots were removed periodically beginning at 2 min. of immersion time. Complete solution of the resin acid salt occurred at about the reflux temperature (189°) which took approximately 1 min. to reach. The ultraviolet absorption spectra after 2 min. of

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(3) R. B. Bates, R. H. Carnighan, and C. E. Staples, *J. Am. Chem. Soc.*, **85**, 3030 (1963); **85**, 3031, 3032 (1963).

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immersion exhibited in every case a single major peak of λ_{max} 241 mμ with an α value as listed in Table I. For any one acid, the height of the abietic acid peak did not change appreciably from 2 to 30 min. of immersion time. The four reactions were repeated with immersion times of only 2 min. Each reaction mixture was allowed to cool to room temperature under a nitrogen sweep, treated with an excess of a saturated aqueous solution of boric acid, and ether extracted five times; the ether extract was washed with water five times and evaporated to dryness. The yield of mixed acids was quantitative. The acid mixture was treated with an excess of diazomethane and the ether solution was stripped to dryness. The residue was analyzed by g.l.c. on a 10% Versamid 900 column (on Chromosorb W) 15 ft. long and 0.25 in. in diameter. The analysis of the pine gum resin acids on this substrate has been studied previously.[5] The analyses were run at 240° with a helium gas flow of 200 cc./min. The results of the analyses are given in Table I. Several of the peaks were collected and the ultraviolet spectra were determined. The results are given in Table I. The identity of the various resin acids was based upon emergence time (ratios with the added marker methyl primarate) as compared with emergence time ratios of mixtures of the known resin acids.[5]

Extensive refluxing of solutions of levopimaric acid in the following solvents containing the indicated basic catalysts did not result in any significant change in the ultraviolet spectrum of the solutions: potassium *t*-butoxide in dimethylformamide, sodium methylate in dimethylformamide, sodium methylate in dimethyl sulfoxide, and potassium *t*-butoxide in *t*-butyl alcohol.

Blank Run.—A solution of 0.50 g. of levopimaric acid in dry dimethyl sulfoxide exhibited λ_{max} 272 mμ (α 18.8). After a 20-min. nitrogen purge, the flask containing the solution and equipped as described previously was lowered into a 230° oil bath for 2 min. and then removed and an aliquot was taken. This exhibited λ_{max} 272 mμ (α 19.1).

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(5) T. W. Brooks, G. S. Fisher, and R. V. Lawrence, Meeting-in-Miniature of the American Chemical Society, Florida Section, May 8–9, 1964, Tallahassee, Fla.

Reactions of Phosphorus Compounds. VI. A General Synthesis of Cycloalkenes

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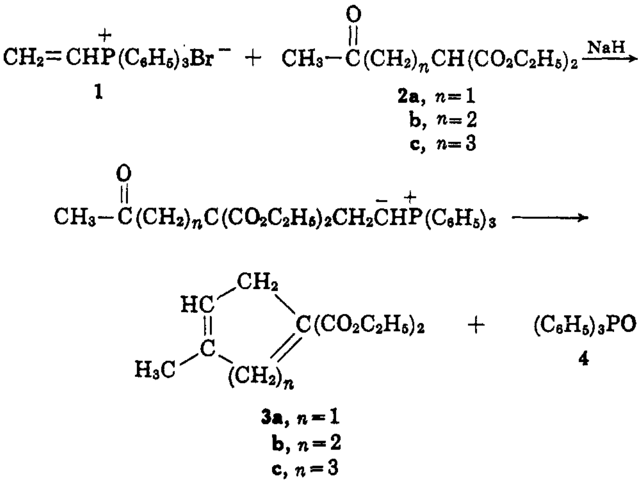
In a recent communication[1] we have outlined a new general ring synthesis whose common feature was the use of vinyltriphenylphosphonium bromide (1). The synthetic usefulness of this reaction has been demonstrated in the published reports of the preparation of a dihydrofuran,[1] a chromene,[1] and a pyridizine.[2] In this paper we wish to demonstrate the utility of this general reaction for the preparation of certain cycloalkenes.

The preparation of 1-phenylcyclopentene[3] and 1-phenylcyclohexene[4] has been accomplished in 24 and 10% yields, respectively, employing the corresponding ω-benzoylalkyltriphenylphosphonium salts as precursors. Other phosphorus ylid cyclizations giving cycloalkylphosphonium salts and ketophosphoranes have been reported.[5,6]

We have prepared diethyl (4-methyl)-3-cyclopentenedicarboxylate (**3a**) in 69% yield and diethyl (4-methyl)-3-cyclohexenedicarboxylate (**3b**) in 51% yield as shown by the following equations. All attempts to synthesize the comparable seven-membered system **3c** following the above reaction scheme were unsuccessful.



Diethyl (3-oxobutyl)malonate (**2b**) prepared according to Spencer, *et al.*,[7] was treated with sodium hydride and vinyltriphenylphosphonium bromide[8] in ether and gave the known[9] diethyl (4-methyl)-3-cyclohexenedicarboxylate (**3b**) in 51% yield. Saponification and decarboxylation of **3b** gave the known[10] 4-methyl-3-cyclohexenecarboxylic acid. In a separate experiment 71% triphenylphosphine oxide (**4**) was recovered along with **3b**. Diethyl (3-methyl)-3 cyclopentenedicarboxylate (**3a**) (69%) was prepared in a similar manner using diethyl (2-oxopropyl)malonate[11] (**2a**) as its precursor.

When 5-bromo-2-pentanone, prepared according to Bachetti and Fiecchi,[12] was treated with sodio diethylmalonate, the expected diethyl (4-oxopentyl)malonate (**2c**) was isolated in 49% yield. Attempts to cyclize **2c** with the vinyl salt **1** to give **3c** were unsuccessful. Numerous attempts were made using sodium hydride in ether, sodium hydride in a 3:1 benzene–DMF mixture, sodium hydride in acetonitrile, and potassium *t*-butylate in *t*-butyl alcohol. The last method listed was a variation on the procedure employed by House and Babad to prepare their seven-membered cyclic ketophosphorane.[6] A viscous polymer-like material was obtained in all cases, and in the *t*-butyl alcohol experiment traces of the starting materials **2c**, **1**, triphenylphosphine, and triphenylphosphine oxide were detected by thin layer and vapor phase chromatography.

Thus, five- and six-membered cycloalkenes are readily available utilizing this new procedure. Work is in progress to include activating groups other than carboxylic esters in order to expand the scope of this reaction to include larger ring sizes.

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