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TRADITIONAL MEDICINAL PLANTS OF THAILAND XIII. FLAVONOID DERIVATIVES FROM *DRACAENA LOUREIRI* (AGAVACEAE)*

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Abstract.-

Fifteen flavonoid derivatives **(1-15)** *have been obtained and characterized from the stems of* Dracaena loureiri *with the help of a variety of one- and two- dimensional nmr-techniques. Two new natural product structure types, the dracaenones and the loureirins, were isolated, together with a range of biogenetically interrelated flavonoids.*

Introduction

The genus *Dracaena,* with perhaps 80 or possibly up to 150 species *(2),* has a slender or occasionally thick stem which may be of considerable height and the leaves vary from linear to broadly lanceolate, for example, *D. draco,* the "Dragon Blood Tree" of the Canary Islands, and *D. reflexa* and *D. arborea* from Mauritius. Other species are slender subshrubs or shrubs, for example *D. cinnabari* on Socotra, *D. schizantha* in Arabia and tropical East Africa, and *D. mannii* in eastern Africa. *D. draco, D. fragrans, D. marginata* and other species are ornamental plants *(3).*

Dracaena species (Dracae-na: Greek, female dragon, the juice when thickened is supposed to resemble dragon's blood) have been used medicinally for a number of years, e.g., the dried leaf of *D. afromontana* for the treatment of rheumatism in Kenya *(4),* the root of *D. deremensis* for malaria and to hasten parturition in East Africa *(5),* the root of *D. fragrans* to alleviate pains in childbirth in East Africa *(5),* the dried wood from *D. loureiri* as antipyretic in Thailand *(6),* and the flower buds of *D. reflexa* as an emmenagogue in Madagascar *(7).* Biological investigations have been reported only for *D. mannii* which was found to possess antimicrobial activity *(8, 9).*

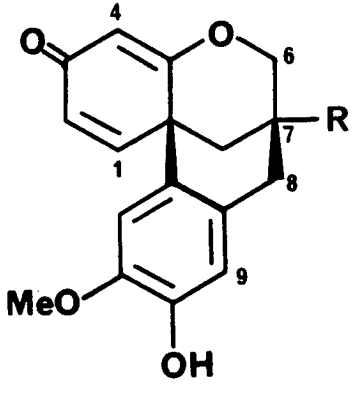
* *For the previous paper in this series, see ref. 1.*

Only three species of *Dracaena* have been phytochemically investigated previously, to afford afromontoside, a cytotoxic steroidal saponin from *D. afromontana (4);* an antimicrobial steroidal dracogenin *(10)* and several flavonoids from *D. draco (11)* and *n*-heptacosane and palmitic acid from *D. mannii (9).*

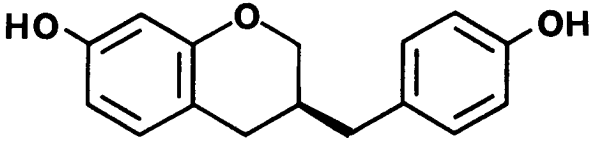
In this investigation of the $CHCl_3$ extract of the Thai medicinal plant *D. loureiri* Gagnep (Syn. *Aletris cochinchinensis* Lour. *(12)* and *Pleomele cochinchinensis* (Lour.) Merr. ex Gagnep *(13).),* which has traditionally been employed for gastrointestinal disturbances, infectious diseases, and as an antipyretic *(6), in vitro* antibacterial activity against *Staphylococcus aureus* and *Bacillus subtilis* was observed. At the initiation of our studies there had been no previous phytochemical work or biological activities reported for this plant. The present study was conducted in order to isolate and identify the constituents responsible for the antibacterial activity, and to evaluate cytotoxicity against murine P-388 lymphocytic leukemia and human carcinoma of the nasopharynx KB cell lines *in vitro (14, 15).*

Results and Discussion

From the stems of *D. loureiri* through a series of chromatographic columns and preparative TLC separations, fifteen flavonoid derivatives were isolated. Two of these, **1** and **2,** were members of the dracaenone series of cyclized homoisoflavans whose structures were established through spectroscopic analysis *(16)* and total synthesis *(17).* A related chromane derivative **3** was also reported at this time *(16).* Four of the isolates, loureirins A - D **(4-7)** were the first members of a new class of natural products, the retrodihydrochalcones *(1).* We report here on the structures of the eight remaining flavonoid derivatives **8 - 15,** comment on some of their spectroscopic data, and on the biogenetic relationships between the isolates.



1 R=H
2 R=OH



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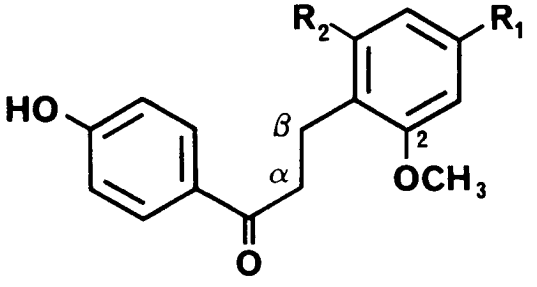
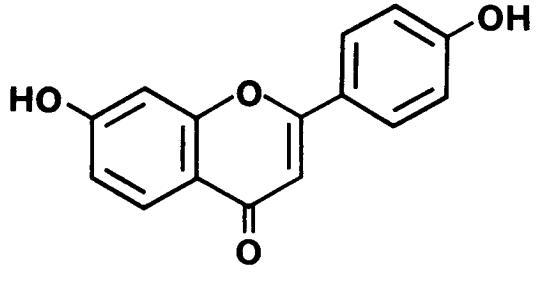


	R_1	R_2
4	OCH_3	H
5	OCH_3	OCH_3
6	OH	H
7	OH	OH

*7, 4' **Dihydroxyflavone (8).***- The structure of this known 5-deoxy flavone was established through comparison with the data available in the literature *(18-21)*. The ^{13}C-NMR spectrum of **8** was unambiguously established through the selective INEPT *(22)* and CSCM 1D *(23)* experiments. Comparison of the observed and published data *(18)* for **8** in DMSO-d_6 indicated that the assignment of C-7 has to be revised.

Previously reported natural occurrences indicate that **8** occurs in legumes *(19-21, 24, 25)*, and rarely non-legumes *(26)*. This is the first reported isolation of this simple flavone from a monocotyledonous plant.



8

(2S)-7-Hydroxyflavanone (9).- The structure of this simple flavanone was deduced from its spectral data in comparison with literature values *(20, 27-29).* ^{1}H and ^{13}C-NMR spectra were assigned unambiguously through the use of selective INEPT and CSCM 1D experiments. At the higher field strength, the chemical shift and multiplicity of the B-ring protons of **9** were deduced, compared with the previous report as a five-proton multiplet.

Since carbon-2 of the flavanone molecule is an asymmetric center, enantiomeric forms are possible. The absolute stereochemistry at C-2 of this simplest naturally occurring flavanone, **9**, was determined as *S* based on its levo-rotation *(30).* This is the first report of the isolation of **9** from a monocotyledonous plant.

(2S)-Pinocembrin (10).- The UV, mass spectral and ^{1}H-nmr data suggested that **10** was the 5-hydroxy derivative of **9** *(31-33).* From the levo-rotation, **10** was concluded to be (2*S*)-5,7-dihydroxyflavanone (pinocembrin). At 360 MHz, the chemical shifts and multiplicities of the B-ring protons, and the overlapping carbon resonances of C-3′/5′ and C-4′ were well separated, and their assignments were confirmed by CSCM 1D experiments.

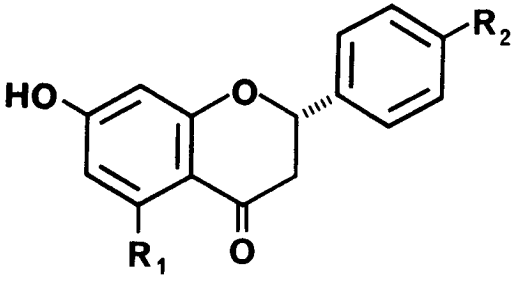
Pinocembrin is widely distributed in the dicots *(34)* and there have been only two previous isolations from the monocots *(35).* This is the first report of the occurrence of **10** in the Agavaceae.

(2S)-7,4′-Dihydroxy-5-methoxyflavanone (11).- The spectral data indicated **11** to be 7,4′-dihydroxy 5-methoxy-flavanone and this was confirmed by comparison with an authentic sample, isolated from *Achyrocline flaccida* (Compositae) *(36, 37),* by means of mixed mp., co-TLC, UV, IR, MS and ^{1}H-NMR. In the original publication *(36),* the optical rotation of the isolate was not mentioned, however, with the authentic sample available a comparison of the absolute configuration at C-2 indicated that the authentic sample had $[\alpha]_D^{20}$ + 5.7° (c 0.071), while the isolate **11** showed $[\alpha]_D^{20}$ -12.8° (c 0.171) in acetone. On the basis of the levo-rotation of **11,** it was established to be (2*S*)-7,4′-dihydroxy-5-methoxyflavanone (naringenin 5-methyl ether).

The complete ^{1}H-NMR assignments of **11** were not presented previously *(36-40).* Unambiguous assignments for H-6 and H-8 were achieved by NOE difference spectroscopy. Thus, irradiation of the methoxy group singlet at 3.74 ppm afforded a substantial NOE enhancement (12.4%) of the proximate proton at 6.06 ppm which could be assigned to H-6, absorbing at lower field than H-8.

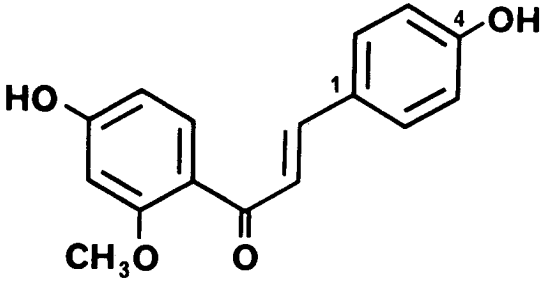
The ^{13}C-NMR assignments of **11** have not been reported previously. In this instance they were assigned with the aid of selective INEPT and CSCM 1D techniques. Selective INEPT transfer from H-2′/6′ (J = 9 Hz) enhanced an oxygenated sp^2 carbon at 157.37 ppm (C-4′), an oxygenated sp^3 carbon at 77.91 ppm (C-2), and a protonated carbon at 127.98 ppm (C-2′/6′). Selective INEPT transfer from H-6 (J = 9 Hz) revealed two oxygenated sp^2 carbons at 164.09 (C-7) and 162.00 ppm (C-5), one quaternary carbon at

104.27 ppm (C-10), and a protonated carbon at 95.43 ppm (C-8). Confirmation of the chemical shift of the C-5 resonance by selective INEPT from a methoxyl proton (J = 4 Hz) enhanced an oxygen-bearing carbon at 162.00 ppm, and confirmation of the C-8 resonance was achieved by using CSCM 1D irradiating the upfield ^{13}C satellite of H-8 to afford a large enhancement of C-8 (95.43 ppm) followed by lesser enhancements of C-6 (93.03 ppm) and C-2 (77.91 ppm).



	R_1	R_2
9	H	H
10	OH	H
11	OCH_3	OH

4,4'-Dihydroxy-2'-methoxychalcone (12).- Based on the UV, ^1H-nmr, and mass spectral data, the isolate was concluded to be 4,4'-dihydroxy-2'-methoxychalcone **(12).** The physicochemical properties of **12** were in close agreement with those published previously *(41-44).*



12

It is well-known that under alkaline conditions, an interconversion occurs between chalcones and their corresponding flavanones. Additionally, many chalcones, characteristically, turn red or orange in the presence of NaOMe *(45)*. That was not the case with the 2′-methoxychalcone, **12** which turned deep yellow. Comparison of the methanolic UV spectrum of **12** with the addition of NaOMe and the published methanolic UV spectrum of liquiritigenin (7,4′-dihydroxyflavanone) *(46)* indicated no similarity. One explanation of this may be that 2′-hydroxychalcone derivatives, in general, are easily isomerized to the corresponding flavanones by a mechanism in which the 2′-hydroxy group undergoes ionization to a phenolate anion followed by cyclization *(47, 48)*. In addition, there seems to be little hindrance to cyclization in any of the additional 6′-substituted chalcones *(47)*. Therefore, the 2′-methoxy group in **12** may suppress the ionization which normally leads to cyclization to the corresponding flavanone under alkaline conditions.

Compound **12** was previously obtained as an active metabolite from the bile excretion of rats following administration of 2′,4,4′-trimethoxy-chalcone, a choleretic drug *(41)*, as a stress metabolite from *Pisum sativum* treated with copper (II) chloride *(42)*, from fungus-inoculated *Broussonetia papyrifera* shoot cortical tissues *(43)* and as a constituent of *Caesalpinia sappan (44)*. It is not clear whether **12** is a normal constituent of *Dracaena loureiri* or whether it is a phytoalexin.

(2R)-7,4′-Dihydroxyflavan (13).- Direct comparison of the observed UV, MS and ^{1}H-NMR spectra with the authentic spectra of 7,4′-dihydroxyflavan **(13)** *(49)* showed them to be identical.

The ^{13}C-NMR spectral assignments of **13** have not been reported previously. Selective INEPT transfer from H-2′/6′ (J = 9 Hz) gave an oxygenated sp^2 carbon at 157.99 ppm (C-4′), two protonated carbons at 128.42, 115.99 ppm (C-2′/6′, C-3′/5′), an oxygenated sp^3 carbon at 78.94 ppm (C-2) and spurious transfer from downfield ^{13}C satellite of H-5 at 130.92 ppm (C-5). Selective INEPT transfer from H-2 (J = 4 Hz) showed an oxygenated sp^2 carbon at 157.09 ppm (C-8a), a quaternary carbon at 134.14 ppm (C-1′), a protonated carbon at 128.42 ppm (C-2′/6′), and two methylene carbons at 31.26, 25.49 ppm (C-3 and C-4).

Flavans unsubstituted in the pyran ring are uncommon natural products, probably owing to their instability (sensitivity to air oxidation)*(50)*. For example, it is known that 7,4′-dihydroxyflavan undergoes rapid self-condensation to dimeric and polymeric compounds in acidic media *(51)* since it turns brown and then greenish yellow following the addition of HCl. Compound **13** has been reported only as a minor constituent in plants in the Amaryllidaceae, Xanthorrhoeaceae *(49)*, Leguminosae *(52)*, Moraceae *(43)*. It is possible that these flavans have taxonomic significance because all the known examples were from monocot plants originally in the family Liliaceae. However, *Dracaena* has been

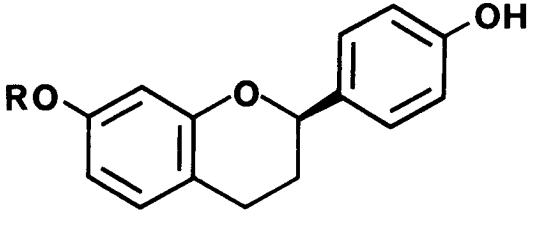
transferred to the family Agavaceae and *Xanthorrhoea* has been placed in the family Xanthorrhoeaceae *(53)*.

The levo-rotatory flavans so far isolated all possess the 2*S*-configuration *(50)*. Therefore, the absolute configuration of C-2 in **13** was assigned the *R* configuration on the basis of a correlation between the sign of the optical rotation with that of all the other natural flavans. 7,4′-Dihydroxyflavan (demethylbroussin) reported by Takasugi *et al. (43)* was assigned the *S* configuration ($[\alpha]_D$ −30.5°, MeOH). The low enantiomeric excess of the *R* form of the isolated **13** ($[\alpha]_D$ +1.8°, MeOH) may be due to a racemic mixture, which might have arisen from the flavan-retrodihydrochalcone interconversion, or the flavan could have epimerized during isolation *(53)*, or it may be a natural product. It was stated by Birch that the optically inacitve trioxygenated flavan isolated from *Xanthorrhoea* seemed unlikely to be an artifact *(54)*.

The preferred conformation of the pyran ring of this 2*R*-flavan in solution came from an evaluation of the coupling constants. The large *trans*-quasi-diaxial coupling constant between H-2 and one of the H-3 indicated that the puckered heterocyclic ring was held somewhere between the half-chair and sofa conformation in which the aromatic ring attached to C-2 was in the quasi-equatorial position.

(2R)-4′-Hydroxy-7-methoxyflavan (14).- Spectroscopic evidence for **14** was very similar to that of **13** apart from changes associated with the replacement of a hydroxy by a methoxy group and was in close agreement with the published data for 4′-hydroxy-7-methoxyflavan *(53)*.

Complete carbon assignments for **14** were achieved with the aid of two-dimensional heteronuclear chemical shift correlation experiment for the protonated carbons and selective INEPT experiments for nonprotonated carbons (Figure). Selective INEPT transfer from H-2′/6′ (J = 9 Hz) gave an oxygenated sp^2 carbon at 155.23 ppm (C-4′), two protonated carbons at 127.60 (C-2′/6′) and 77.71 ppm (C-2), as well as a negative resonance from a residual SPT from a downfield ^{13}C satellite from H-5 at 129.94 ppm (C-5). Transfer from H-2 (J = 4 Hz) enhanced an oxygenated sp^2 carbon at 155.76 ppm (C-8a), two sp^2 carbons at 133.69 (C-1′) and 127.60 ppm (C-2′/6′), and two methylene carbons at 24.50 (C-4) and 29.85 ppm (C-3) with less intensity due to two-bond coupling. Transfer from the methoxyl protons (J = 4 Hz) selectively enhanced only the resonance of C-7 at 158.83 ppm. The difference between this resonance and the other two oxygenated sp^2 carbons implied that the methoxy group was located in ring A which confirmed the structure of **14**.



	R
13	H
14	CH_3

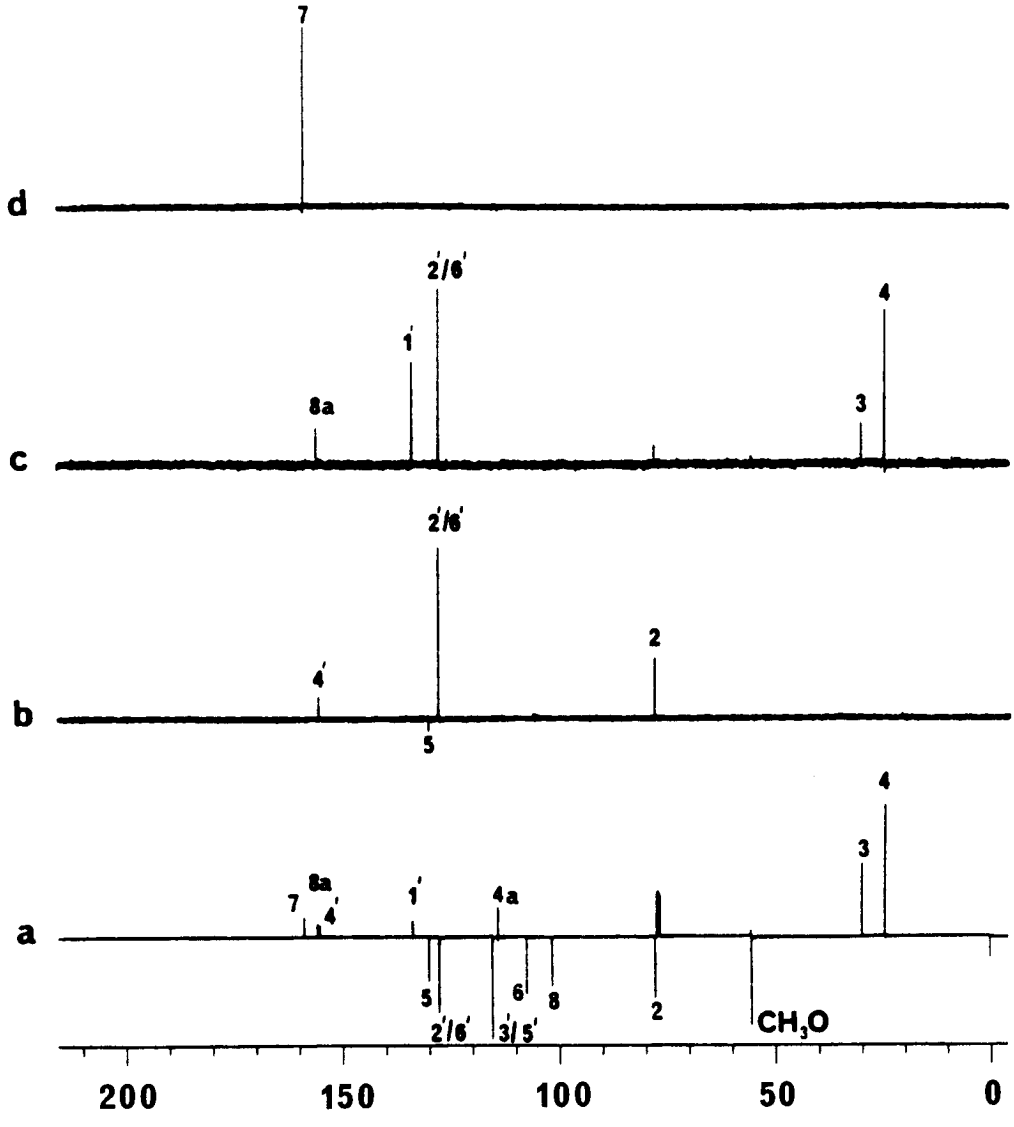
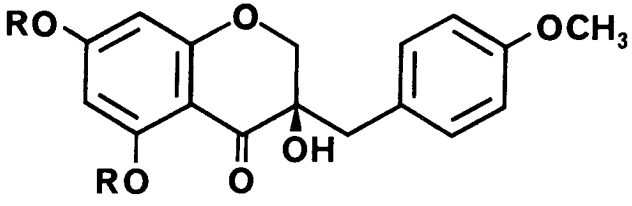


Figure 1. Carbon-13 NMR Spectra of 14. a) APT; b-d, selective, INEPT spectra by irradiation of H-2′/4-6′, H-2 and OCH_3.

A synthesis of the racemic form of compound **14** (mp. 144°) *(15),* as well as isolation of its levo-rotatory form (mp. 148.5-149.5°, $[\alpha]_D^{21}$ -15.6° (c 0.55, EtOH)) *(53)* have been reported. Although the melting point and the optical rotation differred from those of the slightly dextrorotatory form of **14** (mp. 137°, $[\alpha]_D^{20}$ +5.8° (c 0.189, MeOH)), the lack of an authentic sample for comparison made it difficult to establish the enantiomeric excess of **14**. However, based on the structure of **13**, it was tentatively concluded that (+)-4′-hydroxy-7-methoxyflavan possesses the *(R)*-configuration at C-2.

(3R)-Eucomol (15).- The physicochemical and spectroscopic evidence for **15** was in close agreement with the published data of (−)-eucomol possessing the *R*-configuration at C-3 *(56, 57)*. Unambiguous assignment of the two quaternary carbons at C-5 and C-7 could not be achieved by using the selective INEPT technique, because the chemical shifts of H-6 and H-8 were too close. Additionally, acetylation of **15** with immediate work-up yielded a diacetate **16** rather than a monoacetate product. This reaction also revealed the presence of the methoxyl group in ring B due to the downfield shift of only two *meta* protons. Conclusive evidence for the carbon assignments was made by the observation of a heteronuclear NOE difference between C-5 and C-7 in the proton-coupled ^{13}C spectrum.



	R
15	**H**
16	**Ac**

Taxonomic Considerations.- The distribution of flavonoids within the plant kingdom is universal and is variable according to phyla, orders, families *(58)*. There are no obvious correlations at higher taxonomic levels beyond the order. Attention will therefore be focused on situations at lower taxonomic levels.

Chalcones are present in only one monocotyledonous family, the Liliaceae *(30),* and the only monocots reported to possess dihydrochalcones, glycyphyllin and dihydroflavokawin B, were *Smilax glycyphylla* (Liliaceae) *(59)* and *Alpinia speciosa* (Zingiberaceae) *(60),* respectively.

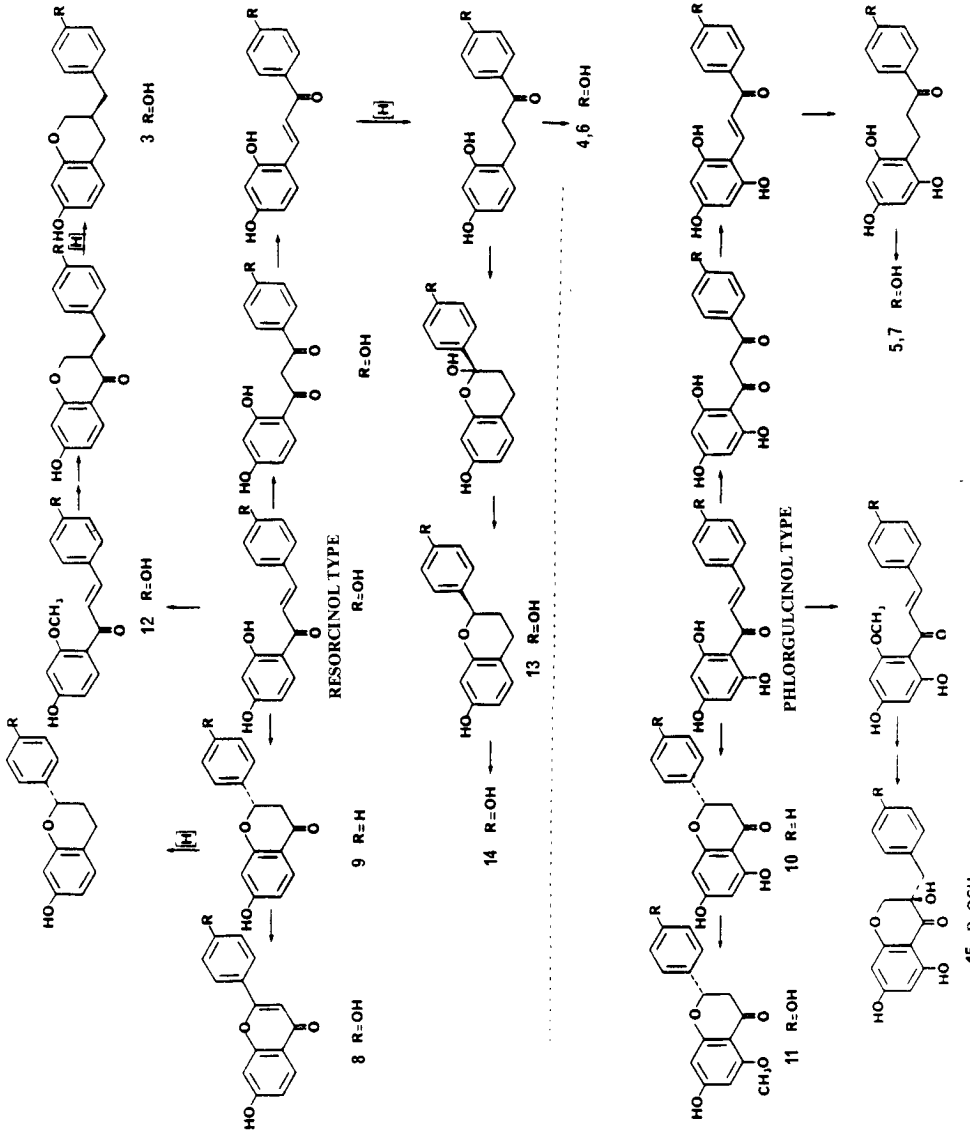
Certain uncommon flavans, unsubstituted in the pyran ring, have been reported in the monocotyledonous plants of the genus *Narcissus* (Amaryllidaceae) *(49), Xanthorrhoea (54), Styphandra (53)* (Xanthorrhoeaceae), *Dianella* (Liliaceae) *(53)* and *Dracaena* (Agavaceae) *(11)*. The highly specific chemical distribution of the homoisoflavonoids in Monocotyledonae was restricted to the genera *Eucomis, Scilla, Muscari, Chinodoxa* and possibly in *Drimopsis maculata* and *Veltheimia capensis,* subfamily Scilloideae of the Liliaceae *(61)*.

In phytochemical studies of 13 genera representing 116 species of Agavaceous plants, only two genera, i.e., *Polyanthes (62, 63)* and *Dracaena (11),* have so far been reported to contain flavonoids. It is noteworthy that the coexistence of the minor flavonoids in monocotyledonous plants may play a role of taxonomic significance at the generic level, since almost all the above genera were from plants which have been included in the family Liliaceae and later transferred to closely related families, e.g., *Dracaena* to the Agavaceae, and *Xanthorrhoea* to the Xanthorrhoeaceae.

Biogenetic Interrelationships.- The *Dracaena loureiri* plant part examined in this study was particularly rich in flavonoids, including two new and unusual flavonoid structures *(1, 16)*. From the determined structures of the isolates, this genus displays the ability to accumulate a series of structurally and biosynthetically inter-related flavonoids at different levels of oxidation and substitution.

Because of the lack of experimental data, discussions of biogenetic relationships must rely heavily on the chemical conversion of various flavonoid classes, on biosynthetic evidence of closely related compounds and information about the natural co-occurrence of various compounds. Very strong supportive evidence for the biogenetic routes were the co-occurrence of intermediates in this plant. It has therefore been possible to interrelate a number of flavonoid isolates and to tentatively propose a biogenetic scheme (Scheme).

All classes of flavonoids are biosynthetically related, with a chalcone being the first common intermediate *(64)*. This skeleton subsequently leads either to flavonoid or, by 1,2-aryl rearrangement, to isoflavonoid nuclei. Chalcones are further catalysed by chalcone isomerase to stereospecifically undergo ring-closure to the corresponding (−) (2*S*)-flavanones. The presence of a high activity of chalcone isomerase allows the plant to exclude chemical isomerization which would lead to a racemic product *(65)*. *In vivo,* chalcones with a resorcinol-type substitution in ring A are exclusive intermediates in the formation of 7-hydroxyflavonoids, while chalcones with a phloroglucinol-type substitution in ring A are selectively converted into 5,7-dihydroxyflavonoids. According to biogenetic theory, the universal flavonoid precursor has an oxygen substituent at the 5-position originating from the intramolecular Claisen condensation of *p*-coumaryl CoA and acetyl-malonyl CoA. The resorcinol-type chalcone may be due to hydroxy-removal during the final stages of chalcone biosynthesis. Flavones lacking a 5-hydroxyl group are rather



Scheme 1. Proposed Biogenesis of the Flavonoids of Dracaenaloureiri.

characteristic of advanced leguminous plants. The presence of 5-deoxyflavonoids was therefore suggested to be a mutation of evolution, possibly an indication of advanced genera in the Agavaceae. Since methyl groups are introduced into flavonoids after formation of the flavonoid ring by flavonoid-specific methyltransferases, which have been found in various plants, it appeared likely that these enzymes, not a general methyltransferase in the pathway of general phenylpropanoid metabolism, might be involved.

Flavans are relatively uncommon natural products. They may arise by reduction of the co-occurring liquiritigenin *(66, 67)*, or possibly by the alkylation of a C_6-unit by a C_9-unit to afford a benzylstyrene which could subsequently cyclize *(52)*. The co-occurrence of retrodihydrochalcones with flavans having similar oxygenation pattern points to their common biogenetic relationship. By analogy to the chalcone to carbinol anhydrobase structural transformation *(68)*, a flavan may arise by cyclization of a 2′-hydroxy-retrodihydrochalcone under appropriate metabolic conditions.

The role of 2′-methoxychalcones as biosynthetic intermediates for homoisoflavanones has been demonstrated by the incorporation of 2′,4′,4-trihydroxy-6′-methoxychalcone and 2′,4′-dihydroxy-4,6′-dimethoxychalcone into eucomin. Mechanisms for cyclization of a chalcone to a chromanone followed by the formation of a homoisoflavanone could occur either by elimination of a proton, or by hydride transfer, or addition of water or hydroxylation *(69)*. Further reduction or deoxygenation of the homoisoflavanone to a homoisoflavan has been proposed.

The co-occurrence of dracaenone derivatives and homoisoflavans in *D. loureiri* suggested that 7-hydroxy-3-(3-hydroxy-4-methoxybenzyl) chromane (3) might cyclize by *para-para* phenolic oxidative coupling to a tetracyclic intermediate which could undergo dienone-phenol rearrangement to the dracaenone skeleton *(16)*.

Biological activity of the isolates.- Although flavonoids may be relatively uninteresting from a structural viewpoint, in terms of biological activity, they belong to a promising and important class of compounds *(70)*. Bacteriostatic activity of 7-hydroxyflavanone **(9)** and pinocembrin **(10)** against *S. aureus* has been studied previously *(71)*. 4,4′-Dihydroxy-2′-methoxychalcone **(12)** possesses significant choleretic activity *(41)*. Racemic and natural levo-rotatory 7,4′-dihydroxyflavan **(13)** showed fungitoxic activity in TLC bioassay against *Botrytis cinerea* and *Cladosporum herbarum (49, 72)*.

Antibacterial activity.- Comparing (2*S*)-7-hydroxyflavanone **(9)**, (2*S*)-pinocembrin **(10)**, and (2*S*)-7,4′-dihydroxy-5-methoxyflavanone **(11)**, the higher activity of **10** was attributed to the chelation of indispensable metals for the bacterial metabolism and direct modification of the cellular membrane *(71)*. The reported MIC against *S. aureus* of pinocembrin varied from Table I, i.e., 100 µg/ml by the broth-dilution method *(71)* and 50 µg/ml by the agar dilution-streak technique *(73)*. This is undoubtedly due, at least,

in part to variable experimental design and interlaboratory variations. Retrodihydrochalcones **(4, 5, 6** and **7)** with more hydrophilic properties had increased activity. Conversion of the C-7 hydroxyl of 7,4′-dihydroxyflavan **(13)** to the less polar methoxy group as in **14** diminished activity. The simple homoisoflavan **3** possessed stronger activity against *S. aureus* than *B. subtilis.*

TALBE I

ANTIBACTERIAL ACTIVITY OF THE ISOLATES FROM *D. LOUREIRI*

Compound	MIC (μg/ml)[a]		
	S. aureus	*B. subtilis*	*E. coli*
(7*S*, 12b*R*)-10-Hydroxy-11-methoxy-dracaenone **(1)**	>500	>500	>500
(7*R*, 12b*R*)-7,10-Dihydroxy-11-methoxy-dracaenone **(2)**[b]	>250	250	>250
(3*S*)-7,4-Dihydroxy-3-(4-hydroxybenzyl) chromane **(3)**	125	250	>500
Loureirin A **(4)**	>500	>500	>500
Loureirin B **(5)**	>500	>500	>500
Loureirin C **(6)**	500	125	>500
Loureirin D **(7)**	250	125	>500
7,4′-Dihydroxyflavone **(8)**	>500	>500	>500
(2*S*)-7-Hydroxyflavanone **(9)**	>500	>500	>500
(2*S*)-Pinocembrin **(10)**	250	125	>500
(2*S*)-7,4′-Dihydroxy-5-methoxyflavanone **(11)**	>500	>500	>500
4,4′-Dihydroxy-2′-methoxychalcone **(12)**[b]	>100	>100	>100
(2*R*)-7,4′-Dihydroxyflavan **(13)**	500	250	>500
(2*R*)-4′-Hydroxy-7-methoxyflavan **(14)**	>500	>500	>500
(3*R*)-Eucomol **(15)**	500	250	>500

[a] Microdilution method.

[b] A limited amount of material was available.

Cytotoxic activity.- All of the isolates were examined for their cytotoxic activity against the KB and P-388 test systems *in vitro* using standard procedures *(14, 15),* the results are shown in Table II. Only 4,4′-Dihydroxy-2′-methoxychalcone **(12)**, whose ED_{50} was 1.8 μg/ml against KB cells *in vitro,* could be considered active. As a class, the dihydrochalcones seem to be remarkably free of toxicity against *in vitro* KB cell line, where ED_{50} values were usually>20 μg/ml *(74).* The retrodihydrochalcones were, however, marginally active.

TABLE II

CYTOTOXIC ACTIVITY OF THE ISOLATES FROM *D. LOUREIRI*

Compound	ED_{50} (μg/ml)[a]	
	KB	P-388
(7*S*, 12b*R*)-10-Hydroxy-11-methoxy-dracaenone **(1)**	_[b]	_[b]
(7*R*, 12b*R*)-7, 10-Dihydroxy-11-methoxy-dracaenone **(2)**	_[b]	_[b]
(3*S*)-7,4′-Dihydroxy-3-(4-hydroxybenzyl)-chromane **(3)**	12.8	12.7
Loureirin A **(4)**	6.4	22.0
Loureirin B **(5)**	22.3	21.7
Loureirin C **(6)**	6.0	15.0
Loureirin D **(7)**	5.5	11.9
7,4′-Dihydroxyflavone **(8)**	29.9	<50
(2*S*)-7-Hydroxyflavanone **(9)**	_[b]	_[b]
(2*S*)-Pinocembrin **(10)**	_[b]	_[b]
(2*S*)-7,4′-Dihydroxy-5-methoxyflavanone **(11)**	31.4	<50
4,4′-Dihydroxy-2′-methoxychalcone **(12)**	1.8	_[b]
(2*R*)-7,4′-Dihydroxyflavan **(13)**	10.0	_[b]
(2*R*)-4′-hydroxy-7-methoxyflavan **(14)**	8.1	14.1
(3*R*)-Eucomol **(15)**	8.2	12.1

[a] A compound is considered active if it has an ED_{50} >4 μg/ml *(14, 15)*.

[b] Not tested.

CONCLUSION

Among the fifteen isolates obtained from the antibacterial plant, *D. loureiri*, a biosynthetically unique retrodihydrochalcone series, the loureirins A, B, C and D **(4-7)** *(1)*, as well as cyclised homoisoflavans **1** and **2** of the dracaenone skeleton *(16)* were fully characterized utilizing modern NMR techniques. Unfortunately, the isolates displayed only marginal antibacterial or cytotoxic activity.

Contrary to normal flavonoids, the isolated dihydrochalcones lacked hydroxy groups at C-2′ and C-6′ in the A-ring and possessed a resorcinol or phloroglucinol type B-ring. Isolation of these compounds, together with a normal chalcone and a 7,4′-dihydroxyflavone has led to the postulation of a biogenetic scheme in *D. loureiri* where the A-rings and C_3 units are derived from cinnamate derivatives and the B-rings are derived from a polyketide moiety. These unusual flavonoids were designated as retrodihydrochalcones.

EXPERIMENTAL

PLANT MATERIAL.- Dried stem material of *D. loureiri* was collected at Prachuabkirikhan Province, Thailand, in January, 1982. The plant material was identified by the Botany Section, Technical Division, Department of Agriculture, Ministry of Agriculture and Cooperatives, Thailand. A herbarium specimen is deposited in the herbarium of the Department of Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand.

EXTRACTION AND INITIAL BIOLOGICAL TESTING.- The chipped, ground and dried stems (630 g) were successively extracted with petroleum ether, $CHCl_3$ and EtOH in a Soxhlet apparatus for 48 h. Evaporation of the solvents gave residues of 11.8, 152.7 and 104.4 g, respectively.

The petroleum ether, $CHCl_3$ and EtOH extracts were tested for antibacterial activity against *Staphylococcus aureus* ATCC 25923, *Bacillus subtilis* ATCC 6633 and *Escherichia coli* ATCC 25922 which are representatives of Gram positive, spore producing and Gram negative bacteria, by the Kirby-Bauer disc diffusion technique *(75)*. Only the $CHCl_3$ soluble fraction displayed antibacterial activity against *S. aureus* and *B. subtilis*. Using an autobiographic method *(76)*, the antibacterial activity of the $CHCl_3$ extract was localized between R_f 0.5-0.6 on silica gel TLC plate developed with petroleum ether and EtOAc (6:1) at the 250μg level. The active extract (152 g) was subjected to silica gel-60 column chromatography (9 × 100 cm), collecting 1 liter fractions and eluting with mixtures of petroleum ether and EtOAc, EtOAc, EtOAc and MeOH of increasing polarity. The fractions, which exhibited inhibition zone against *S. aureus* and *B. subtilis* by the autobiographic method at the 250μg level, were subjected to isolation for their active principles. Fifteen flavonoids were isolated during this study.

7,4'-Dihydroxyflavone (8).- Fractions 69-81, eluted from the silica gel-60 column with petroleum ether and EtOAc (1:2), were further subjected to silica gel-60 chromatography (5 × 78 cm), collecting 500 ml fractions and eluting with mixtures of $CHCl_3$ and MeOH of increasing polarity. Fractions 87-109 afforded small pale red needles of **8** (31.5 mg, 0.005%), mp 318-320°C; $[\alpha]_D^{21}$ 0° (c 0.077, MeOH); R_f $CHCl_3$-MeOH (87:13): 0.24; uv, λ_{max} (MeOH) 229.5 (log ε 3.59), 254 (3.57), 310.5 (sh) (3.85), 329 nm (3.91); λ_{max} (+NaOMe) 214.5 (log ε 4.13), 226.5 (sh) (3.94), 251 (3.84), 264 (sh) (3.77), 329.5 (3.69), 387 nm (4.00); λ_{max} (+$AlCl_3$) 230 (log ε 3.83), 254 (3.59), 310.5 (sh) (3.84), 329 (3.89), 383 nm (2.96); λ_{max} (+$AlCl_3$/HCl) 230 (log ε 3.77), 255 (3.58), 311 (3.73), 331.5 (3.78), 395.5 nm (3.44); λ_{max} (+NaOAc) 235.5 (log ε 4.20), 266 (3.96), 284 (sh) (3.88), 308.5 (3.86), 319.5 (3.83), 360.5 nm (3.84); λ_{max} (+NaOAc/H_3BO_3) 242 (log ε 4.21), 258.5 (sh) (3.95), 283 (4.05), 312 (sh) (3.99), 330 nm (4.01); ir, ν_{max} (KBr) 3204, 3064, 1631, 1603, 1557, 1554, 1383, 1273, 1237, 1224, 1182, 827 cm^{-1}; ^{1}H-nmr (300 MHz, DMSO-d_6)

δ 10.78 (1H, s, exchangeable with D_2O, OH), 10.28 (1H, s, exchangeable with D_2O, OH), 7.92 (2H, d, J = 8.9 Hz, H-2′ and H-6′), 7.87 (1H, d, J = 8.0 Hz, H-5), 6.98 (1H, d, J = 2.2 Hz, H-8), 6.93 (2H, d, J = 8.9 Hz, H-3′ and H-5′), 6.91(1H,dd, J = 8.0, 2.2 Hz, H-6), 6.73 (1H, s, H-3); ^{13}C-nmr (90.8 MHz, DMSO-d_6) δ 176.54 (C-4), 162.64 (C-2), 160.79 (C-7 and C-4′), 157.48 (C-9), 128.26 (C-2′ and C-6′), 126.61 (C-5), 121.88 (C-1′), 116.18 (C-10), 116.04 (C-3′ and C-5′), 114.97 (C-6), 104.55 (C-3), 102.61 (C-8); ms, *m/z* (rel.intensity) 254 (M^+, 19%), 253 (100), 226 (11), 225 (74), 224 (14), 196 (13), 140 (11), 138 (8), 137 (8), 136 (99), 135 (22), 120 (10), 118 (9), 117 (76), 114 (19), 112 (45).

(2S)-7-Hydroxyflavanone (9).- Fractions 20-27, eluted from the silica gel-60 column with petroleum ether and EtOAc (3:1), were further subjected to silica gel-60 chromatography (3 × 60 cm) collecting 150 ml fractions and eluting successively with petroleum ether, $CHCl_3$, and EtOAc (50:50:1). Fractions 5-7 afforded a pink powder of **9**(21.8 mg, 0.004%), mp 184-185°C; $[\alpha]_D^{20}$ -22.0° (c 0.15, acetone); R_f $CHCl_3$-MeOH (94:6): 0.48; uv, λ_{max} (MeOH) 219 (log ε 4.12), 234 (3.99), 276 (4.11), 312 nm (3.82); λ_{max} (+NaOMe) 219 (log ε 4.11), 255 (3.87), 319 (4.09), 345 (sh) nm (4.05); λ_{max} (+$AlCl_3$)219 (log ε 4.13), 234 (3.99), 276 (4.03), 311 nm (3.79); λ_{max} (+$AlCl_3$/HCl) 219 (log ε 4.12), 234 (3.97), 277 (4.02), 311 nm (3.77); λ_{max} (+NaOAc) 229 (log ε 4.19). 256 (3.80), 283 (sh) (3.71), 321 (4.08), 339 (sh) nm (4.06); λ_{max} (+NaOAc/H_3BO_3) 233 (log ε 4.15), 278 (4.03), 311 nm (3.81); ir, ν_{max}(KBr) 3111, 3064, 3034, 2947, 1656, 1651, 1613, 1597, 1574, 1336, 1299, 1259, 1248, 1114 cm^{-1}; ^{1}H-NMR (360 MHz, CD_3OD) δ 7.73 (1H, d, J = 8.7 Hz, H-5), 7.50 (2H, dt, J = 7.5, 1.5, 1.5 Hz, H-2′ and H-6′), 7.40 (2H, td, J = 7.5, 7.5, 1.5 Hz, H-3′ and H-5′), 7.36 (1H, tt, J = 7.5, 7.5, 1.5, 1.5 Hz, H-4′), 6.51 (1H, dd, J = 8.7, 2.2 Hz, H-6), 6.39 (1H, d, J = 2.2 Hz, H-8), 5.48 (1H, dd, J = 12.9, 3.0 Hz, H-2_{ax}), 3.02 (1H, dd, J = 16.9, 12.9 Hz, H-3_{ax} or H-3_{trans}), 2.75 (1H, dd, J = 16.9, 3.0 Hz, H-3_{eq} or H-3_{cis}); ^{13}C-nmr (90.8 MHz, CD_3OD) δ 192.93 (C-4), 166.83 (C-7), 165.32 (C-9), 140.61 (C-1′), 129.85 (C-5), 129.64 (C-4′), 129.51 (C-3′ and C-5′), 127.29 (C-2′ and C-6′), 114.94 (C-10), 111.86 (C-6), 103.83 (C-8), 80.99 (C-2), 45.12 (C-3); ms, *m/z* (rel. intensity) 240 (M^+, 100%), 239 (48), 223 (6), 163 (58), 162 (5), 137 (24), 136 (92), 108 (39), 105 (7), 104 (51), 103 (23), 78 (21), 77 (24).

(2S)-Pinocembrin (10).- Fractions 14-16 eluted from the silica gel-60 column with petroleum ether and EtOAc (4:1) were further subjected to silica gel-60 chromatography (3 × 60 cm), collecting 100 ml fractions, and eluting with $CHCl_3$. Fractions 9-10 afforded pale yellow flakes of **10** (41.4 mg, 0.007%), mp 188-190°C; $[\alpha]_D^{20}$ -62.0° (c 0.089, MeOH); R_f $CHCl_3$-MeOH (94:6): 0.53; λ_{max} (MeOH) 215.5 (log ε 4.26), 229 (sh) (4.41), 289 (4.19), 330 (sh) nm (3.58); λ_{max} (+NaOMe) 218.5 (log ε 4.32), 245.5 (3.82), 323.5 nm (4.34); λ_{max} (+$AlCl_3$) 222.5 (log ε 4.28), 311 (4.31), 375.5 nm (3.54); λ_{max} (+$AlCl_3$/HCl) 222.5 (log ε 4.27), 308.5 (4.28), 373.5 nm (3.52); λ_{max} (+NaOAc) 228.5 (log ε 4.38), 250 (sh) (3.78), 323.5 nm (4.35); λ_{max} (+NaOAc/H_3BO_3) 231.5 (log ε 4.36), 292 (4.17), 330 (sh) nm (3.63); ir, ν_{max}(KBr) 3111, 3011, 2885, 2750, 2638, 1631, 1604, 1584, 1487, 1467, 1454,

1357, 1317, 1302, 1169 cm^{-1}; ^{1}H-nmr (360 MHz, CD_3OD) δ 7.47 (2H, dt, J = 7.0, 1.8, 1.8 Hz, H-2′ and H-6′), 7.40 (2H,td, J = 7.0, 7.0, 1.8 Hz,H-3′ and H-5′), 7.34 (1H, tt, J = 7.0, 7.0, 1.8, 1.8 Hz, H-4′), 5.92 (1H,d, J = 2.1 Hz, H-8), 5.89 (1H, d, J = 2.1 Hz, H-6), 5.41 (1H, dd, J = 12.8, 3.1 Hz, H-2_{ax}), 3.05 (1H, dd, J = 17.1, 12.8 Hz, H-3_{ax} or H-3_{trans}), 2.73 (1H, dd, J = 17.1, 3.1 Hz, H-3_{eq} or H-3_{cis}); ^{13}C-nmr (90.8 MHz, CD_3OD) δ 197.15 (C-4), 168.30 (C-7), 165.37 (C-5), 164.55 (C-9), 140.29 (C-1′), 129.64 (C-3′ and C-5′), 129.57 (C-4′), 127.28 (C-2′ and C-6′), 103.32 (C-10), 97.16 (C-6), 96.21 (C-8), 80.36 (C-2), 44.14 (C-3); ms, *m/z* (rel. intensity) 256 (M^+, 100%), 255 (52), 239 (4), 179 (58), 178 (4), 153 (15), 152 (61), 124 (26), 105 (4), 104 (13), 103 (12), 78 (11), 77 (12).

(2S)-7,4′ Dihydroxy-5-methoxyflavanone (11).- Fractions 123-128 eluted from the silica gel-60 column with EtOAc and MeOH (95:5), afforded yellow needles of **11** (82.7 mg, 0.013%), mp 256-260°C (dec.); $[\alpha]_D^{20}$ −12.8° (c 0.17, acetone); R_f $CHCl_3$-MeOH (9:1): 0.34; uv, λ_{max}(MeOH) 227.5 (log ε 4.36), 283.5 (4.20), 315 (sh) nm (3.71); λ_{max} (+NaOMe) 246 (log ε 4.21), 321 nm (4.40); λ_{max} (+$AlCl_3$) 227.5 (log ε 4.36), 283.5 (4.21), 315 (sh) nm (3.67); λ_{max}(+$AlCl_3$/HCl) 227.5 (log ε 4.34), 283.5 (4.19), 315 (sh) nm (3.67); λ_{max} (+NaOAc) 251 (sh) (log ε 3.95), 284.5 (sh) (4.00), 320 nm (4.35); λ_{max} (+NaOAc/H_3BO_3) 285 (log ε 4.24), 305.5 (sh) nm (log ε 3.95); ir, ν_{max}(KBr) 3228, 3085, 2978, 1635, 1620, 1614, 1588, 1519, 1462, 1270, 1215, 1159, 1111 cm^{-1}; ^{1}H-nmr (360 MHz, DMSO-d_6) δ 9.49 (1H, br s, exchangeable with D_2O, OH), 7.29 (2H, d, J = 8.5 Hz, H-2′ and H-6′), 6.78 (2H, d, J = 8.5 Hz, H-3′ and H-5′), 6.06 (1H, d, J = 1.9 Hz, H-6), 5.96 (1H, d, J = 1.9 Hz, H-8), 5.33 (1H, dd, J = 12.4, 2.1 Hz, H-2_{ax}), 3.74 (3H, s, CH_3O-5), 3.00 (1H, dd, J = 16.1, 12.4 Hz, H-3_{ax} or H-3_{trans}), 2.51 (1H, dd, J = 16.1, 2.1 Hz, H-3_{eq} or H-3_{cis}); ^{13}C-nmr (90.8 MHz, DMSO-d_6) δ 187.60 (C-4), 164.09 (C-7), 164.05 (C-9), 162.00 (C-5), 157.37 (C-4′), 129.15 (C-1′), 127.98 (C-2′ and C-6′), 114.95 (C-3′ and C-5′), 104.27 (C-10), 95.43 (C-8), 93.03 (C-6), 77.91 (C-2), 55.45 (CH_3O-5), 44.63 (C-3); ms, *m/z* (rel. intensity) 286 (M^+, 53%), 285 (30), 269 (5), 258 (6), 257 (2), 193 (29), 180 (20), 179 (3), 168 (20), 167 (100), 166 (87), 165 (2), 164 (1), 138 (54), 137 (8), 124 (8), 123 (27), 121 (13), 120 (98), 119 (21), 107 (16), 95 (24), 94 (6), 93 (4), 92 (6), 91 (29), 89 (5).

4,4′ Dihydroxy-2′-methoxychalcone (12).- Fractions 50-58, eluted from the silica gel-60 column with petroleum ether and EtOAc (1:1), were further subjected to silica gel-60 chromatography (5 × 55 cm), collecting 200 ml fractions, eluting with mixtures of $CHCl_3$ and MeOH of increasing polarity. Fractions 128-149 afforded blunt yellow needles of **12** (3.3 mg, 0.0005%), mp 232-235°C; $[\alpha]_D^{21}$ 0° (c 0.025, MeOH); R_f $CHCl_3$-MeOH (94:6):0.2; uv, λ_{max} (MeOH) 237.5 (log ε 3.65), 349.5 nm (3.95); λ_{max} (+NaOMe) 213.5 (log ε 4.09), 257 (3.66), 321 (sh) (3.40), 418.5 nm (4.07); λ_{max} (+$AlCl_3$) 235.5 (log ε 3.67), 350.5 nm (3.94); λ_{max} (+$AlCl_3$/HCl) 235.5 (log ε 3.66), 350 nm (3.91); λ_{max} (+NaOAc) 226 (log ε 4.18), 256 (sh) (3.56), 326 (sh) (3.67), 396.5 nm (3.93); λ_{max} (+NaOAc/H_3BO_3) 230.5 (log ε 4.16), 355.5 nm (3.94); ir, ν_{max} (KBr) 3282, 3192, 3044, 3019, 1623, 1607, 1590, 1573, 1561, 1514,

1248, 1218, 1201, 1172 cm^{-1}; ^{1}H-nmr (360 MHz, CD_3OD) δ7.57 (1H, d, J = 8.5 Hz, H-6′), 7.56 (1H, d, J = 15.7 Hz, H-ß), 7.50 (2H, d, J = 8.6 Hz, H-2 and H-6), 7.41 (1H, d, J = 15.7 Hz, H-α), 6.81 (2H, d, J = 8.6 Hz, H-3 and H-5), 6.51 (1H, d, J = 2.1 Hz, H-3′), 6.45 (1H, dd, J = 8.5, 2.1 Hz, H-5′), 3.89 (3H, s, CH_3O-2′); ms, *m/z* (rel. intensity) 270 (M^+, 14%), 269 (4), 255 (8), 242 (6), 239 (4), 164 (21), 163 (6), 151 (24), 119 (9), 107 (11).

(2R)-7,4′ Dihydroxyflavan (13).- Fractions 28-32, eluted from the silica gel-60 column with petroleum ether and EtOAc (3:1) were further subjected to silica gel-60 PF 254 chromatography (5.5 × 47 cm), collecting 50 ml fractions, and eluting with mixtures of $CHCl_3$ and MeOH of increasing polarity. Fractions 84-88 afforded glassy pale red crystals of **13** (63.5 mg, 0.010%), mp 191-193°C; $[\alpha]_D^{20}$ +1.8° (c 0.217, MeOH); R_f $CHCl_3$-MeOH (92:8): 0.20; uv, λ_{max} (MeOH) 230 (log ε 3.84), 282 (3.67), 289.5 (sh) nm (3.52); λ_{max} (+NaOMe) 250 (log ε 3.93), 292 nm (3.78); λ_{max} (+$AlCl_3$) 230 (log ε 3.84), 282 (3.63), 290 (sh) nm (3.47); λ_{max} (+$AlCl_3$/HCl) 229 (log ε 3.84), 282 (3.60), 288.5 (sh) nm (3.46); λ_{max} (+NaOAc) 231 (log ε 3.87), 282 (3.66), 290 (sh) nm (3.51); λ_{max} (+NaOAc/H_3BO_3) 231 (log ε 3.87), 282 (3.64), 289 (sh) nm (3.50); ir, ν_{max} (KBr) 3468, 3390, 3027, 2973, 2925, 2874, 1614, 1595, 1519, 1506, 1223, 1207, 1174, 1155, 1110, 1000 cm^{-1}; ^{1}H-nmr (360 MHz, CD_3OD) δ 7.20 (2H, d, J = 8.6 Hz, H-2′ and H-6′), 6.83 (1H, d, J = 8.2 Hz, H-5), 6.78 (2H, d, J = 8.6 Hz, H-3′ and H-5′), 6.32 (1H, dd, J = 8.2, 2.5 Hz, H-6), 6.27 (1H, d, J = 2.5 Hz, H-8), 4.83 (1H, dd, J = 11.1, 2.8 Hz, H-2_{ax}), 2.80 (1H, ddd, J = 16.1, 11.1, 5.4 Hz, H-4_{ax}), 2.61 (1H, ddd, J = 16.1, 5.4, 2.8 Hz, H-4_{eq}), 2.04 (1H, ddt, J = 11.1, 5.4, 2.8, 2.8 Hz, H-3_{eq}), 1.93 (1H, qd, J = 11.1, 11.1, 11.1, 5.4 Hz, H-3_{ax}); ^{13}C-nmr (90.8 MHz, CD_3OD) δ157.99 (C-4′), 157.40 (C-7), 157.09 (C-8a), 134.14 (C-1′), 130.92 (C-5), 128.42 (C-2′ and C-6′), 115.99 (C-3′ and C-5′), 114.24 (C-4a), 109.01 (C-6), 103.98 (C-8), 78.94 (C-2), 31.26 (C-3), 25.49 (C-4); ms, *m/z* (rel. intensity) 242 (M^+, 91%), 136 (23), 123 (65), 120 (100), 119 (13).

(2R)-4′-Hydroxy-7-methoxyflavan (14).- Fractions 14-16, eluted from the silica gel-60 column with petroleum ether and EtOAc (4:1), were further subjected to silica gel-60 chromatography (3 × 60 cm), collecting 100 ml fractions, and eluting with $CHCl_3$. Fractions 2-8 afforded glassy, pale red needles in $CHCl_3$ and long white needles in MeOH of **14** (1.004 g, 0.159%), mp 137°C (MeOH); $[\alpha]_D^{20}$ +5.8° (c 0.189, MeOH); R_f $CHCl_3$-MeOH (99:1): 0.18; uv, λ_{max} (MeOH) 227.5 (log ε 4.13), 282 (3.68), 289 (sh) nm (3.54); λ_{max} (+NaOMe) 218.5 (log ε 4.19), 243.5 (4.20), 284 (3.78), 289 (3.78), 299 (sh) nm (3.39); λ_{max} (+$AlCl_3$) 226.5 (log ε 4.14), 282 (3.68), 288 (sh) nm (3.56); λ_{max} (+$AlCl_3$/HCl) 215 (sh) (log ε 4.10), 226 (4.14), 281.5 (3.66), 289 (sh) nm (3.52); λ_{max} (+NaOAc) 231.5 (log ε 4.20), 282.5 (3.74), 289 (sh) nm (3.63); λ_{max} (+NaOAc/H_3BO_3) 231.5 (log ε 4.23), 281.5 (3.76), 289 nm (3.65); ir, ν_{max} (KBr) 3381, 3026, 2970, 2947, 2919, 2892, 2887, 2875, 2844, 1616, 1588, 1255, 1218, 1202, 1193, 1154, 1109, 999 cm^{-1}; ^{1}H-nmr (360 MHz, $CDCl_3$) δ 7.27 (2H, d, J = 8.5 Hz, H-2′ and H-6′), 6.97 (1H, d, J = 7.9 Hz, H-5), 6.80 (2H, d, J = 8.5 Hz, H-3′ and H-5′),

6.48 (1H, dd, J = 7.9, 2.6 Hz, H-6), 6.47 (1H, d, J = 2.6 Hz, H-8), 4.95 (1H, dd, J = 9.0, 2.8 Hz, H-2_{ax}), 3.74 (3H, s, CH_3O-7), 2.89 (1H, ddd, J = 16.3, 9.0, 5.7 Hz, H-4_{ax}), 2.72 (1H, ddd, J = 16.3, 5.7, 2.8 Hz, H-4_{eq}), 2.13 (1H, ddt, J = 9.0, 5.7, 2.8, 2.8 Hz, H-3_{eq}), 2.04 (1H, qd, J = 9.0, 9.0, 9.0, 5.7 Hz, H-3_{ax}); ^{13}C-nmr (90.8 MHz, $CDCl_3$) δ 158.83 (C-7), 155.76 (C-8a), 155.23 (C-4′), 133.69 (C-1′), 129.94 (C-5), 127.60 (C-2′ and C-6′), 115.32 (C-3′ and C-5′), 113.98 (C-4a), 107.39 (C-6), 101.53 (C-8), 77.71 (C-2), 55.31 (CH_3O-7), 29.85 (C-3), 24.50 (C-4); ms, m/z (rel. intensity) 256 (M^+, 100%), 255 (9), 150 (17), 137 (56), 121 (6), 120 (30), 119 (7).

(3R)-Eucomol (15).- Fractions 61-104, eluted from the silica gel-60 column with petroleum ether and EtOAc (1:3) afforded glassy, pale orange rhomboid crystals of **15** (195.9 mg, 0.031%), mp 131-132°C; $[\alpha]_D^{21}$ -31.5° (c 0.143, $CHCl_3$); R_f petroleum ether-$CHCl_3$-EtOAc(1:2:1): 0.37; uv, λ_{max} (MeOH) 214.5 (log ε 3.91), 224.5 (3.88), 285 (sh) (3.71), 292 (3.75), 328 nm (3.31); λ_{max} (+NaOMe) 225 (sh) (log ε 3.81), 245 (3.30), 277.5 (sh) (2.99), 284 (sh) (3.10), 326 nm (3.99); λ_{max} (+$AlCl_3$) 224 (log ε 4.00), 277 (sh) (3.13), 284 (sh) (3.26), 316.5 (3.87), 380 nm (3.01); λ_{max} (+$AlCl_3$/HCl) 224 (log ε 3.98), 277 (sh) (3.19), 284 (sh) (3.32), 314.5 (3.84), 379 nm(3.01); λ_{max} (+NaOAc) 277.5 (sh) (log ε 3.30), 283.5 (sh) (3.38), 327.5 nm (3.94); λ_{max} (+NaOAc/H_3BO_3) 294 (log ε 3.75), 331 nm (3.20); ir, ν_{max} (KBr) 3451, 3318, 2966, 2935, 2839, 1642, 1635, 1588, 1514, 1301, 1257, 1251, 1175, 1160, 1076 cm^{-1}; ^{1}H-nmr (360 MHZ, CD_3OD) δ 7.14 (2H, d, J = 8.6 Hz, H-2′ and H-6′), 6.82(2H,d, J = 8.6 Hz, H-3′ and H-5′), 5.93 (1H, d, J = 2.2 Hz, H-8), 5.90 (1H, d, J = 2.2 Hz, H-6), 3.99 (2H, AB, J = 11.3 Hz, H-2), 3.75 (3H, s, CH_3O-4′), 2.91 (2H, AB, J = 14.1 Hz, H-9); ^{1}H-nmr (360 MHz, DMSO-d_6) δ 7.09 (2H, d, J = 8.5 Hz, H-2′ and H-6′), 6.79(2H,d, J = 8.5 Hz, H-3′ and H-5′), 5.95 (1H, br s, OH), 5.86 (1H, d, J = 2.0 Hz, H-8), 5.84 (1H, d, J = 2.0 Hz, H-6), 3.88 (2H, br s, H-2), 3.66 (3H, s, CH_3O-4′), 2.80 (2H, br s, H-9); ^{13}C-nmr (90.8 MHz, CD_3OD) δ 199.57 (C-4), 168.46 (C-7), 165.54 (C-5), 164.19 (C-8a), 159.94 (C-4′), 132.65 (C-2′ and C-6′), 127.89 (C-1′), 114.38 (C-3′ and C-5′), 101.27 (C-4a), 97.38 (C-8), 96.14 (C-6), 73.36 (C-3), 72.63 (C-2), 55.53 (CH_3O-4′), 40.55 (C-9); ms, m/z (rel. intensity) 316 (M^+, 5%), 298 (1), 195 (9), 167 (4), 153 (11), 152 (3), 122 (41), 121 (100).

Compound **15** (28.43 mg) was partially acetylated in pyridine-acetic anhydride (1:1, 2 ml) at room temperature. Immediate work-up in the usual way and crystallization from MeOH afforded white needles of **16** (10.2 mg) mp 128°C; $[\alpha]_D^{20}$-59.1° (c 0.107, $CHCl_3$); R_f petroleum ether-$CHCl_3$-EtOAc (1:2:1): 0.63; uv, λ_{max}(MeOH) 220 (log ε 4.43), 261 (4.01), 282 (sh) (3.64), 315 nm (3.60); λ_{max} (+NaOMe) 217 (log ε 4.53), 249 (3.94), 285 (sh) (3.74), 326 nm (4.35); λ_{max} (+$AlCl_3$) 219 (log ε 4.44), 261 (4.02), 312 nm (3.55); λ_{max} (+$AlCl_3$/HCl) 219 (log ε 4.42), 262 (4.01), 312 nm (3.54); (λ_{max}(+NaOAc)228 (log ε 4.60), 250 (3.95), 284 (sh) (3.78), 327 nm (4.32); λ_{max} (+NaOAc/H_3BO_3) 231 (log ε 4.59), 282 (4.11), 312 nm (3.83); ir, ν_{max} (KBr) 3463, 3068, 3013, 2981, 2942, 2909, 2844, 1777, 1774, 1691, 1620, 1514, 1207, 1183, 1136, 1118, 1032 cm^{-1}; ^{1}H-nmr (360 MHz, $CDCl_3$) δ 7.12 (2H, d, J = 8.7 Hz, H-2′ and H-6′), 6.84 (2H, d,

J = 8.7 Hz, H-3′ and H-5′), 6.78 (1H, d, J = 2.1 Hz, H-6), 6.60 (1H, d, J = 2.1 Hz, H-8), 4.16 (2H, AB, J = 11.4 Hz, H-2), 3.79 (3H, s, CH_3O-4′), 2.90 (2H, AB, J = 14.1 Hz, H-9), 2.35 (3H, s, CH_3COO), 2.32 (3H, s, CH_3COO); ^{13}C-nmr (90.8 MHz, $CDCl_3$) δ 193.46 (C-4), 169.05 ($CH_3\underline{C}OO$), 167.83 ($CH_3\underline{C}OO$), 162.97 (C-8a), 158.66 (C-4′), 156.44, 151.38, 131.64 (C-2′ and C-6′), 125.83 (C-1′), 113.60 (C-3′ and C-5′), 110.89 (C-6), 109.37 (C-4a), 108.90 (C-8), 72.52 (C-3), 71.71 (C-2), 55.19 (CH_3O-4′), 39.89 (C-9), 21.20 (CH_3COO), 20.90 (CH_3, COO); ms, m/z (rel. intensity) 400 (M^+, 7%), 315 (1), 298 (2), 195 (20), 167 (2), 153 (9) 152 (5), 122 (28), 121 (100).

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บทคัดย่อ

อนุพันธ์ของฟลาโว่นอยด์ 15 ชนิด (1–15) สกัดได้จากเนื้อไม้จันทน์แดง *(Dracaena loureiri)* และได้กำหนดสูตรโครงสร้างโดยใช้เทคนิคของ nmr ทั้งระบบเอกมิติ และทวิมิติ พบโครงสร้างชนิดใหม่ 2 ชนิด คือ dracaenones และ loureirins พร้อมทั้งสรุปความสัมพันธ์ของกระบวนการชีวสังเคราะห์ของฟลาโว่นอยด์ที่แยกได้