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A Short and Facile Synthetic Route to Prenylated Flavones. Cyclodehydrogenation of Prenylated 2'-Hydroxychalcones by a Hypervalent Iodine Reagent

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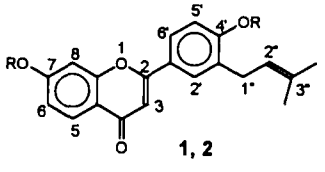
Abstract: The first synthesis of the prenylated flavones kanzonol-D (**1**), -E (**3**) and yinyanghuo-C (**4**) was accomplished by cyclodehydrogenation of the appropriately substituted 2'-hydroxychalcones **16**, **14** and **11**, respectively, in presence of phenyl-iodine(III) diacetate (PIDA) / potassium hydroxide in methanol. The synthesis of kanzonol-B (**13**) was also achieved from the 2'-hydroxychalcone **12**.

Keywords: Flavonoids; flavones; chalcones; hypervalent iodine

Flavones carrying a prenyl substituent and those with a 2,2-dimethyl-2*H*-pyran ring system frequently occur in nature[1,2] and occupy a prominent position among plant phenols owing to their complex biological activity.[3-6] Although several methods for the synthesis of these natural products have been developed,[7-10] most



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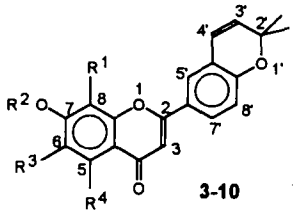

3-10

	R
1	H
2	MOM

	R^1	R^2	R^3	R^4
3	H	H	$Me_2C=CH-CH_2$	H
4	H	H	H	OH
5	H	MOM	H	OMOM
6	H	MOM	H	H
7	H	H	H	H
8	H	MOM	$Me_2C=CH-CH_2$	H
9	$Me_2C=CH-CH_2$	MOM	$Me_2C=CH-CH_2$	H
10	$Me_2C=CH-CH_2$	H	$Me_2C=CH-CH_2$	H

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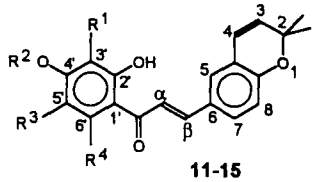
of these procedures suffer from limitations. Recently, we have published[11] a simple method for the synthesis of polyhydroxylated flavones by the cyclodehydrogenation of the appropriately substituted 2'-hydroxychalcones with PIDA / potassium hydroxide in methanol. In continuation of our investigation of naturally occurring biologically active flavonoids[11-14] we have set our sights on the extension of this method for the synthesis of prenylated flavones.

In order to study the scope and limitations of our method in this field, kanzonol-D (**1**) and -E (**3**), new prenylated flavone constituents of *Glycyrrhiza eurycarpa*,[15] and yinyanghuo-C (**4**) with antiplatelet activity isolated from *Vancouveria hexandra*[16] and *Epimedium sagittatum*[17] have been selected as target molecules.

In particular, it is of interest to study whether 2'-hydroxychalcones possessing a 3,3-dimethylallyl or/and 2,2-dimethyl-2*H*-pyran moiety could be transformed into the corresponding flavones without damage to these functional groups. It is well-known from the literature, that the reaction of alkenes with hypervalent iodine reagents showing electrophilic character exhibit interesting features when different functional groups are introduced into the double bond.[18,19]

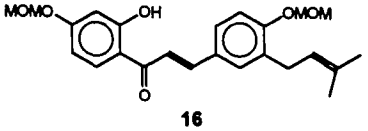
Results and Discussion

The 2'-hydroxychalcone **11** served as a suitable starting material for the synthesis of yinyanghuo-C (**4**), and it was prepared by the condensation of 4,6-bis(methoxymethyl)-phloracetophenone[20] and 2,2-dimethyl-6-formyl-2*H*-chromene[21] in the presence of 50% aqueous sodium hydroxide at room temperature.



11-15

	R^1	R^2	R^3	R^4
11	H	MOM	H	OMOM
12	H	MOM	H	H
13	H	H	H	H
14	H	MOM	$Me_2C=CH-CH_2$	H
15	$Me_2C=CH-CH_2$	MOM	$Me_2C=CH-CH_2$	H



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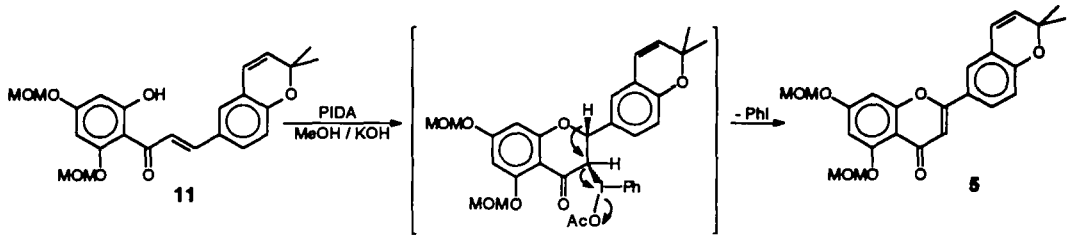
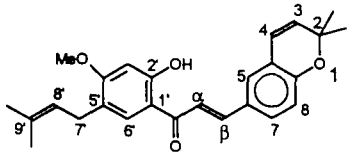
Transformation of **11** with PIDA under the conditions described in our previous paper[11] resulted in the corresponding flavone **5** in good yield (62%). As no other products could be detected by TLC analysis of the reaction mixture, the addition of the reagent (PIDA) to the phenolate anion (generated from the 2'-hydroxyl group of **11** and formation of a 3-phenyliodonium-flavanone intermediate is believed to proceed regioselectively at the double bond adjacent to the carbonyl group. Since in this intermediate the prerequisite of the reductive elimination of iodobenzene and simultaneous loss of hydrogen at C-2 are present, the transformation of **11** took place smoothly to give the prenylated flavone **5**.



Removal the protecting groups of **5** under mild acid conditions afforded yinyanghuo-C (**4**) with m.p. 246-248° which was identical with the natural product in every respect. Cyclodehydrogenation of chalcone **12** also took place without difficulties and gave flavone **6** in 64% yield, whose treatment with dilute hydrochloric acid in methanol afforded **7**.

Besides the two new prenylated flavones kanzanol-D (**1**) and -E (**3**), a novel prenylated chalcone, kanzonol-B (**13**) has also been isolated by Fukai *et al.*[15] from the roots of *Glycyrrhiza eurycarpa*, whose structure was elucidated by spectroscopic methods. It was prepared by a simple demethoxymethylation, under mild acid conditions, of the intermediate **12** from the synthesis of **7**. In fact, treatment of **12** with 18% hydrochloric acid in methanol resulted a crystalline compound with m.p. 189-190°C in 80% yield, which was found to be identical with kanzonol-B (**13**), indicating that the well-documented cyclization of 2',4'-dihydroxychalcones to the corresponding flavanones[22] did not occur in this case. The synthesis of kanzonol-D (**1**) and -E (**3**) could also be accomplished from the chalcones **16** and **14**, respectively, by cyclodehydrogenation with PIDA under standard conditions. These successful transformations (**16** → **2** and **14** → **8**) clearly showed that the attack of the electrophilic reagent (PIDA) took place regioselectively at the olefinic carbon atom neighbouring the carbonyl group which possesses the highest electron density among the olefinic carbons of the molecules in full accordance with quantum chemical calculations. To make a qualitative estimation of the reactivity of the above-mentioned chalcones with an electrophilic reagent (PIDA), we performed a PM3 semiempirical calculation of the electron density of chalcone **18** possessing both a 3,3-dimethylallyl group and a 2,2-dimethyl-2*H*-pyran moiety to assess the different features affecting the reactivity of the double bond atoms.

According to the traditional Löwdin atomic point charges, the C-α carbon should be the most sensitive to the electrophilic attack (see Table 1.).



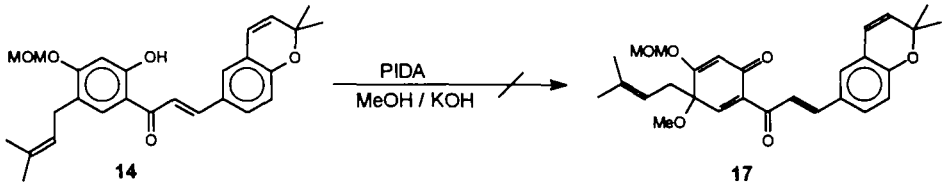
18

	$q_{Löwdin}$	q_{EP}	c_{HOMO}
C-3	-.181	-.185	.178
C-4	-.061	-.153	.103
C-β	.030	.064	-.127
C-α	-.265	-.501	-.233
C-8'	-.169	-.128	-.094
C-9'	-.120	-.252	-.122

Table 1. Quantum chemical data of **18**

The EP charges[23] calculated from the electrostatic potential map are considered more reliable, and reflected the same reactivities of the carbon atoms as the Löwdin charges. Another possibility for the measurement of the reactivity of the atoms toward electrophilic substitution is the frontier electron populations or the coefficients of the HOMO on the carbon atoms.[24] Although the quaternary aromatic carbons at C-1' and C-2' exhibit the highest values, among the olefinic carbons carbon C-α was found to be the most sensitive to electrophilic attack.

It is noteworthy, that dearomatization of ring B of **14** with PIDA, to give the corresponding cyclohexadienone derivative **17**, was not observed under the above conditions. This reagent has been widely



14 **17**

applied to the preparation of 4-alkyl-4-methoxycyclohexadienones in methanol starting from the corresponding *para*-substituted phenols.[25-27] This side-reaction could also be expected in the case of **15**. Since no such a reaction could be recognised, and only cyclodehydrogenation (**15** → **9**) occurred in good yield (63%), therefore PIDA has proved to be a very useful reagent not only for the synthesis of polyhydroxylated flavones,[11] but also for the prenylated analogues starting from the readily available prenylated 2'-hydroxy-chalcone derivatives. The *in vitro* anti-HIV activity of the synthetic compounds is under examination.

Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. 200-MHz ^{1}H-NMR spectra were recorded with a Bruker WP 200 SY instrument with TMS as internal standard. MS spectra were obtained with a VG-7035 GC/MS/DS spectrometer (ion current 0.1 mA, direct insertion technique). Elemental analyses were carried out with a Carlo Erba 1106 analyser. Pre-coated silica gel plates (Kieselgel 60 F254, 0.25 mm, Merck) were used for analytical and preparative TLC. For workup the solutions were dried ($MgSO_4$) and concentrated in vacuo. Phenyliodine(III) diacetate (PIDA) was purchased from Aldrich and 2-hydroxy-4-methoxymethyloxyacetophenone, 2-hydroxy-5-(3,3-dimethylallyl)-4-methoxymethyloxyacetophenone, 3-(3,3-dimethylallyl)-4-methoxymethyloxybenzaldehyde were prepared by known methods.[28-30] Demethoxymethylation of **5**, **6**, **8** and **9** was carried out as described for **13**.

2-Hydroxy-3,5-bis(3,3-dimethylallyl)-4-methoxymethyloxyacetophenone. To a stirred solution of 3,5-bis(3,3-dimethylallyl)-2,4-dihydroxy-acetophenone[31] (3.1 g, 11 mmol) in dry acetone (25 ml) in the presence of K_2CO_3 (5 g) a solution of methoxymethylchloride (2 ml) in dry acetone (10 ml) was added drop wise in 1 h at room temp. After 2 h, potassium carbonate was filtered off, the filtrate was poured into water, the product was extracted with dichloromethane, dried and after evaporation the residue was crystallized from ethanol to give 3.0 g (83%), m.p. 67-68°C as white prisms; ^{1}H NMR ($CDCl_3$): δ = 1.65 and 1.75 (s, 12H, allyl-Me), 2.53 (s, 3H, acetyl-Me), 3.35 and 3.40 (d, J = 5 Hz, 4H, aryl-CH_2), 3.58 (s, 3H, OMe), 5.02 (s, 2H, OCH_2O), 5.20 and 5.30 (t, J = 3 Hz, 2H, allyl-CH), 7.44 (s, 1H, 6-H), 12.55 (s, 1H, 2-OH); Anal. Calcd. for $C_{20}H_{28}O_4$ (332.4): C, 72.26; H, 8.49; found: C, 72.51;1 H, 8.40.

General Procedure for the Preparation of 2'-Hydroxychalcone Derivatives. A solution of the corresponding acetophenone (5 mmol) and aldehyde derivative (5.10 mmol) in ethanol (20 ml) was stirred with 50% (w/w) aqueous NaOH (2 ml) at room temp. After 24 h, the reaction mixture was acidified by passing CO_2 gas through the solution and poured into water. The product was extracted with dichloromethane or ethyl acetate, dried and evaporated. The crude material was purified by crystallisation or by means of flash column chromatography on silica gel using a) n-hexane/ethyl acetate (10:1); b) n-hexane/acetone (10:1); c) n-hexane/acetone (4:1) as the eluent.

(E)-3-(2,2-Dimethyl-2*H*-chromen-6-yl)-1-(2-hydroxy-4,6-dimethoxymethyloxyphenyl)-2-propen-1-one (11). 47%; m.p. 71-73°C (yellow needles from n-hexane); ^{1}H NMR ($CDCl_3$): δ = 1.43 (s, 6H, 2,2-Me), 3.45 and 3.55 (s, 6H, OMe), 5.18 and 5.28 (s, 4H, OCH_2O), 5.68 and 6.35 (d, J = 5 Hz, 2H, 3,4-H), 6.24 (d, J = 1.5 Hz, 1H, 5-H), 6.32 (d, J = 1.5 Hz, 1H, 3'-H), 7.22 (d, J = 1.5 Hz, 1H, 5-H), 7.40 (dd, J = 1.5 and 3.5 Hz,

1H, 7-H), 7.70 (d, J = 10 Hz, 1H, α-H), 7.80 (d, J = 10 Hz, 1H, β-H); Anal. Calcd. for $C_{24}H_{26}O_7$ (426.4): C, 67.59; H, 6.14; found: C, 67.42; H, 6.22.

(E)-3-(2,2-Dimethyl-2*H*-chromen-6-yl)-1-(2-hydroxy-4-dimethoxymethyloxyphenyl)-2-propen-1-one (12). 42%; m.p. 128-129°C (yellow prisms from ethanol); ^{1}H NMR ($CDCl_3$): δ = 1.45 (s, 6H, 2,2-Me), 3.48 (s, 3H, OMe), 5.20 (s, 2H, OCH_2O), 5.68 and 6.35 (d, J = 5 Hz, 2H, 3,4-H), 6.62 (d, J = 1.5 Hz, 1H, 3'-H), 6.58 (m, 1H, 5'-H), 6.80 (d, J = 5 Hz, 1H, 8-H), 7.28 (d, J = 1.5 Hz, 1H, 5-H), 7.40 (m, 1H, 7-H), 7.41 (d, J = 10 Hz, α-H), 7.80 (d, J = 10 Hz, 1H, β-H), 7.82 (d, J = 3 Hz, 6'-H), 13.40 (s, 1H, 2'-OH); Anal. Calcd. for $C_{22}H_{22}O_5$ (366.4): C, 72.12; H, 6.05; found C, 72.24; H, 6.11.

(E)-1-(2',4'-Dihydroxyphenyl)-3-(2,2-dimethyl-2*H*-chromen-6-yl)-2-propen-1-one (Kanzonol-B, 13). The solution of **12** (100 mg, 0.27 mmol) in methanol (5 ml) was treated with 10% hydrochloric acid (0.2 ml) and boiled for 30 min. The reaction mixture was diluted with water. The precipitate separated and purified by preparative TLC (by b.) to give 70 mg (80%) of **13**, m.p. 189-190°C as yellow prisms. Lit. m.p. 190°C[15]; ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ = 1.45 (s, 6H, 2,2-Me), 5.70 and 6.30 (d, J = 5 Hz, 2H, 3,4-H), 7.45 (d, J = 10 Hz, 1H, α-H), 7.78 (d, J = 10 Hz, 1H, β-H), 6.48-7.80 (m, 5H, aromatic H), 7.84 (d, J = 3 Hz, 1H, 6'-H), 10.00 (bs, 1H, 4'-OH), 13.60 (s, 1H, 2'-OH); Anal. Calcd. for $C_{20}H_{18}O_4$ (322.4): C, 74.53; H, 5.62; found C, 74.44; H, 5.62.

(E)-3-(2,2-Dimethyl-2*H*-chromen-6-yl)-1-[2-hydroxy-5-(3,3-dimethylallyl)-4-methoxymethyloxyphenyl]-2-propen-1-one (14). 50%; yellow oil (by a.); ^{1}H NMR ($CDCl_3$): δ = 1.45 (s, 6H, 2,2-Me), 1.70 (s, 6H, allyl-Me), 3.28 (d, J = 5 Hz, 2H, allyl-CH_2), 3.44 (s, 3H, OMe), 5.22 (s, 2H, OCH_2O), 5.30 (t, J = 3 Hz, allyl-CH), 5.70 and 6.35 (d, J = 5 Hz, 2H, 3,4-H), 6.65 (s, 1H, 3'-H), 6.85 (d, J = 3.5 Hz, 1H, 8-H), 7.30 (d, J = 1.5 Hz, 1H, 5-H), 7.40 (dd, J = 1.5 and 3 Hz, 1H, 7-H), 7.45 (d, J = 10 Hz, α-H), 7.65 (s, 1H, 6'-H), 7.85 (d, J = 10 Hz, 1H, β-H), 13.35 (s, 1H, 2'-OH); MS (EI): m/z 434 (M^+, 20), 419 (30), 189 (100), 1783 (70); Anal. Calcd. for $C_{27}H_{30}O_5$ (434.5): C, 74.63; H, 6.96; found C, 74.61; H, 6.89.

(E)-3-(2,2-Dimethyl-2*H*-chromen-6-yl)-1-[2-hydroxy-3,5-bis(3,3-dimethylallyl)-4-methoxymethyloxyphenyl]-2-propen-1-one (15). 47%; yellow oil (by b.); ^{1}H NMR ($CDCl_3$): δ = 1.45 (s, 6H, 2,2-Me), 1.70, 1.75 and 1.80 (s, 12H, allyl-Me), 3.38 (d, J=5 Hz, 4H, aryl-CH_2), 3.60 (s, 3H, OMe), 5.00 (s, 2H, OCH_2O), 5.30 (m, 2H, allyl-CH), 5.65 and 6.35 (d, J=5 Hz, 2H, 3,4-H), 6.85 (d, J=3 Hz, 1H, 8-H), 7.25 (d, J=1.5 Hz, 5-H), 7.40 (dd, J=1.5 and 3 Hz, 7-H), 7.45 (d, J=10 Hz, 1H, α-H), 7.55 (s, 1H, 6'-H), 7.85 (d, J=10 Hz, β-H), 13.05 (s, 1H, 2'-OH); MS (EI): m/z 502 (M^+, 25), 457 (20), 215 (35), 171 (45); Anal. Calcd. for $C_{32}H_{38}O_5$ (502.6): C, 76.47; H, 7.62; found C, 76.51; H, 7.65.

(E)-3-[4-Methoxymethyloxy-3(3,3-dimethylallyl)phenyl]-1-(2-hydroxy-4-methoxymethyloxyphenyl]-2-propen-1-one (16). 78%; yellow oil (by c.); ^{1}H NMR ($CDCl_3$): δ = 1.75 and 1.80 (s, 6H, allyl-Me), 3.35 (d, J = 5 Hz, 2H, allyl-CH_2), 3.50 and 3.55 (s, 6H, OMe), 5.15 and 5.20 (s, 4H, OCH_2O), 5.30 (t, J = 2 Hz, 1H, allyl-CH), 6.60-7.90 (m, 6H, aromatic H), 7.10 (d, J = 10 Hz, 1H, α-H), 7.70 (s, J = 10 Hz, 1H, β-H), 13.40 (s, 1H, 2'-OH); MS (EI): m/z 412 (M^+, 40), 366 (60), 272 (40), 226 (60), 196 (100); Anal. Calcd. for $C_{24}H_{28}O_8$ (412.5): C, 69.88; H, 6.84; found C, 69.81; H, 6.78.

General Procedure for the Cyclodehydrogenation of 2'-Hydroxychalcone Derivatives. To a stirred solution of the 2'-hydroxychalcone (1.39 mmol) in 30 ml absolute methanol a solution of potassium hydroxide (1.39 mmol) in absolute methanol (10 ml) was added over a period of 10 min at 0°C. After stirring for an additional 10 min, PIDA (3.6 mmol) was added in 3 portions during 30 min. The resulting mixture was stirred at room temperature (3-24 h) and the reaction was monitored by TLC. The solution was concentrated and water was added to the residue. The product was filtered off or extracted with dichloromethane, dried and evaporated. The crude material was purified by crystallisation or by means of flash column chromatography on silica gel using a) toluene/acetone (4:1); b) n-hexane/acetone (4:1); c) n-hexane/ethyl acetate (4:1) as the eluent. Demethoxymethylation of **5**, **6**, **8** and **9** was carried out as described for **13**.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-5,7-dimethoxymethyloxy-4*H*-chromen-4-one (5). 62%; pale yellow oil (by a.); ^{1}H NMR ($CDCl_3$): δ = 1.45 (s, 6H, 2',2'-Me), 3.52 and 3.55 (s, 6H, 2 x OMe), 5.25 and 5.35 (s, 4H, 2 x OCH_2O), 5.70 and 6.40 (d, J = 5 Hz, 3',4'-H), 6.54 (s, 1H, 3-H), 6.73 (d, J = 1.5Hz, 1H, 6-H), 6.85 (d, J = 1.5Hz, 1H, 8-H), 7.49 (d, J = 1.5 Hz, 1H, 5'-H), 7.64 (dd, J = 1.5 and 3 Hz, 1H, 6'-H); MS (EI): m/z 424 (M^+, 20), 409 (100), 393 (35), 380 (100), 364 (100); Anal. Calcd. for $C_{24}H_{24}O_7$ (424.4): C, 67.92; H, 5.70; found C, 67.87; H, 5.67.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-7-methoxymethyloxy-4*H*-chromen-4-one (6). 64%; pale yellow oil (hexane/acetone 4:1); ^{1}H NMR ($CDCl_3$): δ = 1.50 (s, 6H, 2',2'-Me), 3.50 (s, 3H, OMe), 5.30 (s, 2H, OCH_2O), 5.70 and 6.40 (d, J = 5 Hz, 3',4'-H), 6.65 (s, 1H, 3-H), 6.90-8.20 (bm, 6H, aromatic H); MS (EI): 364 (M^+, 20), 349 (100), 305 (35), 189 (90); Anal. Calcd. for $C_{22}H_{20}O_5$ (364.4): C, 72.51; H, 5.53; found C, 72.57; H, 5.48.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-6-(3,3-dimethylallyl)-7-methoxymethyloxy-4*H*-chromen-4-one (8). 40%; m.p. 124-126°C (yellow needles by b. and from ethyl acetate/n-hexane); ^{1}H NMR ($CDCl_3$): δ = 1.50 (s, 6H, 2',2'-Me), 1.75 (s, 6H, allyl-Me), 3.40 (d, J = 5 Hz, 2H, aryl-CH_2), 3.50 (s, 3H, OMe), 5.30 (t, J = 3 Hz, 1H, allyl-CH), 5.35 (s, 2H, OCH_2O), 5.70 and 6.40 (d, J = 7 Hz, 2H, 3',4'-H), 6.65 (s, 1H, 3-H), 6.85 (d, J

= 3 Hz, 1H, 8'-H), 7.20 (s, 1H, 8-H), 8.00 (s, 1H, 5-H), 7.55 (d, J = 1.5 Hz, 1H, 5'-H), 7.70 (dd, J = 1.5 and 3 Hz, 1H, 7'-H); Anal. Calcd. for $C_{27}H_{28}O_5$ (432.5): C, 74.98; H, 6.52; found C, 75.10; H, 6.40.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-6,8-bis(3,3-dimethylallyl)-7-methoxymethyloxy-4*H*-chromen-4-one (9). 63%; pale yellow oil (by b.); ^{1}H NMR ($CDCl_3$): δ = 1.40, 1.55, 1.75 and 1.80 (s, 12H, allyl-Me), 3.45 and 3.65 (d, J = 3 Hz, 4H, aryl-CH_2), 3.60 (s, 3H, OMe), 5.05 (s, 2H, OCH_2O), 5.30 (m, 2H, allyl-CH), 5.70 and 6.35 (d, J = 7 Hz, 2H, 3',4'-H), 6.65 (s, 1H, 3-H), 6.85 (d, J = 5.5 Hz, 1H, 8-H), 7.45 (d, J = 1.5 Hz, 1H, 5'-H), 7.60 (dd, J = 1.5 and 3 Hz, 1H, 7'-H), 7.90 (s, 1H, 5-H); MS (EI): m/z 500 (M^+, 10), 413 (50), 401 (100), 189 (40); Anal. Calcd. for $C_{32}H_{36}O_5$ (500.6): C, 76.78; H, 7.25; found C, 76.72; H, 7.22.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-5,7-dihydroxy-4*H*-chromen-4-one (Yinyanghuo-C, 4). 62%; m.p. 246-248°C (yellow needles by b. and from methanol); Lit. m.p. amorphous powder[16], 228-230°C[17]; ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ = 1.46 (s, 6H, 2',2'-Me), 5.82 and 6.40 (d, J = 5 Hz, 2H, 3',4'-H), 6.29 (d, J = 1.5 Hz, 1H, 6-H), 6.49 (d, J = 1.5 Hz, 1H, 8-H), 6.50 (s, 1H, 3-H), 6.87 (d, J = 3 Hz, 1H, 7'-H), 7.51 (d, J = 1.5 Hz, 1H, 5'-H), 7.64 (dd, J = 1.5 and 3 Hz, 1H, 7'-H), 10.1 (s, 1H, 7-OH), 12.80 (s, 1H, 5-OH); Lit.[16] δ (DMSO-d_6) 1.48, 5.71, 6.38, 6.31, 6.45, 6.54, 6.87, 7.63, 10.2 and 13.00 resp.; Anal. Calcd. for $C_{20}H_{16}O_5$ (336.3): C, 71.43; H, 4.79; found C, 71.35; H, 4.69.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-7-hydroxy-4*H*-chromen-4-one (7). 37%; m.p. 258-260°C (yellow prisms from ethanol); ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ = 1.50 (s, 6H, 2',2'-Me), 5.72 and 6.42 (d, J = 5 Hz, 2H, 3',4'-H), 6.62 (s, 1H, 3-H), 6.87 (d, J = 3 Hz, 1H, 8'-H), 6.94 (m, 1H, 6-H), 6.95 (d, J = 1.5 Hz, 1H, 8-H), 7.51 (d, J = 1.5 Hz, 1H, 5'-H), 7.67 (dd, J = 1.5 and 3 Hz, 1H, 7'-H), 8.05 (d, J = 3 Hz, 1H, 5-H); Anal. Calcd. for $C_{20}H_{16}O_4$ (320.3): C, 75.00; H, 5.03; found C, 75.10; H, 5.12.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-6-(3,3-dimethylallyl)-7-methoxymethyloxy-4*H*-chromen-4-one (Kanzonol-E, 3). 75%; m.p. 247-248°C (yellow needles by c. and from hexane/ethyl acetate); Lit. m.p. 246-248°C[15]; ^{1}H NMR (DMSO-d_6): δ = 1.45 (s, 6H, 2',2'-Me), 1.70 and 1.75 (s, 6H, allyl-Me), 3.30 (d, J = 5 Hz, 2H, aryl-CH_2), 5.35 (t, J = 3 Hz, 1H, allyl-CH), 5.85 and 6.55 (d, J = 10 Hz, 2H, 3',4'-H), 6.65 (s, 1H, 3-H), 6.90 (d, J = 3 Hz, 8'-H), 7.00 (s, 1H, 8-H), 7.65 (s, 1H, 5-H), 7.80 (d, J = 1.5 Hz, 5'-H), 7.85 (dd, J = 1.5 and 3 Hz, 1H, 7'-H), 10.9 (brs, 1H, 7-OH), Lit.[15] δ (acetone-d_6) 1.46, 1.74, 1.76, 3.42, 5.40, 5.86, 6.54, 6.61, 7.06, 7.82, 7.74, 7.80, resp.; Lit.[16] (DMSO-d_6) δ = 1.48, 5.71, 6.38, 6.31, 6.45, 6.54, 6.87, 7.63, 10.2 and 13.00 resp.; Anal. Calcd. for $C_{25}H_{24}O_4$ (388.4): C, 77.30; H, 6.23; found C, 77.25; H, 6.12.

2-(2,2-Dimethyl-2*H*-chromen-6-yl)-6,8-bis(3,3-dimethylallyl)-7-methoxymethyloxy-4*H*-chromen-4-one (10). 40%; m.p. 158-160°C (yellow needles from acetone/hexane); ^{1}H NMR ($CDCl_3$): δ = 1.50 (s, 6H, 2',2'-Me), 1.75 and 1.80 (s, 12H, allyl-Me), 3.45 and 3.74 (d, *J* = 5 Hz, 1H, aryl-CH_2), 5.35 (m, 2H, allyl-CH), 5.70 and 6.40 (d, *J* = 7 Hz, 2H, 3',4'-H), 6.15 (s, 1H, 7-OH), 6.65 (s, 1H, 3-H), 6.85 (d, *J* = 5 Hz, 1H, 8'-H), 7.50 (d, *J* = 1.5 Hz, 1H, 5'-H), 7.65 (dd, *J* = 1.5 and 5 Hz, 1H, 7'-H), 7.85 (s, 1H, 5-H); Anal. Calcd. for $C_{30}H_{32}O_4$ (456.6): C, 78.92; H, 7.06; found C, 78.77; H, 7.15.

3'-(3,3-Dimethylallyl)-7,4'-dihydroxy-flavone (Kanzonol-D, 1). 33%; m.p. 229-231°C (yellow needles by b. and from benzene/acetone); Lit. m.p. 229-231°C[15]; ^{1}H NMR (DMSO-d_6): δ = 1.75 (s, 6H, 3",3"-Me), 3.25 (d, *J* = 5 Hz, 2H, 1"-CH_2), 5.35 (t, *J* = 3 Hz, 1H, 2"-H), 6.65 (s, 1H, 3-H), 6.95-7.85 (bm, 6H, aromatic H), 10.3 and 10.8 (s, 2H, 7,4'-OH), Lit.[15] (acetone-d_6) δ = 1.76, 1.77, 3.40, 5.41, 6.58, 6.96-7.96, resp.; Anal. Calcd. for $C_{20}H_{18}O_4$ (322.4): C, 74.51; H, 5.63; found C, 74.12; H, 5.74.

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