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Synthesis of flavonoid-type compounds from methyl dehydroabietates

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Abstract The synthesis of new flavone-type compounds bearing several chiral centres, 12- and 14-(2′-chromonyl)dehydroabietates, are reported. This synthesis started from the aldol condensation of methyl 12- and 14-formyldehydroabietates with 2′-hydroxyacetophenones in order to prepare the corresponding chalcone-type compounds, which were then transformed in the expected flavone-type compounds by cyclodehydrogenation with *DMSO* and a catalytic amount of iodine. All compounds were exhaustively characterised by NMR and MS techniques.

Keywords Chromones; Chalcones; Dehydroabietate derivatives; NMR; MS.

Introduction

Dehydroabietic acid can be easily obtained by catalytic dehydrogenation of abietic-type resin acids, which are very abundant in pine resin [1]. Among resin acids, those of abietic acid-type are the most abundant; they are also the most versatile for chemical synthesis due to the presence of the conjugated double bond system. Dehydroabietic acid has been considered as an interesting starting material for the synthesis of new and more valuable compounds, especially with significant biological properties. It is well-known that many oxygenated diterpenic compounds either synthesized or isolated from natural sources have shown promising biological activities [2–4]. Reactions of the aromatic moiety involving various aromatic substitution reactions are used in the synthesis of natural and bioactive products [5–8]. The dihydroabietic acid, and similar compounds, can also be chemically transformed to obtain new compounds with other potencialities [9].

2′-Hydroxychalcones and flavones are important groups of heterocyclic polyphenolic compounds widely distributed in the plant kingdom, where they participate in several vital functions [10]. Moreover promising pharmaceutical, biocidal, and antioxidant activities have been found for some of these natural compounds and for certain synthetic analogues [11]. The industrial significance of such properties, the search of new and more potent biological active derivatives, the potential synergetic effect with dehydroabietates and our interests on the synthesis of more valuable compounds from dehydroabietic acid [12] and on the synthesis of some flavonoid derivatives [13], led us to study the synthesis of novel flavonoid-dehydroabietates dyads. The stereochemical features of the new products might bring a contribution to potential biological properties.

Results and Discussion

Synthesis

Our synthesis study started with the formylation of **1**. *Vielsmeier* reaction proved to be unsuccessful to prepare the expected formyl derivative **2**. The for-

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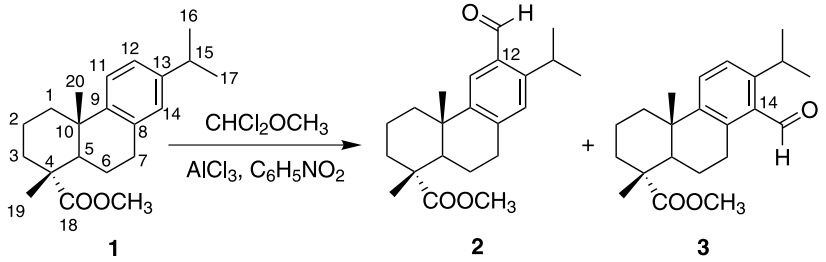


Scheme 1

mylation of **1** with α,α-dichloromethyl methyl ether in the presence of aluminium(III) chloride was attempted according to literature data, using dichloromethane as solvent [14]; compound **2** was then obtained in poor yields (≈15%). However, when the reaction was carried out in nitrobenzene, a solvent commonly used in *Friedel-Crafts* reactions, compound **2** was isolated in 50% yield, and also methyl 14-formyldehydroabietate **3** was isolated in lower yields (≈22%) (Scheme 1).

2′-Hydroxychalcones **4a**–**4c** and **6a**–**6c** were synthesised by base-catalysed aldol condensations of the adequate 2′-hydroxyacetophenones and the benzaldehyde-type compounds **2**, **3** (Scheme 2). In general, it was observed that even with a longer reaction time, chalcones **6a**–**6c** were obtained in lower yields (42–75%) than chalcones **4a**–**4c** (55–85%), due to the higher steric hindrance of position 14.

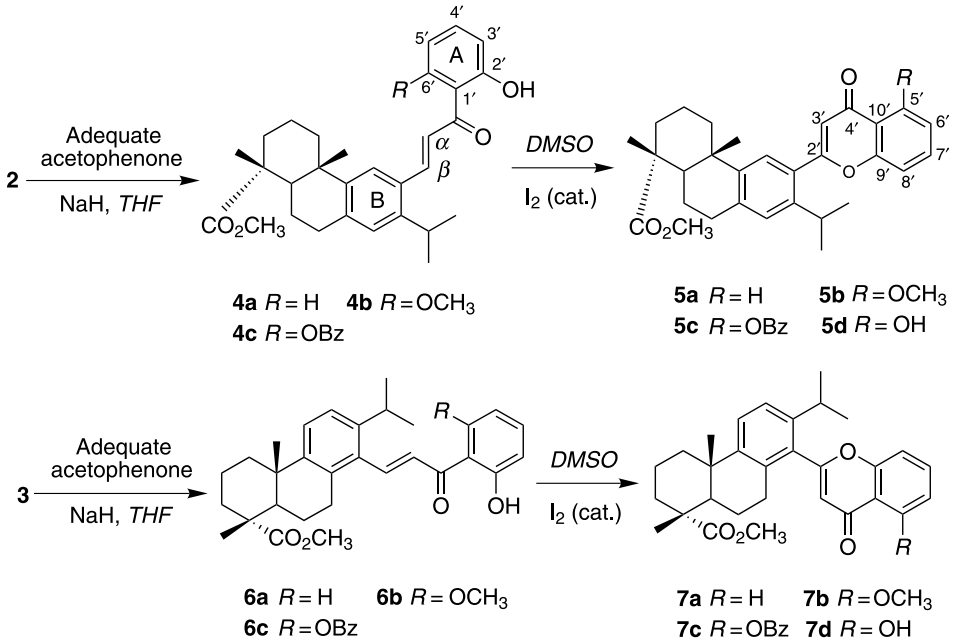
The oxidative cyclization of 2′-hydroxychalcones **4a**–**4c** and **6a**–**6c** into flavones **5a**–**5d** and **7a**–**7d** was carried out in *DMSO* in the presence of a catalytic amount of iodine (Scheme 2) [13]. The formation of flavones **5d** and **7d** can be explained by the oxidative cyclization of the corresponding chalcones **4c** and **6c** followed by cleavage of the benzylic group of compounds **5c** and **7c**, as it has been reported in the synthesis of 5-hydroxychromones [15]. The yields of benzylated and debenzylated products depend mainly on the reaction time: for compounds **5c**/**5d** it was found that, after 15 min, **5c** was formed in 90% yield and **5d** in only 5%; on the other hand, after 120 min, only **5d** was isolated in 87% yield.

Finally, it was also found that the cyclization of chalcones **6a**–**6c** yielded more complex mixtures and lower yields than those found for chalcones **4a**–**4c**; in the case of chalcone **6b** the corresponding cyclization product was never isolated. When compared with compounds **4a**–**4c** this difference in reactivity should again be due to the higher hindrance of position 14. In the case of compound **7c**, it can be isolated (8%) from the reaction media after 15 min; and after 120 min a complete debenzylation took place yielding compound **7d** in 10% yield.

Structural characterisation

The most important features of the spectra of **2** are the proton and carbon resonances of the formyl group ($\delta_H = 10.27$ and $\delta_C = 192.2$). In the case of **3**, these signals appear at δ_H 10.63 ppm and δ_C 195.7 ppm. The two doublets at δ_H 7.24 and 7.42 ppm, with J values characteristic of *ortho* protons ($J = 8.4$ Hz) in the ^{1}H NMR spectrum of **3** instead of two singlets in that of **2**, confirm that positions 11 and 12 are not functionalized and therefore the presence of a 14-formyl group. ^{1}H and ^{13}C resonances of the methyl protons of the isopropyl group of **3** appear at different chemical shift values, as it was already described for 12-substituted derivatives [12], due to the steric hindrance caused by the 14-substituent.

In the ^{1}H NMR spectra of chalcones **4a**–**4c** and **6a**–**6c** the β-proton resonances appear at higher frequency values (δ_H 7.85–8.35 ppm) than those of α-protons (δ_H 7.18–7.74 ppm), which is due to the deshielding mesomeric effect of the carbonyl group. The coupling constants $J_{H\alpha\text{-}H\beta}$ 15–16 Hz indicate a *trans* configuration for these vinylic systems. The existence of strong hydrogen bonds involving the carbonyl groups and the 2′-hydroxyl proton was confirmed by the presence of proton resonances at δ_H 12.78–13.24 ppm. In the ^{1}H NMR spectrum of **4c**, H-1*eq* and H-20 resonances were shifted to lower frequency values relatively to other chalcones **4a**, **4b**, due to the anisotropic shielding effect of the phenyl ring of the 2′-benzyloxy group. This phenomenon was confirmed by the close proximities of H-β to H-15, H-α to H-11, and H-20 to H-2″,6″ (phenyl ring of the benzyloxy group), infered from the cross peaks observed in its N*O*ESY spectrum. These N*O*E effects allowed us to assign the structure of com-



Scheme 2

pounds **4a**–**4c** as depicted in Scheme 2 and to suggest the absence of free rotation about the bond C-β–C-12. In the N*O*ESY spectrum of compound **6c** N*O*E cross peaks between the resonances of H-α and H-β and those of H-7 and H-15 indicate that there is a free rotation around the bond C-β–C-14.

The assignment of H-3′ and H-5′ resonances of compounds **4b**, **4c** and **6b**, **6c** was performed by using HETCOR and one-dimensional selective INEPT. Upon irradiation of 2′-OH resonance (δ_{OH} = 12.94–13.24 ppm), signal enhancements were observed at δ_C = 118.8–112.6, 164.4–165.0 and 101.5–110.9 ppm, which were therefore assigned to C-1′, C-2′, and C-3′. After the assignment of C-3′, based on the HETCOR spectra, it was possible to assign H-3′ ressonances to the double doublet at δ_H = 6.62–6.64 ppm and therefore confirmed the assignment of H-5′ to the double doublet at δ_H 6.40–6.50 ppm.

It is known that the resonances of some protons of 2′-hydroxychalcones are quite sensitive to the B ring substituents [13], which in the present case corresponds to the aromatic ring of the methyl dehydroabietate moiety. Compounds **6a**–**6c** have two alkyl substituents in the *ortho* positions relatively to the α,β-unsaturated system (while compounds **4a**–**4c** have only one), leading to a non-coplanarity of the B ring with the other part of the 2′-hydroxychalcone moiety. The referred absence of coplanarity in chalcone **6a**–**6c** is responsible for the higher frequency values of H-7, H-15, H-α, H-β, and 2′-OH resonances (δ_H = 2.91–2.94, 3.36, 7.50–7.74, 8.22–8.35, and 12.92–13.24 ppm) relatively to those of **4a**–**4c** (δ_H = 2.67–2.77, 3.15–3.25, 7.18–7.39, 7.85–8.03, and 12.78–13.14 ppm). Another effect of the non-coplanarity is the higher frequency values of the C-β resonance of compounds **6a**–**6c** relatively to those of **4a**–**4c** (δ_C = 142.6–145.6 and 141.0–143.8 ppm), due to the lack of conjugation between the α,β-unsaturated system and the B ring.

The main feature in the NMR spectra of flavones **5a**–**5d** and **7a**–**7d** are the resonances of the H-3′ and C-3, which appear at δ 6.24–6.45 and 110.2–115.4 ppm. In the ^{1}H and ^{13}C NMR spectra of flavones **7a**–**7d**, some signals appeared in a duplicated form, suggesting the presence of two conformations for each compound, differing in the orientation of the chromonyl moiety relatively to the rest of the molecule. The N*O*E cross peaks of H-3′ with H-7 signals of one form and also of H-3′ with H-16 and H-17 signals of the other form, led us to conclude that H-3′ is close to H-7 in the former and close to the isopropyl group in the latter. Attempts to separate the two forms of each compound **7a**–**7d** by preparative TLC were not successful. However the separation of the two forms of flavone **7d** by HPLC revealed the presence of two chromatographic peaks which were collected in separate fractions. The purity of each fraction was confirmed immediately after

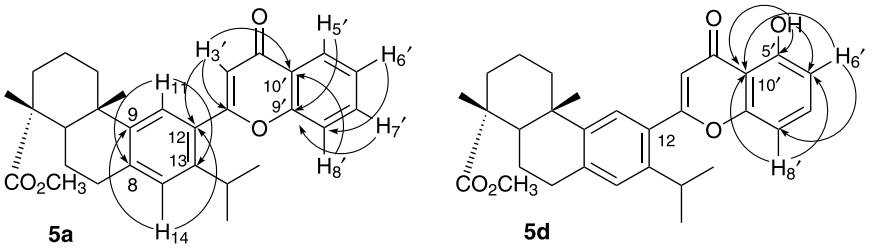


Fig. 1 Connectivities found in the HMBC spectrum of flavone-type compounds **5a** and **5d**

the HPLC isolation and solvent evaporation and revealed that each fraction becomes again a mixture. This observation confirms that each compounds **7a**–**7d** exists as a mixture of two conformers that can be easily interconverted. Additionally it was observed that the referred duplication of proton resonances at room temperature disappeared at 57°C, thus meaning that at this temperature the energy barrier between the two conformers can be easily overcome.

The unequivocal assignement of carbon resonances of flavone-type compounds **5a**–**5d** and **7a**–**7d** were based on HETCOR and HMBC spectra; being the main connectivities found in the HMBC spectrum of **5a** and **5d** shown in Fig. 1 as representatives.

The analysis of the electronic impact mass spectra of the synthesised compounds must take into consideration the characteristic fragmentations of methyl dehydroabietate [16] and of the substituents being present at positions 12 or 14. In the diterpenic moiety of the molecule, the most relevant fragmentations correspond to the loss of 10–CH_3 $[M\text{-}15]^+$, followed by the loss of HCO_2CH_3 $[M\text{-}75]^{+\bullet}$, or the direct loss of CO_2CH_3 $[M\text{-}59]^+$, and the loss of isopropyl group $[M\text{-}43]^+$.

Apart from the fragmentation of the diterpenic moiety of the molecule, the mass spectra of the compounds **4a**–**4c** and **6a**–**6c** also show the characteristic fragmentations of chalcone type compounds, involving mainly the cleavage of C–C bonds around the carbonyl group. Thermal isomerization of chalcones into flavanones sometimes occurs in the ionisation chamber, then a series of ions derived from the isomeric flavanones in spectra of chalcones can be observed [17]. This situation was observed for chalcones **4a**, **4b** and **6a**, **6b**. In addition, for compound **6a**, a $[M+2]^{+\bullet}$ fragment, probably arising from the reduction of the α,β-unsaturation in the ionisation chamber, was also observed. In compounds **4b**, **4c** and **6b**, **6c** the characteristic fragments resulting from demethylation/debenzylation $[M\text{–}Bz]^{+\bullet}$/ $[M\text{–}Me]^{+\bullet}$ followed by the loss of CO were observed. For compounds **4c** and **6c** the fragment at m/z 91, characteristic for a tropylium ion is also detected.

Finally, compounds **5a**–**5d** and **7a**–**7d** show very intense molecular ions (≈100%) and the characteristic fragmentation of flavones resulting from the retro-*Diels-Alder* cleavage of the chromonyl moieties.

Conclusion

The synthesis of chalcone derivatives of methyl 12- and 14-formyldehydroabietates was achieved in good yields. The corresponding flavone-type structures were obtained in good yields in the case of 12-substituted derivatives **5**, whereas in the case of 14-substituted derivatives **7** only moderate yields were obtained, probably due to the high steric hindrance of this position.

Experimental

Melting points were determined in a *Reichert* Thermovar apparatus fitted with a microscope. NMR spectra were recorded on a Bruker AMX 300 spectrometer (300.13 MHz for ^1H and 75.47 MHz ^{13}C), with $CDCl_3$ as solvent. Chemical shifts (δ) are reported in ppm values and coupling constants (J) in Hz. The internal reference was *TMS*. ^1H assignments were made using N*O*ESY spectra (mixing time 800 ms), while ^{13}C assignments were made using 1D selective INEPT [18] (long-range C/H coupling constants optimised to 7 Hz) and 2D HETCOR and HMBC (the low-pass J-filter portion of the experiment was optimised for an average of one-bond heteronuclear coupling of 145 Hz. The delay for evolution of long-range couplings was optimised for 7 Hz) experiments. Mass spectra (EI, 70 eV) were measured on a VG Autospec Q and M mass spectrometer (HRMS data were in good agreement (±5 ppm) with the calculated values). Elemental analyses were obtained with a Carlo Erba 1108 CHNS analyser and were in good agreement (±0.4%) with the calculated values. Preparative thin layer chromatography was carried out with Riedel silica gel 60 DGF254, and column chromatography using Merk silica gel 60, 70–230 mesh. All chemicals and

solvents used were obtained from commercial sources and used as received or dried using standard procedures. High performance liquid chromatography was performed on a GILSON equipped with a Spherisorb – S5W column, a UV-Vis detector GILSON 118 set at $\lambda = 298$ nm, and a Shimadzu C-R1B integrator. A mixture of cyclohexane:ethyl acetate (94:6) was used as eluent (1 cm^3/min). Methyl dehydroabietate (**1**) was obtained by catalytic dehydrogenation of methylated resin according to Ref. [1].

*Formylation of methyl dehydroabietate (**1**)*
$AlCl_3$ (1.1 g, 8.0 mmol) and 190 mm^3 $CHCl_2OCH_3$ (2.1 mmol) were added to a solution of 500 mg methyl dehydroabietate (**1**) (1.6 mmol) in 10 cm^3 nitrobenzene, at room temperature. After stirring for 2.5 h, the solution was poured into a 20 cm^3 saturated solution of $NaHCO_3$. This mixture was extracted with $CHCl_3$ (3×100 cm^3), the combined organic layers were dried over anhydrous sodium sulfate, and the solvent was evaporated to dryness. The residue was taken in 5 cm^3 CH_2Cl_2 and purified by preparative thin-layer chromatography using CH_2Cl_2 as eluent. After several elutions two spots were isolated; the one with higher R_f value was identified as compound **2** (274 mg, 50%) and that with lower R_f value as compound **3** (120 mg, 22%).

Methyl 12-formyldehydroabietate (**2**, $C_{22}H_{30}O_3$)
Yellow oil; ^{1}H NMR: $\delta = 1.22$ (s, H-20), 1.26, 1.28 (d, $J = 6.6$ Hz, H-16, H-17), 1.29 (s, H-19), 1.61–1.79 (m, H-1,2,3,6), 2.20 (dd, $J = 2.2$, 12.8 Hz, H-5), 2.41 (d, $J =$ 11.7 Hz, H-1), 2.92–2.975 (m, H-7), 3.68 (s, 18-OCH_3), 3.88 (heptet, $J = 6.6$ Hz, H-15), 7.08 (s, H-14), 7.71 (s, H-11), 10.27 (s, 12-C*H*O) ppm; ^{13}C NMR: $\delta = 16.5$ (C-19), 18.4 (C-2), 21.3 (C-6), 23.7, 24.0 (C-16, C-17), 25.0 (C-20), 27.2 (C-15), 30.3 (C-7), 36.6 (C-3), 36.9 (C-10), 37.8 (C-1), 44.6 (C-5), 47.5 (C-4), 52.0 (18-O*C*H$_3$), 126.8 (C-11), 128.1 (C-14), 131.0 (C-12), 142.4 (C-8), 147.6 (C-13), 148.1 (C-9), 178.9 (C-18), 192.2 (12-*C*HO) ppm; MS (EI): m/z (%) = 342 (53) $[M]^{+\bullet}$, 325 (22), 297 (14), 283 (73), 267 (100), 255 (12), 217 (10), 213 (12), 201 (16), 197 (11), 181 (14), 169 (11), 155 (13), 143 (11), 141 (14), 129 (14), 128 (13), 55 (12).

Methyl 14-formyldehydroabietate (**3**, $C_{22}H_{30}O_3$)
Yellow oil; ^{1}H NMR: $\delta = 1.23$ (s, H-20), 1.23, 1.28 (2d, $J = 6.8$ Hz, H-16, H-17), 1.27 (s, 19), 1.45–1.86 (m, H-1,2,3,6), 2.21 (dd, $J = 2.0$, 12.6 Hz, H-5), 2.30 (d, $J =$ 11.4 Hz, H-1), 3.08–3.14 (m, H-7), 3.53 (heptet, $J = 6.8$ Hz, H-15), 3.67 (s, 18-O*C*H$_3$), 7.24 (d, $J = 8.4$ Hz, H-12), 7.42 (d, $J = 8.4$ Hz, H-11), 10.63 (s, 14-*C*HO) ppm; ^{13}C NMR: $\delta = 16.4$ (C-19), 18.5 (C-2), 21.4 (C-6), 23.9, 24.2 (C-16, C-17), 25.0 (C-20), 28.1 (C-15), 28.2 (C-7), 36.3 (C-3), 37.3 (C-10), 38.2 (C-1), 43.9 (C-5), 47.4 (C-4), 52.0 (18-O*C*H$_3$), 123.7 (C-12), 129.1 (C-11), 132.6 (C-14), 136.0 (C-8), 147.8 (C-9,13), 178.9 (C-18), 195.7 (14-*C*HO) ppm; MS (EI): m/z (%) = 342 (95) $[M]^{+\bullet}$, 282 (13), 267 (100), 249 (12), 239 (17), 227 (11), 214 (11), 213 (23), 211 (13), 201 (18), 199 (11), 197 (10), 195 (19), 183 (16), 181 (12), 169 (18), 167 (11), 165 (13), 155 (16), 153 (11), 143 (12), 141 (18), 129 (15), 128 (16), 115 (12), 59 (12), 55 (14).

*General method for the synthesis of 2′-hydroxychalcones **4a–4c***
Dry sodium hydride (7 mg, 0.31 mmol) was added to a dried solution of the appropriate acetophenone (0.15 mmol) in 10 cm^3 *THF* under nitrogen. After stirring for 5 min, 50 mg methyl 12-formyldehydroabietate (**2**) (0.15 mmol) were added and the reaction mixture was stirred for 20 h. After this period, the mixture was poured into 20 cm^3 H_2O, 30 g ice, and commercial HCl (*pH* of resulting mixture adjusted to 2). The obtained mixture was extracted with $CHCl_3$ (3×30 cm^3), and the combined organic layers were dried with anhydrous sodium sulfate, and the solvent was evaporated to dryness. The residue was taken in 2 cm^3 CH_2Cl_2 and purified by preparative thin-layer chromatography using dichloromethane as eluent. With 2′-hydroxyacetophenone as starting material **4a** was obtained (38 mg, 55%); 2′-hydroxy-6′-methoxyacetophenone gave **4b** (59 mg, 80%), and 2′-benzyloxy-6′-hydroxyacetophenone gave **4c** (72 mg, 85%).

Methyl 12-[2-(2-hydroxybenzoyl)vinyl]dehydroabietate (**4a**, $C_{30}H_{36}O_4$)
Yellow oil; ^{1}H NMR: $\delta = 1.24$, 1.27 (2d, $J = 6.8$ Hz, H-16, H-17), 1.26 (s, H-20), 1.30 (s, H-19), 1.42–1.90 (m, H-1,2,3,6), 2.25 (dd, $J = 2.1$, 12.5 Hz, H-5), 2.42 (d, $J =$ 11.4 Hz, H-1), 2.91–2.96 (m, H-7), 3.36 (heptet, $J = 6.8$ Hz, H-15), 3.68 (s, 18-OCH_3), 6.96 (dt, $J = 1.1$, 7.6 and 7.7 Hz, H-5′), 7.02 (s, H-14), 7.03 (d, $J = 8.0$ Hz, H-3′), 7.50 (dd, $J = 7.6$, 8.0 Hz, H-4′), 7.50 (d, $J = 15.2$ Hz, H-α), 7.56 (s, H-11), 7.94 (dd, $J = 1.4$, 7.7 Hz, H-6′), 8.35 (d, $J =$ 15.2 Hz, H-β), 12.92 (s, 2′-O*H*) ppm; ^{13}C NMR: $\delta = 16.5$ (C-19), 18.4 (C-2), 21.4 (C-6), 23.6, 23.9 (C-16, C-17), 25.1 (C-20), 28.8 (C-15), 30 (C-7), 36.6 (C-3), 37 (C-10), 37.9 (C-1), 44.6 (C-5), 47.6 (C-4), 52 (18-O*C*H$_3$), 118.6 (C-3′), 118.8 (C-5′), 120.1 (C-α), 120.3 (C-1′), 122.6 (C-11), 126.3 (C-14), 129.6 (C-6′), 130.2 (C-12), 136.2 (C-4′), 138.8 (C-8), 143.8 (C-β), 145.9 (C-13), 147.4 (C-9), 163.6 (C-2′), 178.9 (C-18), 193.8 (C=O) ppm; MS (EI): m/z (%) = 460 (9) $[M]^{+\bullet}$, 417 (100), 385 (11), 121 (24).

Methyl 12-[2-(2-hydroxy-6-methoxybenzoyl)vinyl]dehydroabietate (**4b**, $C_{31}H_{38}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.24$, 1.27 (2d, $J = 6.8$ Hz, H-16, H-17), 1.25 (s, H-20), 1.29 (s, H-19), 1.42–1.93 (m, H-1,2,3,6), 2.25 (dd, $J = 2.2$, 12.5 Hz, H-5), 2.36 (d, $J =$ 11.6 Hz, H-1), 2.90-2095 (m, H-7), 3.36 (heptet, $J = 6.8$ Hz, H-15), 3.67 (s, 18-OCH_3), 3.94 (s, 6′-OCH_3), 6.44 (dd, $J = 0.7$, 8.3 Hz, H-5′), 6.62 (dd, $J = 0.7$, 8.3 Hz, H-3′), 7.00 (s, H-14), 7.36 (t, $J = 8.3$ Hz, H-4′), 7.54 (s, H-11), 7.74 (d, $J = 15.3$ Hz, H-α), 8.22 (d, $J = 15.3$ Hz, H-β), 13.24 (s, 2′-O*H*) ppm; ^{13}C NMR: $\delta = 16.5$ (C-19), 18.5 (C-2), 21.5 (C-6), 23.5, 23.9 (C-16, C-17), 25.2 (C-20), 26.7 (C-15), 29.9 (C-7), 36.5 (C-3), 36.9 (C-10), 37.9 (C-1), 44.6 (C-5), 47.5 (C-4), 51.9 (18-O*C*H$_3$), 55.8 (6′-O*C*H3), 101.5 (C-3′), 110.9 (C-5′), 112 (C-1′), 122.9 (C-11), 126.1 (C-14), 128.1 (C-α), 130.9 (C-12), 135.7 (C-4′), 138 (C-8), 141.3 (C-β), 145.6 (C-13), 147.1 (C-9), 160.9 (C-2), 164.8 (C-2′), 178.9 (C-18), 194.5 (C=O) ppm; MS (EI): m/z (%) = 490 (7) $[M]^{+\bullet}$, 447 (100 177 (13), 151 (48).

Methyl 12-[2-(6-benzyloxy-2-hydroxybenzoyl)vinyl]dehydroabietate (**4c**, $C_{37}H_{42}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.04$ (s, H-20), 1.22, 1.25 (2d, $J = 6.8$ Hz, H-16, H-17), 1.24 (s, H-19), 1.39–1.85 (m, H-1,2,3,6), 1.90 (d, $J = 12.7$ Hz, H-1), 2.14 (dd, $J = 2.2$, 12.5 Hz, H-5), 2.89–2.93 (m, H-7), 3.36 (heptet, $J = 6.8$ Hz, H-15), 3.68 (s, 18-OCH_3), 5.20 (s, 6′-OCH_2Ph), 6.50 (d, $J = 8.0$ Hz, H-5′), 6.64 (d, $J = 8.3$ Hz, H-3′), 6.98 (s, H-14), 7.13 (t, $J = 7.2$ Hz, H-3″, 5″), 7.22 (t, $J = 7.3$ Hz, H-4″), 7.31 (s, H-11), 7.31–7.37 (m, H-2″,6″, H-4′), 7.74 (d, $J = 15.3$ Hz, H-α), 8.22 (d, $J = 15.3$ Hz, H-β), 12.94 (s, 2′-O*H*) ppm; ^{13}C NMR: $\delta = 16.4$ (C-19), 18.4 (C-2), 21.4 (C-6), 23.5, 24.0 (C-16, C-17), 25 (C-20), 28.6 (C-15), 29.9 (C-7), 36.5 (C-3), 36.7 (C-10), 37.3 (C-1), 44.5 (C-5), 47.5 (C-4), 51.9 (18-OCH_3), 70.8 (6′-OCH_2*Ph*), 103 (C-3′), 111.1 (C-5′), 112.6 (C-1′), 122.7 (C-11), 125.9 (C-14), 126.5 (C-2″, 6″), 126.5 (C-4″), 128 (C-3″, 5″), 128.5 (C-α), 130.6 (C-12), 135.6 (C-4′), 136 (C-1″), 137.9 (C-8), 141.0 (C-β), 145.6 (C-13), 147.2 (C-9), 159.9 (C-6′), 164.4 (C-2′), 179 (C-18), 194.6 (C=O) ppm; MS (EI): m/z (%) = 566 (8) $[M]^{+\bullet}$, 523 (100), 475 (14), 433 (10), 403 (11), 325 (10), 137 (47), 91 (90).

General method for the synthesis of 2′-hydroxychalcones ***6a–6c***
NaH (7 mg, 0.31 mmol) was added to a solution of the appropriate acetophenone (0.15 mmol) in 10 cm^3 dry *THF* under nitrogen. After stirring for 5 min, 50 mg methyl 14-formyldehydroabietate (**3**) (0.15 mmol) were added and the reaction mixture was stirred for 30 h. After this period, the mixture was poured into H_2O and commercial HCl (*pH* of resulting mixture adjusted to 2). This mixture was extracted with $CHCl_3$ (3×30 cm^3), the combined organic layers were dried with anhydrous sodium sulfate, and the solvent was evaporated to dryness. The residue was taken in 2 cm^3 CH_2Cl_2 and purified by thin-layer chromatography using CH_2Cl_2 as eluent. With 2′-hydroxyacetophenone as starting material **6a** was obtained (52 mg, 75%); 2′-hydroxy-6′-methoxyacetophenone gave **6b** (48 mg, 65%), and 2′-benzyloxy-6′-hydroxyacetophenone gave **6c** (36 mg, 42%).

Methyl 14-[2-(2-hydroxybenzoyl)vinyl]dehydroabietate (**6a**, $C_{30}H_{36}O_4$)
Yellow oil; ^{1}H NMR: $\delta = 1.19$, 1.23 (2d, $J = 6.8$ Hz, H-16, H-17), 1.24 (s, H-20), 1.27 (s, H-19), 1.30–1.83 (m, H-1,2,3,6), 2.23 (dd, $J = 2.0$, 12.5 Hz, H-5), 2.33 (d, $J = 12.5$ Hz, H-1), 2.73–2.78 (m, H-7), 3.17 (heptet, $J = 6.8$ Hz, H-15), 3.65 (s, 18-OCH_3), 6.91 (ddd, $J = 1.1$, 7.7, 7.9 Hz, H-5′), 7.03 (dd, $J = 1.1$, 8.1 Hz, H-3′), 7.18 (d, $J = 15.9$ Hz, H-α), 7.20 (d, $J = 8.3$ Hz, H-12), 7.29 (d, $J = 8.3$ Hz, H-11), 7.49 (ddd, $J = 1.5$, 7.7, 8.1 Hz, H-4′), 7.79 (dd, $J = 1.5$, 7.9 Hz, H-6′), 8.03 (d, $J = 15.9$ Hz, H-β), 12.78 (s, 2′-O*H*) ppm; ^{13}C NMR: $\delta = 16.4$ (C-19), 18.5 (C-2), 21.6 (C-6), 23.8, 24.2 (C-16, C-17), 25 (C-20), 29.4 (C-7), 29.6 (C-15), 36.4 (C-3), 37.2 (C-10), 38.1 (C-1), 44.2 (C-5), 47.4 (C-4), 51.9 (18-OCH_3), 118.6 (C-3′), 118.9 (C-5′), 119.7 (C-1′), 123.1 (C-12), 124.9 (C-11), 126.5 (C-α), 129.7 (C-6′), 132.8 (C-14), 133.8 (C-8), 136.5 (C-4′), 143.6 (C-13), 145.6 (C-β), 147 (C-9), 163.7 (C-2′), 178.9 (C-18), 193.3 (C=O) ppm; MS (EI): m/z (%) = 462 (7) $[M + 2]^{+\bullet}$, 444 (74), 419 (100), 385 (34), 367 (41), 338 (10), 263 (12), 121 (99), 83 (11).

Methyl 14-[2-(2-hydroxy-6-methoxybenzoyl)vinyl]dehydroabietate (**6b**, $C_{31}H_{38}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.19$, 1.23 (d, $J = 6.8$ Hz, H-16, H-17), 1.24 (s, H-20), 1.27 (s, H-19), 1.40–1.87 (m, H-1,2,3,6), 2.23 (dd, $J = 2.0$, 12.5 Hz, H-5), 2.33 (d, $J = 11.7$ Hz, H-1), 2.75–2.80 (m, H-7), 3.25 (heptet, $J = 6.8$ Hz, H-15), 3.65 (s, 18-OCH_3), 3.86 (s, 6′-OCH_3), 6.40 (dd, $J = 0.7$, 8.3 Hz, H-5′), 6.63 (dd, $J = 0.7$, 8.3 Hz, 3′), 7.18 (d, $J = 8.5$ Hz, H-12), 7.27 (d, $J = 8.5$ Hz, H-11), 7.31 (d, $J = 15.9$ Hz, H-α), 7.36 (t, $J = 8.3$ Hz, H-4′), 7.90 (d, $J = 15.9$ Hz, H-β), 13.08 (s, 2′-O*H*) ppm; ^{13}C NMR: $\delta = 16.4$ (C-19), 18.6 (C-2), 21.7 (C-6), 23.8, 24.2 (C-16, C-17), 25.1 (C-20), 29.4 (C-15), 29.5 (C-7), 36.5 (C-3), 37.3 (C-10), 38.2 (C-1), 44.3 (C-5), 47.5 (C-4), 51.9 (18-OCH_3), 55.8 (6′-OCH_3), 101.4 (C-5′), 110.9 (C-3′), 111.8 (C-1′), 123 (C-12), 124.6 (C-11), 133.1 (C-14), 133.4 (C-α), 134.3 (C-8), 136 (C-4′), 142.7 (C-β), 143.7 (C-13), 146.9 (C-9), 161 (C-6′), 164.9 (C-2′), 179 (C-18), 194.2 (C=O) ppm; MS (EI): m/z (%) = 490 (11) $[M]^{+\bullet}$, 472 (76), 457 (13), 447 (83), 415 (19), 397 (40), 338 (21), 263 (16), 177 (23), 153 (44), 151 (100), 137 (18).

Methyl 14-[2-(6-benzyloxy-2-hydroxybenzoyl)vinyl]dehydroabietate (**6c**, $C_{37}H_{42}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.06$, 1.09 (d, $J = 6.8$ Hz, H-16, H-17), 1.23 (s, H-20), 1.26 (s, H-19), 1.33–1.79 (m, H-1,2,3,6), 2.18 (dd, $J = 2.1$, 12.5 Hz, H-5), 2.34 (d, $J = 12.0$ Hz, H-1), 2.63–2.70 (m, H-7), 3.15 (heptet, $J = 6.8$ Hz, H-15), 3.60 (s, 18-OCH_3), 5.15 (s, 6′-OCH_2*Ph*), 6.42 (d, $J = 8.1$ Hz, H-5′), 6.62 (dd, $J = 0.8$, 8.1 Hz, H-3′), 7.08–7.17 (m, H-3″,5″, H-4″, H-12), 7.21–7.26 (m, H-2″,6″, H-11), 7.31 (t, $J = 8.1$ Hz, H-4′), 7.39 (d, $J = 15.8$ Hz, H-α), 7.85 (d, $J = 15.8$ Hz, H-β), 13.14 (s, 2′-O*H*) ppm; ^{13}C NMR: $\delta = 16.4$ (C-19), 18.6 (C-2), 21.6 (C-6), 23.7, 24.1 (C-16, C-17), 25.1 (C-20), 29.3 (C-15), 29.4 (C-7), 36.5 (C-3), 37.3 (C-10), 38.2 (C-1), 44.3 (C-5), 47.5 (C-4), 51.9 (18-OCH_3), 70.9 (6′-OCH_2Ph), 102.4 (C-3′), 111.1 (C-5′), 112 (C-1′), 123 (C-4″), 124.5 (C-11), 126.9 (C-2″,6″), 128 (C-12), 128.5 (C-3″,5″), 132.9 (C-14), 133.7 (C-α), 134 (C-8), 135.7 (C-1″), 136 (C-4′), 142.6 (C-β), 143.7 (C-13), 146.7 (C-9), 160 (C-6′), 165 (C-2′), 178.9 (C-18), 194.3 (C=O) ppm; MS (EI): m/z (%) = 566 (26) $[M]^{+\bullet}$, 548 (38), 523 (82), 475 (51), 457 (30), 431 (10), 425 (14), 415 (28), 397 (30), 383 (11), 339 (13), 338 (13), 325 (10), 263 (17), 227 (24), 138 (10), 137 (90), 91 (100).

General method for the synthesis of flavones ***5a–5d*** *and* ***7a–7d***
Iodine (0.5 mg) was added to a solution of the appropriate chalcone **4a–4c** and **6a–6c** (0.10 mmol) in 2 cm^3 *DMSO* under nitrogen. The reaction mixture was heated at reflux during the necessary time. After this period, the mixture was poured into H_2O with some crystals of sodium thiosulfate. This mixture was extracted with $CHCl_3$ (3×30 cm^3), the combined organic layers were dried with anhydrous sodium sulfate, and the solvent was evaporated to dryness. The residue was taken in 3 cm^3 CH_2Cl_2 and purified by thin-layer chromatography using CH_2Cl_2 as eluent. With **4a** as starting material **5a** was

obtained (38 mg, 84%) after 30 min of reaction; **4b** gave **5b** (42 mg, 87%) after 30 min of reaction, **4c** gave **5c** (51 mg, 90%) and **5d** (3 mg, 5%) after 15 min of reaction and gave **5d** (41 mg, 87%) after 2 h of reaction, **6a** gave **7a** (14 mg, 30%) after 30 min of reaction, **6c** gave **7c** (3 mg, 5%) after 15 min of reaction and gave **7d** (5 mg, 10%) after 2 h of reaction.

Methyl 12-(2-chromonyl)dehydroabietate (**5a**, $C_{30}H_{34}O_4$)
Yellow oil; ^{1}H NMR: $\delta = 1.24$ (s, H-20), 1.25, 1.28 (2d, $J = 6.8$ Hz, H-16, H-17), 1.29 (s, H-19), 1.41–1.94 (m, H-1,2,3,6), 2.25 (dd, $J = 2.2$, 12.5 Hz, H-5), 2.29 (d, $J =$ 13.1 Hz, H-1), 2.94–2.99 (m, H-7), 3.11 (heptet, $J = 6.8$ Hz, H-15), 3.68 (s, 18-OCH_3), 6.45 (s, H-3′), 7.10 (s, H-14), 7.29 (s, H-11), 7.44 (ddd, $J = 1.0$, 7.7, 7.9 Hz, H-6′), 7.47 (d, $J =$ 7.7 Hz, H-8′), 7.69 (dt, $J = 1.7$, 7.7 Hz, H-7′), 8.27 (dd, $J = 1.7$, 7.9 Hz, H-5′) ppm; ^{13}C NMR: $\delta = 16.5$ (C-19), 18.4 (C-2), 21.4 (C-6), 24.1, 24.3 (C-16, C-17), 25.1 (C-20), 29.9 (C-7), 29.9 (C-15), 36.6 (C-3), 37 (C-10), 37.8 (C-1), 44.6 (C-5), 47.5 (C-4), 52 (18-OCH_3), 112 (C-3′), 118.1 (C-8′), 123.8 (C-10′), 125.1 (C-11), 125.6 (C-5′), 125.7 (C-5′), 126.8 (C-14), 129.6 (C-12), 133.6 (C-7′), 138.4 (C-8), 144.4 (C-13), 147.4 (C-9), 156.4 (C-9′), 167.5 (C-2′), 178.4 (C-4′), 178.9 (C-18) ppm; MS (EI): m/z (%) = 458 (64) $[M]^{+\bullet}$, 443 (52), 383 (100), 341 (12), 337 (28), 317 (18), 261 (10), 165 (11), 121 (43).

Methyl 12-[2-(5-methoxychromonyl)]dehydroabietate
(**5b**, $C_{31}H_{36}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.23$ (s, H-20), 1.23, 1.26 (2d, $J = 6.8$ Hz, H-16, H-17), 1.29 (s, H-19), 1.41–1.93 (m, H-1,2,3,6), 2.24 (dd, $J = 2.2$ and 12.6 Hz, H-5), 2.29 (d, $J =$ 15.8 Hz, H-1), 2.93–2.97 (m, H-7), 3.09 (heptet, $J = 6.8$ Hz, H-15), 3.67 (s, 18-OCH_3), 4.01 (s, 5′-OCH_3), 6.36 (s, H-3′), 6.84 (dd, $J = 0.7$, 8.6 Hz, H-6′), 7.02 (dd, $J = 0.7$, 8.6 Hz, H-8′), 7.08 (s, H-14), 7.27 (s, H-11), 7.56 (t, $J = 8.6$ Hz, H-7′) ppm; ^{13}C NMR: $\delta = 16.5$ (C-19), 18.4 (C-2), 21.4 (C-6), 24.1, 24.3 (C-16, C-17), 25.1 (C-20), 29.9 (C-7), 36.6 (C-3), 37 (C-10), 37.9 (C-1), 44.6 (C-5), 47.5 (C-4), 52 (18-OCH_3), 56.5 (2′-OCH_3), 106.3 (C-8′), 110.2 (C-3′), 113.5 (C-6′), 114.5 (C-10′), 125.6 (C-11), 126.7 (C-14), 129.2 (C-12), 133.6 (C-7′), 138.3 (C-8), 144.4 (C-13), 147.4 (C-9), 158.5 (C-9′), 159.8 (C-5′), 165.2 (C-2′), 178.3 (C-4′), 178.9 (C-18) ppm; MS (EI): m/z (%) = 488 (100) $[M]^{+\bullet}$, 459 (10), 413 (21), 151 (13).

Methyl 12-[2-(5-benzyloxychromonyl)]dehydroabietate
(**5c**, $C_{37}H_{40}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.23$, 1.26 (2d, $J = 6.8$ Hz, H-16, H-17), 1.24 (s, H-20), 1.29 (s, H-19), 1.41–1.94 (m, H-1,2,3,6), 2.25 (dd, $J = 2.2$, 12.5 Hz, H-5), 2.29 (d, $J =$ 14.8 Hz, H-1), 2.93–2.98 (m, H-7), 3.12 (heptet, $J = 6.8$ Hz, H-15), 3.68 (s, 18-OCH_3), 5.32 (s, 5′-OCH_2*Ph*), 6.35 (s, H-3′), 6.86 (dd, $J = 0.7$, 8.4 Hz, H-6′), 7.02 (dd, $J = 0.7$, 8.4 Hz, H-8′), 7.09 (s, H-14), 7.28 (s, H-11), 7.30–7.43 (m, H-3″,4″,5″), 7.50 (t, $J = 8.4$ Hz, H-7′), 7.64 (d, $J = 7.1$ Hz, H-2″,6″) ppm; ^{13}C NMR: $\delta = 16.5$ (C-19), 18.4 (C-2), 21.4 (C-6), 24.1, 24.3 (C-16, C-17), 25.1 (C-20), 29.9 (C-7), 36.6 (C-3), 37 (C-10), 37.8 (C-1), 44.6 (C-5), 47.5 (C-4), 52 (18-OCH_3), 70.8 (2′-OCH_2*Ph*), 108.5 (C-8′), 110.5 (C-3′), 113.6 (C-6′), 115 (C-10′), 125.5 (C-11), 126.6 (C-2″,6″), 126.7 (C-14), 127.6 (C-4″), 128.5 (C-3″,5″), 129.2 (C-12), 133.5 (C-7′), 136.6 (C-1″), 138.3 (C-8), 144.4 (C-13), 147.4 (C-9), 158.5 (C-9′), 158.6 (C-5′), 165 (C-2′), 178.1 (C-4′), 178.9 (C-18) ppm; MS (EI): m/z (%) = 564 (100) $[M]^{+\bullet}$, 563 (19), 487 (11), 474 (20), 459 (19), 458 (32), 443 (10), 399 (16), 384 (10), 383 (29), 137 (13), 91 (76).

Methyl 12-[2-(5-hydroxychromonyl)]dehydroabietate
(**5d**, $C_{30}H_{34}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.24$ (s, H-20), 1.25, 1.28 (2d, $J = 6.6$ Hz, H-16, H-17), 1.29 (s, H-19), 1.42–1.91 (m, H-1,2,3,6), 2.24 (dd, $J = 2.1$, 12.6 Hz, H-5), 2.29 (d, $J =$ 14.7 Hz, H-1), 2.94–2.99 (m, H-7), 3.09 (heptet, $J = 6.6$ Hz, H-15), 3.68 (s, 18-OCH_3), 6.37 (s, H-3′), 6.82 (d, $J = 8.3$ Hz, H-6′), 6.91 (d, $J = 8.3$ Hz, H-8′), 7.11 (s, H-14), 7.27 (s, H-11), 7.54 (t, $J = 8.3$ Hz, H-7′), 12.62 (s, OH) ppm; ^{13}C NMR: $\delta =$ 16.4 (C-19), 18.4 (C-2), 21.4 (C-6), 24.1, 24.3 (C-16, C-17), 25.1 (C-20), 29.9 (C-7), 36.5 (C-3), 36.9 (C-10), 37.8 (C-1), 44.5 (C-5), 47.5 (C-4), 52 (18-OCH_3), 107.1 (C-8′), 110.4 (C-3′), 110.7 (C-10′), 111.3 (C-6′), 125.5 (C-11), 126.9 (C-14), 129 (C-12), 135.3 (C-7′), 138.8 (C-8), 144.4 (C-13), 147.5 (C-9), 156.6 (C-9′), 160.8 (C-5′), 168.8 (C-2′), 178.8 (C-18), 183.5 (C-4′) ppm; MS (EI): m/z (%) = 474 (100) $[M]^{+\bullet}$, 459 (26), 400 (26), 399 (64), 357 (10), 337 (11), 333 (14), 137 (32).

Methyl 14-(2-chromonyl)dehydroabietate (**7a**, $C_{30}H_{34}O_4$)
Yellow oil; ^{1}H NMR: $\delta = 1.16$ (d, $J = 6.8$ Hz, H-16, H-17), 1.21, 1.20 (d, $J = 6.8$ Hz, H-16, H-17), 1.26 (s, H-19), 1.26 (s, H-20), 1.31–1.84 (m, H-1,2,3,6), 2.23 (dd, $J = 1.9$ and 12.2 Hz, H-5), 2.26 (dd, $J = 2.0$, 12.2 Hz, H-5), 2.35 (d, $J = 12.0$ Hz, H-1), 2.76–2.80 (m, H-7), 2.82 (heptet, $J =$ 6.8 Hz, H-15), 2.90 (hept, $J = 6.8$ Hz, H-15), 3.63 (s, 18-OCH_3), 3.65 (s, 18-OCH_3), 6.35 (s, H-3′), 6.36 (s, H-3′), 7.24 (d, $J = 8.4$ Hz, H-12), 7.42 (d, $J = 8.4$ Hz, H-11), 7.45 (ddd, $J = 0.9$, 7.7, 7.9 Hz, H-6′), 7.48 (d, $J = 8.0$ Hz, H-8′), 7.70 (ddd, $J = 1.7$, 7.7, 8.0 Hz, H-7′), 8.29 (dd, $J = 1.7$, 7.9 Hz, H-5′) ppm; ^{13}C NMR: $\delta = 16.3$, 16.4 (C-19), 18.5 (C-2), 21.2, 21.3 (C-6), 23.9, 24.1, 24.2, 24.5 (C-16, C-17), 25.1 (C-20), 27.7, 28.3 (C-7), 30.4, 30.5 (C-15), 36.4, 36.5 (C-3), 37.3, 37.4 (C-10), 38.0, 38.1 (C-1), 44.2 (C-5), 47.5 (C-4), 51.9, 52.0 (18-OCH_3), 113.5, 113.8 (C-3′), 118.2, 118.3 (C-8′), 123.2 (C-12), 123.88, 123.91 (C-10′), 125.3 (C-6′), 125.7, 125.8 (C-5′), 126.8, 126.9 (C-11), 131.2 (C-14), 133.1, 133.2 (C-8), 133.7 (C-7′), 144.5 (C-13), 144.6 (C-13), 147.4 (C-9), 156.8, 156.9 (C-9′), 165.6, 165.7 (C-2′), 178.1, 178.2 (C-4′), 178.8, 178.9 (C-18) ppm; MS (EI): m/z (%) = 458 (48) $[M]^{+\bullet}$, 443 (39), 383 (100), 341 (10), 317 (13), 121 (36).

Methyl 14-[2-(5-benzyloxychromonyl)]dehydroabietate
(**7c**, $C_{37}H_{40}O_5$)
Yellow oil; ^{1}H NMR: $\delta = 1.16$, 1.15 (d, $J = 6.8$ Hz, H-16, H-17), 1.21 (d, $J = 6.9$ Hz, H-16, H-17), 1.26 (s, H-19), 1.26 (s, H-20), 1.29–1.83 (m, H-1,2,3,6), 2.19–2.32 (m, H-5), 2.34 (d, $J = 11.6$ Hz, H-1), 2.65–2.99 (m, H-7, H-15), 3.63 (s, 18-OC*H*3), 3.65 (s, 18-OCH_3), 5.32 (s, 5′-OCH_2Ph), 6.24 (s,

H-3′), 6.26 (s, H-3′), 6.88 (d, $J = 8.2$ Hz, H-6′), 7.03 (d, $J = 8.2$ Hz, H-8′), 7.22 (d, $J = 8.5$ Hz, H-12), 7.31 (t, $J = 7.3$ Hz, H-4″), 7.39–7.44 (m, H-3″, 5″, H-11), 7.51 (t, $J = 8.2$ Hz, H-7′), 7.66 (d, $J = 7.5$ Hz, H-2″,6″) ppm; ^{13}C NMR: $\delta = 16.38$, 16.44 (C-19), 18.5 (C-2), 21.3, 21.4 (C-6), 23.9, 24.1, 24.2, 24.4 (C-16, C-17), 25.2 (C-20), 27.7, 28.3 (C-7), 30.4, 30.5 (C-15), 36.4, 36.6 (C-3), 37.3, 37.4 (C-10), 38.05, 38.13 (C-1), 44.3 (C-5), 47.5 (C-4), 52.0, 52.1 (18-O*C*H$_3$), 70.8 (2′-O*C*H$_2$Ph), 108.3, 108.4 (C-6′), 110.6, 110.7 (C-8′), 115.1 (C-3′,10′), 115.4 (C-3′), 123.1 (C-12), 126.6 (C-2″,6″), 126.76, 126.84 (C-11), 127.6 (C-4″), 128.6 (C-3″,5″), 130.9 (C-14), 133.3, 133.4 (C-8), 133.6 (C-7′), 136.6 (C-1″), 144.6, 144.7 (C-13), 147.4 (C-9), 158.7 (C-5′,9′), 159.0 (C-5′), 163.1 (C-2′), 177.8, 177.9 (C-4′), 178.8, 179.0 (C-18) ppm; MS (EI): m/z (%) = 564 (100) $[M]^{+\bullet}$, 487 (12), 474 (15), 459 (18), 458 (29), 399 (15), 384 (11), 383 (18), 137 (12), 91 (59).

Methyl 14-[2-(5-hydroxychromonyl)]dehydroabietate (**7d**, $C_{30}H_{34}O_5$)

Yellow oil; ^{1}H NMR: $\delta = 1.16$, 1.15 (d, $J = 6.8$ Hz, H-16, H-17), 1.21 (d, $J = 6.9$ Hz, H-16, H-17), 1.26 (s, H-19), 1.26 (s, H-20), 1.38–1.84 (m, H-1,2,3,6), 2.18–2.26 (m, H-5), 2.34 (d, $J = 11.8$ Hz, H-1), 2.64–2.88 (m, H-7, H-15), 3.63 (s, 18-OC*H*$_3$), 3.65 (s, 18-OC*H*$_3$), 6.28 (s, H-3′), 6.29 (s, H-3′), 6.85 (d, $J = 8.4$ Hz, H-6′), 6.91 (dd, $J = 0.6$, 8.4 Hz, H-8′), 7.23 (d, $J = 8.5$ Hz, H-12), 7.42 (d, $J = 8.5$ Hz, H-11), 7.54 (t, $J = 8.4$ Hz, H-7′), 12.57 (s, O*H*) ppm; ^{13}C NMR: $\delta = 16.38$, 16.42 (C-19), 18.5 (C-2), 21.2, 21.3 (C-6), 23.9, 24.2, 24.5 (C-16, C-17), 25.1 (C-20), 28.4 (C-7), 30.5, 30.6 (C-15), 36.4, 36.6 (C-3), 37.3, 37.4 (C-10), 38.0, 38.1 (C-1), 44.2, 44.3 (C-5), 47.5 (C-4), 52.0, 52.1 (18-OCH_3), 107.2, 107.3 (C-8′), 110.8 (C-10′), 111.5 (C-6′), 112.1, 112.4 (C-3′), 123.2 (C-12), 127.1, 127.2 (C-11), 130.8 (C-14), 133.0, 133.2 (C-8), 135.4 (C-7′), 144.5, 144.6 (C-13), 147.51, 147.54 (C-9), 157.1 (C-9′), 160.9 (C-5′), 167.2 (C-2′), 178.9 (C-18), 183.35, 183.43 (C-4′) ppm; MS (EI): m/z (%) = 474 (100) $[M]^{+\bullet}$, 459 (18), 399 (88), 357 (13), 333 (17), 137 (38), 91 (27), 78 (21), 66 (16), 63 (24).

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