Carotenylflavonoids, a novel group of potent, dual-functional antioxidants

Stefan Beutner[a], Susanne Frixel[a], Hansgeorg Ernst[b], Thomas Hoffmann[a], Ines Hernandez-Blanco[a], Claas Hundsdoerfer[a], Nicole Kiesendahl[a], Sebastian Kock[a], Hans-Dieter Martin*[a], Bernhard Mayer[a], Peter Noack[a], Antonio Perez-Galvez[c], Grit Kock[a], Roger Scherrers[a], Wolfgang Schrader[d], Stefan Sell[a], and Wilhelm Stahl[a]

[a] University of Duesseldorf, Universitaetsstr. 1, D-40225 Duesseldorf, Germany
[b] BASF AG, Germany, [c] Instituto de la Grasa (CSIC), Sevilla, Spain, d Max Planck Institute of Coal Research, Muelheim an der Ruhr, Germany
E-mail: martin@uni-duesseldorf.de

Dedicated to Professor Waldemar Adam on the occasion of his 70th birthday

Abstract
We report here on the synthesis and antioxidant properties of novel covalently linked flavonoid-carotenoid hybrids, hereinafter referred to as carotenylflavonoids. By this strategy the essential properties of the protecting systems are improved. Compared with the parent carotenoids or flavonoids, e.g. ß-carotene and a hydroxyflavone, these molecular combinations exhibit improved photoprotective properties, as seen from their UV spectra, and they outperform the individual constituents in their antioxidant properties. The dual functionality is revealed from the time evolution of the peroxidation inhibition assay which clearly displays both phenolic and carotenoid-polyenic contributions to the antioxidant efficiency. Furthermore, these compounds have amphiphilic character, in contrast to symmetrical carotenes and hydroxylated flavones. The antioxidative potential of the carotenylflavonoids is high. They protect cumene against peroxidation more than β-carotene by a factor of about 2.3-2.5, and more than the individual components.

Keywords: Carotenoids, flavonoids, carotenylflavonoids, antioxidants, peroxide inhibition

Introduction

Carotenoids exert many important functions,[1,2] and among them are the outstanding antioxidant effects in lipid phases by free radical scavenging or singlet oxygen quenching.[3,4,5] With regard to antioxidant activity in biological systems carotenoids appear to be involved both in the protection against singlet oxygen and triplet oxygen (as radical chain-breaking antioxidants). Carote-

noids are most effective biological quenchers of $^1O_2$.[5] Singlet oxygen is known to be capable of damaging DNA[6] and of being mutagenic.[7] Furthermore, singlet oxygen can damage lipids.[8,9] Animal and cell culture studies demonstrate anticarcinogenic and antimutagenic properties of these compounds.[10,11] The underlying mechanisms are yet unknown, but the importance of the carotenoids is at least partially discussed in terms of their antioxidant activity.[12]

Polyenes and carotenoids are the best known substances among the compounds that quench $^1O_2$ by efficient energy transfer[5,13]: $^1O_2 + Q \rightarrow {}^3O_2 + {}^3Q$. A large number of modified, synthetic analogues and derivatives have been synthesized in order to prepare even better quenchers than the natural carotenoids β-carotene, canthaxanthin, or astaxanthin. Though in these cases the triplet energy of the carotenoid is the determinant, colour can give an indication of the quenching efficiency: The deeply coloured, magenta, purple and blue carotenoids and polyenes turn out to be excellent quenchers near or at the diffusion limit.[5,13]

Flavonoids constitute a major subclass of antioxidants.[14,15,16] The quenching rate constants for singlet oxygen of flavonoids and phenols are of the order 10^6-10^8 M^{-1} s^{-1}. They are about one to three orders of magnitude lower than those of carotenoids which can reach the diffusion limit (but see ref.[13]).[17,18] However, the inhibition of radical induced oxidation of substrates as cumene or methyl linoleate can be most efficient.[19] Time resolved studies of $^1O_2$ quenching by phenols in aqueous solution at different pH values show that the reaction occurs via a charge transfer from the phenolate PhO^-.[20] Phenols are also excellent chain-breaking antioxidants and good $^1O_2$ quenchers.[17]

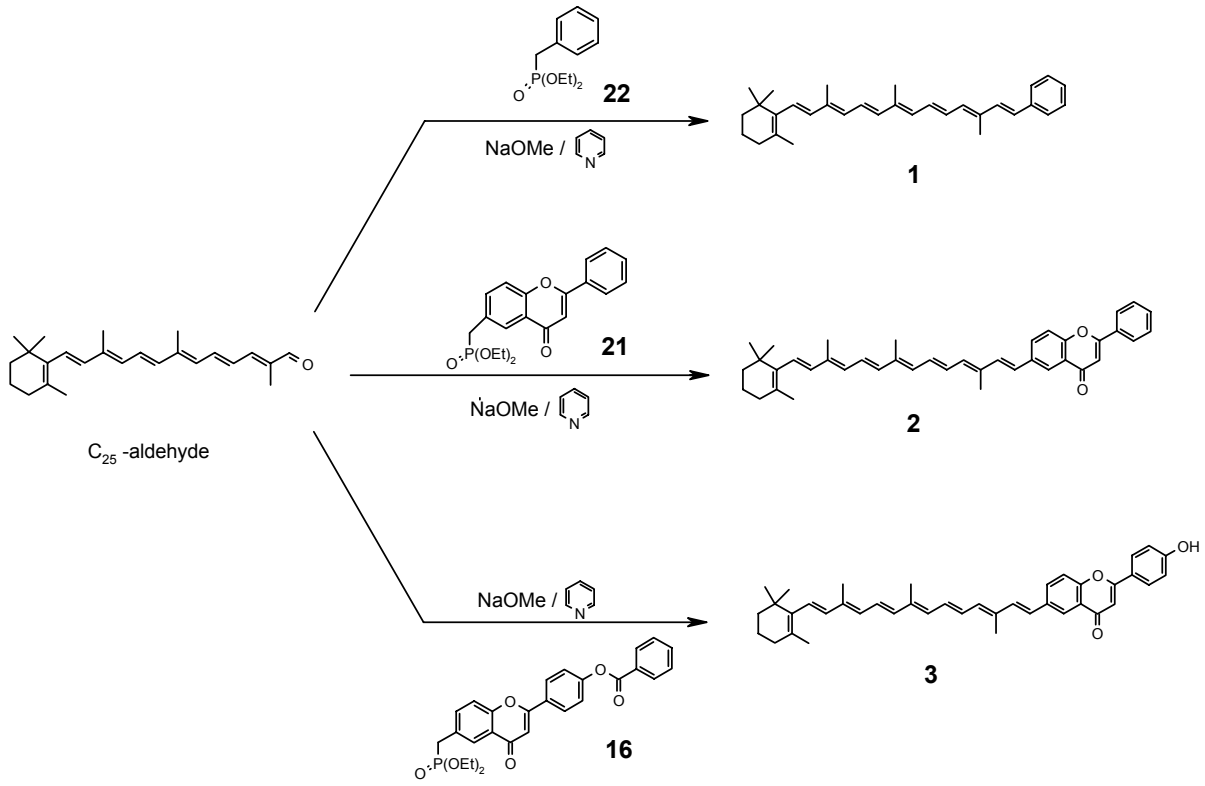
Recently we found that modified flavonoids having small conjugated side-chains excel in singlet oxygen quenching, photoprotection and photostability[21,22]. We therefore extended this research to the synthesis of molecular combinations of flavonoids and carotenoids and the investigation of their antioxidant functions. As a welcome side effect the easy insertion of these amphiphilic dual-functional molecules into lipid bilayers is to be expected, a phenomenon, which is well-known for carotenoids but less or differently observed with hydrophilic flavonoids.

Results and Discussion

The synthetic coupling of the separated chromophores was first tested using non-hydroxylated flavones and was successfully achieved by the use of the well known Wittig-Horner-Emmons-Reaction. In this way non-hydroxylated carotenylflavones **2** and **5** were synthesized that had approximately the same antioxidant properties as ketocarotenoids like echinenone or canthaxanthin[22]. But after introduction of hydroxy groups, as in **3** and **6**, a considerable increase in antioxidant activity was observed (see discussion). The reference compounds **1** and **4** are also needed for quantitative comparisons.

However, to introduce necessary hydroxy groups the strategy has to be changed. Free hydroxyl groups are not stable enough to survive the synthetic route. Therefore, protecting groups

have to be introduced and finally removed again. In these experiments the benzoyl group fulfilled all requirements.

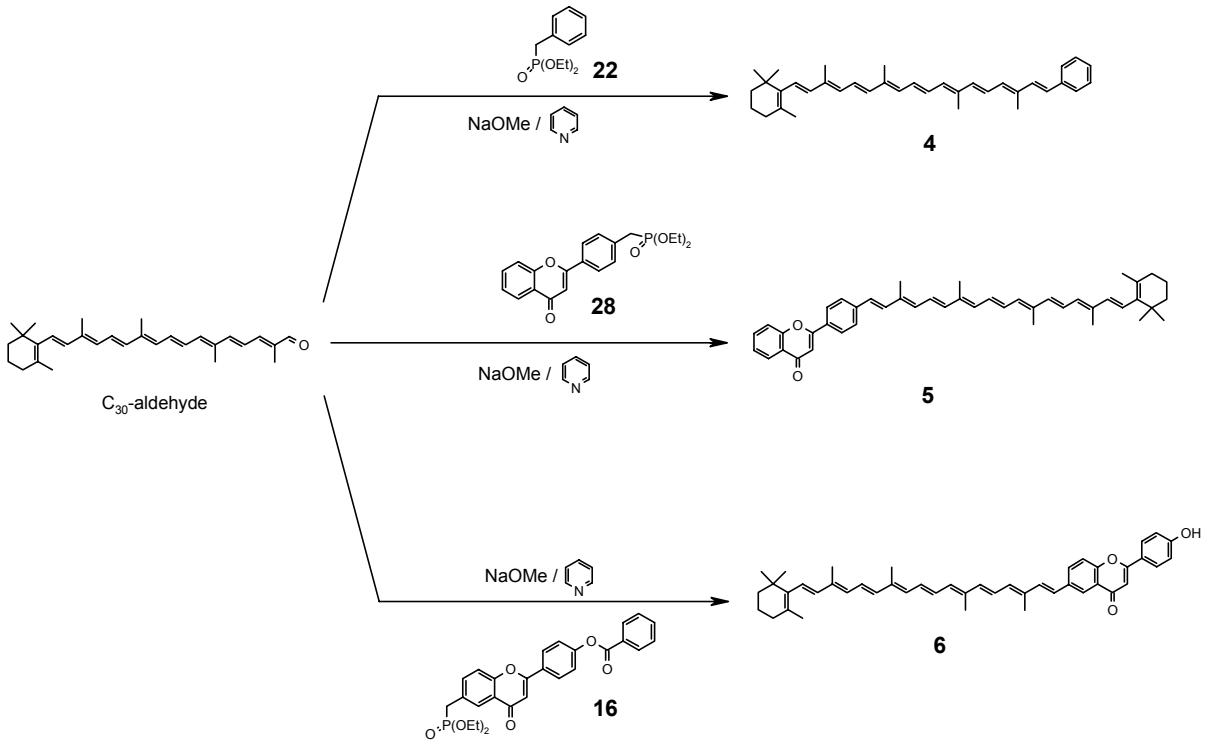


Scheme 1. Synthesis of carotenylflavonoids **2**, **3** and reference compound **1**

For the investigation of antioxidant capacities the method of recording the cumene hydroperoxide formation at 150 torr partial pressure of oxygen was used as has been described in detail[23]. This procedure allows a quantitative assessment of antioxidant capacities, described e.g. in protection factors or inhibition times, and, in addition, a correct time evolution of this behavior is obtained thereby affording parameters like induction periods, inhibition times as well as differential behavior of phenolic and polyenic function.

The antioxidant properties of a compound are evaluated by recording the protection against peroxidation of suitable substrates, e.g. methyl linoleate or cumene. In this work cumene is being preferred as described by Schmidt[23].

The diagram containing the plots of cumene hydroperoxides evolution against time is shown in Figure 1.



Scheme 2. Synthesis of carotenylflavonoids **5**, **6** and reference compound **4**

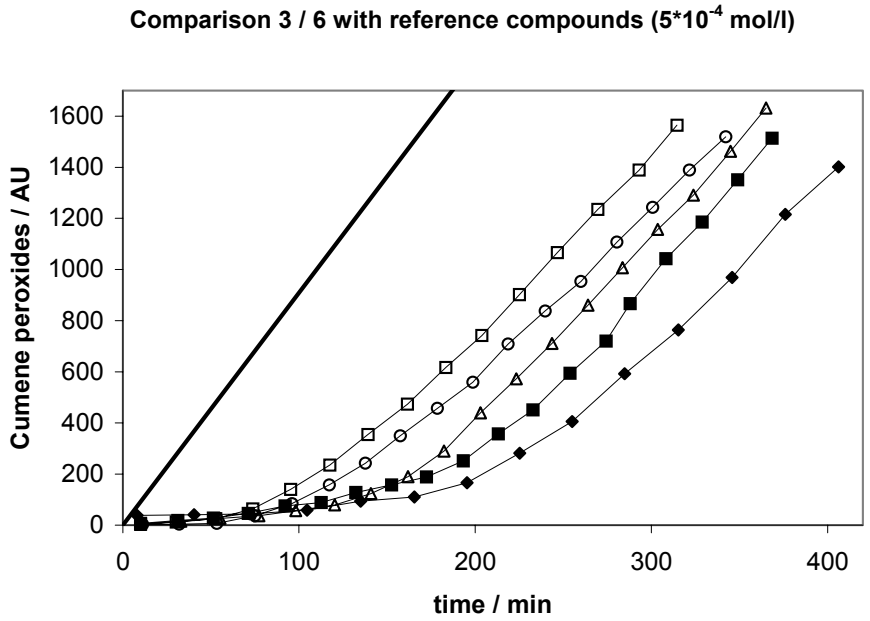


Figure 1. Time evolution of peroxide formation inhibited by: no antioxidant (solid line —), **1 (**open square -□-**)**, **3 (** rhomb -♦-**)**, **4 (**open circle -○-**)**, **6 (**full square -■-**)**-and 4'-hydroxy-6-methyl-flavone **7 (**triangle -△-**).**

A useful comparative discussion of the antioxidant capacities is done by the aid of inhibition times. The inhibition time is determined in the peroxide/time diagram (Fig.1): the straight line of the second stronger rise intersects the time abscissa in the inhibition time (e.g. the final points of **3** define a straight line which intersects at 3.2 h).

It is obvious from Figure 1 that both reference compounds **1** and **4** are moderate carotenoid antioxidants which distinctly inhibit the amount of cumene hydroperoxide, as most carotenoids do, but with short inhibition times which are 1.5 and 1.8 h, respectively. The non-polyenic 4'-hydroxy-6-methylflavone **7**, however, lacking the carotenoid structure, displays a markedly increased antioxidant power with 2.5 h inhibition time and again reduced amount of hydroperoxides. This is due to the completely changed molecular structure: the hydroxyflavone acts primarily as a phenol and in minor contribution as an enone. This differential behavior of phenols (about > 2 h inhibition time) and carotenoids (about < 2 h inhibition time) is a useful mechanistic indicator at concentrations up to 2 x 10^{-3} M, and differentiates clearly between e.g. astaxanthin and α-tocopherol[23].

All reference compounds are, however, outperformed by the two carotenylflavonoids **3** and **6** which reach inhibition times of 3.2 and 3.0 h, respectively (see Fig.2). The time evolution clearly displays both phenolic (the slow onset with very small gradient during the inhibition time) and carotenoid-polyenic (the gradually increasing gradient) contributions to the antioxidant efficiency. The total amount of peroxides is less compared with the other compounds. The differential behavior of phenolics and carotenoids is due to the fact that degradation of carotenoids yields fragments which still show antioxidant capacity whereas phenolics are superior when being present but after being consumed there is much less or no longer any protection (BHT and alpha-tocopherol show steep rises after being consumed!)[23]. Thus it is justified to speak of dual antioxidant function in case of **3** and **6**.

The difference in efficiency between **3** and **6** reflects a well-known fact: carotenoids get more and more unstable and fragile with increasing chain-length. Thus, compound **3** with shorter chain-length lives longer in the reaction mixture and exerts its superior function. In Figure 2 the qualities of these novel antioxidants are visually compared by plotting the inhibition time for each of the compounds. The fact that the combinations **3** and **6** of carotenoid and hydroxylated flavone are superior to the individual chromophores but do not equal the precise sum of the inhibition times of these building blocks may be explained by the conjugative connection: novel π-systems have been built up with their own specific characteristics.

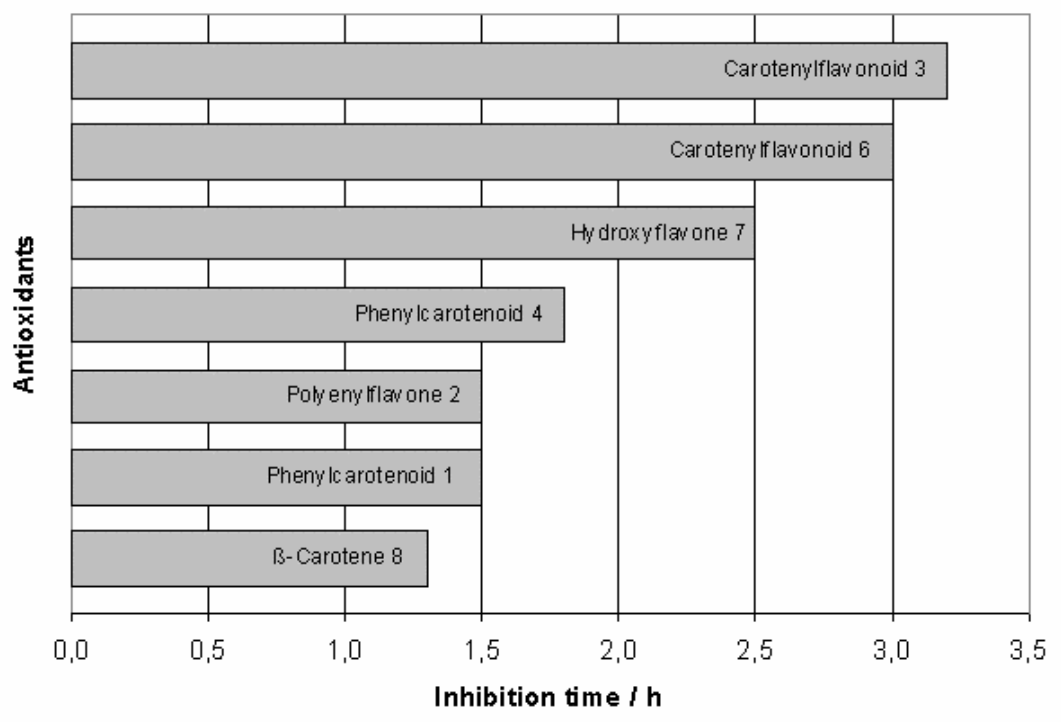


Figure 2. Ranking list of compounds **1**, **2**, **3**, **4**, **6**, **7** and β-carotene **8** using inhibition times taken from graphs in Fig.4 (**1, 3, 4, 6, 7**) or analogous graphs (**2, 8**) (see text for definition).

Conclusions

The covalent combination of flavonoids with carotenoids creates potent, amphiphilic molecular entities which display their dual-functional antioxidative activity clearly in peroxide/time diagrams. Phenolic-flavonoid activity is responsible for the major part of the inhibition time whereas polyenic-carotenoid performance controls the gradually increasing peroxide accumulation which never reaches the peroxide amounts of the unprotected reference experiment and suppresses larger quantities of peroxides for hours. The intrusion of these amphiphilic antioxidants into lipid membranes will open new strategies for membrane protection.

Experimental Section

General Procedures. Melting points were determined with a Buechi SMP-20. UV/Vis spectra were recorded with Perkin Elmer Lambda 19. NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 for ^{1}H-NMR (Bruker AM 500), ^{13}C-{^{1}H}-NMR (Varian VXR 300, Bruker AM 500) and ^{31}P-{^{1}H}-NMR (Varian VXR 300, Bruker AM 500). Internal reference: TMS, 85% H_3PO_4. Combustion elemental analysis: Institute of Pharmaceutical and Medicinal Chemistry. IR:

Bruker Vector 22. UV: Perkin Elmer Lambda 19. HRMS: Max-Planck-Institute Muelheim, MAT 95 Finnigan. MS: EI, CI, GCMS, GC: Thermo Finnigan Trace GC Ultra; MS: Trace DSQ. FAB: Finnigan MAT 8200, MALDI: Bruker Ultra Flex.

Solvents were used p.a. unless specified otherwise. All commercially available chemicals (educts denoted E1-E7) were from Sigma-Aldrich, Merck and Acros, and are indicated with available purity. β-Apo-12‘-carotenal (C25-aldehyde) and β-apo-8‘-carotenal (C30-aldehyde) were provided by BASF (>98%). The antioxidant capacities are evaluated using the peroxidation inhibition assay with cumene as substrate as described in detail by Schmidt[23].

Cumene is treated at 37 °C in a closed vessel with a radical starter (initiator) and with or without the antioxidant (the latter experiment is then taken as reference). The formation of cumene hydroperoxides is followed using High Performance Liquid Chromatography (HPLC) by taking 50 µl samples in intervals from the vessel and injecting them into the HPLC injector. In order to calibrate the system, cumene is first studied without inhibitor: 5 ml cumene, 4 ml chlorobenzene (solvent), 1 ml 0.45 M solution of AMVN (2,2´-azobis(2,4-dimethylvaleronitrile) in chlorobenzene. The concentrations in the reaction vessel are therefore: 3.6 mol/l cumene, 45 mmol/l AMVN. The vessel is closed by a septum which allows samples to be taken out by syringe withdrawal for injection into the HPLC system. The mobile phase is a mixture of hexane/isopropanol (99/1) and the flow rate is 2 ml/min. Silica gel is used as packing material in a 150 x 6.0 mm- 5 µm- column. A Diode-array detector serves for recording UV-Vis spectra in the range 200 – 620 nm. Cumene hydroperoxides are being recorded at 254 nm, retention time is approximately 2.3 min.

p-Tolyl acetate (9).[24] 24.8 g (0.230 mol) *p*-Cresol **E1** (Merck, >98%) and 22.5 g (0.240 mol) acetylchloride **E2** (Merck, >98%) are mixed in a 250 ml flask. The mixture is stirred for 3 h at room temperature. Then the reaction mixture is refluxed for 1 hour and the colourless oil is purified by distillation under reduced pressure. Yield: 31.5 g (0.210 mol, 91 %) **9**, $C_9H_{10}O_2$, M = 150.17 g/mol, bp. 38 °C (0.13 mbar).

2-Hydroxy-5-methylacetophenone (10).[25] 51.9 g (0.350 mol) p-Tolyl acetate **9** and 106 g (0.8 mol) aluminum trichloride are mixed in a 500 ml flask. The mixture is stirred for 30 min at 120-130 °C. After cooling to room temperature the mixture is hydrolyzed with 105 ml of conc. hydrochloric acid and 210 g ice. The yellow oil is extracted with chloroform and the organic phase is washed with water. The product is obtained by recrystallisation from methanol as light yellow needles. Yield: 45.1 g (0.3 mol, 85 %) **10**, $C_9H_{10}O_2$, M = 150.17 g/mol, mp. 50 °C.

4-Methoxybenzoyl chloride (11).[26] 34.0 g (0.253 mol) 4-Methoxybenzoic acid **E5** (Acros, 98%) and 44.6 g (0.381 mol) thionyl chloride are mixed in a 250 ml flask. The reaction mixture is refluxed until gas evolution stops (about 3 h). Excess thionyl chloride is removed under reduced pressure and the colourless oil is vacuum distilled. Yield: 40.9 g (0.240 mol, 95 %) **11**, $C_8H_7ClO_2$, M = 170.59 g/mol, bp. 100 °C (18 mbar).

2-Acetyl-4-methylphenyl 4-methoxybenzoate (12).[27] 15.0 g (0.102 mol) 2-Hydroxy-5-methylacetophenone **10** and 22.2 g (0.131 mol) 4-methoxybenzoyl chloride **11** are dissolved in

20 ml anhydrous pyridine. The mixture is stirred for 20 min at room temperature. The reaction mixture is poured under stirring into 600 ml hydrochloric acid (3%) containing 200 g ice. The grey precipitate is isolated and washed successively with 20 ml methanol and 20 ml water. The product is obtained by recrystallisation from methanol as a white amorphous solid. Yield: 23.1 g, (0.081 mol, 81 %) **12**, $C_{17}H_{16}O_4$, M = 284.3 g/mol, mp. 115 °C.

1-(2-Hydroxy-5-methylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione (13).[27] 23.6 g (0.0831 mol) 2-Acetyl-4-methylphenyl 4-methoxybenzoate **12** are dissolved in 75 ml anhydrous pyridine in a 250 ml flask equipped with a drying tube. The mixture is heated to 50 °C. 7.00 g (0.125 mol) of hot pulverized 85 % potassium hydroxide are added to the solution, and the mixture is stirred mechanically for 15 minutes, while a voluminous precipitate of the yellow potassium salt of the diketone is formed. After the mixture is cooled down to room temperature acidification with 100 ml of 10 % acetic acid yields the diketone as light-yellow needles which are collected on a filter and dried. Yield: 17.3 g, (0.0613 mol, 73 %) **13**, $C_{17}H_{16}O_4$, M = 284.3, mp. 134 °C.

4'-Methoxy-6-methylflavone (14).[27, 28] To a solution of 5.7 g (0.020 mol) of 1-(2-hydroxy-5-methylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione **13** in 30 ml of glacial acetic acid, contained in a 250 ml round-bottomed flask, 1.5 ml of concentrated sulphuric acid are added under shaking. The mixture is refluxed on a steam bath for 1 h with occasional shaking and is then poured with vigorous stirring onto 200 g of crushed ice. After the ice has melted, the crude flavone is collected on a filter, washed with water (about 400 ml) until free from acid, and finally dried at 50 °C. The flavone is obtained as white needles. Yield: 4.7 g, (0.018 mol, 88 %) **14**, $C_{17}H_{14}O_3$, M = 266.3 g/mol, mp. 170 °C. MS, m/z (%): 267 (19.3) [M^++1], 266 (100) [M^+], 265 (10.9) [M^+-1], 238 (10.0), 134 (53.0), 132 (12.2).

4'-Hydroxy-6-methylflavone (7).[29] 5.3 g (0.020 mol) 4'-Methoxy-6-methylflavone **14** are dissolved in 25 ml anhydrous dichloromethane. 40 ml (0.040 mol) of a 1 M solution of boron tribromide in dichloromethane are injected via a septum over 10-15 min under ice cooling. The mixture is stirred for 72 h at room temperature. The reaction mixture is hydrolyzed with ice and extracted with dichloromethane. The combined organic phases are washed with a saturated solution of sodium thiosulphate and dried over magnesium sulphate. The solvent is removed using a rotary evaporator. The product is obtained by recrystallisation from ethanol as light green needles. Yield: 2.4 g, (0.011 mol, 48 %) **7**, $C_{16}H_{12}O_3$, M = 252.3 g/mol, mp. 188 °C, MS m/z (%): 253 (19.3) [M^++1], 252 (100) [M^+], 224 (13.4), 135 (26.8), 134 (63.9), 106 (11.3), 105 (10.4), 78 (13.8), 77 (10.4).

4'-Benzoyloxy-6-methylflavone (15). 25.2 g (0.100 mol) 4'-Hydroxy-6-methylflavone **7** and 28.3 g (0.131 mol) benzoyl chloride **E4** (Merck, >99%) are dissolved in 50 ml anhydrous pyridine. The mixture is stirred for 20 min at room temperature. The reaction mixture is poured under stirring into 600 ml hydrochloric acid (3 %) containing 200 g ice. The grey precipitate is isolated and washed successively with 20 ml methanol and 20 ml water. The product is obtained by recrystallisation from methanol as a white amorphous solid. Yield: 32.4 g, (0.0911 mol, 91 %) **15**, $C_{23}H_{16}O_4$, M = 356.3 g/mol, mp. 177 °C, MS m/z (%): 356 (10.9) [M^+], 253 (17.6), 252 (100), 251 (12.5), 224 (15.3), 135 (26.6), 134 (66.5), 106 (14.6), 105 (74.3), 78 (13.1), 77 (22.6),

92 (35), 91 (67); Anal. Calcd for $C_{23}H_{16}O_4$ (356.3): C 77.51, H 4.52, Found: C 77.20, H 4.50; ^{1}H-NMR ($CDCl_3$): δ = 8.22 (d, 2H), 8.02 (s, 1H), 8.00 (d, 2H), 7.67 (t, 1H), 7.56-7.46 (m, 4H), 7.40 (d, 2H), 6.81 (s, 1H), 2.47 (s, 3H); ^{13}C-NMR ($CDCl_3$): δ = 178.43, 164.69, 162.42, 154.49, 153.44, 135.27, 135.02, 133.91, 130.24, 129.52, 129.03, 128.67, 127.65, 125.06, 123.55, 122.45, 117.80, 107.42, 20.92; IR (KBr): 1736, 1650, 1262, 1059, 708 cm^{-1}.

4-(6-((Diethoxyphosphoryl)methyl)-4-oxo-4*H*-chromen-2-yl)phenyl benzoate (16). 19.9 g (56.0 mmol) 4'-Benzoyloxy-6-methylflavone **15** are dissolved in 150 ml carbon tetrachloride and heated for 30 min. 11.1 g (63.0 mmol) *N*-Bromosuccinimide and 1.5 g azo-bis-isobutyronitrile (AIBN) are added. The mixture is heated under reflux on a steam bath for 6 h. The suspension is slightly cooled and the succinimide is filtered off. The filtrate is cooled down to room temperature and the 4'-benzoyloxy-6-bromomethylflavone crystallized as a light yellow amorphous solid (yield: 10.5 g). Without further purification 8.5 g (0.021 mol) of the 4'-benzoyloxy-6-bromomethylflavone and 4.0 g (0.025 mol) triethyl phosphite (TEP) are heated for 6 h at 140 °C under reflux. The excess TEP is distilled off under reduced pressure. The product is obtained by recrystallisation from toluene as a white amorphous solid. Yield: 7.4 g (0.015 mol, 77 %) **16**, $C_{27}H_{25}O_7P$, M = 492.5 g/mol, mp. 146 °C, MS m/z (%): 492 (9.7) [M^+], 356 (11.9), 104 (100.0), 91 (12.7), 77 (11.0); Anal. Calcd for $C_{27}H_{25}O_7P$ (492.5): C 65.85, H 5.12, Found: C 65.84, H 5.10; ^{1}H-NMR ($CDCl_3$): δ = 8.21 (d, 2H), 8.09 (m, 1H), 8.05-7.96 (m, 2H), 7.74-7.70 (m, 1H), 7.68-7.64 (m, 1H), 7.56-7.50 (m, 3H), 7.42-7.38 (m, 2H), 6.81 (s, 1H), 4.05 (quin, 4H), 3.26 (d, 2H), 1.27 (t, 6H); ^{13}C-NMR ($CDCl_3$): δ = 177.96, 164.65, 162.58, 155.20 (d), 153.52, 135.35 (d), 133.91, 130.21, 129.41 (d), 128.97, 128.65, 127.72, 127.67, 126.35, 126.29, 123.72 (d), 122.48, 118.37 (d), 107.53, 62.24 (d, $^2J(^{31}P\text{-}^{13}C)$ = 6.6 Hz), 33.69 (d, $^1J(^{31}P\text{-}^{13}C)$ = 138.7 Hz), 16.35 (d, $^3J(^{31}P\text{-}^{13}C)$ = 5.7 Hz); ^{31}P-NMR ($CDCl_3$): δ = 26.46; IR (KBr): 3070, 2985, 1731, 1645, 1451, 1268, 1262, 1062, 1025, 711 cm^{-1}.

4'-Hydroxy-6-(3,8,12-trimethyl-14-(2,6,6-trimethylcyclohex-1-enyl)tetradeca-1,3,5,7,9,11,13-heptaenyl)flavone (3). 1.0 g (2.9 mmol) β-Apo-12'-carotenal (C25-aldehyde, BASF, >98%) and 1.2 g (2.9 mmol) 4-(6-((diethoxyphosphoryl)methyl)-4-oxo-4*H*-chromen-2-yl)phenyl benzoate **16** are dissolved in 100 ml anhydrous pyridine. At 0 °C 0.70 g (13 mmol) sodium methoxide are added in portions over 1.5 h. After stirring for 72 h at room temperature the reaction is finished. The reaction mixture is hydrolyzed and extracted with chloroform. The combined organic layers are dried over magnesium sulphate. The solvent is distilled off. Analytically pure orange amorphous product is obtained by column chromatography with a solvent mixture of dichloromethane and diethyl ether (2:1). Yield: 0.19 g, (0.32 mmol, 11 %) **3**, $C_{41}H_{44}O_3$, M = 584.8, mp. 216 °C, MS m/z (%): 584 (13.8) [M^+], 569 (18.0), 328 (18.4), 328 (26.0), 251 (20.9), 209 (18.1), 159 (60.1), 145 (19.1), 133 (34.4), 121 (15.4), 119 (32.1), 115 (17.8), 106 (19.6), 105 (49.5), 93 (18.8), 92 (54.0), 91 (100), 68 (23.7), 38 (32.3); Anal. Calcd for $C_{41}H_{44}O_3$ (584.8): C 84.21, H 7.58, Found: C 84.20, H 7.61; $^1H_{500}$-NMR ($CDCl_3$/ MeOD): δ = 0.97 (s, 6H, -CH_3); 1.40-1.42 (m, 2H, -CH_2 - ring); 1.53-1.58 (m, 2H, -CH_2 - ring); 1.65 (s, 3H, -CH_3); 1.91 (s, 3H, -CH_3); 1.94 (s, 3H, -CH_3); 1.94-1.96 (m, 2H, -CH_2), 1.97 (s, 3H, -CH_3); 6.05-6.14 (m, 3H, CH - chain); 6.21 (d, 1H, CH- chain); 6.30 (d, 1H, -CH - chain); 6.34 (d, 1H, -CH -

chain); 6.57-6.65 (m, 4H, -CH - chain); 6.67 (s, 1H, CO-CH); 6.89 (d, 2H, -CH - aromatic); 6.92 (d, 1H, -CH - chain); 7.45 (d, 1H, -CH - aromatic); 7.71 (dd, 1H, -CH - aromatic); 7.77 (d, 2H, -CH - aromatic); 8.12 (d, 1H, -CH – aromatic); $^{13}C_{75}$-NMR ($CDCl_3$/ MeOD): δ = 12.58, 12.61, 12.64 (-CH_3, chain); 19.13 (-CH_2, ring); 21.60 (-CH_3, ring); 28.82 (2* -CH_3, ring); 32.99, 34.15, 39.53 (-CH_2, ring); 105.02 (-CO-CH); 115.93, 118.29, 125.5, 128.21, 137.01 (-CH, aromatic); 123,61, 125.29, 126.71, 129.32, 130.64, 130.88, 131.48, 132,04; 135.19, 135.23, (-CH, chain); 122.24, 122.41, 129.47, 133.96, 136.17, 137.05, 137.62, 137.79, 155.22 (-C); 160.68 (C-OH); 164.30 (O-C-, aryl); 179.01 (-C=O); IR (KBr): 3030, 2920, 1605, 1561, 1445, 1365, 1175, 965 (all trans), 838 cm^{-1}; UV-Vis (CH_2Cl_2) λ_{max} (ε) = 443 nm (110000 l mol^{-1} cm^{-1}), 320 nm (30000 l mol^{-1} cm^{-1}).

4'-Hydroxy-6-(3,7,12,16-Tetramethyl-18-(2,6,6-trimethylcyclohex-1-enyl)octadeca-1,3,5,7,9,11,13,15,17-nonaenyl)flavone (6). 1.2 g (2.9 mmol) β-Apo-8'-carotenal (C30-aldehyde, BASF, >98%) and 1.2 g (2.9 mmol) 4-(6-((diethoxyphosphoryl)methyl)-4-oxo-4*H*-chromen-2-yl)phenyl benzoate **16** are dissolved in 100 ml anhydrous pyridine. At 0 °C 0.70 g (13 mmol) sodium methoxide are added in portions over 1.5 h. After stirring for 120 h at room temperature the reaction is finished. The reaction mixture is hydrolyzed and extracted with chloroform. The combined organic layers are dried over magnesium sulphate. The solvent is distilled off. Analytically pure dark-red amorphous product is obtained by column chromatography with a solvent mixture of dichloromethane and diethyl ether (2:1). Yield: 0.17 g, (0.27 mmol, 9 %) **6**, $C_{46}H_{50}O_3$, M = 650.9 g/mol, mp.: 198 °C; MS, FAB+NBA m/z (%): 650 (3.9) [M^+]; Anal. Calcd. for $C_{46}H_{50}O_3$ (650.9) C 84.88, H 7.74, Found. C 84.76, H 7.77; $^1H_{500}$-NMR ($CDCl_3$/ MeOD): δ = 0.93 (d, 6H, -CH_3); 1.36-1.40 (m, 2H, -CH_2 - ring); 1.50-1.54 (m, 2H, -CH_2 - ring); 1.62-1.66 (m, 3H, -CH_3); 1.87 (s, 3H, -CH_3); 1.88-1.93 (m, 8H, -CH_2, 2* -CH_3), 1.95 (s, 3H, -CH_3); 6.02-6.12 (m, 3H, CH - chain); 6.16 (d, 1H, CH – chain); 6.21 (d, 1H, CH – chain); 6.24-6.29 (d, d, 2H, -CH - chain); 6.35 (d, 1H, -CH - chain); 6.53-6.59 (m, 5H, -CH - chain); 6.62 (s, 1H, CO-CH); 6.85 (d, 2H, -CH - aromatic); 6.88 (d, 1H, -CH - chain); 7.42 (d, 1H, -CH - aromatic); 7.68 (dd, 1H, -CH - aromatic); 7.72-7.74 (m, 2H, -CH - aromatic); 8.06 (d, 1H, -CH - aromatic); $^{13}C_{75}$-NMR ($CDCl_3$/ MeOD): δ = 12.46, 12.48, 12.53, 12.58 (-**C**H_3, chain); 19.03 (-**C**H_2, ring); 21.47 (-**C**H_3,); 28.75 (2* -**C**H_3, ring); 32.88, 34.04, 39.44 (-**C**H_2, ring); 104.80 (-CO-**C**H); 115.83, 118.20, 125.13, 128.13, 136.97 (-**C**H, aromatic); 123.44, 124.48, 125.06, 126.57, 129.21, 130.42, 130.61, 131.4, 132,16; 133.33, 134.95, 135.26, 135.98, (-**C**H, chain); 122.07, 122.22, 129.67, 134.07, 134.8, 136.06, 137.54, 137.71, 138.76, 155.11 (-**C**); 160.68 (**C**-OH); 164.34 (O-**C**- aryl); 179.04 (-**C**=O); IR (KBr): 3028, 2922, 1605, 1561, 1448, 1365, 1174, 962 (all trans), 838 cm^{-1}; UV-Vis (CH_2Cl_2), λ_{max} (ε) = 475 nm (118000 l mol^{-1} cm^{-1}), 305 nm (49000 l mol^{-1} cm^{-1}).

2-Acetyl-4-methylphenyl benzoate (17).[30] 5.0 g (33 mmol) 2-Hydroxy-5-methylacetophenone **10** and 7.0 g (50 mmol) benzoyl chloride **E4** are dissolved in 20 ml anhydrous pyridine. The mixture is stirred for 20 min at room temperature. The reaction mixture is poured under stirring into 200 ml hydrochloric acid (3%) containing 40 g ice. The grey precipitate is isolated and washed successively with 20 ml methanol and 20 ml water. The product is obtained by recrystal-

lisation from methanol as a white amorphous solid. Yield: 7.1 g, (28 mmol, 84 %) **17**, $C_{16}H_{14}O_3$, M = 254.3 g/mol, mp. 64 °C.

1-(2-Hydroxy-5-methylphenyl)-3-phenylpropane-1,3-dione (18).[27] 6.7 g (26 mmol) 2-acetyl-4-methylphenyl benzoate **17** are dissolved in 25 ml anhydrous pyridine in a 250 ml flask equipped with a drying tube. The mixture is heated to 50 °C. To the solution 2.5 g (45 mmol) of hot pulverized 85 % potassium hydroxide are added, and the mixture is stirred mechanically for 15 min, while a voluminous precipitate of the yellow potassium salt of the diketone forms. The mixture is cooled to room temperature and acidified with 100 ml of 10 % acetic acid. The diketone separated as a light-yellow amorphous precipitate which is collected on a filter and dried. Yield: 5.3 g, (21 mmol, 79 %) **18**, $C_{16}H_{14}O_3$, M = 254.3 g/mol, mp. 91 °C.

6-Methylflavone (19).[27, 31] To a solution of 5.2 g (20 mmol) of 1-(2-hydroxy-5-methylphenyl)-3-phenylpropane-1,3-dione **18** in 30 ml of glacial acetic acid, contained in a 250 ml round-bottomed flask, 1.5 ml of concentrated sulphuric acid is added under shaking. The mixture is heated on a steam bath for 1 h with occasional shaking and is then poured under vigorous stirring onto 200 g of crushed ice. After the ice has melted, the crude flavone is collected on a filter, washed with water (about 400 ml) until free from acid, and finally dried at 50 °C. The flavone is obtained as white needles. Yield: 4.5 g, (19 mmol, 93 %) **19**, $C_{16}H_{12}O_2$, M = 236.3, mp. 122 °C.

6-Bromomethylflavone (20).[32] 4.2 g (18 mmol) 6-methylflavone **19** are dissolved in 50 ml carbon tetrachloride and heated for 30 min. 3.5 g (20 mmol) *N*-bromosuccinimide and 1.5 g azo-bis-isobutyronitrile (AIBN) are added. The mixture is heated under reflux on a steam bath for 6 h. The suspension is slightly cooled and the succinimide is filtered off. The filtrate is cooled down and the 6-bromomethylflavone **20** crystallized as a light yellow amorphous solid. Yield: 3.8 g, (12 mmol, 67 %) **20**, $C_{16}H_{11}BrO_2$, M = 315.2 g/mol, mp. 128 °C.

Diethyl (4-oxo-2-phenyl-4*H*-chromen-6-yl)methylphosphonate (21).[32] A solution of 3.7 g (12 mmol) 6-bromomethylflavone **20** and 1.4 g (15 mmol) triethyl phosphite (TEP) is heated for 6 h at 140 °C under reflux. The excess TEP is distilled off in vacuum. The product is obtained by recrystallisation from toluene as a white amorphous solid. Yield: 3.9 g, (10 mmol, 87 %) **21**, $C_{20}H_{21}O_5P$, M = 372.4 g/mol, mp. 129 °C, ^{31}P-NMR ($CDCl_3$): δ = 26.55.

6-(3,8,12-Trimethyl-14-(2,6,6-trimethylcyclohex-1-enyl)tetradeca-1,3,5,7,9,11,13-heptaenyl) flavone (2). 1.0 g (3.0 mmol) β-Apo-12‘-carotenal (C25-aldehyde, BASF, >98%) and 1.1 g (3.0 mmol) diethyl (4-oxo-2-phenyl-4H-chromen-6-yl)methylphosphonate **21** are dissolved in 30 ml anhydrous pyridine. At 0 °C 0.30 g (5.0 mmol) sodium methoxide are added in portions over 2 h. After stirring for 4 h at room temperature the reaction is finished. The reaction mixture is hydrolyzed and extracted with chloroform. The combined organic layers are dried over magnesium sulphate. The solvent is distilled off. Analytically pure orange-red amorphous product is obtained by column chromatography with a solvent mixture of dichloromethane und diethyl ether (30:1). Yield: 0.42 g (7.4 mmol, 25 %) **2**, $C_{41}H_{44}O_2$, M = 568.8 g/mol, mp. 198 °C (decomp.); HRMS (Finnigan MAT95/ 70eV, EI): Calcd. for $(C_{41}H_{44}O_2)^+$: 568.3341, found: 568.3349; MS, FAB+NBA m/z (%): 569 (15.8) [M^++1], 568 (24.6) [M^+]; $^1H_{500}$-NMR ($CDCl_3$): δ = 1.04 (s, 6H, -CH_3); 1.46-1.49 (m, 2H, -CH_2 - ring); 1.61-1.65 (m, 2H, -CH_2 - ring); 1.73 (s, 3H,

-CH_3); 1.98-2.06 (m, 11H, -CH_2, 3* -CH_3 - chain), 6.12-6.21 (m, 3H, CH - chain); 6.26 (d, 1H, CH - chain); 6.35-6.41 (m, 2H, -CH - chain); 6.62-6.67 (m, 4H, -CH - chain); 6.82 (s, 1H, CO-CH); 6.99 (d, 1H, CH - chain); 7.51-7.54 (m, 4H, -CH - aromatic); 7.75 (dd, 1H, -CH - aromatic); 7.92 (d, 2H, -CH - aromatic); 8.23 (d, 1H, -CH - aromatic); $^{13}C_{75}$-NMR ($CDCl_3$): δ = 12.75, 12.76, 12.88 (-CH_3, chain); 19.30 (-CH_2, ring); 21.74 (-CH_3, ring); 28.99 (2* -CH_3, ring); 33.14, 34.31, 39.73 (-CH_2, ring); 107.52 (-CO-CH); 118.42, 122.55, 125.6, 126.29, 129.05 (-CH, aromatic); 125.43, 126.85, 129.57, 130.77, 131.03, 131.55, 131.62, 132.14, 135.28, 135.41, (-**C**H, chain);131.88, 134.09, 135.08 137.14 (-**C**H, aromatic); 129.41, 134.09, 136.28, 137.18, 137.74, 137.96, 155.39 (-**C**); 163.28 (O-**C**-, aryl); 178.36 (-**C**=O); IR (KBr): 3028, 2926, 1637, 1453, 1362, 967 (all trans) cm^{-1}; UV-Vis λ_{max} (ε) = 442 nm (98900 l mol^{-1} cm^{-1}), 275 nm (36300 l mol^{-1} cm^{-1}).

Diethyl benzylphosphonate (22).[33] A solution of 29.0 g (0.170 mol) bromomethylbenzene **E7** (Merck, >98%) and 35.2 g (0.210 mol) triethyl phosphite (TEP) is heated for 6 h at 140 °C under reflux. The excess TEP is distilled off under vacuum. The colourless oil is obtained by fractionated distillation. Yield: 34.6 g, (0.150 mol, 89 %) **22**, $C_{11}H_{17}O_3P$, M = 228.2 g/mol, bp. 162 °C (23 mbar); ^{31}P-NMR ($CDCl_3$): δ = 27.70.

3,8,12-Trimethyl-14-(2,6,6-trimethylcyclohex-1-enyl)-1-phenyltetradeca-1,3,5,7,9,11,13-heptaene (1). 1.0 g (3.0 mmol) β-Apo-12'-carotenal (C25-aldehyde, BASF, >98%) and 0.96 g (4.2 mmol) diethyl benzylphosphonate **22** are dissolved in 30 ml anhydrous pyridine. At 0 °C 0.30 g (5.0 mmol) sodium methoxide are added in portions over 1 h. After stirring for 2.5 h at room temperature the reaction is finished. The reaction mixture is hydrolyzed and extracted with chloroform. The combined organic layers are dried over magnesium sulphate. The solvent is distilled off. Analytically pure orange amorphous product is obtained by column chromatography with chloroform as solvent. Yield: 0.67 g, (1.60 mmol, 53 %) **1**, $C_{32}H_{40}$, M = 424.7 g/mol, mp. 189 °C (decomp.); HRMS (Finnigan MAT95, 70eV, EI): Calcd. for $(C_{32}H_{40})^+$: 424.3130, found: 424.3135; MS, FAB+NBA m/z (%): 425 (38.3) [M^++ 1], 424 (100.0) [M^+]; $^1H_{500}$-NMR ($CDCl_3$): δ = 1.04 (s, 6H, -CH_3); 1.45-1.49 (m, 2H, -CH_2 - ring); 1.60-1.65 (m, 2H, -CH_2 - ring); 1.73 (s, 3H, -CH_3); 1.98-2.03 (m, 11H, -CH_2, 3* -CH_3 - chain), 6.12-6.20 (m, 3H, CH - chain); 6.26-6.28 (m, 1H, CH - chain); 6.35-6.38 (m, 2H, -CH - chain); 6.62 (d, 1H, CH - chain); 6.64-6.71 (m, 3H, CH - chain); 6.90 (d, 1H, CH - chain); 7.21 (t, 1H, aromatic); 7.32 (t, 2H, -CH aromatic), 7.43 (d, 2H, -CH aromatic); $^{13}C_{75}$-NMR ($CDCl_3$): δ = 12.77, 12.10, 12.40 (-CH_3, chain); 19.27 (-CH_2, ring); 21.77 (-CH_3, ring); 28.98 (2* -CH_3, ring); 33.12, 34.28, 39.66 (-CH_2, ring); 125.18, 126.73, 127.18, 129.73, 130.37, 130.78, 132.22, 133.54, 135.72, 136.73, 137.76 (-**C**H, chain); 126.32, 127.59, 128.63 (-**C**H, aromatic); 129.40, 133.10, 136.13, 137.17, 137.78, 137.92 (-**C**); IR (KBr): 3028, 2926, 965 (all trans), 749, 692 cm^{-1}; UV-Vis (CH_2Cl_2): λ_{max} (ε) = 433 nm (96300 l mol^{-1} cm^{-1}).

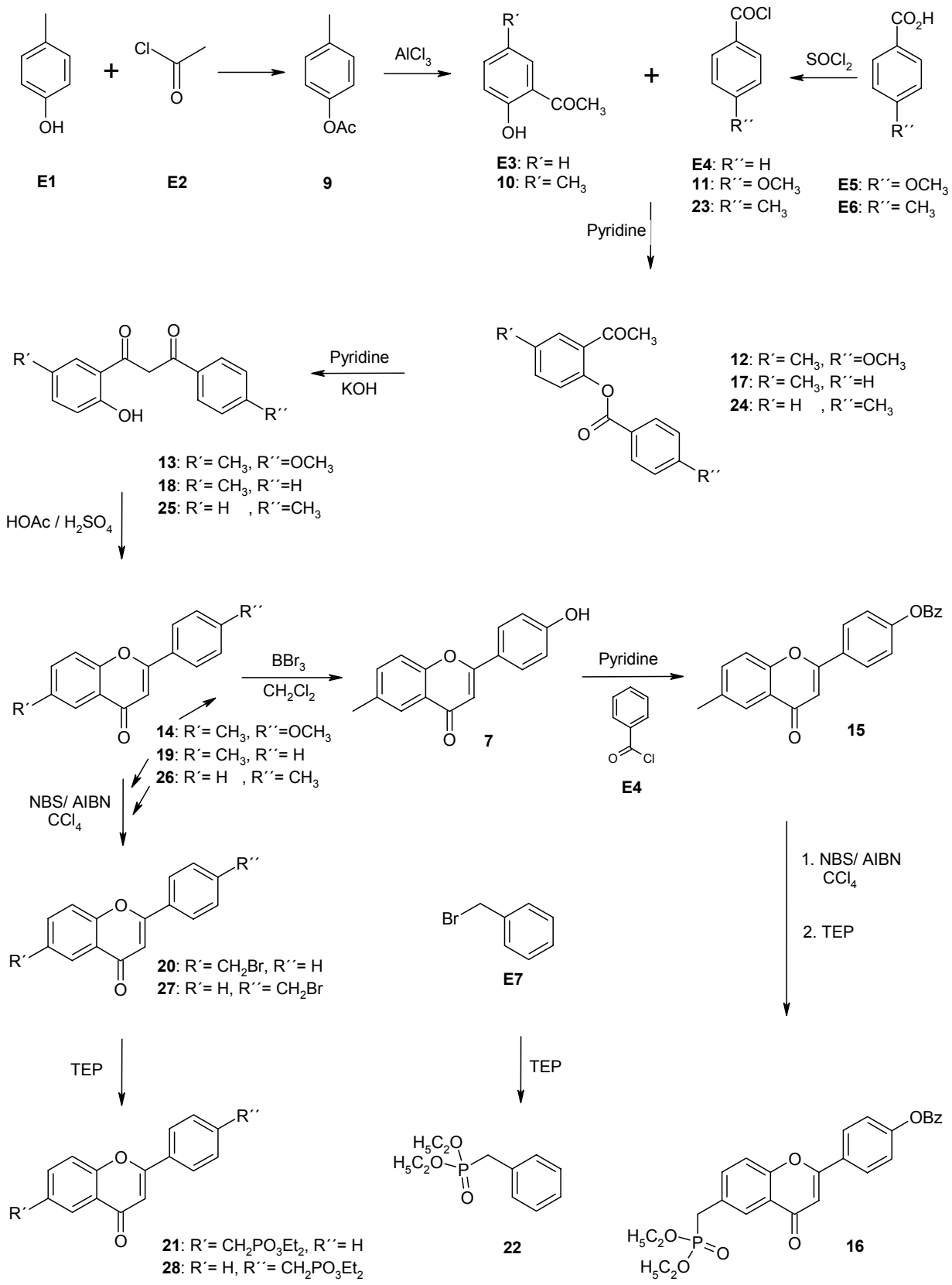
3,7,12,16-Tetramethyl-18-(2,6,6-trimethylcyclohex-1-enyl)-1-phenyloctadeca-1,3,5,7,9,11,13,15,17-nonaene (4). 1.2 g (3.0 mmol) β-Apo-8'-carotenal (C30-aldehyde, BASF, >98%) and 0.96 g (4.2 mmol) diethyl benzylphosphonate **22** are dissolved in 30 ml anhydrous pyridine. At 0 °C 0.30 g (5.0 mmol) sodium methoxide are added in portions over 1 h. After stir-

ring for 2.5 h at room temperature the reaction is finished. The reaction mixture is hydrolyzed and extracted with chloroform. The combined organic layers are dried over magnesium sulphate. The solvent is distilled off. Analytically pure red-violet amorphous product is obtained by column chromatography with chloroform as solvent. Yield: 0.67 g, (1.37 mmol, 46 %) **4**, $C_{37}H_{46}$, M = 490.8 g/mol, mp. 175 °C (decomp.); HRMS (Finnigan MAT95, 70eV, EI): Calcd. for $(C_{37}H_{46})^+$: 490.3599, found: 490.3606; MS, FAB + NBA m/z (%): 490 (100) [M^+]; $^1H_{500}$-NMR ($CDCl_3$): δ = 1.03 (s, 6H, -CH_3); 1.46-1.50 (m, 2H, -CH_2 - ring); 1.59-1.64 (m, 2H, -CH_2 - ring); 1.71-1.76 (m, 3H, -CH_3); 1.98-2.05 (m, 14H, -CH_2, 3* -CH_3 - chain); 6.12-6.20 (m, 3H, CH - chain); 6.25-6.39 (m, 4H, CH - chain); 6.41 (d, 1H, -CH - chain); 6.58 (d, 1H, CH - chain); 6.64-6.70 (m, 3H, CH – chain); 6.91 (d, 1H, CH - chain); 7.20 (t, 1H, aromatic); 7.32 (t, 2H, -CH aromatic); 7.43 (d, 2H, -CH aromatic); $^{13}C_{75}$-NMR ($CDCl_3$): δ = 12.77, 12.80, 12.84, 12.89 (-CH_3, chain); 19.27 (-CH_2, ring); 21.77 (-CH_3, ring); 28.98 (2* -CH_3, ring); 33.12, 34.28, 39.66 (-**C**H_2, ring); 124.85, 125.20, 126.74, 127.13, 129.90, 130.40, 130.82, 132.37, 133.22, 133.65, 135.42, 136.32, 136.77, 137.81 (-**C**H, chain); 126.3, 127.36, 128.63 (-**C**H, aromatic); 129.41, 133.14, 136.14, 137.19, 137.76, 137.92, 138.3 (-**C**); IR (KBr): 3028, 2926, 965 (all trans), 748, 690 cm^{-1}; UV-Vis (CH_2Cl_2) λ_{max} (ε) = 467 nm (109000 l mol^{-1} cm^{-1}).

4-Methylbenzoyl chloride (23).[34] 34.0 g (0.250 mol) 4-Methylbenzoic acid **E6** (Acros, 98%) and 44.6 g (0.381 mol) thionyl chloride are mixed in a 250 ml flask. The reaction mixture is then refluxed until gas evolution stops (about 3 h). Excess thionyl chloride is removed under reduced pressure and the colourless oil is vacuum distilled. Yield: 36.8 g (0.240 mol, 95 %) **23**, C_8H_7ClO, M = 154.6 g/mol, bp. 100 °C (18 mbar).

2-Acetylphenyl 4-methylbenzoate (24).[35] 13.6 g (0.100 mol) 2-Hydroxyacetophenone **E3** (Merck, >98%) and 21.1 g (0.131 mol) 4-methylbenzoyl chloride **23** are dissolved in 20 ml anhydrous pyridine. The mixture is stirred for 20 min at room temperature. The reaction mixture is poured under stirring into 600 ml hydrochloric acid (3 %) containing 200 g ice. The light violet precipitate is isolated and washed successively with 20 ml methanol and 20 ml water. The product is obtained by recrystallisation from methanol as a white amorphous solid. Yield: 21.6 g, (0.085 mol, 85 %) **24**, $C_{16}H_{14}O_3$, M = 254.3 g/mol, mp. 98 °C; ^{1}H-NMR ($CDCl_3$/TMS): δ = 2.45 (s, 3H), 2.54 (s, 3H), 8.12-7.21 (m, 8H).

1-(2-Hydroxyphenyl)-3-*p*-tolyl-propane-1,3-dione (25).[35] 20 g (0.083 mol) 2-Acetyl-phenyl 4-methylbenzoate **24** are dissolved in 75 ml anhydrous pyridine in a 250 ml flask equipped with a drying tube. The mixture is heated to 50 °C. To the solution 7.0 g (0.12 mol) of hot pulverized 85 % potassium hydroxide are added, and the mixture is stirred mechanically for 15 min, while a voluminous precipitate of the yellow-brown potassium salt of the diketone is formed. The mixture is cooled down to room temperature and acidification with 100 ml of 10 % acetic acid yields the diketone as yellow needles which are collected on a filter and dried. Yield: 16 g, (0.063 mol, 80 %) **25**, $C_{16}H_{14}O_3$, M = 254.3, mp.: 108 °C; ^{1}H-NMR ($CDCl_3$/TMS): δ = 2.42 (s, 3H), 6.79 (s, 2H), 7.90-6.88 (m, 8H), 12.1 (s, 1H, OH).


E1
E2
9
E3: R´= H
10: R´= CH3
E4: R´´= H
11: R´´= OCH3
23: R´´= CH3
E5: R´´= OCH3
E6: R´´= CH3
Pyridine
12: R´= CH3, R´´=OCH3
17: R´= CH3, R´´=H
24: R´= H , R´´=CH3
13: R´= CH3, R´´=OCH3
18: R´= CH3, R´´=H
25: R´= H , R´´=CH3
HOAc / H2SO4
14: R´= CH3, R´´=OCH3
19: R´= CH3, R´´= H
26: R´= H , R´´= CH3
7
15
E4
NBS/ AIBN
CCl4
20: R´= CH2Br, R´´= H
27: R´= H, R´´= CH2Br
E7
1. NBS/ AIBN
CCl4
2. TEP
TEP
21: R´= CH2PO3Et2, R´´= H
28: R´= H, R´´= CH2PO3Et2
22
16

Scheme 3

4'-Methylflavone (26).[35] To a solution of 16 g (0.063 mol) of 1-(2-Hydroxy-phenyl)-3-*p*-tolyl-propane-1,3-dione **25** in 90 ml of glacial acetic acid in a 250 ml round-bottomed flask 3.5 ml of concentrated sulphuric acid are added under shaking. The mixture is heated under reflux on a steam bath for 1 h with occasional shaking and is then poured with vigorous stirring onto 500 g of crushed ice. After the ice has melted, the crude flavone is collected on a filter, washed with water (about 1000 ml) until free from acid, and finally dried at 50 °C. The flavone is obtained as white needles. Yield: 13 g, (0.057 mol, 91 %) **26**, $C_{16}H_{12}O_2$, M = 236.3 g/mol, mp. 117 °C; ^{1}H-NMR ($CDCl_3$/TMS): δ = 2.41 (s, 3H), 6.77 (s, 1H), 8.23-7.27 (m, 8H); UV-Vis (CH_2Cl_2): λ_{max} (ε) = 299 nm (28200 l mol^{-1} cm^{-1}), 252 nm (17400 l mol^{-1} cm^{-1}).

4'-Bromomethylflavone (27).[32] 13.2 g (56.0 mmol) 4'-Methylflavone **26** are dissolved in 150 ml carbon tetrachloride and heated for 30 min. 11.1 g (63.0 mmol) *N*-Bromosuccinimide and 1.5 g azo-bis-isobutyronitrile (AIBN) are added. The mixture is heated under reflux on a steam bath for 6 h. The suspension is slightly cooled and the succinimide is filtered off. The filtrate is cooled down and the 4'-bromomethylflavone **27** crystallized as a light yellow solid. Yield: 12.2 g, (39.0 mmol, 70 %) **27**, $C_{16}H_{11}BrO_2$, M = 315.2 g/mol, mp. 132 °C; ^{1}H-NMR ($CDCl_3$/TMS): δ = 4.53 (s, 2H), 6.83 (s, 1H), 8.24-7.27 (m, 8H).

Diethyl 4-(4-Oxo-4*H*-chromen-2-yl)benzylphosphonate (28).[32] A solution of 12 g (39 mmol) 4'-bromomethylflavone **27** and 8.1 g (49 mmol) triethyl phosphite (TEP) is heated under reflux for 6 h at 140 °C. The excess TEP is distilled off in vacuum. The product is obtained by recrystallisation from toluene as a white amorphous solid. Yield: 16 g, (44 mmol, 78 %) **28**, $C_{20}H_{21}O_5P$, M = 372.4 g/mol, mp. 163 °C; ^{31}P-NMR ($CDCl_3$): δ = 26.48, ^{1}H-NMR ($CDCl_3$/TMS): δ = 1.28 (t, 6H), 3.24 (d, 2H), 4.06 (m, 4H), 6.82 (s, 1H), 8.25-7.29 (m, 8H).

4'-(3,7,12,16-Tetramethyl-18-(2,6,6-trimethylcyclohex-1-enyl)octadeca-1,3,5,7,9,11,13,15,17-nonaenyl)flavone (5). 1.0 g (2.4 mmol) β-Apo-8'-carotenal (C30-aldehyde, BASF, >98%) and 1.1 g (3.0 mmol) diethyl 4-(4-oxo-4*H*-chromen-2-yl)benzylphosphonate **28** are dissolved in 35 ml anhydrous pyridine. At 0 °C 0.64 g (11 mmol) sodium methoxide are added in portions over 2 h. After stirring for 3 h at room temperature the reaction is finished. The reaction mixture is hydrolyzed and extracted with chloroform. The combined organic layers are dried over magnesium sulphate. The solvent is distilled off. Analytically pure dark-red amorphous product is obtained by column chromatography with a solvent mixture of dichloromethane und diethyl ether (20:1). Yield: 1.1 g, (1.8 mmol, 78 %) **5**, $C_{46}H_{50}O_2$, M = 634.9 g/mol, mp. 173 °C (decomp.); HRMS (Finnigan MAT95, 70eV, ESIpos [CH_2Cl_2/MeOH]): Calcd. for $(C_{46}H_{50}O_2Na)^+$: 657.3703, found: 657.3698; MS m/z (%): 634 (26) [M^+], 91 (100); $^1H_{500}$-NMR ($CDCl_3$): δ = 1.04 (s, 6H, -CH_3); 1.46-1.49 (m, 2H, -CH_2 - ring); 1.60-1.64 (m, 2H, -CH_2 - ring); 1.72-1.76 (m, 3H, -CH_3); 1.98-2.03 (m, 11H, -CH_2, 3* -CH_3 - chain); 2.06 (s, 3H, CH_3); 6.12-6.22 (m, 3H, CH - chain); 6.26 (d, 1H, CH - chain); 6.31 (d,1H, -CH - chain); 6,36 (d, 1H, -CH - chain); 6.41 (d, 1H, -CH - chain); 6.46 (d, 1H, -CH - chain); 6.58-6.69 (m, 5H, -CH - chain); 6.82 (s, 1H, CO-CH); 7.01 (s, 1H, CH - chain); 7.55 (m, 3H, -CH - aromatic); 7.69 (t, 1H, -CH - aromatic); 7.87 (d, 2H, -CH - aromatic); 8.23 (d, 1H, -CH - aromatic); $^{13}C_{75}$-NMR ($CDCl_3$): δ = 12.75, 12.77, 12.82, 12,84 (-CH_3, chain); 19.26 (-CH_2, ring); 21.76 (-CH_3,

ring); 28.97 (2* -CH_3, ring); 33.12, 34.28, 39.65 (-CH_2, ring); 107.00 (-CO-CH); 118.02, 125.38, 126.57, 126.69, 129.77, 141.32 (-CH, aromatic); 124.59, 125.15, 125.69, 125.88, 126.80, 130.78, 130.83, 133.67, 134.97, 134.99, 136.00, 136.15, 137.09 (-**C**H, chain); 124.03, 129.44, 132.29, 133.83, 136.28, 137.11, 137.72, 137.90, 139.36, 156.22 (-**C**); 163.12 (O-**C**-, aryl) 178.39 (-**C**=O); IR (KBr): 3028, 2922, 1644, 1370, 964 (all trans) cm^{-1}; UV-Vis (CH_2Cl_2) λ_{max} (ε) = 491 nm (115000 l mol^{-1} cm^{-1}), 319 nm (25700 l mol^{-1} cm^{-1}).

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