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Rapid Preparation of 3-Deoxyanthocyanidins and Novel Dicationic Derivatives: New Insight into an Old Procedure

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Common 3-deoxyanthocyanidins and original dicationic flavylium-benzopyrylium derivatives are easily and efficiently synthesized through reactions between the corresponding phenols and aryl ethynyl ketones in the presence of aqueous hexafluorophosphoric acid. The mechanism of the reaction is discussed and two competitive pathways are consistent with our results.

Introduction

The flavylium (2-phenylbenzopyrylium) skeleton **1** is the chromophoric core of one of the most widely encountered family of natural pigments found in the plant kingdom: the anthocyanins (Figure 1). Flavylium-derived pigments are indeed largely responsible for cyanic colours going from salmon pink, through red and violet, to dark blue in most flowers, fruits and leaves of angiosperms.[1]

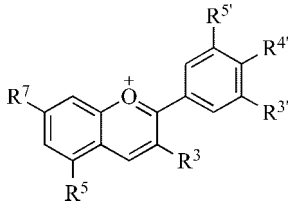

Figure 1. The flavylium chromophore (**1**: $R^3 = R^5 = R^7 = R^{3'} = R^{4'} = R^{5'} = H$), the two flavylium-derived families of pigments (anthocyanidin **2**: $R^3 = OH$ and 3-deoxyanthocyanidin **3**: $R^3 = H$) and the most common 3-deoxyanthocyanidin patterns: apigeninidin (**4**: $R^3 = R^{3'} = R^{5'} = H$ and $R^5 = R^7 = R^{4'} = OH$), luteolinidin (**5**: $R^3 = R^{5'} = H$ and $R^5 = R^7 = R^{3'} = R^{4'} = OH$) and tricetanidin (**6**: $R^3 = H$ and $R^5 = R^7 = R^{3'} = R^{4'} = R^{5'} = OH$).

In these water-soluble natural pigments, the flavylium chromophore is usually substituted and/or functionalized in various and numerous ways. Nature has used sophisticated tools such as hydroxylation, alkylation, acylation and/or glycosylation to adjust the properties of these pigments. Also, because of the impressive number of possible combinations, it is not surprising that new anthocyanins are regularly isolated from natural sources so that, at the present time, about 580 pigments from this family are already listed in the literature, ranging from simple to very complicated structures (Figure 2).[2] At a structural level, it is also worthwhile to distinguish 3-oxygenated aglycones **2** (anthocyanidins) from their 3-deoxy analogues **3** (3-deoxyanthocyanidins) (Figure 1). Unlike the red-coloured anthocyanidins **2**, which are colour-unstable and therefore seldom found naturally in their free forms, 3-deoxyanthocyanins **3** are yellow-orange pigments quite stable in acidic media, and such aglycones **3** – in particular apigeninidin (**4**), luteolinidin (**5**) and tricetanidin (**6**) – have been isolated from food plants such as corn, sorghum and black tea leaves (Figure 1).[4]

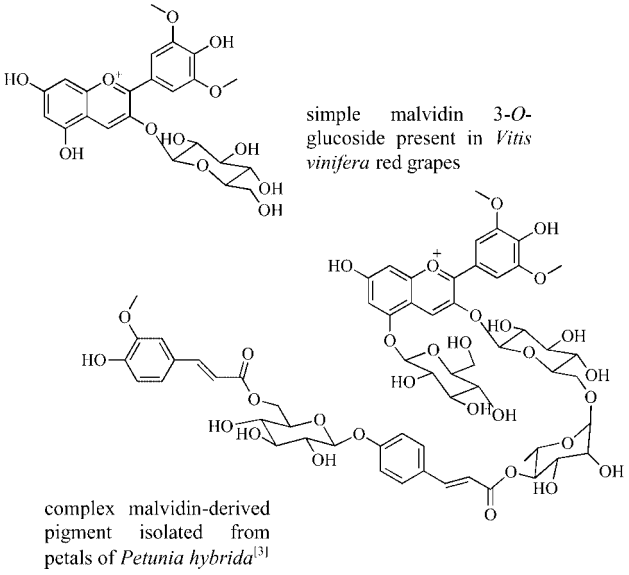

Figure 2. Illustration of the exceptional diversity existing around the flavylium nucleus with two characteristic malvidin-derived pigments.

Anthocyanins, and especially 3-deoxyanthocyanidins, have long been used as food colorants,[5] but during the last decade many other attractive applications have been developed. They have been advanced as potential hair dyes,[6]

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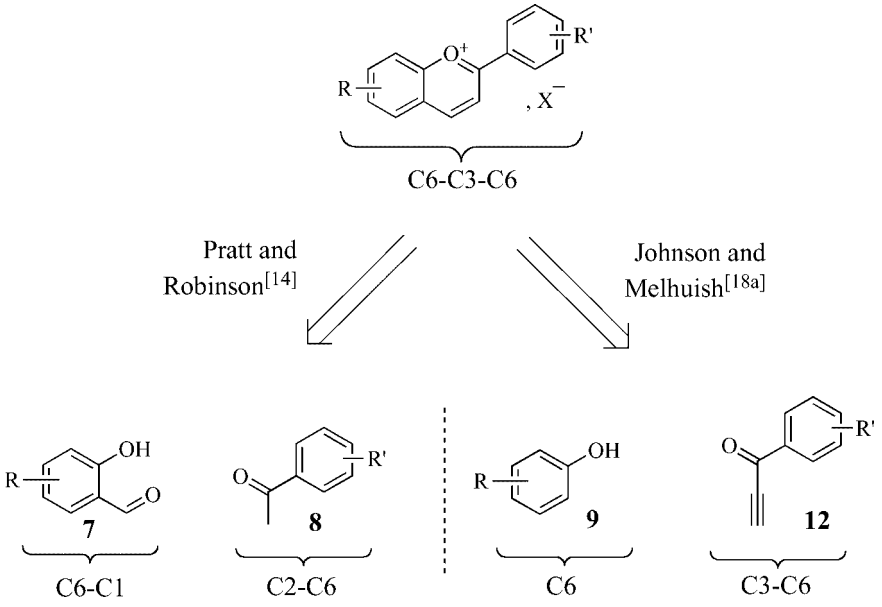
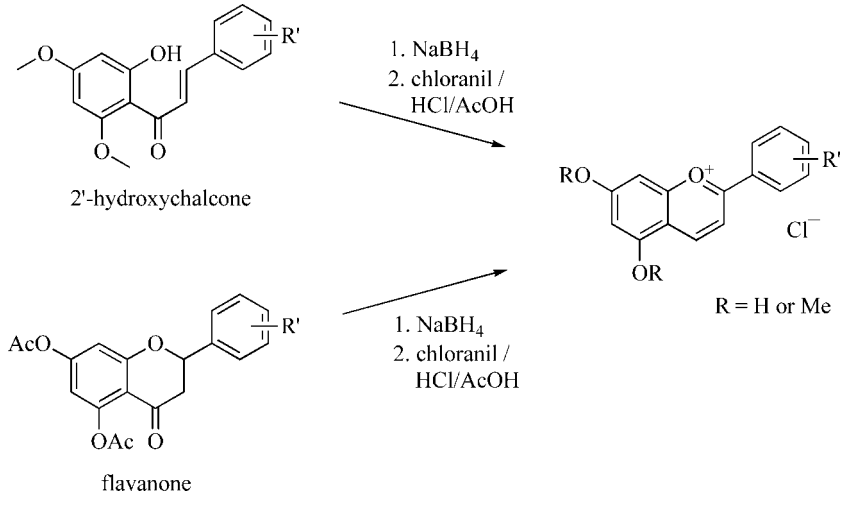
laser dyes,[7] or sensitizers for solar cells.[8] Molecular-level memory systems[9] have been based on such structures and their use in the area of self-assembled and interface systems has been reported.[10] Moreover, unlike most of the other classes of flavonoids, anthocyanins were only recently demonstrated to possess biological properties beneficial to human health: for illustration, regular consumption of anthocyanins (and also other polyphenols) from fruits, vegetables, wines, jams and preserves is closely associated with reduced risks of chronic diseases such as cancer, cardiovascular diseases and Alzheimer's disease.[11] In this pharmacological context, anthocyanins are thus regarded as important potential nutraceuticals for humans.

For all these reasons and because such compounds constitute good models for studying the structural[12] and the redox[13] behaviours of anthocyanins in aqueous medium, we decided to elaborate synthetic methodologies to prepare 3-deoxyanthocyanidin derivatives **3**. Here we report a convenient and efficient strategy allowing precisely the preparation of these monocationic flavylium derivatives but also the preparation of novel dicationic flavylium-benzopyrylium derivatives.

Despite the longstanding interest in flavylium-derived pigments, only a few synthetic approaches towards 3-deoxyanthocyanidins **3** have been reported in the literature until now.[5a] The standard synthetic method, pioneered in the early 1930s by Pratt and Robinson, is based on an acid-mediated condensation between a protected salicylaldehyde derivative **7** and a substituted acetophenone **8**, this strategy being analogized to a "C6–C1 + C2–C6" synthetic approach (Scheme 1).[14] Although this method was the first to allow the preparation of both apigeninidin (**4**) and luteolinidin (**5**) (in moderate yields), the Robinson's condensation presents severe limitations and cannot accommodate any kind of salicylaldehyde reagent. Indeed, when the salicylaldehyde is a phloroglucinol-type derivative, it is well



Scheme 1. Reported retrosynthetic analyses of the 3-deoxyanthocyanidin skeleton.



Scheme 2. Synthetic routes to 3-deoxyanthocyanidins through the chemical modification of a flavonoid precursor.[17]

known that Robinson's conditions give rise to a hard-to-purify mixture of organic salts, among which the targeted flavylium salt **3** is generally isolated in very limited amounts (5–20% yields).[14] However, two alternatives, circumventing this structural restriction, have recently been proposed: Kuhnert et al. developed an efficient $BF_3{\cdot}Et_2O$-mediated version,[15] while T. Mas optimized the condensation by using the peracetylated derivative of phloroglucinaldehyde as reagent and by performing the reaction in acidic methanol.[16]

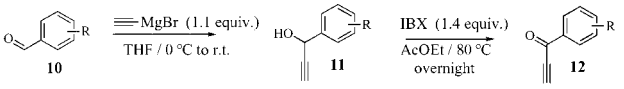
Another classic route to 3-deoxyanthocyanidins **3** is based on the chemical modification of a flavonoid precursor already possessing the appropriate carbon skeleton. Sweeny and Iacobucci, for example, described two reduction/oxidation sequences that, when applied to 2′-hydroxychalcones and flavanones, allowed access to phloroglucinol-type 3-deoxyanthocyanidins (Scheme 2).[17] This approach, however, is inherently limited by the oxidation step, which generally proceeded in moderate yields (30–70%). The other drawback of this approach is that it requires the native C6–C3–C6 flavonoid skeleton, which is not always easily accessible.

In view of these different synthetic limitations, we looked for a more general approach towards 3-deoxyanthocyanidins **3** and, more particularly, phloroglucinol-type derivatives. On the basis of a report by Johnson and Melhuish dating back to 1947, we investigated the acid-mediated condensation between a phenolic derivative **9** and an aryl ethynyl ketone **12**, corresponding to a "C6 + C3–C6" synthetic strategy (Scheme 1).[18] Surprisingly, we noted that this approach had never been optimized or even used since its description sixty years ago. Our goals were therefore on one hand to study this neglected procedure further, and on the other to explore its scope.

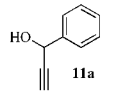
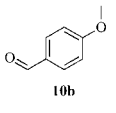
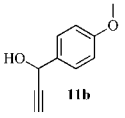
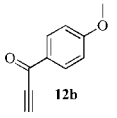
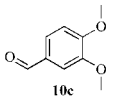
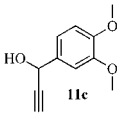
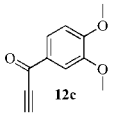
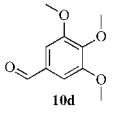
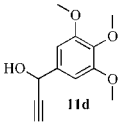
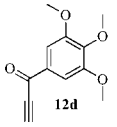
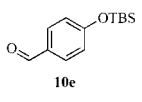
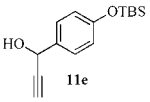
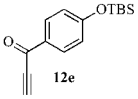
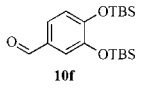
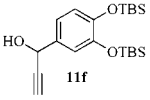
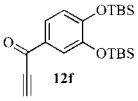
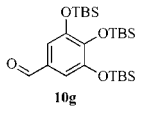
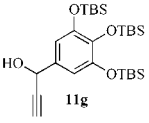
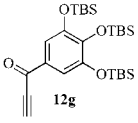
Results and Discussion

In order to prepare the required aryl ethynyl ketone synthons **12**, we have developed a simple and efficient two-step nucleophilic addition/oxidation sequence (Table 1). The nucleophilic addition of ethynylmagnesium bromide to benzaldehyde derivatives **10a**–**g** resulted in 1-arylprop-2-yn-1-ols **11a**–**g** (**10a**–**d** are commercially available materials and **10e**–**g** were obtained from the corresponding commercially available phenols by conventional *O*-silylation methods). We then considered the oxidation of these 1-arylprop-2-yn-1-ols **11** and although various conditions had already been reported (chromium salts, Swern conditions, oxovanadium complexes, Dess–Martin reagent),[19] use of the IBX/ethyl acetate system for the oxidation of propargylic alcohols had so far never been described.[20] Interestingly, this easy-to-use oxidative system proved to be very efficient and thus represents a good alternative for the preparation of ynones (Table 1). By this two-step sequence, all desired synthons **12a**–**g** were synthesized in good to excellent overall yields (74–90%).

Table 1. Synthesis of aryl ethynyl ketone patterns.



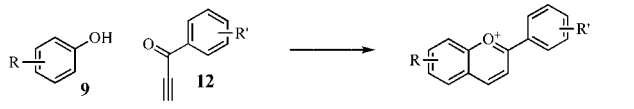
10 11 12

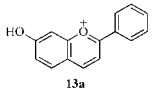
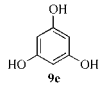
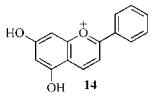
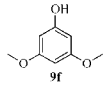
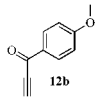
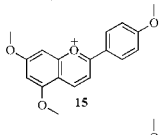
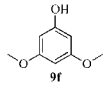
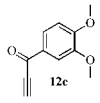
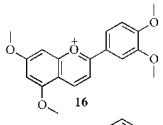
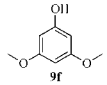
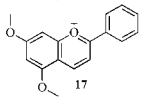
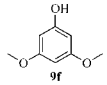
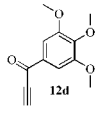
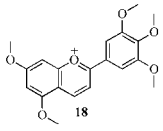
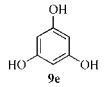
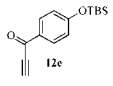
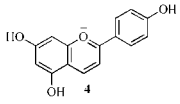
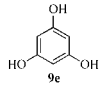
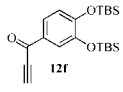
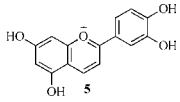
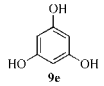
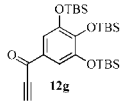
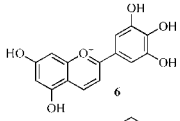
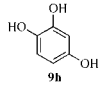
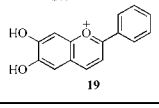
Entry	10	11	12	Overall yield for 12 (%) [a]
1	 10a	 11a	 12a	74
2	 10b	 11b	 12b	90
3	 10c	 11c	 12c	88
4	 10d	 11d	 12d	88
5	 10e	 11e	 12e	88
6	 10f	 11f	 12f	89
7	 10g	 11g	 12g	81

[a] Isolated yield after purification by column chromatography.

We then investigated the acid-mediated key-step condensation involving a phenolic derivative **9** as the nucleophilic entity and an aryl ethynyl ketone **12** as its electrophilic partner (Table 2). In order to improve the condensation procedure adopted by Johnson and Melhuish (concentrated H_2SO_4/AcOH/room temp.; then recrystallization from dilute HCl),[18] we decided to substitute concentrated sulfuric acid with dilute hexafluorophosphoric acid. This choice was motivated by the fact that we had recently examined various acidic conditions for the formation of flavylium salts (i.e., aqueous HCl, HBr, HBF_4 or HPF_6) and had observed that flavylium hexafluorophosphates exhibited the lowest solubility products in acetic acid and so could easily be reco-

Table 2. Formation of 3-deoxyanthocyanidin derivatives from various phenol/aryl ethynyl ketone combinations.



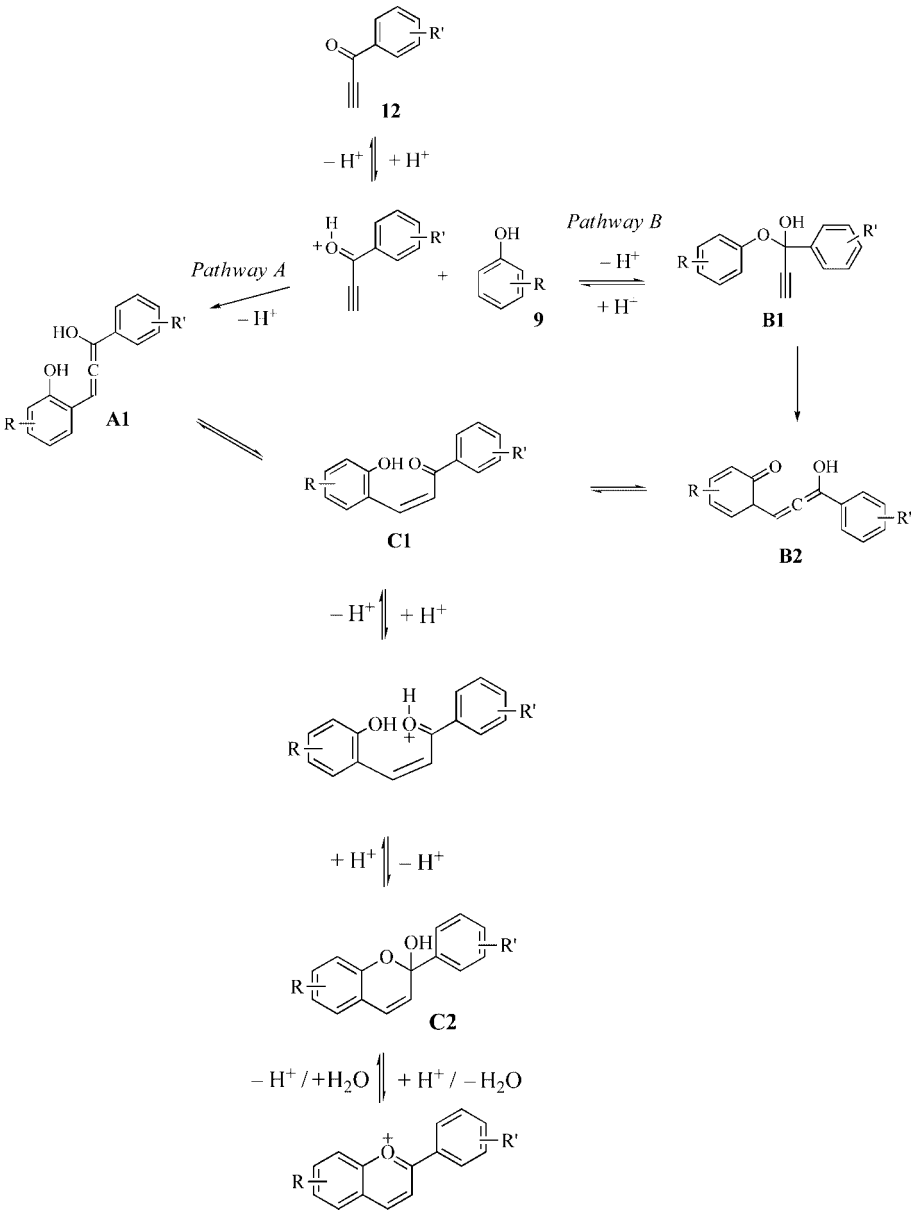
Entry	Phenol **9**	Aryl ethynyl ketone **12**	Product	Yield (%) ref.[a]/ **studied**[b]
1			-	- [c]/ - [c]
2			-	- [c]/ - [c]
3			-	- [c]/ - [c]
4				- [d] [e] / **56**
5				37 / **91**
6				82 / **93**
7				73 / **94**
8				- [f]/ **99**
9				- [f]/ **95**
10				- [f]/ **82**
11				- [f]/ **84**
12				- [f]/ **75**
13				- [f]/ **86**[e]

[a] Reference conditions: concentrated H_2SO_4/AcOH/room temp., then recrystallization from dilute HCl.[18] [b] Studied conditions: HPF_6 (50% in water)/AcOH/room temp./24 to 48 h. [c] No reaction. [d] Successful reaction, but corresponding yield not given in the reference. [e] Only regioisomer observed. [f] Not tested under the reference conditions.

vered in pure form. In addition, whereas flavylium chlorides,[16] tetrafluoroborates,[15,21] or triflates[21] have already been described, flavylium hexafluorophosphates had never previously been disclosed in the literature.

In this context, we initially studied the effect of HPF_6 on some **9**/**12** combinations already reported by Johnson and Melhuish so that we could check the potential of these modified conditions (Entries 1–7). On one hand, in terms of workability of the process, the comparison between the two conditions showed strong analogies. Although the condensation is still inefficient in the case of phenol (**9a**), *m*-cresol (**9b**) and *p*-cresol (**9c**) (Entries 1–3), it is nevertheless efficient in the case of resorcinol (**9d**), phloroglucinol (**9e**) and phloroglucinol dimethyl ether (**9f**) (Entries 4–6). It is worth noting that the interaction between resorcinol (**9d**) and phenyl ethynyl ketone (**12a**) resulted in the selective formation of the single compound 7-hydroxyflavylium (**13a**), with a distinctive AMX-type system of spins on its A ring (no traces of its isomer **13b** – i.e., 5-hydroxyflavylium compound presenting a different but also distinctive AMX system – could be detected by NMR). The origin of this regioselectivity is explained later when the mechanism of the condensation is discussed (Scheme 3). Anyway, all these preliminary results confirmed that the success of the condensation is directly dependent on the nucleophilic character of the phenolic derivative. Indeed, this condensation requires a minimal nucleophilicity in the phenolic partner; otherwise it does not work at all and the starting materials are recovered even after stirring for 72 hours. On the other hand, in terms of efficiency of the process, it clearly appeared that the use of HPF_6 instead of H_2SO_4 induced a significant increase in the condensation process, providing the corresponding 3-deoxyanthocyanidin derivatives in good to excellent yields (Entries 4–7). The most significant improvement involved the preparation of chrysinidin (**14**) through the interaction between phloroglucinol (**9e**) and phenyl ethynyl ketone (**12a**), the yield increasing from 37% with H_2SO_4 to 91% with HPF_6 (Entry 5).

We next checked whether this method could be generalized to other 3-deoxyanthocyanidin derivatives. We first corroborated the efficiency of the procedure for the preparation of polymethylated 3-deoxyanthocyanidin derivatives [i.e., chrysinidin dimethyl ether (**17**) and tricetanidin pentamethyl ether (**18**); Entries 8 and 9]. Permethylated derivatives were often used as synthetic precursors of their phenolic analogues but it is noteworthy that the demethylation step is generally effective in only moderate yields.[15,22] We therefore focused on a one-step synthesis of polyphenolic 3-deoxyanthocyanidins by the procedure investigated here. Further to the promising result obtained with the use of phloroglucinol (**9e**) as the nucleophilic entity (Entry 5), we decided to subject **9e** to the condensation process with aryl ethynyl ketones possessing phenolic functions protected with an appropriate group. We chose the acid-labile *tert*-butyldimethylsilyl group, and the reaction between phloroglucinol (**9e**) and silyl-protected **12e**–**g** resulted in the one-step formation of polyphenolic **4**, **5** and **6** (Entries 10–12). As a consequence, here we have performed total syntheses



Scheme 3. Plausible mechanistic pathways for the acid-mediated condensation between an aryl ethynyl ketone and a phenolic derivative.

of the natural apigeninidin (**4**), luteolinidin (**5**) and tricetanidin (**6**) in four steps with high overall yields starting from the corresponding unprotected benzaldehydes (69%, 72% and 61%, respectively).

Moreover, by analogy with the interaction between resorcinol (**9d**) and phenyl ethynyl ketone (**12a**) (Entry 4), we investigated the selectivity of the condensation with unsymmetrical 1,2,4-trihydroxybenzene (**9g**) as the nucleophilic partner (Entry 13). Although four regioisomers could be expected (i.e., 5,6-, 5,8-, 6,7- and 6,8-dihydroxyflavylium derivatives), we observed the exclusive formation of one isomer, which was shown to be 6,7-dihydroxyflavylium hexafluorophosphate (**19**). Indeed, the NMR spectrum of the obtained product showed two characteristic signals in the aromatic region (i.e., one singlet at δ = 6.81 ppm and one doublet at δ = 7.67 ppm) and **19** is precisely the only regioisomer that is in agreement with this observation.

Until now, no mechanism has been proposed for this acid-mediated condensation, so it seemed constructive to us to discuss our mechanistic hypothesis here. What is sure is that such a condensation would involve a cascade of successive events, resulting in the overall formation of one C–C bond and one C–O bond, together with the establishment of the benzopyrylium aromatic character. The question is to determine how these events would occur and, in fact, two competitive pathways could be envisaged, especially with regard to the way in which the C–C bond could be formed (Scheme 3). It is noteworthy that both would give the same retrochalcone-type intermediate **C1**. On one hand, *Pathway A* involves the formation of the C–C bond through the nucleophilic 1,4-addition of a carbon atom of **9** to acid-activated **12** to generate intermediate **A1**, in which proton migration produces the expected intermediate **C1**. On the other hand, *Pathway B* involves a more complex pathway

to **C1**, starting with the formation of the hemiketal intermediate **B1** through the nucleophilic addition of **9** through its phenolic position to acid-activated **12**. The intermediate **B1** thus presents a suitable propargyl vinyl ether pattern precursor to a Claisen-type rearrangement to afford the intermediate **B2**, which could progress towards **C1** through a simple tautomerization process. Once the intermediate **C1** is produced, we then join the common pathway involving the establishment of the C–O bond through a 6-*exo*-*trig* cyclization of the retrochalcone **C1**. Finally, the resulting cyclic hemiketal **C2** could aromatize after protonation and elimination of water, creating the aromatic benzopyrylium nucleus of the flavylium salt. From our results, it is evident that the condensation process is effective whatever the electrophilic partner **12**, as long as the phenolic derivative **9** is nucleophilic enough, the *C*-nucleophilicity of the phenol clearly emerging as the key parameter of the process. Nevertheless, this fact is not decisive for explaining the mechanistic pathway, because the C-nucleophilic character of the phenol could suggest either *Pathway A* involving the formation of **A1** or *Pathway B* with the formation of **B2**. Moreover, the regioselectivity observed with resorcinol (**9d**) or 1,2,4-trihydroxybenzene (**9g**) could also be explained by both proposed pathways. In these two cases, the regioselectivity would result from the selective formation of the C–C bond, which could, for electronic and steric reasons, progress either through the intermolecular alternative, to afford **A1** (*Pathway A*), but also through the intramolecular alternative from the corresponding intermediate **B1** (*Pathway B*). In the case of **9g**, it is also possible to imagine that the corresponding intermediate **B1** could be produced through the nucleophilic addition of **9g** through the phenolic position 4, which could be seen as its most reactive phenolic site. Consequently, the interpretation of the mechanism of this condensation process is not facile, *Pathway A* and *Pathway B* both being plausible and difficult to differentiate.

To expand the scope of this condensation further, we envisaged the application of our procedure to the synthesis of bispyrylium salts and, more precisely, those possessing a flavylium-benzopyrylium skeleton **20** (see 3a in Figure 3). To the best of our knowledge, no such sophisticated skeleton has ever been encountered in natural pigments but it could nevertheless exhibits interesting properties, especially thanks to its dicationic character. Until now, the only synthetic approach to such derivatives has been that described in 1969 by Reynolds and Van Allan.[23] In their work, the authors mentioned the formation of the derivative **23** through a double Robinson condensation between two equivalents of salicylaldehyde **21** and one equivalent of diketone **22** in a poor yield of 8% (see 3b in Figure 3). As a new alternative, we imagined that, by starting from bis(propynoyl)benzene derivatives, a double condensation with two equivalents of phloroglucinol derivatives could also provide flavylium-benzopyrylium salts.

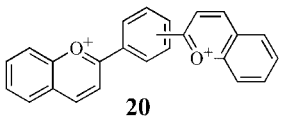
By analogy, the application of our condensation process required the initial preparation of an aryl diethynyl diketone pattern. Thus, by starting from the commercially available isophthalic carboxaldehyde (**24**) and terephthaldehyde (**25**), the synthesis of two aryl diethynyl ketone patterns **26** and **27** was achieved through the same two-step sequence as described above for the preparation of aryl ethynyl ketone synthons **12** (Scheme 4). Each of the two aryl diethynyl diketone patterns **26** and **27** were then engaged in a condensation step in the presence of HPF_6 with phloroglucinol (**9e**) or phloroglucinol dimethyl ether (**9f**). In this manner, three new flavylium-derived pigments **28**, **30** and **31** were obtained in excellent yields. Unfortunately, the reaction between one equivalent of **26** and two equivalents of **9e** gave a hard-to-purify mixture of organic salts, among which the expected dicationic derivative **29** was detected but only in a very limited amount.

Conclusions

In conclusion, we have reactivated and optimized a simple and very efficient method for the synthesis of 3-deoxyanthocyanidins through reactions between activated phenols and aryl ethynyl ketones in acetic acid in the presence of HPF_6. At the same time, by the same method, we have succeeded in the synthesis of novel dicationic flavylium-benzopyrylium skeletons.

Further works, not only to study the behaviour of the newly synthesized dicationic pigments in aqueous media

3a The flavylium-benzopyrylium skeleton:



20

3b Reynolds and Van Allan:[23]

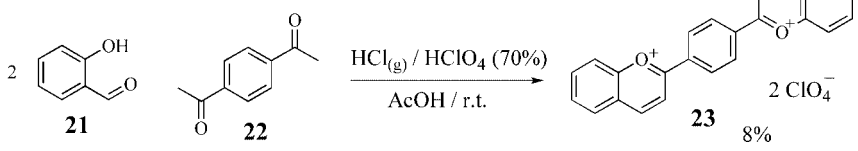
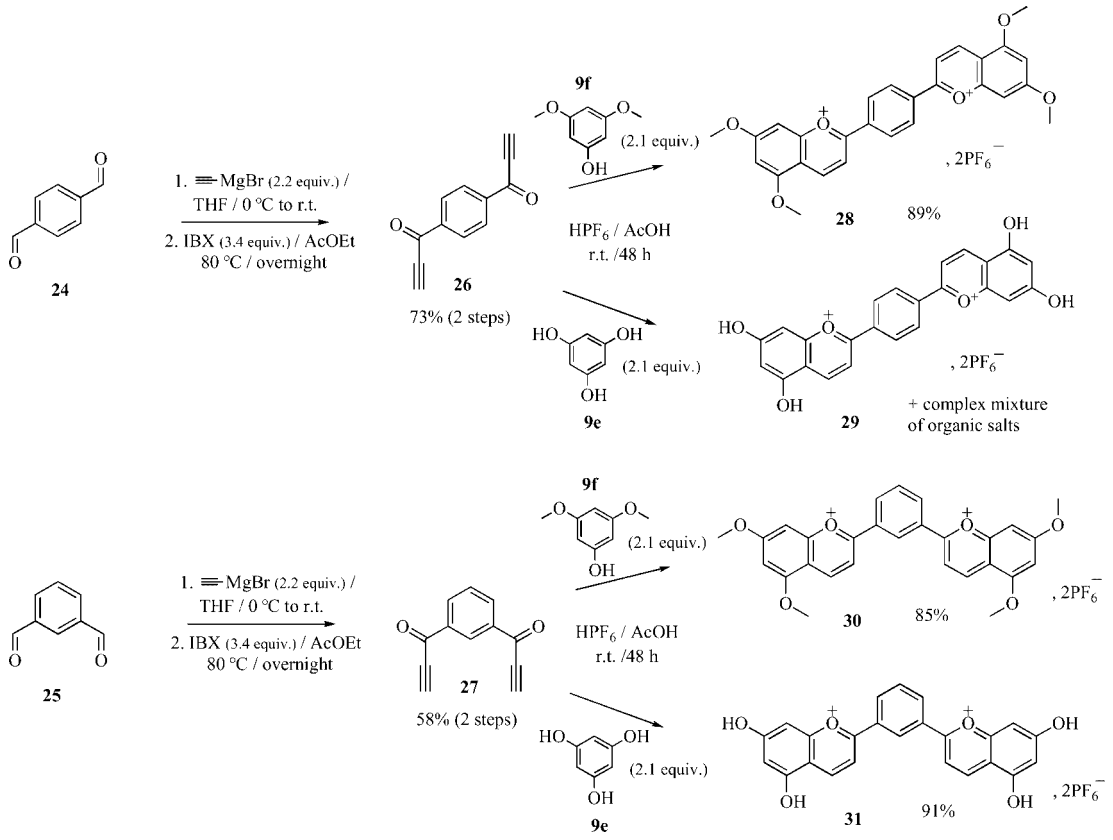


Figure 3. The flavylium-benzopyrylium skeleton: nature and the only synthetic approach developed until now.

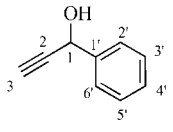


Scheme 4. Synthesis of dicationic flavylium-benzopyrylium derivatives.

but also to continue to broaden the scope of this reaction, are now underway.

Experimental Section

General Remarks: Most reactions were performed under argon with magnetic stirring and in anhydrous solvents. All starting materials were commercially available and were used without further purification. The reactions were monitored by thin-layer chromatography carried out on silica plates (silica gel 60 F_{254}, Merck) with use of UV light for detection. Column chromatography was performed on silica gel 60 (0.040–0.063 mm, Merck) with the eluents indicated. Melting points (m.p.) were determined with a Bibby–Stenlin Stuart SMP3 melting point apparatus and are uncorrected. IR spectra were recorded with a Perkin–Elmer FTIR 1600 spectrometer (KBr disc) and values are reported in cm^{-1}. UV/Vis spectra were measured with a 8452A Hewlett–Packard spectrophotometer in the solvents indicated. ^1H and ^{13}C NMR spectra were recorded with a Bruker AC 300 spectrometer at 300 and 75 MHz, respectively. Chemical shifts (δ) and coupling constants (J) are given in ppm and Hz, respectively. Low- and high-resolution mass spectra were obtained with a Bruker micro-TOF instrument (ESI).



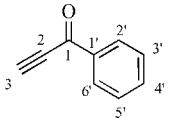
General Procedure for the Preparation of 1-Arylprop-2-yn-1-ols 11a–g: A solution of ethynylmagnesium bromide (0.5 M in THF, 26 mL, 13 mmol, 1.3 equiv.) was added at 0 °C to a solution of the corresponding benzaldehyde **10a**–**g** (10 mmol) in THF (20 mL). After the mixture had been stirred for 2 h at room temperature, a saturated solution of NH_4Cl (20 mL) was added to the solution and the THF was evaporated under vacuum. The aqueous phase was extracted three times with ethyl acetate and the organic layers were washed with water and brine and then dried with Na_2SO_4. After evaporation of the solvent, the resulting crude product was purified by column chromatography (heptane/ethyl acetate) to give **11a**–**g** in pure form.

1-Phenylprop-2-yn-1-ol (11a): Yellow oil. Yield 79%. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.49 (d, $^3J_{OH-1}$ = 6.2 Hz, 1 H, O*H*), 2.66 (d, $^4J_{3-1}$ = 2.2 Hz, 1 H, 3-H), 5.45 (dd, $^3J_{1-OH}$ = 6.2 Hz, $^4J_{1-3}$ = 2.2 Hz, 1 H, 1-H), 7.37 (m, 3 H, 2′-H/ 4′-H/ 6′-H), 7.55 (m, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 64.4 (C-1), 74.9 (C-2), 83.5 (C-3), 126.6 (C-2′ and C-6′), 128.6 (C-4′), 128.7 (C-3′ and C-5′), 140.0 (C-1′) ppm. IR (KBr): $\tilde{\nu}$ = 3335 (O–H), 3290 (≡C–H), 2115 (C≡C) cm^{-1}. MS (ESI, positive mode): *m*/*z* (%) = 139 (100) $[M + Li]^+$, 111 (40). HRMS: calcd. for C_9H_8LiO: 139.0730; found: 139.0730.

1-(3′,4′-Dimethoxyphenyl)prop-2-yn-1-ol (11c): White solid. Yield 90%. M.p. 98 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.32 (d, $^3J_{OH-1}$ = 5.9 Hz, 1 H, O*H*), 2.67 (d, $^4J_{3-1}$ = 2.2 Hz, 1 H, 3-H), 3.87 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 5.41 (dd, $^3J_{1\text{-}OH}$ = 5.9 Hz, $^4J_{1-3}$ = 2.2 Hz, 1 H, 1-H), 6.85 (d, $^3J_{5'-6'}$ = 8.8 Hz, 1 H, 5′-H), 7.08 (d, $^4J_{2'-6'}$ = 2.2 Hz, 1 H, 2′-H), 7.08 (dd, $^3J_{6'-5'}$ = 8.8 Hz, $^4J_{6'-2'}$ = 2.2 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 55.8 (OCH_3), 55.9 (OCH_3), 64.0 (C-1), 74.6 (C-2), 83.8 (C-3), 109.8 (C-2′), 110.9 (C-5′), 119.0 (C-6′), 132.8 (C-1′), 148.9/149.0 (C-3′ and C-4′) ppm. IR (KBr): $\tilde{\nu}$ = 3330 (O–H), 3300 (≡C–H), 2110 (C≡C) cm^{-1}. MS (ESI, positive mode): *m*/*z* (%) = 215 (40) [M +

Na]$^+$, 199 (100) [M + Li]$^+$, 175 (15). HRMS: calcd. for $C_{11}H_{12}LiO_3$ 199.0941; found: 199.0952.

1-(4′-*tert*-Butyldimethylsilyloxyphenyl)prop-2-yn-1-ol (11e): Yellow oil. Yield 94%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.20 [s, 6 H, Si(CH_3)$_2$], 0.98 [s, 9 H, SiC(CH_3)$_3$], 2.24 (d, $^3J_{OH-1}$ = 6.2 Hz, 1 H, O*H*), 2.66 (d, $^4J_{3-1}$ = 2.2 Hz, 1 H, 3-H), 5.41 (dd, $^3J_{1-OH}$ = 6.2 Hz, $^4J_{1-3}$ = 2.2 Hz, 1 H, 1-H), 6.84 (m, AA′ part of an AA′MM′ system, 2 H, 3′-H and 5′-H), 7.42 (m, MM′ part of an AA′MM′ system, 2 H, 2′-H and 6′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 4.4, 18.2, 25.7, 64.1 (C-1), 74.7 (C-2), 83.6 (C-3), 120.2 (C-3′ and C-5′), 128.0 (C-2′ et C-6′), 132.9 (C-1′), 156.0 (C-4′) ppm. IR (KBr): $\tilde{\nu}$ = 3330 (O–H), 3310 (≡C–H), 2120 (C≡C) cm^{-1}. MS (ESI, positive mode): *m*/*z* (%) = 269 (100) [M + Li]$^+$, 245 (35). HRMS: calcd. for $C_{15}H_{22}LiO_2Si$ 269.1544; found: 269.1534.

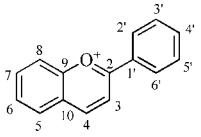


General Procedure for the Preparation of Aryl Ethynyl Ketones 12a–g: IBX (2.8 g, 10 mmol, 2 equiv.) was added in one portion to a solution of the corresponding 1-arylprop-2-yn-1-ol **11a**–**g** (5 mmol, 1 equiv.) in ethyl acetate (25 mL). The mixture was heated at 80 °C and stirred overnight. After recooling to room temperature, the mixture was filtered and ethyl acetate was evaporated under vacuum. The resulting crude product was purified by column chromatography (heptane/ethyl acetate) to give **12a**–**g** in pure form.

Phenyl Ethynyl Ketone (12a): Yellow solid. Yield 94%. M.p. 55 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.47 (s, 1 H, 3-H), 7.47 (m, AA′ part of a AA′BMM′ system, 2 H, 3′-H and 5′-H), 7.59 (m, MM′ part of a AA′BMM′ system, 1 H, 4′-H), 8.13 (m, AA′ part of a AA′BMM′ system, 2 H, 2′-H and 6′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 80.2 (C-2), 81.0 (C-3), 128.7/129.7 (C-2′, C-3′, C-5′ and C-6′), 134.5 (C-4′), 136.1 (C-1′), 177,4 (C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3230 (≡C–H), 2090 (C≡C), 1645 (C=O) cm^{-1}. UV/Vis (MeOH): λ_{max} (ε) = 264 (18900) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 137 (100) [M + Li]$^+$. HRMS: calcd. for C_9H_6LiO 137.0573; found: 137.0568.

3,4-Dimethoxyphenyl Ethynyl Ketone (12c): White solid. Yield 98%. M.p. 118 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.38 (s, 1 H, 3-H), 3.93 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 6.92 (d, $^3J_{5′-6′}$ = 8.4 Hz, 1 H, 5′-H), 7.59 (d, $^4J_{2′-6′}$ = 2.2 Hz, 1 H, 2′-H), 7.86 (dd, $^3J_{6′-5′}$ = 8.4 Hz, $^4J_{6′-2′}$ = 2.2 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 56.0 (O*C*H$_3$), 56.2 (O*C*H$_3$), 80.0 (C-2), 80.3 (C-3), 110.1 (C-2′ and C-5′), 126.1 (C-6′), 129.7 (C-1′), 149.1/154.7 (C-3′ and C-4′), 176,0 (C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3235 (≡C–H), 2090 (C≡C), 1635 (C=O) cm^{-1}. UV/Vis (MeOH): λ_{max} (ε) = 294 (7600), 330 (9200) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 197 (100) [M + Li]$^+$, 179 (10). HRMS: calcd. for $C_{11}H_{10}LiO_3$ 197.0785; found: 197.0782.

4-(*tert*-Butyldimethylsilyloxy)phenyl Ethynyl Ketone (12e): White solid. Yield 94%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.24 [s, 6 H, Si(CH_3)$_2$], 0.93 [s, 9 H, SiC(CH_3)$_3$], 3.37 (s, 1 H, 3-H), 6.90 (m, AA′ part of an AA′MM′ system, 2 H, 3′-H and 5′-H), 8.08 (m, MM′ part of an AA′MM′ system, 2 H, 2′-H and 6′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = –4.3, 18.2, 25.5, 80.0 (C-2), 80.4 (C-3), 120.1 (C-3′ and C-5′), 130.0 (C-4′), 132.1 (C-2′ and C-6′), 161.8 (C-1′), 176.0 (C-1) ppm. IR (KBr): $\tilde{\nu}$ = 3210 (≡C–H), 2090 (C≡C), 1630 (C=O) cm^{-1}. UV/Vis (MeOH): λ_{max} (ε) = 300 (17800) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 267 (100) [M + Li]$^+$. HRMS: calcd. for $C_{15}H_{20}LiO_2Si$ 267.1387; found: 267.1386.



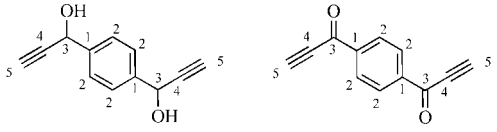
7-Hydroxy-2-phenylbenzopyrylium Hexafluorophosphate (13a): An excess of aqueous hexafluorophosphoric acid (50% in water) was added to a solution of **9d** (55 mg, 0.5 mmol) and **12a** (65 mg, 0.5 mmol) in a minimum of acetic acid. The mixture immediately became dark yellow and was stirred for 48 h at room temperature. The mixture was then plunged into diethyl ether (10 mL) and the flavylium salt precipitated. The resulting yellow powder was recovered by filtration and washed with diethyl ether to give **13a** in pure form (103 mg, 0.28 mmol). Yield 56%. M.p. 117 °C. ^{1}H NMR (300 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 7.50 (dd, $^3J_{6-5}$ = 9.1 Hz, $^4J_{6-8}$ = 2.2 Hz, 1 H, 6-H), 7.58 (dd, $^4J_{8-6}$ = 2.2 Hz, $^5J_{8-4}$ = 0.7 Hz, 1 H, 8-H), 7.71 (m, AA′ part of an AA′BMM′ system, 2 H, 3′-H and 5′-H), 7.83 (m, B part of an AA′BMM′ system, 1 H, 4′-H), 8.19 (d, $^3J_{5-6}$ = 9.1 Hz, 1 H, 5-H), 8.33 (d, $^3J_{3-4}$ = 8.4 Hz, 1 H, 3-H), 8.39 (m, MM′ part of an AA′BMM′ system, 2 H, 2′-H and 6′-H), 9.17 (dd, $^3J_{3-4}$ = 8.4 Hz, $^5J_{4-8}$ = 0.7 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 102.6 (C-8), 113.4 (C-3), 120.4 (C-10), 122.3 (C-6), 128.9 (C-1′), 129.1 (C-3′ and C-5′), 129.9 (C-2′ and C-6′), 133.1 (C-5), 136.2 (C-4′), 155.5 (C-4), 159.9/169.2/172.4 (C-2/C-7/C-9) ppm. IR (KBr): $\tilde{\nu}$ = 3360 (O–H), 1635 (C=O), 860 (P–F) cm^{-1}. UV/Vis (MeOH/5% 1 N HCl): λ_{max} (ε) = 264 (15600), 356 (4700), 436 (21100) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 223 (100) [M]$^+$. HRMS: calcd. for $C_{15}H_{11}O_2$ 223.0754; found: 223.0760.

5,7-Dihydroxy-2-phenylbenzopyrylium Hexafluorophosphate (14): An excess of aqueous hexafluorophosphoric acid (50% in water) was added to a solution of **9e** (dihydrated, 811 mg, 5 mmol) and **12a** (651 mg, 5 mmol) in a minimum of acetic acid. The mixture immediately became dark red and was stirred for 48 h at room temperature. The mixture was then plunged into diethyl ether (100 mL) and the flavylium salt precipitated. The resulting orange powder was recovered by filtration and washed with diethyl ether to give **14** in pure form (1.748 g, 0.455 mmol). Yield 91%. ^{1}H NMR (300 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 6.81 (d, $^4J_{6-8}$ = 2.2 Hz, 1 H, 6-H), 7.11 (dd, $^4J_{8-6}$ = 2.2 Hz, $^5J_{8-4}$ = 0.7 Hz, 1 H, 8-H), 7.72 (AA′ part of an AA′BMM′ system, 2 H, 3′-H and 5′-H), 7.84 (B part of an AA′BMM′ system, 1 H, 4′-H), 8.13 (d, $^3J_{3-4}$ = 8.4 Hz, 1 H, 3-H), 8.35 (MM′ part of an AA′BMM′ system, 2 H, 2′-H and 6′-H), 9.25 (dd, $^3J_{4-3}$ = 8.4 Hz, $^5J_{4-8}$ = 0.7 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 95.7 (C-6), 102.9 (C-8), 111.2 (C-3), 114.4 (C-10), 128.9 (C-3′ and C-5′), 129.1 (C-1′), 130.0 (C-2′ and C-6′), 135.8 (C-4′), 150.5 (C-4), 158.4/159.4/171.1/171.4 (C-2, C-5, C-7 and C-9) ppm. IR (KBr): $\tilde{\nu}$ = 3410 (O–H), 1640 (C=O), 835 (P–F) cm^{-1}. UV/Vis (MeOH/5% 1 N HCl): λ_{max} (ε) = 274 (35400), 474 (36200) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 239 (100) [M$^+$]. HRMS: calcd. for $C_{15}H_{11}O_3$ 239.0703; found: 239.0696.

5,7,4′-Trimethoxy-2-phenylbenzopyrylium Hexafluorophosphate (15): An excess of aqueous hexafluorophosphoric acid (50% in water) was added to a solution of **9f** (771 mg, 5 mmol) and **12b** (801 mg, 5 mmol) in a minimum of acetic acid. The mixture immediately became dark red and was stirred for 48 h at room temperature. The mixture was then plunged into diethyl ether (100 mL) and the flavylium salt precipitated. The resulting purple powder was recovered by filtration and washed with diethyl ether to give **15** in

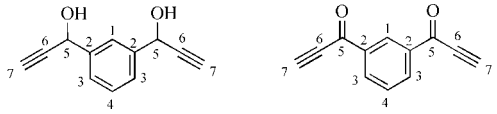
pure form (2.057 g, 0.465 mmol). Yield 93%. M.p. 201 °C. ^{1}H NMR (300 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 3.96 (s, 3 H, OC*H*$_3$), 4.07 (s, 3 H, OC*H*$_3$), 4.09 (s, 3 H, OC*H*$_3$), 6.80 (d, $^4J_{6-8}$ = 2.2 Hz, 1 H, 6-H), 7.19 (m, AA′ part of an AA′MM′ system, 2 H, 3′-H and 5′-H), 7.23 (dd, $^4J_{8-6}$ = 2.2 Hz, $^5J_{8-4}$ = 0.7 Hz, 1 H, 8-H), 8.05 (d, $^3J_{3-4}$ = 8.8 Hz, 1 H, 3-H), 8.32 (m, MM′ part of an AA′MM′ system, 2 H, 2′-H and 6′-H), 9.07 (dd, $^3J_{4-3}$ = 8.8 Hz, $^5J_{4-8}$ = 0.7 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 55.9/57.0/57.2 (O*C*H$_3$), 93.4 (C-6), 99.8 (C-8), 111.3 (C-3), 113.4 (C-10), 115.8 (C-3′ and C-5′), 120.8 (C-1′), 131.9 (C-2′ and C-6′); 148.7 (C-4), 158.8/159.0/167.0/171.4/171.7 (C-2, C-5, C-7, C-9 and C-4′) ppm. IR (KBr): $\tilde{\nu}$ = ca. 1640 (C=O), 835 (P–F) cm^{-1}. UV/Vis (MeOH/5% 1 N HCl): λ_{max} (ε) = 266 (24900), 394 (18000), 460 (13600) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 297 (100) [M]$^+$. HRMS: calcd. for $C_{18}H_{17}O_4$ 297.1121; found: 297.1109.

6,7-Dihydroxy-2-phenylbenzopyrylium Hexafluorophosphate (19): An excess of aqueous hexafluorophosphoric acid (50% in water) was added to a solution of **9g** (48 mg, 0.38 mmol) and **12a** (50 mg, 0.38 mmol) in a minimum of acetic acid. The mixture immediately became dark red and was stirred for 48 h at room temperature. The mixture was then plunged into diethyl ether (10 mL) and the flavylium salt precipitated. The resulting red powder was recovered by filtration and washed with diethyl ether to give **19** in pure form (125 mg, 0.327 mmol). Yield 86%. ^{1}H NMR (300 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 6.81 (s, 1 H, 5-H), 7.67 (d, $^5J_{8-4}$ = 0.7 Hz, 1 H, 8-H), 7.73 (AA′ part of an AA′BMM' system, 2 H, 3′-H and 5′-H), 7.81 (B part of an AA′BMM' system, 1 H, 4′-H), 8.31 (d, $^3J_{3-4}$ = 8,1 Hz, 1 H, 3-H), 8.34 (MM′ part of an AA′BMM′ system, 2 H, 2′-H and 6′-H), 9.04 (dd, $^3J_{4-3}$ = 8.1 Hz, $^5J_{4-8}$ = 0.7 Hz, 1 H, 4-H) ppm. ^{13}C NMR (75 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 102.9 (8-C), 110.4 (5-C), 113.7 (3-C), 121.8 (10-C), 128.5 (3′-C and 5′-C), 129.2 (1′-C), 129.9 (2′-C and 6′-C), 135.4 (4′-C), 148.7 (6-C), 152.7 (4-C), 155.7/159.9/169.7 (2-C/7-C/9-C) ppm. IR (KBr): $\tilde{\nu}$ = 3410 (O–H), 1640 (C=O), 835 (P–F) cm^{-1}. UV/Vis (MeOH/5% 1 N HCl): λ_{max} (ε) = 282 (14600), 440 (23500) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 239 (100) [M]$^+$. HRMS: calcd. for $C_{15}H_{11}O_3$: 239.0703; found: 239.0717.



***p*-Dipropynoylbenzene (26):** A solution of ethynylmagnesium bromide (0.5 M in THF, 40 mL, 20 mmol, 2.7 equiv.) was added at 0 °C to a solution of terephthalaldehyde (**24**, 1.006 g, 7.5 mmol) in THF (75 mL). After the mixture had been stirred for 4 h at room temperature, a saturated solution of NH_4Cl (40 mL) was added and the THF was evaporated under vacuum. The aqueous phase was extracted three times with ethyl acetate and the organic layers were washed with water and brine and then dried with Na_2SO_4. After evaporation of the solvent, the resulting crude product was purified by column chromatography (heptane/ethyl acetate 2:1) to give the expected diol in pure form as a yellow oil (1.229 g, 6.6 mmol). Yield 88%. M.p. 105 °C. ^{1}H NMR (300 MHz, CD_3OD, 25 °C): δ = 2.99 (s, $^4J_{5-3}$ = 2.3 Hz, 2 H, 5-H), 5.40 (d, $^4J_{3-5}$ = 2.3 Hz, 2 H, 3-H), 7.53 (s, 4 H, 2-H) ppm. ^{13}C NMR (75 MHz, CD_3OD, 25 °C): δ = 63.0 (C-3), 74.0 (C-5), 83.7 (C-4), 126.4 (C-1), 141.0 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 3350 (O–H), 3280 (≡C–H), 2120 (C≡C) cm^{-1}. MS (ESI, positive mode): *m*/*z* (%) = 193 (100) [M + Li]$^+$, 175 (15). HRMS: calcd. for $C_{12}H_{10}LiO_2$ 193.0836; found: 193.0835.

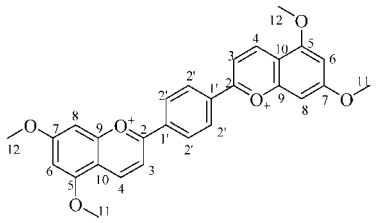
IBX (7.0 g, 25 mmol, 2.5 equiv.) was added in one portion to a solution of the purified diol (935 mg, 5 mmol) in ethyl acetate (25 mL). The mixture was heated at 80 °C and stirred overnight. After recooling to room temperature, the mixture was filtered and ethyl acetate was evaporated under vacuum. The resulting crude product was purified by column chromatography (heptane/ethyl acetate, 4:1) to give **26** in pure form as a yellow solid (756 mg, 4.2 mmol). Yield 84%. M.p. 213 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.55 (s, 2 H, 5-H), 8.27 (s, 4 H, 2-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 80.0 (C-4), 82.2 (C-5), 129.9 (C-1), 140.0 (C-2), 176.5 (C-3) ppm. IR (KBr): $\tilde{\nu}$ = 3220 (≡C–H), 2090 (C≡C), 1655 (C=O) cm^{-1}. UV/Vis (MeOH): λ_{max} (ε) = 280 (25100) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 183 (100) [M + H]$^+$, 149 (15). HRMS: calcd. for $C_{12}H_7O_2$: 183.0441; found: 183.0447.



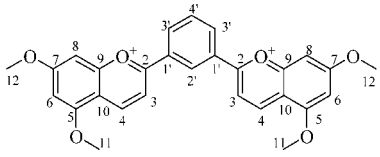
***m*-Dipropynoylbenzene (27):** A solution of ethynylmagnesium bromide (0.5 M in THF, 40 mL, 20 mmol, 2.7 equiv.) was added at 0 °C to a solution of isophthalic dicarboxaldehyde **25** (1.006 g, 7.5 mmol) in THF (75 mL). The solution was stirred at room temperature for 4 h, a saturated solution of NH_4Cl (40 mL) was added, and THF was evaporated under vacuum. The aqueous phase was extracted three times with ethyl acetate and the organic layers were washed with water and brine and then dried with Na_2SO_4. After evaporation of the solvent, the resulting crude product was purified by column chromatography (heptane/ethyl acetate 2:1) to give the expected diol in pure form as a white solid (1.103 g, 5.9 mmol). Yield 79%. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.64 (d, $^4J_{7-5}$ = 2.3 Hz, 2 H, 7-H), 3.57 (s, 2 H, O*H*), 5.38 (d, $^4J_{5-7}$ = 2.3 Hz, 2 H, 5-H), 7.31–7.36 (m, 1 H, 4-H), 7.44–7.49 (m, 2 H, 3-H), 7.61–7.63 (m, 1 H, 1-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 64.0 (C-5), 75.1 (C-7), 83.4 (C-6), 125.0 (C-1), 126.8 (C-3), 129.0 (C-4), 140.5 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 3350 (O–H), 3265 (≡C–H), 2120 (C≡C) cm^{-1}. MS (ESI, positive mode): *m*/*z* (%) = 193 (100) [M + Li]$^+$. HRMS: calcd. for $C_{12}H_{10}LiO_2$: 193.0836; found: 193.0802.

IBX (7.0 g, 25 mmol, 2.5 equiv.) was added in one portion to a solution of the purified diol (935 mg, 5 mmol) in ethyl acetate (25 mL). The mixture was heated at 80 °C and stirred overnight. After recooling to room temperature, the mixture was filtered and ethyl acetate was evaporated under vacuum. The resulting crude product was purified by column chromatography (heptane/ethyl acetate, 4:1) to give **27** in pure form as a yellow solid (656 mg, 3.4 mmol). Yield 67%. M.p. 114 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.56 (s, 2 H, 7-H), 7.66 (t, $^3J_{4-3}$ = 8.0 Hz, 1 H, 4-H), 8.39 (dd, $^3J_{3-4}$ = 8.0 Hz, $^4J_{3-1}$ = 1.7 Hz, 2 H, 3-H), 8.89 (d, $^4J_{1-3}$ = 1.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 79.8 (6-C-6), 82.0 (7-C-7), 129.3/130.9 (C-1 and C-4), 134.8 (C-3), 136.6 (C-2), 176.2 (C-5) ppm. IR (KBr): $\tilde{\nu}$ = 3240 (≡C–H), 2090 (C≡C), 1650 (C=O) cm^{-1}. MS (ESI, positive mode): *m*/*z* (%) = 183 (100) [M + H]$^+$. HRMS: calcd. for $C_{12}H_7O_2$: 183.0441; found: 183.0445.

2,2′-(*p*-Phenylene)bis(5,7-dimethoxybenzopyrylium) Hexafluorophosphate (28): Compound **9f** (390 mg, 2.50 mmol, 2.1 equiv.) and an excess of aqueous hexafluorophosphoric acid (50% in water) were added at room temperature to a solution of **26** (220 mg, 1.20 mmol, 1.0 equiv.) in a minimum of acetic acid. The mixture immediately became dark red and was stirred for 48 h at room



temperature. The mixture was then plunged into diethyl ether (50 mL) and the flavylium salt precipitated. The resulting purple powder was recovered by filtration and washed with diethyl ether to give **28** in pure form (797 mg, 1.07 mmol). Yield 89%. ^{1}H NMR (300 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 4.14 (s, 6 H, OC*H*$_3$), 4.18 (s, 6 H, OC*H*$_3$), 6.93 (d, $^4J_{6-8}$ = 2.0 Hz, 2 H, 6-H), 7.41 (d, $^4J_{8-6}$ = 2.0 Hz, 2 H, 8-H), 8.47 (d, $^3J_{3-4}$ = 8.5 Hz, 2 H, 3-H), 8.63 (s, 4 H, 2′-H), 9.39 (d, $^3J_{4-3}$ = 8.5 Hz, 2 H, 4-H) ppm. ^{13}C NMR (75 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 58.8 (O*C*H$_3$), 59.1 (O*C*H$_3$), 95.0 (C-6), 102.2 (C-8), 114.5 (C-3), 121.5 (C-10), 131.0 (C-2′), 135.5 (C-1′), 152.1 (C-4), 160.8/161.8/169.9 (C-5, C-7 and C-9), 175.4 (2-C) ppm. IR (KBr): $\tilde{\nu}$ = 1643 (C=O), 855 (P–F) cm^{-1}. UV/Vis (MeOH/5% 1 N HCl): λ_{max} (ε) = 370 (7000), 420 (11200), 502 (16000) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 228 (100) [M]$^{2+}$. HRMS: calcd. for $C_{28}H_{24}O_6$ [M]$^{2+}$: 228.0781; found: 228.0777.



2,2′-(*m*-Phenylene)-bis(5,7-dimethoxybenzopyrylium) Hexafluorophosphate (30): Compound **9f** (300 mg, 1.95 mmol, 2.1 equiv.) and an excess of aqueous hexafluorophosphoric acid (50% in water) were added at room temperature to a solution of **27** (170 mg, 0.93 mmol, 1.0 equiv.) in a minimum of acetic acid. The mixture immediately became dark red and was stirred for 48 h at room temperature. The mixture was then plunged into diethyl ether (50 mL) and the flavylium salt precipitated. The resulting red powder was recovered by filtration and washed with diethyl ether to give **30** in pure form (594 mg, 0.79 mmol). Yield 85%. ^{1}H NMR (300 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 4.14 (s, 6 H, OC*H*$_3$), 4.19 (s, 6 H, OC*H*$_3$), 6.92 (d, $^4J_{6-8}$ = 1.8 Hz, 2 H, 6-H), 7.48 (d, $^4J_{8-6}$ = 1.8 Hz, 2 H, 8-H), 8.06 (t, $^3J_{4'-3'}$ = 8.1 Hz, 1 H, 4′-H), 8.46 (d, $^3J_{3-4}$ = 8.4 Hz, 2 H, 3-H), 8.71 (dd, $^3J_{3'-4'}$ = 8.1 Hz, $^4J_{3'-2'}$ = 1.8 Hz, 2 H, 3′-H), 9.21 (t, $^4J_{2'-3'}$ = 1.8 Hz, 1 H, 2′-H), 9.39 (d, $^3J_{4-3}$ = 8.5 Hz, 2 H, 4-H) ppm. ^{13}C NMR (75 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 58.7 (O*C*H$_3$), 59.1 (O*C*H$_3$), 95.1 (6-C-6), 102.1 (8-C-8), 114.1 (3-C-3), 121.5 (10-C-10), 129.7 (2′-C-2′ or 4′-C-4′), 132.2 (1′-C-1′), 132.9 (2′-C-2′ or 4′-C-4′), 135.9 (3′-C-3′), 152.3 (4-C-4), 160.8/161.7/170.4 (C-5, C-7 and C-9), 175.2 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 1645 (C=O), 855 (P–F) cm^{-1}. UV/Vis (MeOH/5% 1 N HCl): λ_{max} (ε) = 394 (18800), 468 (18000) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 228 (100) [M]$^{2+}$. HRMS: calcd. for $C_{28}H_{24}O_6$ [M]$^{2+}$: 228.0781; found: 228.0776.

2,2′-(*m*-Phenylene)-bis(5,7-dihydroxybenzopyrylium) Hexafluorophosphate (31): Compound **9e** (1.162 g, 7.04 mmol, 2.0 equiv.) and an excess of aqueous hexafluorophosphoric acid (50% in water) were added at room temperature to a solution of **27** (622 mg, 3.40 mmol, 1.0 equiv.) in a minimum of acetic acid. The mixture immediately became dark red and was stirred for 48 h at room temperature. The mixture was then plunged into diethyl ether (50 mL) and the flavylium salt precipitated. The resulting red powder was recovered by filtration and washed with diethyl ether to give **31** in pure form (2.139 g, 3.10 mmol). Yield 91%. ^{1}H NMR (300 MHz, CD_3CN/1% [D_1]TFA, 25 °C): δ = 6.87 (d, $^4J_{6-8}$ = 2.1 Hz, 2 H, 6-H), 7.23 (dd, $^4J_{8-6}$ = 1.8 Hz, $^5J_{8-4}$ = 0.6 Hz, 2 H, 8-H), 8.05 (t, $^3J_{4'-3'}$ = 8.1 Hz, 1 H, 4′-H), 8.32 (d, $^3J_{3-4}$ = 8.4 Hz, 2 H, 3-H), 8.69 (dd, $^3J_{3'-4'}$ = 8.1 Hz, $^4J_{3'-2'}$ = 1.8 Hz, 2 H, 3′-H), 9.13 (t, $^4J_{2'-3'}$ = 1.8 Hz, 1 H, 2′-H), 9.38 (dd, $^3J_{4-3}$ = 8.5 Hz, $^5J_{4-8}$ = 0.6 Hz, 2 H, 4-H) ppm. IR (KBr): $\tilde{\nu}$ = 3390 (O–H), 1645 (C=O), 855 (P–F) cm^{-1}. UV/Vis (MeOH/5% 1 N HCl): λ_{max} (ε) = 264 (9500), 298 (7300), 396 (10000), 476 (8800) nm (M^{-1}·cm^{-1}). MS (ESI, positive mode): *m*/*z* (%) = 399 (90) [M – H]$^+$, 200 (100) [M]$^{2+}$. HRMS: calcd. for $C_{24}H_{16}O_6$ [M^{2+}]: 200.0468; found: 200.0494.

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[1] a) T. Goto, T. Kondo, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 17–33; b) R. Brouillard, O. Dangles, in *The Flavonoids: Advances in Research since 1986*, Chapman & Hall, London, **1994**, pp. 565–588.

[2] a) C. F. Timberlake, P. Bridle, in *The Flavonoids*, Academic Press, New York, **1975**, pp. 214–266; b) G. Hrazdina, in *The Flavonoids: Advances in Research*, Chapman & Hall, London, **1982**, pp. 135–188; c) J. B. Harborne, R. J. Grayer, in *The Flavonoids: Advances in Research since 1980*, Chapman & Hall, London, **1988**, pp. 1–20; d) D. Strack, V. Wray, in *The Flavonoids: Advances in Research since 1986*, Chapman & Hall, London, **1994**, pp. 1–22; e) J. B. Harborne, C. A. Williams, *Nat. Prod. Rep.* **1998**, *15*, 631–652; f) J. B. Harborne, C. A. Williams, *Nat. Prod. Rep.* **2001**, *18*, 310–333; g) C. A. Williams, R. J. Grayer, *Nat. Prod. Rep.* **2004**, *21*, 539–573; h) O. M. Andersen, M. Jordheim, in *Flavonoids: Chemistry, Biochemistry and Applications*, CRC Press, Boca Raton, FL, USA **2006**, pp. 471–551.

[3] E. Gonzalez, A. Fougerousse, R. Brouillard, *Phytochemistry* **2001**, *58*, 1257–1262.

[4] a) P. Coggon, G. A. Moss, H. N. Graham, G. W. Sanderson, *J. Agric. Food Chem.* **1973**, *21*, 727–733; b) G. Mazza, E. Miniati, in *Anthocyanins in Fruits, Vegetables and Grains*, CRC Press, Boca Raton, FL, USA **1993**, pp. 225–248.

[5] a) G. A. Iacobucci, J. G. Sweeny, *Tetrahedron* **1983**, *39*, 3005–3038; b) O. Dangles, H. Elhajji, *Helv. Chim. Acta* **1994**, *77*, 1595–1610.

[6] a) P. Darmenton, M. Philippe, L'Oreal S. A. FR 2757383, **1996**; *Chem. Abstr.* **1998**, *129*, 140458n; b) G. Sauter, H.-J. Braun, R. Brouillard, A. Fougerousse, C. Roehri-Stoeckel, Wella S. A., WO 03/000214 A1, **2003**.

[7] P. Czerney, G. Graness, E. Birckner, F. Vollmer, W. Rettig, *J. Photochem. Photobiol. A* **1995**, *89*, 31–36.

[8] a) N. J. Cherepy, G. P. Smestad, M. Grätzel, J. Z. Zhang, *J. Phys. Chem.* **1997**, *101*, 9342–9351; b) M. Grätzel, *J. Chem. Educ.* **1998**, *75*, 752–756.

[9] A. Roque, C. Lodeiro, F. Pina, M. Maestri, R. Ballardini, V. Balzani, *Eur. J. Org. Chem.* **2002**, 2699–2709.

[10] A. C. Fernandes, C. C. Romao, C. P. Rosa, V. P. Vieira, A. Lopes, P. F. Silva, A. L. Maçanita, *Eur. J. Org. Chem.* **2004**, 4877–4883.

[11] a) M. N. Clifford, *J. Sci. Food Agric.* **2000**, *80*, 1063–1072; b) J. M. Kong, L. S. Chia, N. K. Goh, T. F. Chia, R. Brouillard, *Phytochemistry* **2003**, *64*, 923–933; c) D. X. Hou, *Curr. Mol. Med.* **2003**, *3*, 149–159; d) M. A. Lila, in *Plant Pigments and their Manipulation*, CRC Press, Boca Raton, FL, USA **2004**, pp. 248–274.

[12] a) R. Brouillard, J. E. Dubois, *J. Am. Chem. Soc.* **1977**, *99*, 1359–1364; b) R. Brouillard, B. Delaporte, *J. Am. Chem. Soc.* **1977**, *99*, 8461–8468; c) R. Brouillard, in *Anthocyanins as Food Colors*, Academic Press, New York, **1982**, pp. 1–40; d) R. Brouillard, *Phytochemistry* **1983**, *22*, 1311–1323.
[13] O. Dangles, G. Fargeix, C. Dufour, *J. Chem. Soc., Perkin Trans. 2* **2000**, 1653–1663.
[14] a) D. Pratt, R. Robinson, *J. Chem. Soc.* **1922**, 1577–1585; b) D. D. Pratt, R. Robinson, *J. Chem. Soc.* **1923**, 745–758; c) D. Pratt, R. Robinson, *J. Chem. Soc.* **1924**, 188–199; d) D. D. Pratt, R. Robinson, *J. Chem. Soc.* **1924**, 199–207; e) D. D. Pratt, R. Robinson, *J. Chem. Soc.* **1925**, 1128–1138.
[15] N. Kuhnert, M. N. Clifford, A.-G. Radenac, *Tetrahedron Lett.* **2001**, *42*, 9261–9263.
[16] T. Mas, *Synthesis* **2003**, *12*, 1878–1880.
[17] a) J. G. Sweeny, G. A. Iacobucci, *Tetrahedron* **1977**, *33*, 2923–2926; b) J. G. Sweeny, G. A. Iacobucci, *Tetrahedron* **1977**, *33*, 2927–2932.
[18] a) A. W. Johnson, R. R. Melhuish, *J. Chem. Soc.* **1947**, 346–349; b) J. W. Gramshaw, A. W. Johnson, T. J. King, *J. Chem. Soc.* **1958**, 4040–4049.
[19] a) E. V. Vedejs, J. R. Pribish, *J. Org. Chem.* **1988**, *53*, 1593–1599; b) K. Matsuda, N. Nakamura, K. Takahashi, K. Inoue, N. Koga, H. Iwamura, *J. Am. Chem. Soc.* **1995**, *117*, 5550–5560; c) L. De Luca, G. Giacomelli, A. Porcheddu, *J. Org. Chem.* **2001**, *66*, 7907–7907; d) Y. Maeda, N. Kakiushi, S. Matsumura, T. Nishimura, S. Uemura, *Tetrahedron Lett.* **2001**, *42*, 8877–8879; e) Y. Maeda, N. Kakiushi, S. Matsumura, T. Nishimura, T. Kawamura, S. Uemura, *J. Org. Chem.* **2002**, *67*, 6718–6724; f) L. Yu, M. L. Trudell, *Tetrahedron Lett.* **2003**, *44*, 2553–2555; g) Y. Maeda, Y. Washitake, T. Nishimura, K. Iwai, T. Yamauchi, S. Uemura, *Tetrahedron* **2004**, *60*, 9031–9036; h) M. Hunsen, *Tetrahedron Lett.* **2005**, *46*, 1651–1653.
[20] J. D. More, N. S. Finney, *Org. Lett.* **2002**, *4*, 3001–3003.
[21] a) A. R. Katritzky, P. Czerney, J. R. Level, W. Du, *Eur. J. Org. Chem.* **2001**, 4451–4456; b) C. Fichtner, G. Remennikov, H. Mayr, *Eur. J. Org. Chem.* **2001**, 4451–4456.
[22] K. M. Doxsee, M. Feigel, D. S. Kent, J. W. Canary, C. B. Knobler, D. Cram, *J. Am. Chem. Soc.* **1987**, *109*, 3098–3107.
[23] G. A. Reynolds, J. A. Van Allan, *J. Heterocycl. Chem.* **1969**, *6*, 623–626.

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