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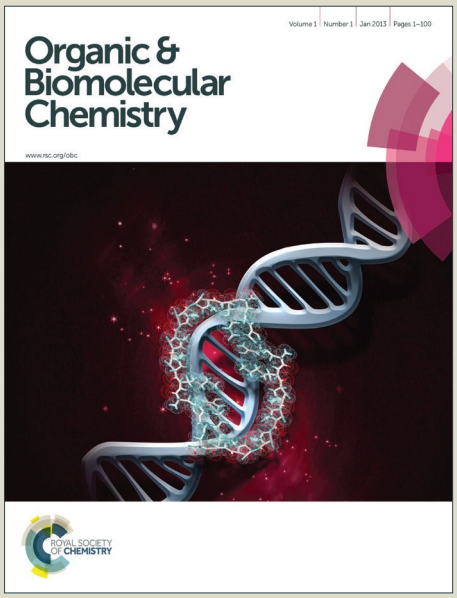

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PAPER

Convenient approach to an advanced intermediate toward the naturally occurring, bioactive 6-substituted 5-hydroxy-4-aryl-1*H*-quinolin-2-ones

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The 5-hydroxy-4-aryl-3,4-dihydro-1*H*-quinolin-2-ones are a small family of natural products, isolated from fungal strains of *Penicillium* and *Aspergillus*. Most of its members, which are insecticides and antihelmintics, carry an isoprenoid C-6 side chain. The synthesis of a 6-propenyl-substituted advanced intermediate for the total synthesis of these natural products is disclosed. This was achieved through the stereoselective construction of a β,β-diarylacrylate derivative from 6-nitro salicylaldehyde, using a Wittig olefination and a Heck-Matsuda arylation, followed by a selective Fe^0-mediated reductive cyclization. Installation of the 6-propenyl side chain was performed by 5-*O*-allylation of the heterocycle, followed by Claisen rearrangement and conjugative migration of the allyl double bond, as key steps. The Grubbs II-catalyzed olefin cross metathesis of the 6-allyl moiety with 2-methylbut-2-ene to afford a precursor of peniprequinolone, is also reported.

Introduction

The quinoline core is a privileged heterocyclic structure found in many natural products and bioactive compounds.[1] Interestingly, filamentous fungi have been the source of relatively few quinoline derivatives;[2] however, certain strains of *Penicillium* and *Aspergillus* produce 5-hydroxy-4-aryl-3,4-dihydro-1*H*-quinolin-2-ones, including those bearing a C-6 alkyl/alkenyl side chain, which form a unique new family of natural products.

Thus, the yaequinolones B-F, J1 and J2 (**1a-1g**, Figure 1)[3a] were isolated from *Penicillium sp.* FKI-2140, along with nine related compounds, including peniprequinolone (**1h**) and the penigequinolones A and B (**1i** and **1j**).[3b-g] The cytotoxic and antifungic[3c] **1h**, previously reported from *P. simplicissimum* and *P. namyslowskii*,[3f] was also found to be a nematicidal antibiotic against the root-lesion nematode *Pratylenchus penetrans*.[3d]

The diastereomeric **1i** and **1j**, pollen growth inhibitors and nematicidal against *Pratylenchus penetrans*,[3d] were also isolated from *Penicillium* sp. NO. 410 and *P. scabrosum*.[3g] On the other hand, the related aspoquinolones A-D (**1k-n**) are cytotoxic and antiproliferative on some cancer cell lines.[2a]

This research also afforded the yaequinolones A1 and A2 (**2a**,**b**) and the quinolinones A and B (**2c**,**d**).[3c,d, 4a] Heterocycles **2a** and **2b** have been previously reported from a *P. janczewskii* strain of marine origin,[3b,4b,c] whereas **2c** and **2d** were originally obtained from *P. simplicissimum* and found to behave as insecticidal antibiotics,[3c] being toxic against various cancer cell lines.[3b]

In addition, two strains of *Aspergillus* were the source of the aflaquinolones A-D (**4a-d**) and the aflaquinolones E-G, which lack the 4'-OMe group.[5a] Some aflaquinolones have also been obtained from the endophyte *A. nidulans* MA-143, together with **1h** and the aniduquinolones A-C. The latter, are analogous to yaequinolones C and F (**1b** and **1e**),[5b] lacking the 4'-OMe group.

More recently, the unusual 22-*O*-(*N*-Methyl-L-valynyl) ester of aflaquinolone B (**4e**) and its epimer **4f** were isolated from the mycelia of *Aspergillus sp.* XS-20090B15, together with the aflaquinolones A and D (or a diastereomer of it).[5c] Compound **4f** exhibited remarkable anti-Respiratory Syncytial Virus activity.

Genomic and biosynthetic studies suggested that this family may derive from anthranilic acid and phenylalanine or tyrosine, through the intermediacy of diketobenzodiazepines,[2a,3d] such as **3a**,**b**, which have been isolated concomitantly.[4c] The latter undergo ring opening and re-cyclization to afford the basic 3,4-dihydro-1*H*-quinolin-2-one core, through the 4-phenylquinoline viridicatin as intermediate.[5d-g] Next, *O*-methylation of the −OH moieties, installation of the C-4 and C-5 −OH groups, attachment the C-6 side chains and further functionalization, would explain their diversity.[5h] The natural products are optically active, displaying a 3*S*,4*S* configuration.[3b,5a]

Ectoparasiticidal and antiproliferative preparations containing some of these heterocycles have been patented.[6a-e] However, synthetic activity in this area has been very scarce.[6f,g]

In pursuit of a common general synthetic approach toward the members of this family of natural products, herein we report a concise route to a potential common key intermediate for the 6-substituted 5-hydroxy-4-aryl-3,4-dihydro-1*H*-quinolin-2-ones, bearing the fundamental structural motif **1**. In addition, the synthesis of a peniprequinolone (**1h**) derivative, lacking the 3,4-glycol monomethyl ether feature, is disclosed.

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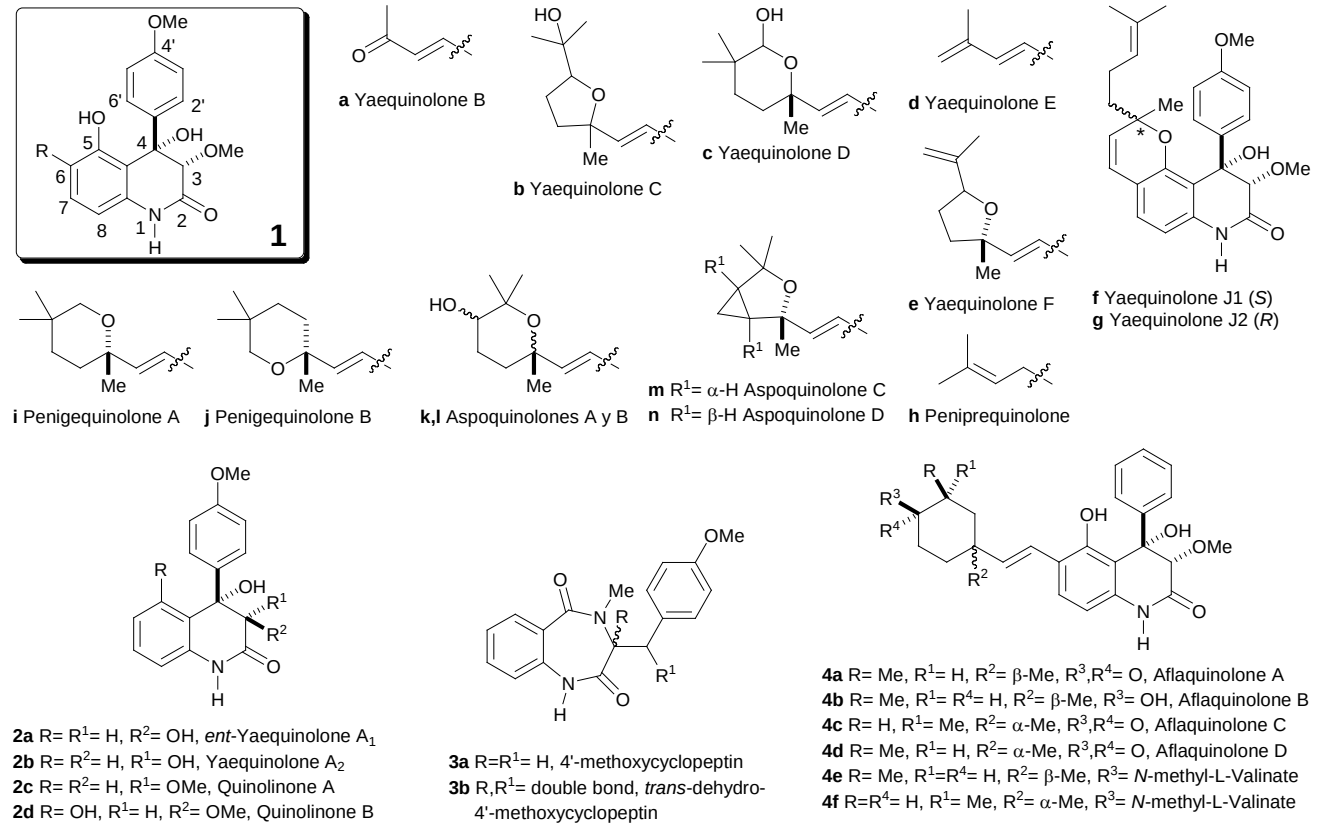

Figure 1. Chemical structures of representative naturally-occurring 6-substituted 5-hydroxy-4-aryl-1*H*-quinolin-2-ones and their congeners. Except for **2a** and **2d**, it is assumed that the heterocycles bear a *cis*-3,4-dioxygenated pattern and exhibit the same 3*S*,4*S* configuration.

Results and discussion

There are five main synthetic approaches toward 4-alkyl/aryl-substituted 1*H*-quinolin-2-ones (Figure 2), which relate to the single bond involved in closing the heterocyclic ring.[7a] These comprise types (a),[7b-g] (b),[8a] (c),[8b] (d),[8c,d] and (e).[8e,f] However, strategies of types (b) and (c) are unsuitable for the synthesis of 5-hydroxy/alkoxy substituted heterocycles, mainly due to their narrow scope and difficult availability of the starting materials, whereas type (a) demands starting from 1,2,4-substituted benzenoids,[9a-g] to block the preferred alternative cyclization mode, en route to 7-hydroxy/alkoxy derivatives.[9h,i]

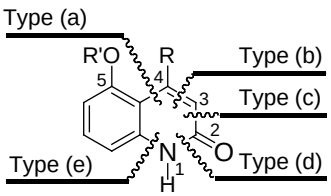

Figure 2. Most relevant general strategies for the synthesis of 4-substituted 1*H*-quinolin-2-ones.

Hence, our approach to the natural products (**5**, Scheme 1) relied on a retrosynthetic analysis involving strategies of types (d) and (e). The C-6 substituent of the target was disconnected at the double bond level, considering that the side chains could be installed by olefin cross-metathesis of a 6-vinyl quinolin-2-one. It was also inferred that the *cis*-3,4-diol monoether system could result from dihydroxylation of a $\Delta^{3,4}$ precursor,[10] and selective alkylation of the less hindered alcohol, uncovering **6** as the suitable common advanced key intermediate sought.

Generally, β-substituted styrenes are less costly and easier to prepare than their styrene counterparts, also being more stable and less prone to undergo homodimerization or spontaneous polymerization.[11a-d] Therefore, it was considered installing a 6-propenyl side chain (**6a**), taking advantage of the 5-OH group.[11e]

Conjecturing that the heterocyclic ring could be accessed by lactamization of a β,β-diarylacrylate with a suitably placed amine attached to the aromatic ring [type (d)],[12a,b] or by *N*-arylation [type (e)],[8e,f,12c,d] unveiled **7** as a potential precursor of **6a** (*Route a*). In turn, it was conceived that β,β-diarylacrylate **7** could be obtained from a cinnamic acid derivative (**8**).[13a,b]

On the other side, it was supposed that compound **9**, which could also be made available from cinnamate **8**, might also be considered a suitable precursor of **6a** (*Route b*); however, previous findings on the reluctance of certain 1*H*-quinolin-2-ones to undergo the Heck reaction on C-4[12c] discouraged exploration of this alternate route as the first choice. Further disconnection of **8** uncovered a precursor aldehyde moiety[14] and unveiled a phenol, suggesting aldehydes **10**, accessible from commercially available phenols **11**, as suitable starting materials.

The type (e) approach was explored first. Therefore, salicylaldehyde (**12**) was submitted to a Williamson etherification with benzyl chloride in absolute EtOH, employing K_2CO_3 as

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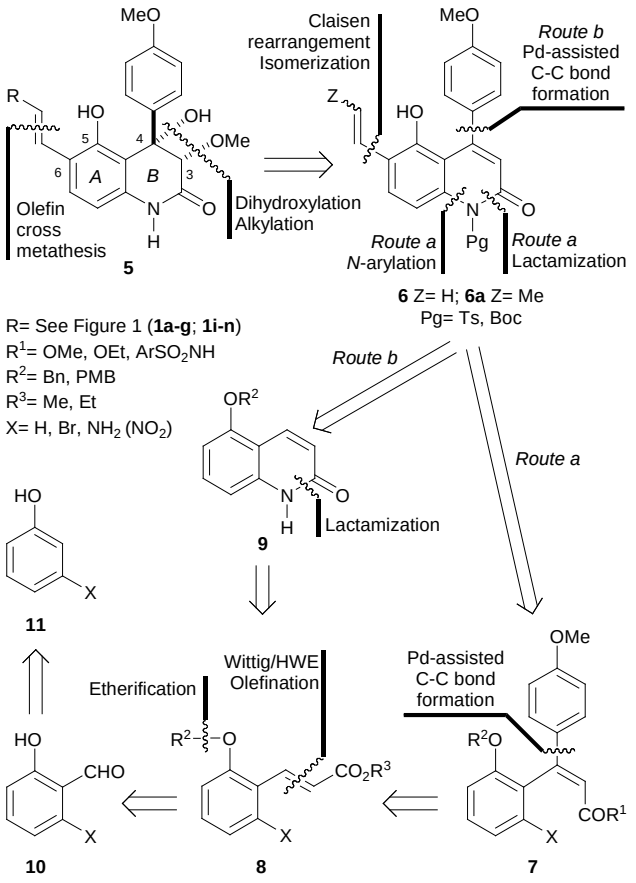
base, which afforded 99% of benzyl ether **13** (Scheme 2). In turn, the aldehyde **13** was exposed to a Hörner-Wadsworth-Emmons (HWE) reaction with $(MeO)_2P(O)CH_2CO_2Me$, furnishing 55% of cinnamate **14**. However, better results were obtained when **13** was subjected to a Wittig olefination with carbethoxymethylene triphenyl phosphorane, which gave 88% of cinnamate **14a**, as a 4:1 mixture of geometric (*E:Z*) isomers, according to the ^{1}H NMR integration

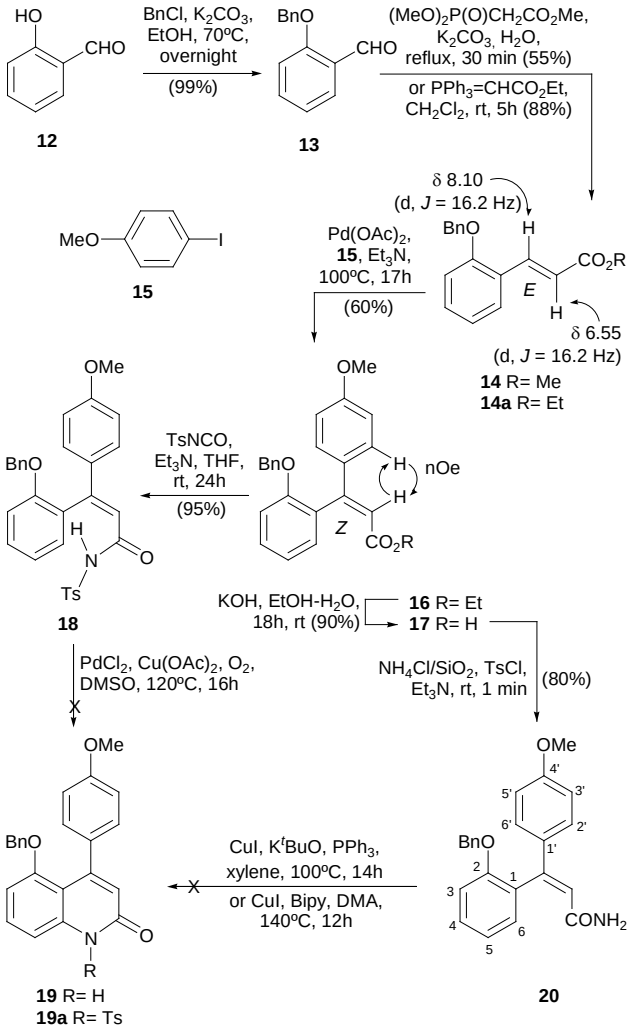


Scheme 1. General retrosynthetic analysis of the natural products **5**. Target heterocycles **6** and **6a** as advanced key intermediates.

Installation of the 4-methoxyphenyl moiety was accomplished by means of a Heck reaction[15] of **14a** with 4-iodoanisole (**15**) in refluxing Et_3N, under $Pd(OAc)_2$ catalysis, which provided the β,β-diphenylacrylate **16** as a 86:14 (^{1}H NMR integration) mixture of geometric isomers, in combined 60% yield. The *Z*-configuration of the main isomer of **16** was ascertained with the aid of nOe experiments, which revealed mutual signal enhancement between the vinylic proton next to the carboxylate ester and the aromatic protons located *meta* to the 4'-methoxy group (2'-H and 6'-H).

In order to insert the required nitrogen atom and properly activate the β,β-diphenylethylene derivative toward cyclization, the ester **16** was saponified (90%) and the resulting carboxylic acid **17** was reacted with tosyl isocyanate in the presence of Et_3N, furnishing the tosylimide derivative **18** (95%).[8e,16] Unfortunately, however, all attempts to cyclize **18** under Pd catalysis, with $Cu(OAc)_2$ as co-catalyst and aerobic conditions,[8e] met with failure, resulting in complete degradation of the tosylimide.

It seems likely that the lability of **18** toward the cyclization conditions that would lead to **19a** may be related to its structure, because exposure of the β,β-diphenylacrylic acid tosylimide to the same cyclization conditions afforded 70% of the expected 4-phenyl-1*H*-quinolin-2-one, fully agreeing with the literature.



Scheme 2. Attempted synthesis of intermediates **19** from salicylaldehyde (**12**).

In view of this outcome, the copper-catalyzed cyclization of amide **20** was explored as an alternative. Amidation of ester **16** with ammonia met with failure;[17a] therefore, the acid **17** was amidated with $NH_4Cl/TsCl$ supported on silica gel, under Et_3N promotion, affording 80% of **20**.[17b] However, exposure of the amide to various copper-mediated C-H activation protocols,[8f,18] resulted in complete recovery of the starting amide **20**.

Therefore, the attention changed to a type (d) strategy, which involves forming the Ar-N bond prior to cyclization or entails using starting materials which already contain the heteroatom.[8d,e]

3-Nitrophenol (**21**) was selected as the new starting material, considering that the nitro moiety could mask the required amino group during the initial stages, and that it could be engaged in a one-pot reductive cyclization (**7**→**6**),[19] under conditions that could also result in the removal of the protecting benzyl ether.

With these ideas in mind, compound **21** was submitted to a

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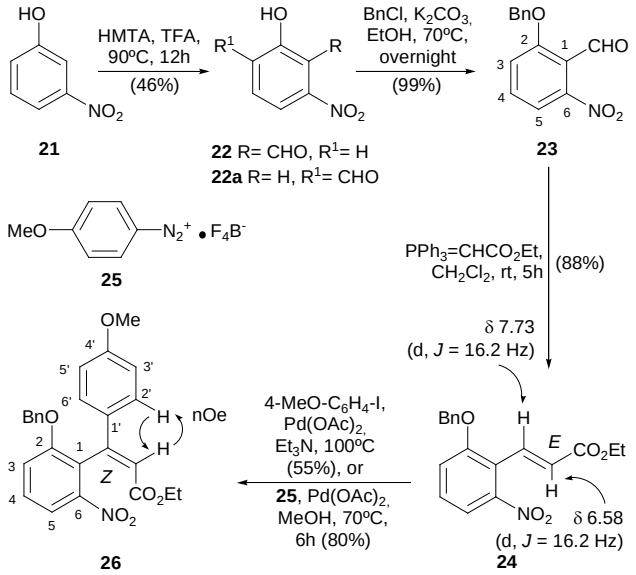
Duff formylation with hexamethylenetetraamine (HMTA) in F_3CCO_2H at 110 ºC during 12h, affording the expected aldehyde **22** as an 85:15 mixture with its isomer **22a**, in combined 54% yield. Notably, previous syntheses of **22** took place with rather lower yields.[20] In turn, phenol **22** was subjected to a Williamson etherification with BnCl in refluxing EtOH, employing K_2CO_3 as base, to give **23** in almost quantitative yield (Scheme 3).



Scheme 3. Synthesis of the intermediate **26** from 3-nitrophenol (**21**).

Introduction of the two-carbon moiety required to build the 1*H*-quinolin-2-one feature was performed by means of a Wittig reaction[21] with ethyl (triphenyl-λ5-phosphanylidene)-acetate, affording 88% of cinnamate **24**.[22] The coupling constants of the vinylic hydrogens (J = 16.2 Hz) unequivocally established the stereochemistry of **24** as *E*.

When the Heck conditions leading to **16** were applied to **24**, the corresponding β,β-diarylacrylate was obtained in 55% yield, confirming previous observations where the reaction was found to loss efficiency when attempting to introduce electron-rich aryl groups.[23] This suggested the need of an alternate strategy.

Despite alternative Heck protocols were available,[24a] the Heck-Matsuda reaction seemed a suitable transformation to fulfil our expectations, since it is apparently devoid of this drawback.[24b-e] Recent examples from the laboratory of Correia were encouraging; furthermore, the *p*-anisidine reagent required to introduce the 4-methoxyphenyl moiety is readily available, and is several times less expensive than *p*-iodoanisol.

Thus, exposure of a refluxing methanolic mixture of cinnamate **24** and the diazonium tetrafluoroborate **25**, derived from *p*-anisidine[24d] to $Pd(OAc)_2$ catalysis, furnished 80% of the β,β-diarylacrylate **26**.

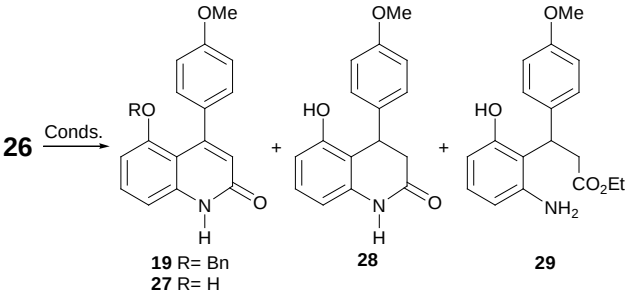
An nOe experiment, revealing mutual signal enhancement between the vinylic proton of the acrylate motif (δ 6.45, singlet), and the neighbouring aromatic protons of the 4-methoxyaryl moiety (δ 7.33, d, J = 8.8 Hz), established the *Z* geometry of **26**. This outcome of the Heck-Matsuda reaction, analogous to that of the Heck arylation,[25] has been explained mechanistically.[26]

Next, the one pot benzyl ether group hydrogenolysis with concomitant reduction of the nitro moiety to the corresponding amino-derivative **29** and further cyclization toward **27** was attempted on **26**. However, when the Pd-mediated catalytic hydrogenation was attempted under a variety of conditions,[27] it exhibited several unforeseen problems, which ranged from partial reduction of the nitro group to concomitant hydrogenation of the acrylate double bond, despite being sterically hindered.

Thus, the hydrogenation with 10% Pd/C in MeOH at room temperature produced equal amounts of **19** and its debenzylated analog **27** in combined 30% yield (Table 1, entry 1), whereas the reaction proceeded more sluggishly in EtOH (entry 2).

However, addition of Et_3N to the ethanolic medium provoked the hydrogenation of the nitro moiety and the subsequent cyclization, but also the debenzylation and hydrogenation of the $\Delta^{3,4}$ double bond, furnishing 61% of **28** (entry 3). On the other side, when the reaction was run in refluxing toluene, a 30:70 mixture of cyclized (**19**) and debenzylated and uncyclized products (**29**) were obtained in 25% combined yield (entry 4).

Table 1. Optimization of the reductive cyclization of **26**.



Entry	Reducing system	Solvent	Time (h)	Temp. (ºC)	Yield (%)	**19**/**27**/**28**/**29**
1	H_2, 10%Pd/C	MeOH	2	rt	30	50/50/0/0
2	H_2, 10%Pd/C	EtOH	3	rt	15	-
3	H_2, 10%Pd/C	EtOH[a]	3	rt	61	0/0/100/0
4	H_2, 10%Pd/C	PhMe	2	110	25	30/0/0/70
5	$SnCl_2$	EtOH	17	rt	40	37/0/0/63
6	$SnCl_2$	EtOH	17	reflux	35	0/0/0/100
7	Fe^0, $CaCl_2$	EtOH	0.5	reflux	decomp.	-
8	Fe^0 (8 equiv.)	AcOH	14	110	74	100/0/0/0

[a] Et_3N was added.

Considering the above results, a stepwise strategy was approached, prioritizing the sequential nitro group reduction-cyclization toward **19**. Unfortunately, $SnCl_2$ in EtOH[28] also gave 40% of a 37:63 mixture of **19** and **29**, when the reaction was performed at room temperature (entry 5) and only **29** was isolated (35%) when the transformation was carried out under reflux (entry 6). The formation of **29** under these different conditions, ruled out employing $SnCl_2$ as the reducing agent for this step.

On the other hand, the use of the Fe/$CaCl_2$ system in refluxing EtOH[29a] unexpectedly furnished solely degradation products (entry 7). However, to our delight, exposure of **26** to elemental iron powder in glacial AcOH at 110 ºC resulted in the selective reduction of the nitro moiety to **30** and subsequent lactamization, cleanly affording 74% of **19**, as the sole product (entry 8).[29b-d]

With the core 1*H*-quinolin-2-one **19** in hands (Scheme 4), the

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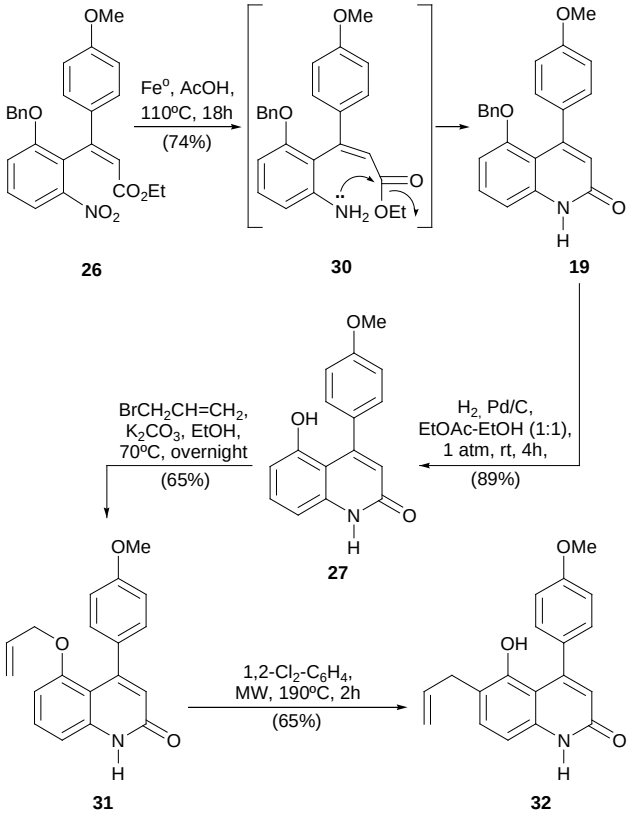
next steps were devoted to the installation of the C-6 β-propenyl side chain. Therefore, proper conditions were sought for the selective debenzylation of **19** and *O*-allylation of **27**.[30a]



Scheme 4. Construction of the 2-quinolonic ring and synthesis of **32**.

The results of Table 1 seemed to confirm literature observations, that characterized the selective debenzylation of aryl benzyl ethers in the presence of C-C double bonds as 'difficult'.[30b] However, in the case of **19**, after several trial and error attempts under different conditions, it was learned that 10% Pd/C in a cold 1:1 (v/v) EtOH-EtOAc solvent mixture under an atmospheric pressure of hydrogen, was an effective system for selectively cleaving the benzyl ether without affecting the $\Delta^{3,4}$ double bond.[30c] Under these conditions, 89% of **27** was reliably obtained after 4 h.

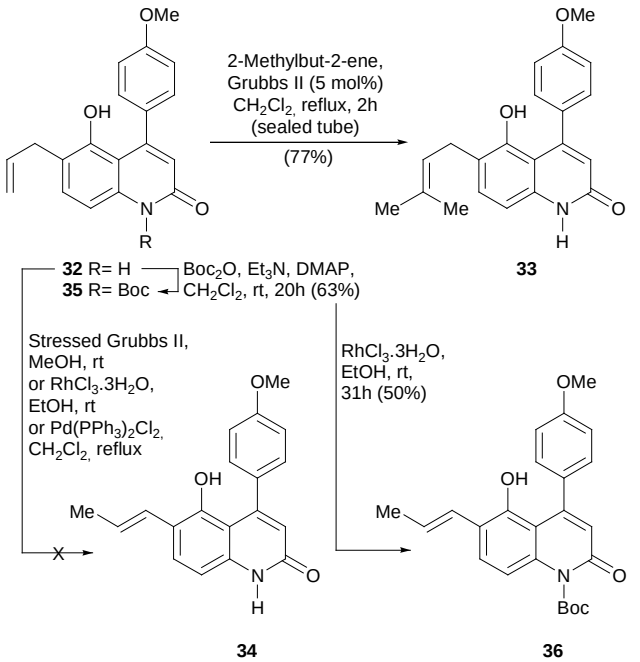
Next, the selective *O*-allylation of the phenol moiety of **27** was undertaken. Literature precedents suggested that the ambident anion at N-1–C-2 is a potentially competitive reaction site [30a,31] and that, in principle the *O*-allylation should predominate.[30a]

In fact, when compound **27** was subjected to a conventional Williamson allylation, with K_2CO_3 in EtOH at 60 ºC, 65% of the expected *O*-allyl derivative **31** was obtained and, to our delight, no other alkylation products were observed. Submission of ether **31** to the projected Claisen rearrangement took place under microwaves irradiation in 1,2-dichlorobenzene, affording 75% of the desired 6-allyl derivative **32**.

Interestingly, the 6-allyl 1*H*-quinolin-2-ones have elicited great synthetic and pharmaceutical interest, having also been used as intermediates toward drugs for treating cardiac diseases, protecting against the UV rays, scavenging active oxygen species, and inhibiting enzymes as well as lipid peroxidation.[32]

The acquisition of compound **32** enabled the proposed synthesis of **33**, a peniprequinolone (**1h**) analog, lacking its 3,4-glycol monoether feature (Scheme 5). This target was conveniently conquered in 77% yield by the olefin cross metathesis of **32** with 2-methylbut-2-ene, under Grubbs II catalyst promotion in refluxing CH_2Cl_2.[33]

However, the achievement of the second and main objective resulted more difficult. Unexpectedly, the isomerization of the terminal double bond of **32** toward **34**, proved to be challenging under a wide range of catalysts and conditions.



Scheme 5. Syntheses of the target compounds **33** and **36**.

The attempts employing stressed Grubbs-II catalyst (MeOH, 60 ºC, 3 h), $RhCl_3.3H_2O$ (EtOH, rt, 7 h), $Pd(PPh_3)_2Cl_2$ ($CHCl_3$, 40 ºC, 4 h) and $[(C_6H_5)_3P]_3Ru(CO)(Cl)H$ (PhMe, 90 ºC, 18 h) met with failure, and the unexpected complete degradation of the starting material with concomitant production of complex mixtures of unidentifiable products, was invariably observed. This was somehow reminiscent of the outcome of a similar attempt at allyl group isomerization during the synthesis of an intermediate for fumimycin.[34]

We speculated that under the isomerization conditions, either the free phenol or the amide of **34** (or even its less contributing phenolic lactim moiety), could lead to structural destabilization of the product, by acid-base or metal-promoted tautomerization to quinone methides, which in turn could undergo degradation.

It has been proposed that quinone methides are formed as intermediates during Pd-catalyzed reactions of 2-vinyl phenols and other conditions involving easily protonable or otherwise reactive benzylic positions and properly placed phenolic groups.[35] These are highly reactive species, capable to undergo different reactions, among them polymerization. Further after observing that **34** was fully recovered after exposure to K^{t}BuO in THF for 12 h at room temperature, it was conceived that perhaps

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the organometallic intermediates and not the isomerized product **34** may be those that trigger the degradation of the heterocycle.

In light of this situation, it was decided to block the possible involvement of the lactam moiety of **32** in the tautomerization reaction, through its protection as the *N*-Boc derivative **35**.[36] This was accomplished in 63% yield with Boc_2O and Et_3N in CH_2Cl_2. Surprisingly, however, the isomerization remained challenging, as compound **35** was also reluctant to cleanly afford the isomerized product. Its exposure to $[(C_6H_5)_3P]_3Ru(CO)(Cl)H$ in toluene for 17 h at 70 ºC did not afford any isomerized product, whereas heating at 90 ºC for 24 h furnished the expected heterocycle **36**, albeit contaminated with PPh_3O, which turned hard to be removed chromatographically. On the other hand, the use of $Pd(PPh_3)_2Cl_2$ ($CHCl_3$, rt, 3 h) gave a mixture of unidentifiable products.

Finally, our expectations were met when exposure of **35** to $RhCl_3.3H_2O$ in absolute EtOH resulted in the smooth isomerization of the allyl moiety, furnishing 50% of the sought product **36**, when the reaction was left 31 h at room temperature. Analysis of its ^1H NMR spectrum, which exhibited signals at δ 6.19 (dd, J = 6.3 and 15.7 Hz, CH_3-C*H*=CH-Ar) and δ 6.36 (d, J = 15.7 Hz, CH_3-CH=C*H*-Ar), unequivocally confirmed the *E*-stereochemistry of the β-methylstyrene unit in **36**.

Conclusions

We have developed a convenient approach towards an advanced common key intermediate for the synthesis of relevant members of the 6-substituted 5-hydroxy-4-aryl-3,4-dihydro-1*H*-quinolin-2-one family of natural products. The synthetic strategy entailed building and cyclization of a substituted β,β-diarylacrylate derivative to construct the heterocyclic core. The sequence was completed by an optimized selective catalytic debenzylation and installation of the anchoring β-propenyl moiety, by an *O*-allylation, followed by Claisen rearrangement and conjugative double bond migration of the resulting 6-allyl-1*H*-quinolin-2-one.

The synthesis took place in nine steps and proceeded in 6.1% overall yield, from the known 2-hydroxy-6-nitrobenzaldehyde, in turn available in one step from commercial 3-nitrophenol.

Further, an analog of peniprequinolone, lacking its 3,4-glycol monomethyl ether feature, was also synthesized by means of a Grubbs II-catalyzed cross metathesis of the 6-allyl-1*H*-quinolin-2-one intermediate with 2-methylbut-2-ene.

Studies are under way in order to establish conditions for the installation of the characteristic C-3–C-4 monoprotected *cis*-diol feature. The results will be communicated in due time.

Experimental section

General information

All the reactions were carried out under dry Nitrogen or Argon atmospheres, employing oven-dried glassware. Anhydrous THF and anhydrous CH_2Cl_2 were obtained from an M. Braun solvent purification and dispenser system. Absolute MeOH and EtOH were accessed by refluxing the solvents over clean Mg/I_2 and distilling from the resulting magnesium alkoxides; anhydrous 1,2-dichlorobenzene was prepared by a 4 h reflux of the solvent over P_2O_5 followed by atmospheric pressure distillation. All other reagents were used as received.

The flash column chromatographies were run with Merck's silica gel 60 H, eluting with hexane/EtOAc mixtures, under positive pressure and employing gradient of solvent polarity techniques.

All new compounds gave single spots on TLC plates (silica gel 60 GF_{254}) run in different hexane/EtOAc and EtOAc/EtOH solvent systems. The chromatographic spots were detected by exposure to 254 nm UV light, followed by spraying with ethanolic *p*-anisaldehyde/sulfuric acid reagent, 1% methanolic $FeCl_3$, ninhydrin or Dragendorff reagent (Munier and Macheboeuf modification),[37] and final careful heating of the plates for improving selectivity.

Apparatus

The melting points were measured on an Ernst Leitz Wetzlar model 350 hot-stage microscope and are reported uncorrected. The IR spectra were recorded with a Shimadzu Prestige 21 spectrophotometer, as thin films held between NaCl cells, as solid dispersions in KBr disks, or with a Pike ATR accessory.

The ^1H NMR spectra were acquired at 300.13 MHz in $CDCl_3$, except when noted otherwise, on a Bruker Avance spectrometer. Chemical shifts are reported in parts per million on the δ scale and J-values are given in Hertz. The peak of the residual protonated solvent ($CHCl_3$ in $CDCl_3$, δ 7.26) was used as the internal standard. The ^{13}C NMR spectra were recorded at 75.48 MHz on a Bruker Avance spectrometer. The solvent peak ($CDCl_3$, δ 77.0) was used as the internal standard. DEPT 135 and DEPT 90 experiments aided the interpretation and assignment of the fully decoupled ^{13}C NMR spectra. In special cases, 2D-NMR experiments (COSY, HMBC and HMQC) were also employed. Pairs of signals marked with an asterisk (*) indicate that their assignments may be exchanged.

The high resolution mass spectra were obtained with a Bruker MicroTOF-Q II instrument (Bruker Daltonics, Billerica, MA). Detection of the ions was performed in electrospray ionization, positive ion mode. The GC-MS experiments were carried out with a Shimadzu QP2010 *plus* instrument. The runs were performed in split injection mode (ratio: 50), column SPB-1 (30 m × 0.25 mm × 0.25 μm); oven temperature program $T_{Init.}$: 50 ºC (3 min.); T_{End}: 300 ºC, at 25 ºC/min; He flow: 1.0 mL/min. Mass spectra were obtained under the following conditions: $T_{Interface}$: 300 ºC; $T_{Ion\ source}$: 230 ºC; Solvent cut time: 3 min; Ionization = 70 eV; range: 60-600 Da. The microwave-assisted reactions were performed in a CEM Discover microwave oven.

2-Hydroxy-6-nitrobenzaldehyde (22)

A solution of 3-nitrophenol (**21**, 1000 mg, 7.20 mmol) in F_3CCO_2H (8 mL), was treated with HMTA (1200 mg, 8.59 mmol) and the mixture was heated at 90 ºC for 12 h. The reaction was poured over ice-water (25 mL), the resultant mixture was stirred for 15 min and then extracted with EtOAc (3 × 40 mL). The organic layers were washed with brine (20 mL), dried under Na_2SO_4 and concentrated in vacuo. Chromatography of the oily residue afforded **22** (560 mg, 46%), as a yellow solid, m.p.: 52-54 ºC (Lit.: 53-54 ºC).[20a] IR (KBr, ν): 3300, 2955, 2922, 2851, 1693, 1645, 1531, 1454, 1352 and 1284 cm^{-1}. ^1H NMR (δ): 7.30 (d, 1H, J = 8.0, H-3), 7.56 (d, 1H, J = 8.0, H-5), 7.63 (t, 1H, J = 8.0, H-4), 10.33 (s, 1H, C*H*O) and 12.11 (s, 1H, O*H*). ^{13}C NMR (δ):

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112.4 (C-1), 116.1 (C-5), 124.2 (C-3), 135.9 (C-4), 151.2 (C-6), 163.3 (C-2) and 193.9 (*C*HO). EI-MS (*m/z*, rel. int., %): 167 (M^+, 7), 149 (39), 137 (61), 120 (25), 119 (25), 109 (19), 107 (13), 92 (59), 91 (32), 93 (11), 81 (100) and 63 (85).

2-Benzyloxy-6-nitrobenzaldehyde (23)

K_2CO_3 (560 mg, 4.00 mmol) was added to a solution of nitrosalicylaldehyde **22** (223 mg, 1.334 mmol) in EtOH (3 mL). The mixture was stirred for 10 minutes at room temperature, when benzyl chloride (338 mg, 2.67 mmol) was added dropwise and the mixture was stirred overnight at 70 °C. After confirming the complete consumption of the starting material, the solvent was evaporated under reduced pressure and the residue was diluted with brine (10 mL) and 1M NaOH (10 mL). The product was extracted with EtOAc (3 × 20 mL); the combined organic extracts were washed with water (10 mL), dried over Na_2SO_4, concentrated and filtered through a short path of silica gel to yield the benzyl ether derivative **23** (342 mg, 99%), as a yellowish oil.[38] IR (film, ν): 3734, 3250, 1646, 1626, 1578, 1368, 1340, 1283, 1153, 1081, 1010, 842 and 669 cm^{-1}. ^1H NMR (δ): 5.22 (s, 2H, OC*H*$_2$Ar), 7.29 (d, 1H, *J* = 8.1, H-3), 7.36-7.41 (m, 5H, ArH of Benzyl), 7.45 (d, 1H, *J* = 8.1, H-5), 7.56 (t, 1H, *J* = 8.1, H-4) and 10.40 (s, 1H, C*H*O). ^{13}C NMR (δ): 71.6 (O*C*H$_2$Ar), 115.9 (C-5), 117.6 (C-3), 121.2 (C-1), 127.2 (C-1' and C-6'), 128.6 (C-4'), 128.9 (C-3' and C-5'), 133.4 (C-4), 135.0 (C-1'), 148.7 (C-3), 158.8 (C-2) and 187.6 (*C*HO).

Ethyl *E*-3-(2'-benzyloxy-6'-nitrophenyl)acrylate (*E*-24)

A mixture of aldehyde **23** (265 mg, 1.03 mmol) and ethyl (triphenyl-λ5-phosphanylidene)-acetate (1180 mg, 2.06 mmol) in dichloromethane (3 mL) was stirred at room temperature for 5 h. Once demonstrated the complete consumption of the starting material by TLC, the solvent was removed under reduced pressure and the residue was chromatographed, affording ***E*-24** (297 mg, 88%), as a yellow solid, m.p.: 80-82 ºC. IR (KBr, ν): 1705, 1521, 1350, 1288, 1273, 1193, 1041, 840 and 746 cm^{-1}. ^1H NMR (δ): 1.32 (t, 3H, *J* = 7.1, OCH$_2$C*H*$_3$), 4.25 (q, 2H, *J* = 7.1, OC*H*$_2$CH$_3$), 5.22 (s, 2H, OC*H*$_2$Ar), 6.58 (d, 1H, *J* = 16.2, CH=C*H*CO$_2$Et), 7.16 (dd, 1H, *J* = 2.0 and 8.0, H-3), 7.35 (dt, 1H, *J* = 2.0 and 8.0, H-5), 7.36 (d, *J* = 8.0, 1H, H-4), 7.38-7.41 (m, 5H, ArH of Benzyl) and 7.73 (d, 1H, *J* = 16.2, C*H*=*C*HCO$_2$Et). ^{13}C NMR (δ): 14.3 (OCH$_2$*C*H$_3$), 60.7 (O*C*H$_2$CH$_3$), 71.4 (O*C*H$_2$Ar), 116.3 (C-3), 116.5 (C-5), 118.7 (C-1), 125.9 (CH=*C*HCO$_2$Et), 127.0 (Benzyl), 128.4 (C-4), 128.6 (Benzyl), 128.8 (Benzyl), 134.3 (*C*H=CHCO$_2$Et), 135.5 (Benzyl), 150.9 (C-6), 157.5 (C-2) and 166.4 (CH=CH*C*O$_2$Et). HRMS *m/z* calcd. for $C_{18}H_{18}NO_5$: 328.1185 $[M + H]^+$; found: 328.1179.

Ethyl *Z*-3-(2-benzyloxy-6-nitrophenyl)-3-(4'-methoxyphenyl) acrylate (26)

A mixture of cinnamate ester **24** (245 mg, 0.749 mmol) and $Pd(OAc)_2$ (17 mg, 0.0749 mmol) in MeOH (3 mL) was vigorously stirred at 80°C for 30 s, when the *p*-anisidine diazonium tetrafluoroborate salt (333 mg, 1.50 mmol) prepared under literature conditions,[24a] was added in one portion. The reaction was further stirred at 80 ºC until complete consumption of the starting material was confirmed by TLC analysis. Then, the reaction mixture was concentrated under reduced pressure and the residue was chromatographed to afford the β,β-diphenylacrylate **26** (194 mg, 60%), as a yellow solid, m.p.: 102-104 ºC. IR (KBr, ν): 2934, 1717, 1603, 1526, 1508, 1448, 1362, 1269, 1163 and 741 cm^{-1}. ^1H NMR (δ): 1.08 (t, 3H, *J* = 7.1, OCH$_2$C*H*$_3$), 3.82 (s, 3H, ArOC*H*$_3$), 3.98 (q, 2H, *J* = 7.1, OC*H*$_2$CH$_3$), 5.02 (q, 2H, *J* = 12.3, OC*H*$_2$Ar), 6.45 (s, 1H, H-3), 6.85 (d, 2H, *J* = 8.8, H-11 and H-13), 7.04 (dd, 2H, *J* = 2.8 and 6.3, ArH of Benzyl), 7.21 (d, 1H, *J* = 8.3, H-8), 7.23-7.26 (m, 3H, ArH of Benzyl), 7.33 (d, 2H, *J* = 8.8, H-10 and H-14), 7.45 (t, 1H, *J* = 8.3, H-7) and 7.72 (d, 1H, *J* = 8.3, H-6). ^{13}C NMR (δ): 14.0 (OCH$_2$*C*H$_3$), 55.3 (O*C*H$_3$), 60.0 (O*C*H$_2$CH$_3$), 70.8 (O*C*H$_2$Ar), 113.9 (C-11 and C-13), 116.0 (C-3), 116.4 (C-6),* 117.0 (C-8),* 124.9 (C-1), 126.9 (2C, Benzyl), 127.9 (C-4'), 128.4 (2C, Benzyl), 128.7 (C-10 and C-14), 129.1 (C-7), 130.6 (C-9), 136.0 (Benzyl), 149.0 (C-7), 149.2 (C-6), 155.9 (C-2), 160.8 (C-4') and 165.6 (*C*O$_2$Et). EI-MS (*m/z*, rel. int., %): 433 (M^+, 1), 416 (10), 151 (58), 150 (100), 133 (20), 122 (47), 121 (21), 115 (29), 107 (22), 106 (30), 105 (31), 104 (20), 103 (59), 94 (36), 93 (28), 91 (56) and 77 (92). HRMS *m/z* calcd. for $C_{25}H_{24}NO_6$ 434.1604 $[M + H]^+$; found: 434.1598.

5-Benzyloxy-4-(4'-methoxyphenyl)-1*H*-quinolin-2-one (19)

Clean iron turnings (206 mg, 3.69 mmol) were added to a stirred solution of β,β-diphenylacrylate **26** (200 mg, 0.461 mmol) in glacial AcOH (2 mL) pre-heated at 110 °C. Stirring was continued during 18 h, when the solution was brought to room temperature, and the precipitate was filtered off and washed with EtOAc (10 mL). The combined organic solutions were evaporated under reduced pressure and the residue was chromatographed to furnish **19** (120 mg, 74%), as a brown solid, m.p.: 207-209 ºC. IR (KBr, ν): 3734, 3250, 1646, 1626, 1578, 1368, 1340, 1283, 1153, 1081, 1010, 842 and 669 cm^{-1}. ^1H NMR (δ): 3.62 (s, 3H, OC*H*$_3$), 4.69 (s, 2H, OC*H*$_2$Ar), 6.28 (s, 1H, H-3), 6.57 (d, 2H, *J* = 8.5, H-3' and H-5'), 6.57 (d, *J* = 8.3, 1H, H-6), 6.74 (d, 2H, *J* = 8.5, H-2' and H-6'), 6.98 (d, 1H, *J* = 8.3, H-8), 7.03-7.14 (m, 5H, ArH of Benzyl), 7.30 (t, 1H, *J* = 8.3, H-7) and 11.71 (s, 1H, N-*H*). ^{13}C NMR (δ): 54.9 (O*C*H$_3$), 70.5 (O*C*H$_2$Ar), 105.1 (C-6), 109.5 (C-8), 110.2 (C-4a), 112.5 (C-3' and C-5'), 122.4 (C-3), 127.2 (C-2' and C-6'), 127.5 (Benzyl), 127.9 (Benzyl), 128.6 (Benzyl), 131.1 (C-7), 134.0 (C-1'), 135.7 (Benzyl), 140.8 (C-8a), 152.3 (C-4), 156.4 (C-5), 158.8 (C-4') and 162.9 (C-2). HRMS *m/z* calcd. for $C_{23}H_{19}NNaO_3$: 380.1257 $[M + Na]^+$; found: 380.1245.

5-Hydroxy-4-(4'-methoxyphenyl)-1*H*-quinolin-2-one (27)

Method A: The benzyloxy derivative **19** (62 mg, 0.174 mmol) was added to a stirred suspension of 10% Pd/C (3 mg) in a 1:1 mixture of EtOH:EtOAc (2 mL), cooled to 0 °C in an ice bath. The system was placed under a hydrogen atmosphere (1 atm.) and stirred during 4 h. Then, the reaction was diluted with EtOAc (10 mL) and filtered through Celite. The filtrate was dried over Na_2SO_4, concentrated in vacuo and chromatographed, affording the 5-hydroxy-1*H*-quinolin-2-one **27** (41 mg, 89%), as a tan crystalline solid, m.p.: 260-262 ºC (Hexanes-EtOAc). IR (KBr, ν): 2928, 2369, 1630, 1607, 1508, 1356, 1281, 1244 and 833 cm^{-1}. ^1H NMR (δ): 3.89 (s, 3H, OC*H*$_3$), 5.59 (s, 1H, N-*H*), 6.41 (s,

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1H, H-3), 6.64 (dd, 1H, *J* = 0.7 and 8.3, H-6), 6.98 (dd, 1H, *J* = 0.7 and 8.3, H-8), 7.06 (d, 2H, *J* = 8.7, H-3' and H-5'), 7.39 (t, 1H, *J* = 8.3, H-7), 7.41 (d, 2H, *J* = 8.7, H-2' and H-6') and 8.53 (s, 1H, O*H*). ^{13}C NMR (δ): 55.5 (OCH_3), 108.3 (C-4a), 108.7 (C-6), 110.4 (C-8), 115.0 (C-3' and C-5'), 121.8 (C-3), 129.4 (C-2' and C-6'), 129.6 (C-1'), 132.1 (C-7), 139.9 (C-8a), 150.2 (C-4), 154.3 (C-5), 160.7 (C-12), and 163.0 (C-2). EI-MS (*m/z*, rel. int., %): 357 (M^+, 6), 91 (100), 73 (14) and 71 (18). HRMS *m/z* calcd. for $C_{16}H_{14}NO_3$: 268.0974 $[M + H]^+$; found: 268.0968.

Method B: A magnetically stirred mixture of compound **26** (24 mg, 0.055 mmol) and 10% Pd/C (1 mg) in anhydrous MeOH (2 mL) was exposed to a hydrogen atmosphere (1 atm.) during 2 h at room temperature. Then, the suspension was filtered through a short pad of Celite and the filtrate was concentrated under reduced pressure. The ensuing light yellow solid was subjected to flash chromatography affording compound **27** (4 mg, 30%) as a brownish crystalline solid. The spectral data of this product were in full agreement with those recorded for the product obtained through *Method A*.

5-Allyloxy-4-(4'-methoxyphenyl)-1*H*-quinolin-2-one (31)

A solution of **27** (316 mg, 1.183 mmol) in absolute EtOH (4 mL), was treated with K_2CO_3 (199 mg, 1.420 mmol). The resulting suspension was stirred at room temperature during 10 min., when allyl bromide (171 mg, 1.420 mmol) was added in one portion and the reaction was heated under reflux during 4 h. After confirming the complete consumption of the starting material by TLC, the reaction mixture was treated with a 1M solution of HCl (10 mL) and the products were extracted with EtOAc (3 × 15 mL). The combined extracts were dried with Na_2SO_4 and concentrated under reduced pressure. The residue was submitted to flash chromatography, affording compound **31** (235 mg, 65%), as a colorless solid, m.p.: 210-212 ºC (CH_2Cl_2). IR (ATR, ν): 3734, 3250, 1646, 1626, 1578, 1368, 1340, 1283, 1153, 1081, 1010, 842 and 669 cm^{-1}. ^{1}H NMR (DMSO-d_6, δ): 3.77 (s, 3H, OCH_3), 4.25 (d, *J* = 5.2, 2H, CH_2=CH-CH_2-Ar), 4.79 (d, *J* = 18.7, 1H, CH_{trans}=CH-CH-Ar), 4.90 (d, *J* = 10.7, 1H, CH_{cis}=CH-CH_2-Ar), 5.36 (ddd, *J* = 5.2, 10.7 and 18.7, 1H, CH_2=C*H*-CH_2-Ar) 5.59 (s, 1H, N*H*), 6.41 (s, 1H, H-3), 6.66 (d, 1H, *J* = 8.2, H-6), 6.89 (d, 2H, *J* = 8.5, H-3' and H-5'), 6.97 (d, 1H, *J* = 8.2, H-8), 7.17 (d, 2H, *J* = 8.5, H-2' and H-6'), and 7.41 (t, 1H, *J* = 8.2, H-7). ^{13}C NMR (DMSO-d_6, δ): 55.5 (OCH_3), 69.2 (CH_2=CH-*C*H_2-Ar), 108.3 (C-4a), 108.7 (C-6), 110.4 (C-8), 115.0 (C-3' and C-5'), 117.1 (*C*H_2=CH-CH-Ar), 121.8 (C-3), 129.4 (C-2' and C-6'), 129.6 (C-9), 132.1 (C-7), 132.8 (CH_2=*C*H-CH-Ar), 139.9 (C-8a), 150.2 (C-4), 154.3 (C-5), 160.7 (C-12) and 163.0 (C-2). HRMS *m/z* for $C_{19}H_{18}NO_3$: 308.1287 $[M + H]^+$; found: 308.1281.

6-Allyl-5-hydroxy-4-(4'-methoxyphenyl)-1*H*-quinolin-2-one (32)

The *O*-allyl derivative (**31**) (200 mg, 0.651s mmol) was dissolved in 1,2-dichlorobenzene (4 mL) and the solution was placed in a sealed tube. The mixture was heated in a microwave reactor (300 W) at 190 °C for 120 min. The crude product was purified by flash chromatography on silica gel, to give **32** (0.150 g, 75%) as a colorless oil, m.p.: > 300 ºC (EtOAc). IR (KBr, ν): 2928, 2369, 1630, 1607, 1508, 1356, 1281, 1244 and 833 cm^{-1}. ^{1}H NMR (δ): 3.33 (d, 2H, *J* = 6.5, H-1'), 3.89 (s, 3H, OCH_3), 4.99 (d, *J* = 15.7, 1H, CH_{cis}=CH-CH_2-Ar), 5.04 (d, *J* = 17.8, 1H, CH_{trans}=CH-CH_2-Ar), 5.93 (ddd, 1H, *J* = 6.5, 15.7 and 17.8, CH_2=C*H*-CH_2-Ar), 6.41 (s, 1H, H-3), 6.99 (d, 1H, *J* = 8.3, H-8), 7.06 (d, 2H, *J* = 8.7, H-3' and H-5'), 7.30 (d, 1H, *J* = 8.3, H-7) and 7.40 (d, 2H, *J* = 8.7, H-2' and H-6'). ^{13}C NMR (δ): 34.0 (CH_2=CH-*C*H_2-Ar), 55.4 (OCH_3), 108.2 (C-4a), 108.4 (C-8), 115.0 (C-3' and C-5'), 115.6 (*C*H_2=CH-CH_2-Ar), 120,6 (C-8a), 121.9 (C-3), 129.5 (C-2' and C-6'), 129,7 (C-1'), 133.3 (C-7), 136.5 (CH_2=*C*H-CH_2-Ar), 138.6 (C-6), 150.2 (C-4), 151.3 (C-5), 160.7 (C-4') and 163.1 (C-2). HRMS *m/z* calcd. for $C_{19}H_{18}NO_3$ 308.1287 $[M + H]^+$; found: 308.1281.

5-Hydroxy-4-(4'-methoxyphenyl)-6-(3-methyl-but-2-enyl)-1*H*-quinolin-2-one (33)

To a stirred solution of the allyl derivative **32** (12 mg, 0.039 mmol) in anhydrous CH_2Cl_2 (0.5 mL) was added the Grubbs II catalyst (1.6 mg, 5 mol%). Then, 2-methyl-but-2-ene (27.4 mg, 0.391 mmol) was dripped in, the system was sealed and the mixture was heated to reflux. After stirring for 2 h, the reaction was cooled to rt and filtered through a silica plug, washing with EtOAc (20 mL). The filtrate was concentrated under reduced pressure to afford **33** (10 mg, 77%) as a brownish solid, m.p.: 222-224 ºC (EtOAc). IR (KBr, ν): 3480, 2926, 2359, 1645, 1634, 1607, 1512, 1454, 1373, 1248, 1178, 1032 and 833 cm^{-1}. ^{1}H NMR (δ): 1.67 (s, 3H, C-CH_3), 1.71 (s, 3H, C-CH_3), 3.25 [d, 1H, *J* = 6.7, CH_2-CH=C(CH_3)$_2$], 3.89 (s, 3H, OCH_3), 5.24 [bs, 1H, CH_2-C*H*=C(CH_3)$_2$], 5.67 (bs, 1H, -N*H*), 6.39 (s, 1H, H-3), 6.94 (d, 1H, *J* = 8.2, H-8), 7.07 (d, 2H, *J* = 8.3, H-3' and H-5'), 7.29 (d, 1H, *J* = 8.2, H-7), 7.40 (d, 2H, *J* = 8.3, H-2' and H-6') and 11.91 (s, 1H, O*H*). ^{13}C NMR (δ): 17.8 (C-*C*H_3), 25.7 (C-*C*H_3), 28.2 [*C*H_2-CH=C(CH_3)$_2$], 55.4 (OCH_3), 108.2 (C-8), 115.0 (C-3' and C-5'), 122.1 (C-3), 122.2 [CH_2-*C*H=C(CH_3)$_2$], 127.3 (C-4a), 128.7 (C-4), 129.5 (C-2' and C-6'), 129.9 (C-9), 132.9 (C-7), 133.2 [CH_2-CH=*C*(CH_3)$_2$], 138.2 (C-8a), 150.2 (C-6), 151.3 (C-5), 160.6 (C-4') and 163.0 (C-2). HRMS *m/z* calcd. for $C_{21}H_{22}NO_3$: 336.1577 $[M + H]^+$; found: 336.1594.

tert-Butyl 6-allyl-5-hydroxy-4-(4'-methoxyphenyl)-2-oxo-2*H*-quinoline-1-carboxylate (35)

To a solution of **32** (146 mg, 0.475 mmol), in anhydrous CH_2Cl_2 (2 mL) was added anhydrous Et_3N (144 mg, 1.425 mmol) and DMAP (17.3 mg, 0.142 mmol). Then, Boc_2O (310 mg, 1.425 mmol) was added in one portion and the resulting mixture was stirred at room temperature for 20 h. After confirming the complete consumption of the starting material by TLC, the reaction was poured on H_2O (10 mL), and the product was extracted with Et_2O (3 × 10 mL). The organic phase was washed with $NaHCO_3$ (10 mL), brine (10 mL), and H_2O (10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue afforded the compound **35** (120 mg, 0.299 mmol) as a pale yellow solid, m.p.: 172-174 ºC (CH_2Cl_2). IR (KBr, ν): 2930, 1666, 1661, 1514, 1371, 1101, 876 and 833 cm^{-1}. ^{1}H NMR (δ): 1.26 (s, 9H, C-(CH_3)$_3$), 3.28 (d, 2H, *J* = 6.5, CH_2-CH=CH_2), 3.88 (s, 3H, OCH_3), 5.03 (m, 1H, CH_{cis}=CH-CH_2-Ar), 5.08 (m, 1H, CH_{trans}=CH-CH_2-Ar), 5.85 (ddd, 1H, *J* = 6.5, 9.4 and 16.2, CH_2=C*H*-CH_2-Ar), 6.54

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(s, 1H, H-3), 6,97 (d, 2H, *J* = 8.6, H-3' and H-5'), 7.32 (d, 2H, *J* = 8.6, H-2' and H-6'), 7.36 (d, 1H, *J* = 8.6, H-8) and 7.42 (d, 1H, *J* = 8.6, H-7). ^{13}C NMR (δ): 27.3 [C-(*C*H$_3$)$_3$], 33.7 (CH$_2$=CH-*C*H$_2$-Ar), 55.3 (O*C*H$_3$), 83.3 [*C*-(CH$_3$)$_3$], 104.3 (C-6), 113.4 (C-9), 113.6 (C-3' and C-5'), 115.0 (C-8), 116.8 (*C*H$_2$=CH-CH$_2$-Ar), 124.0 (C-3), 127.5 (C-3), 131.8 (C-4a), 132.5 (C-2' and C-6'), 135.4 (CH$_2$=*C*H-CH$_2$-Ar), 138.8 (C-8a), 143.2 (C-5), 150.4 [N-(C=O)-O], 151.0 (C-4), 159.4 (C-4') and 163.2 (C-2). HRMS *m/z* calcd. for $C_{24}H_{25}NNaO_5$: 430.1625 [M + Na]$^+$; found: 430.1610.

tert-Butyl 5-hydroxy-4-(4'-methoxyphenyl)-2-oxo-6-propenyl-1*H*-quinoline-1-carboxylate (36)

To a solution of allyl derivative **35** (10 mg, 0.024 mmol) in EtOH (1 mL) was added $RhCl_3.3H_2O$ (2.13 mg, 0.0082 mmol). The resulting mixture was stirred during 31 h to room temperature. Then, the reaction was filtered through silica-pad with EtOAc as eluent. The filtrate was concentrated under reduced pressure to afford compound **36** (5 mg, 50%) as a white solid, m.p.: 139-140 ºC (CH_2Cl_2). IR (KBr, ν): 3690, 2928, 2853, 2370, 1751, 1663, 1549, 1508, 1458, 1248, 1151 and 833 cm^{-1}. ^{1}H NMR (δ): 1.18 [s, 9H, C-(C*H*$_3$)$_3$], 1.78 (d, 3H, *J* = 6.3, C*H*$_3$-CH=CH-Ar), 3.80 (s, 3H, OC*H*$_3$), 6.19 (dd, *J* = 6.3 and 15.7, 1H, CH$_3$-C*H*=CH-Ar), 6.36 (d, *J* = 15.7, 1H, CH$_3$-CH=C*H*-Ar), 6.53 (s, 1H, H-3), 6,95 (d, 2H, *J* = 8.6, H-3' and H-5'), 7.19 (d, 2H, *J* = 8.6, H-2' and H-6'), 7.28 (d, 1H, *J* = 8.8, H-7) and 8.73 (d, 1H, *J* = 8.8, H-8). ^{13}C NMR (DMSO-d_6, δ): 18.6 (*C*H$_3$-CH=CH-Ar), 26.8 [C-(*C*H$_3$)$_3$], 55.1 (O*C*H$_3$), 82.5 [*C*-(CH$_3$)$_3$], 112.3 (C-6), 113.2 (C-3' and C-5'), 114.2 (C-7), 123.2 (CH$_3$-*C*H=CH-Ar), 124.3 (C-3), 124.5 (C-4a), 127.9 (CH$_3$-CH=*C*H-Ar), 128.5 (C-8), 129.1 (C-2' and C-6'), 131.4 (C-9), 139.5 (C-8a), 143.2 (N(C=O)-O), 149.3 (C-4), 149.8 (C-5), 158.8 (C-4') and 160.4 (C-2). HRMS *m/z* calcd. for $C_{24}H_{25}NNaO_5$: 430.1625 [M + H]$^+$; found: 430.1609.

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