Reactivity of 3-Iodo-4-quinolones in Heck Reactions: Synthesis of Novel (*E*)-3-Styryl-4-quinolones

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Abstract: A new and efficient route for the synthesis of (*E*)-*N*-methyl-3-styryl-4-quinolones is described. It involves the Heck reaction of *N*-methyl-3-iodo-4-quinolone, which is obtained by consecutive 3-iodination and NH-methylation of the unsubstituted 4-quinolone, with styrene derivatives. It is demonstrated that such a procedure is only efficient when the 3-iodo-4-quinolone has an N-protecting group. In some cases the branched regioisomers *N*-methyl-3-(1-phenylethenyl)-4-quinolones were also obtained as byproducts.

Key words: 3-iodo-4-quinolones, 3-styryl-4-quinolones, Heck reaction, N-methylation, iodination

Quinolone ring systems are present in a wide range of natural products, especially in alkaloids obtained from plants belonging to the *Rutaceae* family.[1] Therefore, 4-quinolones are known by their extensive variety of clinical applications, such as the treatment of respiratory, gastrointestinal, and gynaecologic infections, sexually transmitted diseases, chronic osteomyelitis, prostatitis, and some skin, bone, and soft tissue infections.[2] The search for new 4-quinolone derivatives has been carried out to improve the spectrum of antimicrobial activity against Gram negative as well as Gram positive bacteria.[3] In recent years, certain 4-quinolones possessing antitumor, anti-HIV-1 integrase and cannabinoid receptor agonist–antagonist activities, have been described.[4]

2-Aryl-4-quinolones, also called azoflavones, are well-known for their significant anticancer activity,[5] but some derivatives also demonstrate other important biological properties, such as antiviral,[6] antibacterial,[7] antiplatelet,[8] and trypanocidal activities.[9] The related 3-aryl-4-quinolones (azoisoflavones) have also shown important biological properties, such as EGFR tyrosine kinase[10] and P-glycoprotein inhibitory activity,[11] good and selective cytotoxic activity against human cancer cell lines,[12] and also extremely high antiplatelet potency.[8] However, despite their structural analogy with isoflavones, this group of compounds have received less attention. In the present communication we report a new method for the synthesis of 3-styryl-4-quinolones, a new type of 4-quinolone structurally related to 3-aryl-4-quinolones and with 3-styryl-chromones.[13] The key transformation of this synthetic route involves the Heck reaction of 3-iodo-4-quinolones with styrene derivatives (Scheme 1).

The Mizoroki–Heck reaction,[14] commonly referred as the Heck reaction, is a highly versatile and useful carbon–carbon bond-forming methodology using aryl halides as substrates and nowadays is a keystone in synthetic organic chemistry.[15]

Firstly, 4-quinolone (**1**) was synthesized,[16] in good yield (70%), by reaction of 2′-aminoacetophenone with methyl formate in the presence of sodium, at 40 °C (Scheme 1).[17] Then, 3-iodo-4-quinolone (**2**)[18] was obtained in good yield (81%) by a recently reported method for the iodination of 2-aryl-4-quinolones,[19] involving the reaction of **1** with iodine in the presence of sodium carbonate in dry THF (Scheme 1).[20]

In the next step to afford (*E*)-3-styryl-4-quinolone (**4**), a range of Heck reaction conditions involving 3-iodo-4-quinolone (**2**) and styrene **3a** were explored (Table 1 shows only pertinent results). In the first attempt, palladium(II) acetate was used as precatalyst and triphenylphosphine (Ph_3P) as ligand and in situ reducing agent of the precatalyst to palladium(0) prior to entering in the Heck catalytic cycle. Under these conditions, **4** was obtained in low yields, 20% being the highest yield obtained when using triethylamine as base, at 150 °C for five hours (Table 1, entry 1) or by using the Heck–Jeffery reaction conditions,[21] at 100 °C for five hours (Table 1, entry 3). On the other hand, the use of tri(*o*-tolyl)phosphine (*o*-TTP) led us

Table 1 Heck Reaction of 3-Iodo-4-quinolone **2** with Styrene **3a**

Entry	Conditions[a]	Yield of **4** (%)	Yield of **5** (%)
1	$Pd(OAc)_2$, Ph_3P, Et_3N, 5 h, 150 °C	20	–
2	$Pd(OAc)_2$, *o*-TTP, Et_3N, 5 h, 100 °C	10	16
3	$Pd(OAc)_2$, Ph_3P, K_2CO_3, TBAB, 5 h, 100 °C	20	–
4[b]	$Pd(PPh_3)_4$, Ph_3P, Et_3N, 5 h, 100 °C	46	trace
5	$Pd(PPh_3)_4$, *o*-TTP, Et_3N, 5 h, 100 °C	16	trace
6	$Pd(PPh_3)_4$, Ph_3P, Et_3N, 5 h, 130 °C	28	–
7	NMP, NaOAc, Pd/C, 140 °C	8	–

[a] Reactions were performed using 5 equiv of styrene, 0.1 equiv of ligand, 1 equiv of base and using NMP as solvent.
[b] 10% of starting material recovered. *o*-TTP = tri(*o*-tolyl)phosphine. TBAB = tetrabutylammonium bromide.

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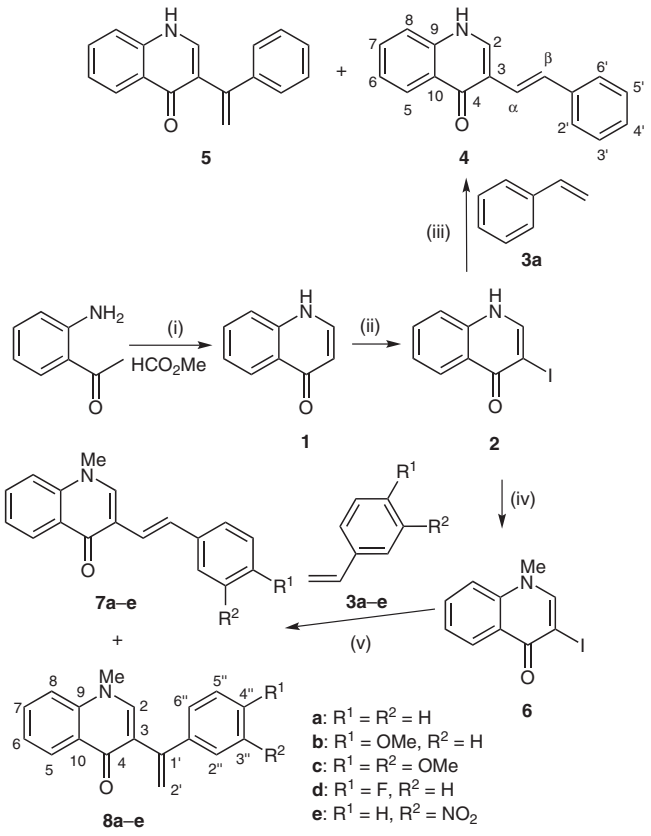

Scheme 1 *Reagents and conditions*: (i) Na, 40 °C, 6 h; (ii) Na_2CO_3, I_2, dry THF, 6 h; (iii) Heck reaction conditions (Table 1); (iv) MeI, PS-TBD, 40 °C, dry THF, 3 h; (v) Heck reaction: classical heating conditions and microwave irradiation (Tables 2,3).

to obtain compound **5** as the main reaction product (Table 1, entry 2). However, the optimal experimental conditions were achieved when palladium(0) was used as catalyst [$Pd(PPh_3)_4$], in the presence of Ph_3P as ligand, and Et_3N as base at 100 °C for five hours (Table 1, entry 4).[22] Under these reaction conditions, the desired (*E*)-3-styryl-4-quinolone (**4**)[23] was obtained in acceptable yield (46%) and traces of the branched regioisomer 3-(1-phenylethenyl)-4-quinolone (**5**) were found (Scheme 1).

All tested cross-coupling reaction conditions led to low or moderate yields of **4** with difficult and time-consuming purification processes. Furthermore, not only the expected linear product **4** was obtained but also its branched regioisomer **5**. These results led us to conclude that the reaction proceeds via two pathways, an ionic one leading to the branched product, and the neutral one, this giving rise to the linear variant.[24]

In order to circumvent these problems we have decided to protect the NH group of 3-iodo-4-quinolone **2**, trying to avoid possible reactions at the NH group and changing the reactivity of this 4-quinolone **2**. Methylation of **2** with an excess of methyl iodide in the presence of PS-TBD,[25] in dry THF at 40 °C, led to the formation of *N*-methyl-3-iodo-4-quinolone (**6**)[26] in good yield (95%) (Scheme 1).[27]

In the first attempt to synthesise 3-styryl-4-quinolones **7a–e**, we used the optimal conditions established above for the reaction of **2** with styrene **3a**; 5 equivalents of styrene, 0.05 equivalents of $Pd(PPh_3)_4$, 0.1 equivalents of Ph_3P and 1 equivalent of Et_3N in NMP (Table 2, entry 1). Under these conditions, (*E*)-*N*-methyl-3-styryl-4-quinolone (**7a**) was isolated as the main product (55%) and *N*-methyl-3-(1-phenylethenyl)-4-quinolone (**8a**)[28] as a byproduct (14%), with 8% recovery of starting compound. Some changes on the procedure were carried out, such as increasing the amount of catalyst (Table 2, entry 2), changing the catalyst source from palladium(0) to palladium(II) (Table 2, entry 3), and the solvent (Table 2, entry 4), but the yield of the expected quinolone **7a** did not improve. It is important to note that under all these conditions the byproduct **8a** was not found or was found in a very low yield.

Table 2 Heck Reaction of *N*-Methyl-3-iodo-4-quinolone (**6**) with Styrene **3a**

Entry	Conditions[a]	Yield of **7a** (%)	Yield of **8a** (%)
1[b]	$Pd(PPh_3)_4$ (0.05 equiv), Ph_3P, Et_3N, NMP, 5 h, 100 °C	55	14
2	$Pd(PPh_3)_4$ (0.05 equiv), Ph_3P, Et_3N, NMP, 5 h, 100 °C	42	–
3	$PdCl_2$ (0.05 equiv), Ph_3P, Et_3N, NMP, 5 h, 100 °C	40	3
4	$Pd(PPh_3)_4$ (0.05 equiv), Ph_3P, Et_3N, CH_3CN, 5 h, 100 °C	22	–

[a] Reactions were performed using 5 equiv of styrene, 0.1 equiv of ligand, 1 equiv of base in 3 mL of solvent.
[b] 8% of starting material was recovered.

The beneficial effect of microwave heating in synthetic organic chemistry is a growing area, since higher yields and shorter reaction times might be obtained.[29] In our case the Heck reaction of *N*-methyl-3-iodo-4-quinolone (**6**) with styrene **3a** under microwave irradiation conditions allowed us to shortening the reaction time but led to lower yields than the purely thermal procedure (e.g., 40% being the highest yield obtained in 1.5 h reaction time).

After these studies on the Heck reaction of 3-iodo-4-quinolones **2** and **6** with styrene **3a** to afford (*E*)-3-styryl-4-quinolones (**4**) and **7a**, we have extended our attention to the reactions of *N*-methyl-3-iodo-4-quinolone **6** with different styrenes **3b–e** and to the optimization of the synthesis of (*E*)-*N*-methyl-3-styryl-4-quinolone derivatives **7b–e**.

Attempts to prepare (*E*)-3-styryl-4-quinolones **7b**,**c** by treating **6** with styrenes **3b**,**c** using the best conditions established in Table 2, were not very successful, the expected compounds being obtained in poor yields (**8b**: 15%, **8c**: 30%). Even when the amount of catalyst was changed [from 0.05 to 0.1 equiv of $Pd(PPh_3)_4$] and the temperature (from 100 °C to 130 °C), the results were not better. Consequently, other conditions were attempted by treating **6** with palladium(II) chloride as catalyst, instead of $Pd(PPh_3)_4$, in the presence of Ph_3P, Et_3N, and using NMP

Table 3 Optimal Heck Reaction Conditions of *N*-Methyl-3-iodo-4-quinolone (**6**) with Styrenes **3b–e**

Compound	Catalyst	Yields under classical heating conditions(%)[a]	Yields under MW condtions (%)[b]
7b	$PdCl_2$	59	36
8b		–	trace
7c	$PdCl_2$	55	30
8c			trace
7d	$PdCl_2$	56	48
8d		trace	–
7e	$Pd(PPh_3)_4$	65	45
8e		–	–

[a] *N*-Methyl-3-iodo-4-quinolone (**6**) was treated with 5 equiv of the appropriate styrene **3b–e**, 0.05 equiv of catalyst, 0.1 equiv of Ph_3P, and 1 equiv of Et_3N, in 3 mL of NMP, at 100 °C for 5 h.
[b] Reaction performed in closed glass vessels under MW irradiation: 2 min ramp to 100 °C and 1.5 h hold at 100 °C.

as solvent, under classical heating conditions (Table 3). The target compounds **7b**,**c**[30] were then obtained in good yields (55–59%). These conditions were also good for obtaining (*E*)-4′-fluoro-3-styryl-4-quinolone (**7d**; 56%), traces of **8d** being obtained as a byproduct (Table 3). When $Pd(PPh_3)_4$ was used as catalyst **7d** was obtained in a slight lower yield (50%). On the other hand, compound **7e** was obtained in good yield (65%) when using $Pd(PPh_3)_4$ as catalyst, but only in 20% yield when $PdCl_2$ was used. The synthesis of **7b–e** were also carried out under microwave irradiation, although the reaction time is significantly lower (1.5 h instead of 5 h), the expected compounds **7b–e** were obtained in lower yields (30–48%, Table 3).

All the new synthesized compounds have been characterized by NMR spectroscopy. The main features in the ^1H NMR spectra that allows the differentiation of **4** from **5** and of **7a** from **8a** are the signals due to the vinylic protons resonances: In compounds **4** and **7a** they appear as doublets with a large coupling constant (J = ca. 16 Hz; $\delta_{H\alpha}$ = 7.27 ppm and $\delta_{H\beta}$ = 7.91 ppm for **4** and $\delta_{H\alpha}$ = 7.19 ppm and $\delta_{H\beta}$ = 7.65 ppm for **7a**), indicative of a *trans* configuration; while in the case of **5** and **8a** they also appear as doublets but with small coupling constants (J = ca. 1.7 Hz; $\delta_{H2'}$ = 5.57 and 5.71 ppm for **5** and $\delta_{H2'}$ = 5.64 and 5.78 ppm for **8a**) indicative of a geminal coupling. It is important to notice the high frequency values of the H-2 resonance, which appears as singlet at δ_H = 7.6–8.2 ppm, due to deshielding effects of the heterocyclic nitrogen atom (inductive effect) and of the carbonyl group (mesomeric effect).

In conclusion, a new methodology for the synthesis of (*E*)-*N*-methyl-3-styryl-4-quinolones has been established. This synthetic route comprises four steps, the synthesis of the unsubstituted 4-quinolone, followed by its 3-iodination and NH-methylation, and finally the Heck reaction of the 3-iodo-*N*-methyl-4-quinolone thus obtained with styrene derivatives. This Heck procedure is only efficient when the 3-iodo-4-quinolone has an N-protecting group. The presence of regioisomeric 3-(1-phenylethenyl)-4-quinolones as byproducts was observed in some cases, depending on the experimental conditions. The beneficial effect of microwave irradiation in the Heck reaction was the shortening of the reaction time although the product yields are disappointingly lower.

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(16) **Physical Data for Quinolin-4 (1*H*)-one (1)**
Mp 196–197 °. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ = 6.35 (d, 1 H, *J* = 7.2 Hz, H-3), 7.43 (ddd, 1 H, *J* = 7.8, 7.7, 0.8 Hz, H-6), 7.59 (d, 1 H, *J* = 8.1 Hz, H-8), 7.72 (ddd, 1 H, *J* = 8.1, 7.8, 1.3 Hz, H-7), 7.99 (d, 1 H, *J* = 7.2 Hz, H-2), 8.26 (d, 1 H, *J* = 7.7 Hz, H-5) ppm. ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 109.8 (C-3), 119.5 (C-8), 125.3 (C-6), 126.1 (C-5), 126.7 (C-10), 133.6 (C-7), 141.5 (C-2, C-9), 180.8 (C-4) ppm. ESI$^+$-MS: *m/z* (%) = 146 (100) [M + H]$^+$. ESI$^+$-HRMS: *m/z* calcd for [C_9H_7NO + H]$^+$: 146.0606; found: 146.0604.
(17) **Optimized Experimental Procedure**
Sodium (0.4 g, 8.70 mmol) was added to a solution of 2′-aminoacetophenone (1 mL, 8.23 mmol) in an excess of methyl formate (23 mL), and the reaction mixture was stirred at 40 °C, under a nitrogen atmosphere. After 6 h, MeOH (10 mL) was added to the reaction mixture to destroy the remaining sodium and the mixture was poured into H_2O (60 mL) and ice (30 g). The organic layer was extracted with EtOAc (4 × 100 mL), dried over anhyd Na_2SO_4, and the solvent evaporated to dryness. The residue was taken in acetone and purified by chromatography column using a (3:2) mixture of acetone–CH_2Cl_2 as eluent. The solvent was evaporated to dryness, and the residue was recrystallized from CH_2Cl_2–light PE to give quinolin-4 (1*H*)-one (**1**) as a yellowish solid (836.5 mg, 70%).
(18) **Physical Data for 3-Iodoquinolin-4 (1*H*)-one (2)**
Mp 217–218 °C. ^{1}H NMR (300.13 MHz, DMSO): δ = 7.38 (ddd, 1 H, *J* = 8.2, 7.6, 1.1 Hz, H-6), 7.58 (d, 1 H, *J* = 8.1 Hz, H-8), 7.69 (ddd, 1 H, *J* = 8.1, 7.6, 1.3 Hz, H-7), 8.10 (d, 1 H, *J* = 8.2 Hz, H-5), 8.52 (s, 1 H, H-2), 12.24 (s, 1 H, NH) ppm. ^{13}C NMR (74.47 MHz, DMSO): δ = 80.7 (C-3), 118.5 (C-8), 122.5 (C-10), 124.1 (C-6), 125.5 (C-5), 131.9 (C-7), 139.6 (C-9), 144.8 (C-2), 173.0 (C-4) ppm. ESI$^+$-MS: *m/z* (%) = 272 (100) [M + H]$^+$, 294 (21) [M + Na]$^+$. ESI$^+$-HRMS: *m/z* calcd for [C_9H_6INO + H]$^+$: 271.9572; found: 271.9579.
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(20) **Optimized Experimental Procedure**
A mixture of quinolin-4 (1*H*)-one (**1**, 300 mg, 2.07 mmol), Na_2CO_3 (329 mg, 3.11 mmol), and iodine (789 mg, 3.11 mmol) in dry THF (20 mL) was stirred at r.t. for 6 h, under a nitrogen atmosphere. After this period, the reaction mixture was poured into a sat. $Na_2S_2O_3$ solution (40 mL). The organic layer was extracted with EtOAc (3 × 100 mL), dried over anhyd Na_2SO_4 and the solvent evaporated to dryness. The residue was recrystallized from CH_2Cl_2–light PE to give 3-iodoquinolin-4 (1*H*)-one (**2**, 454.6 mg, 81%), as a yellow solid.
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(22) **Optimized Experimental Procedure**
A mixture of 3-iodoquinolin-4 (1*H*)-one (**2**, 50 mg, 0.18 mmol), Ph_3P (4.7 mg, 0.018 mmol), Et_3N (25.1 μL, 0.18 mmol), tetrakis(triphenylphosphine)palladium(0) (10.4 mg, 0.009 mmol), and styrene **3a** (103.4 μL, 0.9 mmol) in NMP (3 mL) was stirred at 100 °C for 5 h, under a nitrogen atmosphere. After this period, the reaction mixture was poured into H_2O (40 mL) and ice (30 g). The organic layer was extracted with EtOAc (3 × 100 mL) and washed with H_2O (100 mL). After initial purification by TLC using a (3:1) mixture of CH_2Cl_2–acetone, the solvent was evaporated to dryness and the residue recrystallized from CH_2Cl_2–light PE to give (*E*)-3-styrylquinolin-4 (1*H*)-one(**4**) as a yellow solid (20.5 mg, 46%). Traces of product **5** were found and 10% (5 mg) of the starting material was recovered.
(23) **Physical Data of (*E*)-3-Styrylquinolin-4 (1*H*)-one (4)**
Mp 269–270 °C. ^{1}H NMR (300.13 MHz, CD_3OD): δ = 7.23 (m, 1 H, H-4′), 7.27 (d, 1 H, *J* = 16.2 Hz, H-α), 7.38 (m, 3 H, H-6, H-3′,5′), 7.63 (m, 4 H, H-7, H-8, H-2′,6′), 7.91 (d, 1 H, *J* = 16.2 Hz, H-β), 8.24 (s, 1 H, H-2), 8.36 (dd, 1 H, *J* = 8.4, 0.9 Hz, H-5), 11.11 (s, 1 H, NH) ppm. ^{13}C NMR (75.47 MHz, CD_3OD): δ = 118.6 (C-3), 118.9 (C-8), 124.2 (C-6), 124.7 (C-α), 126.8 (C-5, C-2′,6′), 126.7 (C-10), 127.5 (C-4′), 128.2 (C-β), 129.4 (C-3′,5′), 132.2 (C-7), 138.8 (C-2), 139.8 (C-9), 139.8 (C-1′) 176.6 (C-4) ppm. ESI$^+$-MS: *m/z* (%) = 248 (100) [M + H]$^+$. Anal. Calcd (%) for $C_{17}H_{13}NO$ (247.3): C, 82.57; H, 5.30; N, 5.66. Found: C, 82.47; H, 5.22; N, 5.62.
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(26) **Physical Data for 1-Methyl-3-iodoquinolin-4 (1*H*)-one (6)**
Mp 177–178 °C. ^{1}H NMR (300.13 MHz, DMSO-d_6): δ = 3.00 (s, 3 H, NCH_3), 7.47 (ddd, 1 H, *J* = 7.8, 6.8, 1.2 Hz, H-6), 7.70 (d, 1 H, *J* = 9.0 Hz, H-8) 7.79 (ddd, 1 H, *J* = 9.0, 6.8, 1.6 Hz, H-7), 8.32 (dd, 1 H, *J* = 7.8, 1.6 Hz, H-5) ppm. ^{13}C NMR (75.47 MHz, DMSO-d_6): δ = 40.8 (NCH_3), 80.3 (C-3), 117.3 (C-8), 124.3 (C-10), 125.0 (C-6), 127.5 (C-5), 132.9 (C-7), 141.4 (C-9), 150.2 (C-2), 173.8 (C-4) ppm. ESI$^+$-MS: *m/z* (%) = 286 (100) [M + H]$^+$, 308 (67) [M + Na]$^+$. ESI$^+$-HRMS: *m/z* calcd for [$C_{10}H_8INO$ + H]$^+$: 285.9729; found: 285.9728.
(27) **Optimized Experimental Procedure**
A mixture of 3-iodoquinolin-4 (1*H*)-one (**2**, 200 mg, 0.74 mmol), PS-TBD (1.39 mmol/1 g, 1.33 g, 1.85 mmol) and MeI (0.47 mL, 7.4 mmol) in fresh dry THF (40 mL) was stirred at r.t. for 3 h. After this period, the reaction mixture was poured into a mixture of H_2O (100 mL) and Et_3N (8 mL) and neutralized with HCl (10%). The PS-TBD was filtered off, and the organic layer was extracted with EtOAc (3 × 150 mL), dried over anhyd Na_2SO_4, and the solvent evaporated to dryness. The product 1-methyl-3-iodoquinolin-4 (1*H*)-one (**6**) was recrystallized from CH_2Cl_2–light PE and obtained as a yellow solid (200.4 mg, 95%).
(28) **Physical Data for 1-Methyl-3-(1-phenylvinyl)quinolin-4 (1*H*)-one (8a)**
^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, NCH_3),

5.65 (d, 1 H, *J* = 1.7 Hz, H-2′), 5.78 (d, 1 H, *J* = 1.7 Hz, H-2′), 7.31 (m, 3 H, H-3″,4″,5″), 7.44 (m, 4 H, H-6, H-8, H-2″,6″), 7.55 (s, 1 H, H-2), 7.70 (ddd, 1 H, *J* = 7.8, 7.4, 1.6 Hz, H-7), 8.52 (dd, 1 H, *J* = 8.3, 1.6 Hz, H-5) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 40.7 (NCH_3), 115.1 (C-8), 116.6 (C-2′), 122.4 (C-3), 123.8 (C-6), 127.1 (C-10), 127.2 (C-2″,6″), 127.5 (C-4″), 127.7 (C-5), 128.3 (C-3″,5″), 132.0 (C-7), 140.0 (C-9), 141.3 (C-1″), 143.5 (C-2), 143.8 (C-1′), 176.2 (C-4) ppm. ESI$^+$-HRMS: *m/z* calcd for [$C_{18}H_{15}NO$ + H]$^+$: 262.1232; found: 262.1226.

(29) (a) Loupy, A. *Microwaves in Organic Synthesis*; Wiley-VCH: Weinheim, **2002**. (b) Kappe, C. O. *Angew. Chem. Int. Ed.* **2004**, *43*, 6250. (c) Arvela, R. K.; Leadbeater, N. E. *J. Org. Chem.* **2005**, *70*, 1786. (d) Kappe, C. O.; Dallinger, D. *Nat. Rev. Drug Discovery* **2006**, *5*, 51.

(30) **Physical Data for (*E*)-3-(4-Methoxystyryl)-1-methylquinolin-4 (1*H*)-one (7b)**
Mp 134.7–135.0 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 3.83 (s, 3 H, NCH_3), 6.87 (d, 2 H, *J* = 8.7 Hz, H-2′,6′), 7,01 (d, 1 H, *J* = 16.3 Hz, H-α), 7.38 (m, 2 H, H-6, H-8), 7,44 (d, 2 H, *J* = 8.7 Hz, H-3′,5′), 7.56 (d, 1 H, *J* = 16.3 Hz, H-β), 7.65 (ddd, 1 H, *J* = 7.8, 7.4, 1.4 Hz, H-7), 7.69 (s, 1 H, H-2), 8.52 (d, 1 H, *J* = 7.5 Hz, H-5) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 40.9 (OCH_3), 55.3 (NCH_3), 114.0 (C-3′,5′), 115.2 (C-8), 118.8 (C-3), 120.4 (C-α), 123.8 (C-6), 126.5 (C-10), 127.2 (C-5), 127.5 (C-2′,6′), 127.8 (C-β), 131.0 (C-1′), 131.7 (C-7), 139.2 (C-9), 141.6 (C-2), 158.9 (C-4′), 176.1 (C-4) ppm. ESI$^+$-MS: *m/z* (%) = 292 (100) [M + H]$^+$, 314 (10) [M + Na]$^+$. ESI$^+$-HRMS: *m/z* calcd for [$C_{19}H_{17}NO_2$ + H]$^+$: 292.1338; found: 292.1335.