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Research Article

Ultrasound-Assisted Wittig Reaction for the Synthesis of 3-Substituted 4-Chloroquinolines and Quinolin-4(1*H*)-ones with Extended π-Conjugated Systems

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3-(Vinyl-/buta-1,3-dien-1-yl/4-phenylbuta-1,3-dien-1-yl)-4-chloro quinolines and quinolin-4(1*H*)-ones were synthesized by ultrasound-assisted Wittig reaction of the corresponding 4-chloro-3-formylquinoline and 3-formylquinolin-4(1*H*)-ones with nonstabilized ylides. Ease execution, mild conditions, and high yields make this method exploitable for the generation of libraries of 3-substituted 4-chloroquinolines and quinolin-4(1*H*)-ones with extended π-conjugated systems. To demonstrate the usefulness of these compounds as precursors for the synthesis of more complex structures, 3-vinylquinolin-4(1*H*)-ones were used as dienes in the Diels–Alder reaction with *N*-methylmaleimide to produce novel acridone derivatives. The attempted Diels–Alder reaction with 3-(buta-1,3-dien-1-yl)quinolin-4(1*H*)-one did not afford the expected cycloadduct; instead, 2-methyl-2*H*-pyrano[3,2-*c*] quinoline was obtained. The structures and stereochemistry of the new compounds were established by NMR studies.

1. Introduction

Quinolines (**I**), also known as 1-azanaphthalene or benzo[*b*] pyridine, are aromatic nitrogen heterocyclic compounds of natural or synthetic origin (Figure 1). These compounds were first isolated in 1834 by Runge from coal tar, which has remained the main source of commercial quinoline [1]. The reactivity of quinolines as well as their physicochemical and biological properties have always attracted the attention of researchers. For instance, quinolines behave as weak tertiary amine bases, can form salts with acids, and undergo reactions similar to those of pyridine and benzene [2–5]. Moreover, quinolines have been found to possess antimalarial, antibacterial, antifungal, anticancer, and anti-HIV activities [6]. The most common quinoline-related derivatives are the 4-quinolones (**II**) (or quinolin-4(1*H*)-ones, Figure 1) [7]. Since the discovery of nalidixic acid in the early 1960s by Lescher and his colleagues, the use and development of 4-quinolones have increased impressively [8–14]. 4-Quinolones consist of an aromatic ring fused with a pyridine ring with a nitrogen atom at position 1 and a ketone group at C-4 [8, 9].

Quinolones and their analogues are ubiquitous in nature and synthetically accessible. They play a very important role in organic synthesis, as evidenced by the huge number of synthetic methods developed to achieve these scaffolds and for their synthetic modifications [15–17], and are well recognized for their remarkable pharmacological activities, such as antibacterial, anti-inflammatory, antifungal, antioxidant, antimalarial, anticancer, and anti-HIV, among other important activities [18, 19]. In particular, 2-vinyl-(**III**) and 2-alkenyl (**IV**) derivatives of 4-quinolones (Figure 1), which were identified from a Chinese *Pseudomonas aeruginosa* isolate, are known to possess interesting antimicrobial activities [20]. Since this discovery, related compounds have been synthesized for biological studies [21], but to the best of

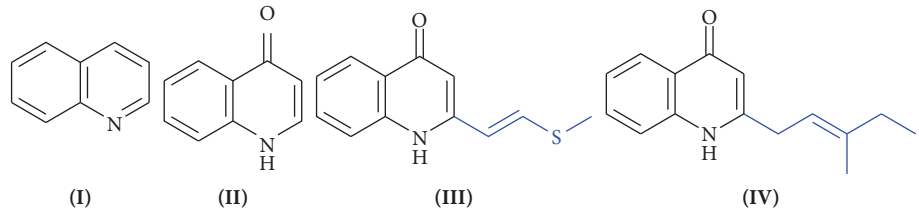


Figure 1: Structures of quinoline (**I**), quinolin-4(1*H*)-one (**II**), and the two natural derivatives (*E*)-2-[2-(methylthio)vinyl]quinolin-4(1*H*)-one (**III**) and (*E*)-2-(3-methylpent-2-en-1-yl)quinolin-4(1*H*)-one (**IV**).

our knowledge, studies on the isomeric 3-substituted (3-vinyl and 3-alkenyl) derivatives are rare.

Despite the interesting structure of vinyl- and alkenyl-quinolones, access to these molecules remains very restricted, limiting their use in organic synthesis. As far as we know, only a few studies have been carried out in this field [22–24]. In 2012, Bach and coworkers reported the use of the Wittig reaction in the synthesis of some 3-vinyl- and 3-alkenyl-2-quinolones from 3-formyl-2-quinolone. The exocyclic double bond of the formed product undergoes enantio- and regioselective epoxidation catalyzed by a ruthenium(II) porphyrin [22]. Coppola reported the formation of 3-vinyl-4-quinolones via the Horner reaction of phosphonates with aldehydes [23]. In 2018, Boháč and coworkers described an efficient method for the synthesis of 2*H*-pyrano[3,2-*c*]quinolin-2-ones from 3-formyl-4-quinolones and monosubstituted acetic acid. The treatment of the obtained products with a solution of sodium hydroxide led to the formation of 3-(2-arylvinyl)-4-quinolones containing a carboxylic acid group at the β-position [24]. Based on these works, we envisioned that 3-formyl(quinoline and quinolones) (Figure 2) can be suitable substrates for the preparation of their corresponding highly conjugated 3-vinyl and 3-buta-1,3-dien-1-yl derivatives via Wittig reactions with nonstabilized ylides.

The advantages of ultrasound-assisted synthesis over conventional thermal methods, such as high reaction rates, better yields, high purity of the products, and high product selectivity, have been reported in recent publications [25, 26]. Moreover, ultrasound-assisted synthesis is considered more environmentally friendly and cost-effective [27]. In fact, ultrasonic irradiation has been used to assist diverse reactions at ambient temperature [28], in aqueous media [29], or using ionic liquids [30] as an alternative to organic solvents, as well as catalyst-free organic reactions for the synthesis of biologically relevant heterocycles, including the synthesis of dihydroquinolines and diverse fused quinolone derivatives [31]. Therefore, we have also explored the benefits of ultrasound irradiation to promote the Wittig reactions studied in this work.

2. Materials and Methods

2.1. General. Reagents and solvents were purchased as reagent-grade and used without further purification unless otherwise stated. Methyltriphenylphosphonium bromide (CAS 1779-49-3), allyltriphenylphosphonium bromide (CAS 1560-54-9), and cinnamyltriphenylphosphonium bromide (CAS 7310-74-9) were purchased from Sigma-Aldrich. Ethyl 3-formyl-6-methoxyquinolone-1(4*H*)-carboxylate (**2c**) was available in our laboratory. Melting points were determined with a Büchi melting point B-540 apparatus and are uncorrected. NMR spectra were recorded with 300 or 500 MHz (300.13 MHz (^{1}H), 75.47 MHz (^{13}C), or 500.16 MHz (^{1}H), 125.77 MHz (^{13}C)) Bruker Avance III NMR spectrometers, with tetramethylsilane (TMS) as the internal reference and $CDCl_3$ as the solvent, unless otherwise stated. Unequivocal ^{1}H assignments (δ, ppm) and ^{13}C assignments (δ, ppm) were made based on NOESY and 2D *g*HSQC (^{1}H/^{13}C) and *g*HMBC (delays for one-bond and long-range $J_{C/H}$ couplings were optimised for 145 and 7 Hz, respectively) experiments. Positive-ion electrospray (ESI^+) mass spectra were performed using a linear ion trap mass spectrometer LXQ (ThermoFinnigan, San Jose, CA). Data acquisition and analysis were performed using the Xcalibur Data System (version 2.0, ThermoFinnigan, San Jose, CA). High-mass-resolving ESI-MS were conducted in a *Q*-Exactive® hybrid quadrupole Orbitrap® mass spectrometer (Thermo Fisher Scientific, Bremen, Germany). The instrument was operated in positive mode with a spray voltage at 3.0 kV and interfaced with a HESI II ion source. The analysis was performed through direct infusion of the prepared solutions at a flow rate of 10 μL·min^{-1} into the ESI source, and the operating conditions were as follows: sheath gas (nitrogen) flow rate 5 (arbitrary units), auxiliary gas (nitrogen) 1 (arbitrary units), capillary temperature 320°C, and S-lens rf level 50. Spectra were analysed using the acquisition software Xcalibur version 4.0 (Thermo Scientific, San Jose, CA, USA).

2.2. Preparation Procedure of the Target Compounds 1, 2a-2b. The synthesis of 4-chloroquinoline-3-carbaldehyde (**1**) was performed following a procedure already reported in the literature [32]. The compound was obtained as a yellow solid with a 66% yield at mp 138-139°C (mp 141-142°C, Lit.) [33]. Structural characterization data (^{1}H and ^{13}C NMR spectra) of this compound are presented in the Electronic Supporting Information (ESI).

The synthesis of 4-oxo-1,4-dihydroquinoline-3-carbaldehyde (**2a**) was performed following a procedure already reported in the literature [32]. The compound was obtained as a yellow solid in 96% yield, mp 260–275°C (decomposition) (mp > 278°C (decomposition), Lit.) [32]. Structural characterization data (^{1}H and ^{13}C NMR spectra) of this compound are presented in the ESI.

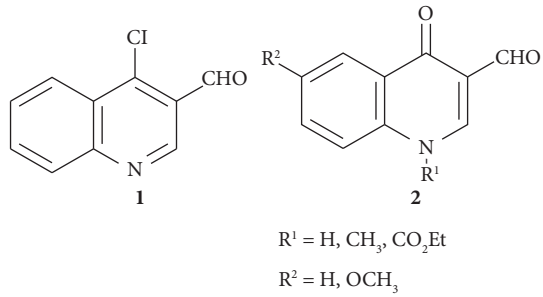


Figure 2: Structures of 3-formyl (quinoline **1** and 4-quinolones **2**) used in the Wittig reactions.

2.2.1. Synthesis of 1-Methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde (2b). NaH (69.1 mg, 2.88 mmol) was added to a stirred suspension of 4-oxo-1,4-dihydroquinoline-3-carbaldehyde (**2a**) (500 mg, 2.88 mmol) in anhydrous THF (40 mL), and the mixture was stirred at room temperature for 30 min. After that period, excess CH_3I (3.62 ml, 58.2 mmol) was added, and the reaction mixture was stirred for 22 h. Then, it was poured over H_2O (20 mL), ice (20 g), and Et_3N and acidified with HCl to pH 6. The obtained solution was extracted with $CHCl_3$ (3×50 mL), dried with anhydrous Na_2SO_4, and concentrated to dryness. Compound **2b** was obtained as a white solid (523 mg, 97% yield), mp 207–209°C (mp 212-213°C, Lit.) [23]. Structural characterization data (^{1}H and ^{13}C NMR spectra) of this compound are presented in the ESI.

2.2.2. General Procedure for the Wittig Reaction of 4-Chloroquinoline-3-carbaldehyde (1) with Ylides 4a and 4b. A mixture of NaH (2.6 mmol, 62.4 mg) and the appropriate triphenylphosphonium bromide salt (1.3 mmol), in freshly dried THF (10 mL), was stirred in the ultrasound bath under nitrogen for 25–45 min at room temperature; the appearance of a yellow to red color (depending on the triphenylphosphonium bromide salt used) and disappearance of the suspension of the phosphonium salt indicated the ylide formation. Subsequently, 4-chloroquinoline-3-carbaldehyde (**1**) (0.26 mmol) was added. The mixture was stirred at room temperature until the complete consumption of the starting 4-chloroquinoline-3-carbaldehyde (**1**). After, the reaction mixture was poured onto ice (20 g) and water (20 mL), and the pH was adjusted to 4-5 with diluted (10%) hydrochloric acid. The organic layer was extracted with $CHCl_3$ (3×50 mL), dried with anhydrous Na_2SO_4 and the organic solvent was evaporated to dryness.

2.2.3. Data for Compound 4-Chloro-3-vinylquinoline (5a). Yield: 50% (24.7 mg), white solid crystals obtained after purification by TLC (EtOAc/hexane, 6 : 4), mp 91.4°C. ^{1}H NMR ($CDCl_3$, 300.13 MHz): $\delta = 9.06$ (s, 1H, H-2), 8.27 (ddd, *J* 8.3, 1.5, 0.6 Hz, 1H, H-5), 8.10 (dd, *J* 8.3, 1.2 Hz, 1H, H-8), 7.73 (ddd, *J* 8.3, 6.9, 1.5 Hz, 1H, H-7), 7.64 (ddd, *J* 8.3, 6.9, 1.2 Hz, 1H, H-6), 7.24 (dd, *J* 17.7, 11.3 Hz, 1H, H-α), 6.00 (d, *J* 17.7 Hz, 1H, H-β), 5.61 (dd, *J* 11.3, 0.5 Hz, 1H, H-β'). ^{13}C NMR ($CDCl_3$, 75.47 MHz): $\delta = 148.1$ (C-2), 147.8 (C-8a), 139.8 (C-4), 131.0 (C-α), 130.0 (C-7), 129.4 (C-8), 128.2 (C-3), 128.0 (C-6), 126.3 (C-4a), 124.5 (C-5), and 119.0 (C-β). MS (ESI$^+$): *m*/*z* (%) = 192 (^{37}Cl, 33) $[M+H]^+$; 190 (^{35}Cl, 100) $[M+H]^+$. HRMS (ESI$^+$): *m*/*z* $[M+H]^+$ calcd for $C_{11}H_9ClN$: 190.0418; found: 190.0405.

2.2.4. Data for Compound (1Z,3E)-3-(Buta-1,3-dien-1-yl)-4-chloroquinoline (5b). Yield: 63% (35.3 mg), white crystals obtained after purification by TLC (hexane/EtOAc, 8 : 2 then 7 : 3), mp 85.7°C. ^{1}H NMR ($CDCl_3$, 300.13 MHz): $\delta = 8.86$ (s, 1H, H-2), 8.28 (dd, *J* 8.4, 1.5 Hz, 1H, H-5), 8.11 (d, *J* 8.4 Hz, 1H, H-8), 7.76 (ddd, *J* 8.4, 6.9, 1.5 Hz, 1H, H-7), 7.65 (ddd, *J* 8.4, 6.9, 1.3 Hz, 1H, H-6), 6.74–6.51 (m, 3H, H-γ, H-α, H-β), 5.55–5.48 (m, 1H, H-δ), 5.38–5.30 (m, 1H, H-δ). ^{13}C NMR ($CDCl_3$, 75.47 MHz): $\delta = 151.2$ (C-2), 147.7 (C-8a), 140.6 (C-4), 133.9 (C-β), 132.3 (C-γ), 130.0 (C-7), 129.6 (C-8), 128.9 (C-3), 127.9 (C-6), 126.3 (C-4a), 124.3 (C-α), 124.2 (C-5), and 122.1 (C-δ). MS (ESI$^+$): *m*/*z* (%) = 218 (^{37}Cl, 33) $[M+H]^+$; 216 (^{35}Cl, 100) $[M+H]^+$. HRMS (ESI$^+$): *m*/*z* $[M+H]^+$ calcd for $C_{13}H_{11}ClN$: 216.0575; found: 216.0577.

2.2.5. Data for Compound (1E,3E)-3-(Buta-1,3-dien-1-yl)-4-chloroquinoline (6b). Yield: 20% (11.2 mg), obtained after purification by TLC (hexane/EtOAc, 8 : 2 then 7 : 3), mp 60°C. ^{1}H NMR ($CDCl_3$, 500.16 MHz): $\delta = 9.09$ (s, 1H, H-2), 8.26 (dd, *J* 8.2, 1.3 Hz, 1H, H-5), 8.09 (d, *J* 8.4 Hz, 1H, H-8), 7.72 (ddd, *J* 8.4, 6.9, 1.3 Hz, 1H, H-7), 7.64 (ddd, *J* 8.2, 6.9, 1.2 Hz, 1H, H-6), 7.12–6.98 (m, 2H, H-α, H-γ), 6.67–6.60 (m, 1H, H-β), 5.54–5.49 (m, 1H, H-δ), 5.36 (d, *J* 10.0 Hz, 1H, H-δ). ^{13}C NMR ($CDCl_3$, 125.77 MHz): $\delta = 147.9$ (C-2), 147.6 (C-8a), 139.5 (C-4), 136.8 (C-β), 133.9 (C-γ), 129.9 (C-7), 129.6 (C-8), 128.0 (C-6), 127.8 (C-3), 126.4 (C-4a), 126.3 (C-α), 124.5 (C-5), and 120.5 (C-δ). MS (ESI$^+$): *m*/*z* (%) = 433 (^{37}Cl, 59) $[2M+H]^+$, 431 (^{35}Cl, 93) $[2M+H]^+$, 218 (^{37}Cl, 38) $[M+H]^+$, 216 (^{35}Cl, 100) $[M+H]^+$. HRMS (ESI$^+$): *m*/*z* $[M+H]^+$ calcd for $C_{13}H_{11}ClN$: 216.0575; found: 216.0582.

2.2.6. General Procedure for the Wittig Reaction of 4-Chloroquinoline-3-carbaldehyde (1) with Ylide 4c. A mixture of NaH (1.1 mmol, 26.4 mg) and the appropriate

triphenylphosphonium bromide salt **3c** (0.55 mmol), in freshly dried THF (10 mL), was stirred in the ultrasound bath under nitrogen for 45 min at room temperature; the appearance of a red to brown color and disappearance of the suspension of the phosphonium salt indicated the ylide formation. Subsequently, 4-chloroquinoline-3-carbaldehyde (**1**) (0.11 mmol) was added, and the mixture was stirred at room temperature until the complete consumption of the starting material. After, the reaction mixture was poured onto ice (20 g) and water (20 mL), and the pH was adjusted to 4-5 with diluted (10%) hydrochloric acid. The organic layer was extracted with $CHCl_3$ (3×50 mL), dried with anhydrous Na_2SO_4 and the organic solvent was evaporated to dryness.

2.2.7. Data for Compound (1Z,3E)-4-Chloro-3-(4-phenylbuta-1,3-dien-1-yl)quinoline (5c). Yield: 60% (19.2 mg), obtained after purification by TLC (hexane/EtOAc, 8 : 2), mp 108-109°C. ^{1}H NMR ($CDCl_3$, 300.13 MHz): $\delta = 8.98$ (s, 1H, H-2), 8.29 (dd, *J* 8.3, 1.5 Hz, 1H, H-5), 8.13 (dd, *J* 8.4, 1.3 Hz, 1H, H-8), 7.77 (ddd, *J* 8.4, 6.9, 1.5 Hz, 1H, H-7), 7.66 (ddd, *J* 8.3, 6.9, 1.3 Hz, 1H, H-6), 7.38 (dd, *J* 8.2, 1.7 Hz, 2H, H-2′, 6′), 7.33–7.21 (m, 3H, H-4′, 3′, 5′), 7.20–7.06 (m, 1H, H-γ), 6.83 (d, *J* 15.4 Hz, 1H, H-δ), 6.71 (dd, *J* 5.1, 1.7 Hz, 2H, H-α, H-β). ^{13}C NMR ($CDCl_3$, 75.47 MHz): $\delta = 151.2$ (C-2), 147.7 (C-8a), 140.6 (C-4), 137.2 (C-δ), 136.6 (C-1′), 133.5 (C-β), 130.0 (C-7), 129.7 (C-8), 129.2 (C-3), 128.8 (C-3′, 5′), 128.3 (C-4′), 127.9 (C-6), 126.9 (C-2′, 6′), 126.5 (C-4a), 124.2 (C-5), 124.0, and 123.9 (C-α and C-γ). MS (ESI$^+$): *m*/*z* (%) = 294 (^{37}Cl, 29) $[M+H]^+$; 292 (^{35}Cl, 87) $[M+H]^+$. HRMS (ESI$^+$): *m*/*z* $[M+H]^+$ calcd for $C_{19}H_{15}ClN$: 292.0888; found: 292.0874.

2.2.8. Data for Compound (1E,3E)-4-Chloro-3-(4-phenylbuta-1,3-dien-1-yl)quinoline (6c). Yield: 39% (12.4 mg), yellow crystals obtained after purification by TLC (hexane/EtOAc, 8 : 2), mp 151–153°C. ^{1}H NMR ($CDCl_3$, 300.13 MHz): $\delta = 9.03$ (s, 1H, H-2), 8.14 (dd, *J* 8.4, 1.4 Hz, 1H, H-5), 7.97 (dd, *J* 8.4, 1.2 Hz, 1H, H-8), 7.60 (dt, *J* 8.4, 6.9, 1.4, 1H, H-7), 7.52 (td, *J* 8.4, 6.9, 1.2 Hz, 1H, H-6), 7.38 (dd, *J*7.7, 1.5 Hz, 2H, H-2′, 6′), 7.26 (t, *J* 7.7 Hz, 2H, H-3′, 5′), 7.17 (tt, *J* 7.7, 1.5 Hz, 1H, H-4′), 7.11–7.03 (m, 2H, H-α, H-β), 6.96 (ddd, *J* 15.1, 6.1, 3.9 Hz, 1H, H-γ), 6.72 (*d*, *J* 15.1, 1H, H-δ). ^{13}C NMR ($CDCl_3$, 75.47 MHz): $\delta = 148.0$ (C-2), 147.6 (C-8a), 139.0 (C-4), 136.8 (C-1′), 135.6 (C-δ), 133.5 (C-β), 129.7 (C-7), 129.6 (C-8), 128.8 (C-3′, 5′ and C-γ), 128.2 (C-4′), 128.1 (C-3), 128.0 (C-6), 126.8 (C-2′, 6′), 126.5 (C-4a), 126.0 (C-α), and 124.5 (C-5). MS (ESI$^+$): *m*/*z* (%) = 294 (^{37}Cl, 32) $[M+H]^+$; 292 (^{35}Cl, 100) $[M+H]^+$. HRMS (ESI$^+$): *m*/*z* $[M+H]^+$ calcd for $C_{19}H_{15}ClN$: 292.0888; found: 292.0874.

2.2.9. General Procedure for the Wittig Reaction of 4-Oxo-1,4-dihydroquinoline-3-carbaldehyde (2a) and 1-Methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde (2b) with Ylides 4a–4c. A mixture of NaH (10 equiv) and the appropriate triphenylphosphonium bromide salt (5 equiv) in freshly dried THF (25 mL) was stirred in the ultrasound bath under nitrogen for 45–90 min (depending on the triphenylphosphonium bromide salt used) at room temperature. The appearance of an orange, red, brown, or yellow color and the disappearance of the suspension of the phosphonium salt indicated ylide formation. Subsequently, 4-oxo-1,4-dihydroquinoline-3-carbaldehyde (**2a**) (0.78 mmol for **7a, 8d** and 0.11 mmol for **8f**), 1-methyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde (**2b**) (0.78 mmol for **7b**, 0.39 mmol for **7e,** and 0.11 mmol for **7g**), or ethyl 3-formyl-6-methoxy-4-oxoquinoline-1(4*H*)-carboxylate (**2c**) (0.36 mmol) was added. The mixture was stirred normally at room temperature until the total consumption of the starting material was reached. After, the reaction mixture was poured onto ice (20 g) and water (20 mL), and the pH was adjusted to 4-5 with dilute (10%) hydrochloric acid. The organic layer was extracted with $CHCl_3$ (3×50 mL), dried with anhydrous Na_2SO_4 and the organic solvent was evaporated to dryness.

2.2.10. Data for Compound 3-Vinylquinolin-4(1H)-one (7a). Yield: 97% (130 mg), white crystals obtained after purification by TLC ($CHCl_3$/acetone, 8 : 2), mp 210.2°C. ^{1}H NMR (CD_3OD, 300.13 MHz): $\delta = 8.32$ (ddd, *J* 8.2, 1.5, 0.6 Hz, 1H, H-5), 8.17 (s, 1H, H-2), 7.69 (ddd, *J* 8.3, 6.9, 1.5 Hz, 1H, H-7), 7.57 (d, *J* 8.3 Hz, 1H, H-8), 7.42 (ddd, *J* 8.2, 6.9, 1.2 Hz, 1H, H-6), 6.90 (dd, *J* 17.8, 11.4 Hz, 1H, H-α), 6.00 (dd, *J* 17.8, 1.8 Hz, 1H, H-β), and 5.24 (dd, *J* 11.4, 1.8 Hz, 1H, H-β'). ^{13}C NMR (CD_3OD, 75.47 MHz): $\delta = 176.9$ (C-4), 139.1 (C-8a), 137.5 (C-2), 131.7 (C-7), 130.2 (C-α), 125.4 (C-4a), 125.2 (C-5), 123.9 (C-6), 118.4 (C-3), 118.0 (C-8), and 112.4 (C-β). MS (ESI$^+$): *m*/*z* (%) = 172 (100) $[M+H]^+$. HRMS (ESI$^+$): *m*/*z* $[M+H]^+$ calcd for $C_{11}H_{10}NO$: 172.0757; found: 172.0760.

2.2.11. Data for Compound 1-Methyl-3-vinylquinolin-4(1H)-one (7b). Yield: 96% (139 mg), obtained after purification by TLC (CH_2Cl_2), 175–235°C (decomposition). ^{1}H NMR ($CDCl_3$, 300.13 MHz): $\delta = 8.47$ (dd, *J* 8.3, 1.7 Hz, 1H, H-5), 7.65–7.59 (m, 1H, H-7), 7.62 (s, 1H, H-2), 7.39–7.34 (m, 2H, H-6,8), 6.78 (dd, *J* 17.7, 11.3 Hz, 1H, H-α), 6.03 (dd, *J* 17.7, 1.8 Hz, 1H, H-β), 5.23 (dd, *J* 11.3, 1.8 Hz, 1H, H-β'), and 3.80 (s, 3H, NCH_3). ^{13}C NMR ($CDCl_3$, 75.47 MHz): $\delta = 176.2$ (C-4), 141.7 (C-2), 139.6 (C-8a), 131.9 (C-7), 130.5 (C-α), 127.2 (C-5), 126.8 (C-4a), 123.8 (C-6), 118.7 (C-3), 115.2 (C-8), 113.6 (C-β), and 40.9 (NCH_3). MS (ESI$^+$): *m*/*z* (%) = 186 (100) $[M+H]^+$.

2.2.12. Data for Compound 6-Methoxy-3-vinylquinolin-4(1H)-one (7c). Yield: 98% (71 mg), yellow crystals obtained after purification by TLC (EtOAc/acetone, 9 : 1), mp 128–130°C. ^{1}H NMR (CD_3OD, 300.13 MHz): $\delta = 8.14$ (s, 1H, H-2), 7.72 (d, *J* 2.9 Hz, 1H, H-5), 7.54 (d, *J* 9.1 Hz, 1H, H-8), 7.34 (dd, *J* 9.1, 2.9 Hz, 1H, H-7), 6.93 (dd, *J* 17.8, 11.4 Hz, 1H, H-α), 5.98 (dd, *J* 17.8, 1.8 Hz, 1H, H-β), 5.24 (dd, *J* 11.4, 1.8 Hz, 1H, H-β'), 3.93 (s, 3H, 6-OCH_3). ^{13}C NMR (CD_3OD, 75.47 MHz): $\delta = 176.0$ (C-4), 157.0 (C-6), 136.5 (C-2), 133.9 (C-8a), 130.3 (C-α), 126.4 (C-4a), 122.9 (C-7), 119.7 (C-8), 117.5 (C-3), 112.2 (C-β), 103.8 (C-5), and 54.7 (6-OCH_3). MS

(ESI$^+$): m/z (%) = 202 (100) $[M+H]^+$. HRMS (ESI$^+$): m/z $[M+H]^+$ calcd for $C_{12}H_{12}NO_2$: 202.0863; found: 202.0869.

2.2.13. Data for Compound (1E,3E)-3-(Buta-1,3-dien-1-yl) quinolin-4(1H)-one (8d). ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 12.44 (s, 1H, N*H*), 8.41–8.30 (dd, *J* 8.2, 1.3 Hz, 1H, H-5), 7.21 (ddt, *J* 8.2, 6.8, 1.3, 2H, H-6,7), 6.67–6.50 (m, 2H), 6.19 (t, *J* 11.3 Hz, 1H), 5.08–4.93 (m, 1H), and 5.30–5.17 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ = 177.2 (C-4), 139.7, 138.3, 133.3, 133.0, 131.6, 131.3, 129.2, 129.0, 126.0, 125.6, 125.0, 123.3, 118.4, 118.3, 117.9. MS (ESI$^+$): m/z (%) = 395 (10) $[2M+H]^+$; 198 (100) $[M+H]^+$.

2.2.14. Data for Compound (1Z,3E)-3-(Buta-1,3-dien-1-yl)-1-methylquinolin-4(1H)-one (7e). Yield: 83% (68.4 mg), white crystals obtained after purification by TLC (CH_2Cl_2/acetone, 9 : 1), mp 153.1°C. ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 8.51 (dd, *J* 8.4, 1.6 Hz, 1H, H-5), 7.72–7.66 (m, 1H, H-7), 7.66 (br s, 1H, H-2), 7.43–7.38 (m, 2H, H-6,8), 6.75 (dddd, *J* 16.9, 11.4, 10.1, 1.2 Hz, 1H, H-γ), 6.61 (dt, *J* 11.4, 1.2 Hz, 1H, H-α), 6.32 (tt, *J* 11.4, 0.9 Hz, 1H, H-β), 5.38 (ddt, *J* 16.9, 1.8, 0.9 Hz, 1H, H-δ), 5.25–5.11 (m, 1H, H-δ), 3.85 (s, 3H, NCH_3). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ = 176.5 (C-4), 143.0 (C-2), 139.9 (C-8a), 133.0 (C-γ), 132.0 (C-7), 129.8 (C-β), 127.0 (C-5), 126.3 (C-4a), 124.1 (C-α), 123.7 (C-6), 119.0 (C-δ), 118.5 (C-3), 115.4 (C-8), 40.9 (NCH_3). MS (ESI$^+$): m/z (%) = 212 (100) $[M+H]^+$. HRMS (ESI$^+$): m/z $[M+H]^+$ calcd for $C_{14}H_{14}NO$: 212.1070; found: 212.1056.

2.2.15. Data for Compound (1E,3E)-3-(4-Phenylbuta-1,3-dien-1-yl)quinolin-4(1H)-one (8f). Yield: 96% (28.9 mg), yellow solid obtained after purification by TLC ($CHCl_3$/acetone, 8 : 2), 292–294°C. ^{1}H NMR (DMSO-d_6, 300.13 MHz): δ = 12.14 (d, *J* 6.3 Hz, 1H, N*H*), 8.24 (d, *J* 6.3 Hz, 1H, H-2), 8.19 (dd, *J* 8.2, 1.5 Hz, 1H, H-5), 7.65 (ddd, *J* 8.4, 6.8, 1.5 Hz, 1H, H-7), 7.59–7.52 (m, 1H, H-8), 7.58–7.48 (m, 1H, H-β), 7.51 (d, *J* 7.1 Hz, 2H, H-2′, 6′), 7.35 (m, 3H, H-6, H-3′, 5′), 7.28–7.18 (m, 1H, H-4′), 7.05 (dd, *J* 15.6, 10.8 Hz, 1H, H-γ), 6.78 (d, *J* 15.6 Hz, 1H, H-α), 6.62 (d, *J* 15.6 Hz, 1H, H-δ). ^{13}C NMR (DMSO-d_6, 75.47 MHz): δ = 175.5 (C-4), 139.0 and 138.9 (C-2 and C-8a), 137.9 (C-1′), 131.9 (C-7), 131.5 (C-γ), 130.6 (C-δ), 129.1 (C-3′, 5′), 129.0 (C-α), 128.3 (C-β), 127.6 (C-4′), 126.5 (C-2′, 6′), 125.9 (C-5), 125.7 (C-4a), 124.0 (C-6), 118.9 (C-8), 117.4 (C-3). MS (ESI$^+$): m/z (%) = 547 (100) $[2M+H]^+$; 274 (100) $[M+H]^+$. HRMS (ESI$^+$): m/z $[M+H]^+$ calcd for $C_{19}H_{16}NO$: 274.1226; found: 274.1208.

2.2.16. Data for Compound (1Z,3E)-1-Methyl-3-(4-phenylbuta-1,3-dien-1-yl)quinolin-4(1H)-one (7g). Yield: 45% (14.1 mg), yellow residue obtained after purification by column chromatography (CH_2Cl_2 and then CH_2Cl_2/acetone 9 : 1), mp 218–220°C. ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 8.54 (dd, *J* 8.3, 1.4 Hz, 1H, H-5), 7.72 (s, 1H, H-2), 7.71 (ddd, *J* 8.3, 7.6, 1.4 Hz, 1H, H-7), 7.44 (d, *J* 7.6 Hz, 1H, H-8), 7.42–7.34 (m, 1H, H-6), 7.39 (d, *J* 7.2 Hz, 2H, H-2′, 6′), 7.31 (t, *J* 7.2 Hz, 2H, H-3′, 5′), 7.22 (m, 1H, H-4′), 7.15 (dd, *J* 16.0, 11.0 Hz, 1H, H-γ), 6.73 (d, *J* 16.0 Hz, 1H, H-δ), 6.68 (d, *J* 11.0 Hz, 1H, H-α), 6.48 (t, *J* 11.0 Hz, 1H, H-β), 3.88 (s, 3H, NCH_3). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ = 176.7 (C-4), 143.0 (C-2), 139.9 (C-8a), 137.5 (C-1′), 134.1 (C-δ), 132.2 (C-7), 129.5 (C-β), 128.7 (C-3′,5′), 127.6 (C-4′), 127.5 (C-5), 126.5 (C-2′,6′), 126.3 (C-4a), 125.1 (C-γ), 124.4 (C-α), 123.9 (C-6), 119.2 (C-3), 115.3 (C-8), 41.0 (NCH_3). MS (ESI$^+$): m/z (%) = 575 (35) $[2M+H]^+$; 288 (100) $[M+H]^+$. HRMS (ESI$^+$): m/z $[M+H]^+$ calcd for $C_{20}H_{18}NO$: 288.1383; found: 288.1383.

2.2.17. General Procedure for the Diels–Alder Reaction of 3-Vinylquinolin-4(1H)-ones 7a, 7b with N-Methylmaleimide 9. To a solution of the appropriate 3-vinylquinolin-4(1*H*)-one **7a, 7b** (0.29 mmol) in dry toluene (20 mL), *N*-methylmaleimide **9** (1.45 mmol, 161 mg) was added, and the mixture was heated at reflux for 1.5 h. Then, chloranil (1.45 mmol, 356 mg) was added and the mixture was heated for more 20 h. After that period, the solvent was removed under reduced pressure, and the obtained residue was dissolved in chloroform and purified by thin-layer chromatography.

2.2.18. Data for Compound 2-Methyl-1H-pyrrolo[3,4-c]acridine-1,3,6(2H,11H)-trione (11a). Yield 37% (30 mg), dark yellow residue obtained after purification by TLC (hexane/acetone, 6 : 4). ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 9.67 (br s, 1H, N*H*), 8.80 (d, *J* 7.9 Hz, 1H, H-5), 8.47 (dd, *J* 7.4, 1.3 Hz, 1H, H-10), 7.76 (ddd, *J* 8.3, 7.4, 1.5 Hz, 1H, H-9), 7.66 (d, *J* 7.9 Hz, 1H, H-4), 7.43 (d, *J* 8.3 Hz, 1H, H-7), 7.37 (ddd, 1H, *J* 8.3, 7.4, 1.3 Hz, 1H, H-8), 3.25 (s, 3H, NCH_3). ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ = 177.2 (C-6), 169.7 (C-3), 167.8 (C-1), 140.1 (C-10a), 136.8 (C-11a), 136.2 (C-3a), 135.2 (C-5), 134.8 (C-9), 127.7 (C-10), 125.6 (C-5a), 123.2 (C-8), 122.3 (C-6a), 117.1 (C-7), 115.9 (C-11b), 115.1 (C-4), 29.4 (NCH_3). MS (ESI$^+$): m/z (%) = 301(15) $[M+Na]^+$; 279 (100) $[M+H]^+$. HRMS (ESI$^+$): m/z $[M+H]^+$ calcd for $C_{16}H_{11}N_2O_3$: 279.0765; found: 279.0764.

2.2.19. Data for Compound 2,11-Dimethyl-1H-pyrrolo[3,4-c] acridine-1,3,6(2H,11H)-trione (11b). Yield: 45% (38.1 mg), orange solid obtained after purification by TLC (two elutions with hexane: EtOAc, 7 : 3, then 8 : 2), mp 221-222°C. ^{1}H NMR ($CDCl_3$, 500.13 MHz): δ = 8.90 (d, *J* 7.7 Hz, 1H, H-5), 8.47 (dd, *J* 8.3, 1.4 Hz, 1H, H-10), 7.82 (ddd, *J* 8.3, 7.1, 1.7 Hz, 1H, H-9), 7.75 (d, *J* 7.7 Hz, 1H, H-4), 7.60 (d, *J* 8.3 Hz, 1H, H-7), 7.40 (ddd, *J* 8.3, 7.1, 1.4 Hz, 1H, H-8), 4.11 (s, 3H, NCH_3), 3.24 (s, 3H, NCH_3). ^{13}CNMR ($CDCl_3$, 125.77 MHz): δ = 177.5 (C-6), 167.5 (C-1), 167.2 (C-3), 144.6 (C-10a), 141.3 (C-11a), 138.8 (C-3a), 135.4 (C-5), 134.9 (C-9), 128.4 (C-5a), 127.5 (C-10), 123.3 (C-6a), 123.2 (C-8), 118.0 (C-11b), 116.9 (C-7), 115.7 (C-4), 43.9 (NCH_3), 24.4 (NCH_3). MS (ESI$^+$): m/z (%) = 293 (18) $[M+H]^+$. HRMS (ESI$^+$): m/z $[M+H]^+$ calcd for $C_{17}H_{13}N_2O_3$: 293.0921; found: 293.0921.

2.2.20. Data for Compound 2-Methyl-2H-pyrano[3,2-c] quinoline (14). Yield: 23% (9.0 mg) obtained after purification by TLC (EtOAc/hexane, 3 : 2). ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ = 8.49 (s, 1H, H-5), 8.10 (dd, *J* 8.2, 1.5 Hz, 1H, H-10), 7.96 (dd, *J* 8.5, 1.1 Hz, 1H, H-7), 7.64 (ddd, *J* 8.5, 6.9, 1.5 Hz, 1H, H-8), 7.46 (ddd, *J* 8.2, 6.9, 1.1 Hz, 1H, H-9), 6.53 (dd, *J* 9.9, 1.7 Hz, 1H, H-4), 5.71 (dd, *J* 9.9, 3.3 Hz, 1H, H-3), 5.34 (qdd, *J* 6.6, 3.3, 1.7 Hz, 1H, H-2), 1.57 (d, *J* 6.6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ = 156.1 (C-10b), 149.4 (C-6a), 148.7 (C-5), 129.7 (C-8), 129.0 (C-7), 125.7 (C-9), 125.4 (C-3), 121.7 (C-10), 120.7 (C-4), 120.1 (C-10a), 111.9 (C-4a), 73.5 (C-2), and 22.0 (CH_3). MS (ESI$^+$): *m*/*z* (%) = 198 (87) $[M+H]^+$. HRMS (ESI$^+$): *m*/*z* $[M+H]^+$ calcd for $C_{13}H_{12}NO$: 198.0913; found: 198.0901.

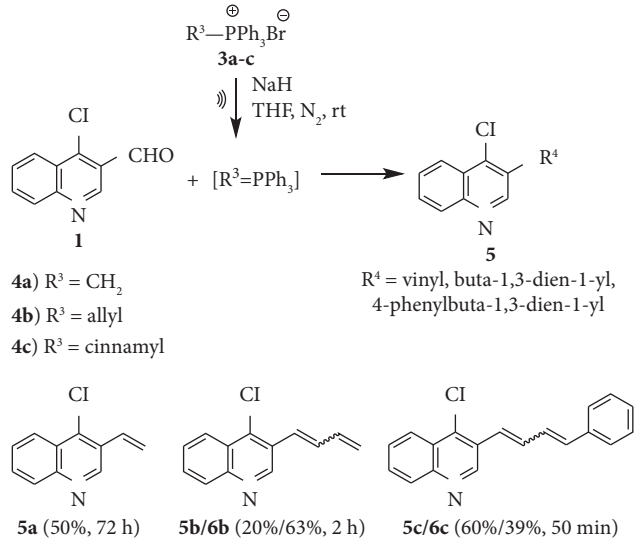
3. Results and Discussion

3.1. Chemistry. The Wittig reaction of 4-chloro-3-formylquinoline **1** with methyltriphenylphosphorane **4a** was initially attempted using the conditions reported by Seixas et al. for the synthesis of 4-chloro-3-styrylquinolines [32, 33]. In the first step, the methyltriphenylphosphorane was prepared from the reaction of the methyltriphenylphosphonium bromide **3a** with 1 molar equiv of sodium hydride (NaH) in freshly dried tetrahydrofuran (THF) at reflux in a nitrogen atmosphere. After the appearance of a yellow color, which is indicative of the formation of the corresponding ylide, the 4-chloro-3-formylquinoline **1** (1 equiv) was added, and the reaction was heated until its complete consumption. However, after the reaction workup, the expected product was not isolated. Wu and coworkers reported that the use of ultrasound in the Wittig reaction contributed to reducing the reaction time and improving the yields [34]. Therefore, it was decided to use ultrasound to promote the Wittig reaction, especially the first step corresponding to the formation of the nonstabilized ylide methyltriphenylphosphorane **4a**. In a first attempt, the ultrasound-assisted Wittig reaction of 4-chloro-3-formylquinoline **1** with methyltriphenylphosphorane **4a** was performed at room temperature (Scheme 1). Ylide **4a** was prepared *in situ* from the treatment of methyltriphenylphosphonium bromide **3a** (5 equiv) with NaH (2 equiv, relatively to the amount of **3a**) in freshly dried THF, under a nitrogen atmosphere, in an ultrasound bath for 25–45 min. The appearance of a yellow to brown color and disappearance of the phosphonium salt indicated the formation of the methyltriphenylphosphorane **4a** (see Materials and Methods section). Then, 4-chloro-3-formylquinoline **1** (1 equiv) was added, and the reaction was stirred at room temperature for 72 h. After the reaction workup, 4-chloro-3-vinylquinoline **5a** was isolated in moderate yield (50%) (Scheme 1). Under similar conditions, the reactions with ylides **4b** and **4c** were performed (Scheme 1) and afforded a diastereomeric mixture of the corresponding quinoline derivatives, (1*Z*,3*E*)-(**5b**) and (1*E*,3*E*)-(**6b**) 3-(buta-1,3-dien-1-yl)-4-chloroquinoline and (1*Z*,3*E*)-(**5c**) and (1*E*,3*E*)-(**6c**) 4-chloro-3-(4-phenylbuta-1,3-dien-1-yl)quinoline in 83% and 99% overall yield, respectively, but in shorter reaction time (Scheme 1).

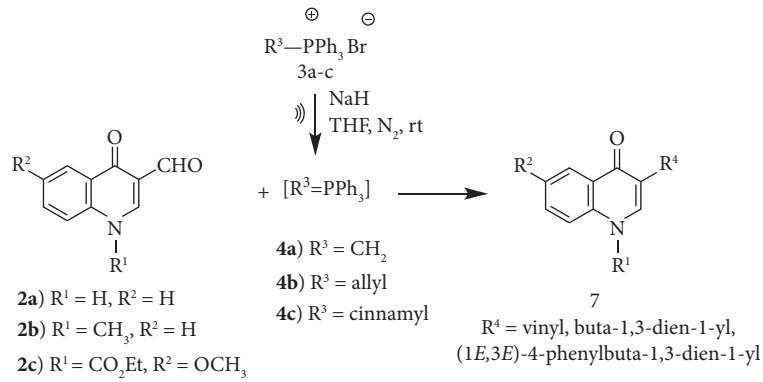
The Wittig reaction of 3-formylquinolone **2a** with methyltriphenylphosphorane **4a** was also carried out with the use of ultrasound. The best conditions found for the formation of the methyltriphenylphosphorane **4a**, with sonication, require the use of an excess of NaH (2 equiv, relatively to the amount of **3a**) in the reaction with the appropriate phosphonium salt **3a** (5 equiv), in freshly dry THF under nitrogen atmosphere (Scheme 2). After the formation of **4a**, 3-formyl-4-quinolone (**2a**, $R^1 = R^2 = H$) (1 equiv) was added, and the reaction mixture was stirred at room temperature for about 2 h, giving 3-vinyl-4-quinolone (**7a**) in a very good yield (97%) after purification by thin layer chromatography (TLC). The reaction of **2a** with ylides **4b** gave the expected (*E,E*)-3-(buta-1,3-dien-1-yl)-4-quinolone **8d,** but in very low amounts, since several purification procedures were necessary to isolate the compound due to difficulties in separating it from the phosphine oxide formed in the reaction. In turn, the reaction of **2a** with ylide **4c** gave only the diastereomer (1*E*,3*E*)-3-(4-phenylbuta-1,3-dien-1-yl)-4-quinolone **8f** in very good yields. The reactions with 1-methyl-3-formyl-4-quinolone (**2b**, $R^1 = CH_3$, $R^2 = H$) with ylides **4a–c** were performed under similar conditions and afforded the expected compounds **7b**,**e** in very good yields and **7g** in a moderate yield (Scheme 2). On the other hand, the reaction of ethyl 3-formyl-6-methoxy-4-quinolone-1-carboxylate (**2c**, $R^1 = CO_2Et$, $R^2 = OCH_3$) with ylide **4a** afforded 6-methoxy-3-vinyl-4-quinolone **7c** in a 98% yield because of the cleavage of the N-1 carbamate protecting group (Scheme 2).

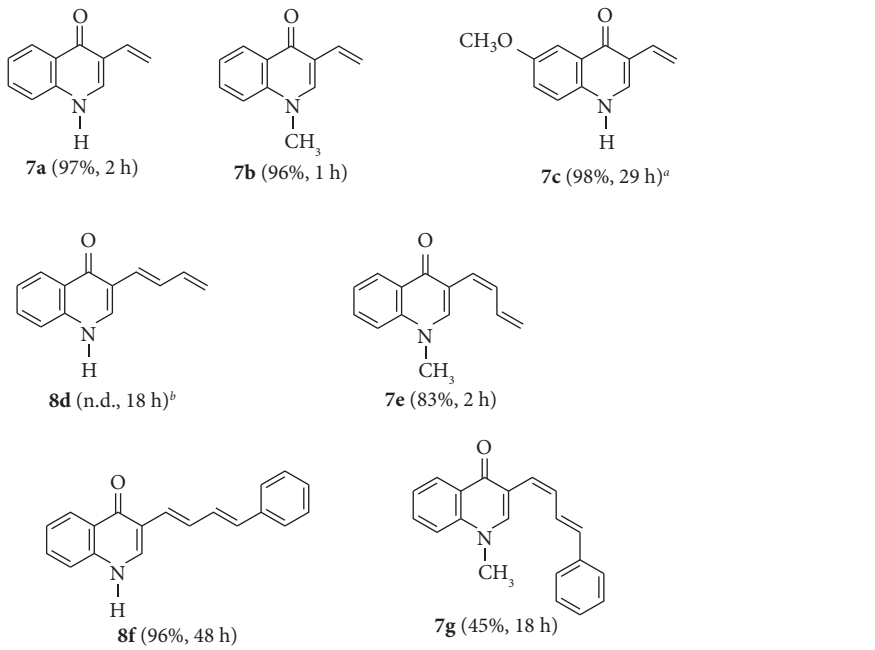
To demonstrate the synthetic utility of the synthesized 3-vinyl-4-quinolones **7a**,**b**, these compounds were used as dienes in the Diels–Alder reaction with *N*-methylmaleimide **9** to prepare acridone-type compounds **11a**,**b** (Scheme 3). An excess of *N*-methylmaleimide (5 equiv) was added to a solution of the 3-vinyl-4-quinolone **7a** in toluene, and the mixture was heated at reflux for 45–60 min. After this period, the TLC of the reaction mixture showed complete consumption of the starting material and the formation of cycloadduct **10**. So, an excess of chloranil (5 equiv) was added to the reaction mixture to promote the formation of the expected acridone **11a** by dehydrogenation of **10a** by refluxing the reaction mixture for 22–24 h. Under this protocol, novel 2-methyl-1*H*-pyrrolo[3,4-*c*]acridine-1,3,6(2*H*,11*H*)-triones (**11a,b**) were obtained in moderate yields (37–45%).

Encouraged by these results, we then focused our attention on the Diels–Alder reaction of (1*E*,3*E*)-3-(buta-1,3-dien-1-yl)-quinolin-4(1*H*)-one (**8d**) with *N*-methylmaleimide **9** (Scheme 4). The analysis of the ^{1}H NMR spectra of the isolated compound did not match with the structure of the expected cycloadduct **12,** but it fits with the structure of 2-methyl-2*H*-pyrano[3,2-*c*]quinoline (**14**) (see NMR Spectroscopy section and ESI). In fact, the formation of this compound can be explained considering the tautomerization of quinolone **8d** into the corresponding 4-hydroxyquinoline **13,** which after a nucleophilic attack of the hydroxy oxygen atom to the γ-position of the allyl group led to the formation of **14** (Scheme 4). In fact, we have previously reported a similar reaction on the formation of (*E*)-2-aryl-4-styrylfuro[3,2-*c*]quinolines from (*E,E*)-2,3-distyryl-4-quinolones [35, 36].

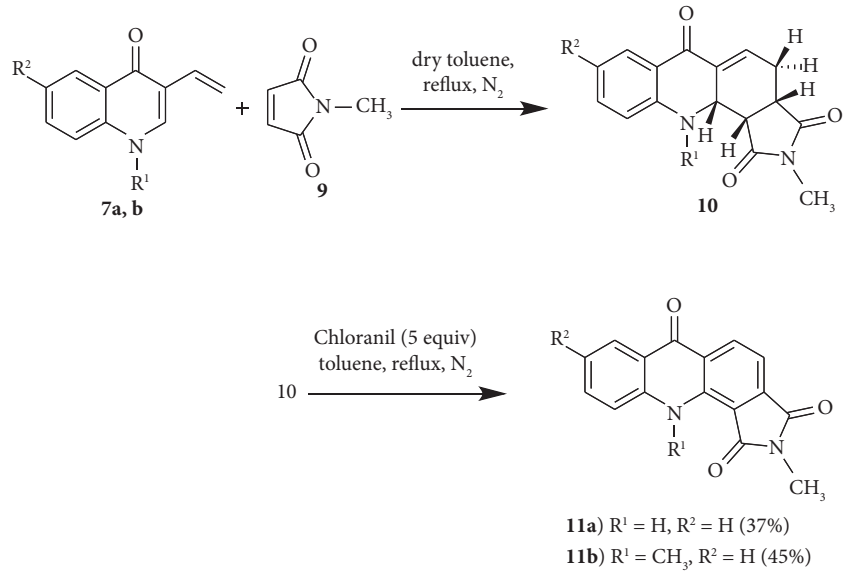


Scheme 1: Wittig reaction of 4-chloro-3-formylquinoline **1** with nonstabilized ylides **4a–c** to prepare the 3-substituted-4-chloroquinolines **5a–c**, **6b,** and **6c**.

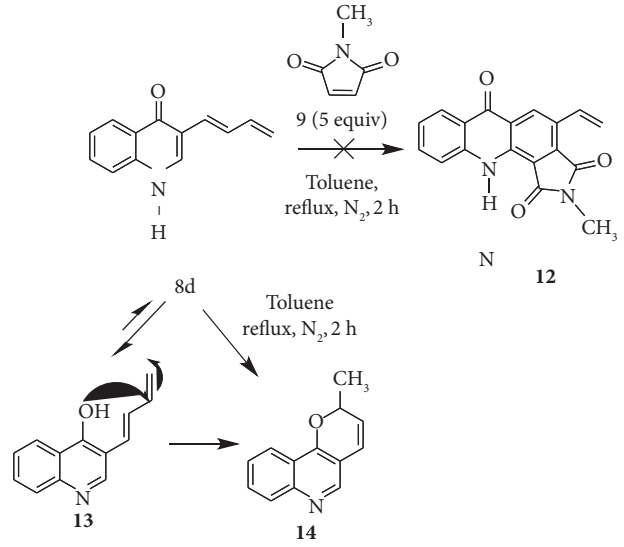




Scheme 2: Wittig reaction of 3-formyl-4-quinolones **2a–c** with nonstabilized ylides **4a–c** to prepare the 3-substituted 4-quinolones **7a–c**, **e**, **g,** and **8d**, **f**. [a]Compound **7c** obtained starting from ethyl 3-formyl-6-methoxy-4-quinolone-1-carboxylate **2c**. [b]The yield of **8d** was not determined because the low amount of isolated compound presented some contamination with phosphine oxide formed in the reaction.



Scheme 3: Diels–Alder reaction of 3-vinyl-4-quinolones **7a**, **b** with *N*-methylmaleimide **9** to give novel acridones **11a**, **b**.



Scheme 4: Synthesis of 2-methyl-2(*H*)-pyrano[3,2-c]quinoline (**14**) starting from (1**E**,3**E**)-3-(buta-1,3-dien-1-yl)quinolin-4(1**H**)-one (**8d**).

3.2. NMR Spectroscopy. All the new synthesized compounds have been characterized by 1D (^{1}H, ^{13}C) and 2D (HSQC, HMBC, and NOESY) NMR techniques. The most characteristic signals in the NMR spectra of 4-chloro-1-vinylquinolines **5a–c** are due to the resonances of H-2 at high frequency values and of the protons of the 3-substituent. For compound **5a**, the resonance of H-2 appears as a singlet at δ_H 9.06 ppm (δ_C 148.1 ppm). For compounds **5b**,**c** and **6b**,**c**, the chemical shift of H-2 is affected by the stereochemistry of the exocyclic double bonds, being more deshielded in the (*E,E*)-isomers **6b,c** (δ_H 9.03–9.09 ppm) than in the (*Z,E*)-isomers **5b,c** (δ_H 8.86–8.98 ppm). Regarding the 3-substituent, in the case of 4-chloro-3-vinylquinoline (**5a**), three signals were assigned to the vinyl group: a doublet of doublets at δ_H 5.61 ppm due to H-β' (*J* 11.3, 0.5 Hz), a doublet at 6.00 ppm assigned to H-β (*J* 17.7 Hz), and a doublet of doublets at δ_H 7.24 ppm due to the resonance of H-α (*J* 17.7, 11.3 Hz). Additionally, were observed two signals in the ^{13}C NMR spectra corresponding to the resonance of C-β at δ_C 119.0 ppm and C-α at δ_C 131.0 ppm.

The most characteristic signals in the NMR spectra of 3-vinyl-4-quinolones **7a–c** are due to the 3-vinyl group. Three sets of doublet of doublets were observed; the most protected is due to the resonance of H-β' at δ_H 5.23–5.24 ppm, followed by the signal of H-β at δ_H 5.98–6.03 ppm and the signal of H-α at δ_H 6.78–6.93 ppm. Depending on the conformation of the double bond, both H-α and H-β can be deprotected by the anisotropic effect of the carbonyl group,

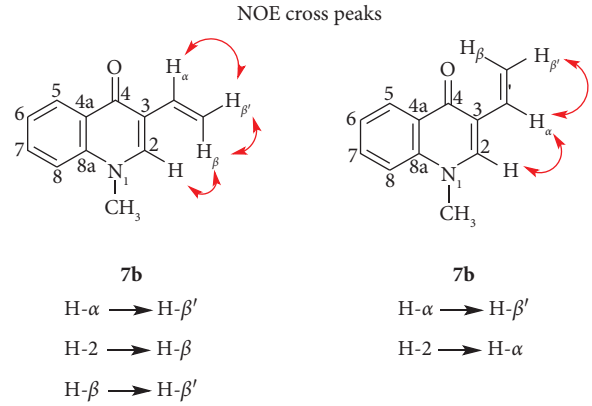


Figure 3: Main NOE cross peaks observed in the NOESY spectrum of compound **7b** and different conformations of the vinyl group.

as shown in Figure 3. Three different coupling constants were calculated for the protons of the vinyl group: the *trans* coupling $^{3}J_{trans}$ 17.7–17.8 Hz, the *cis* coupling $^{3}J_{cis}$ 11.3–11.4 Hz, and the geminal coupling $^{2}J_{\text{gem}}$ 1.8 Hz. The strong NOE cross peaks between H-2 and H-β and H-α indicate a free rotation around the C3-Cα bond and explain the high-frequency values of the resonance of H-α and H-β due to the anisotropic deshielding effect of the carbonyl group.

Another typical signal found in the spectra of compounds **7a–c** is the singlet due to the resonance of H-2 at high frequency (δ_{H} 7.62–8.17 ppm; δ_{C} 136.5–141.7 ppm), due to the inductive and mesomeric deshielding effects of the heterocyclic nitrogen atom and the carbonyl group, respectively. Moreover, in compound **7c**, the absence of signals due to the resonance of the protons and carbons of the ethyl carboxylate group of **2c** confirms the cleavage of this group in the Wittig reaction conditions.

The most important signals in the NMR spectra of the diastereomers (1*Z*,3*E*)-(**5b**) and (1*E*,3*E*)-(**6b**) 3-(buta-1,3-dien-1-yl)-4-chloroquinoline are the protons' resonances of the exocyclic double bonds (Figure 4). Although the accurate calculation of the coupling constants $^{3}J_{\text{H}\alpha\text{-H}\beta}$ and $^{3}J_{\text{H}\gamma\text{-H}\delta}$ was difficult because the signals overlapped, some differences were observed when comparing the spectra of **5b** and **6b**. For example, in the case of **6b,** a multiplet was assigned to the H-α and H-γ resonances that appears at higher frequency values (δ_{H} 6.98–7.12 ppm) than in the diastereomer **5b** (δ_{H} 6.51–6.74 ppm). Moreover, H-2 is more deshielded in **6b** (δ_{H} 9.09 ppm) than in **5b** (δ_{H} 8.86 ppm). For (1*Z*,3*E*)-4-chloro-3-(4-phenylbuta-1,3-dien-1-yl]quinoline (**5c**), the resonance of H-γ (δ_{H} 7.06–7.20 ppm) appears at high frequency than the other vinylic protons, H-α and H-β (δ_{H} 6.71 ppm) and H-δ (δ_{H} 6.83 ppm). The typical coupling constant value of $^{3}J_{\text{H}\gamma=\text{H}\delta}$ 15.4 Hz confirmed the *trans*-stereochemistry of the $C_{\gamma}=C_{\delta}$ double bond. For (1*E*,3*E*)-4-chloro-3-(4-phenylbuta-1,3-dien-1-yl]quinoline (**6c**), the resonance of H-α and H-β (δ_{H} 7.03–7.11 ppm) appears at higher frequency values than H-γ (δ_{H} 6.96 ppm) and H-δ (δ_{H} 6.72 ppm). The coupling constant value $^{3}J_{\text{H}\gamma=\text{H}\delta}$ 15.1 Hz confirms the *trans*-configuration of this vinylic system. In the ^{1}H NMR spectra of (1*E*,3*E*)-3-(4-phenylbuta-1,3-dien-1-yl)quinolin-4(1*H*)-one (**8f**), the resonance of H-β (δ 7.48–7.58 ppm) appears at higher frequency values than the other vinylic protons, H-γ (δ 7.05 ppm), H-α (δ 6.78 ppm), and H-δ (δ 6.62 ppm). The stereochemistry of both vinylic systems was established as trans based on the characteristic coupling constant values ($^{3}J_{\text{H}\alpha\text{-H}\beta}$ 15.6 Hz and $^{3}J_{\text{H}\gamma\text{-H}\delta}$ 15.6 Hz). In the ^{1}H NMR spectrum of (1*Z*,3*E*)-1-methyl-3-(4-phenylbuta-1,3-dien-1-yl)quinolin-4(1*H*)-one (**7g**), the resonance of H-β (δ 6.48 ppm) appears at lower frequency values than the other vinylic protons, H-α (δ 6.68 ppm), H-δ (δ 6.73 ppm), and H-γ (δ 7.15 ppm). The stereochemistry of both vinylic systems was established as *cis*, *trans*-based on the characteristic coupling constant values ($^{3}J_{\text{H}\alpha\text{-H}\beta}$ 11.0 Hz and $^{3}J_{\text{H}\gamma\text{-H}\delta}$ 16.0 Hz) and supported by the NOE cross peaks observed in NOESY spectrum (see ESI) of (1*Z*,3*E*)-1-methyl-3-(4-phenylbuta-1,3-dien-1-yl)quinolin-4(1*H*)-one, between H-β and H-δ and this with H-2′, 6′, and also between H-2 and H-γ (Figure 4).

The most characteristic signals in the NMR spectra of 2-methyl-1*H*-pyrrolo[3,4-*c*]acridine-1,3,6(2*H*,11*H*)-triones **11a,b** are as follows: (i) the singlet due to the resonance of the methyl protons of the maleimide unit at δ_{H} 3.24–3.25 ppm (δ_{C} 24.4–29.4 ppm); (ii) the doublet at δ_{H} 7.66–7.75 ppm due to the resonance of H-4; and the doublet at δ_{H} 8.80–8.90 ppm (H-5) at a higher frequency due to the anisotropic deshielding effect of the carbonyl group. In the ^{13}C NMR spectra, it is possible to observe the presence of a signal at δ_{C} 177.2–177.5 ppm due to the resonance of the carbonyl (C-6) of the acridone and the signals at δ_{C} 167.5–167.8 and 167.2–169.7 ppm (C-1 and C-3) due to the resonance of the two carbonyl groups of the maleimide moiety.

The formation of the 2-methyl-2*H*-pyrano[3,2-*c*]quinoline **14** was corroborated by the most typical signals observed in the NMR spectra: (i) the doublet at δ_{H} 1.57 ppm (δ_{C} 22.0 ppm) due to the resonance of the protons of the methyl group; (ii) the signal of H-2 that appears as a quartet of doublet of doublets at δ_{H} 5.34 ppm (δ_{C} 73.5 ppm); (iii) the doublet of doublets at δ_{H} 5.71 ppm (δ_{C} 125.4 ppm) assigned to the resonance of H-3; (iv) the doublet of doublets at δ_{H} 6.53 ppm (δ_{C} 120.7 ppm) due to the resonance of H-4; and (v) the singlet at high frequency, δ_{H} 8.49 ppm (δ_{C} 148.7 ppm) assigned to the resonance of H-5. The

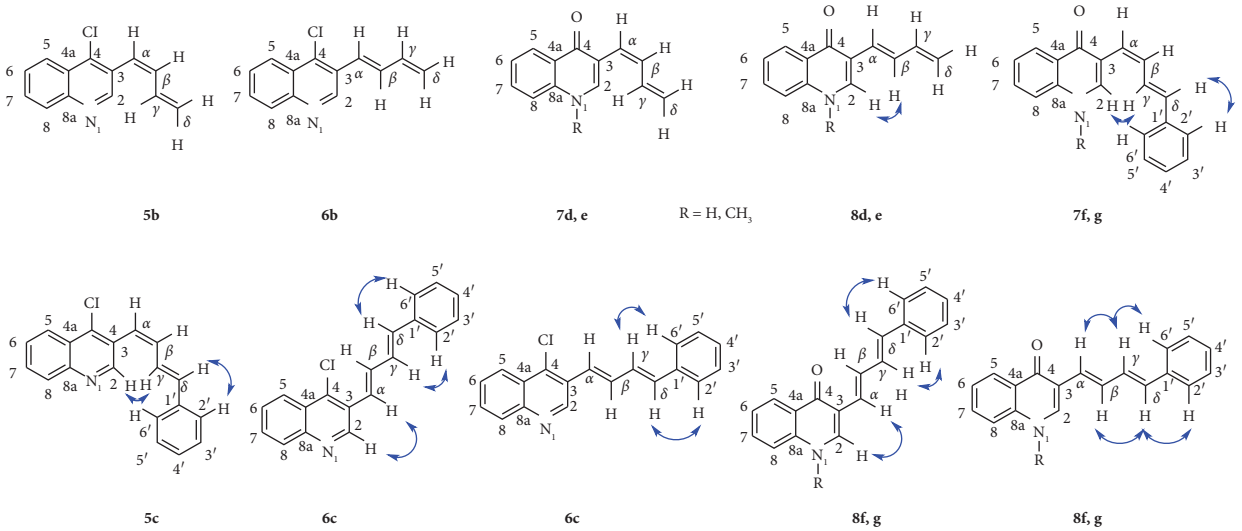


Figure 4: Structures of compounds **5b**-**c** and **7d**–**g**, their respective diastereomers, and the main NOE cross peaks observed in their NOESY spectra.

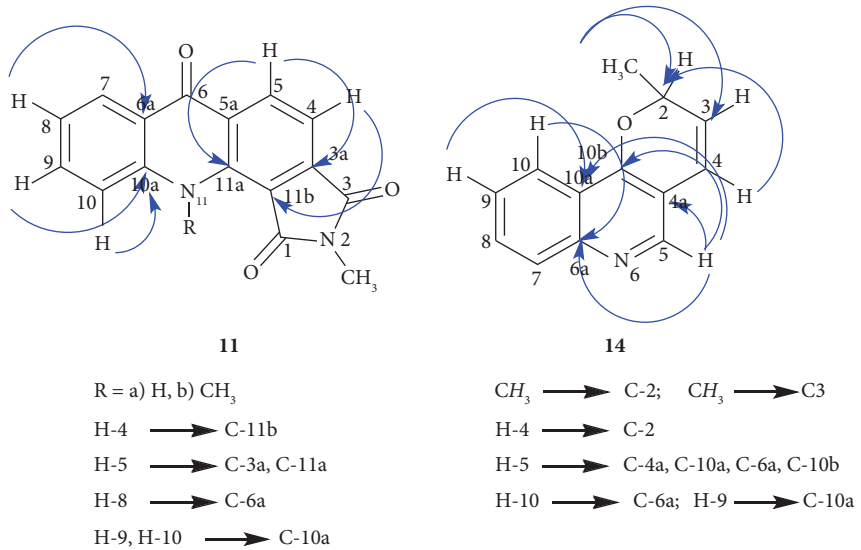


Figure 5: Structures and important correlations observed in the HMBC spectra of compounds **11a**, **b** and **14**.

assignments of C-2 and the quaternary carbons C4a, C-10a, C-6a, and C-10b at δ_C 111.9, 120.1, 149.4, and 156.1 ppm, respectively, were made based on the correlations observed in the HMBC spectra, as shown in Figure 5.

4. Conclusion

In conclusion, 3-substituted 4-chloroquinolines and 4-quinolones with extended π-conjugated systems were synthesized in very good yields by ultrasound-promoted Wittig reaction of the corresponding 4-chloro-3-formylquinoline and 3-formyl-4-quinolones with nonstabilized ylides. The structure of the novel compounds was unequivocally established by means of 1D and 2D NMR spectroscopy. It was demonstrated that 3-vinyl-4-quinolones can be used as building blocks for the synthesis of more complex structures, namely, 2-methyl-1*H*-pyrrolo[3,4-*c*]acridine-1,3,6(2*H*,11*H*)-triones. These compounds were obtained through the Diels-Alder reaction of 3-vinyl-4-quinolones with *N*-methylmaleimide and further oxidation with chloranil. Moreover, it was demonstrated that 3-(buta-1,3-dien-1-yl)-4-quinolones are useful as precursors for the synthesis of 2-methyl-2*H*-pyrano[3,2-*c*]quinoline.

Data Availability

The data included in this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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Supplementary Materials

The supporting information contains ^{1}H NMR and ^{13}C NMR spectra for all the target compounds. (*Supplementary Materials*)

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