Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 61 (2005) 9042–9051
Tetrahedron

Synthesis of *n*-chloroquinolines and *n*-ethynylquinolines (*n* = 2, 4, 8): homo and heterocoupling reactions

J. Gonzalo Rodríguez,* Cristobal de los Rios and Antonio Lafuente

Departamento de Química Orgánica, Universidad Autónoma, Cantoblanco, 28049 Madrid, Spain

Received 31 May 2005; revised 11 July 2005; accepted 14 July 2005

Abstract—The *n*-(ethynyl)quinolines were satisfactorily prepared by heterocoupling reaction between the appropriate *n*-chloroquinoline and 2-methyl-3-butyn-2-ol, catalyzed by palladium, followed by treatment with a catalytic amount of powdered sodium hydroxide in toluene. The *n*-(ethynyl)quinolines were transformed in the corresponding conjugate 1,4-bis[*n*′-(quinolyl)]buta-1,3-diynes by oxidative dimerization, catalyzed by cuprous chloride, with excellent yields. Moreover, the heterocoupling between *n*′-haloquinoline and *n*′-(ethynyl)quinoline (*n*′, 2′ or 3′), catalyzed by palladium, gives 2′,2′-bis(quinoline) or 1,2-di(3′-quinolyl)ethyne, respectively. The same coupling reaction with zerovalent nickel complexes, gives a mixture of 1,2,4- and 1,3,5-tri(*n*′-quinolyl)benzene.

1. Introduction

Earlier, some chloroquinolines had been synthesized as antimalarial precursors,[1] and more recently it has been reported that the 4-aminoquinoline nucleus in chloroquine and related antimalarials having the 7-chloro group act by complexing ferriprotoporphyrin IX.[2] However, quinolines have not been used for the preparation of molecular organic compounds,[3] although some quinoline derivatives are good candidates to form part of new materials with conductive and optical properties.

The use of molecular organic materials as conductors and in nonlinear optics is of considerable interest since such materials have inherent synthetic flexibility, which permits the design of specific molecular properties.[4] In this way, the solid state polymerization of 1,3-diynes to form crystalline conjugated polydiynes has attracted much attention,[5] although many of them are inactive in the solid state, they do undergo liquid crystal polymerization.[6]

Here we describe an efficient synthesis of the 2-, 3-, and 4-quinolylacetylene units (**11**–**14**), the oxidative dimerization to 1,4-bis(*n*-quinolyl)buta-1,3-diyne (**4a**–**c**), their structural thermal analysis and their catalysed coupling reactions. The acetylene derivatives (**11**–**14**) were also obtained for the synthesis of π-conjugated polyenes and furthermore, serve for the synthesis of nanostructures containing those useful units.[7] Poly(vinylquinolines) and their fluorescence properties have been previously reported.[8]

2. Results and discussion

Conjugated ethynyl derivatives having a heterocyclic ring such as pyridine has been reported,[7] and we are now interested in the synthesis and structural analysis of conjugated ethynylquinolines as starting units to prepare molecular networks.

2.1. *n*-(Ethynyl)quinolines

The conjugated *n*-(ethynyl)quinolines (**11**–**14**) (*n* = 2, 3, 4) were satisfactory obtained by cross-coupling reaction between the appropriate *n*-chloroquinoline (compounds **1**, **2**, **6**) and 2-methyl-3-butyn-2-ol catalysed by the palladium–copper system (Sonogashira method).[9a] A modification on the hydrolysis treatment of the crude reaction products was employed,[10] which consists in the incorporation of a small amount of potassium cyanide to a saturated ammonium chloride aqueous solution that permits the pure isolation of the corresponding 2-methyl-4-(*n*′-quinolyl)-3-butyn-2-ol in good to practically quantitative yield. The potassium cyanide avoids the quinoline–palladium complexes separation. The cross-coupling reaction with 3-chloroquinoline fails while 3-bromoquinoline was used with excellent results.[10] However, 2-chloroquinoline was recently used in carbonylation reactions catalysed by palladium.[11]

Keywords: Chloroquinolines; Ethynylquinolines; 1,3-Butadiynes; Homocoupling; Heterocoupling.
* Corresponding author. Tel.: +34 914974715; fax: +34 914973966; e-mail: gonzalo.rodriguez@uam.es

0040–4020/$ - see front matter © 2005 Published by Elsevier Ltd.
doi:10.1016/j.tet.2005.07.043

Finally, the *n*-ethynylquinolines were obtained by treatment of the corresponding 2-methyl-4-(*n'*-quinolyl)-3-butyn-2-ol with catalytic amounts of powdered sodium hydroxide (10–15% mol), in toluene at the reflux temperature, in good to excellent yields (**11**–**13**), in short reaction times (half to 4 h), (Scheme 1). The purification of the *n*-ethynylquinolines was carried out by silica gel column chromatography (**11**, **14**) or by sublimation in a cold-finger surface, giving a microcrystalline white solid (**12**, **13**). We have also used the purification by sublimation in the preparation of the ethynylpyridines.[10]

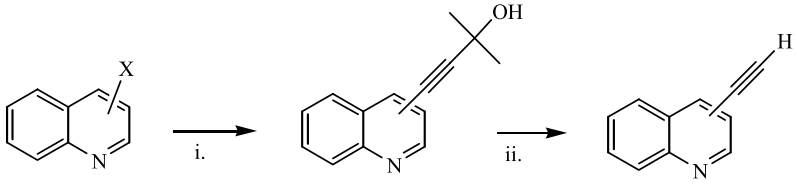
2.2. *n*-Chloroquinolines

The starting 2-chloro (**1**) and 4-chloro (**2**) quinolines were prepared by reaction of anhydrous quinoline-*N*-oxide,[3] with phosphoryl trichloride,[12] yielding a mixture of both isomers, which were isolated by chromatography as yellow solids (47 and 32%, respectively), (Scheme 2).

The 2,8-dichloroquinoline (**6**) was obtained by reaction of anhydrous 8-chloroquinoline-*N*-oxide with phosphoryl trichloride, as the unique product, in moderate yield (52%), while 4,8-dichloroquinoline was detected only as traces in the crude product. Hence, the high regiospecificity of the reaction was due to the serious sterical hindrance of the chloro atom in position 8, although the reaction can be interpreted through an oxyphosphorane adduct anion in a rapid concerted mechanism, Scheme 2.

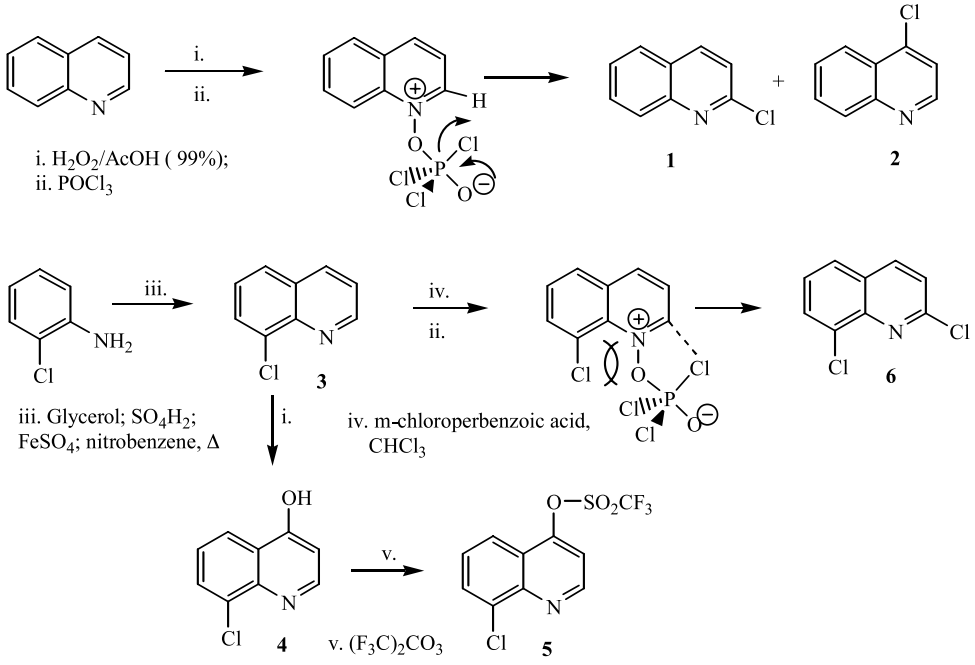
The starting 8-chloroquinoline (**3**) was prepared by the Skraup synthesis between *o*-chloroaniline and 1,2,3-trihydroxypropane catalysed by sulfuric acid, in good yield (78%).[13] The structure of **3** was confirmed by ^{1}H NMR spectrum, which shows unequivocally the H-2 and H-4 protons at 8.97 and 8.09 ppm with *ortho* and *meta* coupling constants (J=4.3, 1.6 Hz and J=8.6, 1.6 Hz, respectively).

A remarkable fact takes place in the preparation of 8-chloroquinoline-*N*-oxide under the same conditions used for the preparation of quinoline-*N*-oxide. 8-chloro-4-hydroxyquinoline (**4**) was obtained in good yield (62%) as the unique transformation product, which mechanism probably proceeds by *N*-protonation followed by water



X= 2-Cl **1**	**7**	n,2		92%	**11**	n,2		91%
X= 3-Br	**8**	n,3		97%	**12**	n,3		95%
X= 4-Cl **2**;	**9**	n,4		86%	**13**	n,4		86%
X= 2-Cl,8-Cl **6**	**10**	n,2	8-Cl	91%	**14**	n,2	8-Cl	65%

Scheme 1.



Scheme 2.

addition, (Scheme 2). The 4-hydroxyquinoline was treated with triflic anhydride yielding the triflate derivative (mp 108–110 °C), which confirms the 4-hydroxyquinoline structure (Scheme 2).

The 8-chloroquinoline-*N*-oxide was obtained by reaction of 8-chloroquinoline with *m*-chloroperbenzoic acid in chloroform with low yield (32%) but, the untransformed starting quinoline was completely recovered.

2.3. 1,4-Di(*n*-quinolyl)-1,3-butadiynes

To increase the π-extended conjugation of the *n*-ethynylquinolines carried out was the catalytic oxidative dimerization to the 1,4-di(*n*-quinolyl)-1,3-butadiynes. Recognized earlier was the oxidative coupling dimerization of the terminal acetylenes in the presence of cupric salts in pyridine, giving symmetric conjugate 1,3-diynes in good yields (Eglinton reaction).[14] A modified method using catalytic amounts of cuprous and ammonium salts in the presence of an oxidizing agent, also provides good yields (Glaser reaction) because of the triple bond oxidative specificity.[14]

Recently, been proposed is a mechanism for the reaction, which takes into account the Cu(I)/O_2 interaction and the easy redox interconversion Cu(I)/Cu(III),[15] as intermediates in the homocoupling reaction.

2.4. 1,4-Di(*n′*-quinolyl)-1,3-butadiyne (15–18)

The oxidative dimerization of *n*-ethynylquinolines (**11**–**14**) under the Glaser conditions, in the presence of catalytic amounts of cuprous chloride, pyridine as the base was carried out at 40 °C, under oxygen atmosphere, giving 1,4-di(*n′*-quinolyl)-1,3-butadiyne (**15**–**18**), which were isolated as microcrystalline white powder, in good to excellent yield, (Scheme 3).

The 1,3-butadiynes **15**–**17** are photosensitive to the sunlight and decompose, with the darkness of the samples, near to the melting point, which were determined by differential scanner calorimetry (DSC).[16]

2.5. 1,4-Di(3′-quinolyl)-1,3-butadiyne (16)

Oxidative dimerization of compound **12** affords 1,4-di(3′-quinolyl)-1,3-butadiyne (**16**) (80%). Crystals of **16** were photosensitive to the sunlight and under exposure turn to insoluble deep-blue crystals. A crystalline powder sample of compound **16**, after sunlight exposure for 2 days, was analysed by mass spectrometry, using the MALDI-TOF technique.

Thus, a mixture of topooligomers were detected by complete volatilization of the sample, in the following distribution: 1,3-diyne monomer **16**, 42.4%; 1,3-diyne dimer 31.4%; 1,3-diyne trimer 22.7%; 1,3-diyne tetramer 3.2%; 1,3-diyne pentamer 0.3%; and 1,3-diyne hexamer in traces.

2.6. 1,4-Di(4′-quinolyl)-1,3-butadiyne (17)

Oxidative coupling of compound **13** affords 1,4-di(4′-quinolyl)-1,3-butadiyne (**17**) in practically quantitative yield (97%). The diyne **17** shows a clear melting point at 215–216 °C.

2.7. 1,4-Di[2′-(8′-chloroquinolyl)]-1,3-butadiyne (18)

The oxidative dimerization of compound **14** affords 1,4-di[2′-(8′-chloroquinolyl)]-1,3-butadiyne (**18**) (30%), (Scheme 3), but all of the untransformed starting product was recovered. The presence of the 8′-chloro atoms in the 1,3-butadiyne **18** produce a clear melting point at 212–214 °C and stability under sunlight exposure.

2.8. Structural analysis of the 1,4-di(*n′*-quinolyl)-1,3-butadiynes 15–18

The 1,3-butadiynes **15**–**18** in the ^{1}H NMR spectrum show the characteristic pyridine proton signals as doublets. Thus, H-3, H-4 and H-2, H-4 appears for compound **15** at 7.57 and 8.16 ppm (J=8.6 Hz); compound **16** at 9.00 and 8.37 ppm (J=1.9 Hz); compound **17** at 8.81 and 7.61 ppm (J=3.9 Hz); and compound **18** at 7.46 and 8.30 ppm (J=8.6 Hz), respectively.

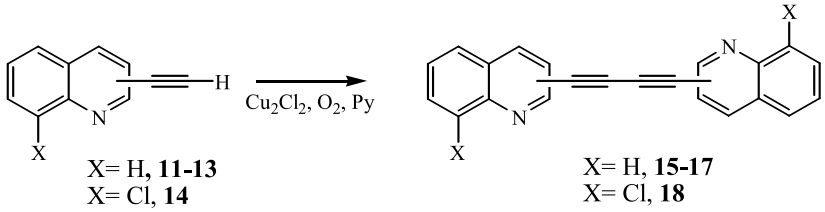
The mass spectrum of the 1,3-butadiynes **15**–**18** show the molecular as the base peak at 304 (372 for **18**) and the double charge M^{+2} molecular peak at 152 (186 for **18**) that is the following more significant in the spectrum and was characteristic of the 1,4-diaryl-1,3-butadiynes.[10]

2.9. Coupling reaction between *n*-haloquinolines and *n*-ethynylquinolines

The coupling between a *n*-haloquinoline and a *n*-ethynylquinoline catalyzed by palladium can give the 1,2-di(*n′*-quinolyl)ethynes, which can be used as starting compounds for the catalytic cyclotrimerization analysis to obtain the hexa-(*n*-quinolyl)benzene derivatives.

2.10. Coupling reaction between 2-chloroquinoline and 2-ethynylquinoline

The coupling between 2-chloroquinoline (**1**) and 2-ethynylquinoline (**11**) in presence of dichloro bis(triphenylphosphine)



Scheme 3.

palladium/cuprous iodide catalyst system, in diethylamine yields the homocoupled of **1** to 2,2′-bis(quinoline) **19** as the unique product, (Scheme 4).

However, the reaction between 2-chloroquinoline (**1**) and 2-ethynylquinoline (**11**), with dichloro bis(triphenylphosphine) nickel–zinc catalyst system, affords the cyclotrimerization of the acetylene **11**, giving a mixture of 1,3,5- (**20**) and 1,2,4-tris(2′-quinolyl)benzene (**21**) (43%) (64:36 molar ratio, respectively, by ^{1}H NMR), (Scheme 4).

2.11. Coupling reaction between 3-bromoquinoline and 3-ethynylquinoline (12)

The coupling between 3-bromoquinoline and 3-ethynylquinoline (**12**), catalyzed by the palladium–copper system, gives the heterocoupled 1,2-di(3′-quinolyl)ethyne (**22**) in good yield (70%), (Scheme 5). Compound **22** was a stable white crystalline solid, which shows fluorescence radiation emission in dichloromethane with two maxima at 354 and 371 (quantum yield Φ, 18%, referred to a solution of 2-aminopiridine).

Compound **22** was employed for the cyclotrimerization with several homogeneous catalyst systems, such as $Cl_2Pd(Ph_3P)_2$–$SiMe_3Cl$,[17] $V(acac)_3$–$AlEt_3$,[18] $Cl_2Ni(Ph_3P)_2$–Zn[19] and also with transfer phase agents, but in all the cases compound **22** was recovered untransformed, (Scheme 5).

However, the same coupling reaction between 3-bromoquinoline and acetylene **12** was also carried out with zerovalent nickel complexes[20–22] but only a mixture of 1,2,4-/1,3,5-tris(3′-quinolyl)benzene was obtained in good yield (80%).

3. Conclusions

2-Chloro, 4-chloro and 2,8-dichloroquinoline were especifically obtained by treatment of the corresponding dehydrated *N*-oxide with phosphoryl chloride in good yield. The ethynylquinolines can be efficiently obtained by heterocoupling with 2-methyl-3-butyn-2-ol catalyzed by palladium, followed of propanone elimination. In this way, 2-ethynyl-8-chloroquinoline was specifically isolated. The *n*-(ethynyl)quinolines can be transformed in the corresponding conjugate 1,4-bis[*n*′-(quinolyl)]buta-1,3-diynes in the presence of cuprous chloride catalyst, with excellent yields.

The heterocoupling between 2-chloroquinoline and 2-(ethynyl)quinoline, catalyzed by palladium, affords 2,2-bis(quinoline). However, the heterocoupling between 3-bromoquinoline and 3-(ethynyl)quinoline, catalyzed by palladium, affords to 1,2-di(3′-quinolyl)ethyne.

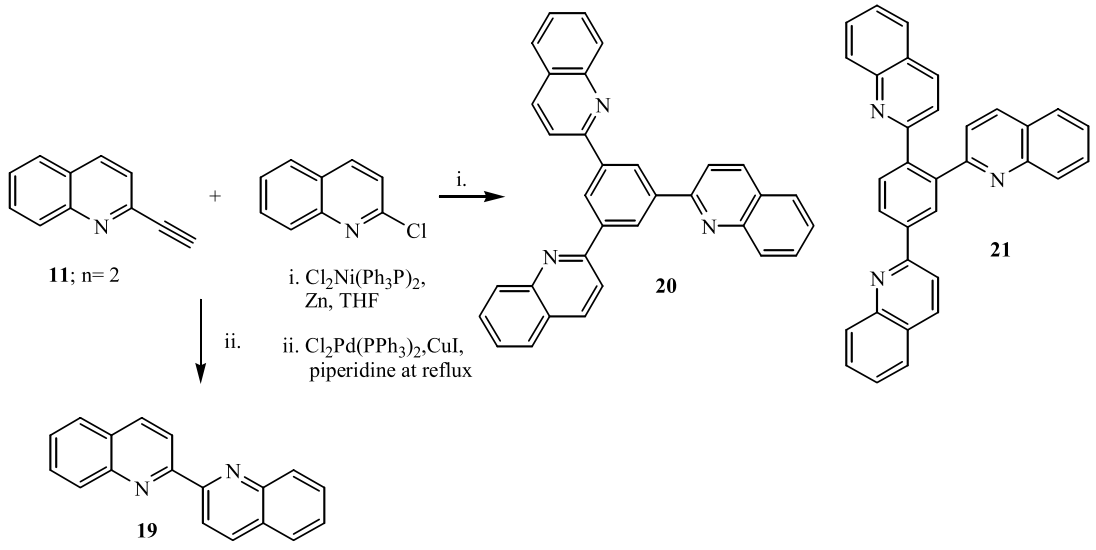
The coupling reaction between 2-chloroquinoline and 2-ethynylquinoline (or 3-bromoquinoline and 3-ethynylquinoline) with zerovalent nickel complexes, gives only a mixture of 1,2,4- and 1,3,5-tris(2′-quinolyl)benzene (or 1,2,4- and 1,3,5-tris(3′-quinolyl)benzene).

4. Experimental

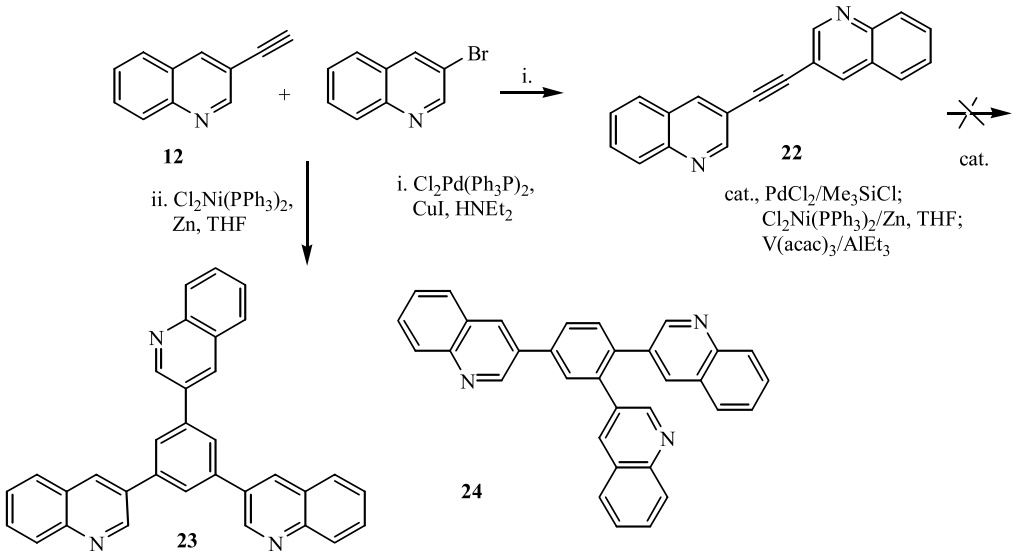
4.1. General methods

Melting points were determined using a Buchi or Reichert stage microscope and are uncorrected, the differential scanning calorimetric measures (DSC) were recorded using a Perkin–Elmer apparatus. IR spectra were recorded using a Bruker Vector 22 spectrophotometer, and the wave numbers are given in cm^{-1}. The ^{1}H NMR spectra were recorded using a Bruker Aspect spectrometer (200 or 300 MHz). Chemical shifts are given in δ with TMS as internal reference and constants coupling *J* are given in Hz. Mass spectra were recorded using a VG AutoSpec spectrometer and the MALDI-TOF spectra were recorded using a Bruker Reflex III spectrometer. UV–vis spectra were recorded using a Hewlett Packard 8453 spectrometer, frequency are given in nm and ε en L mol^{-1} cm^{-1}.Yields are given after chromatography column or solvent extraction.

4.1.1. 2-Chloroquinoline (1) and 4-chloroquinoline (2). A solution of anhydrous quinoline *N*-oxide (7.52 g, 0.052 mol)



Scheme 4.



Scheme 5.

in phosphoryl trichloride (43.8 mL, 0.465 mol) was prepared by slow addition at 0 °C. The mixture was refluxed for 3 h and then poured on ice, neutralized with aqueous ammonium hydroxide and extracted with dichloromethane. The extracts were dried on sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/dichloromethane, 1:5), giving 2-chloroquinoline (**1**) (3.98 g, 47%) as a yellow solid, mp 36–38 °C and 4-chloroquinoline (**2**) (2.71 g, 32%) as a yellow solid, mp 33–34 °C.[12]

2-Chloroquinoline (**1**). ν_{max}(KBr)/cm^{-1} 3055 (ArC–H st), 1616, 1585, 1562, 1496, 1462 and 1420 (C=C and C=N st conj.), 1135 and 1094 (ArC–H (ip), 815, 778 and 742 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 7.38 (d, 1H, $J_{3-4}=8.3$ Hz, H-3), 7.56 (ddd, 1H, $J_{5-6}=8.1$ Hz, $J_{6-7}=7.0$ Hz, $J_{6-8}=1.2$ Hz, H-6), 7.72 (ddd, 1H, $J_{7-8}=8.3$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.4$ Hz, H-7), 7.80 (dd, 1H, $J_{5-6}=8.1$ Hz, $J_{5-7}=1.4$ Hz, H-5), 8.01 (dd, 1H, $J_{7-8}=8.3$ Hz, $J_{6-8}=1.2$ Hz, H-8) and 8.08 (d, 1H, $J_{3-4}=8.3$ Hz, H-4); δ_C (50 MHz, $CDCl_3$) 122.1 (C-3), 126.6 (C-4a), 126.7 (C-6), 127.3 (C-5), 128.3 (C-7), 130.3 (C-8), 138.6 (C-4), 147.6 (C-8a) and 150.3 (C-2); λ_{max}(CH_2Cl_2)/nm 233, 273, 304 and 318. C_9H_6NCl (163.60). Anal. Calcd C 66.07, H 3.70, N 8.56, Cl 21.67; found: C 65.93, H 3.61, N 8.43.

4-Chloroquinoline (**2**). δ_H (200 MHz, $CDCl_3$) 7.47 (d, 1H, $J_{2-3}=4.3$ Hz, H-3), 7.62 (ddd, 1H, $J_{5-6}=8.3$ Hz, $J_{6-7}=7.0$ Hz, $J_{6-8}=1.7$ Hz, H-6), 7.75 (ddd, 1H, $J_{7-8}=8.3$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.3$ Hz, H-7), 8.12 (dd, 1H, $J_{5-6}=8.3$ Hz, $J_{5-7}=1.3$ Hz, H-5), 8.20 (dd, 1H, $J_{7-8}=8.3$ Hz, $J_{6-8}=1.7$ Hz, H-8) and 8.77 (d, 1H, $J_{2-3}=4.3$ Hz, H-2); δ_C (50 MHz, $CDCl_3$) 121.1 (C-3), 124.0 (C-6), 126.4 (C-4a), 127.5 (C-5), 129.7 (C-7), 130.2 (C-8), 142.5 (C-4), 149.0 (C-8a) and 149.7 (C-2); λ_{max}(CH_2Cl_2)/nm 230, 281, 304 and 316. C_9H_6NCl (163.60). Anal. Calcd C 66.07, H 3.70, N 8.56, Cl 21.67; found: C 66.23, H 3.49, N 8.64.

4.1.2. 8-Chloroquinoline (3). Following the Skraup reaction, to a solution of *o*-chloroaniline hydrochloride (20 g, 122 mmol), and glycerol (17.8 mL, 244 mmol) in nitrobenzene (12.6 mL), was added $FeSO_4 \cdot 7H_2O$ (2.0 g, 7.2 mmol) and SO_4H_2 (33 mL, 98%). The mixture was stirred for 5 h at 80 °C and after neutralized with NaOH (12 N) and extracted with dichloromethane. The organic layer was washed (2×50 mL) with hydrochloric acid (10%). The extracts were dried with sodium sulfate, filtered and the solvent removed under reduced pressure yielding a brown oil, which was distilled at reduced pressure yielding 8-chloroquinoline as a colorless oil, 15.51 g (bp 175 °C at 30 mm Hg, 78%,[11b]). Purification can also be carried out by silica gel column chromatography (dichloromethane/hexane 4:1 ($R_f=0.19$).

ν_{max}(film)/cm^{-1}: 1593, 1490, 1459, 1380, 1304, 1209, 1062, 980, 823, 784; δ_H (200 MHz, $CDCl_3$): 9.07 (1H, dd, $J_1=4.3$ Hz, $J_2=1.61$ Hz, H-2), 8.21 (1H, dd, $J_1=8.6$ Hz, $J_2=1.61$ Hz, H-4), 7.86 (1H, dd, $J_1=7.53$ Hz, $J_2=1.08$ Hz, H-7), 7.77 (1H, dd, $J_1=8.06$ Hz, $J_2=1.08$ Hz, H-5), 7.48 (1H, dd, $J_1=8.06$ Hz, $J_2=7.53$ Hz, H-6); 7.43 (1H, dd, $J_1=8.6$ Hz, $J_2=4.3$ Hz, H-3); *m/z* 163/5 (M^+, 100); 136/8 (9); 128 (30); 127 (13); 101 (13); 75 (13); 74 (9); 68 (11); 51 (9); 50 (12); 44 (51). C_9H_6NCl (163.60). Anal. Calcd C 66.07, H 3.70, N 8.56, Cl 21.67; found C 65.87, H 3.44, N 8.62.

4.1.3. 4-Hydroxy-8-chloroquinoline (4). To a solution of 8-chloroquinoline (**3**) (6.42 g, 39.24 mmol) and acetic acid (99%, 9.42 g, 157 mmol), under argon atmosphere was added hydrogen peroxide (30%, 12 mL, 118 mmol), and warmed at 60 °C for 20 h. Then the solvent was evaporated under reduced pressure, neutralized with concentrated sodium carbonate and extracted with dichloromethane. The resulting extract was dried with sodium sulfate, filtered and the solvent was removed under reduced pressure. The residue was purified by flash silica gel column cromatography (dichloromethane/hexane, 10:1) to give **4**, 4.37 g (62%) as a yellow solid, mp 225 °C (dec); ν_{max}(KBr)/cm^{-1} 3600–3000 (OH and N–H st), 1689 (C=O st), 1616, 1586, 1504, and 1467 (C=C and C=N st conj.), 995 and 964 (ArC–H (ip), 757 and 670 (ArC–H (oop); δ_H (200 MHz, MeOD), 8.57 (d, 1H, $J_{2-3}=2.7$ Hz, H-2), 7.47 (d, 1H, $J_{2-3}=2.7$ Hz, H-3), 7.37 (t, 1H, $J_{5-6,6-7}=8.1$ Hz, H-6), 7.55 (dd,

1H, J_{6-7}=8.1 Hz, J_{5-7}=1.2 Hz, H-7), 7.62 (dd, 1H, J_{5-6}= 8.1 Hz, J_{5-7}=1.2 Hz, H-5); δ_C (50 MHz, MeOD) 118.3 (C-3), 126.8 (C-5 and C-7), 127.8 (C-6), 132.9 (C-4a), 133.3 (C-8), 138.9 (C-8a), 146.5 (C-2) and 155.6 (C-4); *m/z* 179 (M^+, 100), 151 (7), 124 (7), 116 (11) and 89 (23).

C_9H_6NClO (179.60). Anal. Calcd C 60.19, H 3.37, N 7.80; found: C 59.89, H 3.44, N 7.55.

4.1.4. 8-Chloro-4-trifluoromethylsulfonyloxyquinoline (5). To a solution of 4-hydroxy-8-chloroquinoline (**4**) (200 mg, 1.11 mmol) in dry dichloromethane (15 mL), under argon atmosphere, at 0 °C were added 4-dimethylaminopyridine (28 mg, 0.22 mmol), 2,6-lutidine (0.19 mL, 1.55 mmol) and triflic anhydride (0.23 mL, 1.33 mmol). The mixture was stirred at 0 °C for 2 h and 1 h at room temperature and then was treated with water. The organic layer was dried with sodium sulfate, filtered and solvent removed at reduced pressure, to yield a residual solid, which was purified by silica gel column chromatography (dichloromethane), giving 8-chloro-4-trifluoromethilsulfonyloxyquinoline (**5**) (280 mg, 81%) as a white solid, mp 108–110 °C.

ν (KBr): 1616, 1586, 1504 and 1467 (C=C, C=N), 1348 (S=O), 1245, 1140, 995, 964, 750 (C–F); δ_H (200 MHz, MeOD), 8.91 (d, 1H, J_{2-3}=2.7 Hz, H-2), 8.10 (d, 1H, J_{2-3}= 2.7 Hz, H-3), 7.88 (dd, 1H, J_{5-6}=8.1 Hz, J_{5-7}=1.1 Hz, H-5), 7.77 (dd, 1H, J_{6-7}=8.1 Hz, J_{5-7}=1.1 Hz, H-7), 7.54 (t, 1H, $J_{5-6,6-7}$=8.1 Hz, H-6); δ_C (50 MHz, MeOD), 144.1 (C-2), 143.1 (CF_3), 133.9 (C-8a), 130.8 (C-7), 129.0 (C-4), 128.4 (C-5), 127.3 (C-6), 127.0 (C-3), 121.8 (C-8), 115.4 (C-4a); *m/z*, 311 (M^+, 47), 178 (10), 150 (100), 123 (32), 88 (10).

$C_{11}H_8ClF_3NO_3S$ (326.69). Anal. Calcd C 40.44, H 2.47, N 4.29; found: C 40.59, H 2.44, N 4.13.

4.1.5. 8-Chloroquinoline-*N*-oxide. To a solution of 8-chloroquinoline (**3**) (6.37 g, 38.93 mmol) in chloroform (10 mL), under argon atmosphere at 0 °C, was slowly added *m*-chloroperbenzoic acid (11 g, assay 57–90%). The mixture was stirred at 40 °C during 5 days and then the solvent was removed under reduced pressure, giving a brown residual oil, which was purified by silica gel flash column cromatography (dichloromethane/tetrahydrofuran, 2:1). The 8-chloroquinoline *N*-oxide (2.22 g, 32%) was isolated as a white solid, mp 103–105 °C.

ν_{max}(KBr)/cm^{-1}: 1654, 1592, 1558 and 1467 (C=C and C=N st conj.), 952 (ArC–H (ip), 790 and 743 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 7.29 (dd, 1H, J_{3-4}=8.6 Hz, J_{2-3}=6.3 Hz, H-3), 7.47 (t, 1H, $J_{5-6,6-7}$=7.8 Hz, H-6), 7.69 (d, 1H, J_{5-6}=7.8 Hz, H-5), 7.73 (d, 1H, J_{6-7}=7.8 Hz, H-7), 7.75 (dd, 1H, J_{3-4}=8.6 Hz, J_{2-4}=1.6 Hz, H-4) and 8.51 (dd, 1H, J_{2-3}=6.3 Hz, J_{2-4}=1.6 Hz, H-2).

C_9H_6ONCl (179.60). Anal. Calcd C 60.19, H 3.37, N 7.80; found: C 59.87, H 3.66, N 7.85.

4.1.6. 2,8-Dichloroquinoline (6). A solution of 8-chloroquinoline-*N*-oxide (365 mg, 2.03 mmol) and phosphoryl trichloride (1.82 mL, 18.29 mmol) at 0 °C, was heated to reflux temperature for 3 h and then poured onto ice, neutralized with a saturated aqueous ammonium chloride solution and extracted with dichloromethane. The extracts were dried with sodium sulfate, filtered and solvent removed, giving a brown solid, which was purified by flash silica gel column cromatography (hexane/dichloromethane, 2:1). Then, solvent was removed and 2,8-dichloroquinoline was isolated (208 mg, 52%) as a white solid, mp 104–105 °C; δ_H (200 MHz, $CDCl_3$) 7.46 (d, 1H, J_{3-4}=8.6 Hz, H-3), 7.49 (dd, 1H, J_{5-6}=8.3 Hz, J_{6-7}= 7.5 Hz, H-6), 7.75 (dd, 1H, J_{5-6}=8.3 Hz, J_{5-7}=1.5 Hz, H-5), 7.85 (dd, 1H, J_{6-7}=7.5 Hz, J_{5-7}=1.5 Hz, H-7) and 8.13 (d, 1H, J_{3-4}=8.6 Hz, H-4); δ_C (50 MHz, $CDCl_3$) 123.4 (C-3), 126.5 (C-6), 126.9 (C-5), 128.1 (C-4a), 130.6 (C-7), 132.6 (C-8), 139.2 (C-4), 144.2 (C-8a) and 151.7 (C-2); *m/z* 197 (M^+, 100), 162 (85), 126 (26), 99 (20) and 75 (15); $\lambda_{max}(CH_2Cl_2)$/nm 239, 289, 307 and 321.

$C_9H_5NCl_2$ (198.05). Anal. Calcd C 54.58, H 2.54, N 7.07; found: C 54.38, H 2.82, N 7.15.

4.1.7. 2-Methyl-4-(2′-quinolyl)-but-3-yn-2-ol (7). General method. To a solution of 2-chloroquinoline (**1**) (3.3 g, 20.17 mmol) and 2-methylbut-3-yn-2-ol (2.19 mL, 22.19 mmol) in freshly distilled diethylamine (10 mL), under argon atmosphere, were added dichloro bis(triphenylphosphine) palladium (141.6 mg, 0.2 mmol) and cuprous iodide (7.68 mg, 0.04 mmol). The mixture was stirred for 30 min at 40 °C and after, the excess of diethylamine was removed under reduced pressure. The residual solid was washed with an aqueous solution of ammonium chloride and potassium cyanide and finally extracted with dichloromethane. The extract was dried with sodium sulfate, filtered and the solvent evaporated to afford a yellow solid that was purified by flash silica gel column chromatography (hexane/ethylacetate, 2:1). The 2-methyl-4-(2′-quinolyl)-but-3-yn-2-ol (**7**) (3.93 g, 92%) was isolated as a yellow solid, mp 103–104 °C. ν_{max}(film)/cm^{-1} 3340 (O–H st), 2220 (C≡C st), 1610, 1587, 1545, 1495, 1455 and 1422 (C=C and C=N st conj.), 1380 and 1360 (CH_3 δ si), 829 and 753 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 1.68 (s, 6H, 2×CH_3), 3.22 (s, 1H, OH), 7.44 (d, 1H, J_{3-4}=8.2 Hz, H-3), 7.52 (ddd, 1H, J_{5-6}=7.8 Hz, J_{6-7}=6.8 Hz, J_{6-8}=1.0 Hz, H-6), 7.68 (ddd, 1H, J_{7-8}=8.8 Hz, J_{6-7}=6.8 Hz, J_{5-7}=1.3 Hz, H-7), 7.72 (dd, 1H, J_{5-6}=7.8 Hz, J_{5-7}=1.3 Hz, H-5), 8.06 (d, 1H, J_{3-4}=8.2 Hz, H-4) and 8.11 (dd, 1H, J_{7-8}=8.8 Hz, J_{6-8}= 1.0 Hz, H-8); δ_C (50 MHz, $CDCl_3$) 31.2 (2×CH_3), 65.4 (C–OH), 82.5 (Ar*C*≡C), 94.6 (ArC≡*C*), 124.2 (C-3), 127.1 (C-6), 127.4 (C-5), 129.2 (C-7), 130.0 (C-8), 136.1 (C-4), 143.2 (C-8a) and 148.0 (C-2).

$C_{14}H_{13}ON$ (211.26). Anal. Calcd C 79.59, H 6.20, N 6.63; found: C 79.38, H 6.34, N 6.52.

4.1.8. 2-Methyl-4-(3′-quinolyl)-but-3-yn-2-ol (8). Following the preparation of **7**, a mixture of 3-bromoquinoline (5.06 g, 24.3 mmol), 2-methylbut-3-yn-2-ol (2.25 mL, 26.7 mmol) in freshly distilled diethylamine (15 mL), under argon atmosphere was added, dichloro bis(triphenylphosphine) palladium(II) (174 mg, 0.25 mmol) and cuprous iodide (10.0 mg, 0.05 mmol). The mixture was stirred at 40 °C for 1 h, giving 2-methyl-4-(3′-quinolyl)-but-3-yn-2-ol (**8**) (4.98 g, 97%) as colourless crystals, mp 112–113 °C.[9b] δ_H (200 MHz, $CDCl_3$) 1.70 (s, 6H, 2×CH_3),

3.50 (s, 1H, OH), 7.54 (ddd, 1H, $J_{5-6}=8.1$ Hz, $J_{6-7}=7.0$ Hz, $J_{6-8}=1.1$ Hz, H-6), 7.70 (ddd, 1H, $J_{7-8}=8.1$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.6$ Hz, H-7), 7.75 (dd, 1H, $J_{5-6}=8.1$ Hz, $J_{5-7}=1.6$ Hz, H-5), 8.10 (dd, 1H, $J_{7-8}=8.1$ Hz, $J_{6-8}=1.1$ Hz, H-8) and 8.20 (d, 1H, $J_{2-4}=2.1$ Hz, H-4) and 9.04 (d, 1H, $J_{2-4}=2.1$ Hz, H-2).

$C_{14}H_{13}ON$ (211.26). Anal. Calcd C 79.59, H 6.20, N 6.63; found: C 79.38, H 6.34, N 6.52.

4.1.9. 2-Methyl-4-(4′-quinolyl)-but-3-yn-2-ol (9). Following the preparation of **7**, a mixture of 4-chloroquinoline (**2**) (2.0 g, 12.22 mmol), 2-methylbut-3-yn-2-ol (1.33 mL, 13.45 mmol) in freshly distilled diethylamine (7 mL), was added dichloro bis(triphenylphosphine) palladium (86 mg, 0.12 mmol, 0.9%) and cuprous iodide (4.7 mg, 0.02 mmol, 0.15%). The mixture was stirred for 2 days at the reflux temperature, giving (**9**) (2.19 g, 86%) as a yellow solid, mp 100–102 °C. δ_H (200 MHz, $CDCl_3$) 1.71 (s, 6H, $2\times CH_3$), 3.54 (s, 1H, OH), 7.13 (d, 1H, $J_{2-3}=4.7$ Hz, H-3), 7.31 (ddd, 1H, $J_{5-6}=8.6$ Hz, $J_{6-7}=7.0$ Hz, $J_{6-8}=1.1$ Hz, H-6), 7.50 (ddd, 1H, $J_{7-8}=8.6$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.6$ Hz, H-7), 8.00 (dd, 1H, $J_{5-6}=8.6$ Hz, $J_{5-7}=1.6$ Hz, H-5), 8.06 (dd, 1H, $J_{7-8}=8.6$ Hz, $J_{6-8}=1.1$ Hz, H-8) and 8.66 (d, 1H, $J_{2-3}=4.7$ Hz, H-2). $C_{14}H_{13}ON$ (211.26). Anal. Calcd C 79.59, H 6.20, N 6.63; found: C 79.63, H 6.10, N 6.33.

4.1.10. 2-Methyl-4-[-2′-(8′-chloroquinolyl)]-but-3-yn-2-ol (10). Following the preparation of **7**, a mixture of 2,8-dichloroquinoline (**6**) (367 g, 1.85 mmol), 2-methylbut-3-yn-2-ol (0.2 mL, 2.02 mmol) in freshly distilled diethylamine (2 mL) were added dichloro bis(triphenylphosphine) palladium (37 mg, 0.05 mmol) and cuprous iodide (2 mg, 0.01 mmol). The mixture was stirred for 1 h at 40 °C, giving 2-methyl-4-[2′-(8′-quinolyl)]-but-3-yn-2-ol (**10**) (415 mg, 91%) as a yellow solid, mp 78–80 °C. δ_H (200 MHz, $CDCl_3$) 1.67 (s, 6H, $2\times CH_3$), 3.22 (s, 1H, OH), 7.44 (dd, 1H, $J_{5-6}=8.6$ Hz, $J_{6-7}=7.8$ Hz, H-6), 7.54 (d, 1H, $J_{3-4}=8.6$ Hz, H-3), 7.70 (dd, 1H, $J_{5-6}=8.6$ Hz, $J_{5-7}=1.6$ Hz, H-5), 7.83 (dd, 1H, $J_{6-7}=7.8$ Hz, $J_{5-7}=1.6$ Hz, H-7) and 8.11 (d, 1H, $J_{3-4}=8.6$ Hz, H-4); δ_C (50 MHz, $CDCl_3$) 31.2 ($2\times CH_3$), 64.9 (C–OH), 83.9 (Ar*C*≡C), 96.8 (ArC≡*C*),125.1 (C-3), 126.6 (C-6), 126.9 (C-5), 128.3 (C-4a), 130.2 (C-7), 132.4 (C-8), 136.8 (C-4), 143.9 (C-8a) and 153.3 (C-2); *m/z* 245 (M^+, 50), 230 (100), 202 (75), 188 (78) and 162 (28). $C_{14}H_{12}ONCl$ (245.70). Anal. Calcd C 68.44, H 4.92, N 5.70; found: C 68.70, H 4.74, N 5.76.

4.1.11. 2-Ethynylquinoline (11). General method. To a solution of 2-methyl-4-(2′-quinolyl)-but-3-yn-2-ol (**7**) (379 mg, 1.79 mmol) in dry toluene (2 mL), under argon atmosphere, was introduced powder of sodium hydroxide (10 mg, 0.25 mmol) and refluxed for 1 h. Then, the reaction mixture was filtered and the solvent was removed giving a brown oil, which was purified by flash silica gel column chromatography (hexane/ethylacetate, 3:1). The 2-ethynylquinoline (**11**) (168 mg, 61%) was isolated as a yellow solid, mp 46–47 °C. ν_{max}(KBr)/cm^{-1} 3172 (≡C–H st), 2103 (C≡C st), 1616, 1593, 1552, 1500, 1457 and 1422 (C=C and C=N st conj.), 833 and 758 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 3.25 (s, 1H, C≡CH), 7.53 (d, 1H, $J_{3-4}=8.1$ Hz, H-3), 7.54 (ddd, 1H, $J_{5-6}=8.1$ Hz, $J_{6-7}=7.0$ Hz, $J_{6-8}=1.6$ Hz, H-6), 7.72 (ddd, 1H, $J_{7-8}=8.6$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.6$ Hz, H-7), 7.77 (dd, 1H, $J_{5-6}=8.1$ Hz, $J_{5-7}=1.6$ Hz, H-5), 8.10 (dd, 1H, $J_{7-8}=8.6$ Hz, $J_{6-8}=1.6$ Hz, H-8) and 8.12 (d, 1H, $J_{3-4}=8.1$ Hz, H-4); δ_C (50 MHz, $CDCl_3$) 77.5 (ArC≡*C*–H), 83.3 (Ar*C*≡C–H), 124.0 (C-3), 127.3 (C-4a, C-5 and C-6), 129.2 (C-7), 130.0 (C-8), 136.1 (C-4), 142.3 (C-8a) and 147.9 (C-2); *m/z* 153 (M^+, 100), 126 (30) and 76 (19); $\lambda_{max}(CH_2Cl_2)$/nm 240, 285, 316 and 330.

$C_{11}H_7N$ (153.18). Anal. Calcd C 86.25, H 4.61, N 9.14; found: C 86.36, H 4.65, N 9.27.

4.1.12. 3-Ethynylquinoline (12). Following the preparation of **11**, 2-methyl-4-(3′-quinolyl)but-3-yn-2-ol (**8**) (4.5 g, 21.3 mmol) in dry toluene (15 mL) and powder of sodium hydroxide (0.1 g, 2.5 mmol) at reflux temperature for 4 h, gave an orange solid, which was purified by sublimation on a cool-finger surface (40 Torr) at 50 °C. The 3-ethynylquinoline (**12**) was isolated as colourless crystals, 2.84 g, 87%, mp 78–79 °C.[9b] ν_{max}(KBr)/cm^{-1} 3165 (≡C–H st), 2095 (C≡C st), 1620, 1600, 1560, and 1490 (C=C and C=N st conj.), 790 and 750 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 3.28 (s, 1H, C≡CH), 7.58 (br dd, 1H, $J_{5-6}=7.8$ Hz, $J_{6-7}=7.0$ Hz, H-6), 7.73 (ddd, 1H, $J_{7-8}=8.6$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.6$ Hz, H-7), 7.79 (dd, 1H, $J_{5-6}=7.8$ Hz, $J_{5-7}=1.6$ Hz, H-5), 8.10 (br d, 1H, $J_{7-8}=8.6$ Hz, H-8), 8.29 (d, 1H, $J_{2-4}=2.3$ Hz, H-4), and 8.95 (d, 1H, $J_{2-4}=2.3$ Hz, H-2); $\lambda_{max}(CH_2Cl_2)$/nm 239 (ε, 30,054), 282 (ε, 7717), 316 (ε, 3579), and 330 (ε, 3659 L mol^{-1} cm^{-1}).

$C_{11}H_7N$ (153.18). Anal. Calcd C 86.25, H 4.61, N 9.14; found: C 86.12, H 4.39, N 8.93.

4.1.13. 4-Ethynylquinoline (13). Following the preparation of **11**, 2-methyl-4-(4′-quinolyl)but-3-yn-2-ol (**9**) (190 mg, 0.9 mmol) in dry toluene (2 mL), and powder of sodium hydroxide (4 mg, 0.1 mmol) at reflux temperature for 30 min, gave 4-ethynylquinoline (**13**) as a white solid, mp 96–97 °C (103 mg, 75%). ν_{max}(KBr)/cm^{-1} 3187 (≡C–H st), 2088 (C≡C st), 1579, 1560, 1503, 1464 and 1420 (C=C and C=N st conj.), 851, 811 and 803 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 3.67 (s, 1H, C≡CH), 7.53 (d, 1H, $J_{2-3}=4.5$ Hz, H-3), 7.60 (ddd, 1H, $J_{5-6}=8.3$ Hz, $J_{6-7}=6.7$ Hz, $J_{6-8}=1.6$ Hz, H-6), 7.74 (ddd, 1H, $J_{7-8}=8.6$ Hz, $J_{6-7}=6.7$ Hz, $J_{5-7}=1.6$ Hz, H-7), 8.11 (dd, 1H, $J_{5-6}=8.3$ Hz, $J_{5-7}=1.6$ Hz, H-5), 8.27 (dd, 1H, $J_{7-8}=8.6$ Hz, $J_{6-8}=1.6$ Hz, H-8) and 8.87 (d, 1H, $J_{2-3}=4.5$ Hz, H-2); $\lambda_{max}(CH_2Cl_2)$/nm 302, 311 and 325.

$C_{11}H_7N$ (153.18). Anal. Calcd C 86.25, H 4.61, N 9.14; found: C 86.41, H 4.39, N 9.15.

4.1.14. 8-Chloro-2-ethynylquinoline (14). Following the preparation of **11**, 2-methyl-4-[2′(8-chloroquinolyl)]but-3-yn-2-ol (**10**) (414 mg, 1.68 mmol) in dry toluene (10 mL) and powder of sodium hydroxide (7 mg, 0.17 mmol) at reflux temperature for 1 h, gave 8-chloro-2-ethynylquinoline (**14**) as an orange solid, mp 92–95 °C (202 mg, 65%).

ν_{max}(KBr)/cm^{-1} 3199 (≡C–H st), 2098 (C≡C st), 1609, 1593, 1542, 1500, 1491 and 1422 (C=C and C=N st conj.), 834, 760 and 670 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 3.29 (s, 1H, C≡CH), 7.47 (dd, 1H, $J_{5-6}=8.1$ Hz, $J_{6-7}=7.0$ Hz,

H-6), 7.60 (d, 1H, $J_{3-4}=8.5$ Hz, H-3), 7.72 (dd, 1H, $J_{5-6}=8.1$ Hz, $J_{5-7}=1.2$ Hz, H-5), 7.85 (dd, 1H, $J_{6-7}=7.3$ Hz, $J_{5-7}=1.2$ Hz, H-7) and 8.15 (d, 1H, $J_{3-4}=8.5$ Hz, H-4); δ_C (50 MHz, $CDCl_3$) 78.7 (ArC≡*C*–H), 83.3 (Ar*C*≡C–H), 125.1 (C-3), 126.6 (C-6), 127.2 (C-5), 128.6 (C-4a), 130.2 (C-7), 133.4 (C-8), 136.6 (C-4), 143.1 (C-8a) and 144.4 (C-2); *m/z* 187 (M^+, 100), 152 (28), 125 (10) and 84 (17); $\lambda_{max}(CH_2Cl_2)$/nm 219, 251, 308 and 334.

$C_{11}H_6NCl$ (187.62). Anal. Calcd C 70.42, H 3.22, N 7.47; found: C 70.33, H 3.03, N 7.16.

4.1.15. 1,4-Di(2′-quinolyl)-1,3-butadiyne (15). General method. A solution of cuprous chloride (10 mg, 0.1 mmol) and 2-ethynylquinoline (**11**) (85 mg, 0.55 mmol) in freshly distilled pyridine (30 mL), under oxygen atmosphere at 40 °C, was stirred for 150 min. Then, the solvent was removed at reduced atmosphere giving a brown solid, which was washed with an aqueous ammonium chloride solution and extracted with dichloromethane. The joining extracts were dried with anhydrous sodium sulfate, filtered and the solvent was evaporated affording a brown solid that was crystalized from acetonitrile/hexane (1:1). The 1,4-di(2′-quinolyl)-1,3-butadiyne (**15**) was isolated as a white solid (76 mg, 89%), mp 210 °C (dec). ν_{max}(KBr)/cm^{-1} 1616, 1589, 1550, 1496, 1456 and 1422 (C=C and C=N st conj.), 1111 (ArC–H (ip), 823, 785, 768 and 740 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 7.57 (d, 2H, $J_{3-4}=8.6$ Hz, H-3 and H-3′), 7.60 (m, 2H, H-6 and H-6′), 7.74 (m, 2H, H-7 and H-7′), 7.80 (m, 2H, H-5 and H-5′), 8.07 (m, 2H, H-8 and H-8′) and 8.16 (d, 2H, $J_{3-4}=8.6$ Hz, H-4 and H-4′); *m/z* 304 (M^+, 100), 152 (14), 128 (6) and 76 (7); $\lambda_{max}(CH_2Cl_2)$/nm 223 (ε, 84,170), 256 (ε, 146,670), 335 (ε, 80,580), 344 (ε, 77,010) and 360 (ε, 94,390 L mol^{-1} cm^{-1}).

$C_{22}H_{12}N_2$ (304.35). Anal. Calcd C 86.82, H 3.97, N 9.20; found: C 86.65, H 3.52, N 9.35.

4.1.16. 1,4-Di(3′-quinolyl)-1,3-butadiyne (16). Following the preparation of **15**, cuprous chloride (20 mg, 0.2 mmol) and 3-ethynylquinoline (**12**) (200 mg, 1.3 mmol) in pyridine (30 mL) at 60 °C, was stirred for 6 h affording 1,4-di(3′-quinolyl)-1,3-butadiyne (**16**) as a white solid, 160 mg, 80%, mp 233.7 °C (DSC). Compound **16** is photosensitive in the solid state and turns to a dark-blue solid by sunlight exposure. ν_{max}(KBr)/cm^{-1} 1610, 1598, 1550, 1490, 1461 and 1422 (C=C and C=N st conj.), 860, 790, 760 and 750 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$): 7.60 (br dd, 2H, $J_{5-6}=7.6$ Hz, H-6 and H-6′), 7.77 (ddd, 2H, $J_{7-8}=8.2$ Hz, $J_{6-7}=7.2$ Hz, $J_{5-7}=1.4$ Hz, H-7 and H-7′), 7.82 (dd, 2H, $J_{5-6}=7.6$ Hz, $J_{5-7}=1.4$ Hz, H-5 and H-5′), 8.12 (br d, 2H, $J_{7-8}=8.2$ Hz, H-8 and H-8′), 8.37 (d, 2H, $J_{2-4}=1.9$ Hz, H-4 and H-4′) and 9.00 (d, 2H, $J_{2-4}=1.9$ Hz, H-2 and H-2′); *m/z* 304 (M^+, 100), 152 (14), 124 (11); $\lambda_{max}(CH_2Cl_2)$/nm 221 (ε, 61,260), 254 (ε, 81,940), 316 (ε, 39,160), 335 (ε, 53,300) and 360 (ε, 56,220 L mol^{-1} cm^{-1}).

$C_{22}H_{12}N_2$ (304.35). Anal. Calcd C 86.82, H 3.97, N 9.20; found: C 86.60, H 4.05, N 9.11.

4.1.17. 1,4-Di(4′-quinolyl)-1,3-butadiyne (17). Following the preparation of **15**, cuprous chloride (5.4 mg, 0.054 mmol) and 4-ethynylquinoline (**13**) (82.4 mg, 0.54 mmol) in pyridine (4 mL), at 40 °C was stirred for 30 min, giving 1,4-di(4′-quinolyl)-1,3-butadiyne (**17**) as a white solid (79 mg, 97%), mp 215–216 °C; ν_{max}(KBr)/cm^{-1} 1573, 1503, 1460 and 1417 (C=C and C=N st conj.), 1077 and 1021 (ArC–H (ip), 851, 802 and 757 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 7.61 (d, 2H, $J_{2-3}=3.9$ Hz, H-3 and H-3′), 7.64 (ddd, 2H, $J_{5-6}=8.1$ Hz, $J_{6-7}=7.0$ Hz, $J_{6-8}=1.6$ Hz, H-6 and H-6′), 7.75 (ddd, 2H, $J_{7-8}=8.6$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.6$ Hz, H-7 and H-7′), 8.06 (dd, 2H, $J_{5-6}=8.1$ Hz, $J_{5-7}=1.6$ Hz, H-5 and H-5′), 8.27 (dd, 2H, $J_{7-8}=8.6$ Hz, $J_{6-8}=1.6$ Hz, H-8 and H-8′) and 8.81 (d, 2H, $J_{2-3}=3.9$ Hz, H-2 and H-2′); *m/z* 304 (M^+, 100), 275 (23), 249 (9), 152 (23) and 124 (12); $\lambda_{max}(CH_2Cl_2)$/nm 228, 271, 334, 345 and 371.

$C_{22}H_{12}N_2$ (304.35). Anal. Calcd C 86.82, H 3.97, N 9.20; found: C 86.59, H 3.87, N 8.94.

4.1.18. 1,4-Di[2′-(8′-chloroquinolyl)-1,3-butadiyne (18). Following the preparation of **15**, cuprous chloride (5 mg, 0.051 mmol) and 8-chloro-2-ethynylquinoline (**14**) (70 mg, 0.373 mmol) in pyridine (6 mL), The mixture was stirred at 40 °C for 4 h 30 min, affording 1,4-di[2′-(8′-chloroquinolyl)-1,3-butadiyne (**18**) as a yellow solid, mp 212–214 °C, (42.06 mg, 30%). ν_{max}(KBr)/cm^{-1} 1598, 1552, 1525, 1498, 1455 and 1426 (C=C and C=N st conj.), 1089 and 1032 (ArC–H (ip), 839, 793 and 758 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$); 7.46 (d, 2H, $J_{3-4}=8.6$ Hz, H-3 and H-3′), 7.79 (dd, 2H, $J_{5-6}=8.1$ Hz, $J_{6-7}=7.5$ Hz, H-6 and H-6′), 7.87 (dd, 2H, $J_{6-7}=7.5$ Hz, $J_{5-7}=1.6$ Hz, H-7 and H-7′), 8.15 (dd, 2H, $J_{5-6}=8.1$ Hz, $J_{5-7}=1.6$ Hz, H-5 and H-5′), and 8.30 (d, 2H, $J_{3-4}=8.6$ Hz, H-4 and H-4′); *m/z* 372 (M^+, 100), 337 (14), 302 (8), 210 (17), 186 (14), 168 (9), 163 (37), 151 (7), 127 (7) and 75 (5); λ_{max} (CH_2Cl_2)/nm 240, 269, 305, 344 and 365.

$C_{22}H_{10}N_2Cl_2$ (373.24). Anal. Calcd C 70.79, H 2.70, N 7.51; found: C 70.87, H 2.94, N 7.33.

4.1.19. Coupling reaction between 2′-chloroquinoline 11 and 2′-quinolylacetylene. (a) *$Cl_2Pd(Ph_3P)_2$–Cu_2I_2.* To a solution of 2-chloroquinoline (**1**) (278 mg, 1.7 mmol) and 2-ethynylquinoline (**11**) (200 mg, 1.3 mmol) in freshly distilled piperidine (15 mL), under argon atmosphere were successively added dichloro bis(triphenylphosphine) palladium (70 mg, 0.1 mmol) and cuprous iodide (10 mg, 0.05 mmol). The mixture was stirred for 3 days at reflux temperature, monitoring by TLC. Then, the piperidine was removed under reduced pressure and the residual solid was washed with an aqueous solution of ammonium chloride and potassium cyanide and extracted with dichloromethane. The joining extracts were dried on sodium sulfate, filtered and solvent evaporated under reduced pressure, giving a dark oil, which was purified by silica gel column cromatography (dichloromethane/acetonitrile, 10:1). The starting 2-ethynylquinoline (**11**) was isolated and also an orange solid (132 mg, 61%) mp 192–194 °C, that was identified as 2,2′-bis(quinoline) (**19**),[12b] δ_H (200 MHz, $CDCl_3$) 7.59 (ddd, 2H, $J_{5-6}=8.1$ Hz, $J_{6-7}=7.0$ Hz, $J_{6-8}=1.3$ Hz H-6 and H6′), 7.77 (ddd, 2H, $J_{7-8}=8.6$ Hz, $J_{6-7}=7.0$ Hz, $J_{5-7}=1.6$ Hz, H-7 and H-7′), 7.89 (dd, 2H, $J_{5-6}=8.1$ Hz, $J_{5-7}=1.6$ Hz, H-5 and H-5′), 8.25 (dd, 2H, $J_{7-8}=8.6$ Hz, $J_{6-8}=1.3$ Hz H-8 and H-8′), 8.34 (d, 2H, $J_{3-4}=8.6$ Hz, H-3 and H-3′), and

8.86 (d, 2H, J_{2-3}=8.6 Hz, H-4 and H-4′); *m/z* (%): 256 (M^+, 100), 128 (30) and 101 (13). $C_{18}H_{12}N_2$ (256.30). Anal. Calcd C 84.35, H 4.72, N 10.93; found: C 84.08, H 4.55, N 10.67.

(b) *$Cl_2Ni(PPh_3)_2$–Zn*. A suspension of dichloro bis(triphenylphosphine) nickel (0.4 g, 0.61 mmol) and triphenylphosphine (0.321 g, 1.22 mmol) and zinc powder (40 mg, 0.61 mmol) in dry THF (7 mL), was stirred at room temperature for 30 min. Then, a solution of 2-chloroquinoline (**1**) (100 mg, 0.61 mmol) and 2-ethynylquinoline (**11**) (118 mg, 0.76 mmol) in dry THF (8 mL), was added. The mixture was stirred at room temperature, under argon atmosphere, for 48 h and then filtered and the solvent removed under reduced pressure, giving a residual solid, which was washed with an aqueous solution of ammonium chloride and extracted with dichloromethane. The extract was dried with sodium sulfate, filtered and solvent evaporated under reduced pressure, giving a red solid, which was purified by flash silica gel column cromatography (hexane/ethyl acetate, 2:1). The starting 2-chloroquinoline (**2**) and a red oil that was identified as the mixture of 1,3,5- (**20**) and 1,2,4-tris(2′-quinolyl)benzene (**21**) (36:64, respectively) (50 mg, 43%). Isolation of the cyclotrimers was not possible and both were analyzed themselves; ν_{max}(KBr)/cm^{-1} 1644, 1618, 1596, 1558, 1503, 1461 and 1425 (C=C and C=N st conj.), 1096 and 1024 (ArC–H (ip), 865, 802 and 700 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 7.06 (d, J=7.5 Hz, H-3), 7.15 (d, J=8.1 Hz, H-3′), 7.54 (m, H-6 and H-6′), 7.73 (m, H-7, H-7′, H-5 and H-5′), 8.15 (m, H-4, H-4′, H-8, H-8 and H-c), 8.49 (dd, J=8.1 Hz, J=1.6 Hz, H-b), 8.71 (d, J=1.6 Hz, H-a) and 8.94 (s, H-a′); by GC/MS separation, 1,3,5-tris(2′-quinolyl)benzene (**20**) *m/z* 459 (M^+, 89%), 458 (100), 329 (6), 229 (25) and 128 (14); 1,2,4-tris(2′-quinolyl)benzene (**21**) *m/z* 459 (M^+, 41), 458 (49), 229 (14) and 128 (100). $C_{33}H_{21}N_3$ (459.54). Anal. Calcd C 86.25, H 4.61, N 9.14; found: C 86.26, H 4.44, N 8.87.

4.1.20. Coupling reaction between 3-bromoquinoline and 12: 1,2-di(3′-quinolyl)ethyne (22). To a solution of 3-bromoquinoline (0.62 g, 3 mmol) and 3-ethynylquinoline (**12**) (0.35 g, 2.29 mmol) in freshly distilled diethylamine (10 mL), under argon atmosphere, were introduced dichloro bis(triphenylphosphine) palladium (50 mg, 0.02 mmol, 3%) and cuprous iodide (8 mg, 0.04 mmol). The mixture was stirred for 6 days at reflux temperature and then the excess of diethylamine was removed at reduced pressure. The residual solid was washed with an aqueous solution of ammonium chloride and potassium cyanide and extracted with dichloromethane. The joining extracts were dried with sodium sulfate, filtered and the solvent evaporated to give a dark solid that was purified by flash silica gel column cromatography (dichloromethane/acetonitrile, 6:1). The 1,2-di(3′-quinolyl)ethyne (**22**) was isolated as a white solid, mp 164–169 °C (0.45 g, 70%); ν_{max}(KBr)/cm^{-1} 1616, 1599, 1564, 1487, 1466 and 1422 (C=C and C=N st conj.), 907, 787, 749 and 736 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) 7.60 (ddd, 2H, J_{5-6}=8.1 Hz, J_{6-7}=7.0 Hz, J_{6-8}=1.6 Hz, H-6 and H-6′), 7.76 (ddd, 2H, J_{7-8}=8.6 Hz, J_{6-7}=7.0 Hz, J_{5-7}=1.6 Hz, H-7 and H-7′), 7.84 (dd, 2H, J_{5-6}=8.1 Hz, J_{5-7}=1.6 Hz, H-5 and H-5′), 8.13 (dd, 2H, J_{7-8}=8.6, J_{6-8}=1.6 Hz, H-8 and H-8′), 8.39 (d, 2H, J_{2-4}=2.1 Hz, H-4 and H-4′) and 9.06 (d, 2H, J_{2-4}=2.1 Hz, H-2 and H-2′); δ_C (50 MHz, $CDCl_3$) 89.7 (Ar–C(C–Ar), 116.7 (C-3 and C-3′), 127.0 (C-4a and C-4a′), 127.3 (C-6 and C-6′), 127.6 (C-5 and C-5′), 129.3 (C-7 and C-7′), 130.3 (C-8 and C-8′), 138.5 (C-4 and C-4′), 146.9 (C-8a and C-8a′) and 151.8 (C-2 and C-2′); *m/z* 280 (M+, 100), 251 (9), 140 (11), 126 (9) and 100 (6); λ_{max}(CH_2Cl_2)/nm 227, 251, 267, 320, 334 and 347; UV–vis. λ_{max}(CH_2Cl_2)/nm 347 (46,100). Fluorescence λ (CH_2Cl_2), 354 and 371 (quantum yield Φ, 18%, referred to 2-aminopiridine in CH_2Cl_2).

$C_{20}H_{12}N_2$ (280.32). Anal. Calcd C 85.69, H 4.31, N 9.99; found: C 85.52, H 4.27, N 9.78.

4.1.21. 3′-Quinolylacetylene (12): cyclotrimerization to 1,3,5-tris(3′-quinolyl)benzene (23) and 1,2,4-tris(3′-quinolyl)benzene (24). *$Cl_2Ni(PPh_3)_2$–Zn*. A solution of dichloro bis(triphenylphosphine) nickel (0.22 g, 0.335 mmol), triphenylphosphine (0.161 g, 0.61 mmol) and zinc powder (20 mg, 0.31 mmol) in dry THF (4 mL), was stirred for 30 min at room temperature. Then, a solution of 3-ethynylquinoline (**12**) (60 mg, 0.38 mmol) in dry THF (4 mL), was added. The mixture was stirred at room temperature, under argon atmosphere, for 24 h, and finally, was filtered and the solvent removed under reduced pressure yielding a residual solid, which was washed with an aqueous solution of ammonium chloride and extracted with dichloromethane. The extract was dried with sodium sulfate, filtered and the solvent evaporated under reduced pressure, giving a red oil, which was purified by silica gel flash cromatography using hexane/ethyl acetate (2:1) as eluent. The red oil was isolated and identified as a mixture (40:60) of 1,3,5-tris (**23**) and 1,2,4-tris(3′-quinolyl)benzene (**24**) (69 mg, 80%). The separation of both cyclotrimers was not possible and both were analyzed themselves; ν_{max}(KBr)/cm^{-1}: 1644, 1618, 1596, 1558, 1503, 1461 and 1425 (C=C and C=N st conj.), 1096 and 1024 (ArC–H (ip), 865, 802 and 700 (ArC–H (oop); δ_H (200 MHz, $CDCl_3$) of the mixture: 1,2,4-tris(3′-quinolyl)benzene; 9.31 (d, J=2.3 Hz, H-2), 8.67 (d, J=8.0 Hz, H-8), 8.46 (d, J=2.3 Hz, H-4), 7.45–7.85 (m, H-5, H-6, H-7); 1,3,5-tris(3′-quinolyl)benzene; 9.34 (d, J=2.3 Hz, H-2), 8.50 (d, J=2.3 Hz, H-4), 8.67 (d, J=8.0 Hz, H-8), 7.95 s (s, H-2, H-4, H-6); *m/z* of the mixture; 459 (M^+, 100), 431 (8), 230 (24). $C_{33}H_{21}N_3$ (459.54). Anal. Calcd C 86.25, H 4.61, N 9.14; found: C 86.03, H 4.36, N 8.77. DSC analysis of the mixture **23** and **24** shows two endothermic peaks at 202 and 209 °C in 40:60 molar ratio.

References and notes

1. Heindel, N. D.; Bechara, I. S.; Ohnmacht, C. J.; Molnar, J.; Lemke, T. F.; Kennewell, P. D. *J. Med. Chem.* **1969**, 797.
2. Egan, T. J.; Hunter, R.; Kaschula, C. H.; Marques, H. M.; Misplon, A.; Walden, J. *J. Med. Chem.* **2000**, *43*, 283–291.
3. (a) Rodriguez, J. G.; Canoira, L.; Benito, Y. *Appl. Organometal. Chem.* **1987**, *1*, 535. (b) Rodríguez, J. G.; Benito, Y.; Baeza, J. G.; Fernández, C.; Gómez-Antón, M. R. *Eur. Polym. J.* **1990**, *26*, 689–693. (c) Benito, Y.; Rodríguez, J. G. *Eur. Polym. J.* **1994**, *30*, 661.

4. (a) Bunz, U. H. F. *Chem. Rev.* **2000**, *100*, 1605. (b) Irie, M. *Chem. Rev.* **2000**, *100*, 1685. (c) Delaire, J. A.; Nakatani, K. *Chem. Rev.* **2000**, *100*, 1817.
5. (a) *Polydiacetylenes*; Bloor, D., Chance, R. R., Eds.; NATO ASI series E, No. 102; Matinus Nijkoff: Boston, 1985. (b) Stiegman, A. E.; Graham, E.; Perry, K. J.; Khundkard, R.; Cheng, L. T.; Perry, J. W. *J. Am. Chem. Soc.* **1991**, *113*, 1658 and references cited therein.
6. (a) Wegner, G. *J. Polym. Sci., Part B* **1971**, *9*, 133. (b) Ozcayir, Y.; Asrar, J.; Blumstein, A. *Mol. Cryst. Liq. Cryst.* **1984**, *110*, 1424. (c) Milburn, G. H.; Wernick, A. R.; Tsibouklis, J.; Bolton, E.; Thomson, G.; Shand, A. *Polymer* **1989**, *30*, 1004.
7. Rodríguez, J. G.; Tejedor, J. L. *Eur. J. Org. Chem.* **2005**, 360. Rodríguez, J. G.; Tejedor, J. L. *Tetrahedron* **2005**, *61*, 2047.
8. Rodríguez, J. G.; Gómez-Antón, M. R.; Pierola, I. F. *Macromolecules* **1986**, *19*, 2932. Rodríguez, J. G.; Benito, Y.; Baeza, J. G.; Fernández-Sánchez, C.; Gómez-Antón, M. R. *Eur. Polym. J.* **1990**, *26*, 689. Benito, Y.; Rodríguez, J. G. *Eur. Polym. J.* **1994**, *30*, 661.
9. (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *50*, 4467. (b) Ames, D. E.; Bull, D.; Takundwa, C. *Synthesis* **1981**, 364.
10. Rodriguez, J. G.; Martín-Villamil, R.; Cano, F. H.; Fonseca, I. *J. Chem. Soc., Perkin Trans. 1* **1997**, 709–714.
11. Ciufolini, M. A.; Mitchell, J. W.; Roschangar, F. *Tetrahedron Lett.* **1996**, *37*, 8281.
12. (a) Bachman, G. B.; Cooper, D. E. *J. Org. Chem.* **1944**, *9*, 302. (b) *Handbook of Chemistry and Physics*; Weast, R. C., Ed. 61th ed.; CRC: Boca Raton, FL, 1980–1981.
13. Cohn, E. W. *J. Am. Chem. Soc.* **1930**, *52*, 3685. Lewis, I. K.; Russel, G. B.; Topsom, R. D.; Vaughan, J. *J. Org. Chem.* **1964**, *29*, 1183.
14. March, J. *Advanced Organic Chemistry* 4th ed.; Wiley, 1992; pp 714–715. For reviews, see Simándi In *The Chemistry of Functional Groups, Supplement C, pt 1*; Patai, S., Rappoport, Eds.; Wiley: New York, 1983; pp 529–534.
15. (a) Karlin, K. D.; Kaderli, S.; Zuberbühler, A. D. *Acc. Chem. Res.* **1997**, *30*, 139. (b) Kitajima, N.; Moro-oka, Y. *Chem. Rev.* **1994**, *94*, 737.
16. Rodríguez, J. G.; Lafuente, A.; de los Rios, C. *J. Polym. Sci., A: Polym. Chem.* **2004**, *42*, 6031 and references cited therein.
17. Jhingan, A. K.; Maier, W. F. *J. Org. Chem.* **1987**, *52*, 1161.
18. Rodríguez, J. G.; Lafuente, A.; Martín, R. *J. Polym. Sci., A: Polym. Chem.* **2005**, *43*, 1228.
19. Rodríguez, J. G.; Ramos, S.; Martín-Villamil, R.; Fonseca, I.; Albert, A. *J. Chem. Soc., Perkin Trans. 1* **1996**, 541.
20. Guo, J.; Mayr, A. *Inorg. Chim. Acta* **1997**, *261*, 141–146.
21. Rodríguez, J. G.; Lafuente, A.; Martín-Villamil, R.; Martinez-Alcazar, M. P. *J. Phys. Org. Chem.* **2001**, *14*, 859–868.
22. Rodríguez, J. G.; Oñate, A.; Martín, R.; Fonseca, I. *J. Organomet. Chem.* **1996**, *513*, 71.