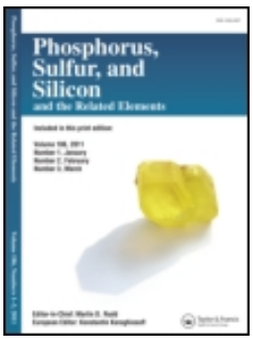

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The behavior of 2-chloroquinoline-3-carbaldehyde and 2-oxoquinoline-3-carbaldehyde toward stabilized methylenetriphenylphosphoranes and secondary amines

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ABSTRACT

In this study use was made of the Wittig carbonyl olefination reaction and stereo-identification of the resulting alkenes. Condensation of 2-chloroquinoline-3-carbaldehyde with some selected stabilized phosphonium ylides yielded a mixture of the corresponding E and Z olefins in each case. On the other hand reaction of 2-oxoquinoline-3-carbaldehyde with the selected ylides afforded the respective olefins only in one of the possible stereoisomers. The reaction of 2-chloroquinoline-3-carbaldehyde with acetylmethylenetriphenylphosphorane produced the respective olefine together with acridin-3-ol. Heating of (E) and/or (Z)-methyl 3-(2-chloroquinolin-3-yl)acrylate with hydrazine hydrate yielded the corresponding propan-1-ol derivative. Dechlorination of (E)-ethyl 3-(2-chloroquinolin-3-yl)acrylate and/or (E)-4-(2-chloroquinolin-3-yl)but-3-en-2-one was effected upon treatment with morpholine or piperidine in absolute ethanol to give the respective enone derivatives.

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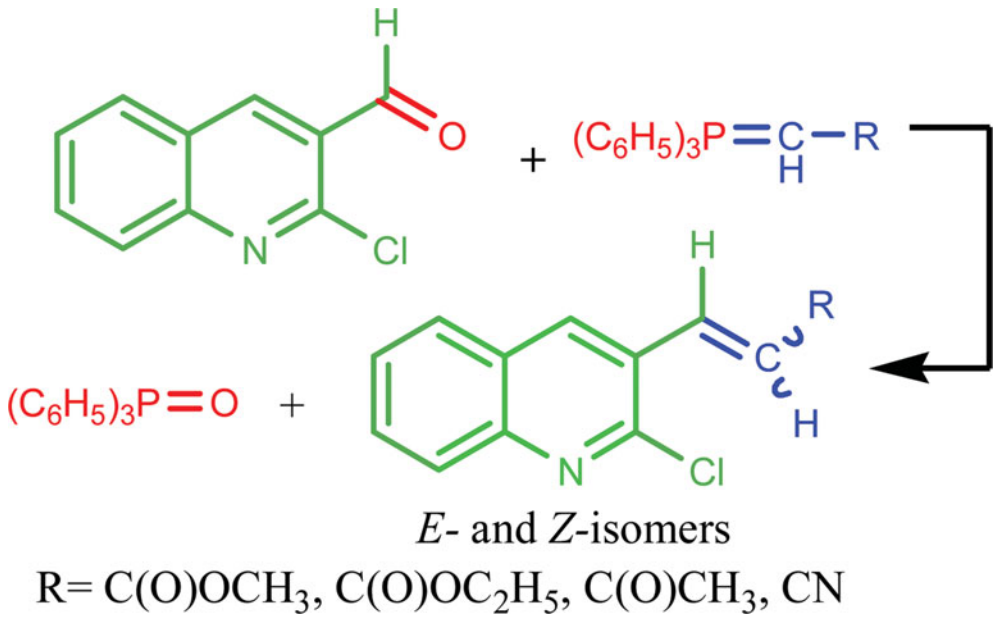
GRAPHICAL ABSTRACT



Introduction

The Wittig reaction is the most widely recognized method for carbonyl olefination.[1,2] It is a reliable method for the synthesis of a wide range of alkenes, often with high *E* and *Z* stereoselectivity, which is of great importance, particularly in medicinal practice and drug action.[3] Correlation between the biological potency and stereochemical aspects is well established.[4,5] For some therapeutics, however, single stereoisomer formulations are needed to provide greater selectivity for their biological targets, improved therapeutic indices and/or better pharmacokinetics than a mixture of stereoisomers.[3] On the

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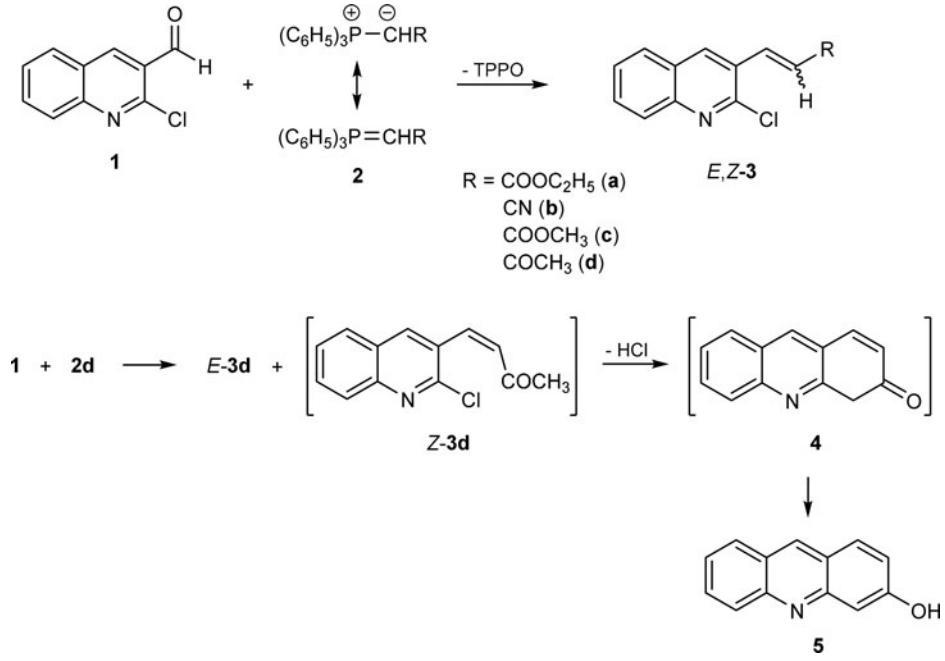


Scheme 1. Synthesis of olefins *E,Z*-**3a-c**, *E*-**3d,** and acridin-3-ol **5**.

other hand, quinolines are ubiquitous and important class of *N*-heterocycles.[6-8] They are the core structure in many alkaloid families[9] and well recognized by virtue of their wide range of applications as pharmaceuticals, agrochemicals, dye stuffs[10] as well as synthetic building blocks.[11] In response to our interest in this area[12] and in the organophosphorus chemistry of carbonyl compounds,[1,13-17] we have now studied the carbonyl olefination of 2-chloroquinoline-3-carbaldehyde (**1**) and 2-oxoquinoline-3-carbaldehyde (**6**) by stabilized methylenetriphenylphosphoranes (Wittig reagents, **2b**–**d**) (Schemes 1, 2). Special attention is devoted to the isolation of the resulting alkenes in pure *E* and/or *Z* forms. Replacement of the chlorine atom in **3** by hydrazines and secondary amines was also studied (Scheme 3).

Results and discussion

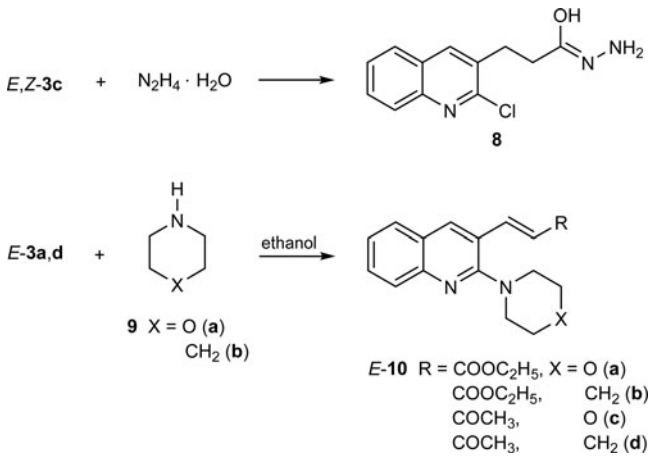
It has been now found that compound **1** reacts with carbethoxymethylenetriphenylphosphorane (**2a**) in absolute ethanol at room temperature. The precipitated colorless substance was identified as (*E*)-ethyl 3-(2-chloroquinolin-3-yl)acrylate (*E*-**3a**) (36% yield) (Scheme 1). The ^{1}H NMR spectrum of *E*-**3a** ($CDCl_3$) showed, that the ethylenic protons give rise to two doublets at $\delta = 6.56$ ($^3J_{HH} = 15.5$ Hz, α-H) and $\delta = 8.11$ ($^3J_{HH} = 16.1$ Hz, ß-H), which is typical for α,ß-unsaturated esters.

The filtrate of the reaction mixture after evaporation of the solvent under reduced pressure till dryness was carefully chromatographed to give two ethylenic products along with triphenylphosphine oxide (TPPO) (cf. Experimental). The first product (23% yield) was identified as (*Z*)-ethyl 3-(2-chloroquinolin-3-yl)acrylate (*Z*-**3a**). The main characteristic features of the ^{1}H NMR spectrum of *Z*-**3a** are two doublets at $\delta = 6.22$ ($^3J_{HH} = 12.2$ Hz, α-H) and at $\delta = 7.23$ ($^3J_{HH} = 11.4$ Hz, ß-H). The comparatively low coupling constant ^3J points to a *Z*-alkene.

The second product (20% yield) was proved to be (*E*)-ethyl 3-(2-chloroquinolin-3-yl)acrylate (*E*-**3a**) by comparing its mp, IR, ^{1}H NMR, and mass spectra with those of the precipitated substance isolated before.

In the same sense, aldehyde **1** reacted with the ylidenephosphorane **2b** under similar conditions to give a mixture of the corresponding ethylenes (*E*- and *Z*-**3b**). Compatible analytical and spectroscopic results were recorded for both isomers (Experimental). TPPO was also isolated and identified in this reaction.

Scheme 2. Synthesis of olefins **7b–d.**



Scheme 3. Synthesis of compound **8** and compounds **10a–d.**

The interesting isolation of *E* and *Z* isomers of compounds **3a** and **3b** has prompted us to reinvestigate the reaction of aldehyde **1** with methylenetriphenylphosphorane **2c**, which has been reported to yield the *E* isomer (*E*-**3c**) as the sole product.[18] We have found that carrying out this reaction in absolute ethanol at room temperature a colorless substance was obtained, which was identified as (***E***)-methyl 3-(2-chloroquinolin-3-yl)acrylate (*E*-**3c**) (32% yield) by comparing its mp, IR, ^{1}H NMR and mass spectra with the reported data.[18] Besides, the filtrate of the reaction mixture after evaporation of the solvent under reduced pressure till dryness and column chromatography on silica gel yielded two ethylenic products along with TPPO. The first product (15% yield) was confirmed to be (***E***)-methyl 3-(2-chloroquinolin-3-yl)acrylate (*E*-**3c**), while the second product (19% yield) was identified as (***Z***)-methyl 3-(2-chloroquinolin-3-yl)acrylate (*Z*-**3c**). Its ^{1}H NMR spectrum ($CDCl_3$) displayed a signal at $\delta = 3.74$ (s, 3H, OCH_3). The ethylenic protons give rise to two doublets at $\delta = 6.22$ (d, $^3J_{HH} = 12.3$ Hz, α-H) and $\delta = 7.22$ (d, $^3J_{HH} = 12.3$ Hz, ß-H). The comparatively lower coupling constant ^3J points to a *Z*-alkene.

When aldehyde **1** and acetylmethylenetriphenylphosphorane (**2d**) were stirred together in absolute ethanol at room temperature, a colorless substance was formed, filtered, and proved to be (***E***)-4-(2-chloroquinolin-3-yl)but-3-en-2-one (*E*-**3d**) (36% yield). The ^{1}H NMR spectrum of *E*-**3d** ($CDCl_3$) showed the presence of a signal at $\delta = 2.47$ (s, 3H, $COCH_3$). The ethylenic protons (2H) gave rise to two doublets at $\delta = 6.75$ ($^3J_{HH} = 16.1$ Hz, α-H) and $\delta = 7.88$ ($^3J_{HH} = 16.1$ Hz, ß-H).

The filtrate of the reaction mixture after evaporation of the solvent under reduced pressure till dryness and chromatography on silica gel yielded two products along with TPPO. The first product (18% yield) was confirmed to be (***E***)-4-(2-chloroquinolin-3-yl)but-3-en-2-one (*E*-**3d**) from its mp, IR, ^{1}H NMR, and mass spectra.

The second product (24% yield) was identified as acridin-3-ol (**5**) for the following reasons: (a) its microanalyses revealed the absence of chlorine in its molecule and its molecular weight determination corresponded to $C_{13}H_9NO$; MS: *m/z* 196 (M+H, 100%); (b) its IR spectrum (KBr, cm^{-1}) showed the presence of a band at 3446 (OH) and absence of bands around 1670 (CO) or around 740 (Cl-C). Apparently, proximity of the acetyl group to the chlorine atom in the presumably formed intermediate *Z*-**3d** would facilitate elimination of HCl molecule. This is followed by enolization of the resulting ketone **4** to give **5** (Scheme 1).

Furthermore, the reaction of 2-oxoquinoline-3-carbaldehyde (**6**) with ylidenetriphenyl-phosphoranes **2b**–**d** was carried out in absolute ethanol at room temperature to give products for which the structures **7b**–**d** were assigned, respectively (Scheme 2).

TPPO was also isolated and identified in each reaction. Structural assignment for (***E***)-methyl 3-(quinolin-2-on-3-yl)acrylate (*E*-**7c**) is based upon the following data: (a) correct elemental analysis and molecular weight determination for **7c**, corresponding to $C_{13}H_{11}NO_3$, MS: *m/z* 229, M^+, r.i. 14%; (b) its IR spectrum shows the CO absorption band of the ester carbonyl at 1698 cm^{-1}; (c) The ^{1}H NMR spectrum of *E*-**7c** ($CDCl_3$) shows a signal at $\delta = 3.83$ (s, 3H, $COOCH_3$) and the ethylenic protons (2H) give rise to two doublets at $\delta = 7.20$ ($^3J_{HH} = 16.0$ Hz, α-H) and at $\delta = 7.79$ ($^3J_{HH} = 16.0$ Hz, ß-H). Compatible elementary and spectroscopic results were also obtained for **7b**,**d** (Experimental).

The behavior of compounds **3** toward hydrazine hydrate and secondary amines was also investigated. Thus, heating of *E*-**3c** or *Z*-**3c** with hydrazine hydrate in absolute ethanol yielded a crystalline product, which proved to be 3-(2-chloroquinolin-3-yl)propanehydrazonic acid (**8**) (Scheme 3). Correct elementary and molecular weight determination for **8** corresponded to $C_{12}H_{12}ClN_3O$, MS: *m/z* 231 (233), (M - H_2O), r.i. 24% (7.8%).

On the other hand heating *E*-**3a** or *E*-**3d** with morpholine (**9a**) or piperidine (**9b**) under the same condition yielded crystalline products **10a**–**d**, in which the chlorine atom was replaced by morpholinyl or piperidinyl group (Scheme 3). Thus, heating *E*-**3a** with morpholine in absolute ethanol yielded a product, which was identified as (***E***)-ethyl 3-(2-morpholino-quinolin-3-yl)acrylate (*E*-**10a**). The main characteristic features of the ^{1}H NMR spectrum of *E*-**10a** are two doublets at $\delta = 6.55$ ($^3J_{HH} = 16.3$ Hz, α-H) and at $\delta = 7.86$ ($^3J_{HH} = 16.3$ Hz, ß-H).

Experimental

Solvents were purified and dried according to the usual procedures. 2-Chloroquinoline-3-carbaldehyde (**1**),[19] the stabilized phosphoniumylides (**2a**-**c**)[20-22] and 2-oxoquinoline-3-carbaldehyde (**6**)[23] were prepared according to known procedures. The reactions were monitored (TLC) and purity of the isolated products was controlled by using silica gel with fluorescent indicator F_{254} coated on aluminum sheets of layer thickness 0.2 mm [Fluka]. Column chromatography was performed on silica gel, grain size 0.063–0.2 mm (Merck). Melting points were determined with an Electrothermal Digital Melting Point Apparatus and are uncorrected. Elemental analytical data were obtained at the analytical laboratory of the National Research Centre. The IR spectra were recorded using KBr pellets with a Jasco Fourier Transform Infrared Spectrophotometer model FT/IR-300E. The ^{1}H NMR spectra were recorded in deuterated chloroform ($CDCl_3$) or in deuterated dimethylsulphoxide (DMSO-d_6) with a JEOL 500 AS (at 500 MHz) or with a Varian Mercury VX-300 (at 300 MHz) spectrometer using tetramethylsilane (TMS) as internal reference. ^{13}C NMR spectra were recorded with a JEOL 500 AS (at 125 MHz) or with a Varian Mercury VX-300 (at 75.46 MHz) instrument. Mass spectra (EI-MS) were measured at 70 eV with a Finnigan MAT SSQ 7000 spectrometer. The Supplemental Materials file contains sample spectra (^{1}H, ^{13}C NMR, IR, and mass spectra) for all products (Figures S1–S54).

General procedure for the preparation of compounds 3a–d and 5

To a stirred solution of 2-chloroquinoline-3-carbaldehyde (**1**) (0.95 g, 5 mmol) in absolute ethanol (30 mL) the ylide **2a**–**d** (5 mmol) was added. The reaction mixture was stirred at room temperature for 2–4 h (TLC controlled). The colorless precipitate was filtered and recrystallized from absolute ethanol to give compounds *E*-**3a**–**d**, respectively. From the filtrate, the solvent was evaporated under reduced pressure till dryness and the residual substance was collected and chromatographed on silica

gel to give compounds *E,Z*-**3a–c**, *E*-**3d,** and **5** along with triphenylphosphine oxide (TPPO), which was obtained at 75/25 v/v (petroleum ether (60–80°C)/acetone as an eluent) as colorless crystals (80% yield) (comparative mp. mixed mp. with authentic sample).[24]

(Z)-Ethyl 3-(2-chloroquinolin-3-yl)acrylate (Z-3a)

Eluent: petroleum ether (60–80°C) / acetone (95/5, v/v); Yellowish crystals, mp 80–81°C; IR (KBr), ν (cm^{-1}): 3050 (C–H aromatic), 2977 (C–H aliphatic), 1724 (CO ester), 1617, 1585 (C=N, C=C), 1194 (CO stretching), 745 (Cl-C); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.18$ (t, $^3J_{HH} = 7.7$ Hz, 3H, $OCH_2C\underline{H}_3$), 4.12 (q, $^3J_{HH} = 7.7$ Hz, 2H, $OC\underline{H}_2CH_3$), 6.22 (d, $^3J_{HH} = 12.2$ Hz, 1H, CH=C<u>H</u>-CO), 7.23 (d, $^3J_{HH} = 11.5$ Hz, 1H, C<u>H</u>=CH-CO), 7.58 (m, 1H, CH-6), 7.83 (m, 1H, CH-7), 7.85 (d, $^3J_{HH} = 7.6$ Hz, 1H, CH-5), 8.05 (d, $^3J_{HH} = 7.6$ Hz, 1H, CH-8), 8.44 (s, 1H, CH-4); MS (EI, 70 eV) *m/z* (%) 226 (63) [M^+– Cl]; Anal. Calcd. for $C_{14}H_{12}ClNO_2$ (261.7): C, 64.25; H, 4.62; N, 5.35, Found: C, 64.37; H, 4.59; N, 5.28%.

(E)-Ethyl 3-(2-chloroquinolin-3-yl)acrylate (E-3a)

Eluent: petroleum ether (60–80°C) / acetone (93/7, v/v); colorless crystals, mp 129–130°C. IR (KBr), ν(cm^{-1}): 3060 (C–H aromatic), 2989, 2936 (C–H aliphatic), 1712 (CO ester), 1614, 1580 (C=N, C=C), 1286 (CO stretching), 746 (Cl-C); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.35$ (t, $^3J_{HH} = 7.7$ Hz, 3H, $OCH_2C\underline{H}_3$), 4.31 (q, $^3J_{HH} = 7.7$ Hz, 2H, $OC\underline{H}_2CH_3$), 6.56 (d, $^3J_{HH} = 15.5$ Hz, 1H, CH=C<u>H</u>-CO), 7.84 (m, 1H, CH-6), 7.94 (m, 1H, CH-7), 8.02 (d, $^3J_{HH} = 8.4$ Hz, 1H, CH-5), 8.03 (d, $^3J_{HH} = 8.5$ Hz, 1H, CH-8), 8.11 (d, $^3J_{HH} = 16.1$ Hz, 1H, C<u>H</u>=CH-CO), 8.38 (s, 1H, CH-4); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.4$ ($OCH_2\underline{C}H_3$), 61.1 ($O\underline{C}H_2CH_3$), 123.0, 127.8 128.2, 128.6, 131.7, 136.2, 139.4, 148.0, 166.0 (ethylenic and quinolinyl carbon atoms), 188.3 (C=O); MS (EI, 70 eV) *m/z* (%) 261 (13), [M^+]; Anal. Calcd. for $C_{14}H_{12}ClNO_2$ (261.7): C, 64.25; H, 4.62; N, 5.35, Found: C, 64.31; H, 4.60; N, 5.26%.

(E)-3-(2-Chloroquinolin-3-yl)acrylonitrile (E-3b)

Eluent: *n*-hexane/acetone (90/10, v/v); colorless crystals, mp 171–173°C. IR (KBr), ν(cm^{-1}): 3056 (C–H aromatic), 2950 (C–H aliphatic), 2211 (CN), 1608, 1578 (C=N, C=C), 747 (Cl-C); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 6.05$ (d, $^3J_{HH} = 16.8$ Hz, 1H, CH=C<u>H</u>-CO), 7.63 (m, 1H, CH-6), 7.83 (m, 1H, CH-7), 7.86 (d, $^3J_{HH} = 7.0$ Hz, 1H, CH-5), 7.89 (d, $^3J_{HH} = 15.8$ Hz, 1H, C<u>H</u>=CH-CO), 8.03 (d, $^3J_{HH} = 7.0$ Hz, 1H, CH-8), 8.32 (s, 1H, C*H*-4); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 100.7$ (CN), 117.2, 126.3, 126.6, 127.9, 128.1, 128.3, 128.4, 132.2, 135.8, 145.4, 148.1 (ethylenic and quinolinyl carbon atoms); MS (EI, 70 eV) *m/z* (%) 214 (44), [M^+]; Anal. Calcd. for $C_{12}H_7ClN_2$ (214.6): C, 67.15; H, 3.29; N, 13.05, Found: C, 66.89; H,3.33; N, 13.23%.

(Z)-3-(2-Chloroquinolin-3-yl)acrylonitrile (Z-3b)

Eluent: *n*-hexane/acetone (88/12, v/v); colorless crystals, mp 133–134°C. IR (KBr), ν(cm^{-1}): 3057 (C–H aromatic), 2969 (C–H aliphatic), 2216 (CN), 1607, 1582 (C=N, C=C), 754 (Cl-C); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 5.75$ (d, $^3J_{HH} = 12.3$ Hz, 1H, CH=C<u>H</u>-CO), 7.63 (m, 1H, CH-6), 7.65 (d, $^3J_{HH} = 12.2$ Hz, 1H, C<u>H</u>=CH-CO), 7.81 (m, 1H, CH-7), 7.94 (d, $^3J_{HH} = 8.4$ Hz, 1H, CH-5), 8.02 (d, $^3J_{HH} = 8.4$ Hz, 1H, CH-8), 8.89 (s, 1H, CH-4). ^{13}C NMR (75 MHz, DMSO): $\delta = 99.7$ (CN), 116.0, 125.9, 127.9, 128.3, 128.5, 132.1, 138.0, 144.0, 146.0 (ethylenic and quinolinyl carbon atoms); MS (EI, 70 eV) *m/z* (%) 214 (65) [M^+]; Anal. Calcd. for $C_{12}H_7ClN_2$ (214.6): C, 67.15; H, 3.29; N, 13.05, Found: C, 66.97; H, 3.40; N, 12.90%.

(Z)-Methyl 3-(2-chloroquinolin-3-yl)acrylate (Z-3c)

Eluent: petroleum ether (60–80°C)/acetone (95/5, v/v); colorless crystals, mp 97–98°C. IR (KBr), ν(cm^{-1}): 3050 (C–H aromatic), 2948 (C–H aliphatic), 1722 (CO ester), 1634, 1561 (C=N, C=C), 1296 (CO stretching), 752 (Cl-C); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.74$ (s, 3H, $COOC\underline{H}_3$), 6.22 (d, $^3J_{HH} = 12.3$ Hz, 1H, CH=C<u>H</u>-CO), 7.22 (d, $^3J_{HH} = 13.0$ Hz, 1H, C<u>H</u>=CH-CO), 7.58 (m, 1H, CH-6), 7.76 (m, 1H, CH-7), 7.85 (d, $^3J_{HH} = 8.4$ Hz, 1H, CH-5), 8.01 (d, $^3J_{HH} = 7.7$ Hz, 1H, CH-8), 8.45 (s, 1H, CH-4); MS (EI, 70 eV) *m/z* (%) 247 (<5) [M^+]; Anal. Calcd. for $C_{13}H_{10}ClNO_2$ (247.6): C, 63.04; H, 4.07; N, 5.66, Found: C, 62.78; H, 4.02; N, 5.60%.

(E)-Methyl 3-(2-chloroquinolin-3-yl)acrylate (E-3c)

Eluent: petroleum ether (60–80°C)/acetone (93/7, v/v); colorless crystals, mp 147–148°C. IR (KBr), ν(cm^{-1}): 3057, 3035 (C–H aromatic), 3005, 2948 (C–H aliphatic), 1709 (CO ester), 1613, 1584 (C=N, C=C), 1287 (CO stretching), 746 (Cl-C); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.85$ (s, 3H, $COOCH_3$), 6.57 (d, $^3J_{HH} = 16.1$ Hz, 1H, CH=C<u>H</u>-CO), 7.60 (m, 1H, CH-6), 7.78 (m, 1H, CH-7), 7.86 (d, $^3J_{HH} = 8.4$ Hz, 1H, CH-5), 8.02 (d, $^3J_{HH} = 8.4$ Hz, 1H, CH-8), 8.13 (d, $^3J_{HH} = 16.1$ Hz, 1H, C<u>H</u>=CH-CO), 8.38 (s, 1H, CH-4). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 52.0$ ($COO\underline{C}H_3$), 122.3, 126.9, 127.4, 127.6, 128.0, 128.4, 131.5, 136.1, 139.5, 147.9 (ethylenic and quinolinyl carbon atoms), 180.0 (C=O); MS (EI, 70 eV) *m/z* (%) 247 (10) [M^+]; Anal. Calcd. for $C_{13}H_{10}ClNO_2$ (247.6): C, 63.04; H, 4.07; N, 5.66, Found: C, 62.97; H, 3.77; N, 5.54%.

(E)-4-(2-Chloroquinolin-3-yl)but-3-en-2-one (E-3d)

Eluent: petroleum ether (60–80°C)/acetone (85/15,v/v); colorless crystals, mp 130–132°C. IR (KBr), ν(cm^{-1}): 3058 (C–H aromatic), 2900 (C–H aliphatic), 1677 (α,β-unsaturated ketone), 1602, 1578 (C=N, C=C), 1287 (CO stretching), 743 (Cl-C); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 2.47$ (s, 3H, $COCH_3$), 6.75 (d, $^3J_{HH} = 16.1$ Hz, 1H, CH=C<u>H</u>-CO), 7. 80 (m, 1H, CH-6), 7.86 (m, 1H, CH-7), 7.88 (d, $^3J_{HH} = 16.1$ Hz, 1H, C<u>H</u>=CH-CO), 7.91 (d, $^3J_{HH} = 7.7$ Hz, 1H, CH-5), 8.00 (d, $^3J_{HH} = 8.4$ Hz, 1H, CH-8), 8.40 (s, 1H, CH-4); MS (EI, 70 eV) *m/z* (%) 231(87) [M^+]; Anal. Calcd. for $C_{13}H_{10}ClNO$ (231.6): C, 67.39; H, 4.35; N, 6.05, Found: C, 67.27; H, 4.37; N, 5.84%.

Acridin-3-ol (5)

Eluent: petroleum ether (60–80°C)/acetone (80/20, v/v); colorless crystals, mp 150–152°C. IR (KBr), ν(cm^{-1}): 3446 (OH),

3054 (C–H aromatic), 2980 (C–H aliphatic), 1652, 1436 (C=N, C=C), 1187 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.01 (bs, 1H, OH), 7.46–7.67 (m, 8H, aromatic-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 115.0, 118.9, 122.2, 125.6, 125.7, 128.6, 129.2, 131.6, 137.9, 138.8, 141.0, 146.8 (acridinyl carbon atoms), 159.3 (C-OH). MS (EI, 70 eV) *m/z* (%) 196 (100) [M^++1]; Anal. Calcd. for $C_{13}H_9NO$ (195.2): C, 79.98; H, 4.56; N, 7.17, found: C, 79.77; H, 4.60; N, 7.02%.

General procedure for the preparation of compounds 7b-d

A mixture of 2-oxoquinoline-3-carbaldehyde (**6**) (0.35 g, 2 mmol) and stabilized ylides **2b**–**d** (2 mmol) in absolute ethanol (20 mL) was stirred at room temperature for 2 h. The formed colorless precipitate was filtered and recrystallized from absolute ethanol to give *Z*-**7b**–**d** isomers, respectively. The filtrate was evaporated under reduced pressure till dryness and the residual substances were collected and chromatographed on silica gel using petroleum ether bp 60–80°C/ethyl acetate as eluent to give an additional amount of compounds *Z*-**7b**–**d** along with triphenylphosphine oxide (TPPO), which was obtained at 70/30 v/v (pet. ether (60–80°C)/ethyl acetate as eluent) as colorless crystals (70% yield) (comparative mp. mixed mp. with authentic sample).[24]

(Z)-3-(2-Oxo-1,2-dihydroquinolin-3-yl)acrylonitrile (Z-7b)

Eluent: petroleum ether (60–80°C)/ethyl acetate (85/15, v/v); colorless crystals, mp 279–280°C. IR (KBr), ν(cm^{-1}): 3154 (NH), 3029 (C–H aromatic), 2894, 2835 (C–H aliphatic), 2217 (CN), 1674 (CO amide), 1620, 1607 (C=N, C=C), 1260 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.63 (d, $^3J_{HH}$ = 11.5 Hz, 1H, CH=C<u>H</u>-CO), 7.28–7.90 (m, 5H), 8.78 (s, 1H, CH-4), 11.84 (bs, 1H, NH). MS (EI, 70 eV) *m/z* (%) 196 (100) [M^+]; Anal. Calcd. for $C_{12}H_8N_2O$ (196.2): C, 73.46; H, 4.11; N, 14.28, found: C, 73.14; H, 3.90; N, 13.88%.

(E)-Methyl 3-(2-oxo-1,2-dihydroquinolin-3-yl)acrylate (E-7c)

Eluent: petroleum ether (60–80°C)/ethyl acetate (80/20, v/v); Colorless crystals, mp 232–233°C. IR (KBr), ν(cm^{-1}): 3156 (NH), 3098, 2993 (C–H aromatic), 2943, 2852 (C–H aliphatic), 1698 (CO ester), 1650 (CO amide), 1624, 1598 (C=N, C=C), 1262 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.83 (s, 3H, $COOCH_3$), 7.20 (d, $^3J_{HH}$ = 16.0 Hz, 1H, CH=C<u>H</u>-CO), 7.25 (m, 1H, CH-6), 7.39 (d, $^3J_{HH}$ = 8.4 Hz, 1H, CH-5), 7.58 (m, 1H, CH-7), 7.62 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH-8), 7.79 (d, J_{HH} = 15.3 Hz, 1H, C<u>H</u>=CH-CO), 8.01 (s, 1H, CH-4), 11.73 (bs, 1H, NH); ^{13}C NMR (125 MHz, DMSO): δ = 52.1 ($COO\underline{C}H_3$), 115.6, 119.4, 120.7, 122.8, 125.7, 129.3, 132.3, 139.4, 140.3, 142.1 (ethylenic and quinolinyl carbon atoms), 161.3 (C=O), 167.5 (C=O); MS (EI, 70 eV) *m/z* (%) 229 (12) [M^+]; Anal. Calcd. for $C_{13}H_{11}NO_3$ (229.2): C, 68.11; H, 4.84; N, 6.11, Found: C,68.57; H, 4.60; N, 5.80%.

(E)-3-(3-Oxobut-1-en-1-yl)quinolin-2(1H)-one (E-7d)

Eluent: petroleum ether (60–80°C)/ethyl acetate (80/20, v/v); colorless crystals, mp 293–294°C. IR (KBr), ν(cm^{-1}): 3151 (NH), 3100, 2997 (C–H aromatic), 2943, 2893 (C–H aliphatic), 1686 (α,β-unsaturated ketone), 1650 (CO amide), 1595, 1557 (C=N, C=C), 1272 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.42 (s, 3H, $COCH_3$), 7.25–7.28 (m, 2H, quinolinyl-H), 7.31 (d, $^3J_{HH}$ = 16.3 Hz, 1H, CH=C<u>H</u>-CO), 7.58–7.66 (m, 3H, C<u>H</u>=CH-CO, quinolinyl-H), 8.04 (s, 1H, CH-4), 10.44 (bs, 1H, NH); MS (EI, 70 eV) *m/z* (%) 213.2 (<5) [M^+]; Anal. Calcd. for $C_{13}H_{11}NO_2$ (213.2): C, 73.23; H, 5.20; N, 6.57, Found: C, 72.95; H, 5.31; N, 6.44%.

Preparation of compound 8

To a stirred solution of compound *Z*-**3c** and/or *E*-**3c** (0.26 g, 1 mmol) in absolute ethanol (15 mL), hydrazine hydrate (2 mL) was added dropwise at room temperature. The reaction mixture was heated under reflux for about 3 h. The solvent was evaporated under reduced pressure and the residue was crystallized from chloroform/*n*-hexane to give compound **8**.

3-(2-Chloroquinolin-3-yl)propanehydrazonic acid (8)

Colorless crystals, mp 189–199°C; IR (KBr), ν(cm^{-1}): 3424 (OH), 3221 (NH_2), 3050 (C–H aromatic), 2915 (C–H aliphatic), 1654, 1551 (C=N, C=C), 755 (Cl–C); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.10 (m, 2H, CH_2), 3.26 (m, 2H, CH_2), 7.52 (m, 1H, CH-6), 7.68 (m, 1H, CH-7), 7.77 (d, $^3J_{HH}$ = 7.6 Hz, 1H, CH-5), 7.99 (d, $^3J_{HH}$ = 8.4 Hz, 1H, CH-8), 8.08 (s, 1H, CH-4), 8.18 (bs, 1H, OH). MS (EI, 70 eV) *m/z* (%) 231(24) [M^+- H_2O]; Anal. Calcd. for $C_{12}H_{12}ClN_3O$ (249.07): C, 57.72; H, 4.84; N, 16.83, Found: C, 57.54; H, 4.72; N, 16.50%.

General procedure for the preparation of compounds 10a-d

To a stirred solution of compound **3c** and/or **3d** (1 mmol) in absolute ethanol (20 mL), the cyclic amine **9a** and/or **9b** (1 mmol) was added. The reaction mixture was heated under reflux for 7–10 h (TLC controlled). The volatile materials were evaporated under reduced pressure till dryness and the residue was triturated with diethyl ether to give colorless crystalline compounds **10a**–**d**. The colorless precipitate was filtered and recrystallized from chloroform/*n*-hexane.

(E)-Ethyl 3-(2-morpholinoquinolin-3-yl)acrylate (10a)

Colorless crystals, mp 112–114°C; IR (KBr), ν(cm^{-1}): 3063, 2966 (CH aromatic), 2927, 2894, 2843 (CH aliphatic), 1704 (CO ester), 1603, 1477 (C=N, C=C), 1186 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (t, $^3J_{HH}$ = 6.7 Hz, 3H, $OCH_2\underline{CH_3}$), 3.36 (m, 4H, morpholinyl-H), 3.91 (m, 4H, morpholinyl-H), 4.28 (q, $^3J_{HH}$ = 6.7 Hz, 2H, $OC\underline{H_2}CH_3$), 6.55 (d, $^3J_{HH}$ = 16.3 Hz, 1H, CH=C<u>H</u>-CO), 7.37 (m, 1H, CH-6), 7.63 (m, 1H, CH-7), 7.70 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH-5), 7.83 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH-8), 7.86 (d, $^3J_{HH}$ = 15.3 Hz, 1H, C<u>H</u>=CH-CO), 8.14 (s, 1H, CH-4); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.4 ($OCH_2\underline{CH_3}$), 51.0 (morpholinyl-$\underline{C}H_2$), 60.8 ($O\underline{C}H_2CH_3$), 67.0 (morpholinyl-$\underline{C}H_2$), 119.6, 122.4, 124.9, 125.0, 127.7, 127.9, 130.6, 137.2, 141.8, 147.6, 159.4 (ethylenic and quinolinyl carbon atoms), 166.8 (C=O); MS (EI, 70 eV) *m/z* (%) 312 (24) [M^+]; Anal. Calcd. for $C_{18}H_{20}N_2O_3$ (312.15): C, 69.21; H, 6.45; N, 8.97, found: C, 69.47; H, 6.11; N, 8.36%.

(E)-Ethyl 3-(2-(piperidin-1-yl)quinolin-3-yl)acrylate (10b)

Oil, IR (KBr), $\nu(cm^{-1})$: 3053(CH aromatic), 2930, 2884 (CH aliphatic), 1716 (CO ester), 1610, 1558 (C=N, C=C), 1169 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (t, $^3J_{HH}$ = 6.7 Hz, 3H, $OCH_2C\underline{H_3}$), 1.76 (m, 4H, piperidinyl-H), 3.30 (m, 4H, piperidinyl-H), 3.70 (m, 2H, piperidinyl-H), 4.28 (q, $^3J_{HH}$ = 6.7 Hz, 2H, $OC\underline{H_2}CH_3$), 6.55 (d, $^3J_{HH}$ = 16.3 Hz, 1H, CH=C<u>H</u>-CO), 7.33 (m, 1H, CH-6), 7.59 (m, 1H, CH-7), 7.67 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH-5), 7.80 (d, $^3J_{HH}$ = 8.6 Hz, 1H, CH-8), 7.85 (d, $^3J_{HH}$ = 16.3 Hz, 1H, C<u>H</u>=CH-CO), 8.11 (s, 1H, CH-4); MS (EI, 70 eV) *m/z* (%) 310 (100) [M^+]; Anal. Calcd. for $C_{19}H_{22}N_2O_2$ (310.17): C, 73.52; H, 7.41; N, 9.03, Found: C, 73.12; H, 7.83; N, 8.68%.

(E)-4-(2-Morpholinoquinolin-3-yl)but-3-en-2-one (10c)

Colorless crystals, mp 165–167°C; IR (KBr), $\nu(cm^{-1})$: 3151, 3099 (C-H aromatic), 2998, 2943, 2846 (CH aliphatic), 1653 (α,β-unsaturated ketone), 1602, 1553 (C=N, C=C), 1254 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.25 (s, 3H, $COCH_3$), 2.29, (m, 4H, morpholinyl-H), 3.33 (m, 4H, morpholinyl-H), 7.19 (m, 1H, CH-6), 7.26 (d, $^3J_{HH}$ = 16.0 Hz, 1H, CH=C<u>H</u>-CO), 7.29 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH-5), 7.52 (m, 1H, CH-7), 7.58 (d, $^3J_{HH}$ = 16.3 Hz, 1H, C<u>H</u>=CH-CO), 7.66 (d, $^3J_{HH}$ = 7.7 Hz, 1H, CH-8), 8.40 (s, 1H, CH-4). MS (EI, 70 eV) *m/z* (%) 282.34 (8) [M^+]; Anal. Calcd. for $C_{17}H_{18}N_2O_2$ (282.14): C, 72.32; H, 6.43; N, 9.92, Found: C, 72.36; H, 6.40; N, 9.95%.

(E)-4-(2-(Piperidin-1-yl)quinolin-3-yl)but-3-en-2-one (10d)

Colorless crystals, mp 158–159°C; IR (KBr), $\nu(cm^{-1})$: 3195 (C-H aromatic), 2951, 2838 (CH aliphatic), 1650 (α,β-unsaturated ketone), 1598, 1456 (C=N, C=C), 1267 (CO stretching); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.65–1.83 (m, 6H, piperidinyl-H), 2.15 (s, 3H, $COCH_3$), 3.31–3.34 (m, 4H, piperidinyl-H) 6.81 (d, $^3J_{HH}$ = 16.5 Hz, 1H, CH=C<u>H</u>-CO), 7.33 (m, 1H, CH-6), 7.61 (m, 1H, CH-7), 7.68 (d, $^3J_{HH}$ = 8.4 Hz, 1H, CH-5), 7.74 (d, $^3J_{HH}$ = 16.5 Hz, 1H, C<u>H</u>=CH-CO), 7.83 (d, $^3J_{HH}$ = 8.4 Hz, 1H, CH-8), 8.14 (s, 1H, CH-4); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.6 ($CO\underline{C}H_3$), 26.1, 27.2, 51.2 (piperidinyl-$\underline{C}H_2$), 122.6, 124.4, 124.7, 127.5, 127.8, 128.0, 130.4, 136.6, 139.3, 141.3, 147.6 (ethylenic and quinolinyl carbon atoms), 198.6 (carbonyl carbon); MS (EI, 70 eV) *m/z* (%) 280.39 (15) [M^+]; Anal. Calcd. for $C_{18}H_{20}N_2O$ (280.16): C, 77.15; H, 7.22; N, 9.96, Found: C, 77.11; H, 7.19; N, 9.99%.

Conclusion

Stabilized phosphonium ylides **2a**–**d** have been now successfully utilized for the preparation of new *E*,*Z*-quinolinylethylenes **3a**–**d**. The strategy employed is based upon the Wittig condensation reaction of reagents **2** with 2-chloroquinoline-3-carbaldehyde (**1**). Similarly, the Wittig reaction of **2** with 2-oxoquinoline-3-carbaldehyde (**6**) produced the respective *Z* and / or *E* chalcones (**7**). Compounds **3** as well as compounds **7** belong to the class of chalcones, which display many biological properties like anti-HIV,[25] anticancer,[26] and antimicrobial[27] activities. Both of the *Z* and *E* isomers of **3a**–**c** and *E*-**3d** were isolated and characterized. This stereochemical specification is of marked significance in the design of active principles, particularly in the field of drugs.[5] Dechlorination of compounds *E*3-**a**,**d** succeeded upon their condensation with piperidine and/or morpholine. The stereochemical *E* configuration is retained in the produced ethylenes (**10**). Meanwhile, conversion of ethylenes *E*,*Z*-**3c** to the respective ethane **8** supplements to well-known potency of hydrazine hydrate as a reducing agent for α,β-unsaturated carbonyl compounds.[28]

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