SYNTHESIS AND ANTI-APHID APHIS GOSSYPII GLOVER ACTIVITY OF SOME NEW QUINOLINE DERIVATIVES

Mohamed Ramdan El-Sayed Aly¹, Ahmed Elsayed Mahmoud Abd El-Mageed³
Abdel Kader Mousa Abdel El Kafafy³, Galal Abd Moain Nawwar³*

¹Chemistry Department, Faculty of Science, Port Said University 42523, Egypt
²Chemistry Department, Faculty of Science, Zagazig University 44519, Egypt
³National Research Center, Dokki, Cairo, Egypt

Received: June 5, 2010
Accepted: December 17, 2010

Abstract: A series of quinoline derivatives have been elaborated from reaction of 2-(m- and p-acetylanilino)-quinolines 6a–b with aldehydes under Claisen-Schmidt conditions followed by cyclization with phenyl hydrazine and hydroxylamine. Reaction of 6a and 6b with hydrazine, semicarbazide and thiosemicarbazide, cyanoacetylhydrazide and some subsequent condensation reactions led to diverse quinoline derivatives. Anti-Aphid Aphis gossypii that harm cotton crop in Egypt was screened. Compound 12 showed an LC50 value of 19429E-10 ppm which is much more active than Marshal (Carbosulfan), one of the broad spectrum insecticides widely used in this field.

Key words: insecticides, aphid Aphis gossypii, quinoline, pyrazole, thiosemicarbazide

INTRODUCTION

Cotton aphid, Aphis gossypii Glover (Homoptera: Aphididae), is a piercing-sucking insect that harms cotton Gossypium barbadense L., crop worldwide (Stoetzel et al. 1996; Daughtery et al. 1997). Damage occurs as a result of direct feeding and excretion of its honeydew. This honeydew is rich in monosaccharides and many free amino acids, resulting in associated pathogenic fungal growth and virus transmission causing more than 50 cotton plant diseases (Forlow and Henneberry 2001). Biological control (Kaplan and Eubanks 2002) through natural enemies including predators (bugs and spiders) (Weathersbee III and Hardee 1994) parasitoids (Aphidius gifuensis) (Ma et al. 2006), and pathogens such as the entomopathogenic fungus Neozygites fresenii are well known (Steinkraus and Zawislak 2004; Smith and Hardee 1996). Relay intercropping (Ma et al. 2006) of agricultural co-systems as mutualistic plant protection, and use of transgenic cotton species were valuable in protection of the crop (Runzhi et al. 2000). Ecological effects represented in O₃ (Menéndez et al. 2010) on aphid infestation as well as use of remote sensing for detection of plant damage were investigated (Reising et al. 2004). Chemical control, on the other hand, has gained great interest due to the widespread cultivation of cotton worldwide to satisfy the global requirements.

Despite the diversity of these insecticides (Takahashi et al. 2001; Conway et al. 2003; Zhae et al. 2009), A. gossypii could continuously evolve insecticidal resistance. Insecticides on their own have singularly failed to control this pest (Moores et al. 1996). Application of wide-spectrum insecticides have devastated natural enemies, thus contributing to aphid outbreaks (Liu 2000). A study was

*Corresponding address:
g.nawwar@link.net
done in Egypt on ten insecticides of the carbamates and organophosphates families tested against adult stages of the pest collected from eight Egyptian governorates. The study showed that Marshal 1 and Dursban 2 were the most toxic insecticides (Khalid et al. 2005). Although, quinoline derivatives are of diverse biological activities (Lubenets et al. 2000), only a few, to the best of our knowledge, are of agro-applications. For instance, Quinclorac 6 is used as a herbicide (Worthing and Waiker 1987) (Fig. 1). This prompted us to synthesize a set of quinolines modified with various functionalities encountered in several pesticides, to assess their contribution as anti-aphid candidates for future protection of cotton cultivation.

**MATERIALS AND METHODS**

**Chemistry**

**General**

Melting points were determined on Gallenkamp apparatus and are uncorrected. Elemental analyses were performed on Flash EA1112 in ThermoFischer Center, Milan, Italy. NMR spectra were recorded on the AC200 Bruker instruments from the Technical university in Vienna, and on the varian Mercury VX-300 instrument at Cairo University. IR-spectra were recorded using JASCO FT IR-460 plus spectrometer. The mass spectra were recorded on GCMS-QP 1000Ex Shimadzu spectrometers in the microanalysis unit at Cairo University. Insecticidal activity was done in the plant protection research Institute, Agricultural Research Center, Mansoura branch, Egypt.

**Synthesis and anti-aphid Aphis gossypii Glover activity of some new quinoline derivatives**

**1-[3-(quinolin-2-ylamino)phenyl]ethanethione (6a)**

A mixture of 2-chloroquinoline 4 (16.3 g, 109.0 mmol) and 3-aminoacetophenone 5a (11.0 g, 70%) as reddish crystals, m.p. 127°C. C_{17}H_{14}N_{2}O (262).

**General procedure for synthesis of 7a–d**

A mixture of 6a (2.98 g, 0.01 mol), the appropriate aromatic aldehyde (0.01 mol) and NaOH (1.0 g, 25.0 mmol) in EtOH (30 ml) was heated under reflux for 8 hours then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from benzene to afford 6a (11.0 g, 70%) as reddish crystals, m.p. 127°C. C_{17}H_{14}N_{2}O (262).

**3-(4-Chlorophenyl)-1-[3-(quinolin-2-ylamino)phenyl]prop-2-en-1-one (7c)**

Obtained as yellow crystals in 60% yield; m.p. 171°C; 1H NMR (200 MHz, CDCl_3): δ 8.43 (s, 1H, NH), 7.97–7.26 (m, 15H, Ar, -CH = CH-), 6.94 (d, 1H, J 8.8 Hz, -CH = CH-); EI-MS: m/z (%), 385 (M+, 100), 261 (91), 219 (35). C_{24}H_{18}ClN_{2}O (366).

**3-(4-Hydroxyphenyl)-1-[3-(quinolin-2-ylamino)phenyl]prop-2-en-1-one (7d)**

Obtained as colorless crystals in 75% yield; m.p. 184°C; 1H NMR (200 MHz, CDCl_3): δ 8.31 (s, 1H, NH), 8.00–7.26 (m,15 H, Ar), -CH = CH-; 6.95 (d, 1H, J 8.8 Hz, -CH = CH-); 2.65 (s, 1H, OH). C_{24}H_{17}ClN_{2}O (384).

**1-[3-(quinolin-2-ylamino)phenyl]-4,5-dihydro-1,5-di-phenylpyrazole (8)**

A mixture of 7a (1.75 g, 5.0 mmol) and phenylhydrazine (0.5 ml, 5.0 mmol) in EtOH (10 ml) was heated under reflux for 6 h then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from MeOH to afford 8 (1.09 g, 60%) as colorless crystals; m.p.163°C. 1H NMR (200 MHz, CDCl_3): δ 8.06–6.80 (m, 21H, 2 Ph, 2 Ar, NH), 5.31 (dd, J_{4`},5 = 7.8 Hz, H-5 pyr), 3.87 (t, 1H, J_{4`},5 = 15.8 Hz, H-4 pyr), 3.17 (dd, 1H, J_{4`},5 = 15.8, J_{4`},6 = 7.8 Hz, 1 H, H-4 pry). C_{30}H_{24}N_{4}O (440.2).

**3-(3-Quinolin-2-ylamino)phenyl]-4,5-dihydro-5-(4-methoxyphenyl)-isoxazole (9)**

A mixture of 7b (1.9 g, 5.0 mmol), hydroxylamine hydrochloride (0.34 g, 5.0 mmol) and NaOH (0.01 mol) in EtOH (15 ml) was heated under reflux for 7 h then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from MeOH to afford 9 (1.3 g, 70%) as colorless crystals; m.p. 146°C. IR (KBr): 3,427–3,314 (NH str), 3,378 (NH str), 3,378 (NH str), 3,378 (NH str); 1H NMR (200 MHz, CDCl_3): δ 7.97–7.26 (m, 15H, Ar, -CH), 6.95 (d, 1H, J 8.8 Hz, -CH = CH-), 5.41 (s, 1H, NH), 3.87 (t, 1H, J_{4`},5 = 15.8 Hz, H-4 pyr), 3.17 (dd, 1H, J_{4`},5 = 15.8, J_{4`},6 = 7.8 Hz, 1 H, H-4 pry). C_{30}H_{24}N_{4}O (395.1).

**3-(3-Quinolin-2-ylamino)phenyl]-4,5-dihydro-5-(4-methoxyphenyl)isoxazole (10)**

A mixture of 7b (1.9 g, 5.0 mmol), hydroxylamine hydrochloride (0.34 g, 5.0 mmol) and NaOH (0.01 mol) in EtOH (15 ml) was heated under reflux for 7 h then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from MeOH to afford 9 (1.3 g, 70%) as colorless crystals; m.p. 146°C. IR (KBr): 3,378 (NH str), 1,607 (C = N str), 1,678 (C = O str); 1H NMR (200 MHz, CDCl_3): δ 8.02 (s, 1H, NH, 7.83–6.89 (m, 14H, Ar), 5.51 (dd, 1H, J_{4`},5 = 11.0, J_{4`},6 = 9.0 Hz, H-5 pyr), 3.88–3.69 (m, 4H, H-4 pry, OMe), 3.36 (dd, 1H, J_{4`},5 = 9.0, J_{4`},6 = 16.8 Hz, H-4 pry). EI-MS: m/z (%): 395 (M+, 52.6), 260 (73.2), 219 (47.4), 128 (71.1), 77 (100). C_{24}H_{17}ClN_{2}O_{2} (395.1).

**1-[3-(quinolin-2-ylamino)phenyl]ethan-1-one hydrazone (11a)**

A mixture of 6a (2.98 g, 0.01 mol), hydrazine hydrate (3.4 g, 0.05 mol) and NaOH (0.01 mol) in EtOH (15 ml) was heated under reflux for 7 h then left to reach ambient temperature. The precipitate formed was filtered and recrystallized from MeOH to afford 10 (1.28 g, 80%) as colorless crystals; m.p. 178°C. 1H NMR (500 MHz, DMSO-d_6): δ 9.54 (s, 1H, NH), 8.53–6.93 (m, 12 H, Ar), 3.21 (brs, 2H, NH_2), 2.37 (s, 3H, CH_3). C_{17}H_{16}N_{4} (276.1).

**3-(quinolin-2-ylamino)phenyl]ethan-1-one hydrazone (10)**

A mixture of 6a (2.98 g, 0.01 mol), hydrazine hydrate (3.4 g, 0.05 mol) and NaOH (0.01 mol) in EtOH (15 ml) was stirred at rt for 2 h. The precipitate formed was filtered and recrystallized from EtOH to afford 10 (2.38 g, 80%) as colorless crystals; m.p. 218°C. IR (KBr): 3,427–3,314 (NH str), 3185 (NH str), 1678 (C = O str), 3185 (NH str).
1-(4-quinolin-2-ylamino)phenyl]ethan-1-one thiosemicarbazone (11b)

A mixture of 6b (2.98 g, 0.01 mol) and thiosemicarbazide (0.91 g, 0.01 mol) in EtOH (20 ml) containing H2SO4 (0.01 ml) was stirred at ambient temperature for 3 h. The precipitate formed was filtered and recrystallized from EtOH to afford 11b (2.0 g, 70%) as yellow crystals; m.p. 181°C. IR (KBr): 3,366–3,230 (NH), 1,683 (C = O), 1,543 (C = N), 1,402 (C = N), 1,376 (C = N), 1,272, 1,206 (C = N). EI-MS: m/z (%) 342 (M+, 2), 295 (1.3), 273 (1.2), 219 (0.8), 195 (0.8), 133 (1.0), 116 (49), 81 (1.0), 50 (1.0), 39 (1.0), 38 (1.1), 37 (20), 29 (1.1), 27 (1.1). NMR (200 MHz, DMSO-d6): δ 11.11 (s, 1 H, -N = CH-), 8.23–8.02 (2s, 2 H, 2 NH), 7.87–7.43 (m, 15H, Ar), 2.46 (s, 3H, CH3); EI-MS: m/z (%): 423 (M+, 1.1), 365 (0.9), 342 (1.0), 317 (1.1), 299 (1.1), 261 (1.2), 234 (0.5). C20H16N6O2 (372).

2-cyano-N'-[1-(3-(quinolin-2-ylamino)phenyl]ethylideneacetohydrazide (13)

A mixture of 6a (2.987 g, 0.01 mol) in EtOH (10 ml) was heated under reflux for 3 h then left at ambient temperature overnight. The precipitate formed was filtered and recrystallized from MeOH to afford 13 (2.24 g, 75%) as colorless crystals; m.p. 224°C. IR (KBr): 3,343–3,450 (NH str), 2,264 (CN str), 1,672 (C = N str), 1,605 (C = N str); 1H NMR (200 MHz, DMSO-d6): δ 9.49 (s, 1H, N-NH-), 8.07–7.08 (m, 10H, Ar), 3.58 (s, 3H, CH3). EI-MS: m/z (%): 335 (M+, 1.0), 292 (0.9), 273 (1.0), 254 (0.7), 235 (0.6), 171 (0.4), 154 (0.3), 133 (1.0), 116 (49), 81 (1.0), 50 (1.0), 39 (1.0), 38 (1.1), 37 (20), 29 (1.1), 27 (1.1). NMR (200 MHz, DMSO-d6): δ 9.70 (s, 1H, N-NH-), 8.69 (s, 1H, NH), 8.10–7.08 (m, 10H, Ar), 3.36 (s, 1H, OH), 2.51 (s, 3H, CH3). C26H20ClN7O2 (481).

2-cyano-2-(4-chlorophenyl diazeneyl)-N'-[1-(3-(quinolin-2-ylamino)phenyl]ethylideneacetohydrazide (16)

A mixture of 13 (3.43 g, 0.01 mol), NaOAc (3 g, 0.3 mol) in dioxiane (20 ml) was stirred at 0°C then treated with p-chlorobenzene diazium chloride (0.01 mol). The precipitate formed was recrystallized from EtOH to afford 16 (2.22 g, 65%) as colorless crystals; m.p. 174°C. IR (KBr): 3,366–3,230 (NH), 2.215 (CN), 1.690 (C = O), 1.599 (C = N); 1H NMR (500 MHz, DMSO-d6): δ 12.72, 12.06, 10.48, 9.64 (4s, 3H, 3 N-H D2O exchangeable), 8.53–7.01 (m, 15 H, Ar), 2.34 (s, 3H, CH3). C20H10ClN6O (481).

Toxicological studies

Samples of cotton leaves infested with cotton aphid, A. gossypii were collected from the cotton fields of the Dakahlia Governorate, Egypt, in June, 2008 and transferred to the laboratory. The slide dip technique adopted by Thistlewood et al. (1992) was applied to evaluate the efficiency of the tested modified heterocyclic compounds, in addition to the recommended insecticide Marshal (carbosulfan) 25% WP, against aphids. A piece of double-faced scotch tape was pressed tightly to the surface of a glass slide, using a moist brush. At least six concentrations for each compound were used. Three replicates with 10 aperter adult (1–2-days-old) each, were made for each concentration. The aphids were stuck to the tape on their backs so that their legs and antennae were free. Slides with aphids were dipped into a beaker containing compound solutions which were mixed with Triton X at a concentration of 0.3%. The aphids were immersed for 10 seconds to ensure complete wetting. Control aphids were similarly dipped in water with Triton X at a concentration of 0.3%. When withdrawn, slides were placed down, on their edges, on absorbent paper towelling and then allowed to dry at room temperature. The treated slides were then placed into a glass slide holding chamber to conserve the moisture. Mortality counts were tallied after 24 hours of treatment. Aphids responding to touch from a brush were considered alive. Mortality data were corrected according to the Abbott formula (Abbott 1952) and the corrected mortality percentage of each compound was statistically computed according to Finney (1971). From which the corresponding concentration probit lines (LC-p lines) were estimated in addition to determination of 25, 50 and 90% mortalities. Slope values of tested compounds were also estimated. In addition, the efficiency of different compounds was measured by comparing the tested compound with the most effective compound by using the following equation: Toxicity index = LC50 of the most effective compound/LC50 of the tested compound x 100, Sun et al. (1950).
RESULTS AND DISCUSSION

Chemistry

For our endeavor, substrates 6a and 6b (Kamel et al. 1986) were obtained by nucleophilic substitution of 2-chloroquinoline 4 with the appropriate acetylaniline derivative 5a–b, in refluxing EtOH containing drops of HCl. The acetyl moieties in these derivatives are active enough to carry diverse functionalizations that might lead to new insecticide candidates. The first group that we thought about was the chalcone derivatives 7a–d, and some of their derived heterocycles 8–9 (Fig. 2), were then prepared. Compounds 7a–d were obtained in 60–75% yields via condensation of 6a with the appropriate aldehyde under Claisen-Schmidt condensation conditions, with modified NaOH proportion into 2.5 equivalents as the substrate is a hydrochloride form.1H NMR spectra of 7a–d showed a doublet for one of the two olefinic protons at δ 6.94–6.99 ppm (J 8.4–9.0 Hz). The second one was overlapping, as the imine proton, with the aromatic protons in the range δ 7.26–8.43 ppm. The methoxy protons of 7b were observed as singlet at 3.86 ppm, and the molecular ion peak of 7c was observed as the base peak at m/z 385. Pyrazole 8 was obtained in 60% yield via Michael-addition of phenyl hydrazine to 6a in refluxing EtOH (Fig. 2). The methylene protons of the pyrazole moiety, H-4pyrazole, were diastereotopic. They appeared as a pair of doublet-of-doublets at δ 3.17 and 3.87 ppm with common germain coupling constant, J_gem, of 15.8 Hz. The pyrazole proton H-5 was observed consequently, as doublet-of-doublet at higher shift, δ 5.31 ppm, with two different J values of 6.4 and 7.8 Hz. Isoxazole 9 (Fig. 2), was obtained in 70% yield by treatment of 7b with hydroxylamine hydrochloride. The H-4 methylene protons of the isoxazole moiety were diastereotopic as in the pyrazole ring in the 1H NMR spectrum with the exception of the overlapping of one of these protons with the methoxy protons giving a multiplet at δ 3.69–3.88 ppm. H-5 was observed, as expected, at higher shift, δ 5.71 ppm, compared with 8, δ 5.31 ppm, due to the electronegativity difference between oxygen and nitrogen. The molecular ion peak for 9, m/z 395, was observed at an intensity of 52%.

The second class of derivatives whose synthesis we thought about is the carbazides. Their derivatives and analogues, as some semicarbazides and thiosemicarbazides, are commercially available insecticides. Therefore, the acetyl moieties of 6a–b are quite suitable to graft quinoline with these active motif and related groups. Thus, condensation of 6a with excess of hydrazine hydrate in refluxing EtOH contained a drop of conc. H_2SO_4 afforded hydra-

![Diagram](image-url)
zone 10 (Fig. 2), in 80% yield. 1H NMR revealed a singlet at δ 2.37 ppm for the methyl group protons, a multiplet for the aromatic protons at δ 6.93–8.53 ppm and a D₂O exchangeable proton singlet at δ 9.54 corresponding to the hydrazone moiety NH₂-group. Semicarbazone 11a (Fig. 2), was obtained in 65% yield by refluxing 6a with semicarbazide in EtOH. IR-spectrum showed stretching bands for the groups NH at 3,314–3,427, NH₂ at 3,185, C = O at 1678 and C = N at 1571 cm. MS revealed a molecular ion peak at m/z 319 with intensity of 66% while 1H NMR showed D₂O exchangeable broad singlets at δ 6.60 ppm for the NH₂ group, 9.59 and 11.20 ppm for the two NH groups. Thiosemicarbazone 11b (Fig. 2), was obtained analogously from 6b and thiosemicarbazide in 70% yield. IR-spectrum revealed stretching bands at 3,261–3,423 for the NH group, 3,062 for the NH₂ group and 1,660 cm for the C = N group. Molecular ion peak of m/z 335 was observed at an intensity of 1%. Condensation of 11b with benzaldehyde in refluxing EtOH afforded Schiff-like-base 12 (Fig. 2), in 65% yield. MS showed the molecular ion peak, m/z 423 at an intensity of 0.1%, whereas, the characteristic aldimine proton signal was observed satisfactorily in the 1H NMR spectrum as singlet at δ 10.20 ppm.

Condensation of 6a with cyanoacetohydrazide was studied (Fig. 2), the reaction was conducted in refluxing EtOH affording the active methylene containing derivative 13 in 75% yield. The molecular ion peak, m/z 342 was observed at an intensity of 2%. 1H NMR spectrum showed that amide proton was observed as two singlets at δ 11.17 and 11.01 ppm due to tautomerism, while, the protons of the active methylene moiety were observed as a singlet at δ 4.29 ppm. Treatment of 13 with Et₃N in refluxing dioxane afforded oxadiazole 14 in favour of a pyrazolone. This was deduced based on the persistence of the active methylene protons signal in 1H NMR spectrum and change in melting point of 13.

Finally, condensation of 13, with nitrous acid prepared in situ at 0°C, afforded oxime 15 in 70% yield (Fig. 3). The two NH proton signals, 1H NMR spectrum, were observed at δ 9.70 and δ 8.69 ppm while oxime-OH was observed at δ 3.36 ppm. Azo-dye derivative 16 was obtained by coupling of 13 with benzene diazonium chloride at 0°C in 65% yield. Disappearance of the active methylene protons signal, 1H NMR spectrum, was decisive for this coupling (Nawwar et al. 1993; Shafik et al. 2006; Abd El Salam et al. 2009).

**Toxicological studies**

Toxicological assay of compounds 6–16, table 1 revealed that the thiosemicarbazide Schiff base derivative 12 is the most toxic one in this quinoline series with LC₅₀ value of 19,429x10⁻¹⁰ ppm which is much more toxic than Marshal. Coming next to this derivative and with a near-by range of toxicity is the hydrazone 10, semicarbazide 11a and then the pyrazole 8. These derivatives are more toxic than Marshal but very less toxic than 12. The cyanoacetylhydrazone series (Fig. 3), was found to be a whole series that was more toxic than Marshal. Oxadiazole 14 was the most toxic one and followed 8 directly, and separated from the rest of the series with the hydroxylated chalcone like derivative 7d. This chalcone derivative was the only active derivative among the other chalcones.

---

**Fig. 3.** Reagents and conditions: (a) EtOH, rfx., 75% for 13; (b) Et₃N, Dioxane, rfx., 60% for 14; (c) NaNO₂, HCl, 0°C, 70% for 15; (d) p-ClC₆H₄N=NCI, NaOAc, 0°C, 65% for 16.
Synthesis and anti-aphid Aphis gossypii Glover activity of some new quinoline derivatives compared with the reference insecticide. This result adds an impact to the intriguing biological activity (Jang et al. 2007) of chalcones which is attributed, in most cases, to the affinity of its enone-system to free sulphydryl groups in proteins (Aly et al. 2006) which might target some insect proteins elaborating this insecticidal activity. Following 7d in toxicity were oxime 15 then the azo-dye derivative 16, and finally cyanoacetylhydrazone 13 which was still more toxic than Marshal. Although, 12 showed the highest anti-aphid activity, its thiosemicarbazide precursor 11b was less toxic than the reference insecticide and so were the rest of the chalcones 7a–c and oxazoline 9.

In general, treatment of the cotton aphids, Aphis gossypii (Glover) with these quinoline derivatives, in comparison with the recommended insecticide, Marshal (Carbosulfan) 25% WP resulted in two groups (Table 1). The first group is more toxic than the insecticide Marshal, The compounds of the first group are 12, 10, 11a, 8, 14, 7a, 15, 16, and 13. The second group is less toxic than Marshal. The compounds of the second group are 11b, 7a, 7b, 6b, 6a, 9 and 7c.

These results reflect the impact of these derivatives as new insecticide candidates for cotton cultivation which are in accordance with our hypothesis.

**CONCLUSIONS**

Condensation reactions of 2-acetylanilinoquinolines were good leads for new quinoline derivatives grafted with several functionalities frequently encountered in commercial pesticides. Some of these derivatives were more toxic than Marshal which is one of the best anti-aphid pesticides on the market. These results put quinoline derivatives of these series, as leads for developing new potential pesticides.

**REFERENCES**


Polish Summary

**SYNTEZA NOWYCH POCHODNYCH ZWIĄZKÓW GUINOLINY I ICH AKTYWNOŚĆ PRZECIWKO AHPIS GOSSYPII (GLOVER)**

Opracowano serię pochodnych związków quinoliny w wyniku reakcji 2-(m i p-acetylanilino)-quinolin 6a-b z aldehydami według Clainsen-Schmidt’a, a następnie poprzez cyklizację z fenoloforydrzaną i hydroksyloamną. Reakcja 6a i 6b z hydroxylazoarmiemiczonymi bezwodnikiem diisocianowym oraz kolejne reakcje kondensacji doprowadziły do powstania pochodnych związków quinoliny. Przedmiotem badań był skuteczność przeciwmęczniczą Aphis gossypii, szkodnikow ugrawa bawełny w Egipcie. Komponent 12 o wartości LC₅₀, dla 19429E-10 ppm okazał się bardziej skuteczny niż preparat Marchal (karbosulfan), jeden z powszechnie stosowanych insektycydów w zwalczaniu A. gossypii.