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Synthesis, characterization and bioefficacy of some cyclic ketones against houseflies

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ABSTRACT

Synthesis of some cyclic ketones which include (2E)-3-(2-chloroquinolin-3-yl)-l-phenyl-2-propen-1-one, (2E)-3-(2-Chloro-6-methylquinolin-3-yl)-1-phenyl-2-propen-1-one, (2E)-3-(2,7-Dichloroquinolin-3-yl)-1-phenyl-2-propen-1-one, (2E)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-phenyl-2-propen-1-one, 2E)-3-(6-Bromo-2-chloroquinolin-3-yl)-1-phenyl-2-propen-1-one were achieved through the condensation of 3-fomylquinolines with acetophenone and 3-acetyl-4-hydroxyquinolin-2(1H)-one with different heterocyclic aldehydes. The synthesized ketones have been screened for insect attractant activities and insecticidal effect against houseflies. All the ketones have shown significant insect attractant properties.

Key words: Insect attractant, ketones, insecticidal effect, 3-fomylquinolines, 3-acetyl-4-hydroxyquinolin-2(1H)-one, acetophenone.

INTRODUCTION

Insect pests reduce crop yields, destroy forests and wood products, carry diseases that affect plants, man and animals and damage food and other stored products. Although synthetic organic pesticide appeared to provide a solution to the problems of insect control, it has become apparent that repeated application of insecticides can be inadequate method of control. Exercise reliance on insecticide use has been accompanied by the development of insect resistance and problems of environmental pollution. To minimize these problems, Pest control should be considering it's entirely and by combining several elements into an integrated system, undesirable consequences of overreliance on a single technique, such as chemical treatment, may be obviated. The term "integrated pest management" (IPM) has been coined to describe a planned combination of individual disciplines and strategies that can be used to reduce the impact of pests. However the effective application of an integrated system depends on the understanding of individual components, their potential applications and their interactions. The emerging alternative agriculture and worldwide shift toward integrated pest management (IPM) are bringing semiochemicals or behavior-modifying chemicals (BMC)[1]. Insect attractant have played as behavior-modifying chemicals and will continue to play an important part in the management of insect pest. However, their potential has not been fully exploited, and research efforts continue in order to provide a basis for their grater utilization. The field has developed rapidly during the past decade as a result of analytical developments that have simplified the identification of minute quantities of unknown organic compounds that occur in nature. Chemicals that act as attractants or carry other messages across distances are volatile (quick to evaporate) compounds. When released into the air, they can be detected by certain insects (those receptive to a specific compound) a few inches to hundreds of yards away. The insect depend upon attractants guide them to host plant[2-7], opposite sex[8], food supply[9] and animals[10,11] on which they deposit their

eggs or larvae. Recently, quite a large number of synthetic insecticides have been prepared which may contain one or more functional group, for example, nitro cyano, fluoro, chloro, alkyl chains of different lengths and systems as allylic and unsaturated carbonyl systems etc. which seem to be responsible for insecticidal activity it has been reported that anisyl acetone, benzyl acetone [12], and other like ketones[13] possess a strong insect attractant[14] was determined by means of an olfactometer. However, despite all the various techniques and formulations used to combat flying insects, they remain incorrigible pests to any human adventuring outdoors. Thus, there is a continual need in the art for new and improved methods and compositions that can be used to protect humans from flying insects. The present study demonstrates synthesis, characterization and bioefficacy of some cyclic ketones against houseflies.

MATERIAL AND METHODS

All the required chemicals were purchased from Merck Company and were used as such. 2-chloro-3-formylquinollnes and N-substituted-3-acetyl-4-hydroxyqulnolin-2(1H)-one were synthesized by using the methods reported in literature[15] with slight modification. IR spectra were recorded on Perkin Elmer spectrum-1 X. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker DPX-400 instrument at 400 and 100 MHZ, respectively. Chemical shifts are reported in ppm referenced to the residual solvent signal. FAB^{+}-MS spectra were recorded on JEOL SX-102 Using Perkin Elmer 2400-CHN Analyzer performed elemental analyses. Melting points were recorded on open capillary method and were uncorrected. Aluminum coated TLC plates were purchased from Merck for monitoring of reaction and purity of compounds. Bioefficacy were carried out with an olfactometer in the laboratory.

Compound 1: (2E)-3-(2-chloroquinolin-3-yl)-l-phenyl-2-propen-1-one

It was prepared by adding aqueous sodium hydroxide (2 ml, 25%) to a mixture of 2-chloro-3-formylqulnoline (1. 0 g, 5.2 mmol,), acetophenone (0.6 g, 5.2 mmol) and 25 ml ethanol (95%). The reaction mixture was stirred for 90 min at room temperature and the reaction was monitored by TLC. The pH of the reaction mixture was adjusted to 6.0 by adding 10% hydrochloric acid. The organic mass was extracted with chloroform. The chloroform layer was dried over anhydrous magnesium sulfate and evaporated. The crude product was purified by column chromatography (n-hexane/ethyl acetate 7:3). The compound was obtained yield: 76%), mp 180-181°C; IR (KBr, cm^{-1}) 1665 (C = 0); 'H-NMR ($CDCl_3$, ppm) δ:8.5 (s, 1H, H4**),** 8.23 (d, J=15.72Hz, 1H,$H_{â}$), 8.04 (brm,5H, H5, H6, H7, H8, $H_{á}$), 7.65 (m, 5H, 5H of phenyl ring) ^{13}C-NMR (100 MHZ, $CDCl_3$) ä: 189.8, 147.9, 139.3, 137.5, 136.2, 133.4, 131.7, 130.4, 128.9, 128.8, 128.7, 128.1, 128.0 and 126.3 mass spectrum (FAB), m/z 295 (M+2, 50%), 297 (M+2+2 17%), 258 (M-Cl, 25%), 216 (M- Ph 10%), 176 (M-Ph-CO-CH, 15%), 105 (Ph-CO, 60%), 77 (Ph 45%). Anal. $C_{18}H_{12}ClNO$: (293.5): Calcd, C, 73.6; H, 4.12; N, 4.77; found: C, 73.45; H, 4.04; N, 4.65%.

Compound 2: (2E)-3-(2-Chloro-6-methylquinolin-3-yl)-1-phenyl-2-propen-1-one

It was prepared from 2-chloro-3-fomyl-6-methylquinolinaen and acetophenone as described for compound-1, yield: 79%),mp 147°C, IR (KBr, cm^{-1}): 1630 (C = 0); 'H-NMR ($CDCl_3$, ppm) δ: 8.34 (s, 1H,H4) 8.16 (d,1H, J=15.76 Hz &$H_{â}$), 8.06 (m,2H,H5,H7),7.8(d, J=8.5Hz 1H,H8) 7.59 (br m, 6H, Há, and 5H of phenyl ring), 2.53 (s, 3H CH_3). ^{13}C-NMR (100 MHZ, $CDCl_3$) ä: 189.8, 149.4, 146.4, 139.0, 137.8, 137.6, 135.5, 133.9, 133.2, 128.9, 128.8, 128.7, 128.6, 128.0, 126.9, 126.8, 125.9, 122.3 and 22.38 Mass spectrum (FAB), m/z 309, (M+2, 70%), 311, (M+2+2 30%), 273, (M+2-HCl 25%), 231, (M+2- Ph 5%). Anal. $C_{19}H_{14}ClNO$: (307.5): Calcd, C, 74.05; H, 4.10; N, 4.55; found: C, 74.05; H, 4.1 0; N, 4.05%.

Compound 3: (2E)-3-(2,7-Dichloroquinolin-3-yl)-1-phenyl-2-propen-1-one

The compound was prepared from 2,7-dichloro-3-fomylquinoline and acetophenone as described for comp.1 and purified by column chromatography with mixture of solvents (n-hexane/ethyl acetate 2:3), yield: 73%, mp 167-8°C; IR (KBr, cm-1): 1670 (C = 0); 'H-NMR ($CDCl_3$, ppm) δ: 8.5(s, 1H, H4), 8.23 (d 1H, J = 15.6 Hz, 1H, Hβ), 8.07 (m, 3H, H5, H6, H8), 7.87 (d J = 15.6 Hz, 1H, Hβ), 7.66 (br m, 5H, 5H of phenyl ring), 7.28 (s, 1H,H8) ^{13}C-

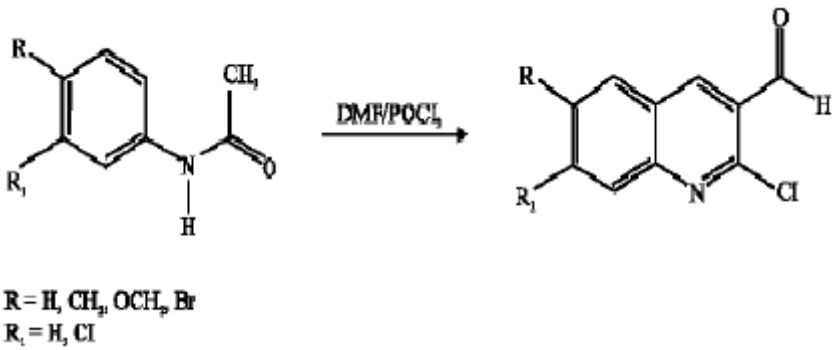
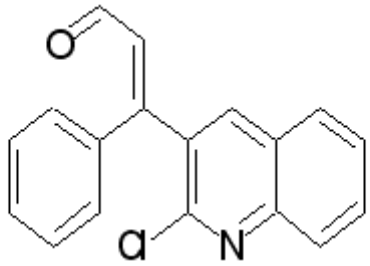
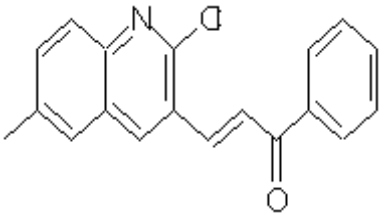


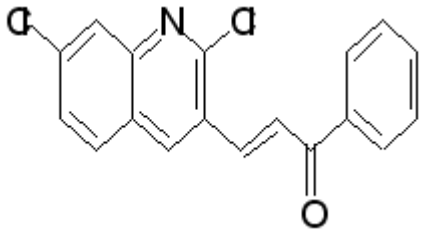
Fig. 1: Scheme for the synthesis of ketones



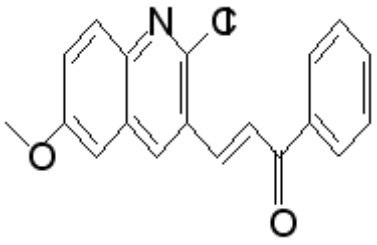
3-(2-chloroquindin-3-yl)-1-phenyl-2-propen-1-one



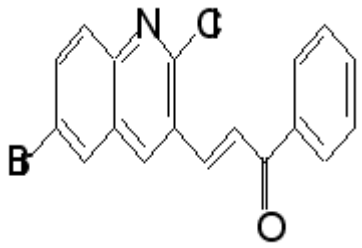
3-(2-chloro-6-methylquinolin-3-yl)
-1-phenyl-2-propen-1-one



3-(2,7-Dichloroquinolin-3-yl)
-1-phenyl-2-propen-1-one



3-(2-chloro-6-methoxyquinolin-3-yl)
-1-phenyl-2-propen-1-one



3-(6-Bromo-2-chloroquinolin-3-yl)
-1-phenyl-2-propen-1-one

Fig. 2: Structures of synthesized cyclic ketones

NMR (100 MHZ, $CDCl_3$) δ: 197.8, 159.9, 146.6, 135.5, 135.3, 128.8, 128.7, 128.6, 128.5, 127.2 and 125.6 mass spectrum (FAB), m/z 329 (M+2 90%), 331 (M+2+2 30%), 292 (M- Cl 45%), 250 (M-Ph 24%), 105 (Ph-CO, 54%), 77 (Ph 40%). Anal. $C_{18}H_{11}Cl_2NO$: (327.5): Calcd, C, 65.87; H, 3.38; N, 4.27; found: C, 65.76; H, 3.42, N, 4.25%.

Compound 4: (2E)-3-(2-Chloro-6-methoxy quinolin-3-yl)-1-phenyl-2-propen-1-one

The compound was prepared from 2-chloro-3-fomyl-6-methoxyquinoline and acetophenone as described for 1, yield: 77%, mp 228°C; IR (KBr, cm-1): 1620 (C = 0); 'H-NMR ($CDCl_3$, ppm) δ: 8.36 (s,1H,H4), 8.16 (d 1H, J=16.00 Hz, Hâ), 8.05 (m, 2H,H5, H7), 7.85 (d 9.2 Hz 1H, H8), 7.57 (m,4H, H2, H4, H6 and Hβ),7.41 (m, 2H, H3, H5), 3.94(s,3H,OCH_3) ^{13}C-NMR (100 MHZ, $CDCl_3$) δ: 189.8, 158.5, 147.8, 139.6, 138.6, 137.6, 134.9, 133.2, 129.9, 128.9, 128.8, 128.7, 126.1, 124.4, 105.3 and 55.7 mass Spectrum (FAB), rn/z 325 (M+2, 1OO%), 327 (M+2+2, 33%), 290 (M+2-HCl 30%), 289 (M+2-HC190%), 245 (M-l -Ph 20%), 105 (Ph-CO 80%), 77 (Ph 43%). Anal. $C_{19}H_{14}ClNO_2$: (323.5), Calcd, C, 70.48; H, 4.36; N, 4.33; found: C, 70.46; H, 4.32; N, 4.30%.

Compound 5: (2E)-3-(6-Bromo-2-chloroquinolin-3-yl)-1-phenyl-2-propen-1-one

The compound was prepared from 6-bromo-2-chloro-3-fomylqulnoline and acetophenone as described for 1 and purified by silica gel column chromatography (n-hexane/ethyl acetate (6: l), yield: 72%, mp 186-7°C; IR (KBr, cm^{-1}): 1675 (C = 0), ^{1}H-NMR ($CDCl_3$, ppm) δ: 8.4 (s, 1H, H4, 8.2 (d J=15.7Hz,1H,Hβ), 8.06 (m, 2H, H5, H7) 7.85 (br m, 2H, H8, Hβ), 7.65 (br m, 5H, 5H of phenyl ring). ^{13}C-NMR (100 MHZ, $CDCl_3$) δ:189.6, 150.8, 145.7,

Table 1: Percent insect attraction of synthesized ketones against houseflies

S. No	Ketones	weight in g.	No. of insects in the test arm	No. of insects in the control arm	percentage insect attraction
1.	(2E)-3-(2-chloroquinolin-3-yl) l-phenyl-2-propen-1-one	0.050	17	8	36
2.	(2E)-3-(2-Chloro-6-methyl quinolin-3-yl) -1-phenyl-2-propen-1-one	0.048	23	2	84
3.	(2E)-3-(2,7-Dichloroquinolin-3-yl) -1-phenyl-2-propen-1-one	0.047	19	6	52
4.	(2E)-3-(2-Chloro-6-methoxy quinolin-3-yl)-1-phenyl-2-propen-1-one	0.052	21	4	68
5.	2E)-3-(6-Bromo-2-chloro quinolin-3-yl)-1-phenyl-2-propen-1-one	0.050	20	5	60

Table 2: Insecticidal effect of synthesized ketones against houseflies

S.No	Ketones	knock down time (min)
1.	(2E)-3-(2-chloroquinolin-3-yl)-l-phenyl-2-propen-1-one	19
2.	(2E)-3-(2-Chloro-6-methylquinolin-3-yl)-1-phenyl-2-propen-1-one	12
3.	(2E)-3-(2,7-Dichloroquinolin-3-yl)-1-phenyl-2-propen-1-one	15
4.	(2E)-3-(2-Chloro-6-methoxyquinolin-3-yl)-1-phenyl-2-propen-1-one	16
5.	2E)-3-(6-Bromo-2-chloroquinolin-3-yl)-1-phenyl-2-propen-1-one	20

138.8, 137.4, 135.0, 134.9, 133.4,130.1, 129.9, 129.1, 128.1, 127.9 and 121.1, mass spectnun (FAB), m/z 372 (M+1 10%), 374 (M+1+2, 1O%), 336, M-Cl 8%), 338 (M+2-Cl, 8%), 176 (M-Ph-CO-CH, 20%), 105 (Ph-CO, 45%), 77 (Ph, 34%). Anal. $C_{18}H_{11}BrClNO$: (372.5): Calcd, C, 58.02; H, 2.98; N, 3.76; found: C, 57.98; H, 2.91; N, 3.69%.

Olfactometer

The experiments were carried out in an olfactometer. It consists of a Y- tube with an opening of each of its arms. One of the Y- shaped arms is known as test arm while the other control arm. The openings in the test and the control arms are joined to the bottles through two mounted glass joints, the other mouth in each case is kept open for the entry of the atmospheric air. This is possible by applying vacuum through the opening in the arm, joining the other two. A definite number of insects contained in the bottle can be introduced in the Y- tube through the opening. The substance to be tested is kept in the bottle for its percent insect attraction to the test arm. On applying vacuum, streams of air of almost the same potency are drawn in the bottle, but because of the odour of the substance in the bottle, the insects are drawn in to the test and the control arms unequally. The number of insects in each of the test and the control arm is then counted after five minutes in each experiment. This time period is arbitrarily fixed for building odour concentration. The percent insect attraction of the substance is then obtains by dividing the difference of the number of insects in the test and the control arms by the total number of insects multiplies by 100.

Percentage insect attraction

The percentage insect attraction were evaluated through the following formula-

$$\% \text{ insect attraction} = \frac{\text{Number of insect in test arm-number of insect in control arm}}{\text{Total number of insect}} \times 100$$

RESULTS AND DISCUSSION

During the present study five cyclic ketones were prepared by condensing 3-fomylquinolines with acetophenone and 3-acetyl-4-hydroxyquinolin-2(1H)-one with different heterocyclic aldehydes. For this purpose a series of substituted 2-chloro-3-fomylquinolines were prepared from acetanilide derivatives using Meth-Cohn and Narine (1978) procedures[15] as per given scheme (Fig. 1). In ^{1}HNMR spectra of these compounds, the protons of α, β unsaturated carbonyl compounds have given two doublets in the range 7.5 ppm for Hβ and 8.5 ppm for Hβ with coupling constant in the range (15-16 Hz). It is anecdotal that they are trans isomers. The rest of signals for protons have appeared in the expected region. Additional structure elucidation is supported by ^{13}CNMR spectra. A signal in the range δ (194-189) ppm in ^{13}CNMR of all the compounds indicates that carbonyl group is present. Interestingly the mass spectra of the prepared ketones have shown the most intense signal $(M+2)^{+}$ in all compounds. The structures of the compounds were given in Figure 2.

Bioefficacy

The newly prepared compounds were screened for their insect attractant activity and insecticidal effect against houseflies using an olfactometer. The preliminary results are encouraging. The insect attractant activities and insecticidal effects were evaluated by measuring the percent insect attraction and knock down time of prepared ketones against houseflies respectively and results were given in Table 1 and 2. On the basis of the observed percent insect attraction and insecticidal effects values, it can be concluded that there is a significant differences in the insect attractant and insecticidal effects of synthesized ketones. Among the synthesized ketones the compounds 2 [(2E)-3-(2-Chloro-6-methyl quinolin-3-yl) -1-phenyl-2- propen-1-one], 4[(2E)-3-(2-Chloro-6-methoxy quinolin-3-yl)-1-phenyl-2-propen-1-one] and 5 [2E)-3-(6-Bromo-2-chloro quinolin-3-yl)-1-phenyl-2-propen-1-one] have shown more insect attractant activity and insecticidal effect against houseflies than rest of ketones. This is might be because of structural features

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