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Synthesis, characterization, anti-bacterial, anti-fungal and nematicidal activities of 2-amino-3-cyanochromenes

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ABSTRACT

Soil-borne plant pathogens such as nematodes, fungi and some bacteria not only affect the plant cultures but also economy and environmental implications. As a result of these pathogens attacks, the yield and quality of crops is affected. Therefore, synthesis of new compounds to control these pathogens is very important and need of time. Chromenes are considered important group of heterocyclic compounds and exhibited significant biological activities. 2-amino-3-cyano chromenes are considered important medicinal scaffolds among the chromenes. We describe three component microwave assisted synthesis of 2-amino-3-cyano chromenes. The versatility of the reaction was examined by varying the aldehydes in the reaction mixture which lead to the synthesis of series of 2-amino-3-cyanochromenes (**1**–**9**). The structural elucidations of the compounds were studied by ^{1}H NMR, ^{13}C NMR, HRMS and FTIR spectrometer and results were well correlated. The synthesized compounds were evaluated for their anti-bacterial, anti-fungal and nematicidal activities. Among the synthesized compounds, compound **6** showed good anti-bacterial activity while compound **9** exhibited high anti-fungal activity. In case of nematicidal activity, compound **8** indicated high activity as compare with other compounds followed by compound **9**. Results indicate that these synthesized compounds could be used as effective control for soil-borne plant pathogens such as nematodes, fungi and bacteria and can help to improve the plant production.

1. Introduction

Chromenes are getting prestigious position in the heterocyclic chemistry due to their extraordinary significance in biologically active molecules, natural products, and synthetic drugs [1]. Among the various types of chromenes, 2-amino-3-cyano chromenes are considered important medicinal scaffolds [2–10] 2-amino-3-cyano chromenes exhibiting numerous biological activities such as anti-bacterial [11], anti-proliferative [12], anti-viral [13,14] anti-cancer [9,10,15] anti-tumor [16] and central nerve activities [17]. Besides this; they are part of many natural products and used in biodegradable agrochemicals [18–21].

Usually, 2-amino-3-cyanochromenes are synthesized by three component reaction employing phenol or resorcinol with malononitrile and arylaldehydes as precursors in the presence of catalyst. Many catalysts are used for such reactions including piperidine [22] basic alumina [23] K_2CO_3 [24] and cetyltrimethylammonium chloride [25]. However, most of the reported work has disadvantage due to long reaction time, toxic solvents, poor yield and limited application [22–24]. Therefore, there is need for the development of an efficient and fast methodology for the synthesis of 2-amino-3-cyano chromenes due to their importance in medicinal chemistry.

Soil-borne plant pathogens (nematodes, fungi and some bacteria) are considered equally important as other pathogens because they affect the plant cultures and finally economy and environmental implications. These pathogens cause severe damage to different vegetables and crops as a result the yield and quality of crops is affected. Some of them infect plant roots and cause disruption of nutrients absorption and water from the soil which may result in mortality. The root-knot nematodes (*Meloidogyne* spp.) are widely distributed and reproduce on over 2000 species of plants [26]. Root-knot nematodes (*Meloidogyne* species) are obligate parasites and cause root cells to become giant and multinucleated. *Macrophomina phaseolina* causes rotting of roots, stem and pods of hundreds of cultivated plant species [27]. *M. phaseolina* has a wide distribution and it can survive in soil and dead plant debris for several years by forming sclerotia. Symptoms including appearance of lesions on roots, stem and other parts of plants which result in stunted growth, yellowing of leaves and reduction in yield [28]. *Fusarium* species are also very common plant pathogens that causes root and stem rot and wilt diseases on a variety of crop plants.

Until now, there is no report for the application of 2-amino-3-cyanochromenes for the remediation of plant pathogens. Herein, we report a fast and efficient three component reaction for the synthesis

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of 2-amino-3-cyanochromenes series by using microwave and screening of their anti-bacterial, anti-fungal and nematicidal activities.

2. Experimental

2.1. General

Reagent grade chemicals and solvents were purchased from Sigma Aldrich and were used without further purification. Thin-layer chromatography (TLC) was performed on silica gel glass plates (Silica gel, 60 F_{254}, Fluka) and spots were visualized under UV lamp. Melting points of the complexes were determined on Gallenkamp apparatus and reported as uncorrected. Infrared (IR) spectra of the compounds were recorded on a Nicolet Impact 410 FT-IR spectrometer (4000–400 cm^{-1}) as a potassium bromide (KBr) pellets. ^1H NMR and ^{13}C NMR spectra were conducted on Varian 400 MHz NMR spectrometer in DMSO-d_6. The proton chemical shifts were reported in parts per million (δ ppm) and coupling constants (J) in Hertz (Hz) and s, d, t, m, br refer to singlet, doublet, triplet, multiplet and broad respectively. JMS-600H high resolution mass spectrometer (JEOL) was used for recording ESI-MS and HRMS spectra of the compounds.

2.1.1. General Method for the Synthesis of Compounds (**1**–**9**)

A stirred mixture of 1-naphthol 1.44 g, (10 mmol), aldehyde (10 mmol), malonitrile (0.660 g, 10 mmol) and two drops of piperidine in bench ethanol (10 mL) was refluxed in microwave reactor at 80 °C (dynamic power 25–30 W) for 5–15 min. The solid product was obtained; it was filtered, washed several times with cold ethanol and dried under vacuum.

2.1.2. 2-Amino-3-cyano-4-phenyl-4H-benzo[h]chromene (**1**)

Yield: 2.77 g (93%); mp: 220–223 °C; IR (KBr pellet, cm^{-1}): 3441, 3299, 3184, 2205, 1653, 1600, 1399;^1H NMR (400 MHz, DMSO-d_6): δ 4.87 (s, 1H), 7.06 (d, J = 8.4 Hz, 1H), 7.15–7.29 (m, 6H), 7.50–7.62 (m, 3H), 7.83 (d, J = 8.4 Hz, 1H), 8.24–8.26 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 41.4, 56.7, 118.4, 121.1, 121.2, 123.2, 124.3, 126.7, 127.1, 127.2, 127.4, 128.1, 129.2, 133.1, 143.2, 146.2, 160.6; HRMS (+ESI): calcd. for $C_{20}H_{14}N_2O$, 298.1101, found 298.1077.

2.1.3. 2-Amino-3-cyano-4-(3-fluorophenyl)-4H-benzo[h]chromene (**2**)

Yield: 2.09 g (66%); mp: 204–206 °C; IR (KBr pellet, cm^{-1}): 3462, 3327, 3196, 2194, 1660, 1635, 1610, 1485, 1447; ^1H NMR (400 MHz, DMSO-d_6): δ 4.94 (s, 1H), 6.99–7.10 (m, 4H), 7.25–7.35 (m, 3H), 7.51–7.62(m, 3H), 7.84(d, J = 8 Hz, 1H), 8.24 (d, J = 8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 40.5, 56.5, 56.1, 114.1, 114.3, 114.7, 114.9, 117.7, 120.9, 121.2, 123.2, 124.2, 124.3, 124.5, 126.5, 127.2, 127.3, 128.1, 131.1, 131.2, 133.2, 143.2, 148.97, 149.03, 160.7, 161.5, 163.96; HRMS (+ESI): calcd. for $C_{20}H_{13}FN_2O$, 316.1006, found 316.0986.

2.1.4. 2-Amino-3-cyano-4-(2-trifluoromethyl)phenyl)-4H-benzo[h]chromene (**3**)

Yield: 2.3 g (63%); mp: 217–219 °C; IR (KBr pellet, cm^{-1}): 3423, 3323, 3195, 3058, 2192, 1658, 1601, 1450, 1403; ^1H NMR (400 MHz, DMSO-d_6): δ 3.41(s, 2H), 5.16 (s, 1H), 6.83 (d, J = 8.4 Hz,1H), 7.26–7.77 (m, 2H), 7.37–7.41 (m, 1H), 7.52–7.58 (m, 2H), 7.61–7.65 (m, 1H), 7.70–7.72 (m, 1H), 7.85 (d, J = 8 Hz, 1H), 8.26(d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 36.7, 56.8, 117.5, 120.17,120.20, 121.3, 123.5, 124.8, 125.39, 125.44, 125.9, 126.2, 126.5, 126.8, 127.3, 127.5, 127.9, 128.1, 132.4, 133.2, 133.9, 143.3, 145.4, 160.4, 160.5; HRMS (+ESI): calcd. for $C_{21}H_{13}F_3N_2O$, 366.0974, found 366.0967.

2.1.5. 2-Amino-3-cyano-4-(3,4-dimethoxyphenyl)-4H-benzo[h]chromene (**4**)

Yield: 2.57 g (72%); mp: 134–139 °C; IR (KBr pellet, cm^{-1}): 3472, 3336,2193, 1659, 1570, 1510, 1466; ^1H NMR (400 MHz, DMSO-d_6): δ 3.67 (s, 6H), 4.81 (s, 1H), 6.96–6.72 (m, 1H), 6.85–6.87 (m, 2H),7.10–7.12 (m, 2H), 7.51–7.62 (m, 3H),7.85 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 55.9, 56.7, 111.8, 112.3, 112.4, 118.5, 120.2, 121.0, 121.1, 123.2, 124.2, 126.7, 127.1, 127.1, 128.1, 133.1, 138.6, 142.9, 148.2, 149.1, 160.5, 161.1; HRMS (+ESI): calcd. for $C_{22}H_{18}N_2O_3$, 358.1312, found 358.1314.

2.1.6. 2-Amino-3-cyano-4-(2-methoxyphenyl)-4H-benzo[h]chromene (**5**)

Yield: 2.26 g (69%); mp: 200–203 °C; IR (KBr pellet, cm^{-1}): 3577, 3458, 3327, 3200, 2190, 1667, 1610, 1573, 1462; ^1H NMR (400 MHz, DMSO-d_6): δ3.77 (s, 3H), 4.40 (m, 0.5H), 5.25 (s, 1H), 6.81–6.85 (m, 1H), 6.96–7.18(m, 6H), 7.49–7.61 (m, 3H), 7.82 (d, J = 8.0 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 19.0, 34.8, 56.0, 112.0, 119.0, 121.08, 121.1, 121.3, 123.2, 124.2, 126.3, 127.0, 128.1, 128.7129.5, 133.1, 133.8143.5, 156.8, 161.3; HRMS (+ESI): calcd. for $C_{21}H_{16}N_2O_2$, 328.1206, found 328.1187.

2.1.7. 2-Amino-3-cyano-4-(3-hydroxyphenyl)-4H-benzo[h]chromene (**6**)

Yield: 2.58 g (82%); mp: 261–263.5 °C; IR (KBr pellet, cm^{-1}): 3391, 2836, 2694, 2171, 1904, 1666, 1481, 1183, 1051; ^1H NMR (400 MHz, DMSO-d_6): δ 4.78 (s, 1H), 6.63–6.73 (m, 3H), 7.08–7.19 (m, 4H), 7.49–7.61 (m, 3H), 7.82 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 9.41 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 41.3, 56.8, 114.5, 114.87, 118.5, 118.8, 121.8, 123.2, 124.3, 126.7, 127.1, 127.2, 128.1, 130.1, 133.1, 143.2, 147.7, 158.2, 160.6; HRMS (+ESI): calcd. for $C_{24}H_{15}ClN_4O$, 410.0929, found 410.0915.

2.1.8. 2-Amino-3-cyano-4-(2-(4-chlorophenyl)pyrimidin-5-yl-4H-benzo[h]chromene (**7**)

Yield: 3.00 g (73%); mp: 239–240 °C; IR (KBr pellet, cm^{-1}): 3458, 3336, 2188, 1663, 1577, 1424; ^1H NMR (400 MHz, DMSO-d_6): δ 5.13 (s, 1H), 7.15 (d, J = 8.8 Hz, 1H), 7.37 (s, 2H), 7.54–7.66 (m, 5H), 7.90 (d, J = 8.0 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H); 8.32–8.34 (m, 2H), 8.81 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 36.4, 54.7, 116.2, 120.7, 121.3, 123.2, 124.8, 126.3, 127.3, 127.6, 128.2, 129.3, 129.9, 133.4, 136.1, 136.2, 137.3, 143.6, 157.6, 160.8, 161.7; HRMS (+ESI): calcd. for $C_{24}H_{15}ClN_4O$, 410.0929, found 410.0915.

2.1.9. 2-Amino-3-cyano-4-(thiophen-2-yl)-4H-benzo[h]chromene (**8**)

Yield: 1.85 g (61%); mp: 152–155 °C; IR (KBr pellet, cm^{-1}): 3466, 3330, 2187, 1657, 1620, 1569,1410, 1373, 1260; ^1H NMR (400 MHz, DMSO-d_6): δ 5.24 (s, 1H), 6.91–6.93 (m, 1H), 7.06–7.07 (m, 1H), 7.22–7.35 (m, 4H), 7.53–7.61 (m, 2H), 7.84–7.91 (m, 1H), 8.20–8.25(1H), 8.67 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 114.1, 114.8, 118.1, 120.9, 121.2, 123.1, 124.4, 125.0, 126.0, 126.5, 127.2, 127.3, 128.1, 129.6, 133.3, 135.8, 139.1, 140.9, 142.8, 151.2, 153.9, 161.7; HRMS (+ESI): calcd. for $C_{18}H_{12}N_2OS$,304.0665, found 304.0650.

2.1.10. 2-Amino-3-cyano-4-(furan-2-yl)-4H-benzo[h]chromene (**9**)

Yield: 0.83 g (30%); mp: 154–157 °C; IR (KBr pellet, cm^{-1}): 3444, 3328, 3194, 2195, 1665, 1604, 1569, 1505, 1409;^1H NMR (400 MHz, DMSO-d_6): δ 5.03 (s, 1H), 6.24 (d, J = 3.2 Hz, 1H), 6.33–6.35 (m, 1H),7.20–7.23 (m, 2H), 7.49–7.64 (m, 3H), 7.89 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 35.0, 53.6, 106.6, 110.9, 115.9, 120.7, 121.1123.2, 124.33, 126.3, 127.2, 127.3, 128.2, 133.3, 143.2, 143.5, 156.8, 161.3; HRMS (+ESI): calcd. for $C_{18}H_{12}N_2O_2$, 288.0893, found 288.0906.

2.2. Biological Studies

2.2.1. Bacterial and Fungal Cultures

Cultures of *Fusarium* species, *Aspergillus niger* and *Bacillus cereus* were obtained from culture collection unit of department of Botany. Culture of *Escherichia coli* was obtained from department of Microbiology, University of Karachi. Fungal cultures were maintained on Potato

dextrose agar (PDA), *B. cereus* was grown on Lauria Bertani agar, while *Escherichia coli* were grown on nutrient agar.

2.2.2. Anti-bacterial and Anti-fungal Activities

Anti-bacterial and anti-fungal activities of all compounds (**1**–**9**) were tested against *Bacillus cereus, Escherichia coli, Fusarium* species and *Aspergillus niger* by disc diffusion technique [29]. Bacterial cells were spread on the surface of agar plate; while 6 mm culture disc of actively growing fungi were placed at the center of agar plate. Each disc (6 mm) was impregnate with 50 μL of compound and placed on inoculated agar surface. Two concentrations (1000 and 500 ppm) for each compound (**1**–**9**) were used. For controls DMSO treated disc was used in each agar plate. Plates were incubated for 48 h (for Bacteria) and 5 days (for fungi) at 37 °C in dark and the zone of growth inhibition was measured to the nearest mm around each of the antibiotic disc.

2.2.3. Nematicidal Activity

Egg masses of root-knot nematodes (*Meloidogyne javanica*) was collected from infested roots with the help of a fine needle under stereomicroscope and transferred into cavity blocks containing sterile distilled water. After hatching, number of second stage juveniles (J2) maintained around 50 to 60/4 mL in each cavity block. 100 μL of compound was added in each cavity block. Two concentrations (1000 ppm and 500 ppm) were assessed for each compound. Cavity blocks with 100 μL of DMSO were considered as controls. Three replicates were made for each treatment. Nematodes were considered dead if they did not move when probed with a fine needle [30]. Data of dead juveniles were expressed as mortality percent.

2.3. Data Analysis

Data were subjected to two factor analysis of variance (ANOVA), followed by Fisher's least significant test [31] using the software STATISTICA version 5.0 (Statsoft Inc., Tulsa, Oklahoma, USA).

3. Results and Discussion

3.1. Chemistry

In our synthesis protocol, we synthesized 2-amino-3-cyanochromenes (**1**–**9**) by a three component reaction of 1-napthol, aryl aldehydes and malononitrile using piperidine as a catalyst. The reaction was performed in ethanol as solvent under microwave irradiation (dynamic power 25–30 W) for 5–15 min (Scheme 1, Table 1). In comparison with microwave method, we also conducted reaction by conventional method using same solvent and catalyst. We found that reaction was completed between 5 and 6 h. The structures of synthesized compounds were elucidated by ^{1}H NMR, ^{13}C NMR, HRMS and FT-IR spectrometer, results show good agreement with the structures.

Table 1
Synthesis of 2-amino-3-cyano-4-phenyl-4H-benzo[*h*]chromenes.

Entry	R	Product	Yield (%)
1	C_6H_5	1	93
2	3-FC_6H_4	2	66
3	2-$CF_3C_6H_4$	3	63
4	3,4-$(OCH_3)_2C_6H_3$	4	72
5	3-$OCH_3C_6H_4$	5	69
6	3-OHC_6H_4	6	82
7	$C_{10}H_6ClN_2$	7	73
8	C_4H_3S	8	61
9	C_4H_3O	9	30

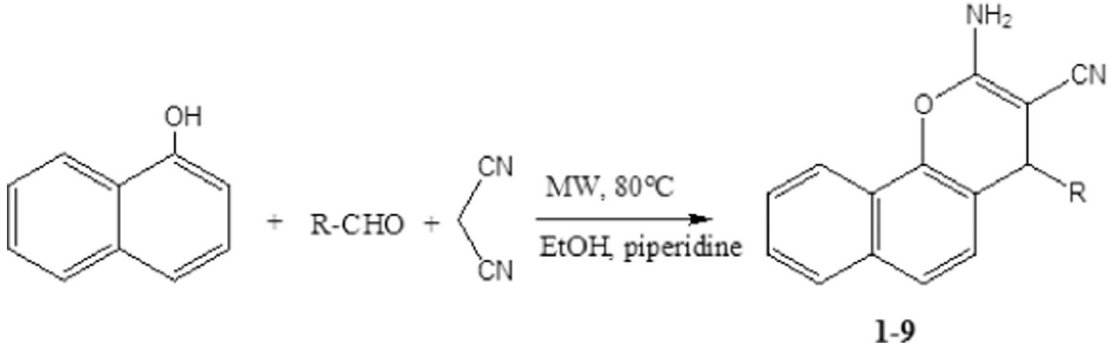
3.2. Biological Studies

The synthesized compounds (**1**–**9**) were evaluated for their biological activities. All the tested compounds showed varied response against variety of microorganisms. However, it was noticed that most of the compounds showed increased activities ($P < 0.001$) at higher tested concentration (1000 ppm) against microorganisms. Compound **6** at 1000 ppm concentration exhibited largest zone (12 mm) of inhibition of *Bacillus cereus* as compare with other compounds. Compounds **3**, **4** and **7** found ineffective against *B. cereus* at both concentrations (500 and 1000 ppm) and showed no zone of inhibition. Similarly, maximum growth of *E. coli* was inhibited by compound **6** at 1000 ppm (12 mm) and largest zone was recorded. Compound **5** produces no effect on growth of *E. coli* at both tested concentrations (Table 2).

Antifungal activities of these compounds were assessed against *Fusarium* species and *Aspergillus niger*. Compound **9** at 1000 ppm concentration greatly inhibited growth of *Fusarium* species, where largest zone of inhibition (16 mm) was observed ($P < 0.001$). Followed by compound **5** at 1000 ppm, where *Fusarium* species showed zone of inhibition of 14 mm, respectively. Most of the other compounds revealed no response to *Fusarium* species at tested concentrations. Similarly, all compounds failed to exhibit any effect on *A. niger*. J2 of root-knot nematodes *Meloidogyne javanica* mortality was tested after 72 h exposure to compounds (**1**–**9**). Significant increased ($P < 0.001$) in mortality was noticed in most of the treatments compared to controls. Highest mortality was noticed by the exposure of compound **8** at 1000 ppm (58%) followed by compound **9** (37%) and compound **4** (18%). However for other compounds, mortality was ranged 4–14%. We also tested the reactants for nematicidal, antibacterial or antifungal activity; however, reactants did not show any activity.

4. Conclusion

A series of 2-amino-3-cyanochromenes were synthesized by utilizing microwave energy by using piperidine as a catalyst and ethanol as a solvent. The method was more efficient as compare with conventional method (5–6 h) and completed within 5–15 min. This methodology has



Scheme 1. Synthesis of 2-amino-3-cyano-4-phenyl-4H-benzo[*h*]chromenes (**1**–**9**).

Table 2
Anti-bacterial, anti-fungal and nematicidal activities of compounds at different concentrations (500 and1000 ppm).

Compounds	*B. cereus*	*E. coli*	*Fusarium* species	*A. niger*	*M. javanica* mortality %
	Zone of inhibition in mm				
Control	0 ± 0	0 ± 0	0 ± 0	0 ± 0	4.96 ± 1.06
1. 500	6.33 ± 0.33	8 ± 0	0 ± 0	0 ± 0	14.30 ± 0.84
1000	9 ± 0	9 ± 0.58	0 ± 0	0 ± 0	12.49 ± 2.88
2. 500	2 ± 2	7.33 ± 0.88	0 ± 0	0 ± 0	11.88 ± 0.38
1000	4 ± 2	8 ± 0.58	10 ± 0	0 ± 0	8.94 ± 2.21
3. 500	0 ± 0	7.33 ± 0.33	0 ± 0	0 ± 0	8.48 ± 1.31
1000	0 ± 0	8 ± 0	0 ± 0	0 ± 0	10.46 ± 1.94
4. 500	0 ± 0	0 ± 0	0 ± 0	0 ± 0	15.90 ± 2.81
1000	0 ± 0	6.33 ± 3.18	0 ± 0	0 ± 0	18.40 ± 3.13
5. 500	8 ± 0.58	0 ± 0	5.67 ± 0.67	0 ± 0	9.08 ± 1.60
1000	10.66 ± 0.33	0 ± 0	14 ± 1	0 ± 0	14.87 ± 3.69
6. 500	6.33 ± 0.33	5.67 ± 0.33	0 ± 0	0 ± 0	9.63 ± 1.22
1000	12 ± 0	12 ± 0.58	0 ± 0	0 ± 0	13.89 ± 4.47
7. 500	0 ± 0	7.66 ± 0.88	0 ± 0	0 ± 0	7.0800.8
1000	0 ± 0	7.8 ± 0.65	0 ± 0	0 ± 0	8.30 ± 0.75
8. 500	6.33 ± 0.33	7.33 ± 0.88	0 ± 0	0 ± 0	48.16 ± 6.04
1000	7.67 ± 0.33	8.67 ± 0.33	0 ± 0	0 ± 0	58.72 ± 7.04
9. 500	0 ± 0	6.33 ± 0.88	0 ± 0	0 ± 0	27.80 ± 3.25
1000	8.33 ± 0.33	7.67 ± 0.67	16 ± 2	0 ± 0	37.31 ± 2.10
[a]$LSD_{0.05}$					
Compound	1.46	1.77	1.14	0	5.96
Concentration	0.623	0.755	0.485	0	2.44

[a] Fisher's least significant difference, Data comprises mean of three replicates ± standard error.

advantages due to mild reaction conditions and simple experimental work up. The synthesized compounds (**1**–**9**) exhibited moderate to high biological activities. Compounds **6**, **9** and **8** exhibited high anti-bacterial, anti-fungal and nematicidal activities respectively. Results indicate that these compounds could be used as effective control for soil-borne plant pathogens (nematodes, fungi and bacteria).

References

[1] G.P. Ellis, I.M. Lockhart, in: G.P. Ellis (Ed.), The Chemistry of Heterocyclic Compounds: Chromenes, Chromanones, and Chromones, 31, Wiley-VCH, Weinheim, Germany 2007, pp. 1–1196.
[2] W. Kemnitzer, J. Drewe, S. Jiang, H. Zhang, Y. Wang, J. Zhao, S. Jia, J. Herich, D. Labreque, R. Storer, K. Meerovitch, D. Bouffard, R. Rej, R. Denis, C. Blais, S. Lamothe, G. Attardo, H. Gourdeau, B. Tseng, S. Kasibhatla, S.X. Cai, J. Med. Chem. 47 (2004) 6299–6310.
[3] A.A. Patchett, R.P. Nargund, Annu. Rep. Med. Chem. 35 (2000) 289–298.
[4] R.W. DeSimone, K.S. Currie, S.A. Mitchell, J.W. Darrow, D.A. Pippin, Comb. Chem. High Throughput Screen. 7 (2004) 473–494.
[5] W. Kemnitzer, S. Kasibhatla, S. Jiang, H. Zhang, J. Zhao, S. Jia, L. Xu, C. Crogan-Grundy, R. Denis, N. Barriault, L. Vaillancourt, S. Charron, J. Dodd, G. Attardo, D. Labrecque, S. Lamothe, H. Gourdeau, B. Tseng, J. Drewea, S.X. Cai, Bioorg. Med. Chem. Lett. 15 (2005) 4745–4751.
[6] S.G. Das, J.M. Doshi, D. Tian, S.N. Addo, B. Srinivasan, D.L. Hermanson, C. Xing, J. Med. Chem. 52 (2009) 5937–5949.
[7] S. Kasibhatla, H. Gourdeau, K. Meerovitch, J. Drewe, S. Reddy, L. Qiu, H. Zhang, F. Bergeron, D. Bouffard, Q. Yang, J. Herich, S. Lamothe, S.X. Cai, B. Tseng, Mol. Cancer Ther. 3 (2004) 1365–1374.
[8] H. Gourdeau, L. Leblond, B. Hamelin, C. Desputeau, K. Dong, I. Kianicka, D. Custeau, C. Bourdeau, L. Geerts, S.X. Cai, J. Drewe, D. Labrecque, S. Kasibhatla, B. Tseng, Mol. Cancer Ther. 3 (2004) 1375–1383.
[9] J.L. Wang, D. Liu, Z.J. Zhang, S. Shan, X. Han, S.M. Srinivasula, C.M. Croce, E.S. Alnemri, Z. Huang, Proc. Natl. Acad. Sci. U. S. A. 97 (2000) 7124–7129.
[10] D.R. Anderson, S. Hegde, E. Reinhard, L. Gomez, W.F. Vernier, L. Lee, S. Liu, A. Sambandam, P.A. Snider, L. Masih, Bioorg. Med. Chem. Lett. 15 (2005) 1587–1590.
[11] M.M. Khafagy, A.H.F. Abd El-Wahab, F.A. Eid, A.M. El-Agody, Farmaco 57 (2002) 715–722.
[12] G. Bianchi, A. Tava, Agric. Biol. Chem. 51 (1987) 2001–2002.
[13] P.W. Smith, S.L. Sollis, P.D. Howes, P.C. Cherry, I.D. Starkey, K.N. Cobley, H. Weston, J. Scicinski, A. Merritt, A. Whittington, P. Wyatt, N. Taylor, D. Green, R. Bethell, S. Madar, R.J. Fenton, P.J. Morley, T. Pateman, A. Beresford, J. Med. Chem. 41 (1998) 787–797.
[14] A. Martinez-Grau, J.L. Marco, Bioorg. Med. Chem. Lett. 7 (1997) 3165–3170.
[15] J. Skommer, D. Wlodkowic, M. Matto, M. Eray, J. Pelkonen, Leuk. Res. 30 (2006) 322–331.
[16] S.J. Mohr, M.A. Chirigos, F.S. Fuhrman, J.W. Pryor, Cancer Res. 35 (1975) 3750–3754.
[17] F. Eiden, F. Denk, Arch. Pharm. (Weinheim, Ger.) (Arch. Pharm.) 324 (1991) 353–354.
[18] E.A. Hafez, M.H. Elnagdi, A.G.A. Elagamey, F.M.A.A. ElTaweel, Heterocycles 26 (1987) 903–907.
[19] M.A. Sofan, M.H. Elnagdi, F.M.A.A. ElTaweel, Liebigs Ann. Chem. 9 (1989) 935–936.
[20] A.M. ElAgrody, M.H. ElHakiem, M.S. Abd El-Latif, A.H. Fakery, E.S.M. El-Sayed, K.A. El-Ghareab, Acta Pharma. 50 (2000) 111–120.
[21] R.S. Varma, R.J. Dahiya, Org. Chem. 63 (1998) 8038–8041.
[22] W. Kemnitzer, S. Kasibhatla, S. Jiang, H. Zhang, J. Zhao, S. Jia, L. Xu, C. Crogan-Grundy, R. Denis, N. Barriault, L. Vaillancourt, S. Charron, J. Dodd, G. Attardo, D. Labrecque, S. Lamothe, H. Gourdeau, B. Tseng, J. Drewe, S.X. Cai, Bioorg. Med. Chem. Lett. 15 (2005) 4745–4751.
[23] R. Maggi, R. Ballini, G. Sartori, R. Sartorio, Tetrahedron Lett. 45 (2004) 2297–2299.
[24] M. Kidwai, S. Saxena, M. Khalilur Rahman khan, S.S. Thukral, Bioorg. Med. Chem. Lett. 15 (2005) 4295–4298.
[25] R. Ballini, G. Bosica, M.L. Conforti, R. Maggi, A. Mazzacani, P. Righi, G. Sartori, Tetrahedron 57 (2001) 1395–1398.
[26] A world perspective on nematology: the role of the society, in: J.N. Sasser, D.W. Freckman, J.A. Veech, D.W. Dickson (Eds.), Vistas on Nematology, Society of Nematologists, Inc., Hyattsville, MD 1987, pp. 7–14.
[27] O.D. Dhingra, J.B. Sinclair, Biology and Pathology of *Macrophomina phaseolina*, Universidade Federal de Vicosa, Brazil, 1978 166.
[28] G.K. Gupta, S.K. Sharma, R. Ramteke, J. Phytopathol. 160 (2012) 167–180.
[29] R.W. Bauer, M.D.K. Kirby, J.C. Sherris, M. Turck, Am. J. Clin. Pathol. 45 (1966) 493–496.
[30] J.C. Cayrol, C. Djian, I. Pijarowski, Revue de Nematologie 12 (1989) 331–336.
[31] J.H. Zar, Biostatistical Analysis, 5th edn Prentice-Hall, Englewoods Cliff, 2009.