chemistry proceedings

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Design, Synthesis and Bioactivity of Benzimidazole–2–Carbamates as Soil–Borne Anti–Fungal Agents †,‡

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† Presented at the 24th International Electronic Conference on Synthetic Organic Chemistry, 15 November–15 December 2020; Available online: https://ecsoc-24.sciforum.net/.

‡ Dedicated to the Memory of Prof. Dr. h. c. Wolfgang Voelter.

Abstract: The design and synthesis of new, safe and potent molecules to apply against soil-borne pathogens is a critical goal for organic and bio-medicinal chemists. Herein, we designed and synthesized a series of benzimidazole-based carbamate derivatives (7a–f), as soil-borne anti-fungals. The derivatives 7a–f were all synthesized in multi-step reactions with acceptable yields. The structures of 7a–f were all identified and characterized using ^{1}H-NMR, IR, HRMS, and melting point calculations. The final compounds were tested on five soil-borne pathogens. The results of various bio-assays showed that compounds 7a-3, 7a-2, 7b-2, 7a-1 and 7b-1 significantly affected the growth of *Pythium aphanidermatum*, a serious pathogen affecting vegetable crops worldwide. Compounds 7a-1 and 7b-1 were the most efficacious, which resulted in a 96% growth inhibition in *Pythium* at 100 mg L^{-1}. In conclusion, we reported the potent carbamate derivatives as soil-borne anti-fungals, and believe that the synthesis of more derivatives related to the current scaffold would be beneficial.

Keywords: anti-fungal; benzimidazole; carbamate; synthesis; soil-borne pathogen

Citation: Al–Harthy, T.; Al-Sadi, A.M.; Zoghaib, W.; Moghadam, E.S.; Stoll, R.; Abdel-Jalil, R. Design, Synthesis and Bioactivity of Benzimidazole–2–Carbamates as Soil–Borne Anti–Fungal Agents. *Chem. Proc.* **2021**, *3*, 64. https://doi.org/10.3390/ecsoc-24-08093

Published: 13 November 2020

1. Introduction

Heterocyclic chemistry plays a critical role in the design and synthesis of bio-active compounds. Some of the most important heterocycles are benzimidazole and its derivatives. The properties of benzimidazole and its derivatives have been studied over more than 100 years. Benzimidazole derivatives are useful intermediates/sub-units for the development of molecules of pharmaceutical or biological interest. Substituted benzimidazole derivatives have been found to have applications in diverse therapeutic areas such as anti-cancer agents, anti-bacterial agents, anti-fungal agents, anti-inflammatory agents, analgesic agents, anti-HIV agents, anti-oxidant agents, anti-convulsant agents, anti-tubercular agents, anti-diabetic agents, anti-leishmanial agents, anti-histaminic agents, anti-malarial agents, and other medicinal agents [1–8]. One of the most important applications of benzimidazole derivatives is its use as an anti-fungal agent in plants. Soil-borne fungi are some of the most important causes of widespread, serious plant diseases. The spores or mycelia of many of these fungi can overwinter or survive adverse conditions in soil or on plant debris, and once an area has become infested with soil-borne fungi, it is generally difficult to get rid of them. There are multiple reported benzimidazole derivatives that are used as fungicides (Figure 1) [9].

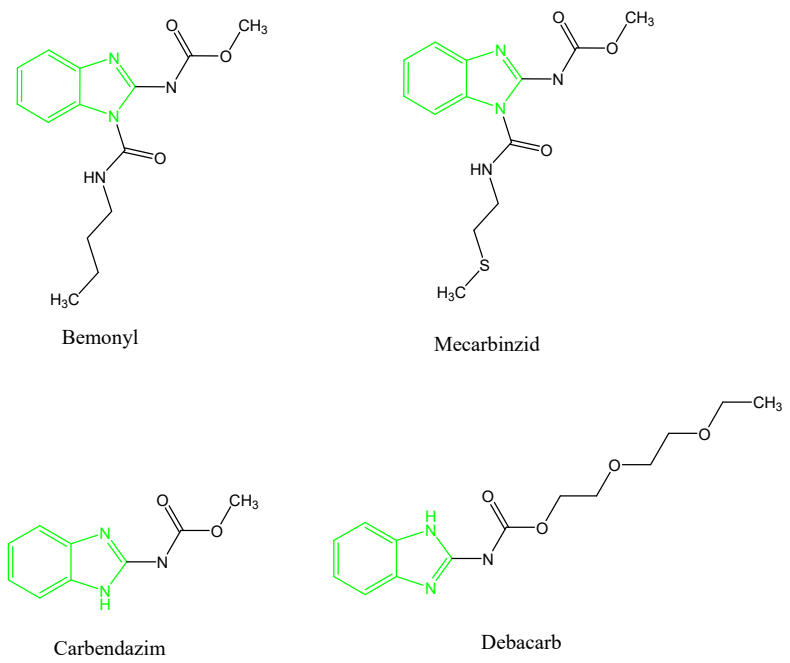


Figure 1. Benzimidazole derivatives used as fungicides.

In parallel with benzimidazole-containing fungicides, a series of fungicides involving a fluorine atom have been developed. Fluorinated heterocycles have attracted attention due to fluorine's ability to act as a polar hydrogen or hydroxyl mimic. The introduction of fluorine at a strategic position of a molecule is a powerful and versatile tool for the development of organic molecules, which gain potential biological activities by changing the steric and electronic mapping of the molecule. The inclusion of fluorine into organic molecules can affect their lipophilicity and thus enhance the rate of cell penetration and transport of a drug to an active site (Figure 2) [10–13].

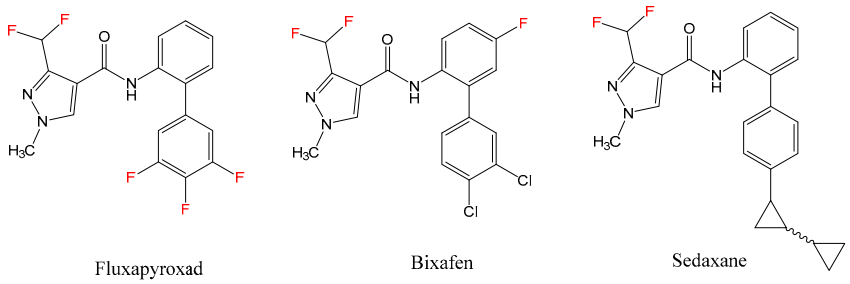


Figure 2. Fluorine-containing fungicides.

Except for the addition of a fluorine atom in the structure of some molecules for exerting anti-fungal activity, using piperazine moiety also led to emergent anti-fungal activities in some structures (Figure 3) [14–19].

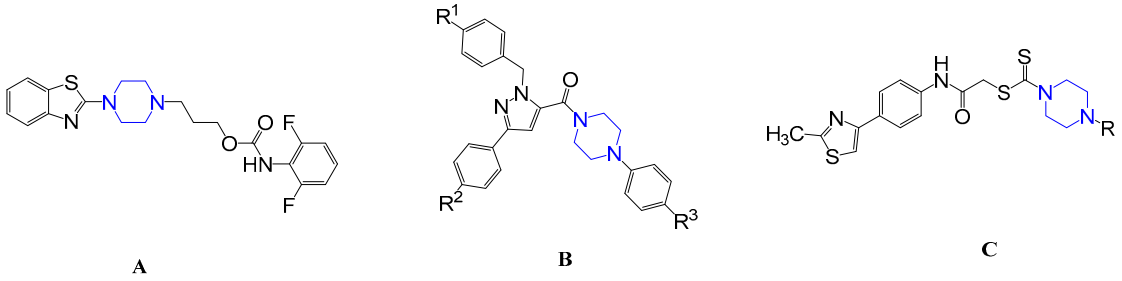


Figure 3. Structures containing a piperazine ring with anti-fungal activities.

With respect to the above explanations and in continuation of our efforts to design and synthesize novel anti-microbial agents containing fluorine and piperazine substituents (Figure 4a), we reported the synthesis of a series of benzimidazole derivatives and their bio-activity as anti-fungal agents (Figure 4b).

Cucumber (*Cucumis sativus*) is the most important greenhouse crop in Oman [20,21]. However, soilborne diseases (i.e., damping-off and vine decline) limit cucumber growth and production. The losses due to these diseases have been reported to exceed 70% in some greenhouses [22–24]. Damping-off and vine decline diseases are also limiting factors to the production of cucumbers and other cucurbits in different parts of the world [25–28].

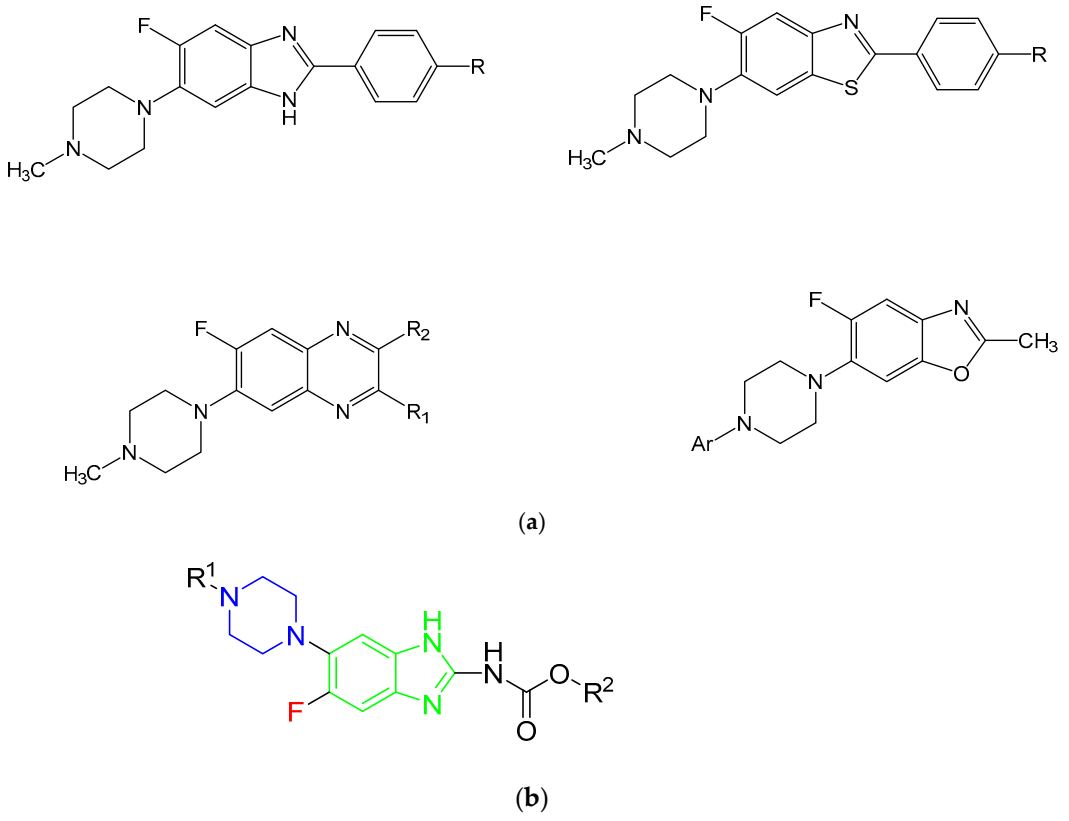


Figure 4. (a) Previous works; (b) current work.

Damping-off and vine decline diseases are caused by different pathogens, including the *Pythium*, *Rhizoctonia* and *Fusarium* species [27,29–31]. *Pythium aphanidermatum* is the most common causal agent of damping-off disease in cucumbers in Oman [22,32,33]. It is also among the two most common pathogens associated with cucumber vine decline [23]. The pathogen is tolerant to heat and has been found to be associated with cucumber root diseases during most of the year.

The management of *Pythium*-induced diseases in cucumbers has relied on the use of imported fungicides, biological control and cultural practices [27,34–37]. Mefenoxam and hymexazol are two common fungicides used to manage Pythium-induced diseases in Oman. Despite their use in different farms, mefenoxam suffers from rapid bio-degradation in soil while resistance to hymexazol has been reported among Pythium species [38–41]. Biological control is a new area of research in Oman. Some bio-control agents have been isolated from Omani soils and plants and tested against Pythium damping-off disease. These agents include *Pseudomonas aeruginosa, Aspergillus terreus, Talaromyces* spp. and *Trichoderma* spp. [42–46]. However, the efficacy of these bio-control agents is limited. Due to limitations in these management methods, it is important to search for new fungicide formulations that can be used to control these diseases.

The objectives of this study were:

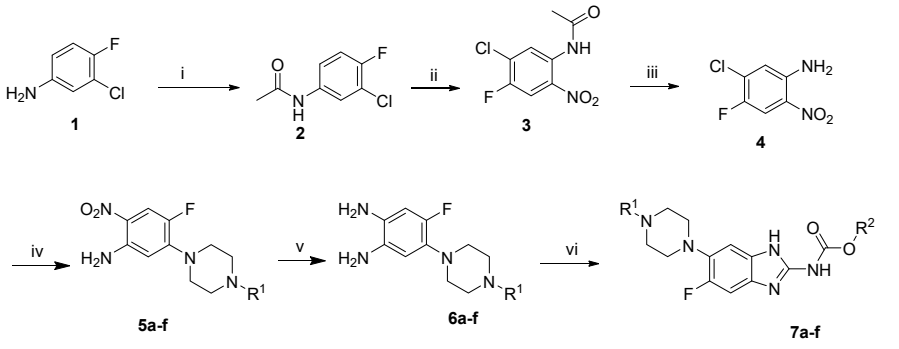
1. To synthesize a novel class of 2-carbamate benzimidazoles.
2. To investigate the efficacy of the new fungicide formulations in suppressing the growth of the most common soil-borne pathogens.

2. Results and Discussion

2.1. Chemistry

The synthetic scheme for the target compounds 7a–f is outlined in Scheme 1. The synthetic strategy involved multi-step synthesis. The 2-carbamate benzimidazole derivatives 7a–f were prepared from the *o*-phenylenediamine 6a–f in a one-pot procedure by reacting with 1,3-bis(substitutedoxycarbonyl)-2-methyl-2-thiopseudourea to produce nine new 2-carbamatebenzimidazoles compounds. The yields of the cyclization reaction ranged from excellent to good.

The chemical structures of the new series of 2-carbamate benzimidazoles 7a–f were elucidated utilizing HRMS, ^{1}H NMR, FTIR and Mp. The new compounds synthesized in this research were characterized using ^{1}H NMR, ^{13}C NMR and IR. In the case of intermediates 6a–f, they were not separated and the crude mixture was used directly for the next step to synthesize the final products. The HRMS spectra of the newly prepared molecules displayed molecular ion peaks at the appropriate m/z values. With FTIR, (NHC=O) was shown as a sharp band in the range of 1743–1716 cm^{-1}. The main characterization techniques for the target carbamates 7a–f are HRMS and ^{1}H NMR spectroscopy.



i:Acetic Anhydride, RT, 3h
ii:H_2SO_4, HNO_3, 0°C - RT, 3h
iii:Ethanol, conc HCl, Reflux, 3h
iv:Piperazine derivatives, DMSO, Reflux ,2h
v: HCl, $SnCl_2$, RT, 2h
vi:1,3-dicarbalkoxy-S-methylisothiourea derivatives, Ethanol, Reflux, overnight

5a,6a: R^1:Me
5b,6b: R^1:Et
5c,6c: R^1:But
5d,6d: R^1:Ph
5e,6e: R^1:4-F-Ph
5f,6f: R^1:2-F-Ph

7a-1: R^1:Me, R^2:Bn
7a-2: R^1:Me, R^2:t-But
7a-3: R^1:Me, R^2:Me
7b-1: R^1:Et, R^2:Bn
7b-2: R^1:Et, R^2:t-But
7b-3: R^1:Et, R^2:Me
7c-1: R^1:But, R^2:Bn
7c-2: R^1:But, R^2:Me

7d-1: R^1:Ph, R^2:Bn
7d-2: R^1:Ph, R^2:t-But
7d-3: R^1:Ph, R^2:Me
7e-1: R^1:4-F-Ph, R^2:Bn
7e-2: R^1:4-F-Ph, R^2:t-But
7e-3: R^1:4-F-Ph, R^2:Me
7f-1: R^1:2-F-Ph, R^2:Bn
7f-2: R^1:2-F-Ph, R^2:t-But
7f-3: R^1:2-F-Ph, R^2:Me

Scheme 1. The synthetic pathway to target compounds 7a–f.

The new 2-carbamatebenzimidazoles 7a–f have been converted to their hydrochloride salts in an attempt to enhance their aqueous solubility,for the biological investigation, due to their poor solubility in organic solvents.

In order to ensure that the structures were maintained as hydrochloride salts after conversion, LC-MS was performed, and the results showed the correct molecular ion peak.

2.2. Biologic Activity

The six fungicide formulations affected the growth of the five fungi at different rates. The growths of *Botrytis* and *Bipolaris* were not affected by any of the fungicide formulations at a concentration of 100 mg L^{-1}. However, the growth of *Pythium* was significantly affected by 7a-3, 7a-2, 7b-2, 7a-1 and 7b-1 (Figure 5). The benzimidazoles with benzyl derivatives (7a-1 and 7b-1) were the most efficacious fungicide formulations in reducing the growth of *Pythium*, resulting in a 96% growth inhibition in *Pythium* at 100 mg·L^{-1}. *Fusarium* and *Alternaria* were only affected by the 7b-1 fungicide formulation (Figure 5).

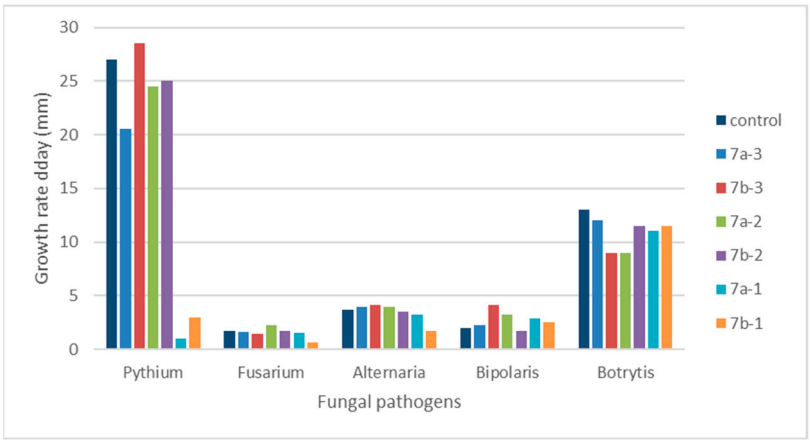


Figure 5. The effect of six fungicide formulations on the growth rates of the *Pythium, Fusarium, Alternaria, Bipolaris* and *Botrytis* species. Bars with the same letter in the same fungus category are not significantly different from each other at $p < 0.05$ (Tukey's Studentized range test, SAS).

3. Conclusions

In conclusion, in this work we reported the synthesis and bio-activity of seventeen benzimidazole-based carbamate derivatives 7a–f as fungicides. The synthesized compounds exhibited an acceptable activity against soil-borne pathogens. The benzimidazoles with benzyl derivatives (7a-1 and 7b-1) showed very high and promising results and were the most efficacious fungicide formulations in terms of reducing the growth of *Pythium*. Future studies should focus on the efficacy of this fungicide on other soil-borne pathogens.

Acknowledgments: We want to thank Sultan Qaboos University for financial support of this project. The Research Center (TRC) for funding this project.

Conflicts of Interest: The authors declare that they have no conflict of interest.

References

1. Keri, R.S.; Hiremathad, A.; Budagumpi, S.; Nagaraja, B.M. Comprehensive Review in Current Developments of Benzimidazole-Based Medicinal Chemistry. *Chem. Biol. Drug Des.* **2015**, *86*, 19–65.
2. Zhou, Y.; Xu, J.; Zhu, Y.; Duan, Y.; Zhou, M. Mechanism of Action of the Benzimidazole Fungicide on *Fusarium graminearum*: Interfering with Polymerization of Monomeric Tubulin But Not Polymerized Microtubule. *Phytopathology* **2016**, *106*, 807–813.
3. Akhtar, W.; Khan, M.F.; Verma, G.; Shaquiquzzaman, M.; Rizvi, M.A.; Mehdi, S.H.; Akhter, M.; Alam, M.M. Therapeutic evolution of benzimidazole derivatives in the last quinquennial period. *Eur. J. Med. Chem.* **2017**, *126*, 705–753.

4. Keri, R.S.; Rajappa, C.K.; Patil, S.A.; Nagaraja, B.M. Benzimidazole-core as an antimycobacterial agent. *Pharmacol. Rep.* **2016**, *68*, 1254–1265.
5. Gaba, M.; Singh, S.; Mohan, C. Benzimidazole: An emerging scaffold for analgesic and anti-inflammatory agents. *Eur. J. Med. Chem.* **2014**, *76*, 494–505.
6. Błaszczak-Świątkiewicz, K.; Olszewska, P.; Mikiciuk-Olasik, E. Biological approach of anticancer activity of new benzimidazole derivatives. *Pharmacol. Rep.* **2014**, *66*, 100–106.
7. Ajani, O.O.; Aderohunmu, D.V.; Ikpo, C.O.; Adedapo, A.E.; Olanrewaju, I.O. Functionalized Benzimidazole Scaffolds: Privileged Heterocycle for Drug Design in Therapeutic Medicine. *Arch. Pharm.* **2016**, *349*, 475–506.
8. Bansal, Y.; Silakari, O. The therapeutic journey of benzimidazoles: A review. *Bioorg. Med. Chem.* **2012**, *20*, 6208–6236.
9. Lucas, G.B.; Campbell, C.L.; Lucas, L.T. Diseases Caused by Soilborne Fungi. In *Introduction to Plant Diseases: Identification and Management*; Springer: Boston, MA, USA, 1992; pp. 162–191.
10. Yu, X.; Teng, P.; Zhang, Y.-L.; Xu, Z.-J.; Zhang, M.-Z.; Zhang, W.-H. Design, synthesis and antifungal activity evaluation of coumarin-3-carboxamide derivatives. *Fitoterapia* **2018**, *127*, 387–395.
11. Shivarama Holla, B.; Sooryanarayana Rao, B.; Sarojini, B.K.; Akberali, P.M.; Suchetha Kumari, N. Synthesis and studies on some new fluorine containing triazolothiadiazines as possible antibacterial, antifungal and anticancer agents. *Eur. J. Med. Chem.* **2006**, *41*, 657–663.
12. Wei, P.; Liu, Y.; Li, W.; Qian, Y.; Nie, Y.; Kim, D.; Wang, M. Metabolic and Dynamic Profiling for Risk Assessment of Fluopyram, a Typical Phenylamide Fungicide Widely Applied in Vegetable Ecosystem. *Sci. Rep.* **2016**, *6*, 33898.
13. Li, C.; Yang, W.; Liu, H.; Li, M.; Zhou, W.; Xie, J. Crystal structures and antifungal activities of fluorine-containing thioureido complexes with nickel(II). *Molecules* **2013**, *18*, 15737–15749.
14. Suryavanshi, H.; Rathore, M. Synthesis and biological activities of piperazine derivatives as antimicrobial and antifungal agents. *Org. Commun.* **2017**, *10*, 228–238.
15. Lv, H.-S.; Wang, L.-Y.; Ding, X.-L.; Wang, X.-H.; Zhao, B.-X.; Zuo, H. Synthesis and Antifungal Activity of Novel (1-Arylmethyl-3-Aryl-1H-Pyrazol-5-yl)(4-Arylpiperazin-1-yl)Methanone Derivatives. *J. Chem. Res.* **2013**, *37*, 473–475.
16. Mohsen, U. Synthesis and Antimicrobial Activity of Some Piperazine Dithiocarbamate Derivatives. *Turk. J. Pharm. Sci.* **2014**, *11*, 347–354.
17. Nishat, N.; Haq, M.M.; Ahamad, T.; Kumar, V. Synthesis, spectral and antimicrobial studies of a novel macrocyclic ligand containing a piperazine moiety and its binuclear metal complexes. *J. Coord. Chem.* **2007**, *60*, 85–96.
18. Kondoh, O.; Inagaki, Y.; Fukuda, H.; Mizuguchi, E.; Ohya, Y.; Arisawa, M.; Shimma, N.; Aoki, Y.; Sakaitani, M.; Watanabe, T. Piperazine Propanol Derivative as a Novel Antifungal Targeting 1,3-β-D-glucan Synthase. *Biol. Pharm. Bull.* **2005**, *28*, 2138–2141.
19. Zhang, Y.; Zhan, Y.-Z.; Ma, Y.; Hua, X.-W.; Wei, W.; Zhang, X.; Song, H.-B.; Li, Z.-M.; Wang, B.-L. Synthesis, crystal structure and 3D-QSAR studies of antifungal (bis-)1,2,4-triazole Mannich bases containing furyl and substituted piperazine moieties. *Chin. Chem. Lett.* **2017**, *29*, 441–446.
20. Kazeeroni, E.A.; Al-Sadi, A.M. 454-Pyrosequencing Reveals Variable Fungal Diversity Across Farming Systems. *Front. Plant Sci* **2016**, *7*, 314–314.
21. Al-Sadi, A.M. Epidemiology and Management of Fungal Diseases in Dry Environments. In *Innovations in Dryland Agriculture*; Farooq, M., Siddique, K.H.M., Eds.; Springer International Publishing: Cham, Switzerland, 2016; pp. 187–209.
22. Al-Sadi, A.M.; Al-Said, F.A.; Al-Kiyumi, K.S.; Al-Mahrouqi, R.S.; Al-Mahmooli, I.H.; Deadman, M.L. Etiology and characterization of cucumber vine decline in Oman. *Crop Prot.* **2011**, *30*, 192–197.
23. Al-Mawali, Q.; Al-Sadi, A.; Fa, A.-S.; Deadman, M. Etiology, development and reaction of muskmelon to vine decline under arid conditions of Oman. *Phytopathol. Mediterr.* **2013**, *52*, 457–465.
24. Al-Mawaali, Q.S.; Al-Sadi, A.M.; Khan, A.J.; Al-Hasani, H.D.; Deadman, M.L. Response of cucurbit rootstocks to *Pythium aphanidermatum*. *Crop Prot.* **2012**, *42*, 64–68.
25. Hatami, N.; Aminaee, M.M.; Zohdi, H.; Tanideh, T. Damping-off disease in greenhouse cucumber in Iran. *Arch. Phytopathol. Plant Prot.* **2013**, *46*, 796–802.
26. Huang, X.; Liu, L.; Wen, T.; Zhang, J.; Shen, Q.; Cai, Z. Reductive soil disinfestations combined or not with Trichoderma for the treatment of a degraded and *Rhizoctonia solani* infested greenhouse soil. *Sci. Hortic.* **2016**, *206*, 51–61.
27. Abbasi, P.A.; Renderos, W.; Fillmore, S. Soil incorporation of buckwheat as a pre-plant amendment provides control of Rhizoctonia damping-off and root rot of radish and Pythium damping-off and root rot of cucumber. *Can. J. Plant Pathol.* **2019**, *41*, 24–34.
28. Al-Fadhal, F.A.; Al-Abedy, A.N.; Alkhafije, D.A. Isolation and molecular identification of *Rhizoctonia solani* and *Fusarium solani* isolated from cucumber (*Cucumis sativus* L.) and their control feasibility by *Pseudomonas fluorescens* and Bacillus subtilis. *Egypt. J. Biol. Pest. Control.* **2019**, *29*, 47.
29. Owen, W.; Jackson, B.; Whipker, B.E.; Fonteno, W.; Benson, M.D. Assessing the severity of damping-off caused by *Pythium ultimum* and *Rhizoctonia solani* in peat-based greenhouse substrates amended with pine wood chip aggregates. *Acta Hortic.* **2019**, *1266*, 27–34.
30. Philosoph, A.; Dombrovsky, A.; Elad, Y.; Koren, A.; Frenkel, O. Insight Into Late Wilting Disease of Cucumber Demonstrates the Complexity of the Phenomenon in Fluctuating Environments. *Plant Dis.* **2019,** *103*, 2877–2883.
31. Ravnskov, S.; Cabral, C.; Larsen, J. Mycorrhiza induced tolerance in *Cucumis sativus* against root rot caused by *Pythium ultimum* depends on fungal species in the arbuscular mycorrhizal symbiosis. *Biol. Control.* **2020**, *141*, 104133.

32. Al-Sadi, A.M.; Al-Masoudi, R.S.; Al-Habsi, N.; Al-Said, F.A.; Al-Rawahy, S.A.; Ahmed, M.; Deadman, M.L. Effect of salinity on Pythium damping-off of cucumber and on the tolerance of *Pythium aphanidermatum*. *Plant Pathol.* **2010**, *59*, 112–120.
33. Al-Sadi, A.M.; Al-Said, F.A.; Al-Jabri, A.H.; Al-Mahmooli, I.H.; Al-Hinai, A.H.; de Cock, A.W.A.M. Occurrence and characterization of fungi and oomycetes transmitted via potting mixtures and organic manures. *Crop Prot.* **2011**, *30*, 38–44.
34. De Corato, U.; Patruno, L.; Avella, N.; Lacolla, G.; Cucci, G. Composts from green sources show an increased suppressiveness to soilborne plant pathogenic fungi: Relationships between physicochemical properties, disease suppression, and the microbiome. *Crop Prot.* **2019**, *124*, 104870.
35. Jaiswal, A.K.; Graber, E.R.; Elad, Y.; Frenkel, O. Biochar as a management tool for soilborne diseases affecting early stage nursery seedling production. *Crop Prot.* **2019**, *120*, 34–42.
36. Wang, H.; Ding, J.; Liu, S.; Bai, X.; Xue, L. Different carbonic supplements induced changes of microflora in two types of compost teas and biocontrol efficiency against *Pythium aphanidermatum*. *Biocontrol Sci. Technol.* **2019**, *29*, 924–939.
37. You, X.; Kimura, N.; Okura, T.; Murakami, S.; Okano, R.; Shimogami, Y.; Matsumura, A.; Tokumoto, H.; Ogata, Y.; Tojo, M. Suppressive Effects of Vermicomposted-Bamboo Powder on Cucumber Damping-Off. *Jpn. Agric. Res. Q.* **2019**, *53*, 13–19.
38. Al-Sa'di, A.M.; Drenth, A.; Deadman, M.L.; Al-Said, F.A.; Khan, I.; Aitken, E.A.B. Association of a second phase of mortality in cucumber seedlings with a rapid rate of metalaxyl biodegradation in greenhouse soils. *Crop Prot.* **2008**, *27*, 1110–1117.
39. Al-Sadi, A.M. Efficacy of mefenoxam is affected by a lag period between application and inactivation of Pythium species. *Phytopathol. Mediterr.* **2012**, *51*, 292–297.
40. Al-Sadi, A.M.; Al-Masoodi, R.S.; Al-Ismaili, M.; Al-Mahmooli, I.H. Population Structure and Development of Resistance to Hymexazol Among *Fusarium solani* Populations from Date Palm, Citrus and Cucumber. *J. Phytopathol.* **2015**, *163*, 947–955.
41. Al-Balushi, Z.; Agrama, H.; Al-Mahmooli, I.; Maharachchikumbura, S.; Al-Sadi, A. Development of Resistance to Hymexazol Among Pythium Species in Cucumber Greenhouses in Oman. *Plant Dis.* **2018,** *102*, 202–208.
42. Halo, B.A.; Al-Yahyai, R.A.; Al-Sadi, A.M. *Aspergillus terreus* Inhibits Growth and Induces Morphological Abnormalities in *Pythium aphanidermatum* and Suppresses *Pythium*-Induced Damping-Off of Cucumber. *Front. Microbiol* **2018**, *9*, 95–95.
43. Al-Daghari, D.S.S.; Al-Abri, S.A.; Al-Mahmooli, I.H.; Al-Sadi, A.M.; Velazhahan, R. Efficacy of native antagonistic rhizobacteria in the biological control of *Pythium aphanidermatum*-induced damping-off of cucumber in Oman. *J. Plant Pathol.* **2020**, *102*, 305–310.
44. Al-Shibli, H.; Dobretsov, S.; Al-Nabhani, A.; Maharachchikumbura, S.S.N.; Rethinasamy, V.; Al-Sadi, A.M. *Aspergillus terreus* obtained from mangrove exhibits antagonistic activities against *Pythium aphanidermatum*-induced damping-off of cucumber. *PeerJ* **2019,** *7*, e7884.
45. Halo, B.A.; Al-Yahyai, R.A.; Maharachchikumbura, S.S.N.; Al-Sadi, A.M. Talaromyces variabilis interferes with *Pythium aphanidermatum* growth and suppresses *Pythium*-induced damping-off of cucumbers and tomatoes. *Sci. Rep.* **2019**, *9*, 11255.
46. Kazerooni, E.; Velazhahan, R.; Al-Sadi, A. *Talaromyces pinophilus* inhibits *Pythium* and *Rhizoctonia*-induced damping-off of cucumber. *J. Plant Pathol.* **2018**, *101*, 377–383.