engineering proceedings

Proceeding Paper

Mini-Review of the Importance of Hydrazides and Their Derivatives—Synthesis and Biological Activity †

Suraj N. Mali [1], Bapu R. Thorat [2,*], Deepa Rani Gupta [2] and Anima Pandey [1]

[1] Department of Pharmaceutical Sciences and Technology, Birla Institute of Technology, Mesra, Jharkhand 835215, India; suraj1695@gmail.com (S.N.M.); apandey@bitmesra.ac.in (A.P.)
[2] Department of Chemistry, Government College of Arts and Science, Aurangabad 431001, India; deepagupta@gmai.com
* Correspondence: bthorat78@gmail.com
† Presented at the 2nd International Electronic Conference on Applied Sciences, 15–31 October 2021; Available online: https://asec2021.sciforum.net/.

Abstract: Organic acid hydrazides include a vast group of organic derivatives of hydrazines containing the active functional group (-C(=O)NHNH$_2$). Acid hydrazones were important bidentate ligands and show keto-enol (amido-iminol) tautomerism. They usually exist in keto form in the solid-state while in equilibrium between keto and enol forms in solution state. Such hydrazones were synthesized in the laboratory by heating substituted hydrazides or hydrazines with corresponding aldehydes or ketones in different organic solvents such as ethanol, methanol, butanol, tetrahydrofuran, etc., and some cases with the ethanol-glacial acetic acid or acetic acid alone. Hydrozones are very important intermediates for the synthesis of heterocyclic compounds and also have different biological activities. The organic chemist would have more interest in the synthesis of acid hydrazides and their derivatives because of their properties. These derivatives having wide applications as chemical preservers for plants, drugs, for manufacturing polymers, glues, etc., in industry and many other purposes. These acid hydrazides and their derivatives were found to be useful synthons for various heterocyclic five, six or seven-membered rings with one or more heteroatoms that were exhibited great biological, pharmacological and industrial applications. This paper will present a review of the chemistry and pharmacological potentials of hydrazide-hydrazones. The various synthetic routes for hydrazone, as well as antibacterial, antifungal and antiviral potentials, have been elaborated in brief.

Keywords: hydrazones; medicinal chemistry; synthesis; pharmacology; organic chemistry

Citation: Mali, S.N.; Thorat, B.R.; Gupta, D.R.; Pandey, A. Mini-Review of the Importance of Hydrazides and Their Derivatives—Synthesis and Biological Activity. *Eng. Proc.* **2021**, *11*, 21. https://doi.org/10.3390/ASEC2021-11157

Academic Editor: Samuel Adeloju

Published: 15 October 2021

1. Introduction

Organic acid hydrazides include the vast group of organic derivatives of hydrazine containing the active functional group (-C(=O)-NH-NH$_2$). Acid hydrazones are important bidentate ligands, which show keto-enol (amido-iminol) tautomerism. They usually exist in the keto form in the solid-state while it retains an equilibrium between keto and enol, when in a solution state (Figure 1).

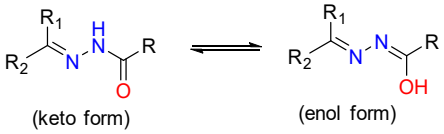


Figure 1. Schematic representation of keto and enol form of acid hydrazones.

Acid hydrazones can react with both electrophiles and nucleophiles simultaneously. They are widely used for the synthesis of heterocyclic compounds. Those compounds

contain nucleophilic nitrogen (imine and amino type), both electrophilic and nucleophilic imine carbon atoms and acidic N-H proton (Figure 2).

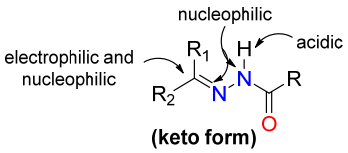


Figure 2. Schematic representation of possible attacking positions in keto form of acid hydrazones.

Such hydrazones were previously synthesized in the laboratory by heating substituted hydrazides or hydrazine with aldehydes or ketones in different organic solvents such as ethanol, methanol, butanol, tetrahydrofuran and, in some cases, with ethanol-glacial acetic acid or acetic acid alone. Hydrazones are very important intermediates for the synthesis of various heterocyclic compounds and usually have wider biological activities. These derivatives have broad applications such as chemical preservers for plants, drugs, for manufacturing polymers, glues, in industry and for many other purposes [1]. These acid hydrazides and their derivatives were found to be useful synthons for the synthesis of various heterocyclic five, six or seven-membered rings with one or more heteroatoms. These compounds were previously exhibited excellent biological, pharmacological and industrial applications such as antibacterial agents, pharmaceuticals, herbicides, antimalarial, antimycobacterial, anticonvulsant, anti-inflammatory, antidepressant, anticancer, antimicrobial activities and dyes [2–12]. Hydrazides and their derivatives could be transformed into various heterocyclic compounds either by cyclisation or cyclo-addition with numerous reagents.

2. Medicinal Chemistry

2.1. Antibacterial Activity

In the past few decades, bacterial and fungal strains have developed resistance towards conventional drugs and, therefore, multidrug-resistant bacterial and fungi infections are becoming serious threats to healthcare settings all over the world. Therefore, for medicinal chemists, the search for new antimicrobial agents is a never-ending and important task. Chemists are constantly looking for different pharmacophores, among them, acid hydrazones/hydrazides are one of the challenging synthons. Numbers of acid hydrazones and their derivatives were synthesized, characterized and evaluated for their antimicrobial activity. There were various reports having hydrazone motif bearing imidazoles (**1**), different thiazolidinone derivatives (**2**, **3**), 1,3,4-thiadiazole based hydrazone derivative (**4**), benzimidazole bearing hydrazone derivative (**5**); benzofuran based hydrazones (**6**); and quinoline-pyridine nucleus containing hydrazones (**7**). These derivatives were also screened for their antibacterial activity against different bacterial strains [13–18] (Figure 3).

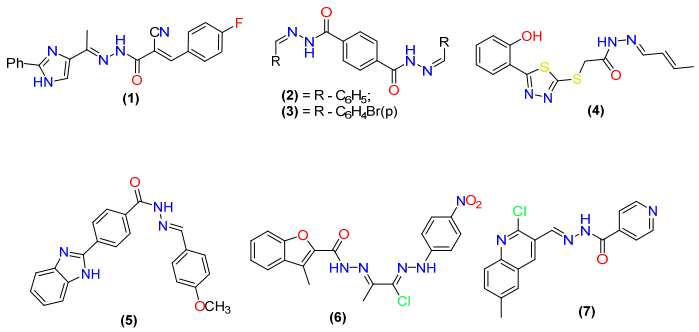


Figure 3. Anti-bacterial compounds (**1**–**7**) based on hydrazide scaffold.

Some amide containing hydrazones (**8**) and (**9**); some piperidine/pyridine based hydrazones (**10**) and (**11**); heterocyclic ring containing hydrazones (**12**); such as Nifurox-

azide; thiophene based hydrazones (**17**); imidazo[2,1-b]thiazole based hydrazones (**13**); imidazo[1,2-a]pyridine based hydrazones (**14**); nitrofurans based hydrazones (**15**); biphenyl-hydrazones (**16**); chloropyrrole based aroylhydrazone (**18**) and (**19**); aryloxyacetic acid hydrazide (**20**); cholic acid-based hydrazones (**21**); benzyledine-hydrazides (**22**); and imidazole bearing hydrazones (**23**, **24**) were demonstrated good antibacterial activities [11,19–33] (Figure 4).

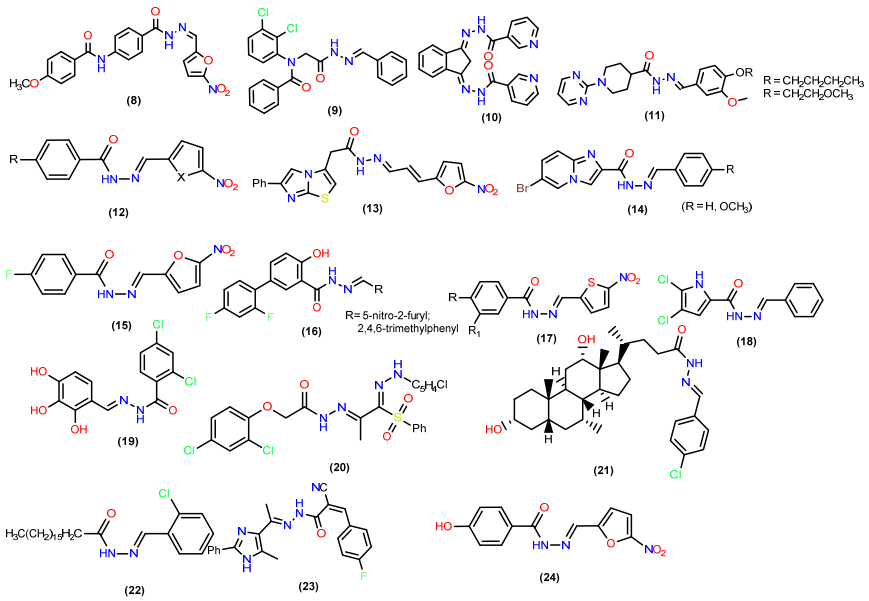


Figure 4. Antimycobacterial compounds (**8**–**24**) based on hydrazide scaffold.

2.2. Anti-Fungal Activities

Many fungal species may cause many superficial or systemic infections in plants, animals, human beings and also in livestock. Today, synthetic chemists are involved in identifying newer antifungal agents with unique mechanisms. There are many synthesized hydrazone derivatives available in the literature which were also studied for their antifungal activity. Some of them were found to be potent antifungal agents or showed promising antifungal activities against different fungi strains, which included scaffolds such as imidazo[1,2-a]pyridine derivative (**25**), tetrazole based acid hydrazide (**26**), benzofuran based hydrazone (**27**) and 5-bromothiophene-2-yl based hydrazones (**28**) [34–37] (Figure 5).

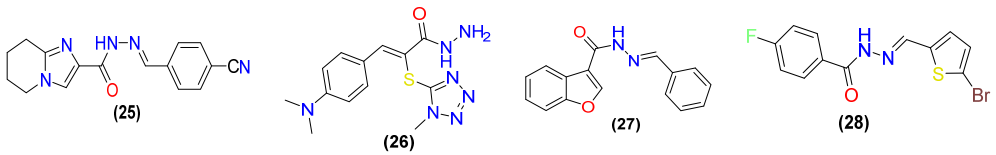


Figure 5. Antifungal compounds (**25**–**28**) based on hydrazide scaffold.

2.3. Antiviral Activity

The virus is a small infectious agent, which can replicate only inside the living cell of an organism. They can cause immense harmful effects to the host body. They mostly infect all types of organisms, including humans, animals and plants. Several reported hydrazones were showed potent antiviral activities against different viral strains or had lower MIC values, such as imidazole-amide containing acid hydrazones (**29**–**31**) and sulfonamide containing acid hydrazones (**32**, **33**) [38–40] (Figure 6).

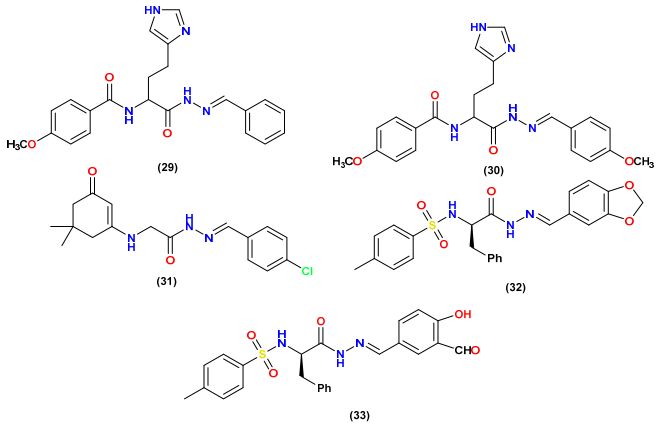


Figure 6. Antiviral compounds (**29**–**33**) based on hydrazide scaffold.

2.4. Antitubercular Activity

Tuberculosis is a highly spreading infectious, chronic and most prevalent disease. It causes more than three million deaths every year [41]. Different strains of *Mycobacterium tuberculosis* can cause infections in the different parts of the body especially in the lungs, liver and bones. Tuberculosis becomes a serious health problem because of the developed resistance to front-line TB drugs such as isoniazid and rifampin. This indicates the need for more effective drugs for the efficient management of tuberculosis. Some hydrazones (**33**–**57**) were synthesized and studied for their anti-TB activity against various strains of *mycobacterium tuberculosis*. These included derivatives such as isoniazid derived hydrazones; pyridylmethyleneamino derivatives of isonicotinoylhydrazones; imidazo[4,5-b]pyridine based hydrazones; 5-nitro-2-furyl based hydrazones; 2-substituted 5-(Pyridine-2-yl)-1,3,4-thiadiazole based hydrazones; 1,2,4-triazole-3-mercaptoacetic acid hydrazones; 5-nitro-thiophene containing arylhydrazone; and diclofenac acid hydrazones [42–57]. Some other hydrazones such as aryloxyhydrazone derivatives, benzofuran-3-carbohydrazide derivatives and 2-substituted quinoline based hydrazones (**52**) were also synthesized, characterized and studied for their anti-TB activities. Several acid hydrazones were also demonstrated potent antimycobacterial activity. Compound (**53**) was the most active (MIC = 1.56 µg/mL, IC_{50} = 5.06 µg/mL and SI = 401) among differently synthesized hydrazone derivatives. Compound (**53**) was found to be better than those of "first-line" or "second line" drugs commonly used to treat TB. Compounds (**54**,**55**), (**56**) and (**57**) were displayed significant and promising antitubercular activity (Figure 7) [42–64].

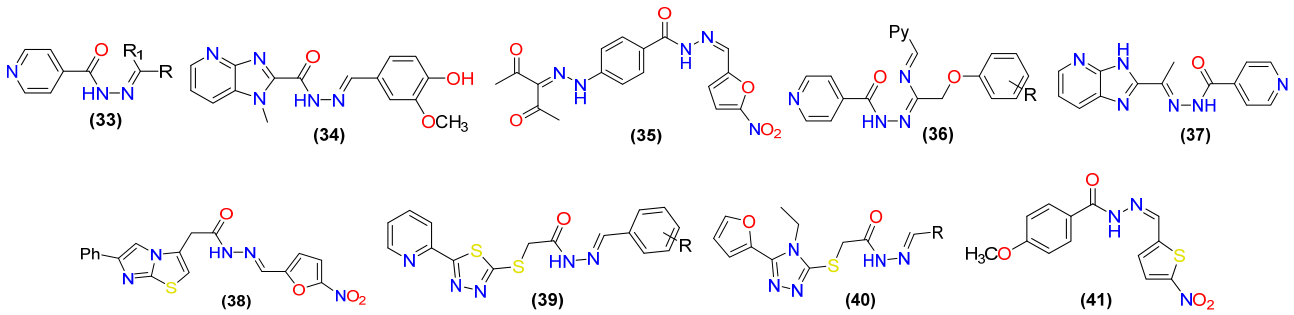


Figure 7. *Cont.*

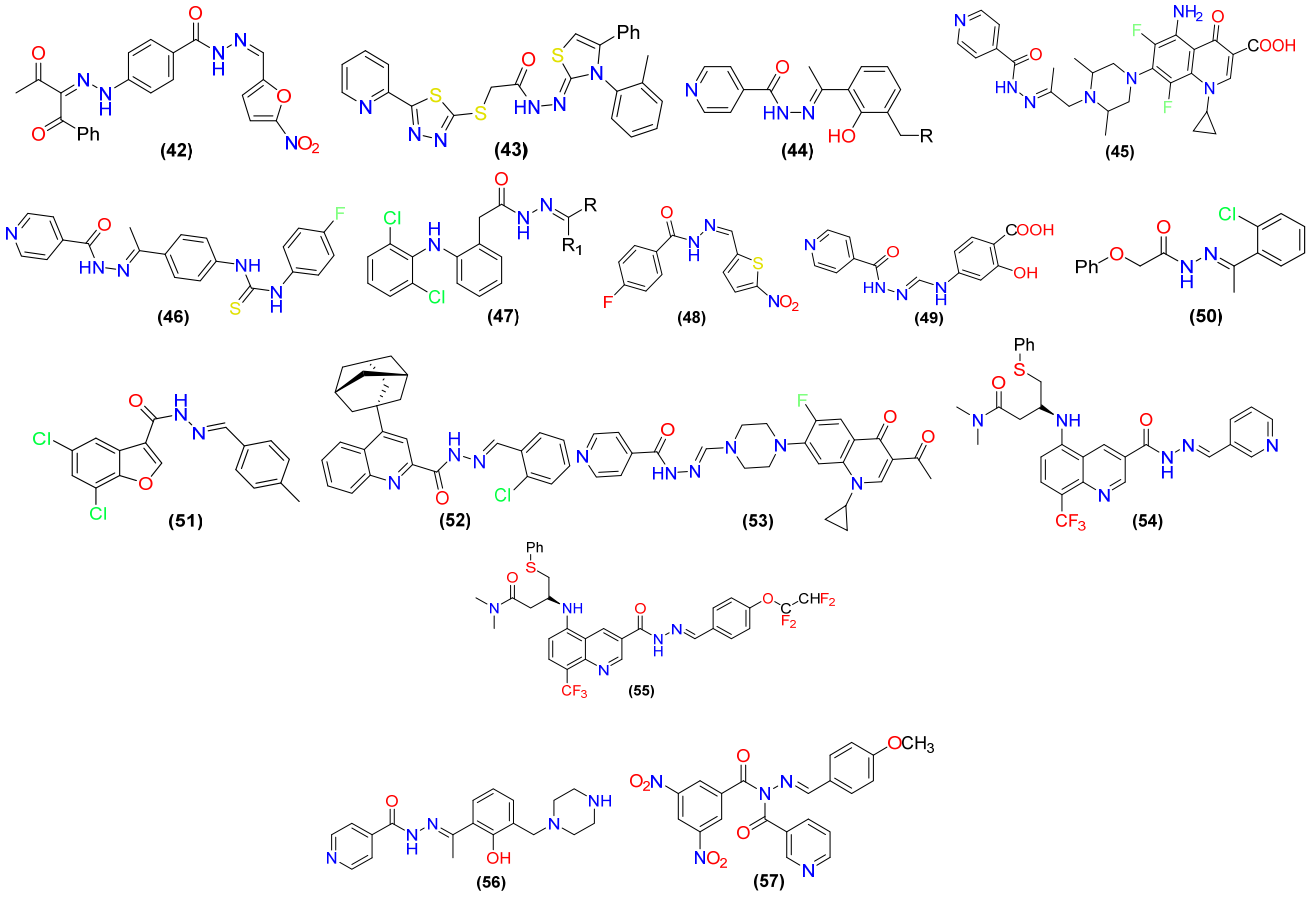
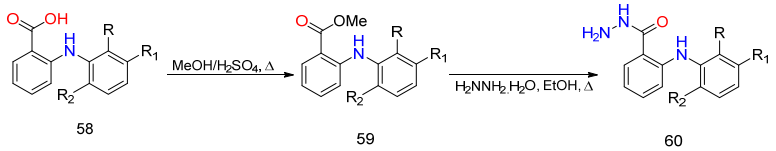


Figure 7. Antimycobacterial compounds (**34**–**57**) based on hydrazide scaffold.

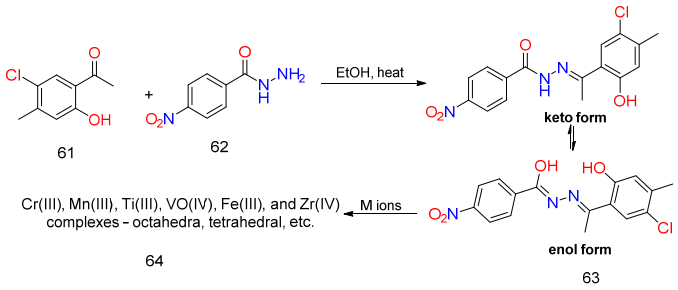
3. Different Synthetic Routes of Hydrazine, Hydrazones and Their Derivatives

Fenamic hydrazides (**60**) were synthesized from corresponding fenamic acids (**58**) through esters intermediates (**59**). Fenamic acids were previously esterified in methanol by using sulfuric acid and under reflux conditions for 12–18 h. These esters were then treated with hydrazine hydrate (under reflux for 1.5–12 h) [65,66] (Scheme 1).



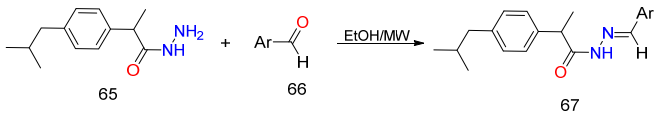
Scheme 1. Synthesis of fenamic acid hydrazides from the corresponding fenamic acids (**58**).

Acyl hydrazones act as mono-nucleating hydrazone ligands, which are easily obtained by condensing acyl hydrazides **62** and substituted aldehydes **61** in ethanol under reflux conditions. These ligands act as a powerful bidentate ligand **63**, **64** and forms complexes with different transition metals. One of the acyl hydrazones, 2-hydroxy-5-chloro-4-methylacetophenone-4-nitrobenzoylhydrazone **63** was synthesized from 4-nitrobenzoyl hydrazide **62** and 2-hydroxy-5-chloro-4-methyl acetophenone **61** in ethanol and got easily coordinated as a tridentate ligand **64** to Cr(III), Mn(III), Ti(III), VO(IV), Fe(III) and Zr(IV) under reflux conditions [67] (Scheme 2).



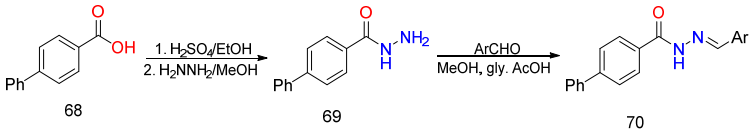
Scheme 2. Synthesis of coordinated tridentate ligands **64**.

A series of substituted ibuprofen-based acyl hydrazones **67** was synthesized under microwave irradiations and by conventional methods using a small quantity of methanol from ibuprofen hydrazide **65** and aryl aldehydes **66** [68] (Scheme 3).



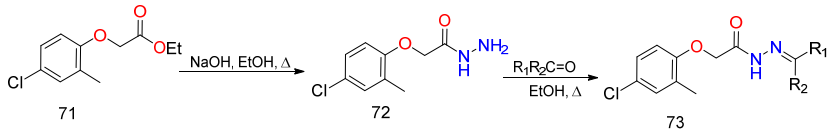
Scheme 3. Synthesis of ibuprofen-based acyl hydrazones.

Several biphenyl-4-carboxylic acid hydrazide-hydrazones **70** were prepared from biphenyl-4-carboxylic acid hydrazide **69** and substituted benzaldehyde using methanol and glacial acetic acid combinations. All synthesized compounds were noted promising antimicrobial activity. Varieties of phenylacetohydrazones were synthesized by using HCl as a catalyst. N-Arylhydrazone derivatives of N-phenyl anthranilic acid were synthesized by condensing 2-(phenylamino) benzohydrazide with various aromatic ketones and aldehydes [10,69,70] (Scheme 4).



Scheme 4. Synthesis of N-Arylhydrazone derivatives.

Acylhydrazide Schiff base derivatives were prepared by acetic acid-catalyzed condensation of acylhyrazide with different aromatic aldehydes and acetophenones in ethanol under reflux conditions [71] (Scheme 5).



Scheme 5. Synthesis of Acyl hydrazide Schiff base derivatives.

4. Conclusions

To summarize, hydrazone coupled motifs are having an immense pharmacological potential and can be used for synthesizing newer novel motifs with higher potencies. We have also summarized various synthetic routes to synthesis these derivatives.

Author Contributions: Conceptualization, S.N.M., A.P., D.R.G. and B.R.T.; methodology, B.R.T.; software, S.N.M.; writing—review and editing, B.R.T. and D.R.G.; visualization, S.N.M. and A.P.; supervision, A.P. All authors have read and agreed to the published version of the manuscript.

Funding: We wish to thank the Department of Pharmaceutical Sciences, Birla Institute of Technology, Mesra, India for financial assistance. S.N.M. is also thankful for the provision of IRF (PhD/PH/10006/20) (Ref. No. GO/Estb/Ph.D./IRF/2020-21/) provided by BIT, Mesra, India.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors would like to thank the Head, Department of Pharmaceutical Sciences and Technology, BIT, Mesra and Department of Chemistry, Government of Maharashtra's Ismail Yusuf College of Arts, Science and Commerce, Mumbai–60 for providing the research facilities for performing the current study.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Thiyagarajan, S.; Gunanathan, C. Direct Catalytic Symmetrical, Unsymmetrical N,N-Dialkylation and Cyclization of Acylhydrazides Using Alcohols. *Organ. Lett.* **2020**, *22*, 6617–6622. [CrossRef]
2. DeMarinis, R.M.; Hoover, J.R.E.; Dunn, G.L.; Actor, P.; Uri, J.V.; Weisbach, J. A new parenteral cephalosporin, SK & F 59962: Chemistry and structure activity relationships. *J. Antibiot.* **1975**, *28*, 463–470.
3. Elnagdi, M.H.; Erian, A.W. New routes to polyfunctionally substituted pyridine, pyridopyridine, quinoline, and pyridazine derivatives. *Arch. Pharm.* **1991**, *324*, 853–858. [CrossRef]
4. Costales, M.J.; Kleschick, W.A.; Ehr, R.J.; Weimer, M.R.U.S. N-(1-Ethyl-4-pyrazolyl)triazoloazinesulfonamide Herbicides. Patent 5,763,359, 9 June 1998.
5. Gemma, S.; Kukreja, G.; Fattorusso, C.; Persico, M.; Romano, M.P.; Altarelli, M.; Savini, L.; Campiani, G.; Fattorusso, E.; Basilico, N.; et al. Synthesis of N1-arylidene-N2-quinolyl-and N2-acrydinylhydrazones as potent antimalarial agents active against CQ-resistant *P. falciparum* strains. *Bioorgan. Med. Chem. Lett.* **2006**, *16*, 5384–5388. [CrossRef] [PubMed]
6. Bijev, A. New heterocyclic hydrazones in the search for antitubercular agents: Synthesis and in vitro evaluations. *Lett. Drug Des. Discov.* **2006**, *3*, 506–512. [CrossRef]
7. Ragavendran, J.V.; Sriram, D.; Patel, S.K.; Reddy, I.V.; Bharathwajan, N.; Stables, J.; Yogeeswari, P. Design and synthesis of anticonvulsants from a combined phthalimide–GABA–anilide and hydrazone pharmacophore. *Eur. J. Med. Chem.* **2007**, *42*, 146–151. [CrossRef]
8. Todeschini, A.R.; de Miranda, A.L.P.; da Silva, K.C.M.; Parrini, S.C.; Barreiro, E.J. Synthesis and evaluation of analgesic, antiinflammatory and antiplatelet properties of new 2-pyridylarylhydrazone derivatives. *Eur. J. Med. Chem.* **1998**, *33*, 189–199. [CrossRef]
9. Ergenç, N.; Günay, N.S.; Demirdamar, R. Synthesis and antidepressant evaluation of new 3-phenyl-5-sulfonamidoindole derivatives. *Eur. J. Med. Chem.* **1998**, *33*, 143–148. [CrossRef]
10. Deep, A.; Jain, S.; Sharma, P.C.; Verma, P.; Kumar, M.; Dora, C.P. Design and biological evaluation of biphenyl-4-carboxylic acid hydrazide-hydrazone for antimicrobial activity. *Synthesis* **2010**, *182*, 183OC.
11. Masunari, A.; Tavares, L.C. A new class of nifuroxazide analogues: Synthesis of 5-nitrothiophene derivatives with antimicrobial activity against multidrug-resistant Staphylococcus aureus. *Bioorgan. Med. Chem.* **2007**, *15*, 4229–4236. [CrossRef]
12. Fahmy, S.M.; Badran, A.H.; Elnagdi, M.H. Synthesis of some new azopyrazole dyes. *J. Chem. Technol. Biotechnol.* **1980**, *30*, 390–395. [CrossRef]
13. Abdel-Wahab, B.F.; Awad, G.E.; Badria, F.A. Synthesis, antimicrobial, antioxidant, anti-hemolytic and cytotoxic evaluation of new imidazole-based heterocycles. *Eur. J. Med. Chem.* **2011**, *46*, 1505–1511. [CrossRef] [PubMed]
14. Palekar, V.S.; Damle, A.J.; Shukla, S.R. Synthesis and antibacterial activity of some novel bis-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles and bis-4-thiazolidinone derivatives from terephthalic dihydrazide. *Eur. J. Med. Chem.* **2009**, *44*, 5112–5116. [CrossRef]
15. Zhong, N.J.; Wang, Y.Z.; Cheng, L.; Wang, D.; Liu, L. Recent advances in the annulation of Morita–Baylis–Hillman adducts. *Organ. Biomol. Chem.* **2018**, *16*, 5214–5227. [CrossRef] [PubMed]
16. Özkay, Y.; Tunalı, Y.; Karaca, H.; Işıkdağ, İ. Antimicrobial activity and a SAR study of some novel benzimidazole derivatives bearing hydrazone moiety. *Eur. J. Med. Chem.* **2010**, *45*, 3293–3298. [CrossRef]
17. Abdel-Aziz, H.A.; Mekawey, A.A. Stereoselective synthesis and antimicrobial activity of benzofuran-based (1E)-1-(piperidin-1-yl)-N2-arylamidrazones. *Eur. J. Med. Chem.* **2009**, *44*, 4985–4997. [CrossRef] [PubMed]
18. Verma, G.; Marella, A.; Shaquiquzzaman, M.; Akhtar, M.; Ali, M.R.; Alam, M.M. A review exploring biological activities of hydrazones. *J. Pharm. Bioallied Sci.* **2014**, *6*, 69–80.
19. Küçükgüzel, Ş.G.; Oruç, E.E.; Rollas, S.; Şahin, F.; Özbek, A. Synthesis, characterisation and biological activity of novel 4-thiazolidinones, 1, 3, 4-oxadiazoles and some related compounds. *Eur. J. Med. Chem.* **2002**, *37*, 197–206. [CrossRef]
20. Asif, M. Pharmacologically potentials of hydrazonone containing compounds: A promising scaffold. *Int. J. Adv. Chem.* **2014**, *2*, 85–103. [CrossRef]

21. Rollas, S.; Gulerman, N.; Erdeniz, H. Synthesis and antimicrobial activity of some new hydrazones of 4-fluorobenzoic acid hydrazide and 3-acetyl-2,5-disubstituted-1,3,4-oxadiazolines. *Il Farmaco* **2002**, *57*, 171–174. [CrossRef]
22. Jubie, S.; Meena, S.; Ramaseshu, K.V.; Jawahar, N.; Vijayakumar, S. Synthesis and biological evaluation of some hydrazones and carbazones of indane-1,3-dione. *Indian J. Chem.* **2010**, *49*, 1261–1263.
23. Govindasami, T.; Pandey, A.; Palanivelu, N.; Pandey, A. Synthesis, characterization and antibacterial activity of biologically important vanillin related hydrazone derivatives. *In. J. Organ. Chem.* **2011**, *1*, 71. [CrossRef]
24. Tavares, L.C.; Chiste, J.J.; Santos, M.G.; Penna, T.C. Synthesis and biological activity of nifuroxazide and analogs. *II Bollettino Chimico Farmaceutico* **1999**, *138*, 432–436.
25. Ulusoy, N.; Çapan, G.; Otük, G.; Kiraz, M. Synthesis and antimicrobial activity of new 6-phenylimidazo[2,1-b]thiazole derivatives. *Bollettino Chimico Farmaceutico* **2000**, *139*, 167–172. [PubMed]
26. Turan-Zitouni, G.; Blache, Y.; Güven, K. Synthesis and antimicrobial activity of some imidazo-[1,2-a]pyridine-2-carboxylic acid arylidenehydrazide derivatives. *Bollettino Chimico Farmaceutico* **2001**, *140*, 397–400.
27. Küçükgüzel, S.G.; Mazi, A.; Sahin, F.; Öztürk, S.; Stables, J. Synthesis and biological activities of diflunisal hydrazide–hydrazones. *Eur. J. Med. Chem.* **2003**, *38*, 1005–1013. [CrossRef]
28. Rane, R.A.; Telvekar, V.N. Synthesis and evaluation of novel chloropyrrole molecules designed by molecular hybridization of common pharmacophores as potential antimicrobial agents. *Bioorgan. Med. Chem. Lett.* **2010**, *20*, 5681–5685. [CrossRef]
29. Lee, J.Y.; Jeong, K.W.; Shin, S.; Lee, J.U.; Kim, Y. Discovery of novel selective inhibitors of Staphylococcus aureus β-ketoacyl acyl carrier protein synthase III. *Eur. J. Med. Chem.* **2012**, *47*, 261–269. [CrossRef]
30. Abdel-Wahab, B.F.; Khidre, R.E.; Awad, G.E. Regioselective synthesis and antimicrobial activities of some novel aryloxyacetic acid derivatives. *Eur. J. Med. Chem.* **2012**, *50*, 55–62. [CrossRef]
31. Ali, M.R.; Marella, A.; Alam, M.T.; Naz, R.; Akhter, M.; Shaquiquzzaman, M.; Saha, R.; Tanwar, O.; Alam, M.M.; Hooda, J. Review of biological activities of hydrazones. *Indones. J. Pharm.* **2012**, *23*, 193–202.
32. Kumar, D.; Judge, V.; Narang, R.; Sangwan, S.; De Clercq, E.; Balzarini, J.; Narasimhan, B. Benzylidene/2-chlorobenzylidene hydrazides: Synthesis, antimicrobial activity, QSAR studies and antiviral evaluation. *Eur. J. Med. Chem.* **2010**, *45*, 2806–2816. [CrossRef]
33. Singh, S.; Sharma, B.; Siddiqi, N.J. HYDRAZONES AS PROSPECTIVE ANTI-HIV AGENT. *Eur. J. Biomed. Pharm. Sci.* **2016**, *3*, 454–458.
34. Devi, T.S.; Rajitha, G. Microwave Assisted Synthesis and Evaluation of N-cinnamoyl aryl hydrazones for Cytotoxic and Antioxidant Activities. *Orient. J. Chem.* **2016**, *32*, 1703–1709. [CrossRef]
35. Altıntop, M.D.; Özdemir, A.; Turan-Zitouni, G.; Ilgın, S.; Atlı, Ö.; İşcan, G.; Kaplancıklı, Z.A. Synthesis and biological evaluation of some hydrazone derivatives as new anticandidal and anticancer agents. *Eur. J. Med. Chem.* **2012**, *58*, 299–307. [CrossRef] [PubMed]
36. Telvekar, V.N.; Belubbi, A.; Bairwa, V.K.; Satardekar, K. Novel N′-benzylidene benzofuran-3-carbohydrazide derivatives as antitubercular and antifungal agents. *Bioorgan. Med. Chem. Lett.* **2012**, *22*, 2343–2346. [CrossRef]
37. Koçyiğit-Kaymakçıoğlu, B.; Oruç-Emre, E.E.; Ünsalan, S.; Tabanca, N.; Khan, S.I.; Wedge, D.E.; İşcan, G.; Demirci, F.; Rollas, S. Synthesis and biological activity of hydrazide–hydrazones and their corresponding 3-acetyl-2,5-disubstituted-2,3-dihydro-1,3,4-oxadiazoles. *Med. Chem. Res.* **2012**, *21*, 3499–3508. [CrossRef]
38. Hiremathad, A.; Patil, M.R.; Chethana, K.R.; Chand, K.; Santos, M.A.; Keri, R.S. Benzofuran: An emerging scaffold for antimicrobial agents. *RSC Adv.* **2015**, *5*, 96809–96828. [CrossRef]
39. El-Sabbagh, O.I.; Rady, H.M. Synthesis of new acridines and hydrazones derived from cyclic β-diketone for cytotoxic and antiviral evaluation. *Eur. J. Med. Chem.* **2009**, *44*, 3680–3686. [CrossRef]
40. Tian, B.; He, M.; Tang, S.; Hewlett, I.; Tan, Z.; Li, J.; Jin, Y.; Yang, M. Synthesis and antiviral activities of novel acylhydrazone derivatives targeting HIV-1 capsid protein. *Bioorgan. Med. Chem. Lett.* **2009**, *19*, 2162–2167. [CrossRef] [PubMed]
41. African American Cultural Collaborative of Mercer County. Available online: https://www.taacf.com/ (accessed on 6 September 2021).
42. Maccari, R.; Ottanà, R.; Vigorita, M.G. In vitro advanced antimycobacterial screening of isoniazid-related hydrazones, hydrazides and cyanoboranes: Part 14. *Bioorgan. Med. Chem. Lett.* **2005**, *15*, 2509–2513. [CrossRef]
43. Shindikar, A.V.; Viswanathan, C.L. Novel fluoroquinolones: Design, synthesis, and in vivo activity in mice against Mycobacterium tuberculosis H37Rv. *Bioorgan. Med. Chem. Lett.* **2005**, *15*, 1803–1806. [CrossRef]
44. Sriram, D.; Yogeeswari, P.; Madhu, K. Synthesis and in vitro antitubercular activity of some 1-[(4-sub) phenyl]-3-(4-{1-[(pyridine-4-carbonyl) hydrazono] ethyl}phenyl) thiourea. *Bioorgan. Med. Chem. Lett.* **2006**, *16*, 876–878. [CrossRef]
45. Imramovský, A.; Polanc, S.; Vinšová, J.; Kočevar, M.; Jampílek, J.; Rečková, Z.; Kaustová, J. A new modification of anti-tubercular active molecules. *Bioorgan. Med. Chem.* **2007**, *15*, 2551–2559. [CrossRef]
46. Cocco, M.T.; Congiu, C.; Onnis, V.; Pusceddu, M.C.; Schivo, M.L.; De Logu, A. Synthesis and antimycobacterial activity of some isonicotinoylhydrazones. *Eur. J. Med. Chem.* **1999**, *34*, 1071–1076. [CrossRef]
47. Bukowski, L.; Janowiec, M. 1-Methyl-1H-2-imidazo [4, 5-b] pyridinecarboxylic acid and some of its derivatives with suspected antituberculotic activity. *Die Pharmazie* **1996**, *51*, 27–30. [CrossRef]
48. Bukowski, L.; Janowiec, M.; Zwolska-Kwiek, Z.; Andrzejczyk, Z. Synthesis and some reactions of 2-acetylimidazo[4,5-b]pyridine. Antituberculotic activity of the obtained compounds. *Die Pharmazie* **1999**, *54*, 651–654. [CrossRef] [PubMed]

49. Küçükgüzel, İ.; Tatar, E.; Küçükgüzel, Ş.G.; Rollas, S.; De Clercq, E. Synthesis of some novel thiourea derivatives obtained from 5-[(4-aminophenoxy)methyl]-4-alkyl/aryl-2,4-dihydro-3H-1,2,4-triazole-3-thiones and evaluation as antiviral/anti-HIV and anti-tuberculosis agents. *Eur. J. Med. Chem.* **2008**, *43*, 381–392. [CrossRef]
50. Küçükgüzel, Ş.G.; Rollas, S. Synthesis, characterization of novel coupling products and 4-arylhydrazono-2-pyrazoline-5-ones as potential antimycobacterial agents. *Il Farmaco* **2002**, *57*, 583–587. [CrossRef]
51. Mamolo, M.G.; Falagiani, V.; Zampieri, D.; Vio, L.; Banfi, E. Synthesis and antimycobacterial activity of [5-(pyridin-2-yl)-1,3,4-thiadiazol-2-ylthio] acetic acid arylidene-hydrazide derivatives. *Il Farmaco* **2001**, *56*, 587–592. [CrossRef]
52. Mamolo, M.G.; Falagiani, V.; Zampieri, D.; Banfi, L.V.E.; Scialino, G. Synthesis and antimycobacterial activity of (3,4-diaryl-3H-thiazol-2-ylidene)-hydrazide derivatives. *Il Farmaco* **2003**, *58*, 631–637. [CrossRef]
53. Ulusoy, N.; Gürsoy, A.; Ötük, G. Synthesis and antimicrobial activity of some 1,2,4-triazole-3-mercaptoacetic acid derivatives. *Il Farmaco* **2001**, *56*, 947–952. [CrossRef]
54. Rando, D.G.; Sato, D.N.; Siqueira, L.; Malvezzi, A.; Leite, C.Q.; Ferreira, E.I.; Tavares, L.C. Potential tuberculostatic agents. Topliss application on benzoic acid [(5-nitro-thiophen-2-yl)-methylene]-hydrazide series. *Bioorgan. Med. Chem.* **2002**, *10*, 557–560. [CrossRef]
55. Bedia, K.K.; Elçin, O.; Seda, U.; Fatma, K.; Nathaly, S.; Sevim, R.; Dimoglo, A. Synthesis and characterization of novel hydrazide–hydrazones and the study of their structure–antituberculosis activity. *Eur. J. Med. Chem.* **2006**, *41*, 1253–1261. [CrossRef]
56. Saeed, A.; Bolte, M. 1-(4-Chlorophenyl)-4,4,6-trimethyl-3,4-dihydropyrimidine-2 (1H)-thione. *Acta Crystallogr. Sect. E: Struct. Rep. Online* **2010**, *66*, o440. [CrossRef] [PubMed]
57. Raja, A.S.; Agarwal, A.K.; Mahajan, N.; Pandeya, S.N.; Ananthan, S. Antibacterial and antitubercular activities of some diphenyl hydrazones and semicarbazones. *Indian J. Chem. Sect. B.* **2010**, *49*, 1384–1388.
58. Rahaman, M.; Hossain, M.M. Convenient Preparation of 3-Ethoxycarbonyl Benzofurans from Salicylaldehydes and Ethyl Diazoacetate. *Org. Synth.* **2019**, *96*, 98–109. [CrossRef]
59. Nayyar, A.; Monga, V.; Malde, A.; Coutinho, E.; Jain, R. Synthesis, anti-tuberculosis activity, and 3D-QSAR study of 4-(adamantan-1-yl)-2-substituted quinolines. *Bioorgan. Med. Chem.* **2007**, *15*, 626–640. [CrossRef]
60. Poggi, M.; Barroso, R.; Costa-Filho, A.J.; Barbosa de Barros, H.; Pavan, F.; Queico Leite, C.; Gambino, D.; Helvecia Torre, M. New isoniazid complexes, promising agents against Mycobacterium tuberculosis. *J. Mex. Chem. Soc.* **2013**, *57*, 198–204. [CrossRef]
61. Eswaran, S.; Adhikari, A.V.; Pal, N.K.; Chowdhury, I.H. Design and synthesis of some new quinoline-3-carbohydrazone derivatives as potential antimycobacterial agents. *Bioorgan. Med. Chem. Lett.* **2010**, *20*, 1040–1044. [CrossRef] [PubMed]
62. Sriram, D.; Yogeeswari, P.; Madhu, K. Synthesis and in vitro and in vivo antimycobacterial activity of isonicotinoyl hydrazones. *Bioorgan. Med. Chem. Lett.* **2005**, *15*, 4502–4505. [CrossRef]
63. Kumar, P.; Narasimhan, B.; Yogeeswari, P.; Sriram, D. Synthesis and antitubercular activities of substituted benzoic acid N′-(substituted benzylidene/furan-2-ylmethylene)-N-(pyridine-3-carbonyl)-hydrazides. *Eur. J. Med. Chem.* **2010**, *45*, 6085–6089. [CrossRef] [PubMed]
64. Baran, A.U. Comparative study of microwave-assisted and conventional synthesis of ibuprofen-based acyl hydrazone derivatives. *Turk. J. Chem.* **2013**, *37*, 927–935. [CrossRef]
65. Narsinghani, T.; Chaturvedi, S.C. QSAR analysis of meclofenamic acid analogues as selective COX-2 inhibitors. *Bioorgan. Med. Chem. Lett.* **2006**, *16*, 461–468. [CrossRef]
66. Lehmann, J.; Kraft, G. Amphiphile Verbindungen, 1. Mitt. Zur Synthese von 1-Aryl-, 1-Aroyl-und 1-Benzyl-2,3,4-5-tetrahydro-1H-1,4-benzodiazepinen. *Arch. Pharmazie* **1984**, *317*, 595–606. [CrossRef]
67. Reddy, L.V.; Suman, A.; Beevi, S.S.; Mangamoori, L.N.; Mukkanti, K.; Pal, S. Design and synthesis of 1-aroyl-2-ylidene hydrazines under conventional and microwave irradiation conditions and their cytotoxic activities. *J. Brazilian Chem. Soc.* **2010**, *21*, 98–104. [CrossRef]
68. Yaul, A.R.; Dhande, V.V.; Aswar, A.S. Synthesis and Characterization of Dioxotungsten (VI) and Dioxomolybdenum (VI) Complexes of Chelating Hydrazone via Their Oxoperoxo Complexes. *World J. Chem.* **2013**, *8*, 38–41.
69. Gunjan, J.; Awadh, D. Synthesis and Biological Evaluation of Some Phenyl Acetic Acid Hydrazone Derivatives. *Int. Res. J. Pharm. (IRJP)* **2011**, *2*, 110–112.
70. Parashar, B.; Punjabi, P.B.; Gupta, G.D.; Sharma, V.K. Synthesis of some novel N-arylhydrazone derivatives of N-phenyl anthranilic acid. *Int. J. ChemTech Res.* **2009**, *1*, 1022–1025.
71. Jamil, W.; Perveen, S.; Shah, S.A.A.; Taha, M.; Ismail, N.H.; Perveen, S.; Ambreen, N.; Khan, K.M.; Choudhary, M.I. Phenoxyacetohydrazide Schiff bases: β-Glucuronidase inhibitors. *Molecules* **2014**, *19*, 8788–8802. [CrossRef]