WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 13, 2022-2032. Review Article ISSN 2277–7105

A REVIEW ON HETEROCYCLIC MOIETIES AND THEIR APPLICATIONS

Rushikesh Natu*, Santosh Waghmare and Hemant Kamble

Loknete Shri Dadapatil Pharate College of Pharmacy, Mandavgoan, Maharashtra, India.

Article Received on
09 Sept. 2021,

Revised on 30 Sept. 2021,
Accepted on 21 Oct. 2021

DOI: 10.20959/wjpr202113-22208

***Corresponding Author**
Rushikesh Natu
Loknete Shri Dadapatil Pharate College of Pharmacy, Mandavgoan, Maharashtra, India.

ABSTRACT

Several described in literature crosslinking methods to obtain heterocyclic moieties were discussed in this review. Selected important properties of polyamides and their synthesis reactions were briefly presented. The heterocyclic moieties displayed a wide range of applications in medicine and industry. New heterocyclic derivatives obtained by linking heterocyclic moiety to amic acids and imides found diverse applications: as surfactants, antimicrobial agents, or corrosion inhibitors. The present article describes the state-of-the art synthesis methods of the heterocyclic compounds and their application.

KEYWORDS: Applications; Corrosion Inhibitors; Heterocyclic moieties; Synthesis.

1 INTRODUCTION

Chemistry of heterocyclic compounds is a field of particular interest of the organic chemists. Heterocyclic compounds have attracted a considerable interest for their highly electron-donating and strong coordination abilities, and still receive much attention because of their applications. Synthesis of secondary and tertiary amines through the N-alkylation of primary amine is the furthermost important and essential reaction in synthetic chemistry. However, N-alkylation using alkyl halides is a traditional method of N-substituted amines synthesis.[1] Polyimides (PIs) have excellent physical and chemical properties and they are used extensively in microelectronic manufacturing as interlayer dielectrics (ILDs), passivation layers and stress buffers.[1,2] PIs rigid imide and phenyl structure cause high modulus, glass transition temperature (Tg) and thermal stability. However, most of them have low solubility in common organic solvents. The PIs film can be prepared by spin-casting of polyamic acids on a Si/metal substrate, followed by the thermal dehydration reaction. However, the release

of water molecules in the thermal immunization process severely deforms the PIs film.[3] The versatile reaction chemistry of benzocyclobutene (BCB)-functionalized thermosets and their excellent properties made them high-performance materials for microelectronic applications.[4-6] Incorporation of the reactive alkyl group to the molecular structure, not only increases the solubility of the BCB monomers, but also provides the photosensitivity when reacted with acid photo-crosslinking agents. In this context we discuss further the chemistry of heterocyclic moieties, synthesis and their applications.

2. Imides

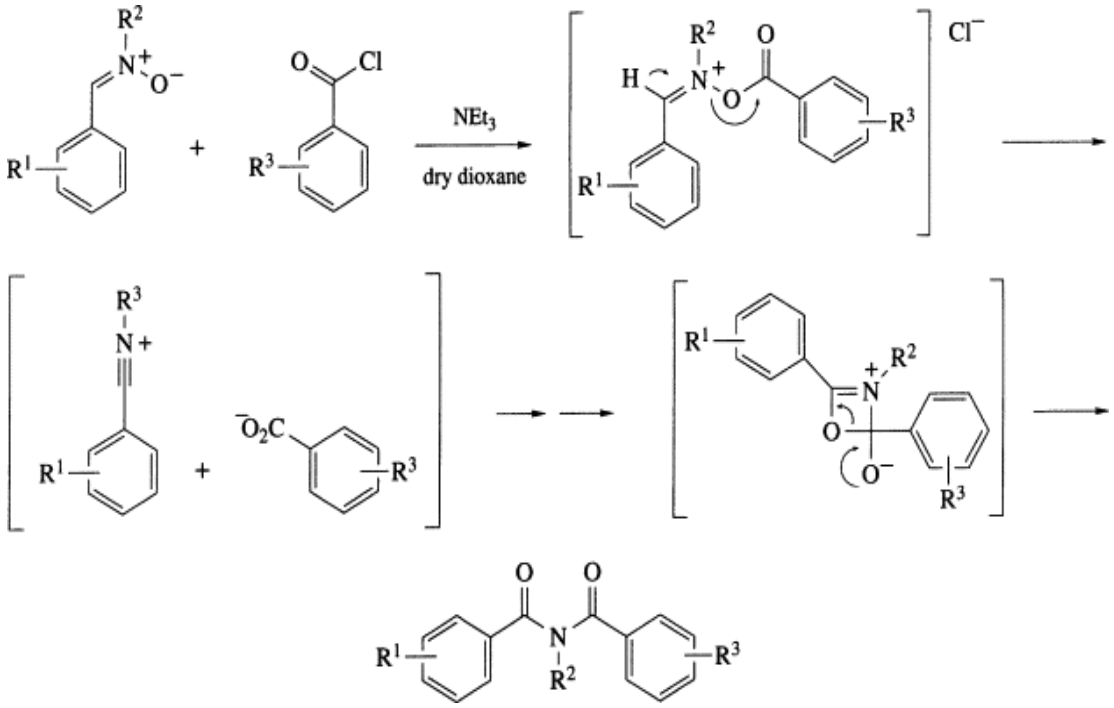
2.1 Chemistry of Imides Noncyclic or 4-, 5-, or 6-cyclic organic compounds of N-monoacyl derivatives or musky, aliphatic imides and their derivatives (Fig. 1) can be obtained by the reaction of carboxylic acids or anhydrides with reagents bearing a receptive amino (-NH2) group. The reaction occur by nucleophilic attack of amino group at a carboxyl carbon atoms of acids or anhydride (Scheme 1).[7] The particular reactivity of imides is a consequence of the relative acidity of the -NH group and the two carbonyl groups.[8] General and extraordinary synthesis conditions, chemical and physical properties, discovery, and usage of cyclic carboxylic monoimides until 1969 have been reviewed by Hargreaves et al.[9]

2.2 Synthesis Methods of Imides

There are a few synthetic methods for the preparation of N-unsubstituted cyclic imides such as abridgment of urea with liquid/gas ammonia, or amide with cyclic anhydrides (Scheme 2).[10]

Also N-unsubstituted imides can be obtained in the reaction of diacid chloride with lithium nitride under tremendously trifling conditions or microwave reaction of cyclic anhydrides with urea or thiourea, benzonitrile, cyanate, thiocyanate, 4-N, N-dimethylamino pyridine, ammonium chloride, ammonium acetate, and hydroxylamine hydrochloride.[11] The conventional simulated pathway (classical twostep method) for N-substituted imides synthesis comprises of the development of amic acids through a reaction of amines and anhydrides. Imidization of amic acids leads to the preferred imides. Dehydration of amic acids produces two isomers, imides and isoimides, contingent upon the kind of dehydrating agent, temperature, and reaction time, nature of amic acid, and the existence or lack of the catalyst.[12] Numerous dehydrating agents have been employed in the imide synthesis, for instance: thionyl chloride, acetyl chloride with triethyl amine, acetic anhydride with

anhydrous sodium acetate (Schemes 3 and 4), phosphorous trichloride, and phosphorous pentaoxide.[13]



2.2 Synthesis Methods of Imides

There are a few synthetic methods for the preparation of N-unsubstituted cyclic imides such as abridgment of urea with liquid/gas ammonia, or amide with cyclic anhydrides (Scheme 2).[10]

Thermal process was utilized to get imides from the analogous amic acids.[14] By implementing this technique numerous N-substituted citraconimides such as N-(hydroxy phenyl) phthalimides, N-(hydroxy phenyl) maleimides, and N-(hydroxy phenyl) citracoimides have been formed (Scheme 5).[15]

A few N-substituted cyclic imides formed from the analogous N-substituted cyclic imides by means of Gabriel synthesis by changing the potassium salt yield after the reaction with alkyl halides (Scheme 6). In this way, phthalimide with N-hydroxy ethyl, N-phenoxy alkyl, N-cyclopentyl, or N-benzyl has been generated.[16] Diels-Alder reaction was carried out to produce imide derivatives like N-substituted derivatives of 1-chloromethyl-1-dibenzo[e.h]bicyclo[2,2,2]octane-2,3-dicarboximide and the achieved imide was then reacted with 1,3-dibromopropane or 1-bromo-4-chlorobutane to produce N-(3-bromopropyl)- or N-

(4-chlorobutyl)-substituted imide, that was condensed with appropriate aryl piperazines generating the novel imides as presented in Scheme 7.[17,18]

Furthermore, some cyclic imides were formed by Mitsunobu reaction (Scheme 8). Principally, Mitsunobu reaction includes condensation of alcohols and acidic components followed by treatment with dialkylazodicarboxylates and trialkyl- or triarylphosphines. This happens mainly due to transposition of the configuration through the proposed transitional oxyphosphonium salts.[19-21] The reaction includes the activation of an alcoholic hydroxyl group and the following carbon-oxygen bond cleavage promoted by an attacking anion to provide the product (esters, ethers, imides etc.) with the complete inversion of the configuration on the alcohol stereo center[22] Synthesis of cyclic imides under microwave irradiation have interesting benefits including improved product yield and reduced reaction time.[23-25] A quick change of lactams to cyclic imides under microwave irradiation was performed using peracetic acid and manganic chloride in ethyl acetate as a solvent (Fig. 2).[26-29]

A straightforward, newly developed, easy and productive synthetic protocol was used for the synthesis of N-aryl phthalimides, maleimides, and succinimides via condensation of cyclic anhydrides with aromatic amine in trifluoroacetic acid (Fig. 3).[30] Advantages of this technique are the short reaction time, accessibility of the reagents, and remarkable yield.

2.3 Applications of Imides

N-Aryl and N-alkyl cyclic imides have attracted much attention of organic and medicinal chemists due to their various applications in biological, synthetic, and polymer chemistry.[31-33] Cyclic imides e.g.: benzoxazines, pyridooxazines and quinazolines can be used as building blocks to create a wide range of heterocyclic compounds.[34] A synthesis of numerous alkaloids and pharmacophores, employs cyclic imides as initial materials and as intermediates. Cyclic imides can also be employed for the synthesis of pesticides because of their substantial biological effects.[35–38] N-phenyl phthalimide was used in the synthesis of numerous herbicides. Its derivatives exhibit hypolipidemic activity, and other biological properties like antimicrobial, antimalarial, antihypertensive, or antiviral.[39–42] Phthalimide derivativeswith phenyl acetic acid and phenyl propionic acid were found to have anti-inflammatory and analgesic properties. Varala et al. synthesized a series of phthalimides linked to mandelic acid using the combination of N-(2-hydroxy ethyl) phthalimide and

substituted mandelic acids (Fig. 4).[43] Additionally, a series of N-phenyl phthalimides connected to substituted pyrazole moiety was synthesized by Pophale et al.[44]

Corrosion Inhibitors Atmospheric degradation of materials over time due to environmental effects is known as corrosion. It is a natural tendency of matter to return to their thermodynamically stable state and most metallic materials form oxides or sulfides. Fortunately, the corrosion rate is slow. Only inert atmospheres or vacuum can provide a corrosion free environment for most of the metallic materials. Usually, iron and steel corrode in the presence of oxygen and water and corrosion rate increase with acidity, water velocity, metal motion, temperature, aeration and certain bacteria.[45] Corrosion inhibitors can protect materials, especially in acidic media.[46] In general, there are three types of inhibitors: inorganic, organic, and mixed (inorganic and organic).[47]

Acid inhibitors are organic compounds that adsorb on the metal surface with the polar groups acting as the reactive centers.[48] Properties of organic inhibitors mainly depend on their structure, presence of functional groups, steric effects and electronic density of structure.[49] Interaction of p-orbitals of the inhibitor with d-orbitals of the surface atoms also enhances the properties of inhibitors.[50] Experimental and theoretical techniques were used to understand the dependence of the efficacy and structural properties of inhibitors.[51] N-heterocyclic derivatives of imidazoline, 1,2,3-triazole, 1,2,4-triazole, benzotriazole, pyrrole, pyridine, pyrazole, bipyrazole, pyrimidine, pyridazine, indole, benzimidazole, quinoline, purine and tetrazole and pyrazine are effective corrosion inhibitors, used for iron or steel in acidic medium. The inhibition impact of N-heterocyclic compounds is caused by the adsorption to metal surface through N-heteroatom, triple or conjugated double bonds or aromatic rings in their molecular structures. In addition, adsorption of inhibitor on steel/solution interface is influenced by the chemical structures, nature and charged surface of a metal, circulation of charge and type of the aggressive medium. Organic inhibitors, e.g. Schiff bases, used in industrial processes to control metal dissolution and the consumption of acid, were invented to replace the inorganic inhibitors. Effectiveness of inhibitor depends on the size of the molecule, orientation, shape and the distribution of the electric charge. The polar organic compounds containing sulfur (thiourea) adsorb on the metal surface and form a charge exchange complex bond between their polar atoms and the metal.[52] Addition of surfactants also modifies the interfaces by controlling, diminishing, or avoiding reactions between a substrate and environment. The corrosion inhibitory potential of surfactants relies on the

classification of surfactants, the substrate type, inhibitor concentration, inhibitor structure, acid type and its pH, salts occurrence, co-surfactant, temperature, and dipping time.[53]

Excellent corrosion inhibition was reported for iron and steel in acidic medium using quaternary ammonium surfactants.[54] Corrosion inhibitor effectiveness increases in the presence of an additional substance in the corrosive medium due to the synergistic effects. For example, halide ions are effective additives for quaternary ammonium surfactants, giving synergistic effect on corrosion inhibition of steel in acidic media. Additionally, surfactants interact with K+, Mg2+, Ba2+, Cu2+, Zn2+, Hg2+, Cd2+, Co2+, Ni2+ and Fe3+ and rare earth cationsgiving detectable change in the corrosion-resisting property of the metal.[55] The adsorption of the gemini surfactants on metal surfaces in acidic medium was affected by length of hydrophobic chains and the spacer length of the gemini surfactants.[56] The corrosion inhibitors are toxic, and thus a great effort was applied to replace harmful inhibitors with effective non-hazardous alternatives. In recent years, several drugs have been used as corrosion inhibitors for various metals and other materials.[57]

CONCLUSIONS

Heterocyclic moieties are important class of organic compounds and acquire much attention because of their applications. The reactivity of imides is a consequence of the relative acidity of the (NH) group and the two carbonyl groups. Because of outstanding physical and chemical properties such as high modulus, high glass transition temperature and high stability, they are commonly used by pharmaceutical and agrochemical industries. Cyclic imides are resourceful compounds used to synthesize diverse heterocyclic systems such as: benzoxazines, pyridooxazines, quinazolines, and pyridopyrimidines. Heterocycles found numerous applications in biological, synthetic, and polymer chemistry and the use of inhibitors derived from heterocyclic moieties is the best practical approaches for shielding materials against corrosion, particularly in acidic medium.

REFERENCES

1. Qian, Z.G. Pang, Z.Z.; Li, Z.X.; He, M.H.; Liu, J.G.; Fan, L. Yang, S.Y. Photoimageable polyimides derived from α,α-(4-amino-3,5- dimethylphenyl)phenylmethane and aromatic dianhydride, J Polym Sci. A Polym Chem, 2002; 40: 3012-3020.
2. Chung, C.-L.; Yang, C.-P.; Hsiao, S.-H. Organosoluble and colorless fluorinated poly(ether imides) from 1,2-bis(3,4-dicarboxyphenoxy)benzene dianhydride and

trifluoromethyl-substituted aromatic bis(ether amine)s. J Polym Sci. A Polym Chem, 2006; 44: 3092-3102.

3. Fukushima, T.; Hosokawa, K.; Oyama, T.; Iijima, T.; Tomoi, M.; Itatani, H. Synthesis and positive-imaging photosensitivity of soluble polyimides having pendant carboxyl groups. J. Polym Sci. A Polym Chem, 2001; 39: 934-946.
4. Burdeaux, D.; Townsend, P.; Carr, J.; Garrou, P. Benzocyclobutene (BCB) dielectrics for the fabrication of high density, thin film multichip modules. J. Electron Mater, 1990; 19: 1357-1366.
5. Kirchhoff, R.-A.; Bruza, K.-J. Benzocyclobutenes in polymer synthesis. Prog Polym Sci, 1993; 18: 85-185.
6. Farona, M.-F. Benzocyclobutenes in polymer chemistry. Prog Polym Sci, 1996; 21: 505-555.
7. Barton, D.; Ollis, W.-D., Eds. Comprehensive organic chemistry: the synthesis and reactions of organic compounds, 1st ed.; Pergamon Press: Oxford, 1979.
8. Chiriac, C.-I; Nechifor, M.; Tanasa. F., Formamide, a novel challenging reagent for the direct synthesis of non-Nsubstituted cyclic imides. Rev. Roumaine De Chim, 2007; 52: 883–886.
9. Hargreaves, M.-K; Pritchard, J.-D; Dave, H.-R. Cyclic carboxylic monoimides. Chem, Rev, 1970; 70: 439-469.
10. Peng, Y.; Song, G.; Qian, X. Imidation of cyclic carboxylic anhydrides under microwave irradiation. Synth. Commun, 2001; 31: 1927-1931.
11. Hijji, Y.-M; Benjamin, E. Efficient Microwave Assisted Syntheses of Unsubstituted Cyclic Imides. Heterocycles, 2006; 68: 2259-2267.
12. Der-Jang, L.; Kung-Li W.; Ying-Chi H.; Kueir-Rarn L.; Juin-Yih L., Chang-Sik H. Advanced polyimide materials: Syntheses, physical properties and applications. Prog Polym Sci, 2012; 37: 907-974.
13. Mohammed, I.-A; Mustapha, A. Synthesis of New Azo Compounds Based on N-(4-Hydroxypheneyl)maleimide and N-(4-Methylpheneyl)maleimide. Molecules, 2010; 15: 7498-7508.
14. Yasin, M. Thermal process was used for preparation of imides from the corresponding amic acids. MSc Thesis, Chem. Dept., Sci. College, Baghdad Univ, 2007.
15. Pyriadi, T.; Al-Azzawi, A. and Al-Obaidi, K. J. Synthesis, characterization and polymerization of n-substituted maleimidylacrylates. Journal of Al-Nahrain University (Sience), 2009; 12: 1-14.

16. Iniaghe, L.; Usifoh, C.-O. Anticonvulsant properties of N-cyclopentylphthalimide and N-benzylphthalimide. Eur. J. Org. Chem., 1999, 2757–2762ä. Res. J. Pharm., Biol. Chem. Sci, 2010; 1: 1068–1072.
17. Klarner, F.-G; Breitkopf, V. The Effect of Pressure on Retro Diels–Alder Reactions. Eur. J. Org. Chem, 1999; 2757-2762.
18. Kossakowski, J.; Predka, A. Synthesis of new N-substituted cyclic imides with an expected anxiolytic activity. XXVI. Derivatives of N-hydroxy-7-diphenylmethylenebicyclo[2.2.1] hept-2-ene-5,6-dicarboximide. Annales Universitatis Mariae Curie-Sklodowska, Sectio AA: Chemia, 2003; 58: 147–153.
19. Castro, B.-R. Replacement of Alcoholic Hydroxyl Groups by Halogens and Other Nucleophiles via Oxyphosphonium Intermediates. Org. React, 1983; 29: 1–162.
20. Macor, J.-E.; Wehner, J.-M. The use of (o-nitroaryl)acetonitriles in the Mitsunobu reaction: mechanistic implications and synthetic applications. Heterocycles, 1993; 35: 349–365.
21. Coleman, R.-S.; Grant, E.-B. A low-temperature Mitsunobu reaction for the inversion of sterically hindered secondary alcohols. Tetrahedron Lett, 1994; 35: 8341–8344.
22. Hughes, D.-L. The Mitsunobu Reaction. Organic Reactions, 1992; 42: 335–656.
23. Ducrocq, C. Wendling, F. Tourbez-Perrin, M. Rivalle, C. Tambourin, P. Pochon, F. and Bisagni, E. Structure-activity relationships in a series of newly synthesized 1-aminosubstituted ellipticine derivatives. J. Med. Chem, 1980; 23: 1212-1216.
24. Reddy, P. Kondo, S. Toru, T. and Ueno, Y. Lewis Acid and Hexamethyldisilazane-Promoted Efficient Synthesis of N-Alkyland N-Arylimide Derivatives. Org. Chem, 1997; 62: 2652-2654.
25. Połoński, T.; Milewska, M.; Gdaniec, M. Synthesis, structure and chiroptical spectra of the bicyclic α-diketones, imides and dithioimides related to santenone. Tetrahedron: Asymmetry, 2000; 11: 3113–3122.
26. You, C.; Würthner, F. Porphyrin−Perylene Bisimide Dyads and Triads: Synthesis and Optical and Coordination Properties. Org. Lett, 2004; 6: 2401–2404.
27. Taherpour, A.-A.; Mansuri, H.-R. Fast Oxidation of Lactams to Cyclic Imides Using Microwave Irradiation. Turk. J. Chem, 2005; 29: 317-320.
28. Lin, Y.; Cheng, J.; Chu, Y. Microwave-accelerated Claisen rearrangement in bicyclic imidazolium [β-3C-im][NTf2] ionic liquid. Tetrahedron, 2007; 63: 10949–10957.

29. Abdel-Aziz, A. M. Novel and versatile methodology for synthesis of cyclic imides and evaluation of their cytotoxic, DNA binding, apoptotic inducing activities and molecular modeling study, Eur. J. Med. Chem, 2007; 42: 614–626.
30. Sunita B. S; Sunil U.T; Sushma S. K; Satish U. D; Rajendra P. M; Rajesh B. N; Vinayak S. S; Vinod V. T; Rajendra P. P. A Facile and Efficient Synthesis of N-aryl Imides Using Trifluoroacetic Acid, Int. J. Indian Chem, 2011; 2: 2228–2232.
31. Shimazawa, R. Takayama, H.; Kato, F.; Hashimoto, Y. Synthesis and qsar of dequalinium analogues AS K+ channel blockers investigations on the role of the 4-amino group. Bioorg. Med. Chem. Lett, 1999; 9: 559–562.
32. Vidal, T.; Petit, A.; Loupy, A.; Gedye, R. Tetrahedron. Re-examination of Microwave-Induced. Synthesis of Phthalimides, 2000; 56: 5473–5478.
33. Jayakumar, R.; Balaji, R.; Nanjudan, S. Studies on copolymers of 2-(N-phthalimido) ethyl methacrylate with methyl methacrylate Eur. Polym. J, 2000; 36: 1659–1666.
34. Ribeiro da Silva, M. A. V. and Cláudia P. F. S. Standard molar enthalpies of formation and sublimation of N-phenylphthalimide. J. Thermal Anal. Calorim, 2007; 87: 21–25.
35. Luzzio, F.; Zacherl, A. A facile scheme for phthalimide ⇌ phthalimidine conversion. Tetrahedron Lett, 1999; 40: 2087–2090.
36. Constantinova T.N; Garbechev I.K. Copolymers containing phthalimide derivatives were used as optical brightening agents, Polym. Int, 1998; 43: 39–43.
37. Lima, L. M.; Brito, F.; Souza, S.; Miranda, A.; Rodrigues, C.; Fraga, A.; Barreiro, E. Novel Phthalimide Derivatives, Designed as Leukotriene D4 Receptor Antagonists Bio org. Med. Chem. Lett, 2002; 12: 1533–1535.
38. Sena V.L, Srivastava R.M, Silva R.O, Lima V.L. Synthesis and hypolipidemic activity of N-substituted phthalimides. Part V. Farmaco, 2003; 58: 1283–1288.
39. James M. C., Jr., P. Josee V., George H. C., Iris H. H. Hypolipidemic activity of phthalimide derivatives. 2. N-Phenylphthalimide and derivatives. J. Med. Chem, 1983; 26: 237–243.
40. Bhawani, S.; Deepika, M.; Lalith, K. B and Talesara, G. L. Synthesis and biological evaluation of 7-N-(n-alkoxyphthalimido)-2-hydroxy-4-aryl-6-aryliminothiazolidino [2,3-b]pyrimidines and Related Compounds. Indian J. Chem, 2004; 43B: 1306–1312.
41. Pandey, V.K.; Sarah, T.; Zehra, T. Thiadiazolyl quinazoolones as potential antiviral and antihypertensive agents. Indian J. Chem, 2004; 43B: 180-183.
42. Mogilaiah, K.; Sakram, B. Microwave assisted synthesis of N-(3-aryl-1,8-naphthyridin-2-yl)…. Indian J. Chem, 2007; 46B: 207–209.

43. Varala, R.; Kotra, V.; Alam, M.; Kumar, N. Synthesis of mandelic acid derived phthalimides, Indian J. Chem, 2008; 47B: 1243–4348.
44. Rasika A. P., Meenakshi N. D. Synthesis and evaluation of novel phthalimide derivatives as analgesic and antiinflammatory agents. Der Pharma Chemica, 2010; 2: 185–193.
45. Afshin Z., Sayyed A. Tabatabai, M. F., Avideh A., Parisa N., Vahideh Z., Abbas S. Synthesis and anticonvulsant activity of new 2-substituted-5-(2-benzyloxyphenyl)-1,3,4-oxadiazoles Bio org. Med. Chem. Lett, 2005; 15: 1863–1865.
46. Pluempanupat, W.; Adisakwattana, S.; Yibchok-Anun S.; Chavasiri, W. Synthesis of N-phenylphthalimide derivatives as alpha-glucosidase inhibitors. Arch. Pharm. Res, 2007; 30: 1501–1506.
47. Mahapatra, S.P., Ghode, P., Jain, D.K., Chaturvedi, S.C., Maiti B.C., and Maity T.K. Synthesis and Hypoglycemic Activity of some Phthalimide Derivatives. J. Pharm. Sci. Res, 2010; 2: 567–578.
48. Cohen, S.; Garland E.; Cano, M.; John, M.; Khanchab, M.; Wehner, J.; Arnold, L. N-substituted phthalimides structures showed inhibitory activities as non-nucleoside HIV-1 reverse transcriptase inhibitors, Carcinogen, 1955; 16: 2743– 2752.
49. Norman, M; Minick, D.; Rigdon, G. Effect of Linking Bridge Modifications on the Antipsychotic Profile of Some Phthalimide and Isoindolinone Derivative. J. Med. Chem, 1996; 39: 149–157.
50. White, H.; Woodhead, J.; Franklin, M. General Principles: Experimental Selection, Quantification, and Evaluation of Anticonvulsant Drugs. In Antiepileptic drugs, 4th Ed.; R. Levy, R. Mattson, B. Meldrum (Eds.) Raven Press, New York, 1995.
51. Haider, N.; Jbara, R.; Käferböck, J.; Traar, U. Synthesis of tetraand pentacyc lic carbazole-fused imides as potential antitumor agents . ARKIVOC, 2009; 6: 38–47.
52. Russo, F.; Romeo, G.; Santagati, N. Synthesis of new thienopyrimidobenzothiazoles and thienopyrimidobenzoxazoles with analgesic and antiinflammatory properties. Eur. J. Med. Chem, 1994; 29: 569–578.
53. Vashi, B.; Mehta, D.; Shah, D. Synthesis and biological activity of 4-thiazolidinones, 2-azetidinones, 4-imidazolinone derivatives having thymol moiety. Indian J. Chem, 1995; 34B: 802–808.
54. Patel, K.; Mehta, A. synthesis and antifungal activity of azetidinone and Thiazolidinones derivatives of 2-amino6-(2-naphthalenyl) thiazolo [3, 2-d] thiadiazole. Eur. J. Chem, 2006; 3: 267–273.

55. Mohan, J.; Kumar, A. Condensed bridgehead nitrogen heterocyclic systems: Synthesis and antimicrobial activity of s-triazolo [3,4-b] [1,3,4] thiadiazoles and s-triazolo [3,4-b] [1,3,4] thiadiazines. J. Ind. Heterocycl. Chem, 2001; 71: 11–21.
56. Bharatham, N.; Bharatham, K.; Lee, K. Quantitative structure activity relationships and molecular docking studies of P56 LCK inhibitors.Bull. Korean Chem. Soc, 2006; 27: 266–272.
57. Bradshaw, T.; Westwell, A. The Development of the Antitumour Benzothiazole Prodrug, Phortress, as a Clinical Candidate. Curr. Med. Chem, 2004; 11: 1241–1253.