Contents lists available at GrowingScience

Current Chemistry Letters

homepage: www.GrowingScience.com

Synthesis of phthalimide and naphthalimide derived Biginelli compounds and evaluation of their anti-inflammatory and anti-oxidant activities

Pradeep Rameshrao Totawar[a], Ravi Varala[b*], Vijay Kotra[c] and Jitendra S. Pulle[d]

[a]*Nagnath Arts, Commerce and Science College, Aundha Nagnath, Hingoli-431705, Maharashtra, India*
[b]*Scrips Pharma, Hyderabad-500 076, Telangana, India*
[c]*Faculty of Pharmacy, Quest International University, Ipoh 30250, Malaysia*
[d]*Shri Guru Buddhi Swami Mahavidyalaya, Purna, Parbhani-431511, Maharashtra, India*

CHRONICLE

Article history:
Received September 20, 2022
Received in revised form
December 20, 2022
Accepted January 12, 2023
Available online
January 12, 2023

Keywords:
Phthalimides
Naphthalimides
Biginelli reaction
Sulfated tin oxide
Anti-inflamamtory
Anti-oxidant activity

ABSTRACT

In the present work, synthesis of phthalimide and naphthalimide derived Biginelli compounds was performed. Allylation of phthalic & naphthalic anhydride, followed by ozonolysis resulted in the formation of *N*-phathalimido/naphpthalimido acetaldehyde (**2** and **7**). These aldehydes were subjected to Biginelli reaction using urea/thiourea and divergent β-keto esters in the presence of sulfated tin oxide (5 mol%) as catalyst in ethanol reflux to produce the corresponding dihydropyrimidinone compounds (**5a-j** and **8a-h**). Additionally, both their antioxidant and anti-inflammatory functions were carried out. Compounds **5e**, **5f**, **5i**, and **5j** have shown potent to moderate potent activity for both antioxidant and anti-inflamamtory activities when compared to standard. Compounds **8c** and **8g** have shown potent antioxidant and anti-inflamamtory activities when compared to other compounds.

1. Introduction

Multi-component reactions (MCRs), which feature selectivity, excellent yields, quicker reaction times, atom economy, and environmental friendliness, are crucial tools in the arsenal of synthetic and medicinal chemists for the production of a wide range of new chemical entities (NCEs).[1] Traditional methodologies required multiple steps and rigorous workup procedures.[2-4] The Biginelli reaction is one of the MCRs, which produces 3,4-dihydropyrimidin-2(1*H*)-ones/thiones from the reaction of aldehydes, urea/thiourea and β-keto esters, with biological relevance,[5-6] such as calcium channel blockers, antihypertensive medicines, anti-inflammatory, anticancer, antiviral, and antibacterial, holds a prominent place among multi-component reactions (**Fig. 1**).[7-13, 35]

Tumor necrosis factor (TNF) inhibitors, analgesic, anticancer, anti-inflammatory, Ca channel blockers, antihypertensive, pesticide, insecticide, herbicide, and other biological actions have been linked to phthalimide derivatives (Figure 2).[14-16] The synthesis of phthalimide analogues is the subject of extensive study because of the wide range of applications they have in medicine. As the primary scaffold for numerous anticancer, anti-inflammatory, antidepressant, anti-protozoal, and antiviral medicines, among others, naphthalimides are a significant class of aromatic heterocycles with significant pharmacological relevance (**Fig. 2**).[17-22] Naphthalimide's tricyclic planar ring system is principally responsible for its intercalation with DNA to disrupt cellular processes, and the molecule's substitution pattern results in a number of other uses. The majority of them, including amonafide, have been dropped, nonetheless, due to their low therapeutic index

* Corresponding author. Tel.: +91-9618286529
E-mail address ravivarala@gmail.com (R. Varala)

doi: 10.5267/j.ccl.2023.1.004

and hemotoxicity. Numerous novel naphthalimide compounds have been created and synthesized in an effort to address these drawbacks and test them for improved efficacy.

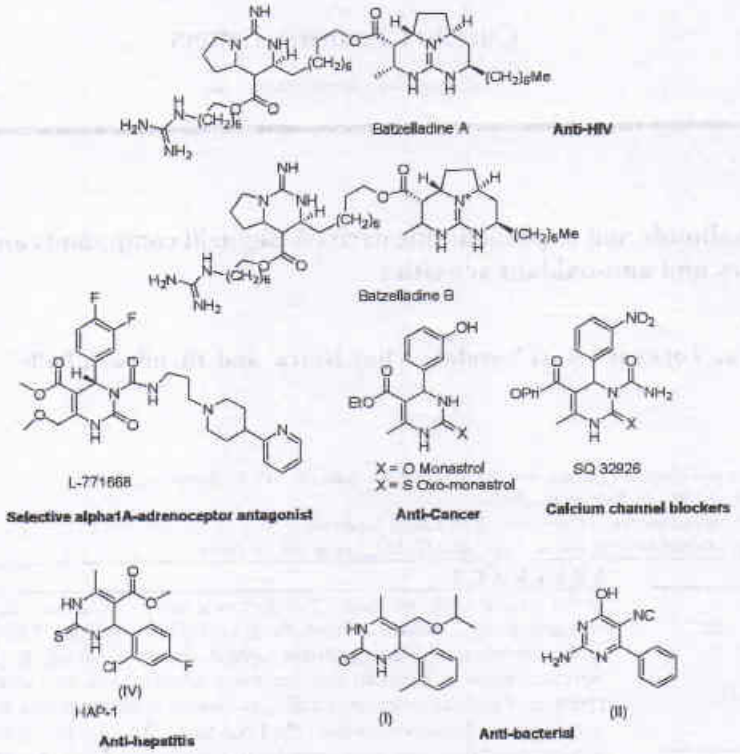


Fig. 1. Dihydropyrimidinone (DHPM) containing various natural and synthetic analogues.[44-45]

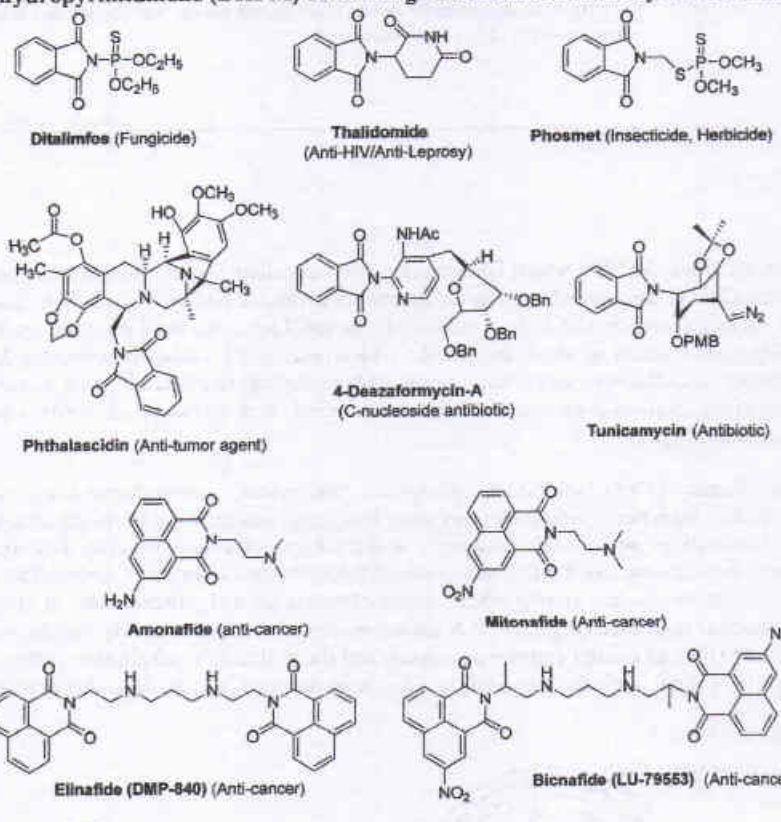


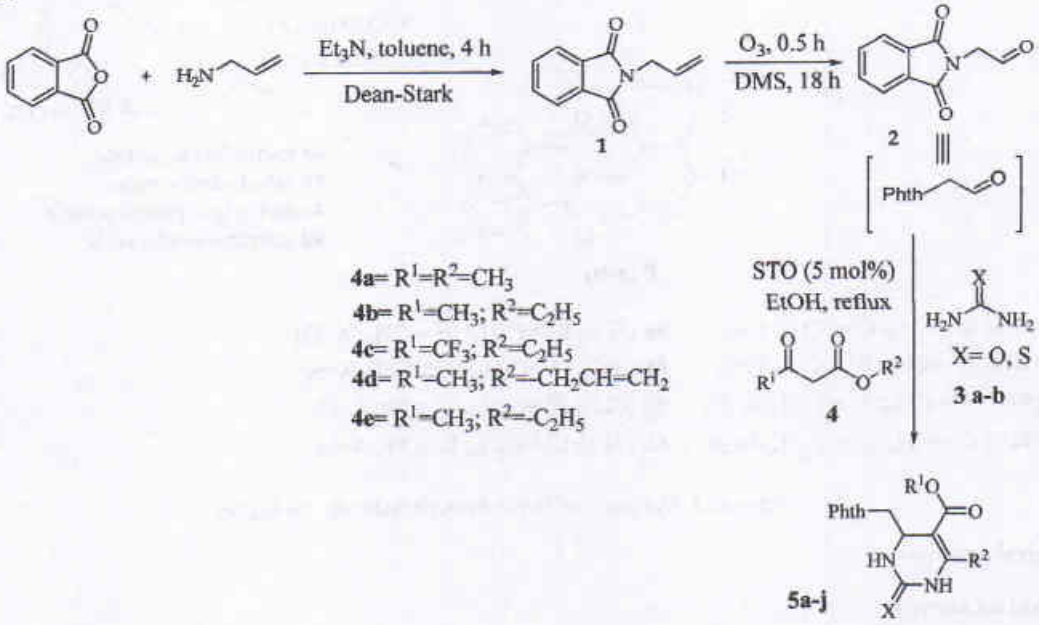
Fig. 2. Representative biologically active phthalimide and naphthalimide analogues.[46-48]

Sulfated tin oxide (hereafter referred to as STO) has received a lot of attention recently in the fields of catalysis and organic synthesis due to its high efficiency, low cost, greater stability, non-corrosive, reuse, and recyclability, as well as its large surface area.[23] As a result, they have been extensively used as a solid acid heterogeneous catalyst in a variety of synthetic transformations.[24]

The hybrid compounds (phthalimide/naphthalimide and dihydropyrimidinone) that contain these two essential heterocyclic scaffolds may exhibit significant or influential therapeutic potential. In keeping with our earlier findings on the chemistry of phthalimides and naphthalimides[25-27] and the synthesis of various dihydropyrimidinones,[28-34] a few hybrid analogues of *N*-naphthalaldehyde derived dihydropyrimidinones were prepared using straightforward chemistry and subjected to studies on their ability to reduce inflammation and fight free radicals.

2. Results and Discussion

As stated in the experimental procedure, initially, we generated *N*-phthalimido acetaldehyde (**2**) from ozonolysis of *N*-allyl phthalimide (**1**) based on our prior strategies (**Scheme 1**).[25-27] The spectral data of the two matched data from the literature.



Scheme 1. Synthesis of Biginelli-phthalimide analogues.

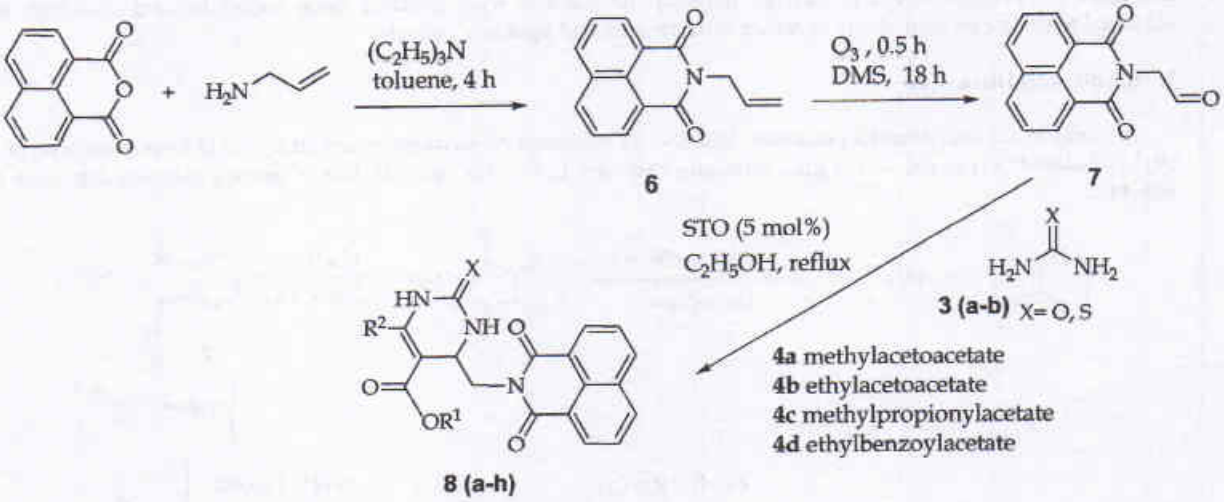
Divergent β-ketoesters (**4**, 1 equiv.), urea/thiourea (**3**, 1.5 equiv.), and *N*-phthalimido acetaldehyde (**2**) (1 equiv.) were allowed to react under reflux conditions with freshly made sulfated tin oxide (STO, 5 mol%) in ethanol (5 mL) as shown in **Scheme 1**. STO loading was increased to 10 mol% without appreciably changing the yield. Alcohol was discovered to be the preferred solvent for the synthesis of biginelli phthalimide analogues among the solvents examined, including acetonitrile, toluene, DMF, xylene, and CCl_4. Different β-ketoesters were given the opportunity to react with thiourea/urea, and this resulted in a variety of products with good yields (83-97%) and quick (2-3.5 h) reaction periods (**Table 1**). There was enough spectral data to characterize every compound that was produced (see Supporting Information). Without losing its reactivity, the catalyst can be recycled and used at least four times (**5c**, 97%, 96%, 94%, and 94%, respectively).

Table 1. STO-Catalyzed synthesis of phthalimide derived Biginelli compounds.

Urea/Thiourea	1,3-diketones	Product	Time(h)	Yield(%)[a]
Urea	Methylacetoacetate	5a	2	90
Thiourea		5b	2.5	92
Urea	Ethylacetoacetate	5c	2	97
Thiourea		5d	2	94
Urea	Ethyl trifluoroacetoacetate	5e	3	83
Thiourea		5f	2.5	85
Urea	Allyl acetoacetate	5g	2.5	90
Thiourea		5h	2	93
Urea	Ethyl benzoylacetate	5i	3	91
Thiourea		5j	3.5	90

[a]Isolated yield

We expanded this approach to include the synthesis of Biginelli compounds produced from naphthalimides because the outcomes from phthalimide hybrid analogues intrigued us. According to the experimental protocol, *N*-allyl naphthalimide (**6**) was ozonolyzed to produce *N*-naphthalimido acetaldehyde (**Scheme 2**).[17] The spectral data of **7** corresponded to data from the literature. Aldehyde **7** was dissolved in ethanol, and then excess urea/thiourea (**3a-b**) and α,β-ketoesters (**4a-d**) were added to the resultant solution. The reaction was accelerated by STO (5 mol%) in ethanol, and when it was conducted out under reflux conditions, the required products (**8a-h**) were produced in yields that ranged from moderate to good (78-94%) (**Scheme 2**).



8a (93%) R^1 =CH_3; R^2 = CH_3; X=O
8b (90%) R^1 =CH_3; R^2 = CH_3; X=S)
8c (89%) R^1 =CH_3; R^2 = C_2H_5; X=O)
8d (94%) R^1 =CH_3; R^2 = C_2H_5; X=S)
8e (87%) R^1 =C_2H_5; R^2 = CH_3; X=O)
8f (78%) R^1 =C_2H_5; R^2 = CH_3; X=S)
8g (82%) R^1 =C_2H_5; R^2 = Ph; X=O)
8h (91%) R^1 =C_2H_5; R^2 = Ph; X=S)

Scheme 2. Synthesis of Biginelli-naphthalimide analogues.

Biological activities

Antioxidant activity:

All of the compounds in the title displayed antioxidant activity by scavenging hydrogen peroxide.[36] Compound **5i** has demonstrated greater activity when compared to standard among the compounds tested for antioxidant activity. Following compound **5j**, which shown strong action, were compounds **5e** and **5f**, which displayed moderate activity (**Table 2** and **Fig. 3**). Compounds **8c** and **8g** from the compounds (**8a-h**) have demonstrated potent action when compared to other compounds activity (**Table 3** and **Fig. 4**).

Table 2. Antioxidant activity of synthesized compounds by hydrogen peroxide scavenging method.

Compound	% inhibition by H_2O_2 scavenging method Concentrations (µg/ml)					IC 50
	100 µg/ml	200 µg/ml	300 µg/ml	400 µg/ml	500 µg/ml	
5a	3.9	6.2	11.29	15.53	20.55	6.1
5b	22.6	29.5	38.4	45.5	55.8	3.85
5c	26.8	36.7	54.5	58.9	59.95	3.67
5d	10.98	16.48	22.54	26.56	30.9	3.88
5e	8.1	16.52	17.21	17.22	26.81	3.00
5f	11.1	19.3	22.43	35.7	41.6	3.02
5g	11.23	15.36	25.45	35.43	55.5	3.09
5h	27.5	40.5	52.95	53.47	59	4.35
5i	4.7	10.30	20.34	41.71	53.13	2.53
5j	10.78	13.07	22.61	38.55	40.63	2.90
Ascorbic acid	23.3	34.78	46.45	52.45	56.46	2.88

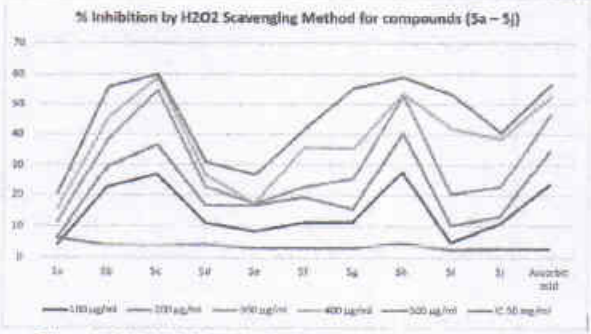


Fig. 3. % Inhibition by H_2O_2 scavenging method for compounds **5a-j**

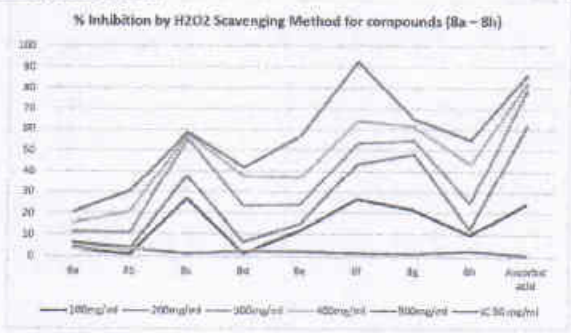


Fig. 4. % Inhibition by H_2O_2 Scavenging Method for compounds **(8a-h)**

Table 3. % inhibition by H_2O_2 scavenging method Concentrations (µg/ml).

Compound	% inhibition by H_2O_2 scavenging method Concentrations (µg/ml)					IC 50 µg/ml
	100 µg/ml	200 µg/ml	300 µg/ml	400 µg/ml	500 µg/ml	
8a	3.8	6.1	11.34	15.49	20.58	6.2
8b	0.76	3.17	10.73	20.75	30.34	3.74
8c	26.79	37.67	55.38	57.82	58.64	1.36
8d	0.99	6.52	23.45	37.34	41.89	2.48
8e	11.67	14.75	23.98	36.83	56.86	2.27
8f	26.49	43.49	53.44	64.12	92.67	1.62
8g	21.62	48.32	54.76	61.43	64.93	1.39
8h	9.82	12.46	24.48	43.62	54.92	2.69
Ascorbic acid	24.2	61.64	78.62	82.26	86.43	0.64

Anti-inflammatory activity

Using a carrageenan-induced acute paw oedema method in rats, all of the title compounds were evaluated for their ability to reduce inflammation.[37] Compounds **5e**, **5f**, **5i**, and **5j** among them have significantly reduced paw oedema **(Table 4, Fig. 5)**. The compound **5i** showed highest protection of 81.67 %, followed by compounds **5j, 5e** and **5f** (80.35, 80.26 and 79.37 % respectively). According to the aforementioned findings, molecules with ethyl benzoyl and ethyl trifluoro groups exhibit more activity than those without these groups. Paw oedema has been significantly reduced by compound **8c** and compound **8g** having ethyl and phenyl substituents, respectively **(Table 5, Fig. 6)**.

Table 4. Anti-inflammatory activity of the phthalimide derived Biginelli compounds.

Compound	1 h	2 h	3 h	4 h	5 h
Control	0.33±0.02	0.59±0.01	0.63±0.02	0.73±0.02	0.85±0.01
5a (200 mg/kg)	0.29±0.01 (10.42%)	0.55±0.03 (29.48%)	0.37±0.02 (34.63%)	0.29±0.03* (60.78%)	0.22±0.01** (72.18%)
5b (200 mg/kg)	0.29±0.04 (10.64%)	0.55±0.04 (29.86%)	0.43±0.04 (37.62%)	0.28±0.03* (62.44%)	0.19±0.03** (74.04%)
5c (200 mg/kg)	0.28±0.04 (12.64%)	0.56±0.04 (24.38%)	0.39±0.03 (44.37%)	0.29±0.04* (62.84%)	0.18±0.04** (74.22%)
5d (200 mg/kg)	0.31±0.03 (08.92%)	0.53±0.01 (34.82%)	0.34±0.04 (46.28%)	0.26±0.02 (70.64%)	0.20±0.01** (73.84%)
5e (200 mg/kg)	0.29±0.03 (10.56%)	0.52±0.04 (36.10%)	0.38±0.02 (43.10%)	0.26±0.01** (70.42%)	0.17±0.04*** (80.26%)
5f (200 mg/kg)	0.25±0.02 (17.32%)	0.53±0.04 (36.86%)	0.33±0.03 (54.54%)	0.24±0.01 (74.22%)	0.18±0.02 (79.37%)
5g (200 mg/kg)	0.25±0.04 (10.34%)	0.55±0.02 (27.38%)	0.40±0.01 (40.16%)	0.30±0.02* (58.62%)	0.18±0.04** (74.52%)
5h (200 mg/kg)	0.26±0.03 (16.28%)	0.54±0.04 (29.64%)	0.36±0.02 (32.88%)	0.26±0.01 (69.86%)	0.17±0.02 (78.46%)
5i (200 mg/kg)	0.28±0.04 (12.64%)	0.52±0.04 (36.87%)	0.34±0.01 (41.48%)	0.25±0.01** (75.29%)	0.16±0.03*** (81.67%)
5j (200 mg/kg)	0.29±0.02 (10.46%)	0.54±0.04 (29.86%)	0.36±0.03 (54.24%)	0.25±0.04** (74.64%)	0.15±0.04*** (80.35%)
Indomethacin (20 mg/kg)	0.26±0.02 (14.44%)	0.54±0.01 (35.83%)	0.32±0.01* (63.28%)	0.24±0.03*** (76.59%)	0.15±0.02*** (82.94%)

All values are mean ± SEM values using 6 animals in each group.
Significant differences with respect to control group was evaluated by ANOVA, Dunnets 't' test.
*P < 0.05, **P < 0.01, ***P < 0.001.

Co-ordinator
IQAC
Shri Guru Buddhiswami Mahavidyalaya
Purna (Jn) Dist. Parbhani - 431511 (M.S.)

Shri Guru Buddhiswami Mahavidyalaya Purna (Jn.) Shikshan Prasarak Sanstha Estd.1983

PRINCIPAL
Shri Guru Buddhiswami Mahavidyalaya
Purna (Jn.) Dist.Parbhani

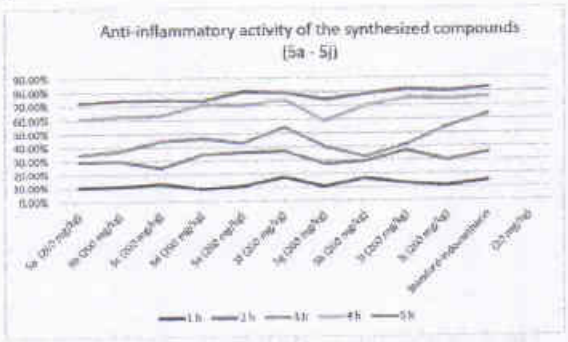


Fig. 5. Anti-inflammatory activity of the synthesized compounds (**5a-j**)

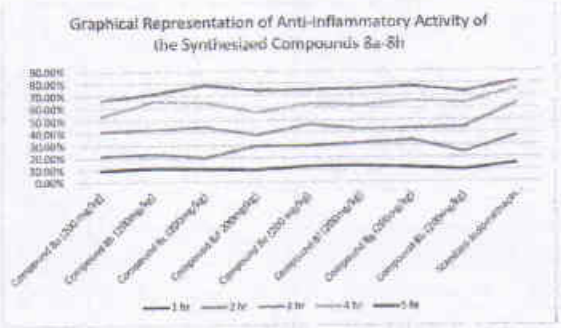


Fig. 6. Anti-inflammatory Activity of the Synthesized Compounds **8a-h**

Table 5. Anti-inflammatory activity of the synthesized compounds **8a-h**

Group	1 h	2 h	3 h	4 h	5 h
Control 1% Water (1 ml/kg)	0.32±0.01	0.58±0.02	0.61±0.02	0.74±0.01	0.83±0.02
8a (200 mg/kg)	0.27±0.02 (9.37%)	0.43±0.01 (21.62%)	0.31±0.02 (41.34%)	0.22±0.03 (53.32%)	0.21±0.02 (66.38%)
8b (200 mg/kg)	0.21±0.02 (11.34%)	0.42±0.02 (22.96%)	0.32±0.02 (42.86%)	0.23±0.01 (65.29%)	0.18±0.04** (71.64%)
8c (200 mg/kg)	0.45±0.02 (10.53%)	0.48±0.03 (20.19%)	0.29±0.02 (44.67%)	0.24±0.02 (64.53%)	0.17±0.02* (78.42%)
8d (200 mg/kg)	0.26±0.01 (09.64%)	0.46±0.02 (29.64%)	0.34±0.03 (38.39%)	0.24±0.02 (56.53%)	0.16±0.01** (74.28%)
8e (200 mg/kg)	0.28±0.02 (12.32%)	0.48±0.03 (29.68%)	0.32±0.02 (46.56%)	0.26±0.01 (63.46%)	0.16±0.02** (74.84%)
8f (200 mg/kg)	0.23±0.03 (12.65%)	0.49±0.03 (31.46%)	0.31±0.02 (42.67%)	0.27±0.02 (62.24%)	0.15±0.03** (75.52%)
8g (200 mg/kg)	0.25±0.01 (11.75%)	0.46±0.03 (33.63%)	0.32±0.02 (43.46%)	0.25±0.03 (65.63%)	0.17±0.01* (77.22%)
8h (200 mg/kg)	0.27±0.02 (9.43%)	0.46±0.01 (24. 24%)	0.33±0.02 (44. 43%)	0.26±0.04 (64.26%)	0.18±0.03** (73.04%)
Indomethacin (20 mg/kg)	0.26±0.01 (14.67%)	0.52±0.02 (37.26%)	0.31±0.01** (63.39%)	0.24±0.03*** (75.47%)	0.14±0.02*** (81%)

All values are mean ± SEM values using 6 animals in each group.
Significant differences with respect to control group was evaluated by ANOVA, Dunnets 't' test .
*P < 0.05, **P < 0.01, ***P < 0.001.

Acute oral toxicity

On the basis of the guidelines for the produced compounds 8a–h, acute oral toxicity was conducted. Following administration of 200 mg/kg body weight for all the compounds, no harmful effects were seen. Therefore, additional anti-inflammatory action was performed at a dose of 100 mg/kg body weight, which was deemed safe because no deaths were noticed.

3. Conclusions

In this study, authors have presented a low-cost, environmentally friendly method for producing phthalimido and naphthalimido-dihydropyrimidine hybrid analogues by reacting *N*-naphthalimido acetaldehyde, divergent β-keto esters with urea/thio-urea under reflux conditions in ethanol with 5 mol% sulfated tin oxide (STO) as a Lewis acid catalyst. The results of screening synthetic compounds for their antioxidant and anti-inflammatory properties are performed. When compared to standards, compounds **5e**, **5f**, **5i**, and **5j** have demonstrated powerful to moderately potent efficacy for both antioxidant and anti-inflammamtory properties. According to the aforementioned findings, molecules with ethyl benzoyl and ethyl trifluoro groups exhibited more activity than those without these groups. When compared to other compounds, compounds **8c** and **8g** with ethyl and phenyl substituents have demonstrated strong antioxidant and anti-inflammatory effects.

Acknowledgements

Dr. RV thanks Dr. Ch. V. Rajasekhar, Scrips Pharma for his continued support and encouragement.

4. Experimental

Please refer to Supporting Information

This paper ensures that applied sciences are very important in nature due to their various uses as reported before.[38-43]

References

1. Brenno A. D. N., Rafael O. R., and Rodrigues M. O. (**2022**) Catalytic Approaches to multicomponent reactions: A critical review and perspectives on the roles of catalysis. *Molecules*, 27, 132; DOI: https://doi.org/10.3390/molecules27010132
2. John S. E., Gulati S., and Shankaraiah N. (**2021**) Recent advances in multi-component reactions and their mechanistic insights: a triennium review. *Org. Chem. Front.*, 8, 4237-4287; DOI: https://doi.org/10.1039/D0QO01480J
3. Graebin C. S., Ribeiro F. V., Rogério K. R., and Kümmerle A. E. (**2019**) Multicomponent Reactions for the Synthesis of Bioactive Compounds: A Review. *Curr. Org. Synth.*, 16(6), 855-899; DOI: 10.2174/1570179416666190718153703
4. Climent M. J., Corma A., and Iborra S. (**2012**) Homogeneous and heterogeneous catalysts for multicomponent reactions. *RSC Adv.*, 2, 16-58; DOI: https://doi.org/10.1039/C1RA00807B
5. Chopda L. V., and Dave P. N. (**2020**) Recent advances in homogeneous and heterogeneous catalyst in Biginelli reaction from 2015-19: A concise review. *ChemistrySelect*, 5, 5552-5572; DOI: https://doi.org/10.1002/slct.202000742
6. Patil R. V., Chavan J. U., Dalal D. S., Shinde V. S., and Beldar A. G. (**2019**) Biginelli Reaction: Polymer supported catalytic approaches. *ACS Comb. Sci.*, 21, 105-148; DOI: 10.1021/acscombsci.8b00120
7. Panda S. S., Khanna P., and Khanna L. (**2012**) Biginelli Reaction: A green perspective. *Curr. Org. Chem.* 16, 507-520; DOI: 10.2174/138527212799499859
8. Mohammadi B., and Behbahani F. K. (**2018**) Recent developments in the synthesis and applications of dihydropyrimidin-2(1*H*)-ones and thiones. *Mol. Divers.*, 22, 405-446; DOI: https://doi.org/10.1007/s11030-017-9806-z
9. George N., Manakkadan A. A., Ariyath A., Maniyamma S., Vijayakumar V., Pai R. G., and Zachariah S. M. (**2019**) Chemistry and pharmacological activities of Biginelli product-A brief overview. *Curr. Drug Discov. Technol.*, 16,127-134; DOI: 10.2174/1570163815666180807141922
10. Marinescu M. (**2021**) Biginelli reaction mediated synthesis of antimicrobial pyrimidine derivatives and their therapeutic properties. *Molecules*, 26, 6022; DOI: https://doi.org/10.3390/molecules26196022
11. Sarrafi Y., Pazokie F., Azizi S., Alimohammadi K., Mehrasbi E., and Chiani, E. (**2014**). Mesoporous SBA-15 nanoparticles: An efficient and eco-friendly Catalyst for one-pot synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones under solvent-free conditions. *Curr. Chem. Lett.*, 3(2), 97-102; DOI: 10.5267/j.ccl.2013.12.003
12. Kaur R., Chaudhary S., Kumar K., Gupta M. K., and Rawal R. K. (**2017**) Recent synthetic and medicinal perspectives of dihydropyrimidinones: A review. *Eur. J. Med. Chem.*, 132, 108-134; DOI: 10.1016/j.ejmech.2017.03.025
13. Khasimbi S., Ali F., Manda K., Sharma A., Chauhan G., and Wakode S. (**2021**) Dihydropyrimidinones scaffold as a promising nucleus for synthetic profile and various therapeutic targets: A review. *Curr. Org. Synth.*, 18(3), 270-293; DOI: 10.2174/1570179417666201207215710
14. Sharma U., Kumar P., Kumar N., and Singh B. (**2010**) Recent advances in the chemistry of phthalimide analogues and their therapeutic potential. *Mini. Rev. Med. Chem.*, 10, 678-704; DOI: 10.2174/138955710791572442
15. Abdulrahman H. S., Mohammed M. H., Al-Ani L. A., Ahmad M. H., Hashim N. M., and Yehye W. A. (**2020**) Synthesis of phthalimide imine derivatives as a potential anticancer agent. *J. Chem.*, Article ID 3928204; DOI: https://doi.org/10.1155/2020/3928204
16. da Silva Júnior J. G., Holanda V. N., Gambôa D. S. R., Siqueira do Monte T. V., de Araújo H. D. A., do Nascimento Júnior J. A. A., Alves do Nascimento Júnior J. A., da Silva Araújo V. F., Callôu M. A. M., de Oliveira Assis S. P., and Lima V. L. M. (**2019**) Therapeutic potential of phthalimide derivatives: A review. *Amer. J. Biomed. Sci. Res.*, 3, 378-384; DOI: 10.34297/AJBSR.2019.03.000699
17. Kamal A., Adil S. F., Tamboli J. R., Siddardha, B., and Murthy U. S. N. (**2008**) Synthesis and anticancer activity of phthalimido and naphthalimido substituted dihydromyrimidone conjugates. *Lett. Drug. Des. Disc.*, 5, 261-270; DOI: 10.2174/157018008784619933
18. Malik M. S., Adil, S. F., Seddigi Z. S., Morad M., Jassas R. S., Thagafi I. I., Altass H. M., Jamal Q. M. S., Riyaz S., Alsantali R. I., Al-Warthan A. A., Ansari M. A., and Ahmed S. A. (**2021**) Molecular modelling assisted design of napthalimide-dihydropyrimidinone conjugates as potential cytotoxic agents. *J. Saudi Chem. Soc.*, 25(5), 101226; DOI: https://doi.org/10.1016/j.jscs.2021.101226
19. Marinov M. N., Naydenova E. D., Momekov G. T., Prodanova R. Y., Markova N. V., Voynikov Y. T., and Stoyanov N. M. (**2019**) Synthesis, characterization, quantum-chemical calculations and cytotoxic activity of 1,8-naphthalimide derivatives with non-protein amino acids. *Anticancer Agents Med. Chem.*, 19(10), 1276-1284; DOI: 10.2174/1871520619666190307115231
20. Jin C., Alenazy R., Wang Y., Mowla R., Qin Y., Tan J., Modi N., Gu X., Polyak S., Venter H., and Ma, S. (**2019**) Design, synthesis and evaluation of a series of 5-methoxy-2,3-naphthalimide derivatives as AcrB inhibitors for the reversal of bacterial resistance. *Bioorg. Med. Chem. Lett.*, 29(7), 882-889; DOI: 10.1016/j.bmcl.2019.02.003
21. Chen R., Yuan C., Jaiswal, Y., Huo L., Li D., Williams L., Zhong J., and Liang Y. (**2020**) Synthesis and biological evaluation of some 1,8-naphthalimide-acridinyl hybrids. *J. Chem.*, Article ID 7989852; DOI: https://doi.org/10.1155/2020/7989852
22. Yildiz U., Kandemir I., Cömert F., Akkoç S., and Coban B. (**2020**) Synthesis of naphthalimide derivatives with potential anticancer activity, their comparative ds- and G-quadruplex-DNA binding studies and related biological activities. *Mol. Biol. Rep.* 47(3), 1563-1572; DOI: https://doi.org/10.1007/s11033-019-05239-y
23. Varala R., Narayana V., Kulakarni S. R., Khan M., Alwarthan A., and Adil S. F. (**2016**) Sulfated tin oxide (STO)-Structural properties and application in catalysis: A review. *Arabian J. Chem.*, 9, 550-573; DOI: https://doi.org/10.1016/j.arabjc.2016.02.015
24. Dubasi N. S., and Varala R. (**2022**) Applications of sulfated tin oxide (STO) in organic synthesis-Update from 2016 to 2021. *Heterocycles*, 104 (5), 843-853; DOI: 10.3987/REV-22-978

Co-ordinator
IQAC
Shri Guru Buddhiswami Mahavidyalaya
Purna (Jn) Dist. Parbhani - 431511 (M.S.)

Shri Guru Buddhiswami Mahavidyalaya Purna (Jn.) Estd.1983

PRINCIPAL
Shri Guru Buddhiswami Mahavidyalaya
Purna (Jn.) Dist.Parbhani

25. Prasad C. S. N., Varala R., and Adapa S. R. (**2002**) A facile preparation of phthalimides and a new approach to the synthesis of indoprofen-Anti- inflammatory agent. *Heterocycl. Commun.*, 281-286; DOI: 10.1515/HC.2002.8.3.281
26. Varala R., and Adapa S. R. (**2005**) A practical and efficient synthesis of thalidomide via Na/liq.NH_3 methodology. *Org. Proc. Res. Dev.*, 9, 853-856; DOI: 10.1021/op050129z
27. Varala R., and Adapa S. R. (**2006**) A novel approach to the synthesis of (R,S)-Baclofen *via* Pd(II)-bipyridine catalyzed conjugative addition. *Synth. Commun.*, 36, 3743-3747; DOI: 10.1080/00397910600946249
28. Varala R., Alam M. M., and Adapa S. R. (**2003**) Bismuth triflate catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2(*1H*)-ones: An improved protocol for the Biginelli reaction. *Synlett*, 67-70; DOI: 10.1055/s-2003-36216
29. Ramu E., Kotra V., Bansal N., Varala R., and Adapa S. R. (**2008**) Green approach for the efficient synthesis of Biginelli compounds promoted by citric acid under solvent-free conditions. *Rasayan J. Chem.*, 1, 188-194
30. Varala R., Kotra V., Alam M. M., Kumar N. R., Ganapaty S., and Adapa S. R. (**2008**) Synthesis of mandelic acid derived phthalimides as a new class of anti-inflammatory and antimicrobial Agents. *Ind. J. Chem. Sec. B*, 47B, 1243-1248
31. Kotra V., Reddy V. V. R., Harika K. S., Babu B. H., Jayashree A., and Varala R. (**2014**) Synthesis of novel 5-carboxynaphthanilide dihydropyrimidine derivatives and evaluation of their biological activity. *Int. J. Pharm. Chem.Sci.*, 3, 915-921
32. Goud K. R., Pagadala R., Boodida S., and Varala R. (**2020**) SO_4^{-2}/SnO_2-catalyzed cyclo-condensation for the synthesis of fully-functionalized pyridines. *J. Het. Chem.*, 57, 923-928; DOI: 10.1002/jhet.3806
33. Pisal P. M., Sawant A. S., Kamble V. T., Varala R., Adil S. F., Khan M., and Siddiqui M. R. H. (**2020**) $ZrCl_4$-Catalyzed one-pot multi-component synthesis of hexahydropyrano pyrimidinone derivatives. *Org. Commun.*, 13, 28-32; DOI: http://doi.org/10.25135/acg.oc.72.20.02.1551.
34. Goud K. R., Pagadala R., Varala R., and Boodida S. (**2021**) An effective process for the synthesis of dihydropyridines *via* SO_4^{-2}/SnO_2 catalyzed Hantzsch reaction. *J. Chin. Chem. Soc.*, 68, 333-337; DOI: https://doi.org/10.1002/jccs.202000264
35. Prasad H., Ananda A., Mukarambi A., Gaonkar N., Sumathi S., Spoorthy H., and Mallu, P. (**2023**). Design, synthesis, and anti-bacterial activities of piperazine based phthalimide derivatives against superbug-Methicillin-Resistant *Staphylococcus aureus*. *Curr. Chem. Lett.*, 12(1), 65-78; DOI: 10.5267/j.ccl.2022.9.005
36. Manasa K., Sidhaye R V., Radhika G., and Nalini C. N. (**2011**) Synthesis, antioxidant activity of quinazoline derivatives.CPR, 1(2), 101.
37. Turner R. A. *Screening Methods in Pharmacology*, (Academic Press, New York), **1965**, 112.
38. Yassin O. M., Ismail S. M., Gameh M. A., Khalil F. A. F., and Ahmed E. M. (**2022**) Evaluation of chemical composition of roots of three sugar beets varieties growing under different water deficit and harvesting dates in Upper Egypt. *Curr. Chem. Lett.*, 11(1), 1-10; DOI: 10.5267/j.ccl.2021.11.003
39. Abdelgalil A., Mustafa A. A., Ali S. A. M., and Yassin O. M. (**2022**) Effect of irrigation intervals and foliar spray of zinc and silicon treatments on maize growth and yield components of maize. *Curr. Chem. Lett.*, 11(2), 219-226; DOI: 10.5267/j.ccl.2021.12.002
40. Abdel-Raheem S. A. A., El-Dean A. M. K., Abdul-Malik M. A., Marae I. S., Bakhite E. A., Hassanien R., Mohamed El-Sayed E. A., Zaki R. M., Tolba M. S., Sayed A. S. A., and Abd-Ella A. A. (**2022**) Facile synthesis and pesticidal activity of substituted heterocyclic pyridine compounds. *Rev. Roum. Chim.*, 67(4-5), 305-309; DOI: 10.33224/rrch.2022.67.4-5.09
41. Abd-Ella A. A., Metwally S. A., Abd ul-Malik M. A., El-Ossaily Y. A., Abd Elrazek F. M., Aref S. A., Naffea Y. A., and Abdel-Raheem S. A. A. (**2022**) A review on recent advances for the synthesis of bioactive pyrazolinone and pyrazolidinedione derivatives *Curr. Chem. Lett.*, 11 (2), 157-172; DOI: 10.5267/j.ccl.2022.2.004
42. Mohamed S. K., Mague J. T., Akkurt M., Alfayomy A. M., Seri S. M. A., Abdel-Raheem S. A. A., and Ul-Malik M. A. A. (**2022**) Crystal structure and Hirshfeld surface analysis of ethyl (3*E*)-5-(4-chlorophenyl)-3-{[(4-chlorophenyl)formamido]-imino}-7-methyl-2*H*,3*H*,5*H*-[1,3]thiazolo[3,2-*a*]pyrimidine-6-carboxylate. *Acta Cryst.* E78, 846-850; DOI: https://doi.org/10.1107/S205698902200603X
43. Kaid, M., Ali A. E., Shamsan A. Q. S., Younes S. M., Abdel-Raheem S. A. A., Abdul-Malik M. A., and Salem W. M. (**2022**) Efficiency of maturation oxidation ponds as a post-treatment technique of wastewater *Curr. Chem. Lett.*, 11(4), 415-422; DOI: 10.5267/j.ccl.2022.4.005
44. Kappe C. O. (**2000**). Biologically active dihydropyrimidones of the Biginelli-type-a literature survey. *Eur. J. Med. Chem.*, 35(12), 1043-1052; DOI: 10.1016/s0223-5234(00)01189-2
45. Sánchez-Sancho F., Escolano M., Gaviña D., Csáky A. G., Sánchez-Roselló M., Díaz-Oltra, S., Del Pozo S. (**2022**) Synthesis of 3,4-dihydropyrimidin(thio)one containing scaffold: Biginelli-like cactions. *Pharmaceuticals* 15(8), 948; DOI: 10.3390/ph15080948
46. Varala R. (**2006**) A facile synthesis of biologically active phthalimides & its analogues-A study, Ph. D Thesis, CSIR-IICT (http://www.csircentral.net/index.php/record/view/78721)
47. Neelottama K., and Kaushik D. (**2016**) Recent advances and future prospects of phthalimide derivatives. *J. Appl. Pharm. Sci.*, 6(3), 159-171; DOI: 10.7324/JAPS.2016.60330
48. Chen Z., Xu Y., Qian, X. (**2018**) Naphthalimides and analogues as antitumor agents: A review on molecular design, bioactivity and mechanism of action. *Chin. Chem. Lett.*, 29(12), 1741-1756; DOI: https://doi.org/10.1016/j.cclet.2018.09.020

Co-ordinator
IQAC
Shri Guru Buddhiswami Mahavidyalaya
Purna (Jn) Dist. Parbhani - 431511 (M.S.)

PRINCIPAL
Shri Guru Buddhiswami Mahavidyalaya
Purna (Jn.) Dist.Parbhani