



Duepetic Solvent based Synthesis and Characterization of different ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate derivative

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Abstract. The current study effectively synthesized a number of distinct ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate derivatives employing an effective and ecologically safe approach. Under ideal reaction circumstances, the synthetic method mainly used a one-pot multicomponent reaction with substituted aromatic aldehydes, ethyl acetoacetate, urea in presence of Duepetic Solvent (Choline Chloride+Sulphamic Acid, 20 mL) and Water (4 mL) are added. High yields, low reaction times, easy operation, and mild reaction conditions. The synthesized compounds were purified and characterized by IR spectroscopy, ¹H NMR, and ¹³C NMR. The study shows how adaptable and appropriate the established technology is for producing a broad variety of structurally varied pyrimidine derivatives. The results of this study offer a useful basis for more biological assessment and medication development research utilizing scaffolds based on pyrimidines. Background

Keywords: Phenylpyrimidine; Duepetic; Dihydropyrimidinones; Biginelli Reaction; DES

1. Introduction

This work described green chemistry as a systematic approach to developing chemical processes that reduce waste, consume less energy, and do not pollute. Proponents of green chemistry emphasize that it is innovative and knowledge-driven, and that it is essential to accomplishing the SDGs (Dobbelaar et al., 2024; Biswas et al., 2025). By connecting chemical advancements with sustainability principles, green chemistry provides a scientific path to cleaner industrial practices and a decrease in the environmental effect of chemical operations (Etzkorn & Ferguson, 2023; Leitner, 1999; Leitner, 1999). New catalyst-based synthesis techniques, eco-friendly alternatives to traditional organic solvents, such as supercritical CO₂, and the use of renewable raw materials to reduce dependency on petroleum-based chemicals are the three primary ways that green chemistry advances. These strategies support SDG 9 (Infrastructure, Innovation, and Industry) by stimulating sustainable industrialization and eco-friendly innovation (Winterton, 2001; Gunbatar et al., 2025; Jalil, 2025). Currently, the development of bio-based solvents to replace dangerous petrochemical solvents in industrial processes is a notable case study that modifies the idea of sustainable manufacturing practices with support for lower environmental risks and aids in the achievement of SDG 12 by supporting cleaner production. All things considered, green chemistry's focus on minimizing hazardous materials, maximizing resource efficiency, and utilizing renewable resources

significantly contributes to the achievement of the UN SDGs. These case studies demonstrate how important sustainable chemical innovation is to building a more equitable and sustainable world (Sah et al., 2025). Because it encourages a circular economy where waste is decreased and materials are reused, using renewable resources is crucial to green chemistry. This strategy focuses on creating environmentally suitable substitutes for conventional chemical processes, such as bio-based synthesis methods that reduce dependency on non-renewable resources by using enzymes, microorganisms, and plant extracts (Slootweg, 2024; Vats, 2022).

The synthesis of novel heterocyclic compounds remains a significant area of interest in medicinal and organic chemistry due to their diverse biological activities (Kabir & Uzzaman, 2022; Abbas, 2023; Heravi & Sadjadi, 2009; Slman et al., 2024). There are some molecules in the asymmetric unit, which are related by an approximate non-crystallographic two fold screw axis. The title compound's molecules have a zigzag configuration due to intermolecular N–HO hydrogen-bond interactions involving the O atoms of the keto groups and the hydrogen atoms of the amino groups (Kurbanova et al., 2009; Nizam et al., 2008; Cheng et al., 2007; Balasubramaniam et al., 2025). Yahia N. Mabkhot, et. Al synthesised Tetrahydropyrimidine Derivatives by mixture of 1,2,3,4-Tetrahydropyrimidine and dimethylformamide-dimethyl in dry xylene was refluxed for 3 h, to give compound Ethyl 6-(2-(dimethylamino)vinyl)-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (Farak et al., 2011).

For the Biginelli reaction, a very effective, environmentally friendly, and reusable procedure has been created. Jagtap et al used biowaste curd water as a catalyst and environmentally friendly solvent to create derivatives of dihydropyrimidinones (Jagtap et al., 2021).

Because of their low toxicity, biodegradability, ease of manufacture, and adjustable physicochemical features, deep eutectic solvents (DESs) have become a class of environmentally friendly and sustainable solvents (Smith et al., 2014). DESs are usually created by combining a hydrogen bond donor (HBD) with a hydrogen bond acceptor (HBA), like choline chloride (ChCl), to create a eutectic combination having a melting point much lower than that of the constituent parts (Wong et al., 2025).

2. Methods

2.1. Experimental

Preparation of DES:- Choline chloride and sulfuric acid were combined in a round-bottom flask at a molar ratio of 3:5 (with a water concentration of 5.5% by weight) to create DES mixes. The flask was then placed in a water bath and continuously stirred for 30 minutes at 100 °C until the ChCl was completely dissolved, forming the clear liquid depicted in scheme 1. Once the viscous liquid had been fully delignified, the boiler was cooled by filtering on a Büchner funnel under reduced pressure. The thick liquid was divided and kept in bottles.

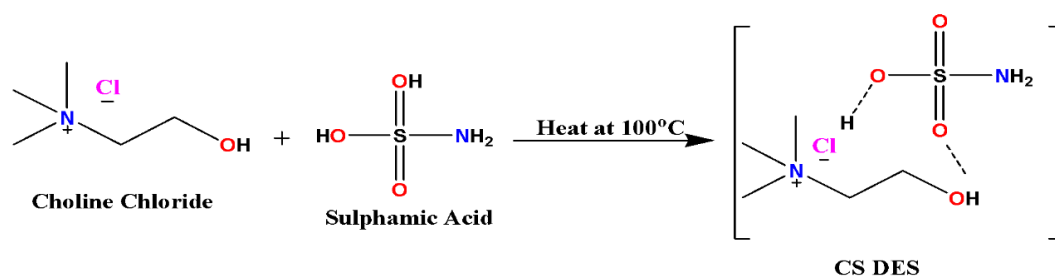


Figure 1. Scheme of the Preparation of deep eutectic solvents

2.2. Preparation of different substituted Ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine - 5 - carboxylate

A deep eutectic solvent made of choline chloride and sulphamic acid (20 mL) and water (4 mL) was added to a round-bottom flask with a cooling system. Aldehyde (12 mmol), urea (12 mmol), and ethyl acetoacetate (8 mmol) were added to this combination. To promote the reaction depicted in Scheme 2, the resultant reaction mixture was constantly stirred at room temperature for about 1.5 hours using a magnetic stirrer.

After completion of the reaction, the mixture was filtered, and the solid residue was washed with a small amount of water and recrystallised by ethanol. The synthesized compound 4a-4j (fig:1) have been characterized by using FT-IR, ^1H -NMR and ^{13}C -NMR spectral studies. DMSO- d_6 was used as a solvent for ^1H and ^{13}C NMR spectra on a Bruker EQUINX55 (400 MHz for ^1H NMR; 101 MHz for ^{13}C NMR) spectrometer.

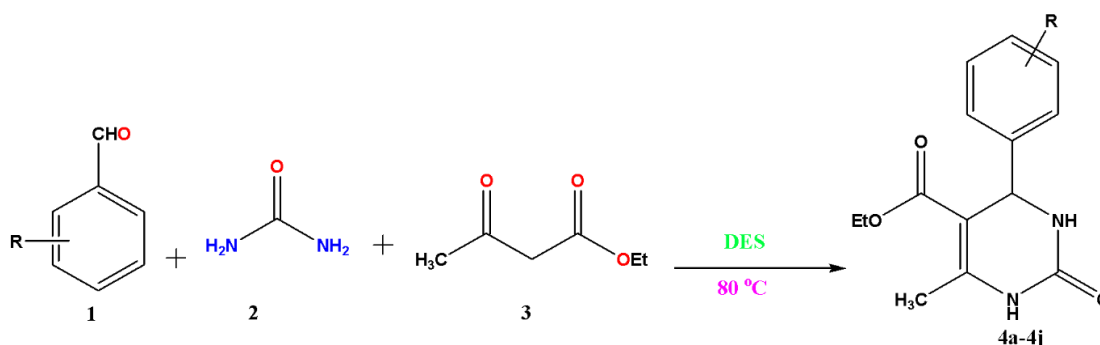


Figure 2. Scheme of the Synthesis of compound 4a to 4j

2.3. Characterizations of DES

2.3.1. FT-IR Spectra of DES

The intermolecular interactions between the hydrogen bond choline chloride and sulphamic acid were examined by recording the FT-IR spectrum of the produced DES. The effective synthesis of the DES and the development of hydrogen bonding networks were verified by characteristic absorption bands. O-H (3400 cm^{-1}) (broad band) shows strong Hydrogen bond, C-H (2930 cm^{-1}) shows stretching vibration, N-C (1620 cm^{-1}) shows carbon carbon double bond, R-SO $_3\text{H}$ (1207 cm^{-1}) confirms sulphonic acid as functional group.

2.3.2. SEM Images of DES Before Use

The material exhibits a highly porous, cavernous, and irregular surface structure with visible voids and deep cavities. This open framework maximizes the available surface area for chemical interactions or adsorption.

2.3.3. SEM Images of DES After Use

The surface morphology transforms significantly, appearing smoother, more continuous, and noticeably filled or covered. The sharp porous features are masked, indicating that a chemical reaction, adsorption process, or structural aggregation has occurred during use.

2.3.4. XRD Patterns of DES at Different Temperatures

In XRD spectra shows the X-ray Diffraction (XRD) patterns of a Deep Eutectic Solvent (DES) at three different temperatures, illustrating a transition from a crystalline solid state to an amorphous liquid state as temperature increases.

- **At 25 °C (Crystalline State):** Displays distinct, sharp diffraction peaks. This indicates a highly ordered solid structure with long-range atomic
- **At 35 °C (Transition State):** Shows a combination of smaller sharp peaks superimposed on a growing broad background. This represents a partial melting or semi-crystalline phase where the crystal lattice begins to break down.
- **At 45 °C (Amorphous/Liquid State):** Features a smooth, broad hump (amorphous halo) without sharp peaks. This confirms the complete absence of long-range structural order, showing that the substance has fully melted into a liquid.

The graph provides clear evidence of a temperature-induced phase transition, where heating the DES disrupts the rigid crystal lattice and converts it into a disordered fluid.

2.3.5 XPS Spectrum of DES

The elemental composition and chemical states of the DES were examined using X-ray photoelectron spectroscopy (XPS). The XPS spectra demonstrated the interactions that led to the development and stability of the deep eutectic solvent and verified the existence of distinctive elements.

2.4. Characterizations of different substituted Ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine - 5 - carboxylate

2.4.1. Ethyl 1,2,3, 4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate (4a)

Color: White solid. Yield: 80%. M.P.: 202°C, ¹H NMR (400 MHz): δ = 1.09(t, 3H), 2.25(s, 3H), 3.99(q, 2H), 5.15(s, H), 7.24-7.34(s, 2H), 7.74(s, NH), 9.19(s, NH) ppm; ¹³C NMR (100 MHz): δ = 20, 40, 50, 55, 100, 128, 130, 132, 145, 150, 155, 166 ppm; MS (ESI): m/z 260.29 [M+1].

2.4.2. Ethyl 1,2,3,4-tetrahydro - 4 - (4 - methoxyphenyl) - 6 - methyl - 2 - oxopyrimidine - 5 carboxylate (4b)

Color: Yellow solid Yield: 88%. M.P.: 200°C, ¹H NMR (400 MHz): δ = 1.10 (t, 3H), 2.26(s, 3H), 3.96(s, 3H), 3.97(q, 2H), 5.13(s, H), 7.16-7.18(s, 4H), 7.70(s, NH), 9.19(s, NH) ppm; ¹³C NMR (100 MHz): δ = 20, 39, 50, 52, 55, 98, 112, 130, 140, 150, 155, 160, 167 ppm; MS (ESI): m/z 290.12 [M+1].

2.4.3. Ethyl 1, 2, 3, 4 - tetrahydro - 4 - (3, 4 - dimethoxyphenyl) - 6 - methyl - 2 - oxopyrimidine - 5 - carboxylate (4c)

Color: White solid Yield: 84%. M.P.: 140 °C, ¹H NMR (400 MHz): δ = 1.12 (t, 3H), 2.27(s, 3H), 3.98(s, 3H), 4.00 (q, 2H), 5.13(s, H), 6.68(s, H), 6.90(dd, 2H), 7.70(s, NH), 9.98 (s, NH) ppm;

¹³C NMR(100 MHz): δ =13,18, 40, 100, 108, 110, 118, 148, 152, 165 ppm; MS (ESI): m/z 320 [M+1].

2.4.4. Ethyl 1, 2, 3, 4 - tetrahydro - 6 - methyl - 2 - oxo - 4 - p - tolylpyrimidine - 5 - carboxylate (4d)

Color: White solid Yield: 90%. M.P.: 204 °C, ¹H NMR (400 MHz): δ = 1.10(t, 3H), 2.25-2.26 (s, 6H), 3.39(q, 2H), 5.12(s, H), 7.12-7.25(s, 4H), 7.69(s, NH), 9.16(s, NH) ppm; ¹³C NMR (100 MHz): δ =12,18, 20,40, 55, 60, 100, 125, 130, 138, 142, 152, 166 ppm; MS (ESI): m/z 274 [M+1].

2.4.5. Ethyl 1, 2, 3, 4 - tetrahydro - 4 - (3 - methoxyphenyl) - 6 - methyl - 2 - oxopyrimidine - 5 - carboxylate (4e)

Color: Light yellow solid Yield: 86%. M.P.: 250°C, ¹H NMR(400 MHz): δ = 1.11 (t, 3H), 2.26(s, 3H), 3.98(s, 3H), 4.1(q, 2H), 5.16(s, H), 6.83(s, 3H), 7.22(s, H), 7.75(s, NH), 9.21 (s, NH) ppm; ¹³C NMR (100 MHz): δ =20, 40, 50, 56, 58, 100, 115, 128, 148, 154, 160, 168 ppm; MS (ESI): m/z 290 [M+1].

2.4.6. Ethyl 4 - (4 - fluorophenyl) - 1, 2, 3, 4 - tetrahydro - 6 - methyl - 2 - oxopyrimidine - 5 - carboxylate (4f)

Color: White solid;Yield: 89%. M.P.: 186°C, ¹H NMR(400 MHz): δ = 1.09(t, 3H), 2.26(s, 3H), 3.99(q, 2H), 5.16(s, H), 7.12(m, 2H), 7.18(m, 2H), 7.29(s, NH), 9.23(s, NH); ¹³C NMR (100 MHz): δ = 16, 18, 40, 55, 60,100, 115, 130, 140, 150, 153, 160 165, 170, MS (ESI): m/z 278 [M+1].

2.4.7. Ethyl 1, 2, 3, 4-tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxopyrimidine-5-carboxylate (4g)

Color: Light yellow solid; Yield: 87%. M.P.: 234°C, ¹H NMR (400 MHz): δ = 1.09 (t, 3H), 2.28 (s, 3H), 3.40(s, H), 3.99(q, 2H), 5.33(s, H), 7.65(m, 2H), 7.72(m, 2H), 7.91(s, NH), 9.38(s, NH); ¹³C NMR(100 MHz): δ = 18, 20, 40,54. 60, 100, 124, 126, 130, 135, 150, 154, 158, MS (ESI): m/z 305.22 [M+1].

2.4.8. Ethyl 4-(3-bromophenyl)-1, 2, 3, 4 - tetrahydro - 6 - methyl - 2 - oxopyrimidine - 5 - carboxylate (4h)

Color: Yellow solid; Yield: 90%. M.P.: 194°C, ¹H NMR (400 MHz): δ = 1.10(t, 3H), 2.28(s, 3H), 4.00(q, 2H), 5.18(s, H), 7.30(m, 2H), 7.31(m, 2H), 7.43(s, NH), 9.29(s, NH); ¹³C NMR (100 MHz): δ =14.1, 17.9, 53.7, 59.4, 98.7, 121, 125, 129, 130, 130.2, 147, 149, 152, 165 MS (ESI): m/z 338.12 [M+1].

2.4.9. Ethyl 4-(2-chlorophenyl)-1,2,3,4-tetrahydro-6-methyl-2-oxopyrimidine-5-carboxylate (4i)

Color: White solid; Yield: 92%. M.P.: 192°C, ¹H NMR (400 MHz): δ = 0.99 (t, 3H), 2.33(s, 3H), 3.90(q, 2H), 5.65(s, H), 7.13(s, H), 7.17(s, 2H), 7.57(s, H), 7.72(s, NH), 9.33(s, NH); ¹³C NMR (100 MHz): δ = 14.0, 17.7, 54.1, 59.1, 98.5, 122.4, 128.5, 128.8, 129,132, 143,149,151,165, MS (ESI): m/z 294.12 [M+1].

2.4.10. Ethyl 4-(2-bromophenyl)-1, 2, 3, 4 - tetrahydro - 6 - methyl - 2 -oxopyrimidine - 5 - carboxylate (4j)

Color: White solid; Yield: 88%. M.P.: 290°C, ^1H NMR (400 MHz): δ = 0.99(t, 3H), 2.32(s, 3H), 3.89(q, 2H), 5.67(s, H), 7.23-7.39(m, 4H), 7.74(s, NH), 9.32(s, NH); ^{13}C NMR (100 MHz): δ = 13.7, 17.7, 51.6, 59.1, 98, 127, 128, 129.1, 129.4, 131, 141, 149, 151, 160 MS (ESI): m/z 338.12 [M+1].

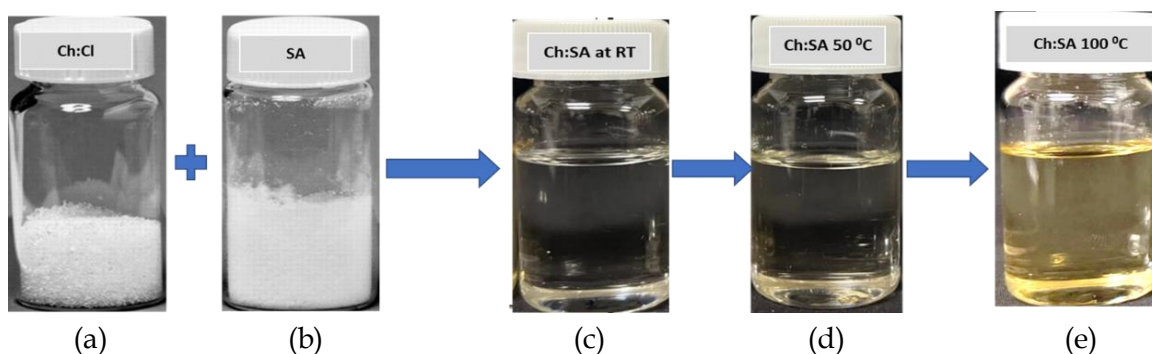


Figure 3. Preparation of deep eutectic solvents (DES): (a) Choline chloride; (b) Sulphamic acid; (c) Choline chloride: Sulphamic acid at room temperature; (d) Choline chloride: Sulphamic acid at 50 °C temperature; (e) Choline chloride: Sulphamic acid at 100 °C temperature

Strong intermolecular interactions inside the DES are facilitated by sulphamic acid, an efficient hydrogen bond donor that increases the DES's acidity and catalytic potential. An acidic DES is created when choline chloride and sulphamic acid are combined. This DES is very helpful in processes like delignification of lignocellulosic biomass, where effective lignin removal is necessary for subsequent cellulose and hemicellulose valorization. Reducing viscosity, enhancing mass transfer, and promoting improved interaction with the biomass matrix are all made possible by the DES system's controlled water content.

DES is a desirable substitute for traditional solvents because its preparation is typically simple and doesn't require complicated purification procedures. Through hydrogen bonding interactions, a homogenous and stable liquid is formed when the components are heated and stirred at the proper molar ratio. Selective delignification, disruption of lignin-carbohydrate complexes, and effective penetration of biomass structure are all made possible by the ensuing viscous liquid. Following treatment, the DES and treated material can be recovered using separation methods including filtration under low pressure. This strategy maximizes efficiency and recyclability while avoiding harmful chemicals and energy consumption, which is consistent with green chemistry principles.

3. Results and Discussion

In present work we have synthesised different substituted Ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate. Choline chloride-based mixes are extensively investigated among DES systems due to their low cost, environmental friendliness, and high efficiency in organic transformations and biomass processing. Here, we report a synthesis a new molecule. In round-bottomed flask fitted with a cooling device, Deepertic Solvent (Choline Chloride+Sulphamic Acid, 20 mL) and Water (4 mL) are added. aldehyde (12 mmol), urea (12 mmol), and ethyl acetoacetate (8 mmol) are introduced into the solution, which is then magnetically stirred at RT for 1.5 hours to allow for a reaction shown

in Scheme:-2. The mixture is subsequently filtered and rinsed with 1 to 2 mL water. The product obtained is recrystallized using ethanol and reaction was monitored by TLC. The synthesized compound 4a-4j shown in fig:1 On completion of the reaction, a solid mass precipitated out, filtered washrd with aq. ethanol. Prepared compounds 4a-f characterized by using sophisticated techniques such as IR, ^1H NMR and ^{13}C NMR etc. The optimization of reaction conditions and yields for compounds(4a-4j)are summarized in Table 1.

Table 1. Optimizations of the reaction conditions for the Synthesis of Compound 4a-4j

Compound	Time (Min)	Yields (%)	Color	M.P. ($^{\circ}\text{C}$)
4a	85	80	White solid	202
4b	90	88	Yellow solid	200
4c	86	84	White solid	140
4d	90	90	White solid	204
4e	80	86	Light yellow solid	250
4f	88	89	White solid;	186
4g	92	87	Light yellow solid	234
4h	86	90	Yellow solid	194
4i	95	92	White solid	192
4j	90	88	White solid	290

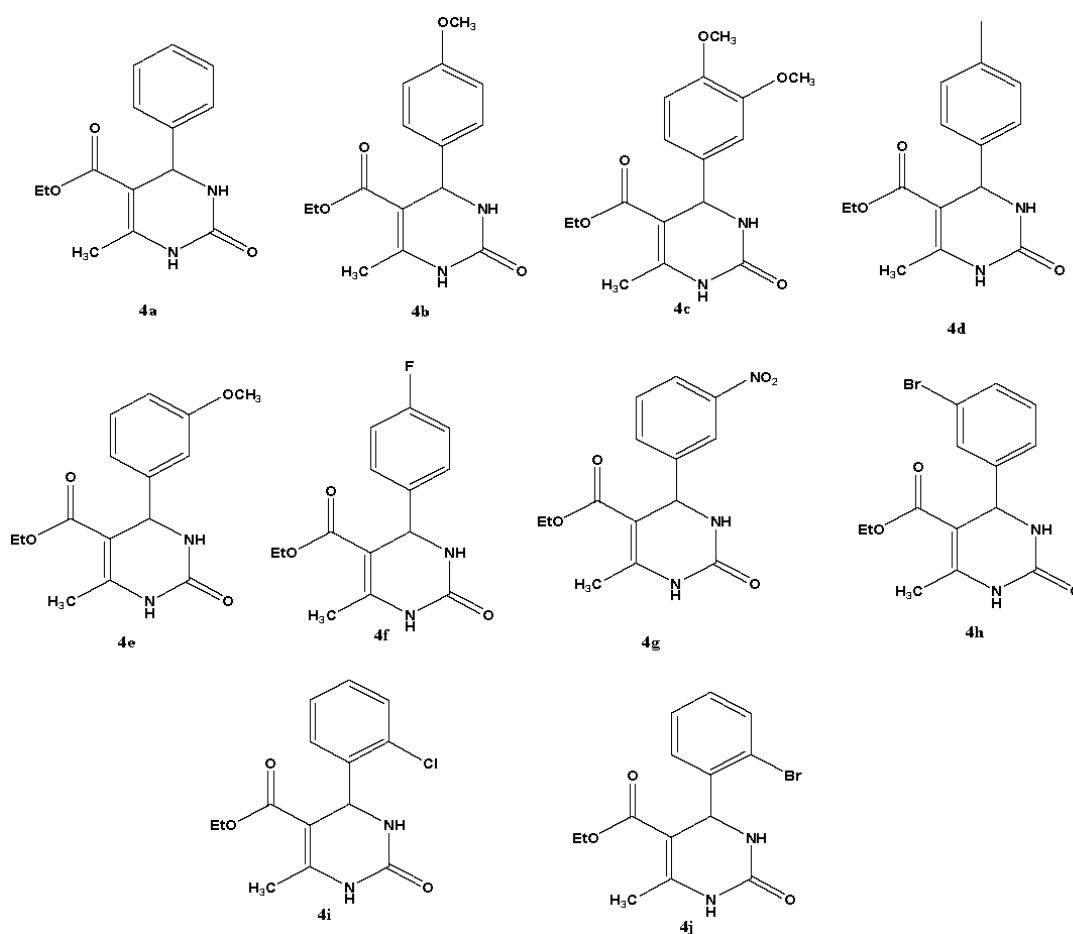


Figure 4. Synthesized different substituted pyrimidine

Strong intermolecular interactions inside the DES are facilitated by sulphamic acid, an efficient hydrogen bond donor that increases the DES's acidity and catalytic potential. An acidic DES is created when choline chloride and sulphamic acid are combined. This DES is very helpful in processes like delignification of lignocellulosic biomass, where effective lignin removal is necessary for subsequent cellulose and hemicellulose valorization. Reducing viscosity, enhancing mass transfer and promoting improved interaction with the biomass matrix are all made possible by the DES system's controlled water content.

Conclusions

A straightforward, effective, and environmentally safe approach for the synthesis of several substituted ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate derivatives (4a-4j) has been created in this study. A DESs system made of sulphamic acid and choline chloride proved to be very successful, providing gentle reaction conditions, ease of use, and a shorter reaction time. At room temperature, the reaction went well, demonstrating the protocol's sustainability and eco-friendliness. The methodology demonstrated good tolerance toward a variety of substituted aldehydes, leading to satisfactory yields of the desired pyrimidine derivatives ie substituted Ethyl 1, 2, 3, 4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate.

There was no need for complicated workup methods because the products were readily separated by straightforward filtration and purified by recrystallization. The suggested structures and the spectral data agreed well. All things considered, this study provides a successful, affordable, and sustainable synthetic route for the production of pyrimidine derivatives with biological significance. The method may be used more in medicinal chemistry and drug discovery due to the structural significance of pyrimidine scaffolds. These findings lay the foundation for next biological studies and optimization targeted at producing powerful bioactive substances.

Acknowledgments

The authors would like to express their gratitude towards all the colleagues and contributors for their continuous support throughout this investigation. VKK also thanks to Head, Department of Chemistry & Principal of Badrinarayan Barwale Mahavidyalaya Jalna and Head, Department of Chemistry & Principal P. S. P. Mandal's, Pratishthan ASC Mahavidyalaya Paithan, District Chhatrapati Sambhajanagar.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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