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(RESEARCH ARTICLE)

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Aqueous extract of *Sea buckthorn* berries: A greener and ecofriendly medium for synthesis of pyrazolopyranopyrimidines

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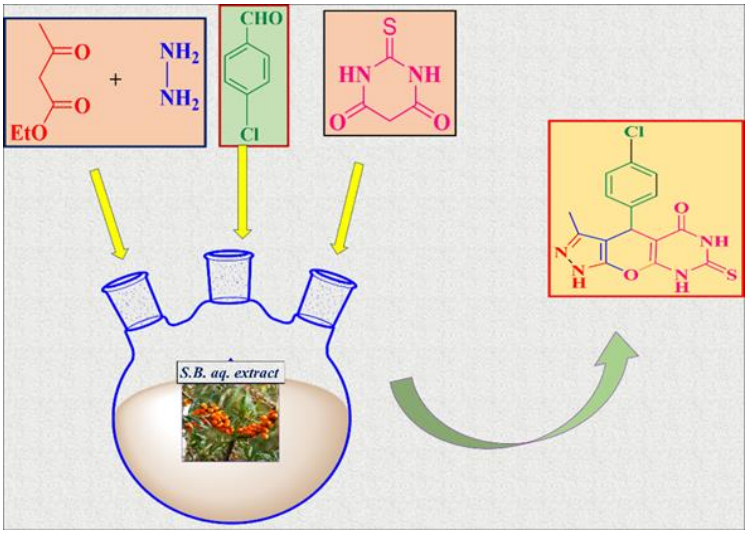
Abstract

Sustainable development and environmental consciousness have become increasingly important, leading to a revolution of industrial processes and organic synthesis methods. The use of organic solvents and their associated emissions has emerged as a significant environmental issue. Consequently, there is a growing emphasis on finding substitutes for volatile solvents and halogenated organic solvents in various synthetic processes. This study focuses on a greener and more eco-friendly approach to synthesizing pyrazolopyrimidine derivatives using sea buckthorn aqueous extract as a sustainable medium. Sea buckthorn berries, rich in phenolic compounds, fatty acids, and vitamins A, C, E, along with high organic acid content, are conducive to multicomponent reactions. Pyrazolyl derivatives are of particular interest due to their role as essential components in various biologically active compounds. Overall, this methodology offers a green and environmentally sustainable alternative to current protocols, with positive implications for both sustainability and economic factors. Additionally, Sea buckthorn berry extract proves to be a recyclable medium, with minimal decrease in product yields upon recycling.

Keywords: Sea Buckthorn; Biocatalyst; Ecofriendly; Multicomponent reaction; pyrazolopyranopyrimidines

Graphical Abstract



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1. Introduction

In recent years, there has been a significant focus on enhancing the sustainability of chemical processes by adopting green chemistry principles [1]-[3]. This effort also involves reducing the use of toxic and hazardous solvents and reagents, while incorporating renewable raw materials [4]. However, despite these advancements, meeting sustainability criteria remains a considerable challenge. One prominent concern revolves around the environmental risks associated with volatile organic solvents. The consumption of solvents during organic transformations is notably higher than that of reagents and the solvents used are often difficult to recycle [5]. To adhere to green chemistry principles, the primary objective is to substitute volatile organic solvents with environmentally friendly alternatives, commonly referred to as "green solvents" [6]. This shift is crucial for aligning chemical processes with sustainability goals and minimizing environmental impact.

In contemporary times, biosynthetic processes utilizing biobased solvents or catalysts have garnered significant attention as promising alternatives for the advancement of green methodologies in organic synthesis [7]-[9]. In accordance with the demand for more sustainable chemistry, the search for more environmentally benign forms of catalysis has received irresistible attention, and one of the leading contestants for environmentally acceptable alternatives is the category of biodegradable and renewable materials [10]. Already, several biodegradable materials, such as chitosan [11], starch [12], glycerol [13], Gluconic acid [14], sulfuric acid-modified PEG (PEG-OSO_3H) [15-16], melamine trisulfonic acid (MTSA) [17]. In addition, a number of organic reactions using natural catalysts such as clay [18]-[20], natural phosphate [21], animal bone [22],[23] and also various fruits juices [24] are reported in the literature. Consideration of nature and environmental sustainability, particularly concerning plants, which represent the most abundant and renewable natural resources is crucial and irreplaceable. Each component, comprising bark, leaves, berries, shells and seeds, harbors a wide array of phytoconstituents such as vitamins, proteins, pectin, starch, sugars, cellulose, polyphenols, flavonoids, lignin, ash, volatile oils, organic acids, and bases. Due to their acidic nature, aqueous fruit juices like those from lemon [25], pineapple [26], coconut [27], *Acacia concinna* [28], *Piper longum* [29] and *Tamarindus indica* [30] have been found to be a suitable replacement for various homogeneous acid catalysts. These diverse chemical constituents are not only beneficial but also serve as a source of inspiration across various scientific domains. Sea buckthorn (SB) has global recognition lately, largely due to its extensively documented traditional uses as well as its medicinal and nutritional value attributed to compounds such as tannins, flavonoids, sterols, carotenoids, tocopherols, and lipids [31]. Over the past decade, numerous studies have highlighted the correlation between SB berries and products with diverse health advantages. This is attributed to the rich content of organic acids, amino acids, sugars, and vitamins found in its fruits contributing a large source of Vitamin C greater than any known fruits and vegetables [32].

Functionalized N-heterocycles are significant in drug discovery, paralleled by the market scrutiny of medications, given pyrimidine's integral role in DNA and RNA within numerous biological functions. Fused pyrazolo and pyrimidine scaffolds hold notable pharmacological significance, especially concerning nucleoside and nucleotide antibiotics, antibacterials, cardiovascular treatments, agrochemicals and veterinary pharmaceuticals [33]. Therefore, the development of a novel method for synthesizing fused heterocyclic compounds is deemed essential in biological science. The enhancing of the biological potential of heterocycles fused pyrimidine ring could be achieved as many conventional drugs encompass this strategy namely, Imatinib, Methotrexate, Imatinib, dasatinib used for cancer therapy approved by US Food and Drug Administration [34].

Considering the aforementioned factors and our continuous efforts in advancing multicomponent reactions and environmentally friendly synthetic methods, we present *Sea Buckthorn* berries aqueous extract as a bio-based catalyst for the one-pot synthesis of pyrazolopyranopyrimidine. This synthesis involves a four-component reaction comprising ethyl acetoacetate, hydrazine hydrate, aromatic aldehydes and barbituric acid. We hypothesized that this remarkable medium could offer a preferable substitute for chemical surfactants and corrosive acids attained to the development of new green approach.

2. Materials and Methods

2.1. General remarks

Solvents and reagents were procured commercially from Sigma Aldrich and utilized without additional purification. Melting points were determined using an open capillary method and are reported without correction. Infrared spectra were acquired using a Perkin Elmer FT-IR spectrophotometer, with samples examined as KBr discs at a concentration of 5% w/w. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker AC spectrometer (300 MHz for ^{1}H NMR and 75

MHz for ^{13}C NMR) using $CDCl_3$ and DMSO-d6 as solvents. Chemical shifts are denoted in parts per million (ppm) with tetramethylsilane (TMS) as the internal reference, and coupling constants are expressed in Hertz (Hz). Mass spectra were recorded using a Shimadzu QP2010 GCMS instrument.

2.2. Preparation of *Sea Buckthorn* aqueous extract

Firstly, 2g *Sea Buckthorn* berries were finely crushed into the powder using mortar and transferred into the beaker containing 100 mL of distilled water. The beaker was then subjected to heating at 70°C for 45 min. Afterwards, the solution was filtered out using Whatmann paper 41 and the filtrate was stored at 4°C for further utilization**.**

2.3. General procedure for the synthesis of pyrazolopyranopyrimidines

In a round bottom flask, stirred a mixture of ethyl acetoacetate (1mmol) and hydrazine hydrate (1 mmol) at room temperature. To this solution substituted aldehyde (1mmol), thiobarbituric acid (1 mmol) and catalyst SB extract (10 mol %) were added. The reaction mixture was stirred for stipulated time and reaction progress was monitored by thin layer chromatography (Methanol: DCM, 7:3). After completion of the reaction the solid product was filtered and washed with water. The synthesized compounds were identified by comparing physical and spectral data. [FT-IR ,^1H NMR, ^{13}C NMR and MS techniques]

3. Result and discussion

Initially, our focus was on preparing an aqueous solution using *Sea Buckthorn* berries. To achieve this, the dried berries of *Sea Buckthorn* were crushed into a fine powder. Subsequently, 5 g of the powder was transferred into the beaker containing 100 mL of distilled water. The beaker was heated at 70 °C for 45 min. The resulting solution was then filtered and the yellow buff coloured solution was stored at 4 °C for further utilization.

Table 1 Qualitative phytochemical analysis of SB aq. extract

Sr.no.	Phytoconstituents	Result
1.	Carbohydrates	+
2.	Tannin	+
3.	Flavonoids	+
4.	Quinones	+
5.	Glycosides	-
6.	Terpenoids	+
7.	Phenols	+
8.	Coumarins	+
9.	Steroids	-
10.	Acids	+

(+) present; (-) absent

Next, we focused our attention towards synthesis of pyrazolopyranopyrimidine derivatives. In the initial phase, we conducted a model one-pot four-component reaction involving EAA (1), hydrazine hydrate (2), thiobarbituric acid (3a), and benzaldehyde (4) in 5 mL of aqueous SB extract. The reaction mixture was stirred at ambient temperature in an open air. The progress of the reaction was monitored by TLC. We were delighted to note that the model reaction proceeded smoothly affording the corresponding product pyrazolopyranopyrimidine (5a) with 95 % yield within 25 min. The most striking feature of the protocol was facile separation of the product from the reaction mixture. The product precipitates out after the completion of the reaction and can be separated by simple filtration. Thus, the acidic nature of the aqueous extract, combined with the surface activity resulting from phytoconstituents, synergistically facilitated the rapid progression of the reaction within a short time. (Figure 1)

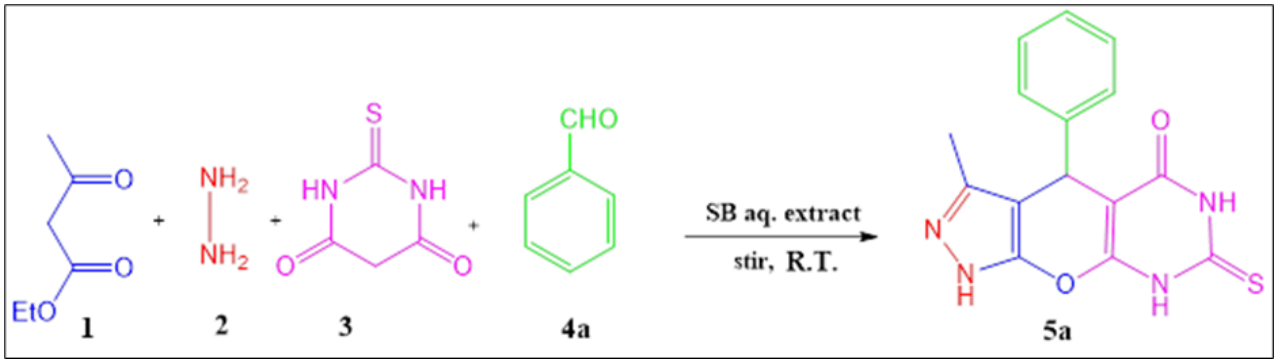


Figure 1 General procedure for the synthesis of pyrazolopyranopyrimidine.

In order to assess the impact of temperature on product yield, the model reaction was conducted at different temperature. Interestingly, the results revealed no discernible effect on the product yield, even with significantly diluted clear solutions. (Table 2)

After the optimization of reaction conditions, the generality of the protocol was established by reacting ethyl acetoacetate (1), hydrazine hydrate (2), thiobarbituric acid (3) with structurally diverse aryl aldehyde (4a). The reaction proceeded smoothly affording the desired pyrazolopyranopyrimidine derivatives in high yield within short reaction time. No anomalies were observed during the reaction. It is noteworthy to mention that the aryl aldehydes bearing electron donating as well as electron withdrawing substitutes reacted equally efficiently affording the corresponding pyrazolopyranopyrimidine derivatives in excellent yields. In addition, sterically congested aryl aldehydes also reacted efficiently, providing the desired pyrimidine derivatives in good yields. Moreover, heteroaryl aldehydes such as thiophene-2-aldehye reacted successfully affording the desired product in high yield.

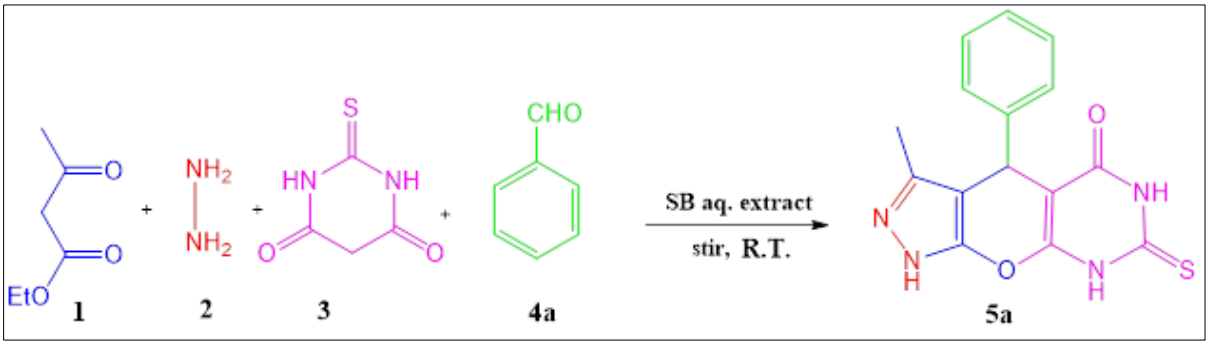


Figure 2 Optimization of reaction conditions in the synthesis of pyrazolopyranopyrimidine

Table 2 General synthesis of pyrazolopyranopyrimidine at optimized reaction temperature using SB aq. extract

Sr. no.	Amount of SB extract (mL)	Temperature (°C)	Reaction time (min.)	% Yield[b]
1	**5**	**RT**	**20**	**93**
2	5	40	22	87
3	5	50	39	84
4	5	60	24	84
5	5	80	30	83
6	5	100	-	No product

[a] Reaction conditions: Ethyl acetoacetate (1.0 mmol), hydrazine hydrate (1 mmol), benzaldehyde (1.0 mmol) and thiobarbituric acid (1.0 mmol) in 5 mL *Sea Buckthorn* aq. extract.[b]

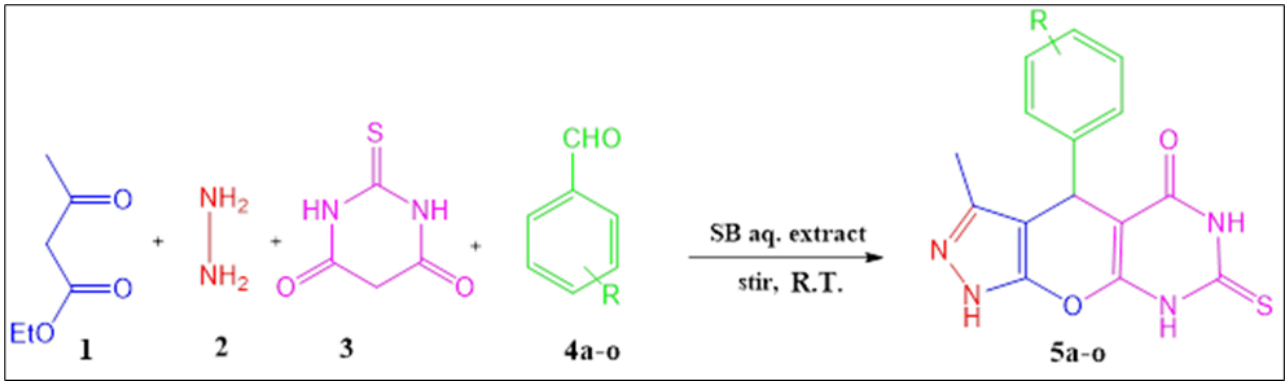
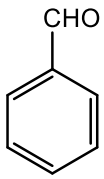
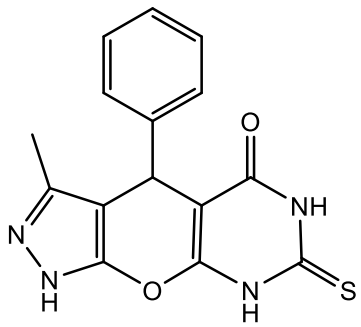
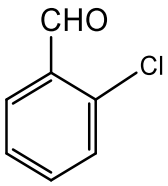
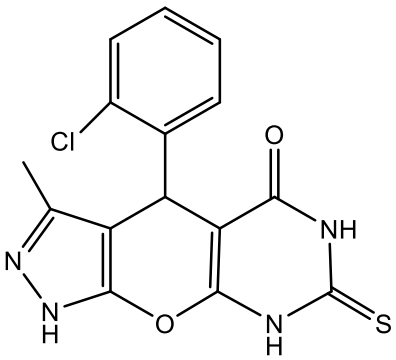
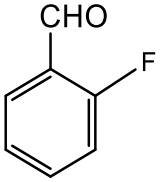
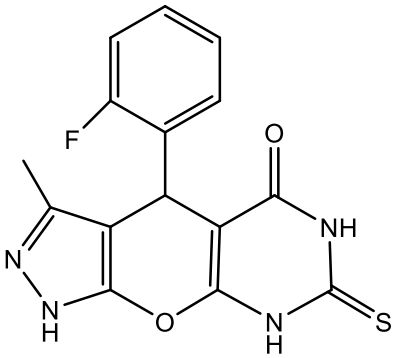
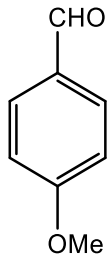
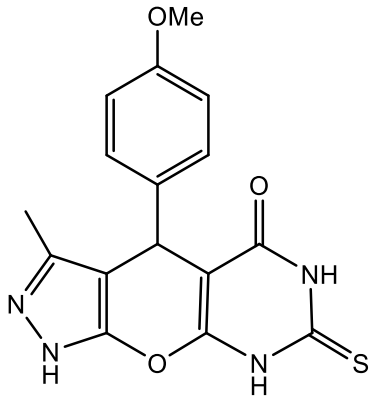
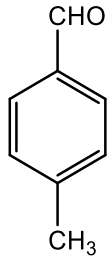
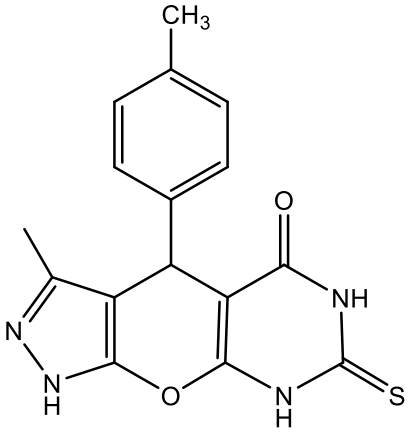
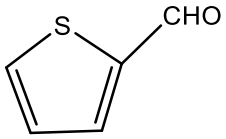
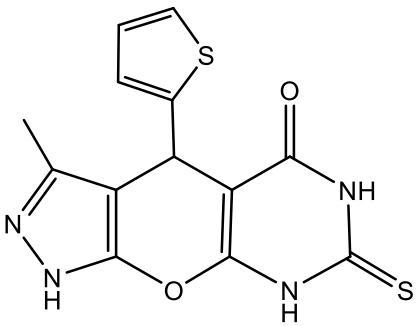
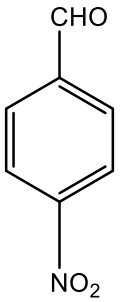
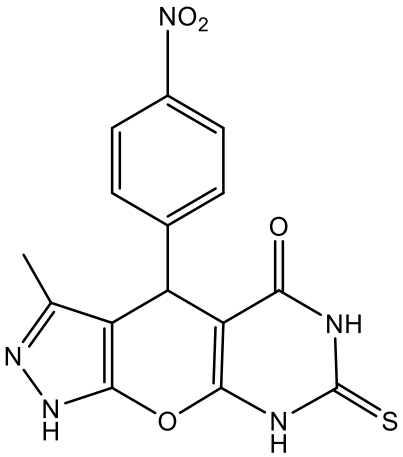
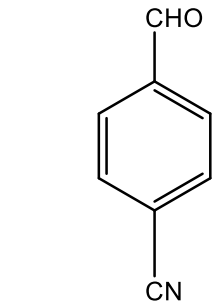
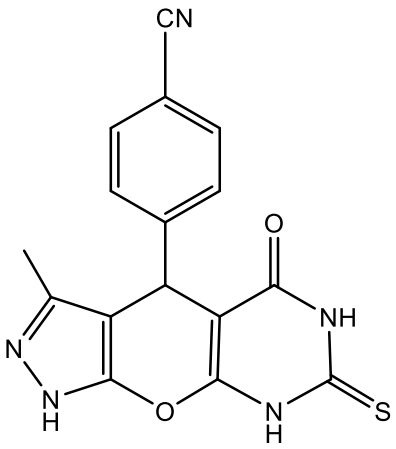
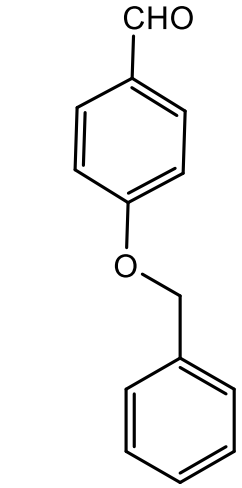
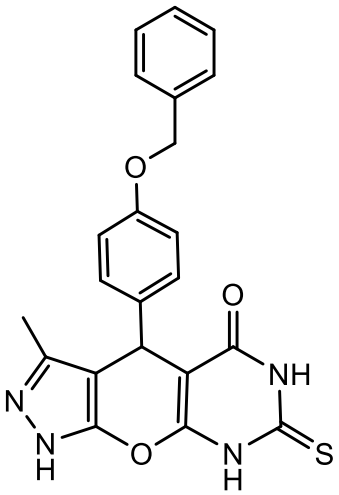
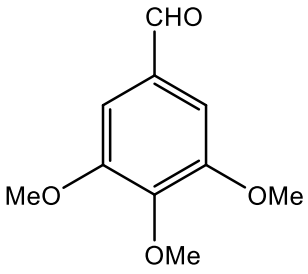
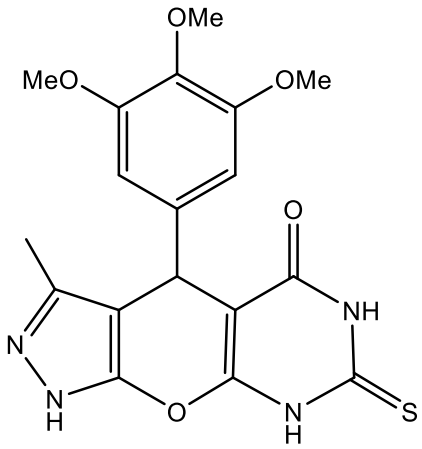


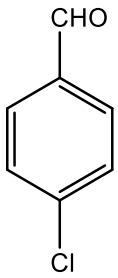
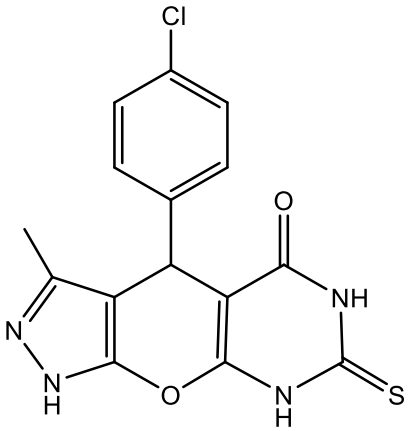
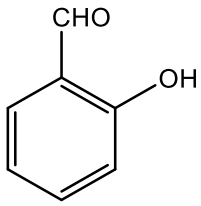
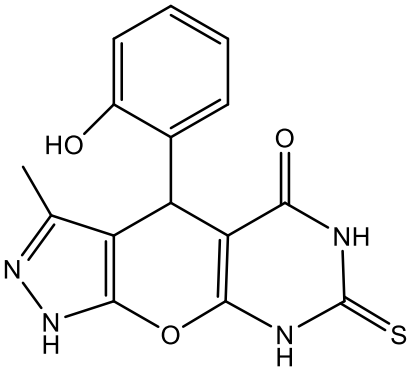
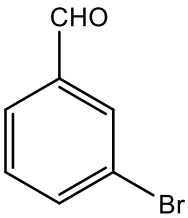
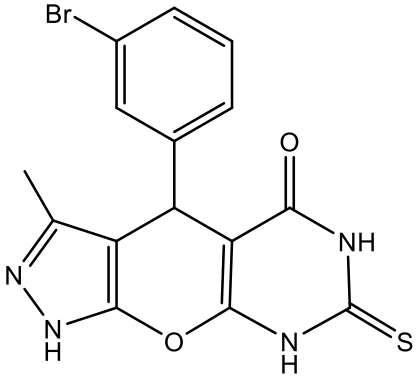
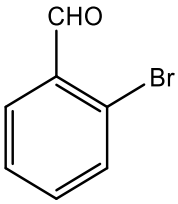
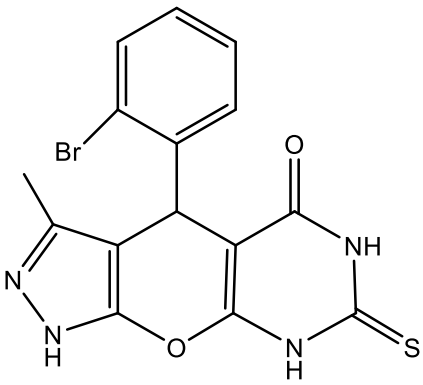
Figure 3 SB aq. extract as a green medium for synthesis of pyrazolopyranopyrimidine

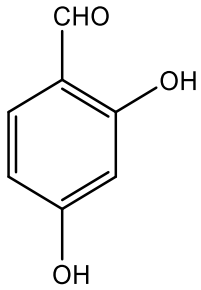
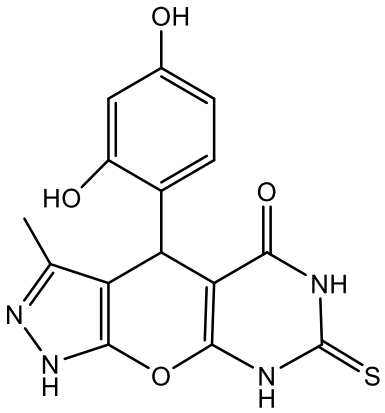
Table 3 Synthesis of pyrazolopyranopyrimidine derivatives using SB aq. extract at optimized reaction conditions

Sr. no.	Aryl aldehyde (4)	Product (5)	Reaction time (min.)	Product yield (%)[b]
a			25	95
b			30	91
c			25	93

d			30	85
e			30	88
f			25	84
g			20	92

h			40	90
i			35	88
j			30	85

k			25	90
l			30	89
m			30	88
n			30	86

o			30	84

[a] Reaction conditions: Ethyl acetoacetate (1.0 mmol), hydrazine hydrate (1 mmol), benzaldehyde (1.0 mmol) and thiobarbaturic acid (1.0 mmol) in 5 mL SB aq. extract at ambient temperature. Isolated yield[b]

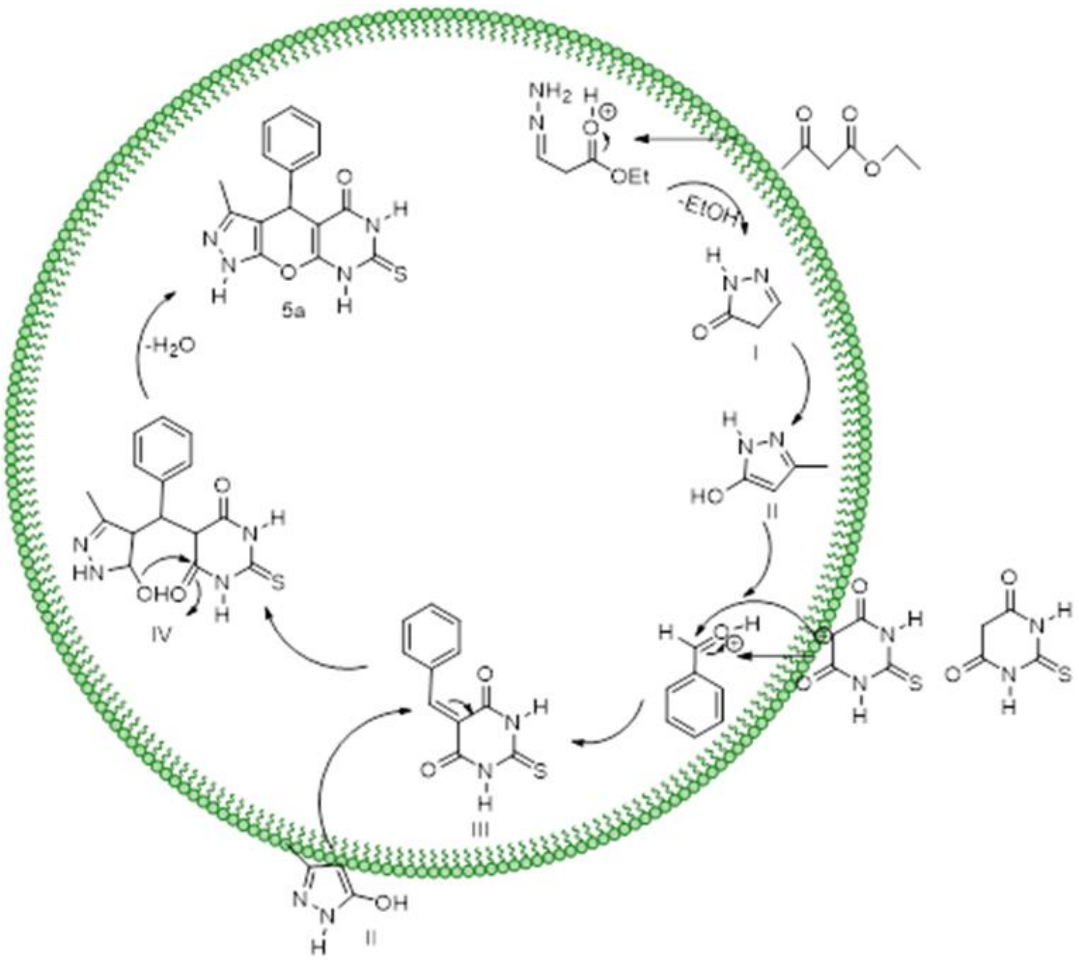


Figure 4 Plausible mechanism for the synthesis of pyrazolopyranopyrimidine in SB extract as a green medium

A plausible mechanism for the synthesis of 5a using SB extract as a green solvent is depicted in Figure 4. Initially, the reaction between ethyl acetoacetate (1) and hydrazine hydrate (2) resulted water soluble 3-methyl-1 H -pyrazol-5(4H)-one (I). The tautomerization of (I) gives stable enolate of pyrazoline. The Knoevenagel condensation between thiobarbituric acid (3) and benzaldehyde (4a) in the presence of SB extract resulted into the intermediate (III). Thereafter, the stable enolate of pyrazoline (II) reacts with intermediate (III) through Michael addition pathway to yield the intermediate (IV). Further, intramolecular cycloaddition of (IV) followed by loss of water molecule afford the desired product 5a.

3.1. Spectroscopic data of representative compounds

- ***3-Methyl-4-phenyl-6,8-dihydropyrazolo[4′,3′:5,6]pyrano[2,3-d]-pyrimidine-5,7(1H,4H)-dione:***White solid; M.P. 218-220 °C, IR (KBr): 3429, 3364, 2895, 2764, 2362, 1675, 1627, 1586, 1542, 1471, 1306, 1097, 814, 778, 697 cm −1 ; ^{1}H NMR (300 MHz, DMSO-d 6): δ2.23 (3 H, s; -CH 3), 5.44 (1H, s; -CH), 7.07-7.04 (2 H, d; Ar-H, *J* = 9 Hz), 7.13-7.10 (1 H, t; Ar-H, *J* = 9 Hz), 7.23-7.20 (2 H, t; Ar-H, *J* = 9 Hz), 10.08 (2 H, s; -NH); ^{13}C NMR (75 MHz, DMSO-d 6): δ10.45, 30.98, 91.90, 106.41, 125.51, 127.09, 127.95, 142.77, 143.83, 151.24, 160.97. 2
- ***4-(2-Chlorophenyl)-3-methyl-4,6-dihydropyrazolo[4',3':5,6]-pyrano[2,3-d]pyrimidin5(2H)-one***:Yellow solid; Yield 90%; M.P. 227–228 °C; 1H NMR (400 MHz, DMSO-d6) δ = 2.40 (s,3H, CH3), 5.26 (s, 1H, CH), 7.06 (d, J = 6.48 Hz, 2H, Ar), 7.21 – 7.25 (m, 2H, Ar), 8.58 (s, 1H,=CH), 10.49 (brs, 1H, NH), 13.77 (s, 1H, CH); 13CNMR (100 MHz, DMSO-d6): 18.3, 34.1,104.3, 111.7, 126.2, 126.3, 127.2, 130.9, 132.2, 136.9, 145.0, 147.4, 150.2, 150.8, 166.5; FT-IR (KBr, cm-1): 3374, 3025, 2342, 1595, 1257; HRMS of [$C_{15}H_{11}N_4O_2Cl$ + 1H] (m/z): 315.0734;Calcd: 315.0737.
- ***3.4-(2-Fluorophenyl)-3-methyl-4,6-dihydropyrazolo[4',3':5,6]-pyrano[2,3-d]pyrimidin5(2H)-one***: Yellow solid; Yield 90%; MP 227–228 °C; 1H NMR (400 MHz, DMSO-d6) δ = 2.40 (s,3H, CH3), 5.26 (s, 1H, CH), 7.06 (d, J = 6.48 Hz, 2H, Ar), 7.21 – 7.25 (m, 2H, Ar), 8.58 (s, 1H,=CH), 10.49 (brs, 1H, NH), 13.77 (s, 1H, CH); 13CNMR (100 MHz, DMSO-d6): 18.3, 34.1,104.3, 111.7, 126.2, 126.3, 127.2, 130.9, 132.2, 136.9, 145.0, 147.4, 150.2, 150.8, 166.5; FT-IR (KBr, cm-1): 3374, 3025, 2342, 1595, 1257; HRMS of [$C_{15}H_{11}N_4O_2F$+ 1H] (m/z): 299.0734;Calcd: 299.0737.
- ***4.3-Methyl-4-(4-methoxyphenyl)-1,4dihydropyrazolo[4′,3′:5,6]pyrano[2,3-d]pyrimidine-5,7(6H,8H)-diones*** Yellow solid; M.P. 230-232 °C, IR (KBr): 3740, 3615, 3180, 3072, 2978, 2845, 2803, 2366, 2320, 1735, 1605, 1510, 1457, 1404, 1267, 1232, 1012, 888, 846, 779, 669, 603 cm −1 ; 1 H NMR (300 MHz, DMSO-d 6): δ2.21 (3 H, s; -CH 3), 3.68 (3 H, s; -OCH 3), 5.37 (1 H, s; -CH), 6.78-6.75 (2 H, d; Ar-H, *J* = 9 Hz), 7.96-6.94 (2 H, d; Ar-H, *J* = 9 Hz); 13 C NMR (75 MHz, DMSO-d 6): δ10.40, 30.23, 55.40, 99.98, 106.48, 113.72, 114.87, 126.91, 128.10, 130.50, 134.70, 144.06, 151.15, 157.59, 160.83, 161.01, 162.16.
- ***5.3-Methyl-4-(p-tolyl)-6,8-dihydropyrazolo[4′,3′:5,6]pyrano[2,3-d]pyrimidine-5,7(1H,4H)dione***White solid; M.P. 204-206 °C, IR (KBr): 3740, 3615, 3180, 3072, 2978, 2845, 2803, 2366, 2320, 1735, 1605, 1457, 1404, 1232, 1012, 888, 846, 779, 669 cm −1 ; 1 H NMR (300 MHz, DMSO-d 6): δ2.22 (6 H, s; -CH 3), 5.38 (1 H, s; -CH), 6.94-6.91 (2 H, d; Ar-H, *J* = 9 Hz), 7.02-6.99 (2 H, d; Ar-H, *J* = 9 Hz), 10.17 (2 H, s; -NH); 13 C NMR (75 MHz, DMSO-d 6): δ10.36, 20.88, 30.68, 91.84, 99.98, 106.33, 126.98, 128.94, 134.84, 139.67, 144.20, 151.22, 160.61.
- ***3-Methyl-4-(3-nitrophenyl)-6,8-dihydropyrazolo[4′,3′:5,6]pyrano[2,3-d]pyrimidin-5,7(6H,8H) one*** White solid; MP 240–242 °C. IR (ν_{max}): 3316, 3053, 1617, 1580 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ(ppm): 2.27 (s, 3H, CH_3), 5.51 (s, 1H,-CH), 7.52–7.54 (d, 2H, *J* = 6 Hz, Ar-H), 7.82 (s, 1H, Ar-H), 8.02-8.04 (d, 1H, *J* = 6 Hz, Ar-H), 11.57(s, 1H, -NH); ^{13}C NMR (75 MHz, DMSO-d_6) δ(ppm): 10.37, 31.20, 95.99, 104.71, 121.43, 130.07, 134.22, 144.29, 144.90, 148.14, 159.08, 163.89, 173.71; HRMS mass calculated for [$C_{15}H_{11}N_5O_4S$] = 341.344 [*m/z*]; obs. mass = [*m/z*], 357.098. Anal. Calcd. for $C_{15}H_{11}N_5O_5$: C (50.42%), H (3.10%), N (19.60%). Found: C (50.38%), H (3.08%), N (19.48%)
- ***8.4-(4-bromophenyl)−3-methyl-4,6-dihydropyrazolo[4′,3′:5,6]-pyrano[2,3-d]pyrimidin-5(2H)-one***White solid; Yield 93%; MP 241–242 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.37 (s, 3H, CH_3), 4.76 (s, 1H, CH), 7.08 (d, *J* = 7.8 Hz, 2H, Ar), 7.47 (d, *J* = 8.28 Hz, 2H, Ar), 8.70 (s, 1H, =CH), 9.94 (brs, 1H, NH), 13.78 (brs, 1H, NH); ^{13}CNMR (100 MHz, $CDCl_3$): 19.5, 35.5, 105.4, 114.5, 127.9, 127.9, 128.4, 129.5, 136.3, 142.8, 144.1, 148.5, 149.1, 160.1, 162.5, 167.0; FT-IR (KBr, cm^{-1}): 3376, 3019, 2345, 1635, 1253; HRMS of [$C_{15}H_{11}N_4O_2$br+ 1 H]$^+$ (*m/z*): 359.0732; Calcd: 359.0732.
- ***10.4-(3,4,5-Trimethoxyphenyl)-3-methyl-4,6-dihydropyrazolo[4',3':5,6]-pyrano[2,3-d] pyrimidin-5(2H)-one*** White solid; Yield 92%; MP 201–203 °C; 1H NMR (400 MHz, DMSO-d6) δ = 2.38 (s, 3H, CH3), 3.73 (s, 3H, OCH3), 3.82 (s, 3H, OCH3), 3.84 (s, 3H, OCH3), 5.28 (s, 1H, CH), 6.69 (s, 2H, Ar), 8.70 (s, 1H, =CH), 10.43 (brs, 1H, NH), 13.30 (brs, 1H, NH); 13CNMR (100 MHz, CDCl3): 18.4, 35.5, 55.9, 60.7, 65.7, 105.3, 112.9, 112.9, 127.7, 127.8, 127.8, 128.3, 136.4, 142.8, 144.3, 148.7, 149.3, 152.7, 167.2; FT-IR (KBr, cm-1): 3328, 3018, 2358, 1602, 1256; HRMS of [$C_{18}H_{18}N_4O_5$ + 1H]+ (m/z): 371.1963; Calcd: 371
- ***4-(4-chlorophenyl)−3-methyl-4,6-dihydropyrazolo[4′,3′:5,6]-pyrano[2,3-d]pyrimidin-5(2H)-one (7g)***White solid; Yield 93%; MP 241–242 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.37 (s, 3H, CH_3), 4.76 (s, 1H, CH), 7.08 (d, *J* = 7.8 Hz, 2H, Ar), 7.47 (d, *J* = 8.28 Hz, 2H, Ar), 8.70 (s, 1H, =CH), 9.94 (brs, 1H, NH), 13.78 (brs, 1H, NH); ^{13}CNMR (100 MHz, $CDCl_3$): 19.5, 35.5, 105.4, 114.5, 127.9, 127.9, 128.4, 129.5, 136.3, 142.8, 144.1, 148.5, 149.1, 160.1, 162.5, 167.0; FT-IR (KBr, cm^{-1}): 3376, 3019, 2345, 1635, 1253; HRMS of [$C_{15}H_{11}N_4O_2Cl$+ 1 H]$^+$ (*m/z*): 315.0732; Calcd: 315.0732.

3.2. Reusability Studies

Recyclability and reusability are the prime factors that play crucial role in assigning the catalytic protocol as a green protocol. In this regard, we investigated the recyclability and reusability of aqueous *Sea buckthorn* berries extract in pyrazolopyranopyrimidine multicomponent synthesis. The *Sea Buckthorn* aq. extract could be easily recycled by removing the insoluble product by simple filtration. We performed model reaction using recycled *Sea buckthorn* aq. extract and we were delighted to note that the extract could be reused for five times without any significant loss in yield of the product. **(Figure 5)**

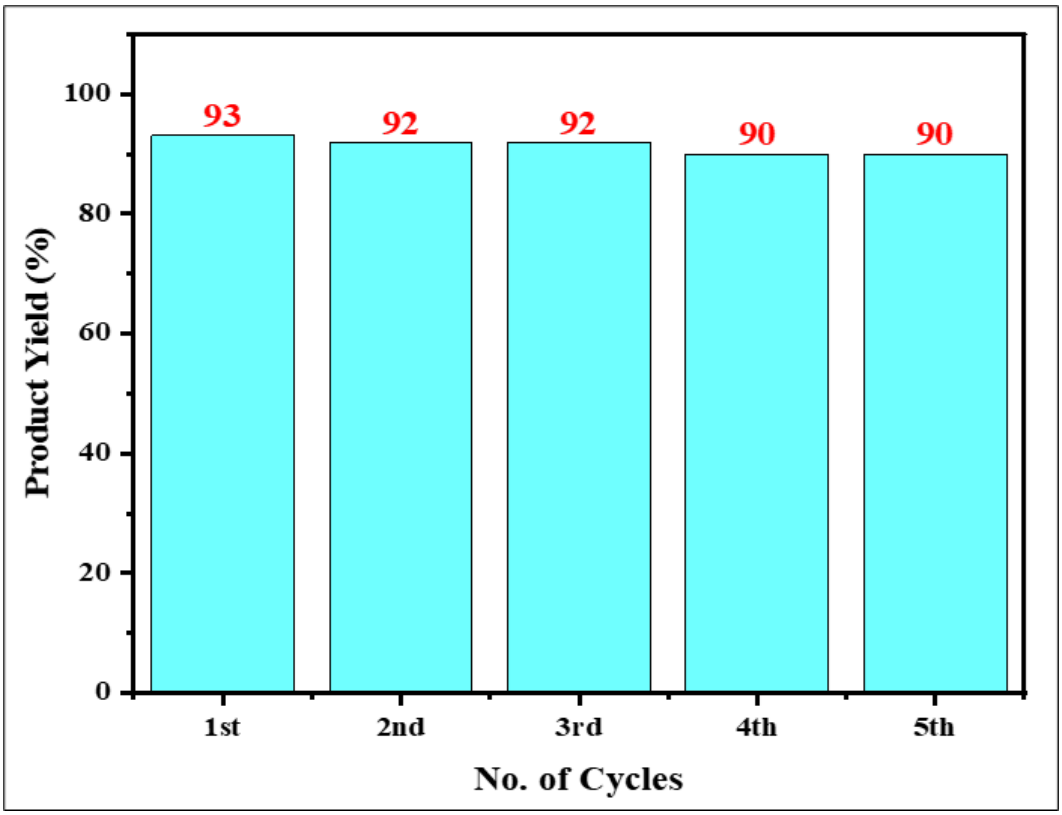


Figure 5 Recyclability of SB aq. extract

4. Conclusion

In conclusion, we present a straightforward bioorganic method for clean and ecofriendly synthesis of triheterocyclic compounds, pyrazolopyranopyrimidine pyrazole, pyran, and pyrimidinone rings *via Sea buckthorn* aqueous extract as a reaction medium. In addition to the ease of product separation and the reaction medium effortless reusability, this protocol boasts significant advantages including the employment of a safe and reusable catalyst, elimination of toxic solvents, attainment of high product yields, brief reaction durations, and a straightforward work-up process.

Compliance with ethical standards

Acknowledgements

We gratefully acknowledge Department of chemistry, Shivaji University, Kolhapur, Sophisticated Analytical Instrument Facility (SAIF) and Common Facility Centre (CFC) Shivaji University, Kolhapur for providing laboratory and characterization facilities.

Disclosure of conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix

Supporting Information

Aqueous extract of *Sea buckthorn* berries: A greener and ecofriendly medium for synthesis of pyrazolopyranopyrimidines.

Prafull Babulal Dandge *, Suraj Dharamu Khot, Komal Rajendra Gouraje, Poonam Manik Ghule, Pragati Vijaykumar Kashid, Rasika Shivaji Lad, Priti Pandurang Ghatage and Snehal Shivaji Ghatage

Compound **5a**, Table 3

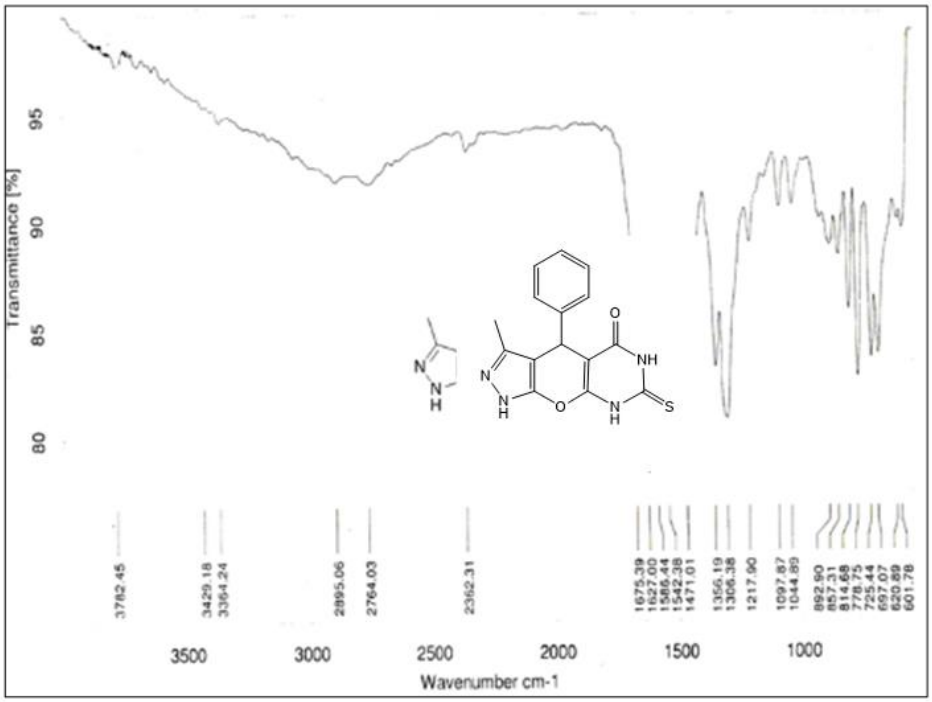

Figure 1 FT-IR spectrum of
4-(3-methyl-5-oxo-7-thioxo-1,4,5,6,7,8-hexahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-4-yl)benzonitrile

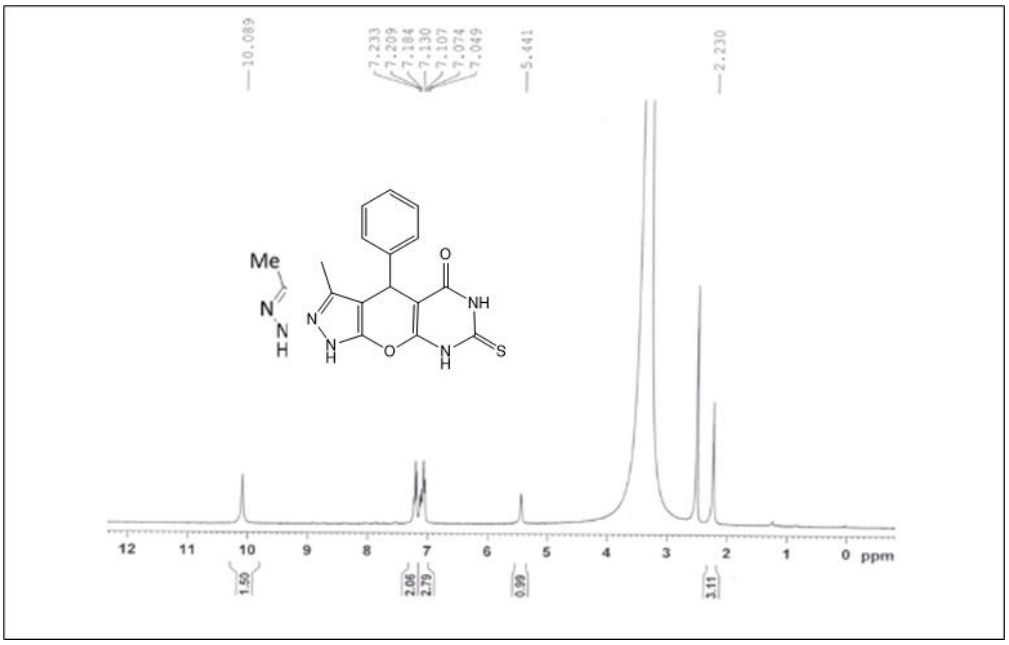

Figure 2 ^{1}H NMR spectrum of

4-(3-methyl-5-oxo-7-thioxo-1,4,5,6,7,8-hexahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-4-yl)benzonitrile

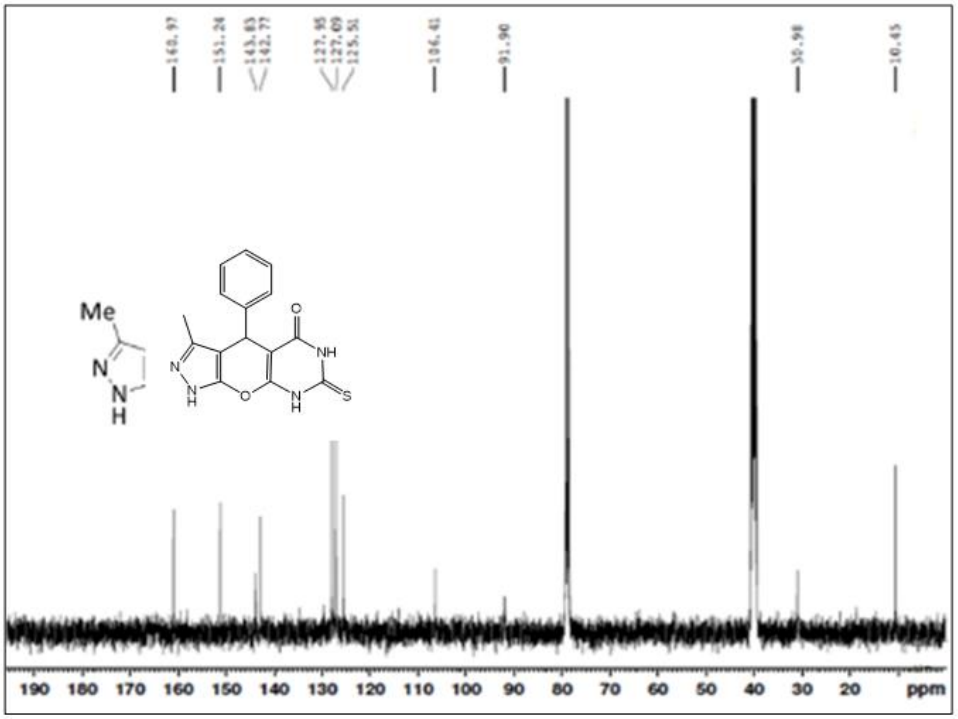

Figure 3 ^{13}C NMR Spectrum of

4-(3-methyl-5-oxo-7-thioxo-1,4,5,6,7,8-hexahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-4-yl)benzonitrile

Compound **5g**, Table 2

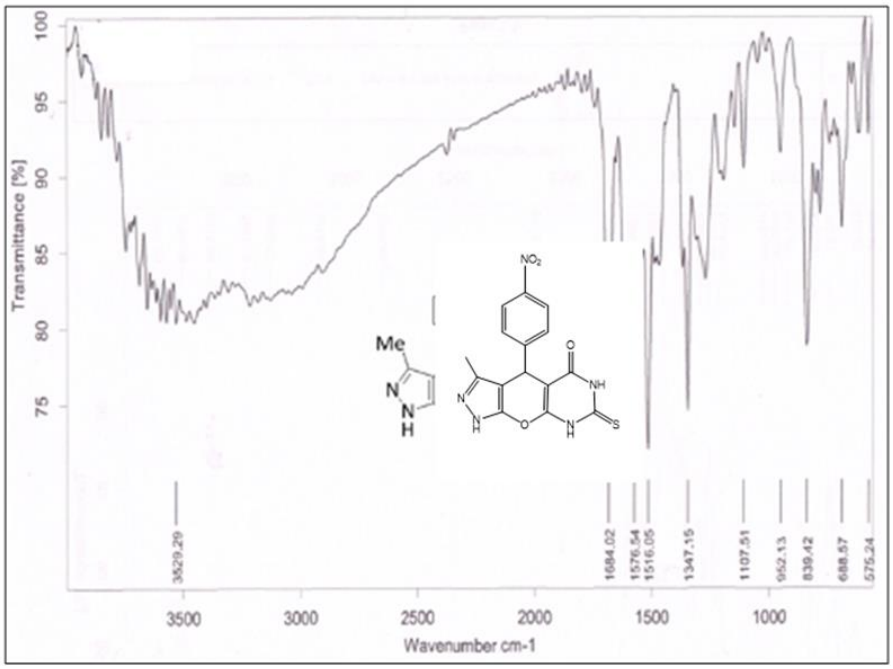

Figure 4 FT-IR spectrum of

3-methyl-4-(4-nitrophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-5(1*H*)-one

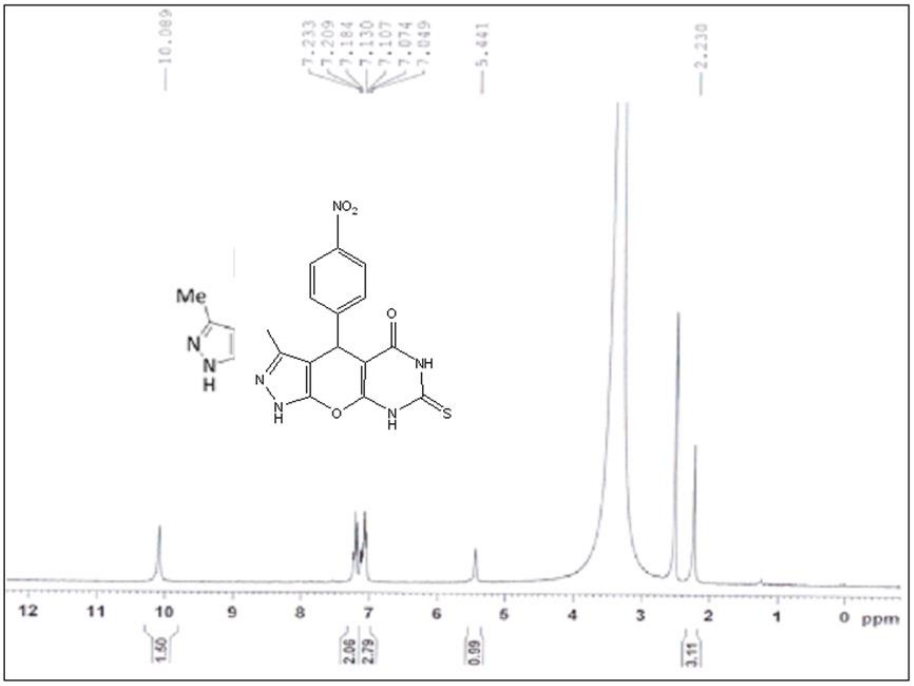

Figure 5 ^{1}H NMR Spectrum of

3-methyl-4-(4-nitrophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-5(1*H*)-one

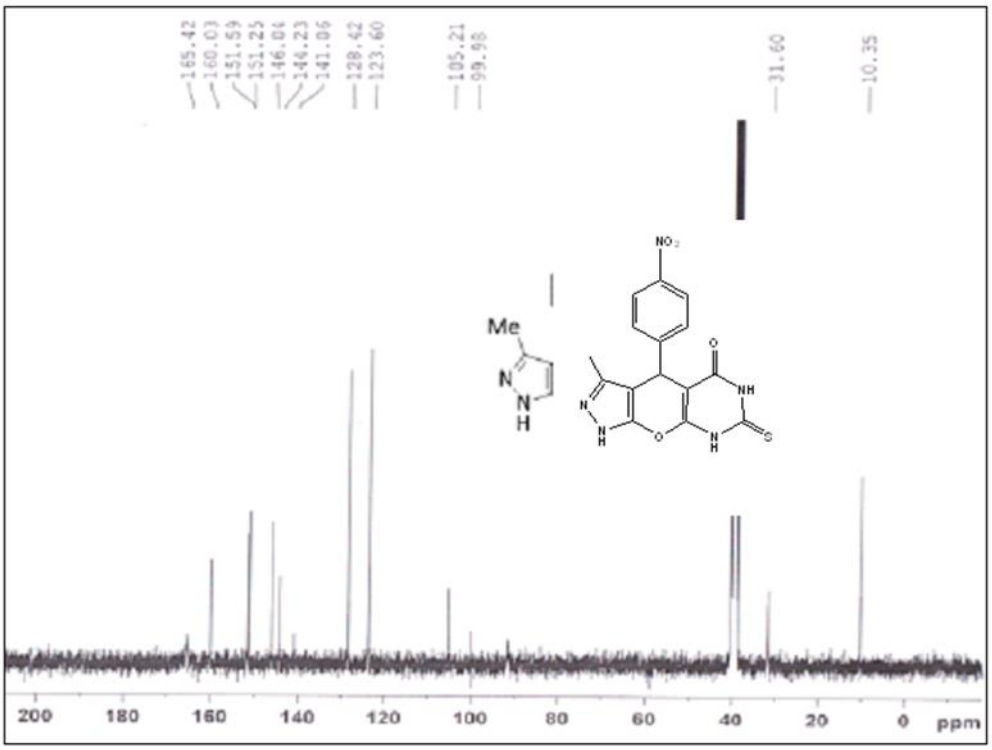

Figure 6 ^{13}C NMR Spectrum of

3-methyl-4-(4-nitrophenyl)-7-thioxo-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-5(1*H*)-one

Compound **5d**, Table 3

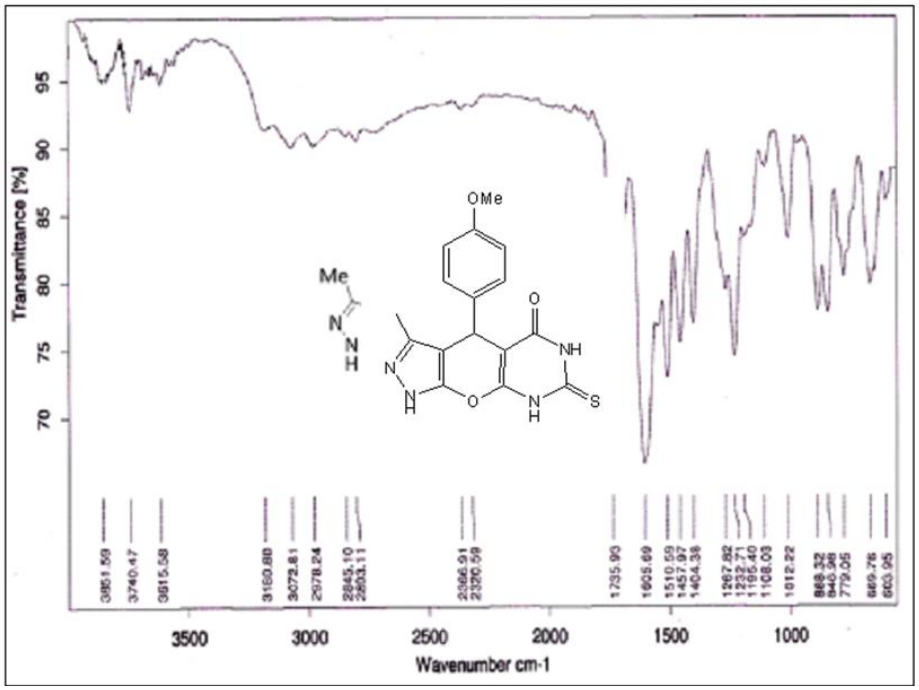

Figure 7 FT-IR Spectrum of

4-(4-methoxyphenyl)-3-methyl-7-thioxo-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-5(1*H*)-one

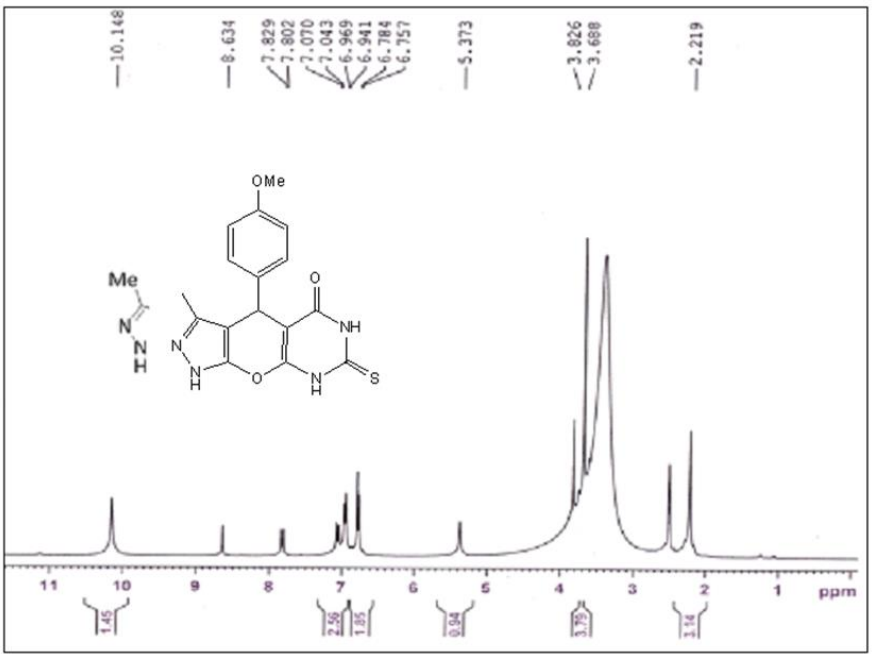

Figure 8 [1]H MNR Spectrum of

4-(4-methoxyphenyl)-3-methyl-7-thioxo-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-5(1*H*)-one

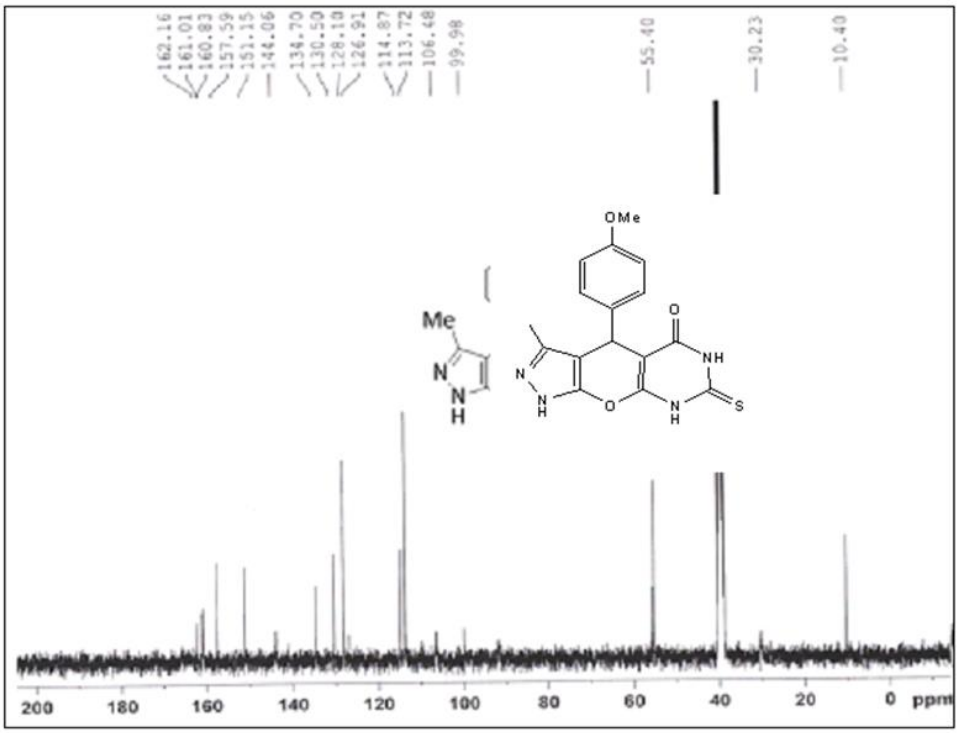

Figure 9 ^{13}C NMR Spectrum of

4-(4-methoxyphenyl)-3-methyl-7-thioxo-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-5(1*H*)-one

Compound **5e**, Table 3

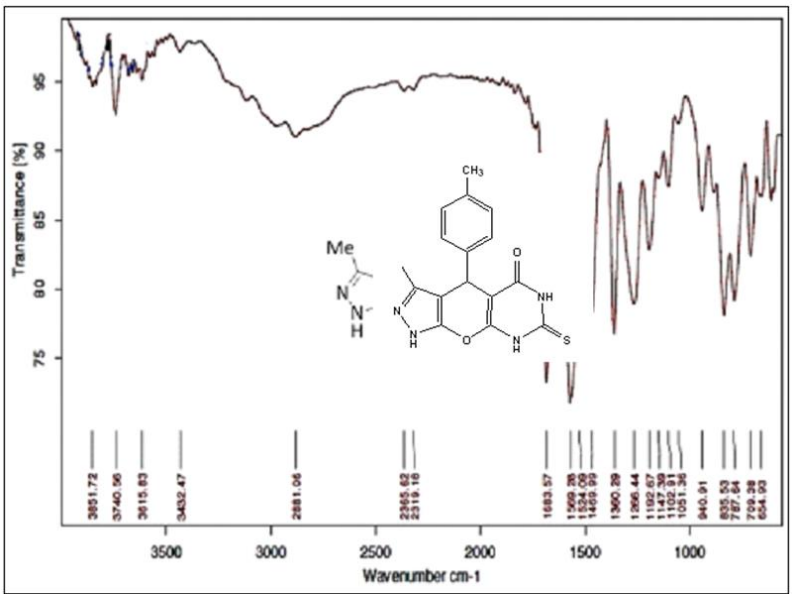

Figure 10 FT-IR Spectrum of
3-methyl-7-thioxo-4-(*p*-tolyl)-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3-*d*]pyrimidin-5(1*H*)-one

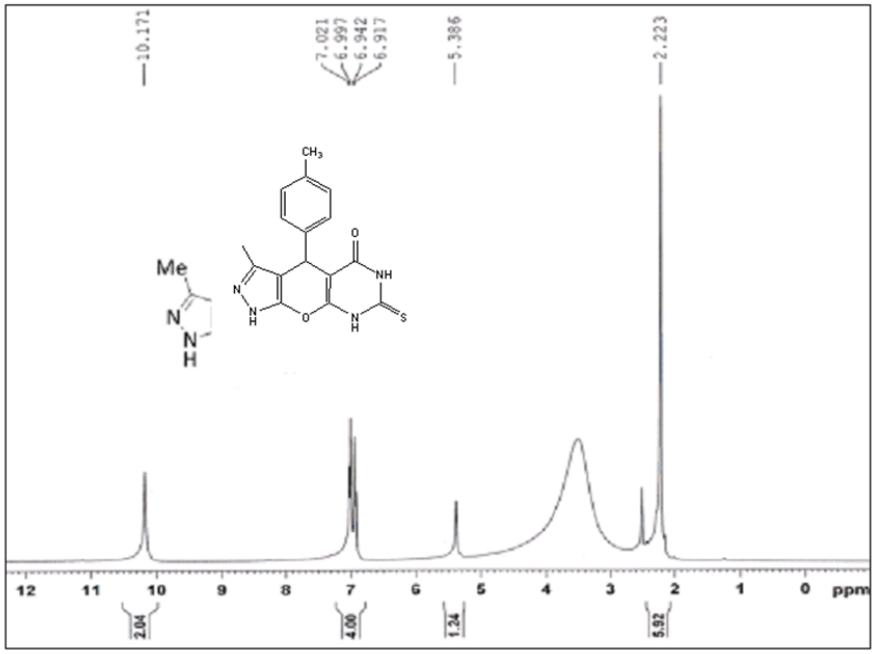

Figure 11 [1]H NMR Spectrum of

3-methyl-7-thioxo-4-(*p*-tolyl)-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3-*d*]pyrimidin-5(1*H*)-one

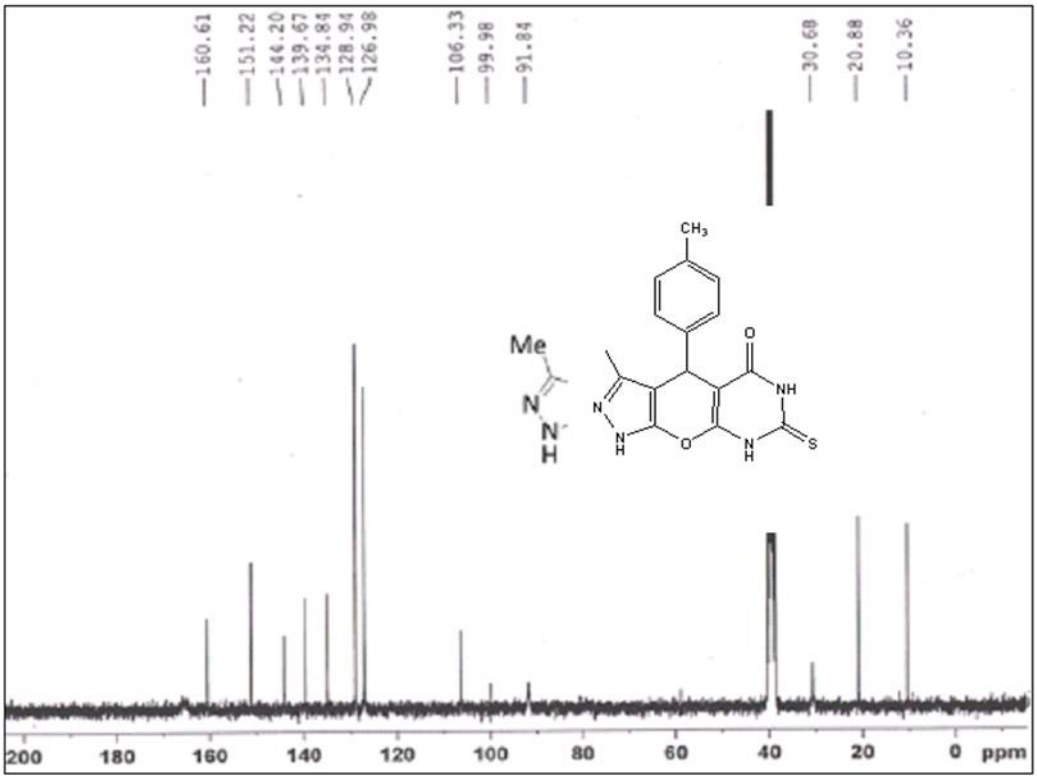

Figure 12 [13]C NMR Spectrum of
3-methyl-7-thioxo-4-(*p*-tolyl)-4,6,7,8-tetrahydropyrazolo[4',3':5,6]pyrano[2,3- *d*]pyrimidin-5(1*H*)-one