Reaction of Coumarin Derivatives with Nucleophiles in Aqueous Medium

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Z. Naturforsch. **2008**, *63b*, 71 – 76; received July 29, 2007

A series of heterocycles was synthesized by the reaction of α,β-unsaturated ketones of benzopyrans or coumarins with various nucleophiles in aqueous medium bearing two points of diversity. Compared to an identical library generated by conventional parallel synthesis, a microwave-assisted procedure dramatically decreased reaction times from hours to minutes, and yields of products and intermediates were improved remarkably. This synthetic approach is ecofriendly in nature which features water as solvent, microwave irradiation, and usage of a "green" catalyst (K_2CO_3).

Key words: Aqueous Medium, Potassium Carbonate, Microwave Irradiation (MWI), Nucleophiles, 4-Hydroxycoumarin

Introduction

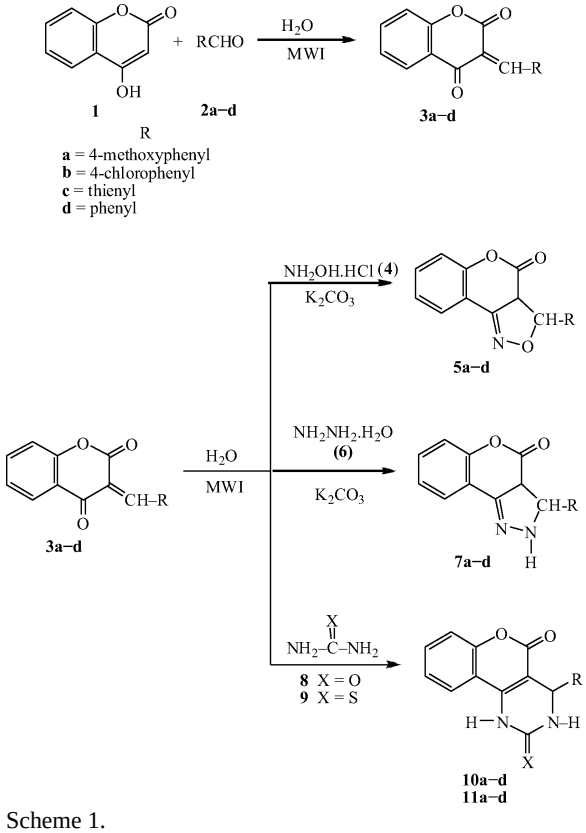
In recent years the combination of two prominent green chemistry principles, "microwaves" and "water", has become very popular and received substantial interest due to work of Leadbeater [1] and others [2] who demonstrated that a great variety of synthetic organic transformations, in particular transition metal-catalyzed processes can be carried out very efficiently and rapidly under these environmentally benign conditions. The use of water as a solvent for organic transformations offers several environmental benefits, and significant rate enhancements are observed in water compared to organic solvents [3 – 5]. This acceleration has been attributed to many factors, including the hydrophobic effect, enhanced hydrogen bonding in the transition state and the cohesive energy and the density of water [6 – 7]. The product isolation may also be facilitated by simple phase separation rather than energy intensive and organic-emitting processes involving distillation of organic solvents. Thus, the development of an efficient synthetic methodology to form carbon-heteroatom bonds in aqueous media appears to be attractive.

Coumarin or [1]benzopyran-2[*H*]-one is an important heterocyclic scaffold in the field of medicinal chemistry and the molecular skeleton is used in laser materials, photosensitizers, brighteners as intermediates for dyes, pesticides as well as in perfume formulations and in enzymoloy as biological probes [8 – 11]. Fusion of coumarin to pyrimidine/isoxazole/pyrazole rings to form polycyclic fused compounds may result in enhanced pharmaceutical efficiency. Isoxazoles, for example, are important intermediates in the synthesis of natural products, and pyrazoles are important ligands in organometallic chemistry, and some of these compounds are used as components of drugs, herbicides and fungicides [12 – 15]. Some of the major advances in chemistry, especially industrial chemistry, over the past generation have been in the area of catalysis. Through the use of catalysts, chemists have found ways of removing the need for large quantities of reagent that would otherwise have been required for chemical transformations and would ultimately have contributed to the waste stream. The use of K_2CO_3 as a catalyst [16] obviates the use of an organic base and also easily gets washed away with water which contributes to the purity of the product.

Motivated by the aforementioned advantages of water-mediated reactions and in continuation of our enduring studies on versatile therapeutically important heterocycles [17], 1-benzopyran-2-one was employed as an addendum in Aldol condensation reactions for investigating the synthesis of pyrazole, isoxazole and pyrimidine derivatives of arylidenechromanediones.

Results and Discussion

In the present study, we disclose a simple and effective synthetic route that produces high yields of a series of potentially active coumarin-fused pyrazoles, isoxazoles and pyrimidine derivatives. Various methods reported for their synthesis so far employed the use of hazardous solvents like diphenylnitrilimine [18], acetic acid [19], pyridine [20], xylene [21] and harmful catalysts like hydrochloric acid [22], triethylamine [23], *etc*. These procedures were "greenified" for the desired organic functional group transformation by conducting the reaction in water. Firstly, 4-hydroxy-2*H*[1]benzopyran-2-one (4-hydroxycoumarin) (**1**) was condensed with aromatic or heteroaromatic aldehydes **2a**–**d** in water under microwave irradiation to yield 3-arylidenechromane-2,4-diones **3a**–**d** (Scheme 1). The use of base required in such reactions was obviated by performing the reaction in water which not only avoided the use of base but also gave good yields (75 – 90 %) within 4.0 – 6.0 minutes of microwave irradiation (MWI). Products **3a**–**d** were easily isolated from the reaction medium



Scheme 1.

Table 1. Comparison of reaction times and yields for **5**, **7**, **10**, **11a** – **d**.

Compound	R	Method B time (h) / yield[a] (%)	Method C time (h) / yield[a] (%)	Method D time (min) / yield[a] (%)
5a	4-$OCH_3C_6H_4$	6.0/48	5.0/62	2.5/80
5b	4-ClC_6H_4	7.5/50	6.5/65	2.5/85
5c	thiophen-2-yl	7.0/52	5.5/67	2.0/84
5d	C_6H_5	6.5/45	5.5/68	2.0/82
7a	4-$OCH_3C_6H_4$	7.5/45	6.5/70	3.0/88
7b	4-ClC_6H_4	7.0/52	5.5/72	2.5/85
7c	thiophen-2-yl	8.0/53	6.5/75	3.0/88
7d	C_6H_5	6.5/40	5.0/66	2.0/86
10a	$OCH_3C_6H_4$	7.5/40	6.0/68	2.5/86
10b	4-ClC_6H_4	5.5/45	4.5/72	1.5/84
10c	thiophen-2-yl	6.5/45	4.5/72	1.5/84
10d	C_6H_5	7.0/53	5.5/74	2.0/90
11a	4-$OCH_3C_6H_4$	6.0/45	4.5/74	2.0/88
11b	4-ClC_6H_4	8.0/56	6.5/76	3.0/90
11c	thiophen-2-yl	7.5/55	6.5/72	3.0/85
11d	C_6H_5	6.5/50	4.5/75	1.5/90

[a] Isolated and unoptimized yields.

as they precipitated as insoluble solids from water, and the structures of the known α,β-unsaturated carbonyl compounds were found to be in consistency with the spectroscopic data [24]. The reaction conditions of the second step (Scheme 1) were optimized for the cyclocondensation of **3a**–**d** with the nitrogen containing nucleophiles (NH_2-G) hydroxylamine hydrochloride, hydrazine, urea and thiourea to afford 3-(substituted aryl)-3,3a-dihydrochromeno[4,3-*c*]isoxazol-4-ones **5a**–**d**, and pyrazol-4-ones **7a**–**d**, 4-substituted-1,2,3,4-tetrahydro-benzopyrano[4,3-*d*]pyrimidine-2,5-diones **10a**–**d** and 4-substituted-1,2,3,4-tetrahydrobenzopyrano[4,3-*d*]pyrimidine-2-thioxo-5-ones **11a**–**d**.

Different solvents such as ethanol, water or benzene with different combinations of temperature and reaction time were studied in order to achieve atom economy within shorter reaction time. In the first experimental trial, the reaction was attempted with ethanol under conventional reflux conditions. In the next attempt, the cyclization of 4-hydroxycoumarin chalcones **3a**–**d** and the nitrogen nucleophile (**4**, **6**, **8**, **9**) was performed conventionally in water using a catalytic amount of K_2CO_3. 4.0 – 7.0 hours were taken to complete the reaction whereas the same reaction was complete within 3.0 minutes when irradiated under microwaves with good to excellent yields (80 – 90 %), indicating that higher temperature facilitated efficient heterocyclization (Table 1). However, the same reaction attempt was unsuccessful when a non-polar solvent like benzene was used with MWI. Hence, the polarity of the solvent also had some effect on the cycliza-

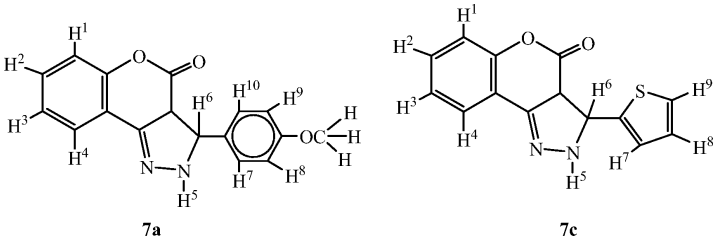


Fig. 1. Structures of compounds **7a** and **7c**.

tion. When water is heated, dissociation to form acid and base, catalyzing the reaction, becomes more significant. Also, the use of near critical water instead of traditional acid-base processes eliminates the need of a neutralization step and avoids the resulting production of waste salts. Thus, water behaves as a tunable solvent with the changes of temperature and microwave power conditions. In the next step water along with K_2CO_3 was used for the synthesis of **5**, **7**, **10** and **11a**–**d**. Here, the use of K_2CO_3 served as a mild inorganic water-soluble base that gets easily washed off with water. Moreover, the use of K_2CO_3 was found to be essential to solubilize **3a**–**d** and to realize the nitrogen nucleophile so that it can react further. The product was obtained after cooling for 10–15 minutes.

The structures of the synthesized compounds **5**, **7**, **10** and **11** were confirmed spectroscopically. The infrared spectra of the products showed a strong peak at 1720 cm^{-1}, a value typical of the coumarin carboxyl group. The ^{1}H NMR spectra showed a doublet at $\delta \sim 5.5$ for **5a**–**d** and at 4.7 ppm for **7a**–**d**, whereas a singlet at ~ 6.1 ppm for **10** and **11a**–**d** is a characteristic signal in favor of the proposed product. Apart from IR and ^{1}H NMR data, mass and ^{13}C NMR spectra as well as elemental analyses also support the structures of the final products.

The structures of **7a** and **7c** (Fig. 1) were further confirmed with NOESY NMR spectra. Cross correlation peaks due to coupling of 5-H protons (NH, $\delta > 11.0$) with 6-H ($\delta > 4.8$) and the protons of the methoxyphenyl group ($\delta < 7.0$) in the case of **7a** (Fig. 1) and between 5-H (NH, $\delta > 11.0$) and 6-H ($\delta > 4.8$) and the thienyl protons ($\delta > 7.0$) in the case of **7c** have been found.

In conclusion, a synthetic route to various fused heterocycles adhering to the green chemistry principles was followed in aqueous solution without using any harsh acids or bases thereby eliminating the need of toxic compounds and solvents. Additionally, the use of MWI resulted in complete conversion of reactants into products without the formation of side products and any noticeable decomposition. We have developed a method which is not only more environmentally benign but also has economic advantages in producing better products less expensively in a short period of time.

Experimental Section

MW irradiation was carried out in a Kenstar-OM 9925E MW oven (800 W, 2450 MHz). The temperature of the reaction mixture was measured with a non-contact mini-gun type IR thermometer (model 8868). IR spectra were recorded with a Perkin-Elmer FTIR-1710 spectrometer using KBr pellets. ^{1}H NMR spectra were obtained with a Bruker Avance Spectrospin 300 spectrometer (300 MHz) using TMS as internal standard. Elemental analyses were performed with a Heraeus CHN-Rapid analyzer. The melting points (uncorrected) were determined with a Thomas Hoover melting point apparatus. ^{13}C NMR spectra were recorded with a Bruker Topspin Spectrometer at 75.6 MHz. Mass spectra were recorded with a TOF MS instrument. All reactants were purchased from Sigma-Aldrich and Lanchester and used without further purification. Solvents used for the reactions were double distilled in a vacuum.

*General procedure for the synthesis of 3-arylidenechromane-2,4-diones **3a**–**d***

Method A

To the mixture of 4-hydroxycoumarin (**1**) (0.01 mol) and aromatic/heteroaromatic aldehydes **2a**–**d** (0.01 mol), 3–4 mL of water was added. The reaction mixture was exposed to microwave irradiation for the appropriate time. The progress of the reaction was monitored by TLC examination (Merck TLC: mean particle size 10–12 μm; particle size distribution 5–20 μm; layer thickness 250 μm; plate height 30 mm). The solid obtained was filtered, washed with water and recrystallized from EtOH.

*General procedure for the synthesis **5a**–**d**, **7a**–**d**, **10a**–**d** and **11a**–**d***

Method B (conventional method)

To the mixture of 3-arylidenechromane-2,4-diones **3a**–**d** (0.01 mol), a nucleophile [hydroxylamine hydrochloride (**4**)

/ hydrazine hydrate (**6**) / urea (**8**) / thiourea (**9**), (0.015 mol)] and K_2CO_3 (1.0 – 1.5 mg) (not in case of urea and thiourea), 10 mL of EtOH was added. The reaction mixture was refluxed for the appropriate time with constant stirring. The reaction was monitored by TLC examination. Upon completion of the reaction, the solid obtained was filtered, and washed with water. Then the product was purified by column chromatography [silica gel, elution with *n*-hexane : EtOAc 8 : 2 (v/v)] followed by recrystallization from EtOH.

Method C (conventional method)

This method is the same as method B except that water was used as solvent.

Method D (microwave-assisted synthesis)

In an Erlenmeyer flask were placed 3-arylidenechromane-2,4-diones **3a** – **d** (0.01 mol), a nucleophile [hydroxylamine hydrochloride (**4**) / hydrazine hydrate (**6**) / urea (**8**) / thiourea (**9**) (0.015 mol)] and K_2CO_3 (not in case of urea and thiourea), and 2 – 3 mL of water. The reaction mixture was subjected to microwave irradiation (MWI) for a specific time (Table 1) at low power (560 W). The progress of the reaction was monitored by TLC examination at intervals of 30 seconds. On completion, the reaction mixture was cooled and filtered, washed with cold water and dried. The rest was the same as in method B.

*3-(4-Methoxyphenyl)-3,3a-dihydro-chromeno[4,3-c]-isoxazol-4-one (**5a**)*

M. p. 188 – 190 °C. – $C_{17}H_{13}O_4N$: calcd. C 69.15, H 4.40, N 4.74; found C 69.13, H 4.38, N 4.72. – IR (nujol): ν = 1605, 1660 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.27 (d, 1 H, *J* = 9.8 Hz), 3.84 (s, 3 H, OCH_3), 5.51 (d, 1 H, CH-O, *J* = 8.0 Hz), 6.86 – 7.53 (m, 8 H, Ar-H). – ^{13}C NMR (75.6 MHz, $CDCl_3$, TMS): δ = 129.6, 125.7, 133.2, 123.5, 154.6, 171.0, 47.2, 66.9, 128.5, 129.7, 134.3, 129.5, 128.6, 139.0, 166.6, 125.1, 61.2. – MS: *m/z* (%) = 295.2 (100) $[M]^+$.

*3-(4-Chlorophenyl)-3,3a-dihydrochromeno[4,3-c]isoxazol-4-one (**5b**)*

M. p. 175 – 177 °C. – $C_{16}H_{10}O_3NCl$: calcd. C 64.10, H 3.33, N 4.67; found C 64.13, H 3.34, N 4.68. – IR (nujol): ν = 1615, 1665 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.25 (d, 1 H, *J* = 9.8 Hz), 5.59 (d, 1 H, CH-O, *J* = 8.0 Hz), 6.80 – 7.55 (m, 8 H, Ar-H). – MS: *m/z* (%) = 299.3 (100) $[M]^+$.

*3-(Thiophene-2-yl)-3,3a-dihydrochromeno[4,3-c]isoxazol-4-one (**5c**)*

M. p. 168 – 170 °C. – $C_{14}H_9O_3NS$: calcd. C 61.99, H 3.32, N 5.16, S 11.80; found C 61.98, H 3.21, N 5.14, S 11.83. – IR (nujol): ν = 1610, 1670 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.28 (d, 1 H, *J* = 9.8 Hz), 5.52 (d, 1 H, CH-O, *J* = 8.0 Hz), 6.75 – 7.40 (m, 7 H, Ar-H + thienyl). – MS: *m/z* (%) = 270.8 (100) $[M]^+$.

*3-Phenyl-3,3a-dihydrochromeno[4,3-c]isoxazol-4-one (**5d**)*

M. p. 166 – 168 °C. – $C_{16}H_{11}O_3N$: calcd. C 72.45, H 4.15, N 5.28; found C 72.35, H 4.18, N 5.30. – IR (nujol): ν = 1615, 1670 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.26 (d, 1 H, *J* = 9.8 Hz), 5.50 (d, 1 H, CH-O, *J* = 8.0 Hz), 6.81 – 7.66 (m, 9 H, Ar-H). – MS: *m/z* (%) = 264.7 (100) $[M]^+$.

*3-(4-Methoxyphenyl)-3,3a-dihydro-2H-chromeno[4,3-c]-pyrazol-4-one (**7a**)*

M. p. 175 – 177 °C. – $C_{17}H_{14}O_3N_2$: calcd. C 69.38, H 4.76, N 9.52; found C 69.36, H 4.78, N 9.50. – IR (nujol): ν = 1615, 1665, 3450 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.47 (d, 1 H, *J* = 9.6 Hz), 3.83 (s, 3 H, OCH_3), 4.81 (d, 1 H, *J* = 8.2 Hz), 6.80 – 7.55 (m, 8 H, Ar-H), 11.21 (s, 1 H, NH). – NOE correlations: 1-H/2-H, 3-H/2-,4-H, 5-H/6-,7-H, 7-H/8-H, -OCH_3/9-,8-H, 10-H/6-,9-H. – MS: *m/z* (%) = 293.5 (100) $[M]^+$.

*3-(4-Chlorophenyl)-3,3a-dihydrochromeno[4,3-c]pyrazol-4-one (**7b**)*

M. p. 188 °C. – $C_{16}H_{11}O_2N_2Cl$: calcd. C 64.32, H 3.68, N 9.38; found C 64.30, H 3.63, N 9.35. – IR (nujol): ν = 1605, 1660, 3450 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.45 (d, 1 H, *J* = 9.6 Hz), 4.83 (d, 1 H, *J* = 8.2 Hz), 6.82 – 7.58 (m, 8 H, Ar-H), 11.23 (s, 1 H, NH). – MS: *m/z* (%) = 299.0 (100) $[M]^+$. – ^{13}C NMR (75.6 MHz, $CDCl_3$, TMS): δ = 129.7, 125.5, 131.3, 122.5, 153.7, 171.0, 56.3, 48.0, 143.5, 129.0, 130.5, 133.8, 131.5, 129.5, 158.6, 128.1.

*3-(Thiophene-2-yl)-3,3a-dihydrochromeno[4,3-c]pyrazol-4-one (**7c**)*

M. p. 172 °C. – $C_{14}H_{10}N_2O_2S$: calcd. C 62.22, H 3.70, N 10.37, S 11.85; found C 62.12, H 3.73, N 10.40, S 11.84. – IR (nujol): ν = 1615, 1670, 3455 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.49 (d, 1 H, *J* = 9.6 Hz), 4.84 (d, 1 H, *J* = 8.2 Hz), 6.77 – 7.69 (m, 7 H, Ar-H + thienyl), 11.24 (s, 1 H, NH). – MS: *m/z* (%) = 270.0 (100) $[M]^+$. – NOE correlations: 1-H/2-H, 3-H/2-,4-H, 5-H/6-,7-H, 8-H/7-,9-H.

*3-Phenyl-3,3a-dihydrochromeno[4,3-c]pyrazol-4-one (**7d**)*

M. p. 164 – 166 °C. – $C_{16}H_{12}O_2N_2$: calcd. C 72.72, H 4.54, N 10.60; found C 72.11, H 4.56, N 10.57. – IR (nu-

jol): ν = 1605, 1660, 3440 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.47 (d, 1 H, J = 9.6 Hz), 4.81 (d, 1 H, J = 8.2 Hz), 6.80 – 7.65 (m, 9 H, Ar-H), 11.25 (s, 1 H, NH). – MS: *m/z* (%) = 264.0 (100) $[M]^+$.

*4-(4-Methoxyphenyl)-1,2,3,4-tetrahydrobenzopyrano[4,3-d]pyrimidine-2,5-dione (**10a**)*

M. p. 242 °C (240 °C [25]). – $C_{18}H_{14}O_4N_2$: calcd. C 67.08, H 4.34, N 8.69; found C 67.05, H 4.31, N 8.73. – IR (nujol): ν = 1660, 3450 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 3.86 (s, 3 H, OCH_3), 6.12 (s, 1 H), 6.85 – 7.55 (m, 8 H, Ar-H), 11.53 (brs, 2 H, 2NH). – MS: *m/z* (%) = 321.8 (100) $[M]^+$.

*4-(4-Chlorophenyl)-1,2,3,4-tetrahydrobenzopyrano[4,3-d]-pyrimidine-2,5-dione (**10b**)*

M. p. 161 – 163 °C (162 – 164 °C [26]). – $C_{17}H_{11}O_3N_2Cl$: calcd. C 62.48, H 3.36, N 8.57; found C 62.49, H 3.36, N 8.54. – IR (nujol) : ν = 1670, 3450 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 6.11 (s, 1 H), 6.89 – 7.65 (m, 8 H, Ar-H), 11.52 (brs, 2 H, 2NH). – MS: *m/z* (%) = 326.0 (100) $[M]^+$.

*4-(Thiophen-2-yl)-1,2,3,4-tetrahydrobenzopyrano[4,3-d]-pyrimidine-2,5-dione (**10c**)*

M. p. 168 – 170 °C. – $C_{15}H_{10}N_2O_3S$: calcd. C 60.40, H 3.35, N 9.39, S 10.73; found C 60.4, H 3.37, N 9.36, S 10.75. – IR (nujol): ν = 1675, 3440 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 6.14 (s, 1 H), 6.79 – 7.65 (m, 7 H, Ar-H + thienyl), 11.55 (brs, 2 H, 2NH). – ^{13}C NMR (75.6 Hz, $CDCl_3$, TMS): δ = 127.6, 126.3, 129.5, 122.3, 153.8, 171.0, 104.5, 54.8, 127.5, 129.5, 126.4, 143.5, 162.0, 149.2, 140.8. – MS: *m/z* (%) = 297.8 (100) $[M]^+$.

*4-Phenyl-1,2,3,4-tetrahydrobenzopyrano[4,3-d]pyrimidine-2,5-dione (**10d**)*

M. p. 162 – 163 °C (162 °C [25]). – $C_{17}H_{12}O_3N_2$: calcd. C 69.86, H 4.10, N 9.58; found C 69.85, H 4.14, N 9.56. – IR (nujol): ν = 1680, 3445 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 6.12 (s, 1 H), 6.79 – 7.65 (m, 9 H, Ar-H), 11.53 (brs, 2 H, 2NH). – MS: *m/z* (%) = 292.0 (100) $[M]^+$.

*4-(4-Methoxyphenyl)-1,2,3,4-tetrahydrobenzopyrano[4,3-d]pyrimidine-2-thioxo-5-one (**11a**)*

M. p. 234 – 236 °C (234 °C [25]). – $C_{18}H_{14}O_3N_2S$: calcd. C 63.85, H 4.14, N 8.28, S 9.46; found C 63.89, H 4.12, N 8.25, S 9.45. – IR (nujol): ν = 1675, 3455 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 3.84 (s, 3 H, OCH_3), 6.07 (s, 1 H), 6.83 – 7.53 (m, 8 H, Ar-H), 11.50 (brs, 2 H, 2NH). – MS: *m/z* (%) = 338.6 (100) $[M]^+$.

*4-(4-Chlorophenyl)-1,2,3,4-tetrahydrobenzopyrano[4,3-d]-pyrimidine-2-thioxo-5-one (**11b**)*

M. p. 187 – 189 °C (188 – 190 °C [26]). – $C_{17}H_{11}O_2N_2ClS$: calcd. C 59.56, H 3.21, N 8.17, S 9.34; found C 59.54, H 3.20, N 8.1, S 9.35. – IR (nujol): ν = 1680, 3450 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 6.08 (s, 1 H), 6.86 – 7.82 (m, 8 H, Ar-H), 11.50 (brs, 2 H, 2NH). – MS: *m/z* (%) = 342.0 (100) $[M]^+$.

*4-(Thiophen-2-yl)-1,2,3,4-tetrahydrobenzopyrano[4,3-d]-pyrimidine-2-thioxo-5-one (**11c**)*

M. p. 245 – 247 °C. – $C_{15}H_{10}N_2O_2S$: calcd. C 57.32, H 3.18, N 8.91, S 20.38; found C 57.31, H 3.15, N 8.71, S 20.34. – IR (nujol): ν = 1680, 3455 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 6.08 (s, 1 H), 6.77 – 7.65 (m, 7 H, Ar-H + thienyl), 11.40 (brs, 2 H, 2NH). – MS: *m/z* (%) = 314.7 (100) $[M]^+$.

*4-Phenyl-1,2,3,4-tetrahydrobenzopyrano[4,3-d]pyrimidine-2-thioxo-5-one (**11d**)*

M. p. 188 – 189 °C (188 °C [25]). – $C_{17}H_{12}O_2N_2S$: calcd. C 62.23, H 3.89, N 9.09, S 10.38; found C 62.21, H 3.87, N 9.07, S 10.39. – IR (nujol): ν = 1670, 3445 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 6.05 (s, 1 H), 6.79 – 7.68 (m, 9 H, Ar-H), 11.48 (brs, 2 H, 2NH). – ^{13}C NMR (75.6 MHz, $CDCl_3$, TMS): δ = 128.6, 125.0, 130.1, 122.3, 152.8, 171.0, 101.9, 58.2, 129.1, 130.3, 128.5, 130.1, 128.9, 144.4, 184.2, 163.2, 129.8. – MS: *m/z* (%) = 308.0 (100) $[M]^+$.

Acknowledgement

The authors are thankful to CSIR, New Delhi, for their financial assistance.

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