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Research Article

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Synthesis and characterization of some new 3, 5-disubstituted pyrimidine and thiopyrimidine derivatives

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ABSTRACT

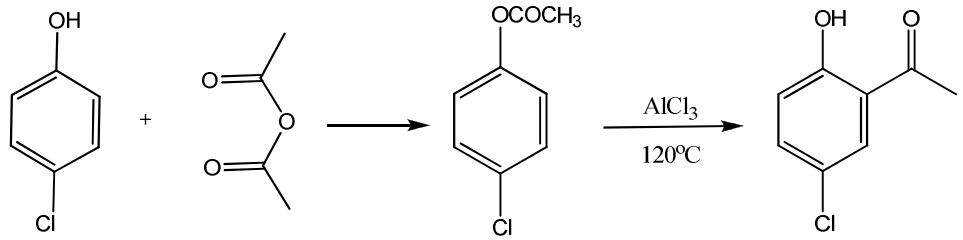
1-(5-chloro-2-hydroxyphenyl)-ethanone (1a) was prepared from 2-chlorophenol through multi-step reaction. Compound (1a) reacts with different aryl aldehyde in the presence of NaOH (40%) to gives 1-(5-chloro-2-hydroxyphenyl)-3-(4-substitutedphenyl)-prop-2-en-1-one (2a-e). 4-(5-chloro-2-hydroxy phenyl)-6-(4-substituted phenyl)-pyrimidin-2-(1H)-one (3a-e) and 4-(5-chloro-2-hydroxyphenyl)-6-(4-substitutedphenyl)-pyrimidin-2-(1H)-thione (4a-e) was achieved through cyclisation of 1-(5-chloro-2-hydroxyphenyl)-3-(4-substitutedphenyl)-prop-2-en-1-one (2a-e) with urea and thiourea in ethanol containing catalytic amount of KOH respectively. All the synthesized compounds were characterized on the basis of spectral data.

Keywords: 2-Chlorophenol, aryl aldehyde, urea and thiourea.

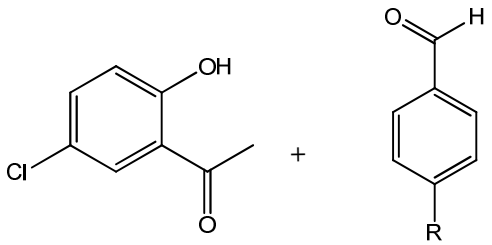
INTRODUCTION

Oxopyrimidines and thiopyrimidines are potential bioactive agents due to their wide spectrum of pharmacological activities like anti-inflammatory [1], antimicrobial [2], calcium channel blockers [3], antihypertensive [4], analgesic [5], antitumor [6], antiviral [7], antibacterial [8], anti-HIV [9] and anticancer [10]. Looking to the diversified activities exhibited and in continuation of our work on the synthesis of biologically active heterocycles, we report here in the reaction of different aryl aldehyde [11, 12, 13] with 1-(5-chloro-2-hydroxyphenyl)-ethanone in the presence of NaOH (40%) afforded gives 1-(5-chloro-2-hydroxyphenyl)-3-(4-substitutedphenyl)-prop-2-en-1-one(2a-e). 1-(5-chloro-2-hydroxy phenyl)-3-(4-substitutedphenyl)-prop-2-en-1-one (2a-e) on cyclization [14,15,16] with urea and thiourea in ethanol containing catalytic amount of KOH to afforded 4-(5-chloro-2-hydroxyphenyl)-6-(4-substitutedphenyl)-pyrimidin-2-(1H)-one (3a-e) and 4-(5-chloro-2-hydroxyphenyl)-6-(4-substitutedphenyl)-pyrimidin-2-(1H)-thione (4a-e) respectively.

The structures of the synthesized compounds (3a-e) and (4a-e) have been confirmed by melting point, TLC, IR spectra and NMR spectra.



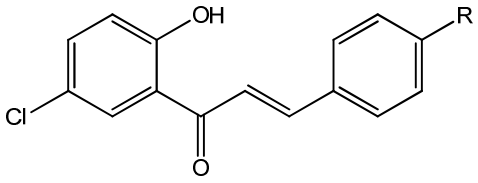
(1a)



(1a) **(1b)**

Where R=H, OCH_3, OH, Cl. $N(CH_3)$

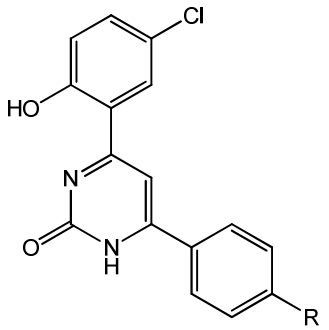
40% NaOH,
EtOH

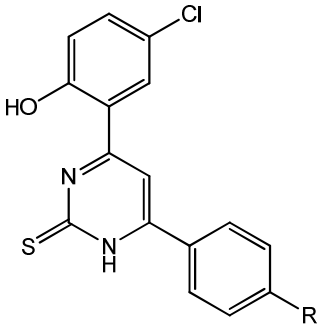


(2a-e)

NH_2-CO-NH_2, KOH
Ethanol

NH_2-CS-NH_2., KOH
Ethanol





(3a-e) **(4a-e)**

SCHEME

EXPERIMENTAL SECTION

Materials: 2-Chlorophenol, Anhydrous $AlCl_3$, Acetic anhydride, Benzaldehyde, 4-Methoxybenzaldehyde, 4-Chlorobenzaldehyde, 4-Hydroxybenzaldehyde, 4-N, N-Dimethylbenzaldehyde, Urea, Thiourea, NaOH, KOH, Ethanol.

All the melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr using Perkin Elmer model 2000 spectrophotometer and reported wave numbers are given in cm^{-1}. ^{1}H-NMR spectra were recorded in $CDCl_3$ on a Brucker Advance II 400 MHz spectrophotometer using TMS as an internal standard. Chemical shift values are shown in δ ppm. Mass spectra were recorded on Agilent 6320 Ion Trap mass spectrometer. The purity of all the synthesized compounds was checked by TLC on silica gel plates by using appropriate solvents.

Synthesis of 1-(3-chloro-6-hydroxyphenyl)-ethanone (1a):
4-Chlorophenyl acetate, which is prepared from 4-chlorophenol & acetic anhydride, were mixed with anhydrous $AlCl_3$ and heated at 120 ^oC for 45 minutes on oil bath. The reaction mixture was decomposed with ice cold water containing little hydrochloric acid to get crude ketone. It was purified by dissolving in acetic acid and pouring the solution dropwise into cold water with stirring. Yellowish white solid was obtained, Yield: 65%, m.p.: 42-45 ^oC.

1-(5-chloro-2-hydroxyphenyl)-3-(4-methoxyphenyl)-prop-2-en-1-one (2a):
1-(3-chloro-6-hydroxyphenyl)-ethanone (1a) (0.01 mol) dissolved in ethanol (40 ml) and 4-methoxybenzaldehyde (0.01 mol) was added with constant stirring at room temperature. Then NaOH solution (40%) was added to the reaction mixture with constant stirring, keeping the temperature of the reaction mixture below 10 ^oC throughout the addition. The flask was corked and kept the reaction mixture for 48 hours at room temperature. Finally the reaction mixture was poured over crushed ice and neutralized with glacial acetic acid. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to afford compound (2a).

Yield: 69%, M.P.: 90-93 ^oC, M.W.: 288.06, Anal. Calculation for $C_{16}H_{13}ClO_3$: Found: C: 65.49, H: 5.23, Calcd. C: 66.56, H: 4.54. IR (KBr, cm^{-1}): 1753 (C=O), 1488 (C=C), 1238 (Ar-O), 1200 (C-O). ^{1}NMR: ($CDCl_3$, 400 MHz): 3.85 (s, 3H, $-OCH_3$), 5.47-5.46 (d, 1H, CO-CH=), 6.93-6.91 (m, 2H, Ar-H), 7.68-6.65 (d 1H, Ar-CH=), 7.91-7.17 (m, 5H, Ar-H). Other compounds of this type (2b-e) were prepared similarly and are recorded in Table-1.

4-(5-chloro-2-hydroxyphenyl)-6-(4-methoxyphenyl)-pyrimidin-2(1H)-one (3a).
A mixture of 1-(1-(5-chloro-2-hydroxyphenyl)-3-(4-methoxyphenyl)-prop-2-en-1-one (2a-e) (0.01 mol) and urea (0.01 mole) in ethanol (30 ml) containing alcoholic KOH (1mL) were refluxed for 12 hours. Cooled the reaction mixture and poured over crushed ice. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to afford compound (3a).

Yield: 71%, M.P.: 63-66 ^oC, M.W.: 350.43, Anal. Calculation for $C_{17}H_{13}ClN_2O_3$: Found: C: 62.49, H: 4.21, N: 8.61 Calcd. C: 62.11, H: 3.99, N: 8.52. IR (KBr, cm^{-1}): 3435 (-OH), 3070 (-NH), 2991 (Ar-CH), 1691 (C=O), 1639 (C=N). ^{1}NMR: ($CDCl_3$, 400 MHz): 3.83 (s, 3H, $-OCH_3$), 5.08 (d, 1H, Ar-H), 6.96-6.94 (s, 2H, Ar-H), 7.26 (s, 1H, -OH), 7.46-7.38 (m, 4H, Ar-H), 7.65-7.63 (d, 1H, Ar-H), 12.87 (s, 1H, -NH). Other compounds of this type (3b-e) were prepared similarly and are recorded in Table-1.

4-(5-chloro-2-hydroxyphenyl)-6-(4-methoxyphenyl)-pyrimidin-2(1H)-thione (4a).
A mixture of 1-(1-(5-chloro-2-hydroxyphenyl)-3-(4-methoxyphenyl)-prop-2-en-1-one (2a-e) (0.01 mol) and thiourea (0.01 mole) in ethanol (30 ml) containing alcoholic KOH (1mL) were refluxed for 12 hours. Cooled the reaction mixture and poured over crushed ice. The product separated out was filtered, washed with water, dried and recrystallized from ethanol to afford compound (4a).

Yield: 67%, M.P.: 180-182 ^oC, M.W.: 344.82, Anal. Calculation for $C_{17}H_{13}ClN_2O_2S$: Found: C: 58.89, H: 3.73, N: 8.02, Calcd. C: 59.21, H: 3.80, N: 8.12. IR (KBr, cm^{-1}): 3436 (-OH), 3069 (-NH), 2992 (Ar-CH), 1638 (C=N), 1612 (C=C), 1171 (C-O). ^{1}NMR: ($CDCl_3$, 400 MHz): 3.87 (s, 3H, $-OCH_3$), 6.98-6.94 (m, 3H, Ar-H), 7.26 (s, 1H, -OH), 7.45-7.40 (m, 2H, Ar-H), 7.65-7.63 (d, 2H, Ar-H), 7.85-7.84 (d, 1H, Ar-H), 12.88 (s, 1H, -NH).Other compounds of this type (4b-e) were prepared similarly and are recorded in Table-1.

Table-1: Physicochemical data of the synthesized compounds

Sr. No.	Compds	R	M.P. (°C)	Yield (%)	Molecular Weight	Molecular Formula
1	2a	OCH_3	90-93	69	288.73	$C_{16}H_{13}ClO_3$
2	2b	H	89-91	62	258.70	$C_{15}H_{11}ClO_2$
3	2c	Cl	165-168	68	293.14	$C_{15}H_{10}Cl_2O_2$
4	2d	OH	135-138	64	274.70	$C_{15}H_{11}ClO_3$
5	2e	$N(CH_3)_2$	140-143	59	301.77	$C_{17}H_{16}ClNO_2$
6	3a	OCH_3	63-66	71	328.75	$C_{17}H_{13}ClN_2O_3$
7	3b	H	65-68	65	298.72	$C_{16}H_{11}ClN_2O_2$
8	3c	Cl	175-180	67	333.17	$C_{16}H_{10}Cl_2N_2O_2$
9	3d	OH	120-122	70	314.72	$C_{16}H_{11}ClN_2O_3$
10	3e	$N(CH_3)_2$	140-143	66	341.79	$C_{18}H_{16}ClN_3O_2$
11	4a	OCH_3	180-182	67	344.82	$C_{17}H_{13}ClN_2O_2S$
12	4b	H	192-195	71	314.79	$C_{16}H_{11}ClN_2OS$
13	4c	Cl	67-70	59	349.23	$C_{16}H_{10}Cl_2N_2OS$
14	4d	OH	95-98	63	330.79	$C_{16}H_{11}ClN_2O_2S$
15	4e	$N(CH_3)_2$	240-243	66	357.86	$C_{18}H_{16}ClN_3OS$

RESULTS AND DISCUSSION

The structures of the synthesized compounds were characterized with the help of TLC, IR and NMR. There are no absorptions in the region of 1600-1700 cm^{-1} indicating the absence of –C=N group in 2a compound. The IR spectrum of compounds 3a and 4a shows the characteristic band at 1600-1700 cm^{-1} indicating the presence of C=N group confirmed the cyclisation in pyrimidine and thiopyrimidine derivatives.

The ^{1}H NMR spectrum of compound 2a showed doublet of –CO-CH= at δ 5.47-5.46 ppm and Ar-CH= at δ 7.68-7.65 ppm, which confirmed the presence of chalcone moiety. The ^{1}H NMR spectrum of compound 3a and 4a showed singlet of -NH near about δ 12.00-13.00 ppm confirmed the cyclisation in pyrimidine and thiopyrimidine derivatives.

CONCLUSION

The present work describes a novel and simple approach for the synthesis of some new 3, 5-disubstituted pyrimidine and thiopyrimidine derivatives. The structures of the synthesized compounds were characterized with the help of TLC, IR and NMR.

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REFERENCES

[1] SS Bahekar and DB Shinde, *Acta Pharm*., **2003**, 53, 223.
[2] AM El-Agrody, FM Ali, FA Eid, Mohammed AA, El-Nassag G, El-Sherbeny and A H Bedair, *Phosphorus, Sulfur and Silicon*, **2006**, 181, 839.
[3] L Guarneri, A Patrizia, I Marina, P Elena, T Carlo, L Amedeo and T Rodolfo, *Arzneimittel Forschung*, **1996**, 46, 15; *Biol Abstr*. **1998**, 101, 32842.
[4] Priyanka Pathak, Ramandeep Kaur and Balbir Kaur, *Arkivok*, **2006** (xvi), 160.
[5] Veerachamy Alagarsamy, Durairaj Shankar and Viswas Raja Solomon, *Arkivok*, **2006** (xvi), 149.
[6] Y. L. Huang, C. F. Lin, Y. J. Lee, W. W. Li and T. C. Chao, *Bio. Org. Med. Chem*., **2003**, 11, 67.
[7] S Shigeta, S Mori, F Watanabe and M Saneyoshi, *Antivir Chem. Chemother*, **2002**, 13, 145.
[8] Somnath Nag, Richa Pathak, Manish Kumar, PK Shukla and Sanjay Batra, *Bioorganic & Medicinal Chemistry*, **2006**, 16, 3824.
[9] GF Sun, YY Kuang, FE Chen, De Clercq and C. Pannecouque, *Arch. Pharm*. (Weinheim), **2005**, 338, 457.
[10] KS Nimavat, KH Popat, SL Vasoya and HS Joshi, *Indian Journal of Heterocyclic Chemistry*, **2003**, 12, 217.
[11] Shankaraiah G Konda, Vishnu T Khedkar and Bhaskar S Dawane, *Journal of Chemical and Pharmaceutical Research*, **2010**, 2(1), 187-191.

[12] OA Fatalla et al., *Arch Pharm Res*, 28(11), **2005**, 1205-1212.
[13] VN Ingle et al, *Indian Journal of chemistry*, **2008**, 47B, 1260-1270.
[14] Raga Basawaraj, Ravi Hassappa, Neelavathi Chillargi and shivanand Noola, *Indian Journal of Heterocyclic Chemistry*, **2010**, 19, 252-256.
[15] ML Ladani, SD Tala, JD Akbari, MF Dhaduk and HS Joshi, *Journal of Indian Chemical Soc*., **2009**, 86, 104-108.
[16] V Harinadha Babu, P Senthil Kumar, KK Srinivasan and G Varadaraja Bhat, *Indian J. Pharm. Sci*., **2004**, 66 (5), 647-652.
[17] SB Zangade, JD Jadhav, Lalpod, YB Vibhute and BS Dawane, *Journal of Chemical and Pharmaceutical Research*, **2010**, 2(1), 310-314.
[18] Kakul Husain, Mohammad Abid and Amir Azan, *European Journal of Medicinal Chemistry*, **2008**, 43(2), 393-403.
[19] Chirag K Patel, CS Rami, B Panigrahi and CN Patel, *Journal of Chemical and Pharmaceutical Research*, **2010**, 2(1), 73-78.