Original Research Paper

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Chemistry

EFFICIENT METHOD FOR SYNTHESIS OF 5-((BENZYLIDENE AMINO)METHYL)-4-(SUBSTITUTED PHENYL),6-METHYL, 3,4-DIHYDROPYRIMIDIN-2(1H)-ONES

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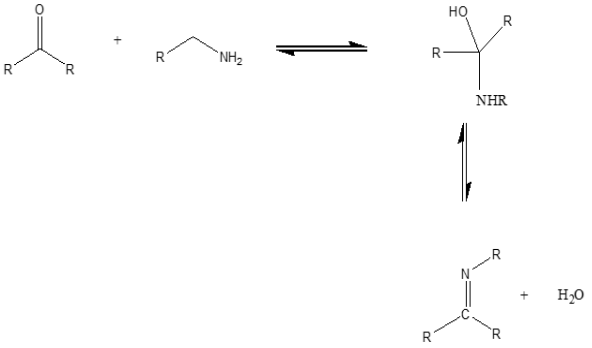
ABSTRACT A Simple and Economic Synthesis of 5-((benzylidene amino)methyl)-4-(substituted phenyl)-6-methyl, 3,4-dihydropyrimidin-2(1H)-ones by using 5-(aminomethyl)-4-(substituted phenyl)- 6-methyl- 3,4-dihydropyrimidin-2(1H)-ones and benzaldehyde in presence of ethanol. When banzaldehyde is react with primary amine i.e. 5-(aminomethyl)-4-(substituted phenyl)- 6-methyl- 3,4-dihydropyrimidin-2(1H)-ones in presence of alcoholic medium it gives formation of corresponding Schiff bases.

KEYWORDS : Benzaldehyde, Ethanol, Schiff bases, 5-(aminomethyl)-4-(substituted phenyl)- 6-methyl- 3,4-dihydropyrimidin-2(1H)-ones etc.

Introduction: Over the last two decades there has been rapid progress in synthetic organic chemistry associated with the search for new organic compounds derivatives with desirable properties. Such compounds are widely used in the pharmacetutical industry[1]. The four-membered cyclic amides commonly known as 2-azetidinones or β-lactams occupy a prominent place in the realm of organic and medicinal chemistry since the structure elucidation of penicillin showed the presence of β -lactam ring in it and the antibacterial activity of Penicillin was attributed to the presence of β -lactam ring. The early investigations in organic chemistry were focused on broadening the spectrum of antibacterial activity. These studies led to development of several novel methodologies for construction of the β -lactam ring and discovery of several β -lactam antibiotics, such as monobactams, cephalosporins, carbapenams, trinems etc[2]. β-lactam antibiotics, since their introduction continue to be chemotherapeutics of incomparable effectiveness, conjugating a broad spectrumof activity with low toxicity[3]. It possess pharmacological activities such as anti-viral[4], antihyperlipidemic[5], human leukocyte elastase[6], antidepressant[7], anti-parkinsonian[8], anti-tumor[9], tubercular[10], enzyme inhibitory [11], and antithrombotic[12].

Hugo Schiff was the first scientist who described Schiff bases in 1864 [13]. The preparation of Schiff bases involves a variety of conditions and is brought about by mixing carbonyl compounds and amines in various proportions and employing a range of solvents. The formation of Schiff bases is generally favored by making use of dehydrating agents. A great care should be taken for the purification of Schiff bases as they are degradable. The acid/base catalysis or heating is employed for the synthesis of Schiff bases as their reactions are mostly reversible[14].

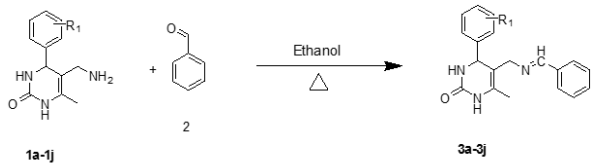


The common structural feature of these compounds is the azomethine group with a general formula RHC=N-R_1, where R and R_1 are alkyl, aryl, cyclo alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines [15]. The nitrogen atom of azomethine may be involved in the formation of a hydrogen bond with the active centers of cell constituents and interferes in normal cell processes. Schiff bases from an important class of the most widely used organic compounds and have a wide variety of applications in many fields including analytical, biological and inorganic chemistry [16].

Schiff bases have been utilized as synthons in the preparation of a number of industrial and biologically active compounds like formazans, 4-thiazolidinies, benzoxazines, 2-azetidinone and so fourth via ring closure, cycloaddition and replacement reactions[17]. Schiff bases have received more attention mainly because of their wide biological activities including anti-tumor[18], antibacterial[19], fungicidal[20], anti-inflammatory[21], antiviral[22], herbicidal[23], antipyretic[24] and anticonvulsant[25]. Schiff bases and their cyclization to produce β -lactam derivatives of biological significance[26].

Result and Discussion : In this communication, the equimolar quantity of 5-(aminomethyl)-4-(substituted phenyl), 6-methyl,3,4-dihydropyrimidin-2(1H)-one (1a-1j) (0.01mol) and benzaldehyde (2) (0.01mol), were taken in Round bottom flask with 5-10ml ethanol as a solvent and the reaction mixture was subjected to reflux for few hours. The product, obtained was poured over crushed ice. The solid separated out was filtered, washed with water and recrystallized from ethanol to afford pure 5-((benzylidene amino)methyl)-4-(substituted phenyl), 6-methyl, 3,4-dihydropyrimidin -2(1H)-ones. (**3a-3j**). And these results are summarized in Table-I.

Reaction:



Scheme 1:
5-((benzylideneamino)methyl),-4-(substituted phenyl),6-methyl, 3,4-dihydropyrimidin-2(1H)-one

Where R_1 = a) –H , b) 4-OCH_3 , c) 4-NO_2 , d) 4-Br , e) 4-Cl f) 4-OC_2H_5 , g) 3-Cl , h) 2-Cl , i) 2-F , j) 2-OC_2H_5 .

Table I : Analytical data of synthesized 5-((benzylidene amino)methyl)-4-(substituted phenyl), 6-methyl, 3,4-dihydropyrimidin-2(1H)-ones.

Sr. No.	Compound	R_1	Reaction time (hrs)	M.F.	M.W.	Yield	M.Pt (^oC)
1	3a	H	1.5	$C_{19}H_{19}ON_3$	305	80%	240^oC
2	3b	p-OCH_3	1	$C_{20}H_{21}O_2N_3$	335	75%	232^oC

3	3c	p-NO_2	0.50	$C_{19}H_{18}O_3N_4$	350	82%	215 ^oC
4	3d	p-Br	1.20	$C_{19}H_{18}ON_3Br$	383.9	80%	239 ^oC
5	3e	p-Cl	0.50	$C_{19}H_{18}ON_3Cl$	339.5	85%	245 ^oC
6	3f	p-OC_2H_5	1.45	$C_{21}H_{23}O_2N_3$	349	90%	222 ^oC
7	3g	m-Cl	1.30	$C_{19}H_{18}ON_3Cl$	339.5	88%	233 ^oC
8	3h	o-Cl	1.30	$C_{19}H_{18}ON_3Cl$	339.5	81%	248 ^oC
9	3i	o-F	1.20	$C_{19}H_{18}ON_3F$	323	76%	240 ^oC
10	3j	o-OC_2H_5	1	$C_{21}H_{23}O_2N_3$	349	79%	242 ^oC

Experimental Section: The melting points of all synthesized compounds were recorded using open capillaries and are uncorrected. The IR spectra were recorded on a PERKIN ELMER Spectophotometer in the frequency range 4000-400 cm^{-1} in Nujol mull and as KBr pellets. 1H NMR spectra were recorded on BRUKER ADVANCE II 400 spectrometer with TMS as internal standard using DMSO as solvents. All the compounds are synthesized in R. B. Flask by using water condenser and refluxed for several times. Purity of the compounds were checked on pre coated silica-G plates by TLC.

Chemicals (Reagents) used in the synthesis of 5-((benzylidene amino)methyl)-4-(substituted phenyl), 6-methyl, 3,4-dihydropyrimidin -2(1H)-ones, were of AR gread.

General Procedure : In this case, the equimolar quantity of 5-(aminomethyl)-4-(substituted phenyl), 6-methyl,3,4-dihydropyrimidin-2(1H)-one (1a-1j) (0.01mol) and benzaldehyde (2) (0.01mol), were taken in Round bottom flask with 5-10ml ethanol as a solvent and the reaction mixture was subjected to reflux for few hours. The product, obtained was poured over crushed ice. The solid separated out was filtered, washed with water and recrystallized from ethanol to afford pure 5-((benzylidene amino)methyl)-4-(substituted phenyl), 6-methyl, 3,4-dihydropyrimidin -2(1H)-ones. (3a-3j).

Spectroscopic data of Representative 5-((benzylidene amino) methyl) - 4-(substituted phenyl) - 6-methyl - 3,4-dihydropyrimidin-2(1H)-ones.

1. 5-((benzylidene amino)methyl)-4-(phenyl), 6-methyl, 3,4-dihydropyrimidin-2(1H)-one.(entry-1): m.p 240^{0}C ,IR(KBr) :[cm^{-1}] 3416, 2929, 1678, 1436, 1388, 934, 713 ; PMR (DMSO-d6):7.7(1H,s,CH),7.9(4H,m,ArH),6.9(1H,bs,NH),2.3(3H,s,CH_3),10.0(1H,s,NH).

2. 5-((benzylidene amino)methyl)-4-(4-methoxy-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-2): m.p 232^{0}C ,IR(KBr) :[cm^{-1}] 3414, 2929, 1678, 1386, 1029, 752 ; PMR (DMSO-d6) :6.9(1H,s,NH),7.4(4H,m,ArH),6.9(1H,bs,NH),2.5(3H,s,CH_3),7.2(1H,s,CH).

3. 5-((benzylidene amino)methyl)-4-(4-nitro-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-3): m.p 215^{0}C ,IR(KBr) :[cm^{-1}] 3624, 3227, 1663, 1341, 1075, 727 ; PMR (DMSO-d6) :7.0(1H,bs,NH),7.6(4H,m,ArH),8.7(1H,bs,NH),2.0(3H,s,CH_3),5.3(1H,s,CH).

4. 5-((benzylidene amino)methyl)-4-(4-bromo-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-4): m.p 239^{0}C ,IR(KBr) :[cm^{-1}] 3487, 3118, 1760, 1442, 1039, 752 ; PMR (DMSO-d6) :8.7(1H,bs,NH),8.2(4H,m,ArH),6.9(1H,bs,NH),2.0(3H,s,CH_3),6.9(1H,s,NH).

5. 5-((benzylidene amino)methyl)-4-(4-chloro-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-5): m.p 245^{0}C ,IR(KBr) :[cm^{-1}] 3435, 3235, 1710, 1402, 1087, 706 ; PMR (DMSO-d6) :7.0(1H,bs,NH),7.6(4H,m,ArH),8.6(1H,bs,NH),2.1(3H,s,CH_3),5.28(1H,s,CH).

6. 5-((benzylidene amino)methyl)-4-(4-ethoxy-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-6): m.p 222^{0}C ,IR(KBr) :[cm^{-1}] 3622, 3187, 1791, 1702, 1499, 1046, 706 ; PMR (DMSO-d6) :8.5(1H,bs,NH),6.8(4H,m,ArH),5.1(1H,bs,NH),2.5(3H,s,CH_3),9.9(1H,s,CH).

7. 5-((benzylidene amino)methyl)-4-(3-chloro-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-7): m.p 233^{0}C ,IR(KBr) :[cm^{-1}] 3327, 2929, 1607, 1436, 996, 717 ; PMR (DMSO-d6) :7.2(1H,bs,NH),7.3(4H,m,ArH),7.5(1H,bs,NH),2.0(3H,s,CH_3),8.6(1H,s,CH).

8. 5-((benzylidene amino)methyl)-4-(2-chloro-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-8): m.p 248^{0}C ,IR(KBr) :[cm^{-1}] 3741, 3018, 1698, 1438, 993, 782 ; PMR (DMSO-d6) :6.9(1H,bs,NH),7.3(4H,m,ArH),7.4(1H,bs,NH),2.0(3H,s,CH_3),5.6(1H,s,CH).

9. 5-((benzylidene amino)methyl)-4-(-fluoro-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-9): m.p 240^{0}C ,IR(KBr) :[cm^{-1}] 3741, 3616, 1557, 1433, 991, 710 ; PMR (DMSO-d6) :6.9(1H,bs,NH),7.2(4H,m,ArH),7.3(1H,bs,NH),2.0(3H,s,CH_3),8.6(1H,s,CH).

10. 5-((benzylidene amino)methyl)-4-(2-chloro-phenyl)-6-methyl-3,4-dihydropyrimidin-2(1H)-one.(entry-10): m.p 242^{0}C ,IR(KBr) :[cm^{-1}] 3622, 3088, 1674, 1450, 1038, 741 ; PMR (DMSO-d6) :7.2(1H,bs,NH),7.1(4H,m,ArH),6.9(1H,bs,NH),2.0(3H,s,CH_3),8.5(1H,s,CH).

In the conclusion, we have developed a simple quick and efficient method or the synthesis of 5-((benzylidene amino)methyl)-4-(substituted phenyl), 6-methyl, 3,4-dihydropyrimidin -2(1H)-ones by using benzaldehyde and ethanol. Apart from its Simplicity, the important advantage of the present protocol is the ability to tolerate variations in all the three components of the reaction. To the best of our knowledge, this is one of the quickest, economical and simple alternatives towards the synthesis of the 5-((benzylidene amino)methyl)-4-(substituted phenyl), 6-methyl, 3,4-dihydropyrimidin -2(1H)-ones. This introduces another important use of Benzaldehyde in the synthetic Organic Chemistry.

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