Turk J Chem
23 (1999) , 401 – 405.

Reactions of N-Aminopyrimidine Derivatives with 1,3-Dicarbonyl Compounds

Zülbiye ÖNAL, Behzat ALTURAL
Erciyes University, Arts and Sciences Faculty,
Department of Chemistry, 38039, Kayseri-TURKEY

Received 15.09.1997

The reactions of 1-Amino-pyrimidine derivatives **(1)** and some 1,3-dicarbonyl compounds **(2)** were realized in the presence of p-toluensulfonic acid catalyst to give convenient enamine **(3)** and/or imine derivatives **(4)**. In the same way, the enamine **(5)** and/or imine derivatives **(6)** were synthesized using **(1)** and 1,3-indanedione which is one of the different 1,3-dicarbonyl compounds. The molecular structures of all the prepared compounds were determined by ^{1}H-nmr, ^{13}C-nmr, i.r. spectra and elemental analyses, and were drawn by taking imine-enamine tautomerism into account.

Key words: Enamine; Imine; 1,3-Diketone; Addition reaction

Introduction

N-Aminopyrimidine derivatives **(1)**, consisting of 1-amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-tione anologue have been repordet recently[1,2]. Several subsequent reactions of **(1)** were realized to synthesize substituted ureas by adding amines to isocyanates[3]. Since pyrimidine derivatives, in general, have become of great interest for biological and medical reasons[4], we have now extended our investigations into the reactions of **(1)** with various 1,3-dicarbonyl compounds.

Experimental

Melting points were determined with a Buchi melting point apparatus and not corrected. The compounds were routinely checked for their homogenity by TLC using kieselgel GF_{254}60 as absorbant. The i.r. spectra were recorded on a Schimadzu spectrophotometer model 435 V-04 using samples in potasium bromide disks. The ^{1}H-nmr spectra were measured with a Gemini-Varian 200 MHz, ^{1}H-nmr using TMS as the internal reference. The elemental analysis was carried out with a Carlo-Erba 1108 Elemental Analyzer. A Buchi RE model 111 type, rotary evaporator was used for evaporating the solvents remaining in the reaction media. Chemicals were from Merck and Aldrich Chemicals Comp. Solvents were distilled before use.

General Procedure to get **(3)** and/or **(4)**:

Compound **(1)** and the corresponding 1,3-dicarbonyl compound **(2)** (molar ratio 1:4 approximately) and p-toluensulfonic acid catalyst were homogeneously mixed. The mixture was heated at 115-125°C and kept at this temperature for 40 min-3h without any solvent in a calcium chloride guard tube fitted round

bottom flask of 50 ml. After cooling to room temperature the residue was treated with dry ether and crude product recrystallized from a suitable solvent (i.e. n-butanol or i-propanol).

1-(5-Benzoyl-4-phenyl-2-oxo-1,2-dihydro-pyrimidinyl-amino)-1-phenyl-2- benzoyleten (3a):

0.2 g **la** and 1 g **2a** (molar ratio 1:7) were heated at 115°C for 40 min yielding 0.2 g 60% **3a**, m.p 294°C (n-butanol). i.r. cm^{-1}:3350-3500 (N-H), 3150-3200 (C=CH), 3000-3050 (arom. C-H), 1690 (C=O), 1600 (C=C and C=N), 1500-1400 (arom. ring skeleton vib.), 660-800 pyrimidine ring skeleton vib.). ^{1}H-nmr (DMSO) δ: 5.85 (N-H), 5.96 (C=CH), 6.67-7.83 (arom. protons). ^{13}C-nmr (DMSO) δ 160.05ppm (NCON), 148.78 (N=C, pyrimidine ring), 58.69 (NH-C), 64.91 (=CH-, olefin), 196.59-196.94 (C=O), 129.12-148.79 (aromat. C's). Anal. calc. for $C_{32}H_{23}N_3O_3$: C 77.25, H 4.65, N 8.44; found: C 77.01, H 4.61, N 8.40.

1-(5-Benzoyl-4-phenyl-2-thioxo-1,2-dihydro-pyrimidinyl-amino)-1-phenyl- 2-benzoyleten (3b):

0.2 g **lb** and 1 g **2b** (molar ratio 1:7) were heated at 115°C for 3 h yielding 0.2 g 60% **3b**, m.p 275°C (n-butanol). i.r. cm^{-1}:3400 (N-H), 3150-3200 (C=CH and C=N), 3020 (arom. C-H), 1690 (C=O), 1600 (C=C and C=N), 1520-1450 (arom. ring skeleton vib). 1220 (C=S), 680-760 (pyrimidine ring skeleton vib.). ^{1}H-nmr (DMSO) δ: 5.89 (N-H), 5.71 (C=CH), 6.66-7.70 ppm (arom. protons). Anal. calc. for $C_{32}H_{23}H_3O_2S$: C 74.78, H 4.50, N 8.18, S 6.24; found: C 74.46, H 4.39, N 7.98, S 5.94.

1-(5-Benzoyl-4-phenyl-2-oxo-1,2-dihydro-pyrimidinyl-amino)-1-metoxy-phenyl- 2-p-metoxybenzoyleten (3c):

0.2 g **lc** and 0.76 g **2c** (molar ratio 1:4) were heated at 115°C for 90 min yielding 0.23 g 64% **3c**, m.p 325°C (n-butanol). i.r. cm^{-1}: 3400-3500 (N-H), 3150-3200 (C=CH), 3050-3100 (arom. C-H), 2800-3000 (OCH_3), 1710-1650 (C=O), 1600-1580 (C=C and C=N), 1510-1430 (arom. ring skeleton vib.), 900-760 (pyrimidine ring skeleton vib.). ^{1}H-nmr (DMSO) δ: 3.36-3.71 (CH3), 6.88-6.92 (N-H), 6.62-6.67 (C=CH), ^{13}C-nmr (DMSO) δ: 164.81 (NCON), 146.43 (N=C, pyrimidine ring), 58.69 (NH-C), 64.91 (=CH-, olefin), 190.93-193.08 (C=O), Anal. calc. for $C_{34}H_{27}H_{27}N_3O_5$: C 73.74, H 4.87, N 7.53; found: C 73.49, H 4.51, N 7.53.

1-(5-Benzoyl-4-phenyl-2-thioxo-1,2-dihydro-pyrimidinyl-amino)-1-p-metoxy-phenyl- 2-p-metoxybenzoyleten (3d):

0.2 g **ld** and 0.76 g **2d** (molar ratio 1:4) were heated at 115°C for 2 h yielding 0.18 g 50% **3b**, m.p. 277°C (n-butanol). i.r. cm^{-1}: 3400-3500 (N-H), 2800-3000 (OCH_3), 3050 (arom.C-H), 1660-1600 (C=O), 1530-1400 (arom. ring skeleton vib.), 1160 (C=S), 600-730 (pyrimidine ring skeleton vib.). ^{1}H-nmr ($CDCl_3$) δ: 3.61-3.66 (CH_3), 5.67-5.71 (C=CH), 5.73-5.77 (N-H), 6.57-7.68 (arom. protons) Anal. calc. for $C_{34}H_{27}H_{27}N_3O_4S$: C 71.18, H 4.74, N 7.32; found: C 70.85, H 4.82, N 7.08, S 5.43.

1-(5-Benzoyl-4-phenyl-2-oxo-1,2-dihydro-pyrimidinyl-amino)-1-methyl-2- acetyleten (3e):

0.2 g **le** and 1,5 ml (1.458 g) **2e** (molar ratio 1:21) were heated at 115°C for 30 min yielding 0.16 g 62% **3e**, m.p. 240°C (n-butanol). i.r. cm^{-1}: 3400-3500 (N-H), 3100-3200 (arom C-CH), 3050 (CH_3) 1720-1690 (arom. ring skeleton vib.), 1340-1240 (CH_3 bend. vib.), 800-690 (pyrimidine ring skeleton vib.). ^{1}H-nmr (DMSO) δ: 2.38-1.88 (CH_3), 5.31 (N-H), 4.32 (C=CH), 7.03-7.37 (arom. protons), 9.80 (enol OH), ^{13}C-nmr (DMSO) δ: 156.81 (NCON), 148.68 (N=C, pyrimidine ring), 68.36 (NH-C), 63.65 (=CH-, ofelin), 196.28 (C=O aliphat.), 205.51 (C=O arom.) Anal. calc. for $C_{22}H_{19}N_3O_3$: C 70.76, H 5.12, N 11.25; found: C 70.37, H 5.24, N 10.96.

1-(5-Benzoyl-4-phenyl-2-thioxo-1,2-dihydro-pyrimidinyl-amino)-1-methyl-2- acetyleten (3f):

0.2 g **lf** and 1,5 ml (1.458 g) **2f** (molar ratio 1:21) were heated at 115°C for 45 min yielding 0.15 g 60% **3f**, m.p. 247°C (n-butanol). i.r. cm^{-1}: 3400-3600 (N-H), 3100-3200 (arom. C-CH), 3000 (CH_3) 1720

(C=O), 1600 (C=C and C=N), 1540-1400 (arom. ring skeleton vib.), 1220- (C=S.), 780-680 (pyrimidine ring skeleton vib.). ^{1}H-nmr ($CDCl_3$) δ: 2.14-2.49 (CH_3), 5.37-5.43 (N-H), 4.10-4.15 (C=CH), 6.99-7.33 (arom. protons), Anal. calc. for $C_{22}H_{19}N_3O_2S$: C 67.85, H 4.91.N 10.79, S 8.22; found: C 67.73, H. 4.74, N 10.41, S 8.15.

1-(5-Benzoyl-4-phenyl-2-oxo-1,2-dihydro-pyrimidinyl-amino)-1-p-methyl-phenyl- 2-p-methylbenzoyleten (3g):

0.2 g **lg** and 0.64 g **2g** (molar ratio 1:4) were heated at 120°C for 2 h yielding 0.23 g 65% **3g**, m.p. 284°C (n-butanol). i.r. cm^{-1}: 3400-3500 (N-H), 3000-3100 (CH_3), 1720-1650 (C=O), 1600 (C=C and C=N), 1500-1650 (arom. ring skeleton vib.), 900-860 (pyrimidine ring skeleton vib.). ^{1}H-nmr (DMSO) δ: 2.08-2.15 (CH_3), 5.64-5.69 (C=CH), 5.80-5.85 (arom. protons), 8.89 (pyrim. ring proton). Anal. calc. for $C_{34}H_{27}N_3O_3$, C 77.69, H 5.17 N 7.99, found: C 77.39, H. 5.19, N 7.71.

1-(5-Benzoyl-4-phenyl-2-thioxo-1,2-dihydro-pyrimidinyl-amino)-1-p-methyl-phenyl- 2-p-methylbenzoyleten (3h):

0.2 g **lh** and 0.65 g **2h** (molar ratio 1:4) were heated at 120°C for 2 h yielding 0.23 g 65% **3h**, m.p. 295°C (n-butanol). i.r. cm^{-1}: 3400-3500 (N-H), 3020-3100 cm^{-1}, (arom. C-CH) 2900-3000 (CH_3), 1660 (C=C and C=N), 1520-1450 (arom. ring skeleton vib.), ^{1}H-nmr (DMSO) δ: 2.22-2.27 (CH_3), 5.83-5.88 (C=CH), 6.35-6.40 (N=H), 6.87-7.89 (arom. protons), Anal. calc. for $C_{34}H_{27}N_3O_2S$, C 75.40, H 5.02, N 7.73, S 5.90; found: C 75.56, H. 4.80, N 7.56, S 5.60.

1-(5-Benzoyl-4-phenyl-2-oxo-1,2-dihydro-pyrimidinyl-amino)-1-p-methyl-phenyl- 2-p-benzoyleten (3i):

0.2 g **li** and 0.65 g **2i** (molar ratio 1:4) were heated at 125°C for 3 h yielding, 0.17 g 50% **3i**, m.p. 293°C (n-butanol). i.r. cm^{-1}: 3400-3500 (N-H), 3000-3100 (arom. C-CH) 2900 (CH_3), 1680-1720, (C=O), 1600 (C=C and C=N), 1500-1400 (arom. ring skeleton vib.) 680-800 (pyrimidine. ring skeleton vib), ^{1}H-nmr (DMSO) δ: 2.07 (CH_3), 5.66-5.70 (C=CH), 5.81-5.86 (N=H), 6.62-7.72 (arom. protons), ^{13}C-mr (DMSO) δ: 160.25 (NCON), 146.64 (N=C), (pyrimidine ring), 68.36 (NH-C), 63.65 (=CH-, olefine), 196.03 (C=O aliphat.), 196.97 (C=O arom) Anal. calc. for $C_{33}H_{25}N_3O_3$; C 77.46, H 4.92, N 8.21. found: C 77.45, H 4.75, N 8.07.

1-(5-Benzoyl-4-phenyl-2-thioxo-1,2-dihydro-pyrimidinyl-amino)-1-p-methyl -phenyl-2-p-benzoyleten (3j):

0.2 g **lj** and 0.66 g **2j** (molar ratio 1:4) were heated at 125°C for 2 h yielding, 0.17 g 50% **3j**, m.p. 265°C (n-butanol). i.r. cm^{-1}: 3400-3500 (N-H), 3050 (arom. C-CH), 3000 (CH_3) 1660 (C=O), 1600 (C=C and C=N), 1530-1400 (arom. ring skeleton vib.) 660-800 (pyrimidine. ring skeleton vib), ^{1}H-nmr (DMSO) δ: 2.10 (CH_3), 5.29-5.35 (C=CH), 5.73-5.80 (N=H), 6.69-7.595 (arom. protons), Anal. calc. for $C_{33}H_{25}N_3O_2S$: C 75.12, H 4.77, N 4.77, N 7.96, S 6.06. found: C 74.92, H 4.47, N 7.91, S 6.36.

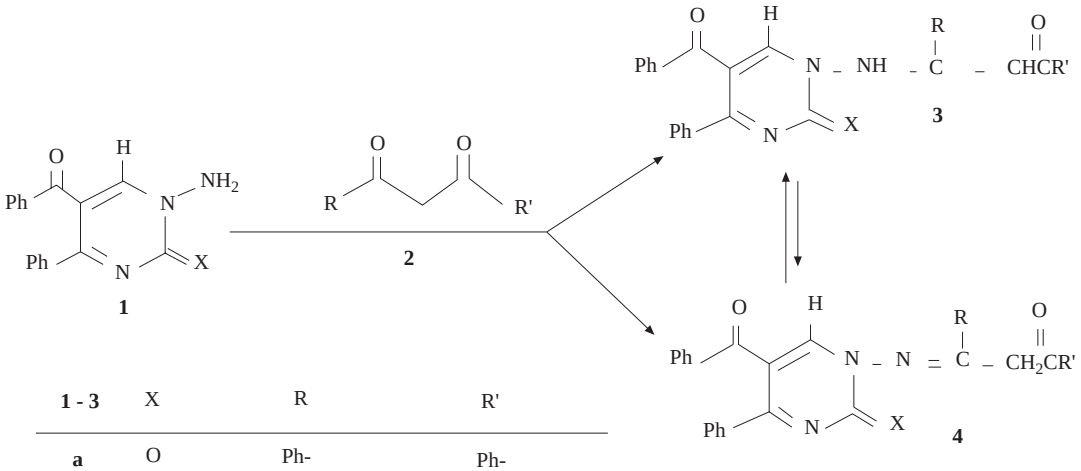
5-Benzoyl-1-(indane-3-one-l-ilydene-amino)-4-phenyl-pyrimidine-2-one (6a):

0.2 g **la** and 0.2 g indane-1,3-dione (molar ratio 1:2) were dissolved in 25 ml ethanol and to this solution was added 0.01 ml conc. HCl as a catalyst. The mixture was stirred by a magnetic stirrer at room temperature for 48 h. The precipitate was separated by filtering and recrystalized from n-butanol to give 0.11 g (40%) of the product, **6a**; m.p 345°C. i.r. cm^{-1}: 3450 (carbonyl overtone), 1700 (C=O) 1590 (C=C and C=N), 1500-1380 (arom. ring skeleton vib.), 760-680 (pyrimidine. ring skeleton vib) ^{1}H-nmr (DMSO) δ 2.51 (CH_2), 7.34-7.92 (arom. protons). ^{13}C-nmr (DMSO) δ: 167.50 (NCON), 110.33 (CH_2), 182.07-192.33 (C=O) Anal. calc. for $C_{26}H_{17}N_3O_3$; C 74.40, H 4.08, N 10.02. found: C 74.47, H 4.25, N 9.25.

5-Benzoyl-l-(indane-3-one-l-ilydene-amino)-4-phenyl-pyrimidine-2-thione (6b):

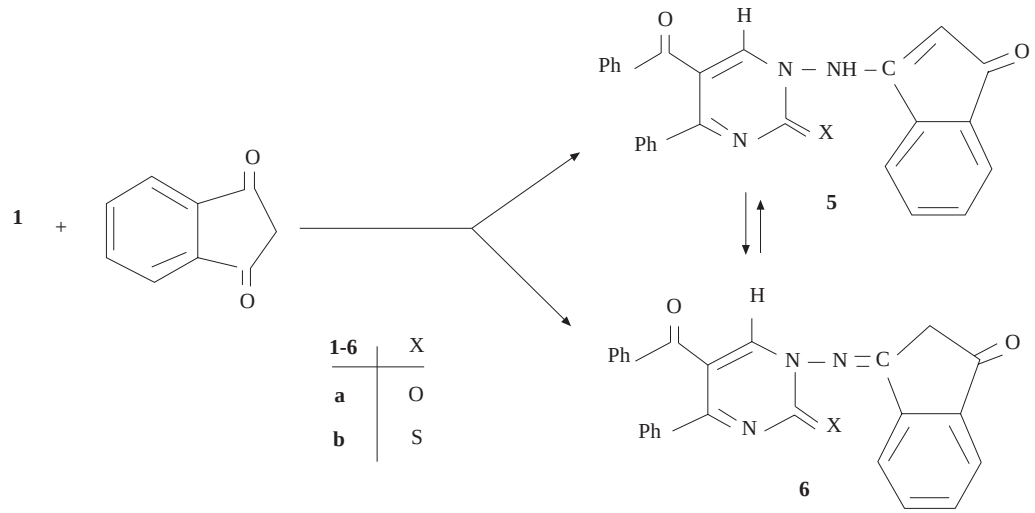
0.2 g **lb** and 0.18 indane-1,3-dione (molar ratio 1:2) were dissolved in 25 ml ethanol and to this

solution was added 0.01 ml conc. HCl as a catalyst. The mixture was stirred by a magnetic stirrer at room temperature for 48 h. The precipitate was separated by filtering and recrystalized from n-butanol to give 0.11 g (40%) of the product, **6b**; m.p 300°C. i.r. cm^{-1}: 3400 (carbonyl overtone), 1700-1660 (C=O) 1590 (C=C and C=N), 1230 (C=S) ^{1}H-nmr (DMSO) δ 2.52 (CH_2), 7.30-7.97 (arom. protons). Anal. calc. for $C_{26}H_{17}N_3O_2S$; C 71.71, H 4.24, N 9.65, S 7.35. found: C 71.99, H 3.70, N 9.02, S 7.00.



1 - 3	X	R	R'
a	O	Ph-	Ph-
b	S	Ph-	Ph-
c	O	4-MeO-C_6H_4-	4-MeO-C_6H_4-
d	S	4-MeO-C_6H_4-	4-MeO-C_6H_4-
e	O	Me-	Me-
f	S	Me-	Me-
g	O	4-MeO-C_6H_4-	4-MeO-C_6H_4-
h	S	4-MeO-C_6H_4-	4-MeO-C_6H_4-
i	O	4-MeO-C_6H_4-	Ph-
j	S	4-MeO-C_6H_4-	Ph-

Scheme 1.



1-6	X
a	O
b	S

Scheme 2.

Results and Discussion

Several enamine derivatives of **3** (see Scheme 1) were easily obtained in moderate yields (40-65%) from nucleophilic addition of **1** to the corresponding derivatives of **2**. The reactions were performed by heating them without any solvent to 115-125 °C (see Experimental Section). In general, when aldehydes and ketones containing an α-hydrogen are treated with ammonia and primary amines, the unstable enamines are formed and they cannot be isolated[5]. In this study, the synthesis of the enamines was realized using the primary amines. The structures of the obtained enamines were confirmed by interpreting their ^{1}H-nmr and ^{13}C-nmr spectra[6]. Enamines in the imine-enamine tautomerization are normally more stable than imines only when there is no hydrogen attached to nitrogen. In addition, conjugation always lowers the energy of unsaturated system by allowing the π-electrons to be delocalized[7,8]. On the other hand, the imino compound **6** was formed from the reaction of 1,3-indanedione and **1**. The structures of the products were determined with the ^{1}H-nmr and ^{13}C-nmr spectra of the compounds. It is interesting to note that both **3** and **4** and in the same manner **5** could exist, particularly in the tautometric form which could not be distinguished clearly by simple spectroscopic methods (see Scheme 1 and Scheme 2). Nevertheless, depending on the ^{1}H-nmr and ^{13}C-nmr spectra, the compounds formed from **3** have predominantly the depicted structure (see Experimental Section).

Acknowledgement

We thank the Erciyes University Research Fund for the financial support of this work.

References

1. Y. Akçamur, B. Altural, E. Sarıpınar, G. Kollenz, O. Kappe, K. Peters, E. M. von Schering, **J. Heterocylic Chem.** 25: 1419 (1998).
2. B. Altural, Y. Akçamur, E. Sarıpınar, I. Yıldırım, G. Kollenz, **Monatsh. Chem.** 120, 101 (1989)
3. B. Altural, G. Kollenz, **Monatsh. Chem.** 121, 677-682 (1990)
4. A. Kleemann, J. Engel, **Pharmazeugt. Wirkstoffe.** 2.Aufl., Thieme, Stuttgart, New York, pp. 25, 225, 375, 478 (1982)
5. T. W. Graham Solomons, *Organic Chemistry*, 4th. Ed. John Wiley and Sons Inc., New York, Chichester, Brisbane, Toronto, Singapore, pp. 966-970 (1988)
6. R. M. Silverstein, G. C. Bassler, T. C. Morrill, **Spectrometric Identification of Organic Compounds,** 4th. Ed. John Wiley and Sons Inc., New York, Chichester, Brisbane, Toronto, Singapore, pp. 757, 968 (1988)
7. J. March, **Advanced Organic Chemistry,** 4th. Ed. Wiley and Sonc Inc., New York Chichester, Brisbane, Toronto, Singapore, pp. 69, 70 (1985)
8. T. W. Graham Solomons, **Organic Chemistry**, 4th. Ed. John Wiley and Sons Inc., New York, Chichester, Brisbane, Toronto, Singapore, pp. 547, 784 (1988)