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Reactions of 1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one/thione Compounds with Unsymmetrically 1,3-Substituted Diketones

ZÜLBIYE ÖNAL
Department of Chemistry, Faculty of Arts and Science
Erciyes University, 38039 Kayseri, Turkey
E-mail: zulbiye@erciyes.edu.tr

1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one/thione (**1**) react with several unsymmetrically 1,3-substituted diketones (**2a-f**) under different conditions to give the new imine derivatives (**3a-f**). Unsymmetrically 1,3-substituted diketones derivatives (**2a-f**) were obtained from 1,5-di-(4-aryl)-4,5-dibromo-1-pentene-3-one and sodium methoxide. All newly synthesized compounds were characterized by elemental analysis, IR and ^{1}H NMR spectral data.

Key Words: 1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one/thione, Unsymmetrically 1,3-Substituted diketones, Addition reactions, Imines.

INTRODUCTION

In recent papers many methods and reactions of cyclic oxalyl compounds have been reported to give substituted heterocyclic compounds[1-4]. The reactions of 2,3-furandiones with several semicarbazones, ureas and their thioanalogues and oximes, amides, anilides and hydrazines have been reported in different solvents and at various temperatures[5-12].

It is obvious that pyrimidine derivatives are an important class of organic compounds and 1-amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one and its pyrimidine-2-thione anologue are synthesized in two steps from 4-benzoyl-5-phenylfuran-2,3-dione[8,9] (**Scheme-I**). 1-Aminopyrimidine derivatives (**1**) exhibits a free N-NH_2- moiety, which should apply to several subsequent reactions. The reactions of (**1**) with several anhydrides and isocyanates have been reported in different conditions[13-15]. The reactions are generally initiated by nucleophilic attack of the nitrogen atom of 1-aminopyrimidine derivatives. In general, pyrimidines have found much interest for biological and medicinal reasons, thus their chemistry has been investigated extensively. Some of these compounds have been shown to exhibit antiallergy, antitumor, antiviral and antiparasitic properties[16-20].

In the present study, we carried out the reaction of (**1**) with several unsymmetrically 1,3-substituted diketones (**2a-f**) yielding a new series of

imine derivatives (**3a-f**). Unsymmetrically 1,3-substituted diketones were synthesized in our laboratories. The general outline of the reactions studied is shown in **Scheme-II**.

EXPERIMENTAL

Melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. Compounds were routinely checked for their homogeneity by TLC using DC Alufolien Kieselgel 60 F_{254} Merck and a Camag TLC lamp (254/366 nm). Microanalyses were performed on a Carlo Erba elemental analyzer, model 1108; the results agreed favorably with the calculated values. The IR spectra were recorded on a Shimadzu Model 435 V-04 spectrometer, using potassium bromide discs. ^{1}H NMR spectra was recorded on a Gemini-Varian 200 MHz instrument. The chemical shifts are reported in ppm from tetramethylsilane and are given in δ (ppm). Solvents were dried by refluxing with the appropriate drying agent and distilled before use. All other reagents were purchased from Merck, Fluka and Aldrich Chemical Co. and were used without further purification.

5-Benzoyl-4-phenyl-1-[(1Z,4Z)-1-(4-hydroxyphenyl)-5-(4-methoxyphenyl)-3-oxopent-4-enylidene]aminopyrimidin-2(1*H*)-one (3a): 1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one (**1a**) (0.2 g, 0.069 mmol), (4E)-1,5-*bis*-(4-methoxyphenyl)pent-4-ene-1,3-dione (**2a**) (1.10 g, 3.5 mmol) and *p*-toluenesulphonic acid catalyst were homogeneously mixed. The mixture was heated at 125 ºC and kept at this temperature for 2 h without any solvent in a calcium chloride guard tube fitted round bottom flask of 50 mL. Then, the residue was treated with ether and filtered and the formed crude product (**3a**) was recrystallized from *n*-butanol and allowed to dry over P_2O_5; yield 0.12 g (60 %); m.f. $C_{36}H_{29}N_3O_5$; m.p. 265 ºC; IR (KBr, ν_{max}, cm^{-1}): 3200-3150 (arom. C-H stretch.), 2900-2850 (OCH_3), 1720, 1650 (C=O), 1600-1580 (C=C and C=N), 800-710 (pyrimidine ring skeleton vib.); ^{1}H NMR (DMSO): δ = 7.50-6.73 (m, 21H, ArH), 3.76 (s, 2H, CH_2), 3.74 (s, 3H, OCH_3), 3.66 ppm (s, 3H, OCH_3). Elemental (%) analysis: Found (calcd.): C = 74.01 (74.09), H = 4.95 (5.00), N = 6.92 (7.20). S = 7.40 (7.51).

5-Benzoyl-4-phenyl-1-[(1Z,4Z)-1-(4-hydroxyphenyl)-5-(4-methoxyphenyl)-3-oxopent-4-enylidene]aminopyrimidin-2(1*H*)-thione (3b): 1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-thione (**1b**) (0.2 g, 0.069 mmol), (4E)-1,5-*bis*-(4-methoxyphenyl)pent-4-ene-1,3-dione (**2b**) (1.02 g, 3.3 mmol) and *p*-toluenesulphonic acid catalyst were homogeneously mixed. The mixture was heated at 130 ºC and kept at this temperature for 3 h without any solvent in a calcium chloride guard tube fitted round bottom flask of 50 mL. Then, the residue was treated with ether and filtered and the formed crude product (**3b**) was recrystallized from *n*-bu-

tanol and allowed to dry over P_2O_5; yield 0.110 g (55 %); m.f. $C_{36}H_{29}N_3O_4S$; m.p. 259 ºC; IR (KBr, ν_{max}, cm^{-1}): 3100-3050 (arom. C-H stretch.), 3000-2800 (OCH_3), 1660, 1610 (C=O), 1600-1580 (C=C and C=N), 1240 (C=S), 820-720 (pyrimidine ring skeleton vib.); ^{1}H NMR (DMSO): δ = 7.87-6.77 (m, 21H, ArH), 3.82 (s, 2H, CH_2), 3.67 (s, 3H, OCH_3), 3.64 ppm (s, 3H, OCH_3). Elemental analysis: Found (calcd.): C = 72.41 (72.11), H = 4.85 (4.87), N = 6.89 (7.01). S = 5.04 (5.34).

5-Benzoyl-4-phenyl-1-[(1E)-3-(4-methoxyphenyl)-1-methyl-3-oxo-propylidene]aminopyrimidine-2(1*H*)-one (3c): 1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one (**1a**) (0.2 g, 0.069 mmol), 1-(4-methoxyphenyl)butane-1,3-dione (**2c**) (0.66 g, 3.4 mmol) and *p*-toluenesulphonic acid catalyst were homogeniously mixed. The mixture was heated at 75 ºC and kept at this temperature for 1 h without any solvent in a calcium chloride guard tube fitted round bottom flask of 50 mL. Then, the residue was treated with ether and filtered and the formed crude product (**3c**) was recrystallized from ethanol and allowed to dry over P_2O_5; yield 0.14 g (70 %); m.f. $C_{28}H_{23}N_3O_4$; m.p. 261 ºC; IR (KBr, ν_{max}, cm^{-1}): 3200-3100 (arom. C-H stretch.), 3000-2900 (aliphatic, C-H), 1700, 1660, 1600 (C=O), 1600-1580 (C=C and C=N), 1520-1460 (aromatic ring skeleton vib.), 780-700 (pyrimidine ring skeleton vib.); ^{1}H NMR (DMSO): δ = 8.05-7.02 (m, 15H, ArH), 4.50 (s, 2H, CH_2), 3.50 (s, 3H, OCH_3), 1.85 ppm (s, 3H, CH_3). Elemental (%) analysis: Found (calcd.): C = 72.30 (72.25), H = 4.95 (4.98), N = 8.89 (9.03).

5-Benzoyl-4-phenyl-1-[(1E)-3-(4-methoxyphenyl)-1-methyl-3-oxo-propylidene]amino-pyrimidine-2(1*H*)-thione (3d): 1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one (**1b**) (0.2 g, 0.069 mmol), 1-(4-methoxyphenyl)butane-1,3-dione (**2d**) (0.66 g, 3.4 mmol) and *p*-toluenesulphonic acid catalyst were homogeneously mixed. The mixture was heated at 75 ºC and kept at this temperature for 1 h without any solvent in a calcium chloride guard tube fitted round bottom flask of 50 mL. Then, the residue was treated with ether and filtered and the formed crude product (**3d**) was recrystallized from ethanol and allowed to dry over P_2O_5; yield 0.136 g (68 %); m.f. $C_{28}H_{23}N_3O_3S$; m.p. 287 ºC; IR (KBr, ν_{max}, cm^{-1}): 3100-3050 (arom. C-H stretch.), 3000-2800 (aliphatic, C-H), 1660, 1600 (C=O), 1600-1580 (C=C and C=N), 1230 (C=S), 730-600 (pyrimidine ring skeleton vib.); ^{1}H NMR (DMSO): δ = 8.09-7.02 (m, 15H, ArH), 5.48 (s, 2H, CH_2), 3.86 (s, 3H, OCH_3), 1.83 ppm (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 195.49 (Ph-C=O), 147.95-110.25 (aromatic carbons), 140.57 (C=S), 63.27 (CH_2), 57.45 ppm (OCH_3). Elemental (%) analysis: Found (calcd.): C = 70.01 (69.85), H = 4.58 (4.81), N = 8.45 (8.73). S = 6.57 (6.65).

5-Benzoyl-4-phenyl-1-[(1Z,4E)-3-oxo-1,5-diphenylpent-4-enylidene]aminopyrimidin-2(1*H*)-one (3e): 1-Amino-5-benzoyl-4-phenyl-

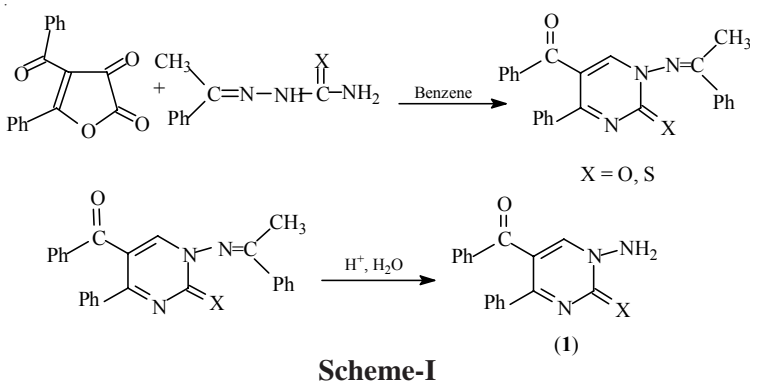
1*H*-pyrimidine-2-one (**1a**) (0.2 g, 0.069 mmol), (4E)-1,5-diphenylpent-4-ene-1,3-dione (**2e**) (0.88 g, 3.5 mmol) and *p*-toluenesulphonic acid catalyst were homogeneously mixed. The mixture was heated at 100 ºC and kept at this temperature for 40 min. without any solvent in a calcium chloride guard tube fitted round bottom flask of 50 mL. Then, the residue was treated with ether and filtered and the formed crude product (**3e**) was washed with hot ethanol several times and allowed to dry over P_2O_5; yield 0.14 g (70 %); m.f. $C_{34}H_{25}N_3O_3$; m.p. 255 ºC; IR (KBr, ν_{max}, cm^{-1}): 3200-3150 (arom., C-H stretch.), 1660, 1600 (C=O), 760-680 (pyrimidine ring skeleton vib.); ^{1}H NMR (DMSO): δ = 7.97-6.70 (m, 21H, ArH), 6.06-5.82 (d, 2H, CH=CH), 3.82 ppm (s, 2H, CH_2). Anal. (%) Calcd. for $C_{34}H_{25}N_3O_3$: C, 77.99; H, 4.81; N, 8.03. Found: C, 77.68; H, 4.79; N, 8.19.

5-Benzoyl-4-phenyl-1-[(1Z,4E)-3-oxo-1,5-diphenylpent-4-enylidene] aminopyrimidin-2(1*H*)-thione (3f): 1-Amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one (**1b**) (0.2 g, 0.069 mmol), (E)-1,5-diphenylpent-4-ene-1,3-dione (**2f**) (0.82 g, 3.3 mmol) and *p*-toluenesulphonic acid catalyst were homogeneously mixed. The mixture was heated at 100 ºC and kept at this temperature for 50 min without any solvent in a calcium chloride guard tube fitted round bottom flask of 50 mL. Then, the residue was treated with ether and filtered and the formed crude product (**3f**) was washed with hot ethanol several times and allowed to dry over P_2O_5; yield 0.13 g (65 %); m.f. $C_{34}H_{25}N_3O_2S$; m.p. 271 ºC; IR (KBr, ν_{max}, cm^{-1}): 3100-3020 (arom., C-H stretch.), 1640, 1600 (C=O), 1180 (C=S), 760-680 (pyrimidine ring skeleton vib.); ^{1}H NMR (DMSO): δ = 8.20-6.95 (m, 21H, ArH), 6.95-6.06 (d, 2H, CH=CH), 3.80 ppm (s, 2H, CH_2). Elemental (%) analysis: Found (calcd.): C = 75.42 (75.69), H = 4.88 (4.67), N = 7.53 (7.79). S = 5.96 (5.93).

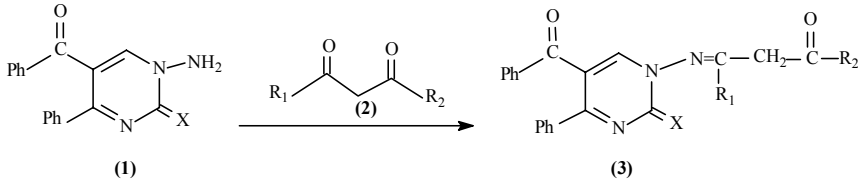
RESULTS AND DISCUSSION

As mentioned above, the reactions of 4-benzoyl-5-phenyl-furan-2,3-dione with acetophenonsemicarbazone/acetophenonthiosemicarbazone yielded 1-methylenaminopyrimidines whose hydrolysis afforded the 1-amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-one/thione (1)[8,9] (**Scheme-I**).

The addition elimination reaction of (**1**) with unsymmetrically 1,3-substituted diketones (**2a-f**) afforded several imine derivatives (**3a-f**), in good yields. The reactions were performed by heating them without any solvent up to 75-130 ºC. Primary amines can add to aldehydes and ketones to give imines. When there is at least one aryl group on the nitrogen or carbon, the compounds are quite stable. In addition, conjugation always lowers the energy of unsaturated system by allowing the π-electrons to be delocalized[21,22]. In this study, the synthesis of the imine compounds (**3a-f**) were realized by using the aromatic aryl amines and ketones.



Scheme-I



1-3	X	R_1	R_3
a	O	*p*- CH_3O-C_6H_4-	*p*-$CH_3OC_6H_4$-CH=CH-
b	S	*p*-CH_3O-C_6H_4-	*p*-$CH_3OC_6H_4$-CH=CH-
c	O	CH_3-	*p*-$CH_3OC_6H_4$-
d	S	CH_3-	*p*-$CH_3OC_6H_4$-
e	O	Ph-	C_6H_5-CH=CH-
f	S	Ph-	C_6H_5-CH=CH-

Scheme-II

All the newly synthesized compounds were purified by recrystallization and their structures were confirmed by elemental analysis and IR, ^{1}H NMR spectroscopic techniques that supported the assigment. The formation of (**3a**) was supported by the result of spectroscopic measurements particularly by the presence of absorbtion bands characteristic for carbonyl groups (IR: 1720, 1650 cm^{-1}). Important structural information (**3a**) can be obtained from its ^{1}H NMR spectrum. The ^{1}H NMR spectrum (**3a**) contains two singlet peaks at 3.74, 3.66 ppm representing the methoxy groups. The multiple peaks beetween (7.53-6.73 ppm) are thought to represent the aromatic protons. The corresponding signals in CH_2 protons were determined at 3.76 ppm. The result of these measurement are listed in the experimental section.

In a similar way, the reaction of the 1-amino-5-benzoyl-4-phenyl-1*H*-pyrimidine-2-thione (**1b**) with (4E)-1,5-*bis*-(4-methoxyphenyl)pent-4-ene-1,3-dione (**2b**) leads to form 5-benzoyl-4-phenyl-1-[(1Z,4Z)-1-(4-hydroxy phenyl)-5-(4-methoxyphenyl)-3-oxopent-4-enylidene]aminopyrimidin-2(1*H*)-thione (**3b**) (**Scheme-II**). In IR spectra of the compound (**3b**), the C=O absorption bands were found to be at (ν = 1660, 1610 cm^{-1}). The C=S

absorption was at (ν = 1240 cm^{-1}). Final confirmation of the structure of (**3b**) can be derived from its ^1H NMR spectrum, the peaks at 3.67, 3.64 ppm belong to the methoxy groups, the peak at 3.82 ppm represents the -CH_2- group. The result of measurements of (**3c-f**) are given in the experimental part.

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REFERENCES

1. E. Ziegler, M. Eder, C. Belegratis and E. Prewedourakis, *Monatshefte für Chemie*, **98**, 2249 (1967).
2. G. Kollenz, C.O. Kappe and H.A. El-Nabi, *Heterocycles*, **32**, 669 (1991).
3. R.W. Saalfrank, T. Lutz, B. Hörner, J. Gündel, K. Peters and H.G. von Schnering, *Chemische Berichte*, **124**, 2289 (1991).
4. E. Saripinar, Y. Güzel, Z. Önal, I.Ö. Ilhan and Y. Akçamur, *J. Chem. Soc. Pak.*, **22**, 308 (2000).
5. G. Kollenz, E. Ziegler, W. Ott and H. Igel, *Zeitschrift für Naturforschung*, **31b**, 1511 (1976).
6. W. Ott, E. Ziegler and G. Kollenz, *Synthesis*, 477 (1976).
7. Y. Akçamur and G. Kollenz, *Org. Prep. Proced. Intern.*, **19**, 52 (1987).
8. Y. Akçamur, B. Altural, E. Saripinar, G. Kollenz, O. Kappe, E.M. Peters and H.G. Von Schnering, *J. Heterocycl. Chem.*, **25**, 1419 (1988).
9. B. Altural, Y. Akçamur, E. Saripinar, I. Yildirim and G. Kollenz, *Monatshefte für Chemie*, **120**, 1015 (1989).
10. I. Yildirim and I.Ö. Ilhan, *J. Heterocycl. Chem.*, **34**, 1047 (1997).
11. E. Saripinar, I.Ö. Ilhan and Y. Akçamur, *Heterocycles*, **57**, 1445 (2002).
12. I.Ö. Ilhan, Y. Akçamur, E. Saripinar and E. Aslan, *Asian J. Chem.*, **15**, 1373 (2003).
13. B. Altural and G. Kollenz, *Monatshefte für Chemie*, **121**, 677 (1990).
14. Z. Önal, E. Saripinar and I.Ö. Ilhan, *J. Heterocycl. Chem.*, **38**, 397 (2001).
15. Z. Önal and B. Altural, *Asian J. Chem.*, **18**, 1061 (2006).
16. P.F. Tuby, T.W. Hudyma, M. Brown, J.M. Essery and R.A. Partyka, *J. Med. Chem.*, **22**, 263 (1979).
17. P.F. Tuby, T.W. Hudyma, M. Brown, J.M. Essery and R.A. Partyka, *J. Med. Chem.*, **25**, 1145 (1982).
18. A.S. Galabov, E. Velichkova, A. Karparov, D. Sidzhakova, D. Danchev and N. Chakova, *Arzneimittelforschung*, **34**, 9 (1984).
19. S. Raic-Malic, D. Svedruzic, T. Gazivoda, A. Marunovic, A. Hergold-Brundic, A. Nagl, J. Balzarini, E. De Clercq and M. Mintas, *J. Med. Chem.*, **43**, 4806 (2000).
20. N. Azas, P. Rathelot, S. Djekov, F. Delmas, A. Gellis, C.D. Giorgio, P. Vanelle and P. Timon-David, *Tetrahedron*, **58**, 7241 (2002).
21. J. March, Advanced Organic Chemistry, J. Wiley and Sons Inc., New York, Chichester, Brisbane, Toronto, Singapore, edn. 4, pp. 796-798 (1985).
22. T.W. Solomons, Organic Chemistry, J. Wiley and Sons Inc., New York, Chichester, Brisbane, Toronto, Singapore, edn. 4 (1988).

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