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Reactions of 1-Amino-5-Benzoyl-4-Phenyl-1H-Pyrimidine-2-Thione with Various Carboxylic Anhydrides

ZÜLBIYE ÖNAL* and BEHZAT ALTURAL
Department of Chemistry, Erciyes University, 38039 Kayseri, Turkey
Fax: (90)(352)4374933; E-mail: zulbiye@erciyes.edu.tr

1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione (**1**) reacts with various carboxylic anhydrides (**2a–e**) under different conditions and gives the new amide and imide derivatives. Reaction of (**1**) with maleic anhydride (**2b**) resulted in acid derivative (**3b**). The structures of these compounds (**3a–f**) were determined by ^{1}H NMR, ^{13}C NMR, IR spectra and elemental analysis.

Key Words: 1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione, Carboxylic anhydride, Condensation, Amide, Imide.

INTRODUCTION

The formation of 1-amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione (**1**) has been reported recently[1,2]. The reactions of (**1**) with 1,3-dicarbonyl compounds and some isocyanates have been reported in different solvents at different temperatures[3,4]. Pyrimidine derivatives have been found generally to be more interesting for biological and medical reasons. Some of these compounds have been shown to exhibit bactericide, fungicide, antiviral and herbicide properties[5–7].

Here, we have now extended our investigations into the reactions of (**1**) with various carboxylic anhydrides (**2a–e**).

EXPERIMENTAL

Solvents were dried by refluxing with the appropriate drying agent and distilled before use. All melting points were determined by use of Büchi melting point apparatus and not corrected. Microanalyses were performed on a Carlo-Erba elemental analyzer Model 1108. The IR spectra were obtained as potassium bromide pellets using a Shimadzu Model 435 V-04 spectrometer. ^{1}H and ^{13}C NMR spectra were obtained from Gemini-Varian 200 MHz, TMS as internal standard (δ in ppm). All experiments were followed by TLC using DC Alufolion Kieselgel 60 GF 254 Merck and with a Model Camag TLC lamp (254/366 nm).

2-(5-Benzoyl-2-thioxo-4-phenyl-1,2-dihydro-1-pyrimidinyl)-1,3-isoindolinedione (3a): 0.2 g 1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione (**1**) and a large excess of phthalic anhydride (**2a**), 2.4 g (molar ratio 1 : 26) were homogeneously mixed. The mixture in a 50 mL round bottomed flask by fitting

calcium chloride guard tube was heated at 190°C for 1 h without any solvent. After cooling to room temperature the residue was treated with dry ether and so formed crude product recrystallized from acetic acid; yield: 0.14 g (70%), yellow crystals; m.p. 305°C; IR (cm^{-1}) (KBr): 3500–3400 ν(C═O, carbonyl overtone), 3000 ν(aromatic C═CH), 1740–1680–1650 ν(C═O carbonyl), 1500–1420 ν(aromatic ring, skeleton vib.), 1260 ν(C═S), 1220–1050 ν(anhydride C—O stretch), 800–700 ν(pyrimidine ring); ^1H NMR (DMSO, δ): 8.90 ppm (s, 1H, pyrimidine ring), 7.96–7.15 (m, 15H, aromatic). Elemental analysis: Found (calcd.): C = 68.64 (68.94), H = 3.43 (3.76), N = 9.61 (9.72), S = 7.31 (7.06).

N-(5-Benzoyl-2-thioxo-4-phenyl-1,2-dihydro-1-pyrimidinyl) acetamide (3b): 0.2 g 1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione **(1)** and 4 mL acetic anhydride **(2b)** (molar ratio 1 : 33) were mixtured at 0°C for 4 h. The residue acetic anhydride was removed by evaporation and the oily residue was treated with anhydrous ether to give a yellow coloured crude solid, which was recrystallized from *n*-butanol; yield: 0.09 g (45%), yellow crystals; m.p. 330°C; IR (cm^{-1}) (KBr)): 3200 ν(N—H), 3030 ν(—CH_3), 1720–1660 ν(C═O groups), 1610–1590 ν(C═C and C═N), 1200 ν(C═S), 800–670 ν(pyrimidine ring, skeleton vib); ^1H NMR (DMSO, δ): 8.50 (s, 1H, pyrimidine ring), 8.10–7.70 ppm (m, 10 H, aromatic), 5.86 (broad, NH), 2.14 (—CH_3). Elemental analysis: Found (Calcd.): C = 65.31 (65.05), H = 4.32 (4.10), N = 12.02 (11.98), S = 9.17 (9.85).

N-(5-Benzoyl-phenyl-2-thioxo-1,2-dihydro-1-pyrimidinyl)-2,5-pyrrolidine dione (3c): 0.2 g 1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione **(1)** and 1.3 g succinic anhydride **(2c)** (1 : 20 molar ratio) were heated at 180°C for 1 h without any solvent. The residue was treated with dry ether and filtered and the so formed crude product was recrystallized from *n*-butanol; yield 0.08 g (40%), yellow crystals; m.p. 330°C; ^1H NMR (DMSO, δ): 8.67 (s, 1H, pyrimidine ring), 7.89–6.87 (m, aromatic 10H), 2.52 ppm (s, CH_2). Elemental analysis: Found (Calcd.): C = 64.35 (64.77), H = 3.80 (3.87), N = 10.50 (10.79), S = 8.05 (8.23).

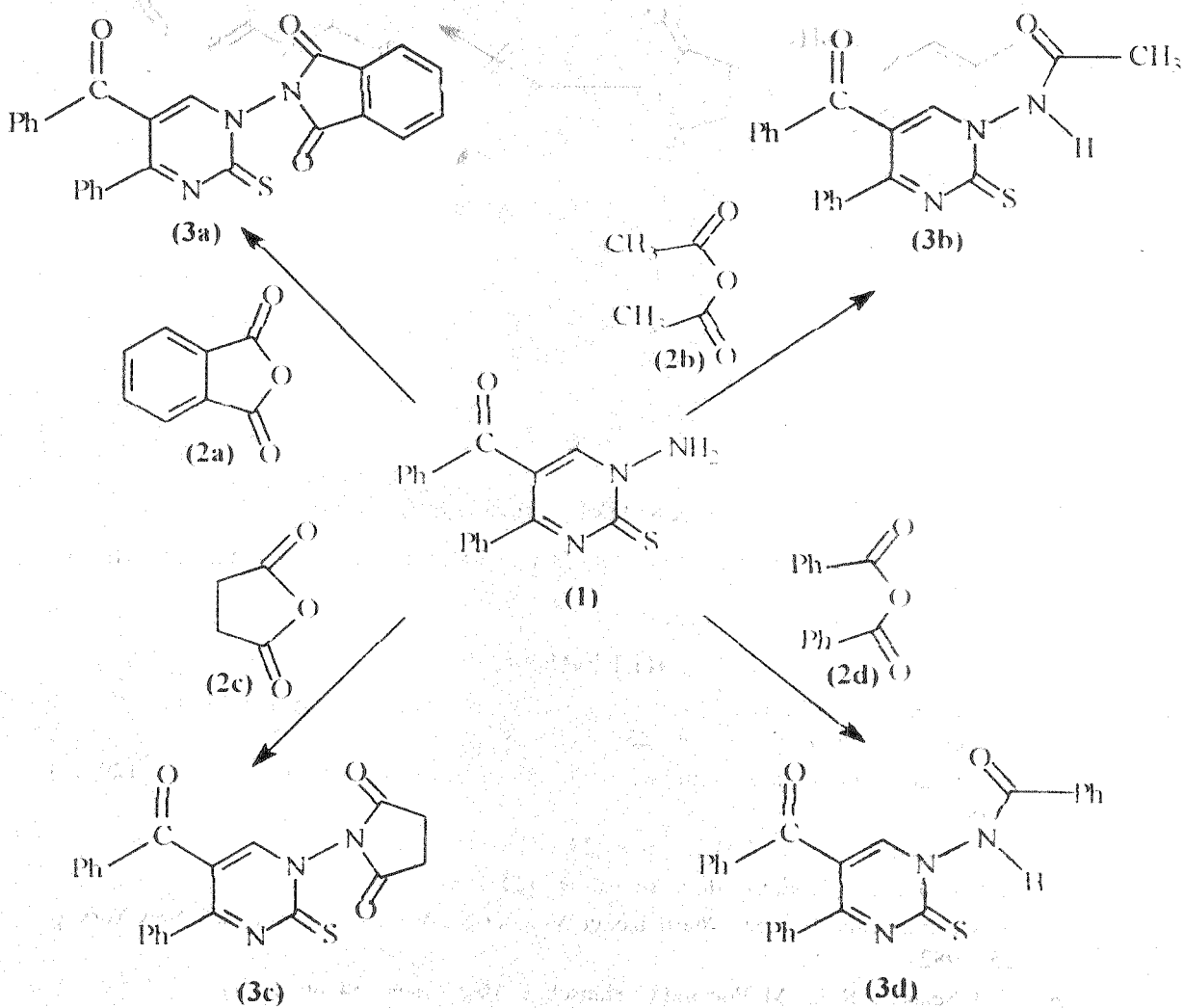
N-(5-Benzoyl-2-thioxo-4-phenyl-1,2-dihydro-1-pyrimidinyl) benzamide (3d): 0.2 g 1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione **(1)** and 2.9 g benzoic anhydride **(2d)** (1 : 20 molar ratio) were homogeneously mixed. The mixture was heated at 40°C for 2 h without any solvent. After cooling to room temperature the residue was treated with dry ether and the formed crude product recrystallized from *n*-butanol; yield: 0.1 g (50%), yellow crystals; m.p. 270°C; ^1H NMR (DMSO, δ): 9.50 (s, 1H, pyrimidine ring), 8.21–6.70 (m, 15H, aromatic), 1.95 ppm (s, 1H, N—H). Elemental analysis: Found (Calcd.): C = 69.80 (70.04), H = 4.05 (4.18), N = 10.10 (10.20), S = 7.47 (7.77).

3-(5-Benzoyl-2-thioxo-4-phenyl-1,2-dihydro-1-pyrimidinyl-carbamoyl)-2-propenoic acid (3e): 0.2 g 1-Amino-5-benzoyl-4-phenyl-1H-pyrimidine-2-thione **(1)** and 0.82 g maleic anhydride **(2e)** (molar ratio 1 : 13) were homogeneously mixed. The mixture was heated at 80°C and kept at this temperature for 2 h without any solvent in a calcium chloride guard tube fitted in a round bottom flask of 50 mL. After cooling to room temperature the residue was treated with dry ether. The precipitated crude yellow product was filtered and washed from benzene; yield: 0.08 g (40%), m.p. 180°C; IR (cm^{-1}) (KBr): 3150 ν(N—H), 2900–2750 ν(broad, acid's O—H), 1720, 1700, 1670, 1650 ν(C═O absorption

bend). 1220 ν(C=S), 780–680 ν(pyrimidine ring). ^{1}H NMR (DMSO, δ): 10.52 (s, —COOH), 9.40 (broad NH), 8.50 (s, 1H, pyrimidine ring), 7.21–6.12 (m, —CH=CH—COOH respectively), 7.90–6.78 ppm (m, 10H, aromatic). ^{13}C NMR (DMSO, δ): 198.510 (s, benzoyl's C=O), 167.530 (s, carboxyl's C=O), 164.710 ppm (s, amide's C=O). Elemental analysis: Found (Calcd.): C = 62.05 (62.21), H = 3.78 (3.72), N = 10.36 (10.16), S = 7.90 (7.60).

RESULTS AND DISCUSSIONS

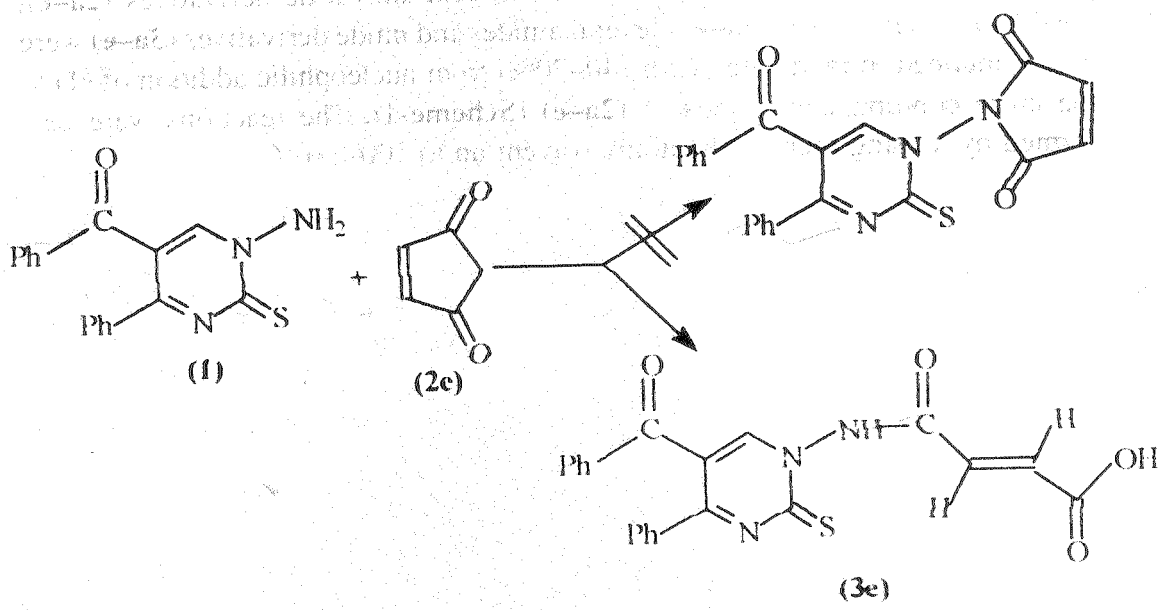
The reactions of the pyrimidine (**1**) with acid anhydride derivatives (**2a–e**), yield N-acyl derivatives (**3a–e**). Several amides and imide derivatives (**3a–e**) were easily obtained in moderate yields (40–70%) from nucleophilic addition of (**1**) to the corresponding compounds of (**2a–e**) (**Scheme-1**). The reactions were performed by heating them without any solvent up to 100–180°C



Scheme-1

The structure of (**3a**) was confirmed by its elemental analysis, IR, ^{1}H NMR specroscopic data (**Scheme-1**). The formation of (**3a**) is supported by the results of spectroscopic measurements in particular in presence of three carbonyl bonds (IR: 1740, 1680, 1650 cm^{-1}).

When the same reactions were attempted with maleic anhyride **(2b)**, the expected maleic imide derivative was not obtained. Instead, **(3b)** was formed with 40% yield **(Scheme-2)**. The structure of this compound **(3b)** was easily determined from its IR and ^{1}H NMR. The NH and OH absorption bands were found at about 3150 and 2900–2750 cm^{-1} (broad) respectively. The absorption bands of ν(C=O) groups were found to be at 1720, 1700, 1670, 1650 cm^{-1}. The absorption band of ν(C=S) group was found to be at 1220 cm^{-1}. The ^{1}H NMR spectrum showed peak of COOH at δ = 10.52 ppm. Amide and alkenyl protons, —NH—CO—CH=CH— were determined at δ = 9.40, 7.21 and 6.12 ppm.



Scheme-2

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