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Reactions of 4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione with Various Anilides

ILHAN ÖZER ILHAN*, EMINE ALTUNTAS and ISMAIL YILDIRIM
Department of Chemistry, University of Erciyes, Kayseri-38039, Turkey
Fax: (90)(352)4378802; E-mail: ilhano@erciyes.edu.tr

4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione (**1**) reacts with acetanilides (**3a-f**) under different conditions and gives open-chain dibenzoylacetic acid derivatives **4a,b**, **5c-f**. It has been demonstrated that with the variation in reaction conditions, the reaction changes leading to different products. All the newly synthesized compounds were characterized by elemental analysis, IR, ^{1}H and ^{13}C NMR spectral data. All were compared with their previous analogues.

Key Words: Furan-2,3-dione, α-Oxoketenes, Anilide, Cyclic oxalyl compounds.

INTRODUCTION

Furan-2-3-diones, belong to an important group of heterocyclic starting compounds have been the subject of extensive study in recent past. Due to their high reactivity, numerous reports have highlighted their chemistry and use[1]. In furan-2,3-diones atoms C-2, C-3, C-5 and C-6 represent electrophilic sites of different reactivity and could be used for the construction of condensed heterocyclic systems upon reaction with various nucleophiles and binucleophiles[2]. The reactions of substituted furan-2,3-diones with some dienophiles in different solvents at various temperatures have also been studied[3]. Moreover, derivatives of heterocyclic 2,3-diones which are α,β-unsaturated carbonyl compounds, have been found to serve as versatile synthetic equivalents in thermolysis reactions[4], cycloaddition reactions[5] and nucleophilic addition reactions[6]. Several attempts to change functional groups in furan- or pyrrol-2,3-diones and related systems have been reported recently[7]. A convenient method for the synthesis and the mechanism of reactions and calculations on the interaction of 2,3-dihydro-2,3-furandiones with several semicarbazones, ureas and their thio-analogues have been reported recently[8]. The reactions are generally initiated by the nucleophilic attack of the nitrogen atom of semicarbazone, urea or hydrazines, directed on to the oxygen atom of the furan ring[9]. The reaction of furan-2,3-dione (**1**), obtained easily from *p*,*p*'-

dimethyldibenzoylmethane and oxalyl chloride[10], with α-naphthylamine, aniline, *p*-toluidine and *o*-toluidine derivatives in benzene at the room temperature led to the formation of the 2-oxo-3-butenoic acid derivative, the pyrrol-2,3-dione, the pyrrol-2-ones and the quinoxaline-2-ones derivatives, respectively[1e]. Thermal decomposition of furan-2,3-diones lead to the formation of highly reactive α-oxoketene intermediates[11]. The general reactivity of ketenes and the mechanism of the reactions with nucleophiles have been reviewed recently and a few *ab initio* and semi-empirical (AM1 and PM3) calculations on a series of differently substituted α-oxoketenes, especially substituent effects on their stability as well as reactivity have been published[12]. Therefore, these *vicinal*-dione compounds like **1** have been used as initial materials in the synthesis of the target heterocycles.

EXPERIMENTAL

Solvents were dried by refluxing over the appropriate drying agent and distilled before use. Melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. Microanalyses were performed on a Carlo Erba elemental analyser, model 1108. The IR spectra were recorded on a Jasco FT IR spectrometer model 460, using potassium bromide pellets. The ^{1}H and ^{13}C NMR spectra were recorded on Varian Gemini 200 instrument. The chemical shifts are reported in ppm from tetramethylsilane as an internal standard and are given in δ (ppm). All experiments were followed by TLC using DC Alufolien Kieselgel 60 F_{254} Merck and Camag TLC lamp (254/366 nm).

***N*,*N*-Bis-(*p*,*p*'-dimethyldibenzoylacetic acid)-*N*-*m*-aminophenylamide (4a):** 4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione (**1**) (0.5 g, 1.63 mmol) and *m*-aminoacetanilide (**3a**) (0.24 g, 1.63 mmol) were refluxed in toluene (50 mL) for 6 h. The solvent was evaporated and the remaining oily residue was treated with dry diethyl ether to give a yellow crude product which was recrystallized from methanol and allowed to dry on P_2O_5. Yield 65% (0.7 g); m.p. 220°C; IR (KBr, cm^{-1}) : 3500-3200 ν(NH, OH), 3050 ν(CH, aromatic), 1705, 1680 ν(C=O, amide and ketonic), 1600, 1540, 1460 ν(C=C); ^{1}H NMR (DMSO, δ): 10.25 (s, -NH), 8.25-8.11 (d, 2H), 7.59-7.45 (m, 20H, Ar-H), 3.36 (s, 2H, under the peak of H_2O in DMSO-d_6, probably), 2.52-2.04 ppm (s, -CH_3). ^{13}C NMR (DMSO, δ) 204.3 (s, C-4, C-4'), 194.27 (s, C-2, C-2'), 160.68 (s, C-5, C-5'), 148.18 (s, C-3, C-3', in enol-form), 136.51-127.11 (m, arom. C), 108.83 (s, C-3, C-3', in keto-form). Elemental analysis (%): found (calcd.): [C= 75.90 (75.61), H= 5.42 (5.51), N= 5.51 (5.35)].

***N*,*N*-Bis-(*p*,*p*'-dimethyldibenzoylacetic acid)-*N*-*p*-bromophenylamide (4b):** 4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione (**1**) (0.5 g, 1.63 mmol) and *p*-bromoacetanilide (**3b**) (0.35 g, 1.63 mmol) were refluxed in xylene (50 mL) for 5 h. The solvent was evaporated and the remaining oily residue was treated with dry diethyl ether to give a yellow crude product which was recrystallized from methanol and allowed to dry on P_2O_5. Yield 50 % (0.6 g); m.p. 212°C; IR (KBr, cm^{-1}): 3550-3250 ν(OH), 3050 ν(CH, aromatic), 1705, 1680 ν(C=O, amide and ketonic), 1600, 1540, 1460 ν(C=C), 1320 ν(C-O); ^{1}H NMR (DMSO, δ): 8.00-7.90 (q, 2H), 7.59-7.45 (m, 20H, Ar-H), 3.34 (s, 2H, probably belonging to the O-H, under the water peak of DMSO-d_6,) 2.52-2.04 ppm (s, -CH_3). ^{13}C NMR (DMSO, δ) 203.3 (s, C-4, C-4'), 194.47 (s, C-2, C-2'), 161.68 (s, C-5, C-5'), 147.40 (s, C-3, C-3', in enol-form), 133.51-126.67 (m, arom. C), 104.30 (s, C-3, C-3', in keto-form) Elemental analysis (%): found (calcd.): [C= 69.23 (69.55), H= 4.67 (4.82), N= 1.92 (1.79)].

3,3-*p*,*p*'-Dimethyldibenzoyl-2-oxopropanoic acid-*N*-acetyl-*N*-phenylamide (5c): 4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione (**1**) (0.5 g, 1.63 mmol) and acetanilide (**3c**) (0.22 g, 1.63 mmol) were refluxed in benzene (50 mL) for 5 h. The solvent was evaporated and the remaining oily residue was treated with dry diethyl ether to give a yellow crude product which was recrystallized from acetic acid and allowed to dry on P_2O_5. Yield 55 % (0.4 g); m.p. 191°C; IR (KBr, cm^{-1}): 3070 and 2950 ν(C-H, aromatic and aliphatic), 1710, 1635 ν(s, C=O), 1580, 1480, 1450 ν(m, C=C); ^{1}H NMR (DMSO, δ): 8.11-8.07 (d, 1H), 7.41-7.30 (m, 13H, Ar-H), 2.52-2.49 (s, 6H, CH_3), 2.42 ppm (s, 3H, CH_3). ^{13}C NMR (DMSO, δ) 192.68 (s, C-7, C-8), 175.29 (d, C-4, C-5), 170.60 (s, C-2), 140.50 (s, C-6, enol-form), 138.11, 135.62 (q, N-Ph), 132.00-129.20 (m, aromatic C), 67.92 (s, C-6, in keto-form), 27.77 (s, C-1), 26.92-25.55 (s, Ar-CH_3). Elemental analysis (%): found (calcd.): [C= 73.46 (73.57), H= 5.21 (5.02), N= 3.17 (3.11)].

3,3-*p*,*p*'-Dimethyldibenzoyl-2-oxopropanoic acid-*N*-acetyl-*N*-*p*-methylphenylamide (5d): 4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione (1) (0.5 g, 1.63 mmol) and *p*-methylacetanilide (**3d**) (0.24 g, 1.63 mmol) were refluxed in benzene (50 mL) for 4 h. The solvent was evaporated and the remaining oily residue was treated with dry diethyl ether to give a white crude product which was recrystallized from methanol and allowed to dry on P_2O_5. Yield 50% (0.37 g); m.p. 160°C; IR (KBr, cm^{-1}): 3040 and 2950 ν(C-H, aromatic and aliphatic), 1710, 1670 ν(s, C=O), 1575, 1480, 1450 ν(m, C=C); ^{1}H NMR (DMSO, δ): 8.12-8.06 (d, 1H), 7.91-7.17 (m, 12H, Ar-H), 2.53-2.50 (s, 6H, CH_3), 2.42 (s, 3H, CH_3), 2.32 ppm (s, 3H, CH_3). ^{13}C NMR (DMSO, δ) 193.7 (s, C-7, C-8), 174.5 (d, C-4, C-5), 170.20 (s, C-2), 140.30 (s, C-6, enol-form), 137.62, 135.6 (q, N-Ph), 131.96-130.10 (m, aromatic C), 67.19 (s, C-6, in keto-form), 27.85 (s, C-1), 26.92-22.44 (s, Ar-CH_3). Elemental analysis (%): found (calcd.): [C= 73.84 (73.83), H= 5.49 (5.51), N= 3.07 (3.00)].

3,3-*p,p*'-Dimethyldibenzoyl-2-oxopropanoic acid-*N*-acetyl-*N*-*p*-aminophenylamide (5e): 4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione (**1**) (0.5 g, 1.63 mmol) and *p*-aminoacetanilide (**3e**) (0.24 g, 1.63 mmol) were refluxed in benzene (50 mL) for 5.5 h. The solvent was evaporated and the remaining oily residue was treated with dry diethyl ether to give a yellow crude product which was recrystallized from methanol and allowed to dry on P_2O_5. Yield 65 % (0.49 g); m.p. 210°C; IR (KBr, cm^{-1}): 3500-3250 ν(N-H), 3050 and 2950 ν(C-H, aromatic and aliphatic), 1700, 1670 ν(s, C=O), 1580, 1480, 1450 ν(m, C=C); ^1H NMR (DMSO,δ): 9.93 ($-NH_2$), 7.42-7.72 (m, 12H, Ar-H), 2.50 (s, 6H, CH_3), 2.42 ppm (s, 3H, CH_3). Elemental analysis (%): found (calcd.): [C= 71.05 (71.11), H= 5.26 (5.50), N= 6.14 (6.02)].

3,3-*p,p*'-Dimethyldibenzoyl-2-oxopropanoic acid-*N*-acetoacetyl-*N*-*p*-phenylamide (5f): 4-(*p*-Methylbenzoyl)-5-(*p*-methylphenyl)furan-2,3-dione (**1**) (0.5 g, 1.63 mmol) and acetoacetanilide (**3f**) (0.29 g, 1.63 mmol) were refluxed in benzene (50 mL) for 5 h. The solvent was evaporated and the remaining oily residue was treated with dry diethyl ether to give a yellow crude product which was recrystallized from acetic acid and allowed to dry on P_2O_5. Yield 52% (0.41 g); m.p. 177°C; IR (KBr, cm^{-1}): 3070 and 2900 ν(C-H, aromatic and aliphatic), 1700, 1670 ν(s, C=O), 1580, 1480, 1450 ν(m, C=C); ^1H NMR (DMSO, δ): 8.13-8.07 (d, 1H), 7.41-7.30 (m, 12H, Ar-H), 4.80 (s, $-CH_2$), 2.52 (s, 6H, CH_3), 2.40 ppm (s, 3H, CH_3). Elemental analysis (%): found (calcd.): [C= 72.05 (72.23), H= 5.17 (5.37), N= 2.90 (3.15)].

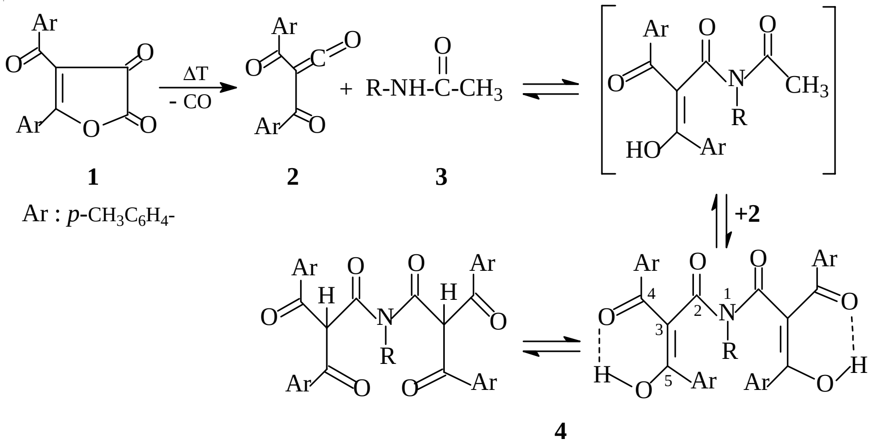
RESULTS AND DISCUSSION

In the present studies the reaction of **1** with various acetanilides **3a-f** under different conditions is presented various substituted amides **4a,b, 5c-f** (**Schemes I and II**) have been synthesized.

The reactions between **1** and **3a,b** were performed either in boiling toluene or xylene (110-140ºC). Obviously (**Scheme-I**), the corresponding dibenzoylacetic acid-*N*-arylamide (**4a,b**) formation goes through the CO disconnection under heating and results in the molecule of ketene **2**. Then the second molecule of **2** combines with the product and we get the final product **4** after CH_3CO_2H disconnection. The ketene formation under conditions mentioned has been proved by different workers[13].

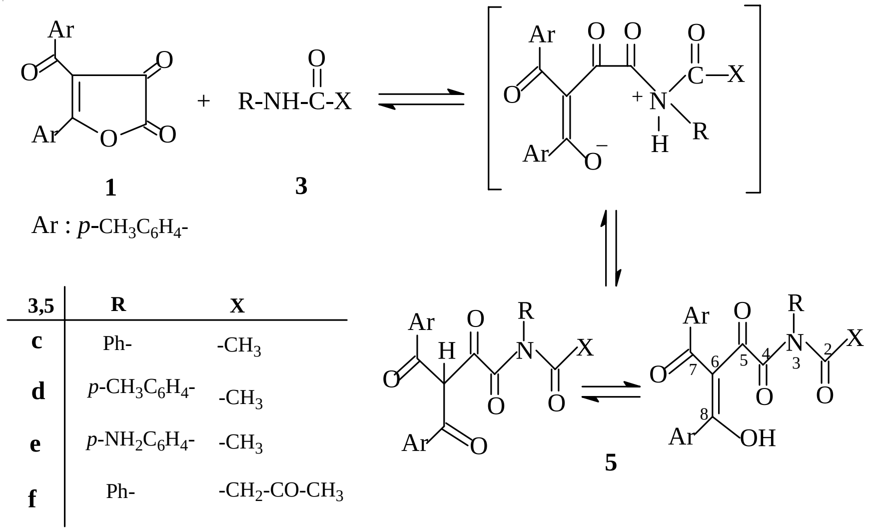
The structures of **4a,b** were confirmed by elemental analysis, IR, ^1H and ^{13}C NMR spectroscopic data. In the IR spectra of compound **4** the C=O exhibit an absorption band at *ca.* 1705, 1680 cm^{-1} (details in Experimental, **4a**). Taking into account the IR and NMR spectral data of compounds **4a,b** indicate the existence of keto-enol tautomerism. For example, ^1H NMR spectra are in the range of δ 10.25, 8.25-7.9 and 2.04 ppm and the ^{13}C

spectra showed peaks at δ = 148.18, 147.40 and 108.83, 104.30 ppm (C-3, C-3'). These weak peaks indicate in favour of keto-enolic forms of the compounds **4a,b**.



R = a : m-$NH_2C_6H_4$- b : p-BrC_6H_4-

Scheme-I



3,5	R	X
c	Ph-	$-CH_3$
d	p-$CH_3C_6H_4$-	$-CH_3$
e	p-$NH_2C_6H_4$-	$-CH_3$
f	Ph-	$-CH_2$-CO-CH_3

Scheme-II

In order to make the reaction selective, we to determined the parameters *i.e.*, the reaction pathways, leading to such different final product. Unlike the previous reaction, under which the ketene is formed in the first stage, the attact of molecule **1** by the molecule of nucleophile **3a** happens without preliminary elimination of CO.

Besides the thermolysis reactions, the compound **1** also reacted with numerous NH-nucleophiles[4c,5c,8d]. The substituted amide derivatives **5c-f** were obtained in 50-65 % yields, respectively from the nucleophilic addition reactions of **1** with acetanilide **3c**, *p*-methylacetanilide **3d**, *p*-aminoacetanilide **3e** and acetoacetanilide **3f** under heating in benzene for 4-5.5 h. By this, the NH-nucleophile attacks the atom C-2 of the furan ring by a Michael-addition type reaction (**Scheme-II**). Structure elucidation of **5c** is mainly based upon ^{13}C NMR spectroscopy, signals at 192.68 (s, C-7, C-8), 175.29 (d, C-4, C-5), 170.60 (s, C-2), 140.50 (s, C-6, enol-form), 138.11, 135.62 (q, N-Ph), 132.00-129.20 (m, aromatic C), 67.92 (s, C-6, in keto-form), 27.77 (s, C-1), 26.92-25.55 (s, Ar-CH_3) could be assigned to the main chain-carbons of **5c**.

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