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Reactions of Substituted Furan-2,3-diones with C- and N-Nucleophiles

ESVET AKBAS*, TAHIR DASKAPAN† and AHMET SENER
Department of Chemistry, Faculty of Science and Arts, Yuzuncu Yil University
65080, Van, Turkey
E-mail: esvakbas@hotmail.com; esvet@yyu.edu.tr

The thermolysis of 5-phenyl-2,3-dihydrofuran-2,3-dione in 4-methoxyphenylacetone yield 2-(4-methoxybenzyl)-2-methyl-6-phenyl-4*H*-1,3-dioxin-4-one *via* α-oxoketene. Reaction of 5-phenyl-2,3-dihydrofuran-2,3-dione with phenylhydrazine afforded 1,6-diphenyl-1,2-dihydropyridazine-3,4-dione. The hydrazine derivatives and 1,2-phenylenediamine react with 4,4-dimethyltetrahydrofuran-2,3-dione to give the corresponding hydrazone derivatives and 3,3-dimethyl-2,3-dihydrofuro[2,3-*b*]quinoxaline, respectively. The structures of compounds were characterized on the basis of elemental analyses, Mass, IR, ^{1}H and ^{13}C NMR spectra.

Key Words: Furan-2, 3-Dione, Pyridazine, Dioxine.

INTRODUCTION

α-Oxoketenes are often used as structure particles in chemical design. Usually they can not be stabilized under reaction conditions. The most common method for the synthesis of these highly reactive molecules are the thermolysis of 2,3-dihydrofuran-2,3-diones and 1,3-dioxin-4-ones. For example, 5-aryl-[1], 5-aryl-4-imidoyl-[2], 5-aryl-4-halogen-[3], 4-benzoyl-5-phenyl-[4], 5-aryl-4- phenyl-[5], 5-aryl-4-quinoxalinyl-2,3-dihydrofuran-2,3-diones[6] and 1,3-dioxin-4-ones-[7] can be used as sources of α-oxoketenes.

The ketenes usually were added to multiple bond systems *via* a [2+2] process across their C=C as well as C=O double bonds, while a-oxoketenes show a pronounced behaviour to form [4π+2π] hetero-Diels Alder adducts when trapped with dienophiles. When the reaction mixture contains an inert reagent, the –COC=C part in primary ketene molecule acts as heterodiene, while the other molecule the C=C bond of ketene acts as heterodienophile[8-10].

For instance, the thermolysis of 5-aryl-4-halo-2,3-dihydrofuran-2,3-diones gives aroyl(halo)ketenes *via* cyclodimerization of 3-aroyl-6-aryl-3,5-dihalo-3,4-dihydro-2*H*-pyran-2,4-diones. The hydrolysis of the latter yields 3-aroyl-6-aryl-5-halo-4-hydroxy-2*H*-pyran-2-ones[3].

†Department of Chemistry, Faculty of Science, Ankara University, 06100, Ankara, Turkey.

The furandiones which is contains no substituent in position 4 is thermally unstable. They undergo decomposition by heating to a temperature near the melting point (135-140°C) give aroylketenes. They were converted into 3-aroyl-6-aryl-3*H*-pyran-2,4-diones as a result of [4+2] cyclodimerization and react with chloral to give 1,3-dioxin-4-ones[11].

Besides, aroylketenes generated from 6-aryl-1,3-dioxin-4-ones frequently give reactions with the analogous of the aroylketenes formed from 5-aryl-2,3-dihydrofuran-2,3-diones[12]. The reaction of acetylacetone, methyl acetyl- and aroylpyruvates with dioxinones formed from 2,3-dihydrofuran-2,3-diones, lead to pyranones[7].

The nucleophilic addition is one of the most characteristic reactions of the ketenes[10,12,13]. N-Acrylamides of aroylacetic acids were obtained by the reaction of the arylketenes with aromatic and heterocyclic amines. The reactions of ketene with 1,1-diamines form the substituted 6-aryl-2-methylene-4*H*-pyrimidin-4-ones[7]. The ketenes towards carbon-nucleophiles converted into 4-pyrone derivative[10].

On the other hand, the 4,4-dimethyldihydrofuran-2,3-dione (**5**)[14] do not generated keten form by heating to a temperature near the melting point. Because of, do not have to exist π bond among with carbons C_4-C_5. But the reactivity of carbonyl groups in compound **5** with some C-, N-, and O-nucleophiles was reported previously[15].

The present work are devoted to the thermolysis of 5-aryl-2,3-dihydrofuran-2,3-dione in the carbonyl compound and N-nucleophile, and the investigation and the interaction of 4,4-dimethyldihydrofuran-2,3-dione with 1,2-phenylenediamine and various hydrazine derivatives.

EXPERIMENTAL

Solvents were dried by refluxing with the appropriate drying agents and distilled before use. Melting points were determined on an Barnstead/Electrothermal-9200 apparatus and are uncorrected. Microanalyses were performed on LECO CHNS 932 Elemental Analyzer. The IR spectra were obtained in as potassium bromide pellets using a Mattson 1000 FTIR spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance DPX-400 spectrometers, using TMS as an internal standard. The mass spectra (100 eV) were run on an AGILENT 1100 MSD mass spectrometer. All experiments were followed by TLC using DC Alufolien Kieselgel 60 F 254 Merck and Camag TLC lamp (254/366 nm).

2-(4-Methoxybenzyl)-2-methyl-6-phenyl-4*H*-1,3-dioxin-4-one (3): A solution of compound **1** (1 mmol) and 4-methoxyphenylacetone (1 mmol) in 10 mL absolute *p*-xylene was maintained for 30-40 min at 138-140°C. The precipitate formed was filtered off and recrystallized from methanol to give compound **3**. Yield: 0.167 g (54 %); m.p. 114-115°C; Analysis (%

calcd./found): for $C_{19}H_{18}O_4$ C: 73.53/73.56, H: 5.85/5.84; IR (KBr, ν_{max}, cm^{-1}), 3180 (H arom.), 3001-2832 (R-H), 1723 (C=O), 1618 (C_5=C_6). ^{1}H NMR ($CDCl_3$): δ 1.71 (3H, s, CH_3), 3.32 (2H, d, CH_2, J= 8 Hz, A part of AB system), 3.45 (2H, d, CH_2, J= 8 Hz, B part of AB system), 3.9 (3H, s, OCH_3), 6.0 (1H, s, C_5-H), 6.9 (2H arom., benzyl, J= 8.6 Hz), 7.2 (2H arom., benzyl, J= 8.6 Hz), 7.5-7.7 (5H arom., m). ^{13}C NMR ($CDCl_3$): δ164.8 (C=O), 161.7, 158.9, 132.2, 131.8, 130.9, 128.9, 126.4, 126.5, 113.8, 107.8, 91.3, 55.3, 43.1, 22.7.

1,6-Diphenyl-1,2-dihydropyridazine-3,4-dione (4): The furandione **1** (1 mmol) and phenyl hydrazine (1 mmol) were refluxed in dry benzene (10 mL) for about 3 h. After cooling, the precipitate was filtered off and washed with cold benzene to give a crude solid that was recrystallized from ethyl alcohol. Yield: 55%; m.p. 240-241°C; Analysis (% calcd./found): for $C_{16}H_{12}N_2O_2$; C: 72.72/73.34, H: 4.58/4.50, N: 10.60/10.65; IR (KBr, ν_{max}, cm^{-1}), 3155 (br. s. NH ⇌ OH), 1620 (C=O). ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 7.3 (1H, s, C_5), 7.4-8.0 (10H arom., m), 11.3 (1H, br. s, NH- exchangable). Mass (100 eV): *m/e*: 266.1, 265.1, 230.0, 229.1, 203.0.

4,4-Dimethyldihydrofuran-2,3-dione-3-(N-phenylhydrazone) (6a): The compound **5** (1 mmol) and phenylhydrazine (1 mmol) was refluxed in 20 mL benzene for 3 h. The solvent was evaporated, then the oily residue was treated with ether and the formed crude product was recrystallized from toluene. Compound **6a** was obtained in yield 50%; m.p. 177-178°C; Analysis (% calcd./found): for $C_{12}H_{14}N_2O_2$ C: 66.04/65.97, H: 6.47/6.46, N: 12.84/12.85; IR (KBr, ν_{max}, cm^{-1}), 3297 (N-H), 3057, 2966 (CH_3, C-H), 1738 (C=O, lactone), 1587 (C=N), 1517 (C=C). ^{1}H NMR (DMSO-d_6): δ 1.5 (6H, s, CH_3), 3.4 (2H, s, CH_2), 6.9-7.3 (4H arom., m), 9.8 (1H, s, NH). ^{13}C NMR ($CDCl_3$): δ165.7, 142.9, 132.2, 129.3, 122.3, 113.5, 80.0, 38.1, 26.6. Mass (100 eV): *m/e*: 220.1, 219.1, 201.1, 195.0, 189.1, 173.1, 163.0, 119.1, 93.1.

4,4-Dimethyldihydrofuran-2,3-dione-3-[N-(2,5-dichlorophenyl) hydrazone] (6b): The compound **6b** was prepared according to the procedure for compound **6a**, it crystallized from 1-butanol, in yield 55 %; m.p. 176-177°C; Analysis (% calcd./found): for $C_{12}H_{12}N_2O_2Cl_2$ C: 50.19/ 50.17, H: 4.21/4.26, N: 9.76/9.79; IR (KBr, ν_{max}, cm^{-1}) 3383 (N-H), 2957 (CH_3, C-H), 1765 (C=O, lactone), 1594 (C=N), 1507 (C=C). ^{1}H NMR (DMSO-d_6): δ 1.5 (6H, s, CH_3), 4.1 (2H, s, CH_2), 7.1-7.5 (3H arom., m), 8.9 (1H, s, NH). Mass (100 eV): *m/e*: 289.0, 288.0, 287.1, 243.0, 241.0, 230.9, 195.0, 189.0, 164.0, 162.9, 161.0, 159.9.

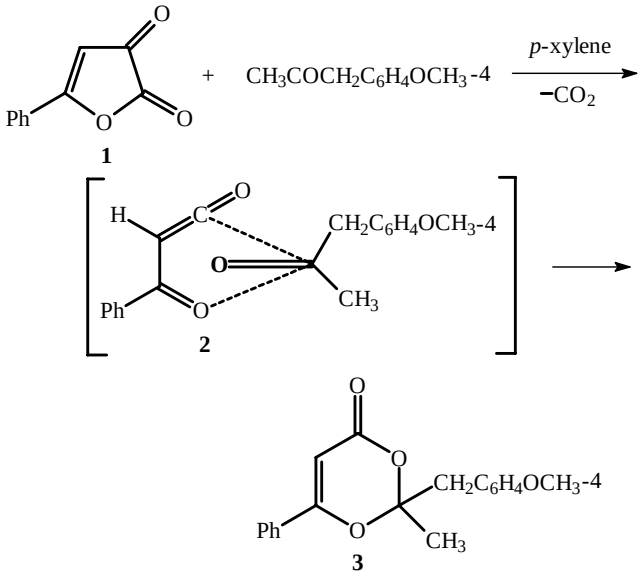
4-{2-[4,4-dimethyl-2-oxodihydrofuran-3(2H)-ylidene]hydrazino}-benzoic acid (6c): The compound **6c** was prepared according to the procedure for compound **6a**, it crystallized from acetic acid, in yield 50 %; m.p. 244-245°C; Analysis (% calcd./found): for $C_{13}H_{14}N_2O_4$ C: 59.54/59.56,

H: 5.38/5.32, N: 10.68/10.65; IR (KBr, ν_{max}, cm^{-1}), 3442-3528 (OH), 3278 (N-H), 3077, 2969, 2872 (CH_3, C-H), 1730 (C=O, lactone), 1673 (C=O, acid), 1583 cm^{-1} (C=N), 1524 cm^{-1} (C=C). ^{1}H NMR (DMSO-d_6): δ 1.3 (6H, s, CH_3), 4.3 (2H, s, CH_2), 7.4 (2H arom., benzoyl, J= 8.56 Hz), 7.8 (2H arom., benzoyl, J = 8.56 Hz), 11.6 (1H, s, NH), 12.1(1H, br. s, OH).

3,3-Dimethyl-2,3-Dihydrofuro[2,3-b]quinoxaline (7): A solution of compound **5** (1 mmol) and 1,2-phenylenediamine (1 mmol) in 20 mL of benzene was refluxed for 4 h. The mixture was cooled to room temperature; the precipitate was filtered off and recrystallized from the mixture of ethanol-water (2/1). Yield: 60%; m.p. 190-191°C; Analysis (% calcd./found): for $C_{12}H_{12}N_2O$ C: 71.98/71.94, H: 6.04/6.10, N: 13.99/13.85; IR (KBr, ν_{max}, cm^{-1}), 3224, 3004 (C-H arom.), 2966, 2892 (CH_3, C-H), 1657 (O–C=N–, ring system[17,18]), 1597, 1550, 1279, 1078 (C-O-C). ^{1}H NMR ($CDCl_3$): δ 1.5 (6H, s, CH_3), 3.8 (2H, s, CH_2), 7.3-7.8 (4H arom., m). ^{13}C NMR ($CDCl_3$): δ166.8, 158.2, 133.8, 133.1, 132.3, 130.9, 126.3, 117.3, 60.8, 46.0, 24.1. Mass (100 eV): *m/e*: 202.1, 201.1, 190.1, 189.1, 187.0, 119.1.

RESULTS AND DISCUSSION

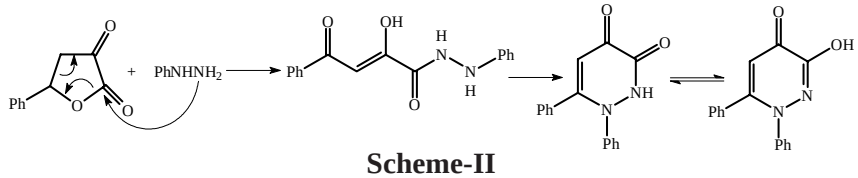
A mixture of compound **1** and 4-methoxyphenylacetone were heated in *p*-xylene at 138-140°C for 25-30 min. Under the thermolysis conditions of compound **1**, with the loss of carbon monoxide give phenylketene (**2**)[11]. The subsequent [4+2] cycloaddition of phenylketene C=C–C=O component at the (C=O) group of ketone afforded 2-[(4-methoxy benzyl)-2-methyl-6-phenyl-4*H*-1,3-dioxin-4-one (**3**) (**Scheme-I**).



Scheme-I

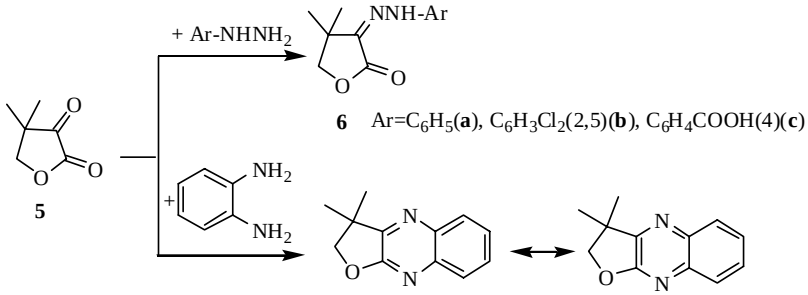
IR spectra of compound **3** show a strong lactone carbonyl band at 1723 cm^{-1}. The observed IR data are in agreement with published data[5,8,11] for analogs of compound **3**. ^{13}C NMR spectrum of compound **3** revealed signal at δ 164.8 (C=O).

The reaction of compound **1** with phenylhydrazine gave 1,6-diphenyl-1,2-dihydropyridazine-3,4-dione (**4**). The IR spectrum of compound **4** showed broad absorption band at 3155 cm^{-1} because of NH ⇌ OH function and carbonyl absorption bands at 1620 cm^{-1}. In the ^1H NMR spectra of compound **4**, the 1-H (C_5) signal appears as a singlet at δ 7.3 ppm, and a broad singlet signal at δ 11.3 was exhibited due to NH proton. The mass spectrum of compound **4** showed the following ion peaks, *m/e*: 266.1, 265.1, 230.0 (**Scheme-II**). This structure is in agreement with published data[16] for analogs of compound **4**.



Scheme-II

On the other hand, the interaction of compound **5** with phenylhydrazine and 2,5-dichlorophenylhydrazine in benzene at refluxing temperature afforded products that were characterized as phenylhydrazon derivatives compounds (**6a**) and (**6b**), respectively. Both products showed NH protons as singlet signals around δ 9.8 and 8.9, in addition to methyl protons singlet near δ 1.5 in their ^1H NMR spectra. Their IR spectra revealed strong absorption bands due to NH and lactone carbonyl functions 3383-3297 cm^{-1} and 1765-1738 cm^{-1}, respectively. When compound **5** were treated with 4-hydrazinobenzoic acid obtained compound **6c**. Its IR spectrum appeared two carbonyl absorption bands 1673 and 1730 cm^{-1}. The ^1H NMR spectrum showed a broad singlet signal at δ 12.1 due to OH proton, in addition to NH proton singlet near δ 11.6 (**Scheme-III**). Their mass ion peaks data are in agreement for all products.



6 Ar=C_6H_5(**a**), $C_6H_3Cl_2$(2,5)(**b**), C_6H_4COOH(4)(**c**)

5

7

Scheme-III

Furthermore, treatment of compound **5** with 1,2-phenylenediamine in benzene led to the formation of quinoxaline derivative compound **7**, in 60 % yield (**Scheme-III**). The product was identified by IR, ^{1}H, ^{13}H NMR, MS spectra and elemental analysis.

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