

Reactions of 4-Benzoyl-5-[(E)-2-phenyl-1-ethenyl]-2,3-dihydro-2,3-furandione with Aromatic Aminonucleophiles

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4-Benzoyl-5-[(E)-2-phenyl-1-ethenyl]-2,3-dihydro-2,3-furandione (1) reacts with various aminonucleophiles (2a–g) and gives the hexadienoic acid derivatives (6-phenyl-3-benzoyl-arylamino-2-oxo-3,5-hexadienoic acids) (3a–g). The structures of the synthesized compounds were determined by being interpreted by their elemental analysis and IR, ¹H- and ¹³C-NMR spectra.

Key Words: 2,3-Dihydro-2,3-furandione, Hexadienoic acids, Aminonucleophiles, Nucleophilic addition reactions.

INTRODUCTION

In early studies, 4-acyl-5-alkyl/aryl-2,3-dihydro-2,3-furandiones were obtained from 1,3-dicarbonyl compounds with oxalyl halides¹. Recently, reactions of cyclic oxalyl compounds were reported to give substituted heterocyclic compounds. In addition, the reactions of substituted 2,3-furandiones have been studied with several semi-/thiosemicarbazones, ureas, thioureas, oximes, various hydrazines, some acetanilides and amides under different conditions². Most of these obtained compounds in general are well known for their potential biological activities³.

In the present study, we carried out the reaction of 4-benzoyl-5-[(E)-2-phenyl-1-ethenyl]-2,3-dihydro-2,3-furandione (1) with phenylhydrazine, *o*-phenylenediamine, *p*-phenylenediamine, α -naphthylamine, 4-methyl-*o*-phenylenediamine, *o*-toluidine and 2-amino-4-methylphenole (2a–g). The compound (1) was prepared from (E)-1,5-diphenyl-4-pentene-1,3-dione with oxalylchloride⁴. The hexadienoic acid derivatives, which are α -keto-carboxylic acids were synthesized from the reactions of the various amines (2a–g) with 4-benzoyl-5-[(E)-2-phenyl-1-ethenyl]-2,3-dihydro-2,3-furandione (1) (Scheme-2).

EXPERIMENTAL

Solvents were dried by refluxing with the appropriate drying agent and distilled before use. Melting points were determined by using Büchi melting point apparatus and are not corrected. Microanalyses were performed on a Carlo-Erba elemental analyzer model 1108. IR spectra were obtained as potassium bromide pellets using a Shimadzu model 435 V-04 spectrometer. The ¹H- and ¹³C-NMR

spectra were recorded on a Varian 4200 Gemini spectrometer using tetramethylsilane as an internal standard. All experiments were followed by TLC using DC Alufolien Kieselgel 60 F₂₅₄ (Merck) and with a model Camag TLC lamp (254/366 nm).

(3Z,5E)-3-Benzyl-6-phenyl-4-(phenylhydrazono)-2-oxo-3,5-hexadienoic acid (3a): To a solution of the compound (1) (0.30 g, 0.10 mmol) in benzene (50 mL), phenylhydrazine (2a) (0.118 g, 0.10 mmol) was added dropwise. After the reaction mixture had been stirred at room temperature for 1 h, the precipitate was filtered and recrystallized from toluene and allowed to dry on P₂O₅; yield 0.12 g (38%); m.p. 145–146°C; IR (cm⁻¹) (KBr): 3650–3100 ν(—NH, —OH); 1730, 1612, 1579 ν(C=O, acid carbonyl, benzoyl C=O, =C—C=O carbonyl), 1496, 1564 ν(N—H), 1234 ν(C=N), 970 ν(CH=CH), 741, 697 ν(mono-substituted benzene); ¹H NMR (DMSO, δ): 8.576 (—NH and —OH), 7.834–6.645 ppm (15H, aromatic H); ¹³C NMR (DMSO, δ): 184.322 (C-3), 177.435 (C-2), 163.400 (C-1), 160.130 (C-4), 149.403 (C-5), 148.253 (C-6), (C-5 and C-6, HC=CH), 144.070–114.194 ppm (aromatic C). Elemental analysis (%): Found (Calcd.): C = 72.44 (72.81), H = 4.75 (4.75), N = 6.60 (6.79).

(3Z,5E)-3-Benzyl-6-phenyl-4-(*o*-phenylenediamino)-2-oxo-3,5-hexadienoic acid (3b): To a solution of the compound (1) (0.30 g, 0.10 mmol) in benzene (50 mL), *o*-phenylenediamine (2b) (1.108 g, 0.10 mmol) was added dropwise. The reaction mixture had been stirred at room temperature for 24 h, the precipitated yellow product was filtered and recrystallized from *n*-propanol and *n*-butanol; yield 0.17 g (55.7%); m.p. 245.4°C; IR (cm⁻¹) (KBr): 3600–3200 ν(O—H and N—H), 1714, 1677, 1658 ν(C=O), 1630 ν(CH=CH), 1579 ν(N—H), 1367 ν(C—N, for C—NH₂), 751 ν(1,2-disubstituted benzene); ¹H NMR (DMSO, δ): 12.12 (s, O—H), 8.88–8.60 (C—NH₂), 7.97–7.19 ppm (m, 14H, Ar—H); ¹³C NMR (DMSO, δ): 190.273 (C-13, Ph—C=O carbonyl C), 183.400 (C-2, CH=CH—C=O), 158.800 (C-1, —COOH), 148.230 (C-4, —CH=C—), 141.977–111.333 ppm (Ar—C); Elemental analysis (%): Found (Calcd.): C = 72.10 (72.82), N = 6.75 (6.79), H = 4.72 (4.85).

(3Z,5E)-3-Benzyl-6-phenyl-4-(*p*-phenylenediamino)-2-oxo-3,5-hexadienoic acid (3c): To a solution of the compound (1) (0.30 g, 0.10 mmol) in benzene (50 mL), *p*-phenylenediamine (2c) (0.108 g, 0.10 mmol) was added. The reaction mixture had been stirred at room temperature for 48 h, the precipitate was separated by filtering and washed with hot ethanol and allowed to dry on P₂O₅, yield 0.18 g (60.5%); m.p. 213–213.5°C; IR (cm⁻¹) (KBr): 3600–3200 ν(OH, N—H), 1676, 1625, 1595 ν(C=O), 3059 ν(C—H), 848 ν(C₆H₄); ¹H NMR (DMSO, δ): 10.896–10.874 (OH and N—H), 7.880–6.930 ppm (14H, Aromatic-H); ¹³C NMR (DMSO, δ): 164.600 (C-1), 143.120–122.140 ppm (aromatic C). Elemental analysis (%): Found (Calcd.): C = 73.50 (72.81), H = 4.90 (4.85), N = 6.57 (6.79).

(3Z,5E)-3-Benzyl-6-phenyl-4-(1-naphthylamino)-2-oxo-3,5-hexadienoic acid (3d): To a solution of the compound (1) (0.30 g, 0.10 mmol) in benzene (50 mL), α-naphthylamine (2d) (0.143 g, 0.10 mmol) was added. The reaction mixture had been stirred at room temperature for 24 h, the precipitate was filtered and washed with ether and allowed to dry on P₂O₅; yield: 0.18 g (62%); m.p.:

140°C; IR (cm^{-1}) (KBr): 3650–3150 $\nu(\text{O—H}$ and $\text{N—H})$, 1706, 1614, 1581 $\nu(\text{C=O})$, 797–763 $\nu(\alpha\text{-substituted naphthalene})$; ^1H NMR (DMSO, δ): 8.020 (OH and N—H), 7.813–7.245 ppm (m, 17H, aromatic H); ^{13}C NMR (DMSO, δ): 184.526 (C-3), 181.800 (C-2), 177.501 (C-1), 144.070–114.190 ppm (Ar—C). Elemental analysis (%): Found (Calcd.) C = 77.40 (77.85), N = 3.01 (3.13), H = 4.82 (4.69).

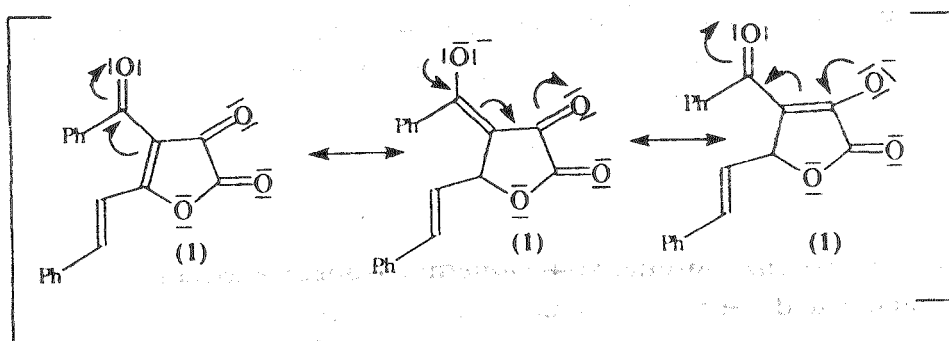
(3Z,5E)-3-Benzyl-6-phenyl-4-(4-methyl-*o*-phenylenediamino)-2-oxo-3,5-hexa-dienoic acid (3e): To a solution of the compound (1) (0.30 g, 0.10 mmol) in benzene (50 mL) 4-methyl-*o*-phenylenediamine (2e) (0.122 g, 0.10 mmol) was added. The reaction mixture had been stirred at room temperature for 24 h, the precipitate was filtered and recrystallized from ethanol and allowed to dry on P_2O_5 ; yield: 0.18 g (58%); m.p.: 206–207°C; IR (cm^{-1}) (KBr): 3600–3100 $\nu(\text{O—H}$, $\text{N—H})$, 1635, 1630, 1628 $\nu(\text{C=O})$, 1447 $\nu(\text{—CH}_3)$; ^1H NMR (DMSO, δ): 12.134 and 12.075 (—NH and —OH), 2.312–2.350 (CH_3), 7.957–7.007 ppm (m, 14H, aromatic H); ^{13}C NMR (DMSO, δ): 196.314 (C-13), 196.102 (C-2), 156.595 (C-1), 148.896 (C-4), 148.340 (C-3), 144.370–117.133 (aromatic C), 22.17 ppm (—CH_3). Elemental analysis (%): Found (Calcd.): C = 73.27 (73.240), H = 5.09 (5.16), N = 6.73 (6.57).

(3Z,5E)-3-Benzyl-6-phenyl-2-oxo-4-(*o*-toluidino)-3,5-hexadienoic acid (3f): To a solution of the compound (1) (0.30 g, 0.10 mmol) in benzene (50 mL), *o*-toluidine (2f) (0.09 mL, 0.10 mmol) was added dropwise. This solution was stirred in benzene at room temperature for 48 h. The crude precipitate was filtered off and washed with ether and left to dry on P_2O_5 ; yield: 0.16 g, (52%); m.p.: 192–193°C; IR (cm^{-1}) (KBr): 3600–3100 $\nu(\text{broad, O—H}$ and $\text{N—H})$, 3061 and 3025 $\nu(\text{—CH}_3)$; 1666, 1685, 1640 $\nu(\text{acid, benzoyl, C}_2, \text{C=O})$, 1590 $\nu(\text{C=C})$, 756 $\nu(1,2\text{-disubstituted Ar—H})$; ^1H NMR (DMSO, δ): $\delta = 9.6$ (O—H and N—H), 6.850–7.750 (m, 14H, Ar—H), 2.30 (—CH_3). Elemental analysis (%): Found (Calcd.): C = 76.22 (75.91), N = 3.67 (3.41), H = 5.14 (5.11).

(3Z,5E)-3-Benzyl-6-phenyl-4-(2-hydroxy-3-methyl anilino)-2-oxo-3,5-hexa-dienoic acid (3g): To a solution of the compound (1) (0.30 g, 0.10 mmol) in benzene (50 mL), 2-hydroxy-3-methyl aniline (2g) (0.123 g, 0.10 mmol) was added. This solution was stirred at room temperature for 24 h. The crude precipitate was filtered off and recrystallized from *n*-propanol and allowed to dry on P_2O_5 ; yield: 0.17 g (56%); m.p.: 156°C; IR (cm^{-1}) (KBr): 3600–3100 $\nu(\text{O—H}$ and $\text{N—H})$, 3020–2920 $\nu(\text{—CH}_3)$, 1684, 1649, 1627 $\nu(\text{C=O})$, 1535 $\nu(\text{N—H eđilmesi})$, 965 $\nu(\text{CH=CH})$, 885–813 $\nu(\text{trisubstituted Ar—H})$; ^1H NMR (DMSO, δ): 9.80 (s, O—H) (—NH not observed), 8.20–6.20 (m, 13H, Ar—H), 2.20 ppm (5.3 H, CH_3). Elemental analysis (%): Found (Calcd.): C = 73.14 (73.06), N = 3.26 (3.27), H = 4.64 (4.91).

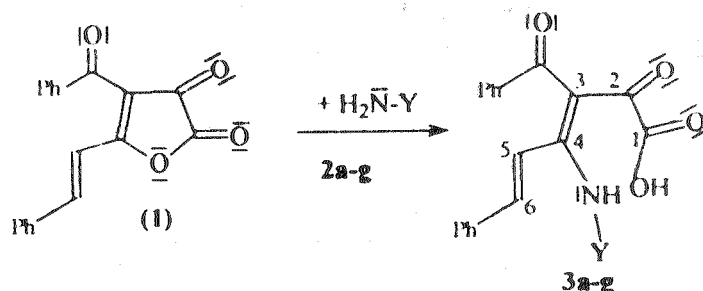
RESULTS AND DISCUSSION

The cyclocondensation reactions of (E)-1,5-diphenyl-4-pentene-1,3-dione with oxalyl chloride regiospecifically afforded 4-benzoyl-5-[(E)-2-phenyl-1-ethenyl]-2,3-dihydro-2,3-furandione (1), which exhibits conjugation with double bonds⁴ (Scheme-1).



Scheme-1

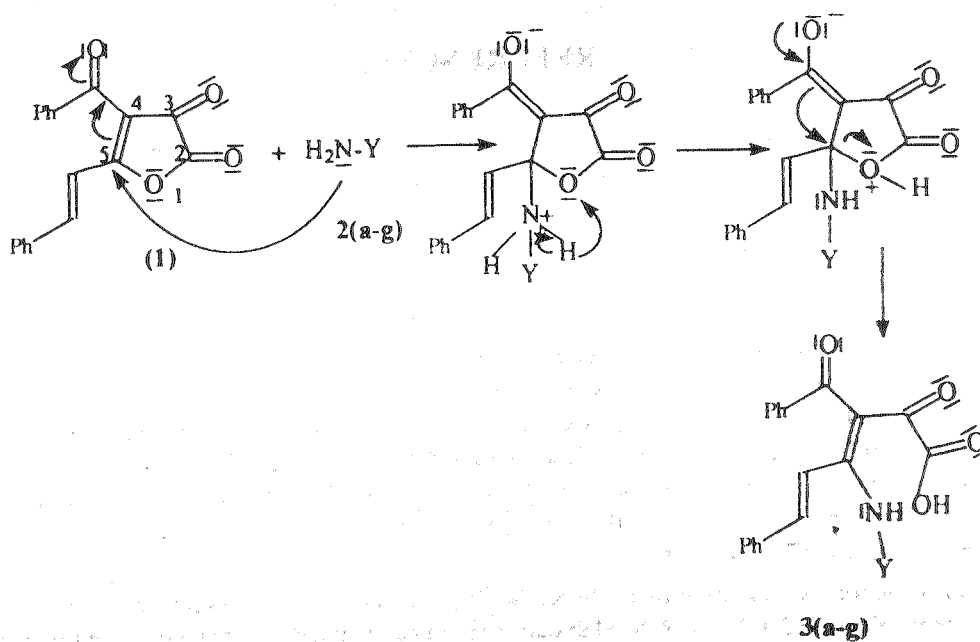
In the present study, we carried out the reaction of the furan-2,3-dione (1) with phenylhydrazine and the various aromatic amine nucleophiles 2(a-g) yielding 3,5-hexadienoic acid derivatives (3a-g) (Scheme-2). At room temperature in benzene, mixing of furandione (1) and corresponding phenylhydrazine and amines (1 : 1 mol) for about 1–3 d led to the formation of the novel compounds (3a-g) in approximately 38–62% yield. In moderate conditions, excellent yields of the reactions can be explained by the chemical behaviour of furandiones similar to the compounds 2(a-g) towards nucleophiles⁵.



| 3(a-g) | Y | Y |
|--------|---|---|
| a | | e |
| b | | f |
| c | | g |
| d | | |
| | | |
| | | |
| | | |
| | | |

Scheme-2

Addition of the nucleophiles to the furandiones usually starts with nucleophilic attack at one of the C-2, C-3 and C-5 positions of the furan ring system⁶. In this reaction, the formation of 3,5-hexadienoic acid derivatives (3a-g) may be viewed as occurring *via* a Michael type addition to C-5 atom of (1) (Scheme-3). The reactions proceeded smoothly at room temperature in benzene for 1–3 d and afforded the corresponding acid derivatives (3a-g) in yield 38–62%. The new compounds (3a-g) can be used as substrate to obtain the new compounds like the pyrrolidione derivatives.



Scheme-3

Structures of synthesized compounds were assigned on the basis of analytical as well as spectroscopic data. Product (3a) was obtained in 37% yield by treating (1) with phenylhydrazine (2a) and stirring in benzene at room temperature for 1 h. In the IR spectra of compound (3a), the —OH and —NH absorption bands of —COOH, —NH₂ groups were found to be at 3650–3100 cm⁻¹. The absorption bands of (C=O) groups were found to be at 1730, 1612, 1579 cm⁻¹. The ¹H NMR signals were at $\delta = 8.576$ ppm (—OH and —NH) and $\delta = 7.834$ –6.645 ppm (m, Ar—H). The ¹³C NMR signals were found to be at 184.322 ppm (C-13), 177.435 ppm (C-2), 163.400 ppm (C-1) and elemental analysis data also support their structure (3a). The reaction pathway from furandione (1) with phenylhydrazine (2a) to hexadienoic acid (3a) is outlined briefly in Scheme-2.

Nucleophilic addition of *o*-phenylenediamine (2b) with furandione (1) provided (3Z,5E)-3-benzyl-6-phenyl-4-(*o*-phenylenediamino)-2-oxo-3,5-hexadienoic acid (3b) in %55.7. At the room temperature in benzene, mixing of furandione (1) and *o*-phenylenediamine (2b) (1 : 1) for 24 h. In the IR spectrum of (3b) characteristic absorption bands at about 3600–3200 cm⁻¹ (OH and NH), 1714, 1677, 1658 cm⁻¹ (C=O) were observed. The ¹H NMR signals were at $\delta = 12.12$ ppm (—OH) and $\delta = 7.970$ –7.190 ppm (m, Ar—H). The ¹³C NMR spectrum of (3b) exhibits significant line broadenings for the carbons 158.800 ppm (C-1), 183.400 ppm (C-2, CH=CH—CO—), 148.230 ppm (C-4) and 190.273 ppm (C-13, Ph—CO—), 141.477–111.333 ppm (Ar—C). Other spectral and analytical data of (3b) are in full agreement with its proposed structure as well.

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REFERENCES

1. (a) E. Ziegler, M. Eder, C. Beleggratis and E. Prewedourakis, *Monatsh Chem.*, **98**, 2249 (1967); (b) R.W. Saalfrank and T. Lutz, *Angew. Chem. Int. Ed. Engl.*, **29**, 1401 (1990); (c) R.W. Saalfrank, T. Lutz, B. Hörner, J. Gündel, K. Peters and H.G. Von Schnering, *Chem. Ber.*, **124**, 2289 (1991); (d) E. Saripinar, Y. Güzel, Z. Önal, I.O. İlhan and Y. Akçamur, *J. Chem. Soc. Pak.*, **22**, 308 (2000).
2. (a) G. Kollenz, E. Ziegler, W. Ott and H. Igel, *Z. Naturforsch.*, **31B**, 1511 (1976); (b) W. Ott, E. Ziegler and G. Kollenz, *Synthesis*, 477 (1976); (c) Y. Akçamur, B. Altural, E. Saripinar, G. Kollenz, C.O. Kappe, E.M. Petres and H.G. Von Schnering, *J. Heterocycl. Chem.*, **25**, 1419 (1988); (d) B. Altural, Y. Akçamur, E. Saripinar, İ. Yildirim and G. Kollenz, *Monatsh. Chem.*, **120**, 1015 (1989); (e) Y. Akçamur and G. Kollenz, *Oppi Briefs*, **19**, 52 (1987); *Chem. Abstr.*, **107**, 7020t (1987); (f) I.O. İlhan, E. Saripinar and Y. Akçamur, *J. Heterocycl. Chem.*, **41**, 1 (2004); (g) İ. Yildirim and I.Koca, *Asian J. Chem.*, **16**, 899 (2004); (h) İ. Yildirim and I.O. İlhan, *Indian J. Chem.*, **36B**, 1138 (1997); (i) E. Saripinar, I.O. İlhan and Y. Akçamur, *Heterocycles*, **57**, 1445 (2002).
3. (a) A. Şener, A. Kasimogullari, M.K. Şener, İ. Bildirici and Y. Akçamur, *J. Heterocycl. Chem.*, **39**, 869 (2002); (b) R.N. Mahajan, F.H. Havaladar and P.S. Fernandes, *J. Indian Chem. Soc.*, **68**, 245 (1991); (c) W.T. Thomson, *Agricultural Chemicals, Book II: Herbicides*, 13th Edn., Thomson Publications, California, USA, pp. 268–278 (1997); (d) C.C. Cheng, *Prog. Med. Chem.*, **67**, (1969); (e) T.J. Lomis, J.F. Suida and R.E. Shepherd, *J. Chem. Soc. Chem. Comm.*, 290.
4. S.H. Ungören, B. Deniz and B. Altural, *Asian J. Chem.*, **16**, 805 (2004).
5. (a) W. Ott, E. Ziegler and G. Kollenz, *Synthesis*, 477 (1976); (b) *Synthesis*, 679 (1973); (c) H.A.A. El-Nabi and G. Kollenz, *Monatsh. Chem.*, **128**, 381 (1997).
6. (a) Y. Akçamur, A.M. İpekoglu and G. Kollenz, *J. Heterocycl. Chem.*, **34**, 221 (1997); (b) İ. Yildirim, E. Saripinar, Y. Gözel, Ş. Patat and Y. Akçamur, *J. Mol. Struct.*, **334**, 165 (1995); (c) İ. Yildirim, M. Tezcan, Y. Gözel, E. Saripinar and Y. Akçamur, *Truk. J. Chem.*, **20**, 27 (1996); (d) E. Saripinar, İ. Yildirim, Y. Gözel and Y. Akçamur, *Monatsh. Chem.*, **127**, 505 (1996); (e) İ. Yildirim, Y. Akçamur, E. Saripinar and G. Kollenz, *Kuwait J. Sci. Eng.*, **29**, 57 (2002).

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