A Simple Synthesis of 2-{(Arylmethylidene)hydrazinylidene]-3-hydroxy-4*H*-furo[3,2-*c*]pyran-4(3*H*)-ones

by **Mehdi Adib***[a]), **Samira Ansari**[a]), **Long-Guan Zhu**[b]), and **Mehdi Rahimi-Nasrabadi**[c])

[a]) School of Chemistry, University College of Science, University of Tehran, P.O. Box 14155–6455, Tehran, Iran (phone/fax: +98-21-66495291; e-mail: madib@khayam.ut.ac.ir)

[b]) Chemistry Department, Zhejiang University, Hangzhou 310027, P. R. China

[c]) Department of Chemistry, Imam Hossein University, Tehran, Iran

A simple synthesis of 2-hydrazinylidene-3-hydroxy-4*H*-furo[3,2-*c*]pyran-4-ones is described. A mixture of (isocyanoimino)(triphenyl)phosphorane, an aromatic aldehyde, and dehydroacetic acid (= 3-acetyl-2-hydroxy-6-methyl-4*H*-pyran-4-one) undergo a 1:1:1 addition reaction under mild conditions to afford the title compounds in excellent yields.

Introduction. – Furo[3,2-*c*]pyrans, fused five/six-membered heterocyclic compounds with two O-atoms (in positions 1 and 5), are of interest because of the occurrence of their saturated and partially saturated derivatives in biologically active compounds and natural products. For example, patulin, 4-hydroxy-4*H*-furo[3,2-*c*]pyran-2(6*H*)-one (*Fig. 1*), is a mycotoxin produced by several species of *Penicillium*, *Aspergillus*, and *Byssochlamys* fungi, with the most commonly encountered species being *Penicillium expansum* [1]. It occurs in unfermented apple juice, grape juice, and field crops [2]. It has antibiotic properties and has been shown to be carcinogenic and mutagenic, and it causes chromosome damage in biological systems [3].

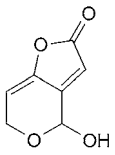
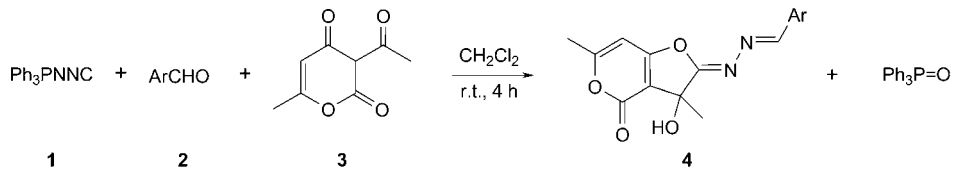


Fig. 1. *Structure of Patulin*

The most common synthetic approaches reported for the preparation of furo[3,2-*c*]pyran ring systems involve: intramolecular *Claisen* condensation of 2-ketomethylfuran-3-carboxylates [4], anhydropyranose annulation [5], CAN (ceric ammonium nitrate; $(NH_4)_2Ce(NO_3)_6$)-mediated reaction of 4-hydroxy-2*H*-pyran-2-ones with alkenes or alkynes [6], reaction between tetrahydro-2-oxofuran-3-yl propanoate and benzaldehyde in the presence of a base *via* a modified benzilic acid rearrangement [7], cyclization of 3-[3-(dimethylamino)prop-2-enoyl]-4-hydroxy-2*H*-pyran-2-ones in the presence of $SOCl_2$ [8], and reaction of 3,4-dihydro-2*H*-pyran-4-ol with 1,2-dibromoethyl ether, followed by radical cyclization of the intermediate [9].

There are several reports on the use of (isocyanoimino)(triphenyl)phosphorane (Ph_3PNNC; **1**; *Scheme 1*) in syntheses of metal complexes [10][11]. Recently, syntheses of 1,3,4-oxadiazepines [12a], 2-aryl-1,3,4-oxadiazoles [12b], α-keto-1,3,4-oxadiazoles [12c], 3-(5-aryl-1,3,4-oxadiazol-2-yl)-3-hydroxybutan-2-ones [12d], N^2,N^2-dicyclohexyl-5-aryl-1,3,4-oxadiazole-2-carboximidamides [12e], 1-chloro-2-(5-aryl-1,3,4-oxadiazol-2-yl)propan-2-amines [12f], 2-(arylamino)-2-(5-aryl-1,3,4-oxadiazol-2-yl)propyl benzoates (and acetates) [12g], and *N*-benzyl-*N*-[1-(5-aryl-1,3,4-oxadiazol-2-yl)cyclobutyl]amines [12h] by using **1** in multicomponent reactions (MCRs) were reported.

Scheme 1. *One-Pot Three-Component Synthesis of 2-[(Arylmethylidene)hydrazinylidene]-3-hydroxy-4*H*-furo[3,2-*c*]pyran-4(3*H*)-ones* **4**



As part of our current studies on new routes for the preparation of biologically active heterocyclic compounds from readily available building blocks [13], we have described the syntheses of 2-aryl-5-(hydroxyalkyl)-1,3,4-oxadiazoles [14a], 3-(1-hydroxyalkyl)[1,2,4]triazolo[4,3-*c*]quinazolines [14b], 3-(5-aryl/alkyl-1,3,4-oxadiazol-2-yl)-3-hydroxy-1,3-dihydro-2*H*-indol-2-ones [14c], 3-aryl-1-(arylmethylideneamino)-pyrrolidine-2,5-diones [14d], and 3,4-disubstituted *N*-aminopyrrolidine-2,5-diones [14e] by using **1** in MCRs.

Results and Discussion. – We report herein an efficient synthesis of functionalized 4*H*-furo[3,2-*c*]pyranes. Thus, a mixture of **1**, an aldehyde **2**, and 3-acetyl-6-methyl-2*H*-pyran-2,4(3*H*)-dione (dehydroacetic acid, **3**) underwent a 1:1:1 addition reaction in CH_2Cl_2 at room temperature to afford the corresponding 2-(arylmethylidenehydrazinylidene)-3-hydroxy-4*H*-furo[3,2-*c*]pyran-4(3*H*)-ones **4a**–**4l** in 85–94% yields (*Scheme 1* and *Table*). All the reactions went to completion within 4 h. ^{1}H-NMR Analysis of the reaction mixtures clearly indicated formation of the corresponding 4*H*-furo[3,2-*c*]pyran-4-ones **4** in excellent yields.

Table. *Synthesis of 4*H*-Furo[3,2-*c*]pyran-4-ones* **4a**–**4l**

Product	Ar	Yield [%][a])	Product	Ar	Yield [%][a])
4a	4-O_2N–C_6H_4	94	**4g**	Pyridin-4-yl	89
4b	4-F–C_6H_4	91	**4h**	4-Cl–C_6H_4	95
4c	3-Cl–C_6H_4	93	**4i**	4-Br–C_6H_4	92
4d	3-MeO–C_6H_4	90	**4j**	Thiophen-2-yl	85
4e	Furan-2-yl	88	**4k**	Ph	89
4f	3,4-$(MeO)_2C_6H_3$	86	**4l**	4-Me–C_6H_4	90

[a]) Yields of the isolated products.

The structures of the isolated products were deduced on the basis of their IR, ^{1}H- and ^{13}C-NMR, and mass spectra, and elemental analysis. The mass spectrum of **4i** displayed the molecular ion (M^+) peaks at m/z 378 and 376, consistent with a 1:1:1 product of **1**, **3**, and 4-bromobenzaldehyde after losing Ph_3P=O. The IR spectrum of **4i** showed absorptions at 3293, 1729, 1712, and 1636 cm^{-1} indicating the presence of OH, C=O, and C=N functionalities. The ^{1}H-NMR spectrum of **4i** exhibited four sharp *singlet*s at 1.82 and 2.33 ppm due to the Me groups, 6.43 ppm arising from OC=CH moiety, and 8.35 ppm for the aldimine H-atom. A fairly sharp signal appeared at 5.25 ppm (exchangeable by D_2O addition) for the OH group along with the characteristic signals with appropriate chemical shifts and coupling constants for the four aromatic H-atoms of the 4-bromophenyl substituent. The ^{1}H-decoupled ^{13}C-NMR spectrum of **4i** showed 14 distinct resonances in agreement with the proposed structure (see *Exper. Part*).

Single-crystal X-ray analysis of **4i** conclusively confirmed its structure and, by analogy, those of other isolated products. An ORTEP diagram of **4i** is shown in *Fig. 2*[1]).

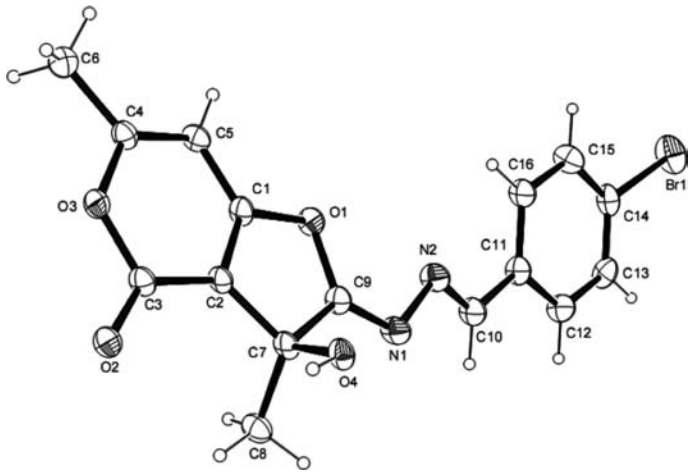


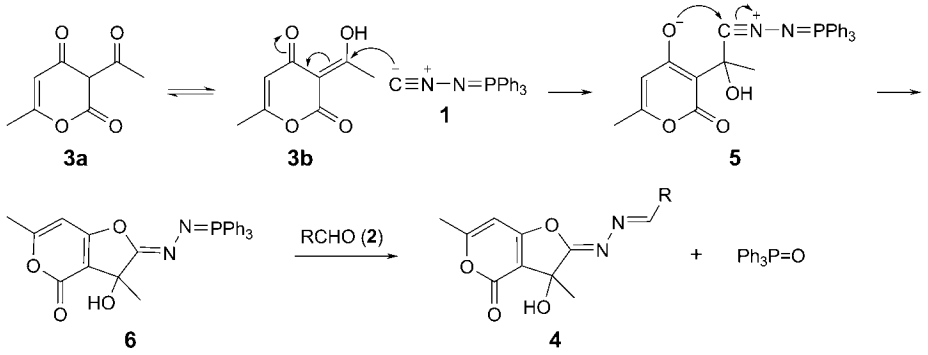
Fig. 2. *ORTEP Diagram of the molecular structure of* **4i**

A plausible mechanism for the reaction is provided in *Scheme 2*. On the basis of the well-established chemistry of isocyanides [15–19], it is reasonable to assume that the first step may involve conjugate addition of the isocyanide **1** on the enol form of dehydroacetic acid **3b** and formation of the enolate intermediate **5**, followed by intramolecular nucleophilic addition of the enolate to the nitrilium moiety and cyclization to give the iminolactone intermediate **6**. Aza-*Wittig* reaction of this

---

[1]) Selected X-ray crystallographic data for compound **4i**: $C_{16}H_{13}O_4N_2Br$, monoclinic, space group $P2_1/c$, $a = 11.319(3)$ Å, $b = 7.9512(19)$ Å, $c = 17.502(4)$ Å, $\beta = 92.264(4)^\circ$, $V = 1573.9(7)$ Å^3, $T = 295(2)$ K, $Z = 4$, $D_{calc.} = 1.583$ g cm^{-3}, $\mu = 2.629$ mm^{-1}, 1368 observed reflections, final $R_1 = 0.055$, $wR_2 = 0.139$, and for all data $R_1 = 0.143$, $wR_2 = 0.200$. CCDC-755586 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data request/cif.

Scheme 2. *Proposed Mechanism*



intermediate with the aldehyde **2** would afford the 4*H*-furo[3,2-*c*]pyran-4(3*H*)-ones **4** by removal of $Ph_3P{=}O$.

In conclusion, we have developed a simple reaction between (isocyanoimino)-(triphenyl)phosphorane, aromatic aldehydes and dehydracetic acid for the efficient synthesis of 4*H*-furo[3,2-*c*]pyran-4-ones, which are of potential synthetic and pharmacological interest. The reactions have been performed under neutral conditions, and the substances have been mixed without any activation or modification.

This work was supported by the *Research Council of the University of Tehran* as research project (6102036/1/03).

Experimental Part

General. All the chemicals were obtained from *Merck* (Germany), and were used without further purification. *(Isocyanoimino)(triphenyl)phosphorane* (**1**) was prepared according to [10]. Column chromatography (CC): silica gel *60* (*Merck*). M.p.: *Electrothermal 9100* apparatus; uncorrected. IR Spectra: *Shimadzu IR-460* spectrometer; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker DRX-500 Avance* (at 500.1 and 125.8 MHz, resp.) and *Bruker DPX-250* (at 250.1 and 62.9 MHz, resp.) instruments; in (D_6)DMSO or (D_6)acetone soln. ; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI-MS (20 eV): *Agilent Technologies* (*HP*) *5973* mass spectrometer; in *m*/*z* (rel. %). Elemental analyses: *Heraeus CHN-O-Rapid* analyzer. X-Ray crystallography: *Bruker SMART* diffractometer; CCD area detector; graphite monochromatized MoK_α radiation.

General Procedure for the Preparation of Compounds **4**. A soln. of the appropriate aldehyde **2** (1 mmol), **1** (0.302 g, 1 mmol), and *3-acetyl-6-methyl-2*H*-pyran-2,4(3*H*)-dione* (=*dehydroacetic acid,* **3**; 0.168 g, 1 mmol) in CH_2Cl_2 (4 ml) was stirred at 25° for 4 h. After complete conversion to the corresponding 4*H*-furo[3,2-*c*]pyran-4-one (TLC monitoring), the precipitated product (in the case of compounds **4a**–**4h**) was filtered and washed with CH_2Cl_2 (2 × 2 ml). For the other compounds, **4i**–**4l**, the solvent was removed, and the residue was purified by CC (SiO_2; hexane/AcOEt 4:1). The solvent was removed to afford the product.

*(2*Z*)-2,3-Dihydro-3-hydroxy-3,6-dimethyl-2-[(2*E*)-(4-nitrobenzylidene)hydrazinylidene]-4*H*-furo[3,2-*c*]pyran-4-one* (**4a**). Pale-yellow powder. Yield: 0.32 g (94%). M.p. 179–180°. IR (KBr): 3529 (OH), 1732 (C=O), 1682, 1639, 1587, 1512, 1447, 1404, 1337, 1248, 1221, 1144, 1123, 1010, 1057, 982, 922, 856, 821, 779, 752. ^1H-NMR (500.1 MHz, (D_6)DMSO): 1.68, 2.30 (2*s*, 6 H); 6.34 (*s*, 1 H); 6.66 (*s*, 1 H); 8.07 (*d*, *J* = 7.2, 2 H); 8.32 (*d*, *J* = 7.2, 2 H); 8.57 (*s*, 1 H). ^{13}C-NMR (125.8 MHz, (D_6)DMSO): 20.2; 23.5; 72.8; 94.9; 105.4; 124.0; 129.2; 139.4; 148.8; 157.8; 158.1; 162.4; 166.0; 168.4. EI-MS: 343 (6, M^+), 328

(83), 277 (6), 194 (17), 180 (34), 168 (27), 153 (96), 149 (24), 125 (13), 103 (17), 85 (30), 76 (13), 69 (23), 43 (100). Anal. calc. for $C_{16}H_{13}N_3O_6$ (343.30): C 55.98, H 3.82, N 12.24; found: C 55.82, H 3.98, N 12.11.

*(2*Z*)-2-[(2*E*)-(4-Fluorobenzylidene)hydrazinylidene]-2,3-dihydro-3-hydroxy-3,6-dimethyl-4*H*-furo[3,2-*c*]pyran-4-one* (**4b**). Cream powder. Yield: 0.28 g (91%). M.p. 166°. IR (KBr): 3402 (OH), 1744 (C=O), 1715, 1693, 1641, 1603, 1578, 1512, 1447, 1425, 1400, 1229, 1198, 1144, 1069, 1040, 978, 926, 839. ^{1}H-NMR (250.1 MHz, (D$_6$)DMSO): 1.67, 2.31 (2*s*, 6 H); 6.30 (*s*, 1 H); 6.67 (*s*, 1 H); 7.35 (*dd*, ^3J(H,H) = 8.6, ^3J(F,H) = 8.9, 2 H); 7.91 (*dd*, ^3J(H,H) = 8.6, ^4J(F,H) = 5.8, 2 H); 8.47 (*s*, 1 H). ^{13}C-NMR (62.9 MHz, (D$_6$)DMSO): 20.2; 23.5; 72.5; 94.8; 105.3; 116.0 (*d*, ^2J(C,F) = 22.0); 130.1 (*d*, ^4J(C,F) = 3.0); 130.5 (*d*, ^3J(C,F) = 8.9); 158.7; 160.0 (*d*, ^1J(C,F) = 240.0); 161.8; 165.8; 166.1; 168.2. EI-MS: 316 (9, M^+), 301 (78), 194 (30), 180 (41), 168 (17), 153 (76), 122 (74), 108 (19), 95 (48), 85 (28), 69 (27), 55 (13), 43 (100). Anal. calc. for $C_{16}H_{13}FN_2O_4$ (316.29): C 60.76, H 4.14, N 8.86; found: C 60.73, H 4.24, N 8.66.

*(2*Z*)-2-[(2*E*)-(3-Chlorobenzylidene)hydrazinylidene]-2,3-dihydro-3-hydroxy-3,6-dimethyl-4*H*-furo[3,2-*c*]pyran-4-one* (**4c**). Cream powder. Yield: 0.31 g (93%). M.p. 173°. IR (KBr): 3310 (OH), 1742 (C=O), 1693, 1643, 1580, 1441, 1402, 1225, 1140, 1061, 980, 910, 883, 795, 682. ^{1}H-NMR (500.1 MHz, (D$_6$)DMSO): 1.67, 2.30 (2*s*, 6 H); 6.30 (*s*, 1 H); 6.66 (*s*, 1 H); 7.50 – 7.58 (*m*, 2 H); 7.79 (*d*, *J* = 6.8, 1 H); 7.86 (*s*, 1 H); 8.44 (*s*, 1 H). ^{13}C-NMR (125.8 MHz, (D$_6$)DMSO): 20.2; 23.6; 72.7; 94.9; 105.4; 126.7; 127.5; 130.8; 131.0; 133.7; 135.7; 158.1; 158.3; 162.1; 166.1; 168.3. EI-MS: 334 (2, M^+(^{37}Cl)), 332 (5, M^+(^{35}Cl)), 319 (21), 317 (57), 194 (24), 180 (37), 168 (24), 153 (71), 138 (37), 125 (13), 111 (31), 85 (25), 75 (24), 69 (23), 43 (100). Anal. calc. for $C_{16}H_{13}ClN_2O_4$ (332.74): C 57.76, H 3.94, N 8.42; found: C 57.80, H 4.07, N 8.15.

*(2*Z*)-2,3-Dihydro-3-hydroxy-2-[(2*E*)-(3-methoxybenzylidene)hydrazinylidene]-3,6-dimethyl-4*H*-furo[3,2-*c*]pyran-4-one* (**4d**). Pale-yellow powder. Yield: 0.29 g (90%). M.p. 172°. IR (KBr): 3356 (OH), 1722 (C=O), 1681, 1604, 1479, 1454, 1353, 1269, 1213, 1161, 1083, 1045, 969, 928, 875, 812, 783, 690. ^{1}H-NMR (250.1 MHz, (D$_6$)DMSO): 1.67, 2.31 (2*s*, 6 H); 3.82 (*s*, 3 H); 6.30 (*s*, 1 H); 6.66 (*d*, *J* = 7.5, 1 H); 7.11 (*s*, 1 H); 7.41 – 7.45 (*m*, 3 H); 8.41 (*s*, 1 H). ^{13}C-NMR (62.9 MHz, (D$_6$)DMSO): 20.7; 24.1; 55.7; 73.1; 95.4; 105.8; 113.3; 117.6; 121.3; 130.5; 135.4; 158.7; 160.1; 161.0; 162.2; 166.7; 168.8. EI-MS: 328 (34, M^+), 313 (100), 268 (12), 253 (9), 194 (17), 180 (33), 153 (60), 134 (73), 120 (16), 107 (36), 92 (24), 77 (32), 43 (35). Anal. calc. for $C_{17}H_{16}N_2O_5$ (328.32): C 62.19, H 4.91, N 8.53; found: C 62.11, H 5.13, N 8.40.

*(2*Z*)-2-{[(2*E*)-(Furan-2-yl)methylidene]hydrazinylidene}-2,3-dihydro-3-hydroxy-3,6-dimethyl-4*H*-furo[3,2-*c*]pyran-4-one* (**4e**). Cream powder. Yield: 0.25 g (88%). M.p. 218°. IR (KBr): 3296 (OH), 1740 (C=O), 1682, 1601, 1585, 1475, 1408, 1384, 1235, 1148, 1126, 1065, 1042, 1018, 980, 935, 908, 823, 768. ^{1}H-NMR (500.1 MHz, (D$_6$)DMSO): 1.64, 2.30 (2*s*, 6 H); 6.26 (*s*, 1 H); 6.67 (*s*, 1 H); 6.69 (*dd*, *J* = 3.3, 1.7, 1 H); 7.10 (*d*, *J* = 3.3, 1 H); 7.93 (*d*, *J* = 1.7, 1 H); 8.29 (*s*, 1 H). ^{13}C-NMR (125.8 MHz, (D$_6$)DMSO): 20.2; 23.6; 72.6; 94.9; 105.3; 112.5; 117.6; 146.7; 148.8; 149.2; 158.1; 162.5; 166.1; 168.3. EI-MS: 288 (29, M^+), 273 (100), 194 (20), 180 (69), 168 (15), 153 (70), 121 (39), 108 (31), 94 (94), 80 (29), 69 (17), 55 (18), 43 (73). Anal. calc. for $C_{14}H_{12}N_2O_5$ (288.26): C 58.33, H 4.20, N 9.72; found: C 58.33, H 4.16, N 9.68.

*(2*Z*)-2-[(2*E*)-(3,4-Dimethoxybenzylidene)hydrazinylidene]-2,3-dihydro-3-hydroxy-3,6-dimethyl-4*H*-furo[3,2-*c*]pyran-4-one* (**4f**). Cream powder. Yield: 0.30 g (86%). M.p. 163°. IR (KBr): 3202 (OH), 1755 (C=O), 1697, 1649, 1599, 1576, 1512, 1461, 1463, 1425, 1381, 1273, 1236, 1213, 1150, 1167, 1065, 1034, 969, 916, 862, 808, 748. ^{1}H-NMR (250.1 MHz, (D$_6$)DMSO): 1.66, 2.31 (2*s*, 6 H); 3.82, 3.83 (2*s*, 6 H); 6.25 (*s*, 1 H); 6.67 (*s*, 1 H); 7.07 (*d*, *J* = 8.5, 1 H); 7.38 (*d*, *J* = 8.5, 1 H); 7.42 (*s*, 1 H); 8.36 (*s*, 1 H). ^{13}C-NMR (62.9 MHz, (D$_6$)DMSO): 20.7; 24.2; 56.0; 56.1; 73.0; 95.5; 105.8; 110.0; 112.0; 123.8; 126.7; 149.4; 152.2; 158.7; 160.4; 161.9; 166.7; 168.7. EI-MS: 358 (100, M^+), 343 (49), 328 (61), 301 (10), 206 (13), 191 (27), 179 (20), 163 (73), 150 (55), 137 (23), 120 (32), 107 (20), 92 (40), 77 (51), 65 (31), 43 (66). Anal. calc. for $C_{18}H_{18}N_2O_6$ (358.35): C 60.33, H 5.06, N 7.82; found: C 60.38, H 5.21, N 7.57.

*(2*Z*)-2,3-Dihydro-3-hydroxy-3,6-dimethyl-2-{[(2*E*)-(pyridin-4-yl)methylidene]hydrazinylidene}-4*H*-furo[3,2-*c*]pyran-4-one* (**4g**). Pale-brown powder. Yield: 0.26 g (89%). M.p. 185°. IR (KBr): 3297 (OH), 1735 (C=O), 1680, 1641, 1605, 1584, 1452, 1406, 1249, 1142, 1130, 1067, 1042, 976, 914. ^{1}H-NMR (250.1 MHz, (D$_6$)DMSO): 1.69, 2.31 (2 *s*, 6 H); 6.36 (*s*, 1 H); 6.68 (*s*, 1 H); 7.76 (*d*, *J* = 5.6, 2 H); 8.46 (*s*, 1 H); 8.73 (*d*, *J* = 5.6, 2 H). ^{13}C-NMR (62.9 MHz, (D$_6$)DMSO): 20.2; 23.4; 72.7; 94.8; 105.3; 121.7; 140.3; 150.4; 157.6; 158.0; 162.0; 166.0; 168.4. EI-MS: 299 (3, M^+), 284 (51), 256 (7), 194 (7), 180 (17), 168 (15), 153 (74), 132 (20), 105 (25), 85 (24), 78 (29), 69 (24), 43 (100). Anal. calc. for $C_{15}H_{13}N_3O_4$ (299.29): C 60.20, H 4.38, N 14.04; found: C 60.14, H 4.42, N 13.88.

*(2Z)-2-[(2E)-(4-Chlorobenzylidene)hydrazinylidene]-2,3-dihydro-3-hydroxy-3,6-dimethyl-4*H-*furo[3,2-c]pyran-4-one* (**4h**). Cream powder. Yield: 0.31 g (95%). M.p. 183–184°. IR (KBr): 3299 (OH), 1739 (C=O), 1687, 1605, 1582, 1438, 1400, 1230, 1144, 1040, 980, 928, 880, 810, 780, 691. ^{1}H-NMR (500.1 MHz, (D_6)acetone): 1.90, 2.32 (2*s*, 6 H); 3.82 (*s*, 1 H); 6.18 (*s*, 1 H); 7.41 (*d*, *J* = 8.5, 2 H); 7.74 (*d*, *J* = 8.5, 2 H); 8.38 (*s*, 1 H). ^{13}C-NMR (125.8 MHz, (D_6)acetone): 21.0; 24.9; 74.0; 95.1; 105.4; 129.2; 129.9; 131.9; 137.8; 159.0; 160.7; 161.9; 166.9; 168.6. EI-MS: 334 (7, M^+(^{37}Cl)), 332 (18, M^+(^{35}Cl)), 319 (30), 317 (76), 274 (10), 221 (15), 194 (33), 180 (51), 153 (100), 138 (63), 125 (20), 111 (25), 89 (19), 69 (15). Anal. calc. for $C_{16}H_{13}ClN_2O_4$ (332.74): C 57.76, H 3.94, N 8.42; found: C 57.57, H 4.10, N 8.23.

*(2Z)-2-[(2E)-(3-Bromobenzylidene)hydrazinylidene]-2,3-dihydro-3-hydroxy-3,6-dimethyl-4*H-*furo[3,2-c]pyran-4-one* (**4i**). Pale-pink crystals. Yield: 0.34 g (92%). M.p. 165°. IR (KBr): 3293 (OH), 1729 (C=O), 1712, 1636, 1580, 1485, 1454, 1408, 1344, 1246, 1138, 1069, 1034, 984, 953, 922, 829, 802, 779, 678. ^{1}H-NMR (500.1 MHz, (D_6)acetone): 1.82, 2.33 (2*s*, 6 H); 5.25 (*s*, 1 H); 6.43 (*s*, 1 H); 7.68 (*d*, *J* = 8.5, 2 H); 7.81 (*d*, *J* = 8.5, 2 H); 8.35 (*s*, 1 H). ^{13}C-NMR (125.8 MHz, (D_6)acetone): 20.7; 24.2; 74.3; 95.3; 106.3; 125.9; 130.8; 132.9; 134.2; 158.8; 159.2; 162.7; 167.4; 169.5. EI-MS: 378 (10, M^+(^{81}Br)), 376 (10, M^+(^{79}Br)), 363 (92), 361 (87), 209 (12), 194 (55), 180 (77), 168 (46), 157 (25), 153 (100), 140 (8), 125 (15), 109 (11), 89 (22), 85 (26), 76 (14), 43 (33). Anal. calc. for $C_{16}H_{13}BrN_2O_4$ (377.19): C 50.95, H 3.47, N 7.43; found: C 50.89, H 3.51, N 7.38.

*(2Z)-2,3-Dihydro-3-hydroxy-3,6-dimethyl-2-{[(2E)-(thiophen-2-yl)methylidene]hydrazinylidene}-4*H-*furo[3,2-c]pyran-4-one* (**4j**). Pale-yellow powder. Yield: 0.25 g (85%). M.p. 157°. IR (KBr): 3395 (OH), 1738 (C=O), 1709, 1686, 1641, 1589, 1443, 1420, 1407, 1381, 1248, 1223, 1144, 1063, 1038, 982, 935, 910, 746. ^{1}H-NMR (250.1 MHz, (D_6)DMSO): 1.66, 2.31 (2 *s*, 6 H); 6.27 (*s*, 1 H); 6.71 (*s*, 1 H); 7.21 (*dd*, *J* = 4.7, 3.5, 1 H); 7.64 (*d*, *J* = 3.5, 1 H); 7.80 (*d*, *J* = 4.7, 1 H); 8.67 (*s*, 1 H). ^{13}C-NMR (62.9 MHz, (D_6)DMSO): 20.8; 24.1; 73.1; 95.5; 105.8; 128.7; 131.7; 134.6; 138.5; 155.7; 158.7; 162.9; 166.7; 168.8. EI-MS: 304 (22, M^+), 289 (86), 253 (24), 225 (13), 194 (20), 180 (60), 168 (16), 153 (72), 137 (36), 125 (24), 110 (100), 96 (39), 85 (28), 69 (24). Anal. calc. for $C_{14}H_{12}N_2O_4S$ (304.33): C 55.25, H 3.97, N 9.21; found: C 55.19, H 4.14, N 9.07.

*(2Z)-2-[(2E)-Benzylidenehydrazinylidene]-2,3-dihydro-3-hydroxy-3,6-dimethyl-4*H-*furo[3,2-c]pyran-4-one* (**4k**). Pale yellow crystals. Yield: 0.26 g (89%). M.p. 149°. IR (KBr): 3269 (OH), 1742 (C=O), 1693, 1639, 1603, 1580, 1450, 1412, 1402, 1317, 1248, 1227, 1144, 1069, 1036, 978, 912, 818, 734, 692. ^{1}H-NMR (250.1 MHz, (D_6)DMSO): 1.70, 2.32 (2*s*, 6 H); 6.32 (*s*, 1 H); 6.67 (*s*, 1 H); 7.50–7.54 (*m*, 3 H); 7.83–7.91 (*m*, 2 H); 8.46 (*s*, 1 H). ^{13}C-NMR (62.9 MHz, (D_6)DMSO): 20.2; 23.5; 72.5; 94.8; 105.3; 128.2; 128.8; 131.3; 133.4; 158.1; 159.8; 161.8; 166.1; 168.2. EI-MS: 298 (9, M^+), 283 (82), 194 (44), 180 (32), 168 (22), 153 (69), 131 (12), 104 (83), 90 (20), 77 (70), 51 (31), 43 (100). Anal. calc. for $C_{16}H_{14}N_2O_4$ (298.30): C 64.42, H 4.73, N 9.39; found: C 64.42, H 4.79, N 9.40.

*(2Z)-2,3-Dihydro-3-hydroxy-3,6-dimethyl-2-[(2E)-(4-methylbenzylidene)hydrazinylidene]-4*H-*furo[3,2-c]pyran-4-one* (**4l**). Cream powder. Yield: 0.28 g (90%). M.p. 159°. IR (KBr): 3307 (OH), 1728 (C=O), 1690, 1634, 1574, 1445, 1412, 1381, 1240, 1177, 1138, 1109, 1026, 978, 951, 924, 833, 783, 760. ^{1}H-NMR (250.1 MHz, (D_6)DMSO): 1.67, 2.31, 2.37 (3*s*, 9 H); 6.27 (*s*, 1 H); 6.68 (*s*, 1 H); 7.32 (*d*, *J* = 8.0, 2 H); 7.74 (*d*, *J* = 8.0, 2 H); 8.42 (*s*, 1 H). ^{13}C-NMR (62.9 MHz, (D_6)DMSO): 20.2; 21.1; 23.5; 72.5; 94.9; 105.2; 128.2; 129.4; 130.8; 141.4; 156.5; 160.0; 161.7; 166.1; 168.2. EI-MS: 312 (11, M^+), 297 (72), 274 (4), 237 (4), 194 (34), 180 (20), 168 (15), 153 (51), 118 (100), 104 (32), 91 (65), 65 (33). Anal. calc. for $C_{17}H_{16}N_2O_4$ (312.33): C 65.38, H 5.16, N 8.97; found: C 65.43, H 5.22, N 8.94.

REFERENCES

[1] G. Engel, M. Teuber, in 'Mycotoxins - Production, Isolation, Separation and Purification', Ed. V. Betina, Elsevier, Amsterdam, 1984, pp. 291–314.
[2] L. Chen, B. H. Ingham, S. C. Ingham, *J. Food Sci. C: Food Chem. Toxicol.* **2004**, *69*, C669.
[3] E. Pfeiffer, K. Gross, M. Metzler, *Carcinogenesis* **1998**, *19*, 1313; F. Dickens, H. E. H. Jones, *Br. J. Cancer* **1961**, *15*, 85; I. Alves, N. G. Oliveira, A. Laires, A. S. Rodrigues, J. Rueff, *Mutagenesis* **2000**, *15*, 229.
[4] L. Mavoungou-Gomès, J. Bruneton, M. Aicart, *J. Heterocycl. Chem.* **1985**, *22*, 1233.

[5] T. H. Al-Tel, Y. Al-Abed, M. S. Shekhani, W. Voelter, *Tetrahedron Lett.* **1993**, *34*, 7717.
[6] K. Kobayashi, K. Sakashita, H. Akamatsu, K. Tanaka, M. Uchida, T. Uneda, T. Kitamura, O. Morikawa, H. Konishi, *Heterocycles* **1999**, *51*, 2881.
[7] S. E. Drewes, N. D. Emslie, J. S. Field, A. A. Khan, N. S. Ramesar, *Tetrahedron Lett.* **1993**, *34*, 1205.
[8] W. Löwe, G. Eggersmann, *Arch. Pharm.* **1984**, *317*, 685.
[9] A. M. Gómez, M. Casillas, S. Valverde, J. C. López, *Tetrahedron: Asymmetry* **2001**, *12*, 2175.
[10] H. Stolzenberg, B. Weinberger, W. P. Fehlhammer, F. G. Pühlhofer, R. Weiss, *Eur. J. Inorg. Chem.* **2005**, *21*, 4263.
[11] T.-W. Chiu, Y.-H. Liu, K.-M. Chi, Y.-S. Wen, K.-L. Lu, *Inorg. Chem.* **2005**, *44*, 6425.
[12] a) A. Souldozi, A. Ramazani, N. Bouslimani, R. Welter, *Tetrahedron Lett.* **2007**, *48*, 2617; b) A. Souldozi, A. Ramazani, *Tetrahedron Lett.* **2007**, *48*, 1549; c) L. Cui, Q. Liu, J. Yu, C. Ni, H. Yu, *Tetrahedron Lett.* **2011**, *52*, 5530; d) A. Ramazani, M. Rouhani, A. Rezaei, N. Shajari, A. Souldozi, *Helv. Chim. Acta* **2011**, *94*, 282; e) F. Zeinali Nasrabadi, A. Ramazani, Y. Ahmadi, *Mol. Diversity* **2011**, *15*, 791; f) A. Ramazani, F. Zeinali Nasrabadi, Y. Ahmadi, *Helv. Chim. Acta* **2011**, *94*, 1024; g) A. Ramazani, Y. Ahmadi, A. Mashhadi Malekzadeh, A. Rezaei, *Heteroat. Chem.* **2011**, *22*, 692; h) A. Ramazani, N. Shajari, A. Mahyari, Y. Ahmadi, *Mol. Diversity* **2011**, *15*, 521.
[13] M. Adib, E. Sheikhi, N. Rezaei, *Tetrahedron Lett.* **2011**, *52*, 3191, and refs. cit. therein.
[14] a) M. Adib, M. Riazati Kesheh, S. Ansari, H. R. Bijanzadeh, *Synlett* **2009**, 1575; b) M. Adib, S. Ansari, S. Feizi, H. R. Bijanzadeh, *Synlett* **2010**, 921; c) M. Adib, E. Sheikhi, A. Kavoosi, H. R. Bijanzadeh, *Synthesis* **2010**, 4082; d) M. Adib, S. Ansari, S. Fatemi, H. R. Bijanzadeh, L.-G. Zhu, *Tetrahedron* **2010**, *66*, 2723; e) M. Adib, S. Ansari, H. R. Bijanzadeh, *Synlett* **2011**, 619.
[15] A. Dömling, *Chem. Rev.* **2006**, *106*, 17.
[16] A. Dömling, I. Ugi, *Angew. Chem., Int. Ed.* **2000**, *39*, 3168.
[17] I. Ugi, 'Isonitrile Chemistry', Academic Press, London, 1971.
[18] I. Ugi, *Angew. Chem., Int. Ed.* **1982**, *21*, 810.
[19] H. M. Walborsky, M. P. Periasamy, in 'The Chemistry of Functional Groups, Supplement C', Eds. S. Patai, Z. Rappaport, Wiley, New York, 1983, Chapt. 20, 835 – 837.

Received August 6, 2012