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SHORT COMMUNICATIONS

Synthesis of Functionally Substituted 2-Imino-3-aryl-2,5-dihydrofurans and Their Chemical Reactions

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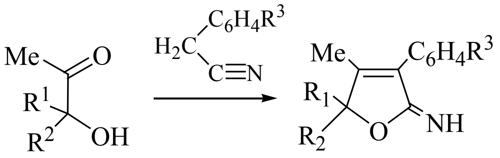
3-Functionalized 2(5*H*)-furanones are known to be contained in the composition of many biologically active compounds and are widely applied in the medicine, agriculture, perfumery, etc. [1]. Depending on the character of substituents the derivatives of 2(5*H*)-furanones exhibit various pharmacological actions [2–4].

In our previous publications we reported on the structure and the process of the formation of the corresponding substituted 2,5-dihydrofurans by condensation of α-ketols with the amides of cyanoacetic acid [5] and with malononitrile [6]. Unlike the reaction with the amides of cyanoacetic acid the reaction of α-ketols with the malonodinitrile led to the simultaneous formation in good yields of two types of compounds, 2-imino derivatives of the corresponding dihydrofurans, and the products of their further reaction with the malonodinitrile, 2-dicyanomethylenedihydrofurans [6].

In extension of the research on the synthesis of new functionally substituted derivatives of 2,5-dihydrofurans and aiming at the preparation of 2-imino derivatives containing aromatic substituents in the position *3* we investigated in this study the reactions of α-ketols with aromatic nitriles. In this reaction unlike that with the malononitrile only 2-imino-3-aryl-4-methyl-5,5-substituted2,5-dihydrofurans **Ia–Id** formed in high yields (up to 90%).

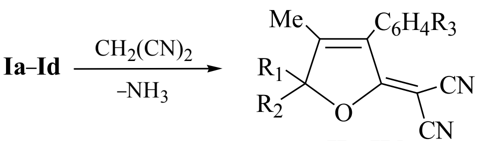
Various factors were studied affecting the course of the reaction, optimum conditions were developed, and it was established that the process easily occurred at room temperature and equimolar amounts of the reagents in the presence of a catalytic quantity of sodium ethylate (1 : 1 : 0.1) in contrast to data of [7] where the sodium ethylate was used in an equimolar amount as a reagent, and the reaction was carried out under the microwave activation (250 MHz, 100 W).

The reaction of 2-imino derivatives **Ia–Id** with malononitrile in the ratio 1 : 1 at room temperature in benzene or ethanol within ~20 h furnished in nearly quantitative yield the corresponding 2-dicyanomethylene derivatives **IIa–IId**.



Ia–Id

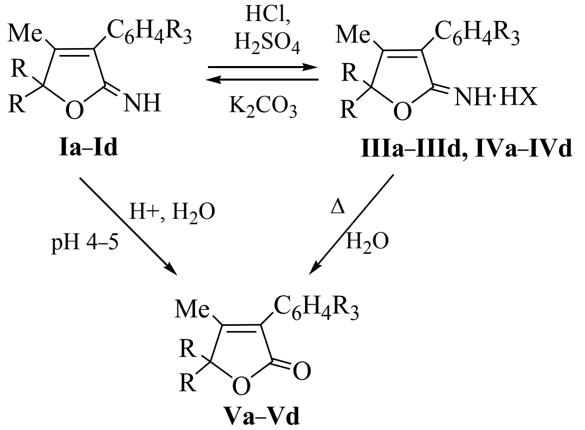
$R^1 = R^2 = Me$, R^3 = H (**a**), Cl (**b**), OMe (**c**); R^1, $R^2 = C_5H_{10}$, R^3 = H (**d**).



IIa–IId

$R^1 = R^2 = Me$, R^3 =H (**a**), Cl (**b**), OMe (**c**); R^1,$R^2 = C_5H_{10}$, R^3 = H (**d**).

At treating with hydrochloric and sulfuric acids at pH 1–2 compounds **Ia–Id** readily and in the quantitative yield formed salts **IIIa–IIId**, **IVa–IVd**. Hydrochlorides **IIIa–IIId** were also obtained at passing gaseous hydrogen chloride through the benzene solutions of compounds **Ia–Id**. The salts obtained are easily titrated with 0.1 N NaOH solution, and at the treatment with the solution of potassium carbonate they are readily converted into the initial imino derivatives **Ia–Id**.



$R^1 = R^2 = Me$, $R^3 = H$ (**a**), Cl (**b**), OMe (**c**); $R^1,R^2 = C_5H_{10}$, $R^3 = H$ (**d**); X = Cl (**III**), HSO_4 (**IV**).

In the presence of acids (pH 4–5) at heating (70–80°C) compounds **Ia–Id** within 3 h are hydrolyzed into the corresponding 3-aryl-4-methyl-5,5-substituted 2(5*H*)-furanones **Va–Vd**. Under similar conditions salts **IIIa–IIId**, **IVa–IVd** in water or ethanol hydrolyze with the formation of the corresponding furanones **Va–Vd**.

2-Imino-3-aryl-4-methyl-5,5-substituted 2,5-dihydrofurans Ia-Id. To a solution of 0.115 g (0.005 mol) of sodium in 10 ml of anhydrous ethanol was added 0.05 mol of tertiary α-ketoalcohol and 0.05 mol of substituted benzonitrile. The reaction mixture was maintained at room temperature for ~20 h (TLC monitoring). The separated precipitate was filteref off, dried, and recrystallized from heptane (or from a mixture benzene–hexane,1:2).

2-Imino-4,5,5-trimethyl-3-phenyl-2,5-dihydrofuran (Ia). Yield 8.6 g (86%), mp 81–82°C (49–50°C [7]). IR spectrum, ν, cm^{-1}: 3283 (NH), 1648 (C=N), 1602 (C=C), 1580 (arom), 1440 (CH_3), 1390 (CH_3), 1140 (C–O–C). ^1H NMR spectrum, δ.ppm: 1.47 s (6H, $2CH_3$), 1.95 and 2.00 s (3H, CH_3), 6.52 s (0.3H, NH), 6.84 s (0.7H, NH), 7.18–7.52 m ($5H_{arom}$). Found, %: C 77.97; H 7.57; N 6.88. $C_{13}H_{15}NO$. Calculated, %: C 77.58; H 7.51; N 6.96.

2-Imino-4,5,5-trimethyl-3-(4-chlorophenyl)-2,5-dihydrofuran (Ib). Yield 10.1g (86%) mp 91–92°C [7]. ^1H NMR spectrum, δ, ppm: 1.45 s (6H, $2CH_3$), 1.85 and 1.90 s (3H, CH_3), 6.50 s (0.3H, NH), 6.80 s (0.7H, NH), 7.20–7.55 m ($4H_{arom}$). Found, %: C 66.01; H 5.73; Cl 15.28; N 5.67. $C_{13}H_{14}ClNO$. Calculated, %: C 66.24; H 5.99; Cl 15.04; N 5.94.

2-Imino-4,5,5-trimethyl-3-(4-methoxyphenyl)-2,5-dihydrofuran (Ic). Yield 8.37 г (72%) oily substance [7]. ^1H NMR spectrum, δ, ppm: 1.40 s (6H, $2CH_3$), 1.90 s (3H, CH_3), 2.76 s (3H, OCH_3), 6.55 s (0.3H, NH), 6.80 s (0.7H, NH), 7.18–7.50 m ($4H_{arom}$). Found, %: C 72.57; H 7.20; N 6.32. $C_{14}H_{17}NO_2$. Calculated, %: C 72.70; H 7.41; N 6.06.

2-Imino-4-methyl-5,5-pentamethylene-3-phenyl-2,5-dihydrofuran (Id). Yield 10.88 g (90%), mp 126–127°C (125–126°C [7]). ^1H NMR spectrum, δ, ppm: 1.25–1.80 m [10H, $(CH_2)_5$], 1.95 s (3H, CH_3), 6.45 s (0.3H, NH), 6.82 s (0.7H, NH), 7.20–7.45 m ($5H_{arom}$). Found, %: C 79.18; H 7.44; N 6.12. $C_{16}H_{19}NO$. Calculated, %: C 79.63; H 7.94; N 5.80.

2-Dicyanomethylene-4-methyl-3-phenyl-5,5-substituted 2,5-dihydrofurans IIa–IId. A mixture of 0.01 mol of compound **Ia–Id** and 0.66 g (0.01 mol) of malononitrile in 10 ml of anhydrous ethanol (or benzene) was maintained at room temperature for ~20 h. The precipitate formed after partial distilling off the solvent in a vacuum was filtered off and recrystallized from a mixture ethanol–water, 2:1.

2-Dicyanomethylene-4,5,5-trimethyl-3-phenyl-2,5-dihydrofuran (IIa). Yield 2.34 g (93%), mp 207–208°C. IR spectrum, ν, cm^{-1}: 2228, 1620, 1588, 1560, 1435, 1390. ^1H NMR spectrum, δ, ppm: 1.55 s (6H, $2CH_3$), 2.30 s (3H, CH_3), 7.2–7.5 m ($5H_{arom}$). Found, %: C 76.57; H 5.41; N 11.61. $C_{16}H_{14}N_2O$. Calculated, %: C 76.78; H 5.60; N 11.19.

2-Dicyanomethylene-4,5,5-trimethyl-3-(4-chlorophenyl)-2,5-dihydrofuran (IIb). Yield 2.8 g (99%), mp 194–195°C. ^1H NMR spectrum, δ, ppm: 1.47 s (6H, $2CH_3$), 1.85 and 1.90 s (3H, CH_3), 7.25–7.50 m ($4H_{arom}$). Found, %: C 67.12; H 4.21; Cl 12.57; N 9.47. $C_{16}H_{13}ClN_2O$. Calculated, %: C 67.49; H 4.60; Cl 12.45; N 9.84.

2-Dicyanomethylene-4,5,5-trimethyl-3-(4-methoxyphenyl)-2,5-dihydrofuran (IIc). Yield 2.36 g (89%), mp 154–155°C. ^1H NMR spectrum, δ, ppm: 1.40 s (6H, $2CH_3$), 1.90 s (3H, CH_3), 2.75 s (3H, OCH_3), 7.20–

7.50 m ($4H_{arom}$). Found, %: C 77.01; H 6.32; N 10.74. $C_{17}H_{16}N_2O$. Calculated, %: C 77.25; H 6.10; N 10.60.

2-Dicyanomethylene-4-methyl-5,5-pentamethylene-3-phenyl-2,5-dihydrofuran (IId). Yield 2.75 g (95%), mp 188–189°C. ^1H NMR spectrum, δ, ppm: 1.25–1.75 m [10H, $(CH_2)_5$], 1.95 s (3H, $2CH_3$), 7.20–7.45 m ($5H_{arom}$). Found, %: C 78.39; H 6.38; N 9.25. $C_{19}H_{18}N_2O$. Calculated, %: C 78.59; H 6.25; N 9.65.

2-Imino-3-aryl-4-methyl-5,5-substituted 2,5-dihydrofurans hydrochlorides IIIa–IIId. *a.* To a solution of 5 mmol of compound **Ia–Id** in anhydrous ethanol was added 0.01 mol (0.5 ml) of 35% HCl till pH 1–2. The separated precipitate was filtered off and washed with anhydrous ethanol.

b. Through a benzene solution of 5 mmol of compound **Ia–Id** was parred gaseous HCl, the separated precipitate was filtered off and washed with anhydrous benzene.

2-Imino-4,5,5-trimethyl-3-phenyl-2,5-dihydrofuran hydrochloride (IIIa). Yield 1.05 g (89%) (*a*), 1.15 g (97%) (*b*), mp 220–222°C. IR spectrum, ν, cm^{-1}: 3480 ($^+NH_2$), 1609 (C=C), 1645 (C=N), 1580 (arom), 1445 (CH_3), 1390 (CH_3). Found, %: C 65.37; H 6.21; Cl 14.27; N 5.32. $C_{13}H_{15}NO\cdot HCl$. Calculated, %: C 65.68; H 6.78; N 5.89; Cl 14.91.

2-Imino-4,5,5-trimethyl-3-(4-chlorophenyl)-2,5-dihydrofuran hydrochloride (IIIb). Yield 1.15 g (84%) (*a*), 1.34 g (98%) (*b*), mp 210–213°C. Found, %: C 57.51; H 5.67; Cl 26.33; N 5.41. $C_{13}H_{14}NOCl\cdot HCl$. Calculated, %: C 57.37; H 5.55; N 5.15; Cl 26.05.

2-Imino-4,5,5-trimethyl-3-(4-methoxyphenyl)-2,5-dihydrofuran hydrochloride (IIIc). Yield 1.1 g (83%) (*a*), 1.15 g (86%) (*b*), mp 207–210°C. Found, %: C 62.61; H 6.29; Cl 13.32; N 5.47. $C_{14}H_{17}NO_2\cdot HCl$. Calculated, %: C 62.80; H 6.78; Cl 13.24; N 5.23.

2-Imino-4-methyl-5,5-pentamethylene-3-phenyl-2,5-dihydrofuran hydrochloride (IIId). Yield 1.2 g (88%) (*a*), 1.30 g (94%) (*b*). mp 223–226°C. Found, %: C 69.42; H 7.41; Cl 12.79; N 5.27. $C_{16}H_{19}NO\cdot HCl$. Calculated, %: C 69.18; H 7.26; Cl 12.76; N 5.04.

2-Imino-3-aryl-4-methyl-5,5-substituted 2,5-dihydrofurans hydrogen sulfates IVa–IVd. To a solution of 0.01 mol of compound **Ia–Id** in anhydrous ethanol was added 0.01 mol (2.2 ml, 45%) of H_2SO_4. The separated precipitate was filtered off and washed with anhydrous ethanol.

2-Imino-4,5,5-trimethyl-3-phenyl-2,5-dihydrofuran hydrogen sulfate (IVa). Yield 2.6 g (87%). mp 193–195°C. Found, %: C 52.23, H 5.74; N 4.51; S 10.62. $C_{13}H_{15}NO\cdot H_2SO_4$. Calculated, %: C 52.16; H 5.72; N 4.68; S 10.71.

2-Imino-4,5,5-trimethyl-3-(4-chlorophenyl)-2,5-dihydrofuran hydrogen sulfate (IVb). Yield 2.82 g (85%). mp 229–231°C. Found, %: C 46.64; H 4.51; Cl 10.53; N 4.30; S 9.67. $C_{13}H_{14}NOCl\cdot H_2SO_4$. Calculated, %: C 46.78; H 4.83; Cl 10.62; N 4.20; S 9.61.

2-Imino-4,5,5-trimethyl-3-(4-methoxyphenyl)-2,5-dihydrofuran hydrogen sulfate (IVc). Yield 2.68 g (82%), mp 223–225°C. Found, %: C 50.98; H 5.57; N 4.31; S 9.85. $C_{14}H_{17}NO_2\cdot H_2SO_4$. Calculated, %: C 51.05; H 5.81; N 4.25; S 9.73.

2-Imino-4-methyl-5,5-pentamethylene-3-phenyl-2,5-dihydrofuran hydrogen sulfate (IVd). Yield 2.8 g (84%), mp 248–250°C. Found, %: C 56.71; H 6.23; N 4.21; S 9.52. $C_{16}H_{19}NO\cdot H_2SO_4$. Calculated, %: C 56.62; H 6.24; N 4.13; S 9.45.

Reaction of compounds IIIa–IIId, IVa–IVd with potassium carbonate. *a.* To a water solution of 0.01 mol of compound **IIIa–IIId** (pH 2–3) was added a concn. solution of K_2CO_3 till pH 7–8. The separated precipitate was filtered off and recrystallized from heptane to obtain compounds **Ia–Id** .

b. To a water solution of 0.01 mol of compound **IVa–IVd** was added a concn. solution of K_2CO_3 till Ph 7–8. Further workup as described in *a*.

Compound **Ia**. Yield 1.85 g (92%) (*a*), 1.76 g (88%) (*b*), mp 81–82°C.

Compound **Ib**. Yield 2.1 g (90%) (*a*), 2.25 g (96%) (*b*), mp 91–92°C.

Compound **Ic**. Yield 1.95 g (85%) (*a*), 1.65 g (72%) (*b*), oily substance.

Compound **Id**. Yield 2.27 g (94%) (*a*), 2.3 g (96%) (*b*), mp 126–127°C.

3-Aryl-4-methyl-5,5-substituted 2(5*H*)-furanones Va–Vd. *a.* To 0.01 mol of compound **Ia–Id** in 5 ml of water was added HCl till pH 4–5, and the solution was heated on a water bath over 3 h. The separated precipitate was filtered off, washed with water, and recrystallized from ethanol.

b. A solution of 0.01 mol of compound **IIIa–IIId** in 10 ml of ethanol (or water) was heated on a water bath over 3 h. The separated precipitate was filtered off and recrystallized from ethanol.

c. A solution of 0.01 mol of compound **IVa–IVd** in

10 ml of ethanol (or water) was heated on a water bath over 3 h. Further workup as described in *b*.

4,5,5-Trimethyl-3-phenyl-2(5*H*)-furanone (Va). Yield 1.75 g (87%) (*a*), 1.73 g (86%) [1.8 g (89%)] (*b*), 1.78 g (88%) [1.8 g (89%)] (*c*), mp 102°C [8].

4,5,5-Trimethyl-3-(4-chlorophenyl)-2(5*H*)-furanone (Vb). Yield 2.2 g (94%), 2 g (86%) [2.1 g (90%)] (*b*), 2 g (87%) [2.1 g (89%)] (*c*), mp 115–116°C [7].

4,5,5-Trimethyl-3-(4-methoxyphenyl)-2(5*H*)-furanone (Vc). Yield 1.85 g (80%), 2 g (86%), [2.1 g (90%)] (*b*), 1.9 g (82%) [2 g (86%)] (*c*), mp 85–86°C [7].

4-Methyl-5,5-pentamethylene-3-phenyl-2(5*H*)-furanone (Vd). Yield 2 g (82%), 1.94 g (80%), [2 g (83%)] (*b*), 2 g (83%) [2.1 g (87%)] (*c*), mp 135–136°C [8].

IR spectra were recorded on a spectrophotometer UR-20 from mulls in mineral oil. ^{1}H NMR spectra were taken on a spectrometer Varian Mercury-300 (300 MHz) from solutions in DMSO-d_6–CCl_4, 1:3, internal reference HMDS. The reaction progress was monitored and the purity of compounds obtained was checked by TLC on Silufol UV-254 plates, eluent acetone–benzene, 1 : 2, development under the iodine vapor or UV irradiation.

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