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Convenient Synthesis of 2-Imino-3-(2-thienyl)-2(5*H*)-furans and Their Certain Transformations

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Abstract—A convenient and efficient method was described of the preparation of 2-imino-3-(2-thienyl)-2,5-dihydrofurans by the condensation of α-ketol with the thiophene-2-acetonitrile and some their chemical transformations were performed.

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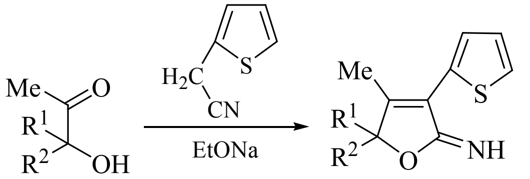
3-Functionalized 2(5*H*)-furanones are relatively wide spread in the nature, they are contained in the composition of many plants and animal bodies and they exhibit a wide range of biologic action [1–5].

The theoretical and practical interest is attracted by functionally substituted 2-furanones containing various substituents in the position *3*. No compounds were described containing in this position heterocyclic substituents, therefore the development of their synthesis was especially interesting.

In extension of the investigation of the synthesis and chemical reactions of new derivatives of iminolactones we carried out in this research the reaction of α-ketols with the thiophene-2-acetonitrile in the presence of sodium ethylate. The reaction proceeds at the equimolar reagents ratio in the presence of the catalytical quantity of the sodium ethylate in anhydrous ethanolover 10 h and results in substituted 2-imino-3-(2-thienyl)-2,5-dihydrofurans **Ia–Id** in high yields (up to 96%).

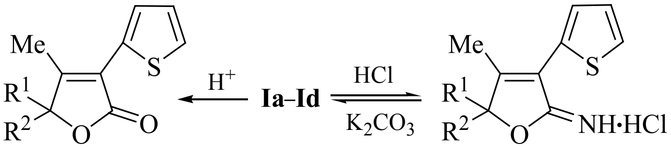


Ia–Id

$R^1 = R^2 = Me$ (**a**); $R^1,R^2 = (CH_2)_5$ (**b**); $R^1 = Me$, $R^2 = Et$ (**c**); Ph (**d**).

The hydrolysis of 2-imino derivatives **Ia–Id** provided previously unknown 3-(2-thienyl)-2,5-dihydrofuran-2-ones **IIa–IId**. The reaction occurred in the presence of acids (pH 4–5) at heating on a water bath for 3 h.

Compounds **Ia–Id** readily formed hydrochlorides at passing the gaseous hydrogen chloride through their benzene solutions. The obtained salts **IIIa–IIId** were easily transformed into the initial 2-imino derivatives **Ia–Id** by treating with a solution of potassium carbonate.



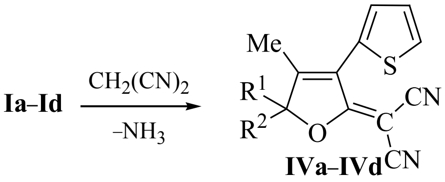
IIa–IId **IIIa–IIId**

$R^1 = R^2 = Me$ (**a**); $R^1,R^2 = (CH_2)_5$ (**b**); $R^1 = Me$, $R^2 = Et$ (**c**); $R^1 = Me$, $R^2 = Ph$ (**d**).

It is known that 2-dicyanomethylene derivatives of furans are chromophores, they possess electrooptical and photorefractive properties [6], and are fluorophores with the fluorescent characteristics [7].

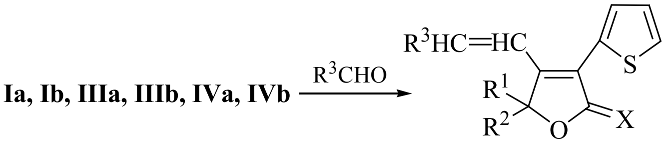
Aiming at the preparation of new dicyanomethylene furan derivatives we studied the reaction of synthesized 2-imino derivatives **Ia–Id** with malononitrile. The reaction proceeded readily at mixing the initial components in the 1:1 ratio at the room temperature with ammonia evolution and the formation of the corresponding

2-dicyanomethylene derivatives **IVa–IVd** in the nearly quantitative yield.



$R^1 = R^2 = Me$ (**a**); $R^1,R^2 = (CH_2)_5$ (**b**); $R^1 = Me$, $R^2 = Et$ (**c**); $R^1 = Me$, $R^2 = Ph$ (**d**).

Taking into account the lability of the hydrogen atoms of the methyl groupattached to the multiple carbon-carbon bond we also studied the reactions of iminolactones **Ia, Ib,** lactones **IIIa, IIIb**, and dicyanomethylenefurans **IVa, IVb** with aromatic aldehydes in the alcoholic solution of NaOH that occurred with the retention of the lactone ring affording derivatives **Va–Vl** with the styryl and furylvinyl substituents in the position *4*. 2-Dicyano-methylene derivatives **Ve, Vf, Vk, Vl** were also obtained by the independent synthesis from the corresponding iminolactones **Va, Vb, Vg, Vh** and malononitrile analogously to the preparation of compounds **IVa–IVd**.



Va–Vl

$R^1 = R^2 = Me$ (**a, c, e, g, i, k**); $R^1,R^2 = (CH_2)_5$ (**b, d, f, h, j, l**); $R^3 = Ph$ (**a–f**), 2-furyl (**g–l**); X = NH (**a, b, g, h**), O (**c, d, i, j**), $C(CN)_2$ (**e, f, k, l**).

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from mulls in mineral oil. ^1H NMR spectra were taken on a spectrometer Varian Mercury-300 (300 MHz) from solutions in DMSO-d_6, 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.

5,5-Substituted 2-imino-4-methyl-3-(2-thienyl)-2,5-dihydrofurans Ia–Id. *a*. To a solution of 0.046 g (2 mmol) of Na in 20 ml of anhydrous ethanol was added 20 mmol of an appropriate tertiary α-ketoalcohol and 2.43 g (20 mmol) of thiophene-2-acetonitrile. The reaction mixture was left standing for 10 h at room temperature (TLC monitoring). The separated precipitate was filtered off, washed with water, dried, and recrystallized from heptane.

b. To a water solution of 5 mmol of compound **IIIa–IIId** (pH 2–3) was added the concentrated solution of K_2CO_3 till pH 7–8. The workup of the precipitate was as in the procedure *a*.

2-Imino-3-(2-thienyl)-4,5,5-trimethyl-2,5-dihydrofuran (Ia). Yield 3.9 g (95%) (*a*), 0.92 g (89%) (*b*), mp 78–79°C. IR spectrum, ν, cm^{-1}: 3290, 1650, 1625, 1040. ^1H NMR spectrum, δ, ppm: 1.43 s (6H, $2CH_3$), 2.10 s (3H, CH_3), 6.85–7.15 m (2H, NH, $H_{thiophene}$), 7.40–7.75 m (2H, $H_{thiophene}$). Found, %: C 63.57; H 6.63; N 6.51; S 15.74. $C_{11}H_{13}NOS$. Calculated, %: C 63.77; H 6.28; N 6.76; S 15.46.

2-Imino-4-methyl-5,5-pentamethylene-3-(2-thienyl)-2,5-dihydrofuran (Ib). Yield 4.77 g (97%) (*a*), 1 g (87%) (*b*), mp 92–93°C. IR spectrum, ν, cm^{-1}: 3270, 1640, 1620, 1040. ^1H NMR spectrum, δ, ppm: 1.20–1.25 m (2H, CH_2), 1.50–1.75 m (8H, $4CH_2$), 1.90 s (3H, CH_3), 6.90–7.20 m (2H, NH, $H_{thiophene}$), 7.52–7.85 m (2H, $H_{thiophene}$). Found, %: C 68.21; H 6.72; N 5.83; S 13.01. $C_{14}H_{17}NOS$. Calculated, %: C 68.02; H 6.89; N 5.67; S 12.96.

2-Imino-4,5-dimethyl-3-(2-thienyl)-5-ethyl-2,5-dihydrofurans (Ic). Yield 3.6 g (82%) (*a*), 0.92 g (84%) (*b*). Oily substance. ^1H NMR spectrum, δ, ppm: 0.85 t (3H, $CH_2\underline{CH_3}$, *J* 16.5 Hz), 1.48 s (6H, $2CH_3$), 1.75–1.80 m (2H, $\underline{CH_2}CH_3$), 6.78–7.10 m (2H, NH, $H_{thiophene}$), 7.35–7.68 m (2H, $H_{thiophene}$). Found, %: C 65.27; H 6.48; N 6.47; S 14.62. $C_{12}H_{15}NOS$. Calculated, %: C 65.27; H 6.48; N 6.47; S 14.48.

2-Imino-4,5-dimethyl-3-(2-thienyl)-5-phenyl-2,5-dihydrofurans (Id). Yield: 4.3 g (80%) (*a*), 1 g (82%) (*b*). Oily substance. ^1H NMR spectrum, δ, ppm: 1.45 s (3H, CH_3), 1.51 s (3H, CH_3), 6.75 m (2H, NH, $H_{thiophene}$), 7.25 d (2H, H_{arom}, *J* 16.5 Hz), 7.37 d (2H, H_{arom}, *J* 16.5 Hz), 7.40–7.45 m (2H, H_{arom}, $H_{thiophene}$). Found, %: C 71.51; H 5.63; N 5.36; S 11.49. $C_{16}H_{15}NOS$. Calculated, %: C 71.38; H 5.58; N 5.20; S 11.89.

3-(2-Thienyl)-2,5-dihydrofuran-2-ones IIa–IId. To a mixture of 10 mmol of compound **Ia–Id** and 5 ml of water was added HCl to pH 4–5, and the mixture was heated on a water bath for 3 h. The separated precipitate was filtered off, washed with water, and dried .

3-(2-Thienyl)-4,5,5-trimethyl-2,5-dihydrofuran-2-

one (IIa). Yield 2 g (95%), mp 82–83°C. IR spectrum, ν, cm^{-1}: 1730, 1630, 1620, 1040. ^{1}H NMR spectrum, δ, ppm: 1.45 s (6H, $2CH_3$), 2.15 and 2.20 s (3H, CH_3), 7.05 m (1H, $H_{thiophene}$), 7.45 m (2H, $H_{thiophene}$). Found, %: C 63.64; H 5.67; S 15.83. $C_{11}H_{12}O_2S$. Calculated, %: C 63.46; H 5.77; S 15.39.

4-Methyl-5,5-pentamethylene-3-(2-thienyl)-2,5-dihydrofuran-2-one (IIb). Yield 2.5 g (98%), mp 116–117°C. Found, %: C 67.47; H 6.54; S 12.49. $C_{14}H_{16}O_2S$. Calculated, %: C 67.74; H 6.45; S 12.90.

4,5-Dimethyl-3-(2-thienyl)-5-ethyl-2,5-dihydrofuran-2-one (IIc). Yield 2.1 g (94%), mp 69–70°C. Found, %: C 64.68; H 6.63; S 14.14. $C_{12}H_{14}O_2S$. Calculated, %: C 64.87; H 6.31; S 14.41.

4,5-Dimethyl-3-(2-thienyl)-5-phenyl-2,5-dihydrofuran-2-one (IId). Yield 2.6 g (97%), mp 74–75°C. Found, %: C 71.31; H 5.51; S 11.58. $C_{16}H_{14}O_2S$. Calculated, %: C 71.11; H 5.19; S 11.85.

2-Imino-3-(2-thienyl)-2,5-dihydrofurans hydrochlorides IIIa–IIId. Through a benzene solution of 4 mmol of compound **Ia–Id** was passed gaseous HCl. The separated precipitate was filtered off, washed with anhydrous benzene, and dried.

2-Imino-4,5,5-trimethyl-3-(2-thienyl)-2,5-dihydrofuran hydrochloride (IIIa). Yield 0.96 г (99%), mp 215–217°C. Found, %: C 54.34; H 5.82; Cl 14.69; N 5.61; S 13.41. $C_{11}H_{14}ClNOS$. Calculated, %: C 54.21; H 5.74; Cl 14.58; N 5.75; S 13.14.

2-Imino-4-methyl-5,5-pentamethylene-3-(2-thienyl)-2,5-dihydrofuran hydrochloride (IIIb). Yield 1.12 g (99%), mp 205–207°C. Found, %: C 59.14; H 6.42; Cl 12.45; N 5.01; S 11.38. $C_{14}H_{18}ClNOS$. Calculated, %: C 59.26; H 6.35; Cl 12.52; N 4.94; S 11.29.

2-Imino-4,5-dimethyl-3-(2-thienyl)-5-ethyl-2,5-dihydrofuran hydrochloride (IIIc). Yield 1 g (96%), mp 202–204°C. Found, %: C 56.04; H 6.33; Cl 13.87; N 5.63; S 12.54. $C_{12}H_{16}ClNOS$. Calculated, %: C 55.92; H 6.21; Cl 13.79; N 5.44; S 12.43.

2-Imino-4,5-dimethyl-3-(2-thienyl)-5-phenyl-2,5-dihydrofuran hydrochloride (IIId). Yield 1.14 d (93%), mp 218–220°C. Found, %: C 62.48; H 5.32; Cl 11.26; N 4.85; S 10.74. $C_{16}H_{16}ClNOS$. Calculated, %: C 62.85; H 5.24; Cl 11.62; N 4.58; S 10.48.

2-Dicyanomethylene-3-(2-thienyl)-4-methyl-2,5-dihydrofurans (IVa–IVd). General procedure. A mixture of 10 mmol of iminolactone **Ia–Id** and 0.66 g (10 mmol) of malononitrile in 10 ml was left standing at room temperature for 15–20 h. After partial removal of the solvent the precipitate was filtered off, washed with water, dried, and recrystallized from a mixture ethanol–water, 2:1.

2-Dicyanomethylene-4,5,5-trimethyl-3-(2-thienyl)-2,5-dihydrofuran (IVa). Yield 2.5 g (98%), mp 208–209°C. IR spectrum, ν, cm^{-1}: 2230, 1630, 1620, 1040. ^{1}H NMR spectrum, δ, ppm: 1.50 s (6H, $2CH_3$), 2.15 s (3H, CH_3), 6.95–7.15 m (3H, $H_{thiophene}$). Found, %: C 65.26; H 4.86; N 10.39; S 12.41. $C_{14}H_{12}N_2OS$. Calculated, %: C 65.63; H 4.69; N 10.94; S 12.50.

2-Dicyanomethylene-4-methyl-5,5-pentamethylene-3-(2-thienyl)-2,5-dihydrofuran (IVb). Yield 2.9 g (96%), mp 168–169°C. ^{1}H NMR spectrum, δ, ppm: 1.28–1.31 m (2H, CH_2), 1.38–1.65 m (8H, $4CH_2$), 1.90 s (3H, CH_3), 6.92–7.12 m (3H, $H_{thiophene}$). Found, %: C 68.29; H 5.50; N 9.54; S 10.18. $C_{17}H_{16}N_2OS$. Calculated, %: C 68.92; H 5.41; N 9.46; S 10.81.

2-Dicyanomethylene-4,5-dimethyl-3-(2-thienyl)-5-ethyl-2,5-dihydrofuran (IVc). Yield 2.5 g (93%), mp 177–178°C. Found, %: C 66.77; H 5.58; N 10.73; S 11.28. $C_{15}H_{17}N_2OS$. Calculated, %: C 66.67; H 5.19; N 10.37; S 11.85.

2-Dicyanomethylene-4,5-dimethyl-3-(2-thienyl)-5-phenyl-2,5-dihydrofuran (IVd). Yield 3 g (92%), mp 145–146°C. Found, %: C 71.96; H 4.45; N 8.58; S 10.18. $C_{19}H_{14}N_2OS$. Calculated, %: C 71.70; H 4.40; N 8.81; S 10.06.

2-Functionally substituted 4-arylvinyl-3-(2-thienyl)-2,5-dihydrofurans Va–Vl. General procedure. A mixture of 10 mmol of compound **Ia, Ib, IIIa, IIIb, IVa, IVb,** 0.01 g of sodium hydroxide, and 12 mmol of an appropriate aldehyde in 10 ml of anhydrous ethanol was heated on a water bath for 4 h. After partial removal of the solvent the precipitate was filtered off, washed with water, dried, and recrystallized from a mixture ethanol–water, 2:1.

2-Imino-5,5-dimethyl-4-styryl-3-(2-thienyl)-2,5-dihydrofuran (Va). Yield 2.3 g (80%) mp 153–154°C. IR spectrum, ν, cm^{-1}: 3260, 1650, 1630, 1620, 1495, 1040. Found, %: C 73.38; H 5.43; N 4.39; S 10.42. $C_{18}H_{17}NOS$. Calculated, %: C 73.22; H 5.75; N 4.75; S 10.85.

2-Imino-5,5-pentamethylene-4-styryl-3-(2-thienyl)-2,5-dihydrofuran (Vb). Yield 2.5 g (81%), mp 141–142°C. Found, %: C 74.12; H 6.97; N 4.22; S 9.78. $C_{21}H_{21}NOS$. Calculated, %: C 75.22; H 6.27; N 4.18; S 9.55.

5,5-Dimethyl-4-styryl-3-(2-thienyl)-2,5-dihydrofuran-2-one (Vc). Yield 2.45 g (84%), mp 137–138°C. Found, %: C 72.83; H 5.62; S 10.49. $C_{18}H_{16}O_2S$. Calculated, %: C 72.97; H 5.41; S 10.81.

5,5-Pentamethylene-4-styryl-3-(2-thienyl)-2,5-dihydrofuran-2-one (Vd). Yield 2.8 g (84%), mp 144°C. Found, %: C 75.14; H 5.89; S 9.65. $C_{21}H_{20}O_2S$. Calculated, %: C 75.00; H 5.95; S 9.52.

2-Dicyanomethylene-5,5-dimethyl-4-styryl-3-(2-thienyl)-2,5-dihydrofuran (Ve). Yield 2.63 g (79%), mp 180–181°C. IR spectrum, ν, cm^{-1}: 2230, 1630, 1620, 1500, 1040. Found, %: C 73.17; H 5.23; N 8.44; S 9.17. $C_{21}H_{16}N_2OS$. Calculated, %: C 72.07; H 5.11; N 8.41; S 9.61.

2-Dicyanomethylene-5,5-pentamethylene-4-styryl-3-(2- thienyl)-2,5-dihydrofuran (Vf). Yield 3.1 g (83%), mp 215–216°C. Found, %: C 75.45; H 5.37; N 7.75; S 8.97. $C_{24}H_{20}N_2OS$. Calculated, %: C 75.00; H 5.21; N 7.29; S 8.33.

2-Imino-5,5-dimethyl-3-(2-thienyl)-4-(2-furylvinyl)-2,5-dihydrofuran (Vg). Yield 2.1 g (80%), mp 149–150°C. ^{1}H NMR spectrum, δ, ppm: 1.60 s (6H, $2CH_3$), 6.50 d (1H, CH=CH, *J* 16.5 Hz), 6.72 d (1H, CH=CH, *J* 16.5 Hz), 7.0–7.2 m (2H, $H_{thiophene}$, H_{furan}), 7.4 m (2H, NH, $H_{thiophene}$), 7.55–7.65 m (3H, $H_{thiophene}$, H_{furan}). Found, %: C 67.83; H 5.54; N 4.28; S 11.16. $C_{16}H_{15}NO_2S$. Calculated, %: C 67.37; H 5.26; N 4.91; S 11.23.

2-Imino-5,5-pentamethylene-3-(2-thienyl)-4-(2-furylvinyl)-2,5-dihydrofuran (Vh). Yield 2.4 g (84%), mp 207–208°C. Found, %: C 70.84; H 5.46; N 4.94; S 11.43. $C_{19}H_{19}NO_2S$. Calculated, %: C 70.15; H 5.85; N 4.31; S 9.84.

5,5-Dimethyl-3-(2-thienyl)-4-(2-furylvinyl)-2,5-dihydrofuran-2-one (Vi). Yield 2.8 g (81%), mp 152–153°C. ^{1}H NMR spectrum, δ, ppm: 1.65 s (6H, $2CH_3$), 6.45 d (1H, CH=CH, *J* 16.5 Hz), 6.70 d (1H, CH=CH, *J* 16.5 Hz), 7.00–7.20 m (2H, $H_{thiophene}$, H_{furan}), 7.35–7.40 m (1H, $H_{thiophene}$), 7.55–7.65 m (3H, $H_{thiophene}$, H_{furan}). Found, %: C 75.14; H 5.89; S 9.65. $C_{21}H_{20}O_2S$. Calculated, %: C 75.00; H 5.95; S 9.52.

5,5-Pentamethylene-3-(2-thienyl)-4-(2-furylvinyl)-2,5-dihydrofuran-2-one (Vj). Yield 2.7 g (83%), mp 174°C. Found, %: C 69.49; H 5.67; S 9.79. $C_{19}H_{18}O_3S$. Calculated, %: C 69.94; H 5.52; S 9.82.

2-Dicyanomethylene-5,5-dimethyl-3-(2-thienyl)-4-(2-furylvinyl)-2,5-dihydrofuran (Vk). Yield 2.9 g (87%), mp 201–202°C. ^{1}H NMR spectrum, δ, ppm: 1.60 s (6H, $2CH_3$), 6.35 m (1H, CH=CH, *J* 16.5 Hz), 6.55 m (1H, CH=CH, *J* 16.5 Hz), 6.95–7.10 m (2H, $H_{thiophene}$, H_{furan}), 7.30–7.45 m (1H, $H_{thiophene}$), 7.60–7.75 m (3H, $H_{thiophene}$, H_{furan}). Found, %: C 68.49; H 4.67; N 8.51; S 9.29. $C_{19}H_{14}N_2O_2S$. Calculated, %: C 68.26; H 4.19; N 8.38; S 9.58.

2-Dicyanomethylene-5,5-pentamethylene-3-(2-thienyl)-4-(2-furylvinyl)-2,5-dihydrofuran (Vl). Yield 3.3 g (89%), mp 209–210°C. Found, %: C 70.65; H 4.25; N 7.18; S 8.42. $C_{22}H_{18}N_2OS$. Calculated, %: C 70.59; H 4.81; N 7.49; S 8.56.

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