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Chemistry of Iminofurans: X.* Synthesis and Hydrolysis of 5-Aryl(hetaryl)-2-[(4,5,6,7-tetrahydro-1-benzothiophen-2-yl)imino]furan-3(2*H*)-ones

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Abstract—5-Aryl(hetaryl)furan-2,3-diones reacted with *N*-(triphenyl-λ^5-phosphanylidene)-4,5,6,7-tetrahydro-1-benzothiophen-2-amines to give 5-aryl(hetaryl)-2-[(4,5,6,7-tetrahydro-1-benzothiophen-2-yl)imino]furan-3(2*H*)-ones whose acid hydrolysis afforded 4-aryl(hetaryl)-2-hydroxy-4-oxo-*N*-(4,5,6,7-tetrahydro-1-benzothiophen-2-yl)but-2-enamides.

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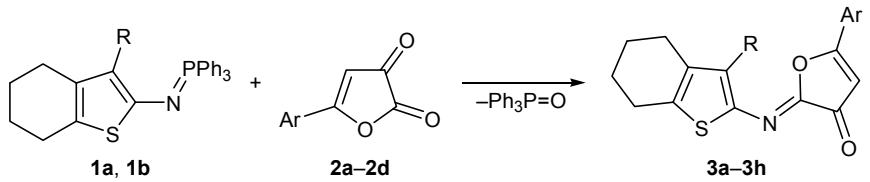
Two methods are presently known to obtain 2-iminofuran-3(2*H*)-ones in high yields. The first method is based on [4+1]-cycloaddition of aroylketenes (generated by thermal decomposition of furan-2,3-diones [2, 3] or 2-diazo-1,3-diketones [3]) to isonitriles. The second method implies the reaction of substituted furan-2,3-diones with *N*-(triphenyl-λ^5-phosphanylidene)anilines, which has been represented by only two examples [4, 5]. 2-Iminofuran-3(2*H*)-one derivatives constitute a poorly explored class of compounds; however, even scarce published data on their reactivity demonstrate their high synthetic potential as starting materials for the preparation of biologically active compounds [6]. In order to extend the synthetic potential of 2-iminofuran-3(2*H*)-ones and obtain new biologically active compounds in the present work we made an attempt to introduce a pharmacophoric Gewald thiophene fragment [7–9] to the imino nitrogen atom.

It is known that furan-2,3-diones react with 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile to give not 2(3)-iminofuran-3(2)-ones but *N*-(3-cyano-4,5,6,7-tetrahydro-1-benzothiophen-2-yl)-4-aryl-2,4-dioxobutanamides as a result of furan ring opening [10]. The most general and widely studied procedure allowing introduction of various substituents to the imino nitrogen atom and avoidance of undesirable reaction pathway is Staudinger imination (aza-Wittig reaction of carbonyl compounds with triphenylphosphine imines [11–13]).

We examined the potential of this procedure with the goal of extending the series of substituted 2-iminofuran-3(2*H*)-ones. For this purpose, we have synthesized *N*-(triphenyl-λ^5-phosphanylidene)thiophen-2-amines **1a** and **1b** from the corresponding thiophen-2-amines according to the procedures reported in [14–17] for the preparation of phosphine imines from primary amines and dibromo(triphenyl)-λ^5-phosphane.

Scheme 1.

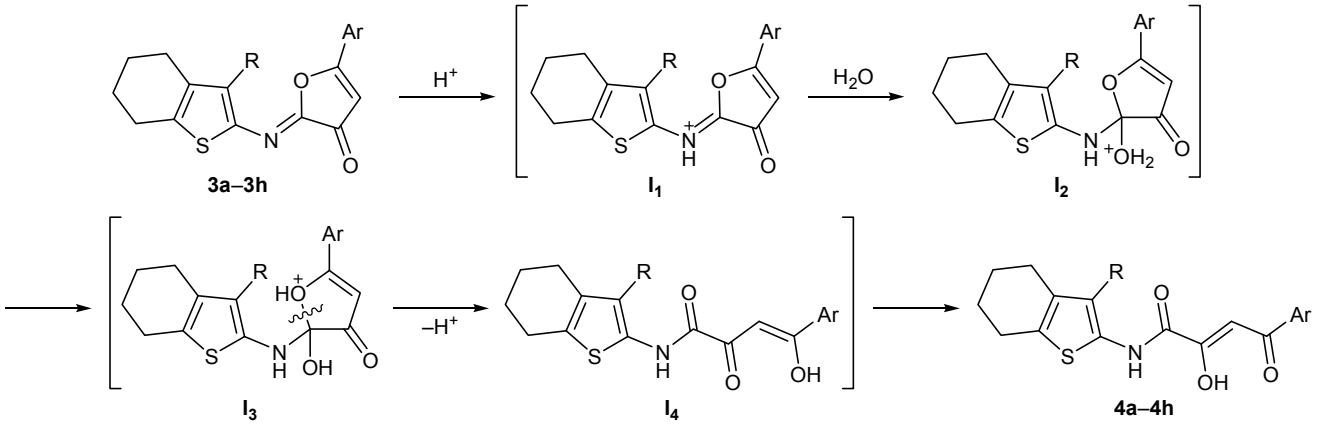


1a, **1b** **2a–2d** **3a–3h**

1, R = CN (**a**), COOEt (**b**); **2**, Ar = Ph (**a**), 4-ClC$_6$H$_4$ (**b**), 4-MeC$_6$H$_4$ (**c**), thiophen-2-yl (**d**); **3**, R = CN, Ar = Ph (**a**), 4-ClC$_6$H$_4$ (**b**), 4-MeC$_6$H$_4$ (**c**), thiophen-2-yl (**d**); R = COOEt, Ar = Ph (**e**), 4-ClC$_6$H$_4$ (**f**), 4-MeC$_6$H$_4$ (**g**), thiophen-2-yl (**h**).

* For communication IX, see [1].

Scheme 2.



R = CN, Ar = Ph (**a**), 4-ClC_6H_4 (**b**), 4-MeC_6H_4 (**c**), thiophen-2-yl (**d**); R = COOEt, Ar = Ph (**e**), 4-ClC_6H_4 (**f**), 4-MeC_6H_4 (**g**), thiophen-2-yl (**h**).

Compounds **1a** and **1b** reacted with 5-substituted furan-2,3-diones **2a**–**2d** to afford a series of 5-aryl-(hetaryl)-2-[(4,5,6,7-tetrahydro-1-benzothiophen-2-yl)-imino]furan-3(2*H*)-ones **3a**–**3h** (Scheme 1).

2-Iminofuranones **3a**–**3h** were isolated as orange crystalline substances which displayed in the IR spectra absorption bands due to substituent in position *3* of the tetrahydrobenzothiophene fragment (CN group in **3a**–**3d**, 2215–2220 cm^{-1}, or ester carbonyl group in **3e**–**3h**, 1686–1693 cm^{-1}) and C^3=O carbonyl group (1693–1717 cm^{-1}). Their ^{1}H NMR spectra showed signals from aromatic protons at δ 7.17–8.01 ppm, a singlet from the vinylic proton in the furan ring at δ 6.20–6.35 ppm, signals from protons in the cyclohexene ring at δ 2.71–2.83 and 1.84–1.90 ppm, and signals from the ester ethyl group (in **3e**–**3h**) at δ 4.38–4.40 and 1.39–1.41 ppm.

The reaction was regioselective, and compounds **3a**–**3h** were formed in almost quantitative yield. Furthermore, it may be regarded as a rare case of reactions of triphenylphosphine imines at the lactone carbonyl, presumably due to increased electron density on C^2 of the furan ring.

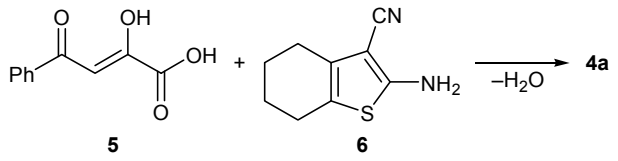
Furan-2,3-diones [18–20], as well as their 3-imino analogs [21–27], readily undergo hydrolysis even by the action of atmospheric moisture. However, 2-iminofuranones **3a**–**3h** remained unchanged on prolonged storage in air and on heating in aqueous solvents. Compounds **3a**–**3h** were hydrolyzed by heating for 15 min in boiling dioxane–water (6:1) containing a catalytic amount of HCl; as a result, amides **4a**–**4h** were obtained (Scheme 2).

Amides **4a**–**4h** are yellow or orange crystalline substances. They showed in the IR spectra absorption bands due to stretching vibrations of the NH group (both H-bonded and not, 3119–3196 and 3350–3365 cm^{-1}, respectively), cyano group (2204–2213 cm^{-1}) or ester carbonyl (1682–1693 cm^{-1}), and amide carbonyl (1665–1691 cm^{-1}). In the ^{1}H NMR spectra of these compounds we observed a singlet from the NH proton (δ 12.50–12.57 ppm, H-bonded, **4e**–**4h**; 9.75–9.88 ppm, free, **4a**–**4d**), signals from aromatic protons (δ 7.19–8.03 ppm), a singlet from the vinylic proton (δ 7.08–7.28 ppm), signals from protons in the cyclohexene fragment (δ 2.63–2.81 and 1.80–1.85 ppm), and signals from the ester ethyl group in **4e**–**4h** (δ 4.38–4.39, 1.40–1.85 ppm).

Presumably, the hydrolysis of **3a**–**3h** begins with protonation of the imino nitrogen atom to form intermediate $\mathbf{I_1}$ which takes up water molecule at C^2 of the furan ring to give intermedate $\mathbf{I_2}$. Proton migration in $\mathbf{I_2}$ to the endocyclic oxygen atom yields intermediate $\mathbf{I_3}$ which undergoes opening of the furan ring at the O^1–C^2 bond with subsequent elimination of proton, and [1,5]-prototropic shift in intermediate $\mathbf{I_4}$ thus formed leads to amides **4a**–**4h** (Scheme 2)

The spectral parameters of **4a**–**4c** coincided with those of the products obtained by reactions of the corresponding 5-arylfuran-2,3-diones with 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile [10], but the melting points were different. The structure of the hydrolysis products was additionally confirmed by independent synthesis of amide **4a** from benzoylpyruvic acid (**5**) and nitrile **6** by heating for a short time in ethanol (Scheme 3). The physical constants and spectral data of samples of **4a** prepared by the two methods were identical.

Scheme 3.



EXPERIMENTAL

The IR spectra were recorded on an FSM-1201 spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on Varian Mercury Plus-300 (300 MHz) and Bruker Avance III spectrometers (400 MHz) using hexamethyldisiloxane as internal standard. The mass spectra were obtained on a Kratos MS-30 instrument (electron impact, 70 eV; ion source temperature 200°C). The elemental compositions were determned on a Leco CHNS-932 analyzer. The progress of reactions and the purity of the isolated compounds were monitored by TLC on Sorbfil PTSKh P-A-UF-254 plates (diethyl ether–benzene–acetone, 10:9:1; detection under UV light or by treatment with iodine vapor). The melting points were measured on an SMP40 melting point apparatus.

Commercially available reagents and solvents were used; acetonitrile of chemically pure grade was subjected to additional purification [28]; rectified ethanol was of deluxe grade. Compounds **2a**–**2d** were synthesized according to [29] from the corresponding aroyl(hetaroyl)pyruvic acids [30, 31]; ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate and 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile (**6**) were prepared as reported in [32].

3-Substituted *N*-(triphenyl-λ^5-phosphanylidene)-4,5,6,7-tetrahydro-1-benzothiophen-2-amines 1a and 1b (*general procedure*). A solution of 0.05 mol of triphenylphosphine in 100 mL of anhydrous benzene was cooled to 5°C, a solution of 0.05 mol of bromine in 30 mL of anhydrous benzene was added dropwise under stirring, and the mixture was stirred for 3 h at room temperature. A solution of 0.1 mol of triethylamine in 30 mL of anhydrous benzene was added to the resulting suspension of dibromo(triphenyl)-λ^5-phosphane, a solution of 0.05 mol of nitrile **6** or ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate in 50 mL of anhydrous benzene was added, and the mixture was stirred for 20 min at 50°C. After cooling, the precipitate of triethylamine hydrobromide was filtered off, the filtrate was evaporated under reduced pressure, and the residue was purified by recrystallization.

2-[(Triphenyl-λ^5-phosphanylidene)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile (1a). Yield 16.4 g (75%), yellow crystals, mp 196.4–196.6°C (from EtOH); published data [14]: mp 198°C. IR spectrum: ν 2209 cm^{-1} (CN). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.71 m (4H, CH_2), 2.32 m (2H, CH_2), 2.49 m (2H, CH_2), 7.44–7.80 m (15H, H_{arom}).

Ethyl 2-[(triphenyl-λ^5-phosphanylidene)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (1b). Yield 18.7 g (77%), yellow crystals, mp 181–182°C (from EtOH); published data [14]: mp 181°C. IR spectrum: ν 1699 cm^{-1} (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 t (3H, Me, J = 7.1 Hz), 1.68 m (4H, CH_2), 2.34 m (2H, CH_2), 2.71 m (2H, CH_2), 4.28 q (2H, OCH_2, J = 7.1 Hz), 7.42–7.85 m (15H, H_{arom}).

5-Aryl(hetaryl)-2-[(3-R-4,5,6,7-tetrahydro-1-benzothiophen-2-yl)imino]furan-3(2*H*)-ones 3a–3h (*general procedure*). A mixture of 0.01 mol of phosphine imine **1a** or **1b** and 0.01 mol of furan-2,3-dione **2a**–**2d** in 20 mL of anhydrous toluene was stirred for 3–5 h at 50–60°C. The mixture was cooled, and the precipitate was filtered off and recrystallized from acetonitrile.

2-{[3-Oxo-5-phenylfuran-2(3*H*)-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile (3a). Yield 2.61 g (78%), orange crystals, mp 254°C. IR spectrum, ν, cm^{-1}: 2196 (CN), 1691 (C^3=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.90 m (4H, CH_2), 2.74 m (2H, CH_2), 2.83 m (2H, CH_2), 6.40 s (1H, CH), 7.55–7.71 m (3H, H_{arom}), 7.94 m (2H, H_{arom}). Mass spectrum, m/z (I_{rel}, %): 334 (91) $[M]^+$, 160 (100), 176 (98), 77 (71) $[Ph]^+$, 102 (53) $[PhC{=}CH]^+$, 69 (48), 188 (46). Found, %: C 68.26; H 4.21; N 8.36; S 9.60. $C_{19}H_{14}N_2O_2S$. Calculated, %: C 68.24; H 4.22; N 8.38; S 9.59. M 334.39

2-{[5-(4-Chlorophenyl)-3-oxofuran-2(3*H*)-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile (3b). Yield 3.24 g (88%), orange crystals, mp 235–236°C. IR spectrum, ν, cm^{-1}: 2215 (CN), 1697 (C^3=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.90 m (4H, CH_2), 2.71 m (2H, CH_2), 2.83 m (2H, CH_2), 6.32 s (1H, CH), 7.38 and 7.81 (2H each, H_{arom}, *AA′BB′*, J = 7.6 Hz). Mass spectrum, m/z (I_{rel}, %): 368 (100) $[M]^+$, 188 (100), 204 (77), 139 (75), 45 (56), 111 (33) $[ClC_6H_4]^+$. Found, %: C 61.90; H 3.56; N 7.63; S 8.70. $C_{19}H_{13}ClN_2O_2S$. Calculated, %: C 61.87; H 3.55; N 7.60; S 8.69. M 368.83.

2-{[5-(4-Methylphenyl)-3-oxofuran-2(3*H*)-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile (3c). Yield 3.45 g (99%), orange

crystals, mp 184–185°C. IR spectrum, ν, cm^{-1}: 2215 (CN), 1697 (C^3=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.89 m (4H, CH_2), 2.39 s (3H, Me), 2.71 m (2H, CH_2), 2.83 m (2H, CH_2), 6.33 s (1H, CH), 7.33 and 7.81 (2H each, H_{arom}, *AA′BB′*, *J* = 8.1 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 348 (100) $[M]^+$, 176 (100) $[C_9H_8N_2S]^+$, 119 (83) $[MeC_6H_4CO]^+$, 161 (47), 204 (69.5) $[C_{10}H_8N_2OS]^+$, 91 (35) $[MeC_6H_4]^+$, 322 (7) $[M - CN]^+$. Found, %: C 68.97; H 4.60; N 8.07; S 9.21. $C_{20}H_{16}N_2O_2S$. Calculated, %: C 68.94; H 4.63; N 8.04; S 9.20. *M* 348.42.

2-{[3-Oxo-5-(thiophen-2-yl)furan-2(3*H*)-ylidene]-amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carbonitrile (3d). Yield 3.34 g (98%), orange crystals, mp 201–202°C. IR spectrum, ν, cm^{-1}: 2220 (CN), 1693 (C^3=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.90 m (4H, CH_2), 2.72 m (2H, CH_2), 2.81 m (2H, CH_2), 6.20 s (1H, CH), 7.30 t (1H, H_{arom}, *J* = 4.2 Hz), 7.83 d (1H, H_{arom}, *J* = 4.8 Hz), 7.88 d (1H, H_{arom}, *J* = 3.0 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 340 (72) $[M]^+$, 277 (100), 111 (100), 204 (67), 312 (53) $[M - CO]^+$. Found, %: C 60.00; H 3.53; N 8.20; S 18.85. $C_{17}H_{12}N_2O_2S_2$. Calculated, %: C 59.98; H 3.55; N 8.23; S 18.84. *M* 340.42.

Ethyl 2-{[3-oxo-5-phenylfuran-2(3*H*)-ylidene]-amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (3e). Yield 2.48 g (65%), orange crystals, mp 146–148°C. IR spectrum, ν, cm^{-1}: 1698 (C^3=O), 1686 (C=O, ester). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.41 t (3H, Me, *J* = 7.2 Hz), 1.82 m (4H, CH_2), 2.73 m (2H, CH_2), 2.81 m (2H, CH_2), 4.38 q (2H, OCH_2, *J* = 7.2 Hz), 6.35 s (1H, CH), 7.47–7.63 m (3H, H_{arom}), 7.93 d (2H, H_{arom}, *J* = 8.4 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 381 (80) $[M]^+$, 308 (65) $[M - COOEt]^+$, 179 (57). Found, %: C 66.10; H 5.00; N 3.65; S 8.42. $C_{21}H_{19}NO_4S$. Calculated, %: C 66.12; H 5.02; N 3.67; S 8.41. *M* 381.45.

Ethyl 2-{[5-(4-chlorophenyl)-3-oxofuran-2(3*H*)-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (3f). Yield 3.20 g (77%), orange crystals, mp 169–170°C. IR spectrum, ν, cm^{-1}: 1715 (C^3=O), 1693 (C=O, ester). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 t (3H, Me, *J* = 7.2 Hz), 1.85 m (4H, CH_2), 2.73 m (2H, CH_2), 2.83 m (2H, CH_2), 4.40 q (2H, CH_2, *J* = 7.2 Hz), 6.34 s (1H, CH), 7.55 and 7.87 (2H each, H_{arom}, *AA′BB′*, *J* = 8.4 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 415 (100) $[M]^+$, 369 (100), 206 (90), 278 (88), 342 (76) $[M - COOEt]^+$, 136 (73) $[ClC_6H_4C{=}CH]^+$, 225 (73), 51 (62), 179 (55). Found, %: C 60.66; H 4.36; N 3.40; S 7.70. $C_{21}H_{18}ClNO_4S$. Calculated, %: C 60.65; H 4.36; N 3.37; S 7.71. *M* 415.89.

Ethyl 2-{[-5-(4-methylphenyl)-3-oxofuran-2(3*H*)-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (3g). Yield 3.08 g (78%), orange crystals, mp 197–198°C. IR spectrum, ν, cm^{-1}: 1714 (C^3=O), 1682 (C=O, ester). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.32 t (3H, Me, *J* = 7.1 Hz), 1.81 m (4H, CH_2), 2.47 s (3H, Me), 2.63 m (2H, CH_2), 2.85 m (2H, CH_2), 4.28 q (2H, OCH_2, *J* = 7.1 Hz), 6.85 s (1H, CH), 7.48 and 7.70 (2H each, H_{arom}, *AA′BB′*, *J* = 8.1 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 395 (20) $[M]^+$, 322 (100) $[M - COOEt]^+$, 116 (80) $[MeC_6H_4C{=}CH]^+$, 206 (75), 121 (73), 43 (53), 349 (43), 91 (42) $[MeC_6H_4]^+$. Found, %: C 66.83; H 5.33; N 3.55; S 8.12. $C_{22}H_{21}NO_4S$. Calculated, %: C 66.82; H 5.35; N 3.54; S 8.11. *M* 395.47.

Ethyl 2-{[3-oxo-5-(thiophen-2-yl)furan-2(3*H*)-ylidene]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (3h). Yield 3.02 g (78%), orange crystals, mp 201–202°C. IR spectrum, ν, cm^{-1}: 1717 (C^3=O), 1690 (C=O, ester). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 t (3H, Me, *J* = 6.9 Hz), 1.84 m (4H, CH_2), 2.75 m (2H, CH_2), 2.81 m (2H, CH_2), 4.38 q (2H, OCH_2, *J* = 6.9 Hz), 6.17 s (1H, CH), 7.28 t (1H, H_{arom}, *J* = 3.9 Hz), 7.86 m (2H, H_{arom}). Found, %: C 58.93; H 4.42; N 3.61; S 16.52. $C_{19}H_{17}NO_4S_2$. Calculated, %: C 58.90; H 4.42; N 3.61; S 16.55.

***N*-(4,5,6,7-Tetrahydro-1-benzothiophen-2-yl)-4-aryl(hetaryl)-2-hydroxy-4-oxobut-2-enamides 4a–4h (*general procedure*).** *a*. A solution of 0.01 mol of furan-3-one **3a**–**3h** in 20 mL of water–dioxane (1:6) containing a catalytic amount of aqueous HCl was heated for 15–20 min under reflux. After cooling to room temperature, the precipitate was filtered off and recrystallized from chloroform–ethanol (1:1).

b. A solution of 0.48 g (2.5 mmol) of benzoylpyruvic acid (**5**) in 3 mL of ethanol was heated to the boiling point, and a solution of 0.445 g (2.5 mmol) of aminothiophene **6** in 3 mL of ethanol, heated to the boiling point, was added. After cooling to room temperature, the precipitate was filtered off and recrystallized from ethanol. Yield of **4a** 0.546 g (62%).

***N*-(3-Cyano-4,5,6,7-tetrahydro-1-benzothiophen-2-yl)-2-hydroxy-4-oxo-4-phenylbut-2-enamide (4a).** Yield 2.85 g (81%, *a*), orange crystals, mp 214–215°C; published data [10]: mp 204–205°C. IR spectrum, ν, cm^{-1}: 3405 (NH), 2218 (CN), 1701 (C=O, amide). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.85 m (4H, CH_2), 2.58–2.73 m (4H, CH_2), 7.25 s (1H, CH), 7.51 m

(2H, H_{arom}), 7.61 m (1H, H_{arom}), 8.01 m (2H, H_{arom}), 9.88 s (1H, NH), 15.02 br.s (1H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 352 (30) $[M]^+$, 69 (100), 178 (75), 147 (53) $[BzCH{=}COH]^+$, 77 (51) $[Ph]^+$, 43 (32) $[NHCO]^+$, 105 (27) $[Bz]^+$. Found, %: C 64.77; H 4.59; N 7.93; S 9.09. $C_{19}H_{16}N_2O_3S$. Calculated, %: C 64.76; H 4.58; N 7.95; S 9.10. *M* 352.41.

4-(4-Chlorophenyl)-*N*-(3-cyano-4,5,6,7-tetrahydro-1-benzothiophen-2-yl)-2-hydroxy-4-oxobut-2-enamide (4b). Yield 2.71 g (70%), yellow crystals, mp 225–226°C; published data [10]: mp 209–211°C. IR spectrum, ν, cm^{-1}: 3356 (NH), 2211 (CN), 1688 (C=O, amide). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.85 m (4H, CH_2), 2.63 m (2H, CH_2), 2.68 m (2H, CH_2), 7.20 s (1H, CH), 7.48 and 7.95 (2H each, H_{arom}, *AA′BB′*, *J* = 8.7 Hz), 9.85 s (1H, NH), 15.48 br.s (1H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 386 (58) $[M]^+$, 181 (100), 69 (91), 139 (54) $[ClC_6H_4CO]^+$, 150 (41), 43 (25) $[NHCO]^+$, 209 (75). Found, %: C 58.97; H 3.90; N 7.24; S 8.32. $C_{19}H_{15}ClN_2O_3S$. Calculated, %: C 58.99; H 3.91; N 7.24; S 8.29. *M* 386.85.

***N*-(3-Cyano-4,5,6,7-tetrahydro-1-benzothiophen-2-yl)-2-hydroxy-4-(4-methylphenyl)-4-oxobut-2-enamide (4c).** Yield 3.55 g (97%), yellow crystals, mp 191–192°C; published data [10]: mp 182–184°C. IR spectrum, ν, cm^{-1}: 3350 (NH), 2213 (CN), 1691 (C=O, amide). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.84 m (4H, CH_2), 2.44 s (3H, Me), 2.63 m (2H, CH_2), 2.67 m (2H, CH_2), 7.21 s (1H, CH), 7.30 and 7.91 (2H each, H_{arom}, *AA′BB′*, *J* = 8.1 Hz), 9.88 s (1H, NH), 15.41 br.s (1H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 366 (50) $[M]^+$, 178 (100), 119 (51) $[MeC_6H_4CO]^+$, 69 (38), 161 (28), 44 (23), 91 (16) $[MeC_6H_4]^+$. Found, %: C 65.53; H 4.97; N 7.62; S 8.75. $C_{20}H_{18}N_2O_3S$. Calculated, %: C 65.55; H 4.95; N 7.64; S 8.75. *M* 366.44.

***N*-(3-Cyano-4,5,6,7-tetrahydro-1-benzothiophen-2-yl)-2-hydroxy-4-oxo-4-(thiophen-2-yl)but-2-enamide (4d).** Yield 3.48 g (97%), yellow crystals, mp 182–183°C. IR spectrum, ν, cm^{-1}: 3365 (NH), 2208 (CN), 1682 (C=O, amide). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.84 m (4H, CH_2), 2.63 m (2H, CH_2), 2.68 m (2H, CH_2), 7.08 s (1H, CH), 7.21 t (1H, H_{arom}, *J* = 4.2 Hz), 7.76 d (1H, H_{arom}, *J* = 4.4 Hz), 7.89 d (1H, H_{arom}, *J* = 3.3 Hz), 9.75 s (1H, NH), 15.02 br.s (1H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 358 (47) $[M]^+$, 153 (100), 179 (77) , 69 (63), 111 (51), 181 (44), 43 (28) $[NHCO]^+$. Found, %: C 56.95; H 3.96; N 7.82; S 17.90. $C_{17}H_{14}N_2O_3S_2$. Calculated, %: C 56.96; H 3.94; N 7.82; S 17.89. *M* 358.43.

Ethyl 2-[(2-hydroxy-1,4-dioxo-4-phenylbut-2-en-1-yl)amino]-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (4e). Yield 2.80 g (70%), orange crystals, mp 168–169°C. IR spectrum, ν, cm^{-1}: 3204 (NH), 1684 (C=O, ester), 1665 (C=O, amide). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.42 t (3H, Me, *J* = 7.5 Hz), 1.81 m (4H, CH_2), 2.70 m (2H, CH_2), 2.81 m (2H, CH_2), 4.39 q (2H, OCH_2, *J* = 7.5 Hz), 7.28 s (1H, CH), 7.47–7.63 m (3H, H_{arom}), 8.00–8.03 m (2H, H_{arom}), 12.57 s (1H, NH), 15.69 br.s (1H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 399 (71) $[M]^+$, 179 (100), 105 (89) $[Bz]^+$, 151 (71), 69 (61), 225 (51). Found, %: C 63.15; H 5.30; N 3.50; S 8.03. $C_{21}H_{21}NO_5S$. Calculated, %: C 63.14; H 5.30; N 3.51; S 8.03. *M* 399.46.

Ethyl 2-{[4-(4-chlorophenyl)-2-hydroxy-1,4-dioxobut-2-en-1-yl]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (4f). Yield 3.69 g (85%), orange crystals, mp 203–204°C. IR spectrum, ν, cm^{-1}: 3211 (NH), 1680 (C=O, ester), 1660 (C=O, amide). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.41 t (3H, Me, *J* = 6.9 Hz), 1.80 m (4H, CH_2), 2.69 m (2H, CH_2), 2.81 m (2H, CH_2), 4.39 q (2H, OCH_2, *J* = 6.9 Hz), 7.25 s (1H, CH), 7.47 and 7.93 (2H each, H_{arom}, *AA′BB′*, *J* = 8.4 Hz), 12.54 s (1H, NH), 15.43 br.s (1H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 433 (29) $[M]^+$, 179 (100), 139 (76) $[ClC_6H_4CO]^+$, 69 (75) $[C_3H_3NO]^+$, 225 (51), 43 (33) $[NHCO]^+$. Found, %: C 58.10; H 4.66; N 3.23; S 7.42. $C_{21}H_{20}ClNO_5S$. Calculated, %: C 58.13; H 4.65; N 3.23; S 7.39. *M* 433.90.

Ethyl 2-{[2-hydroxy-4-(4-methylphenyl)-1,4-dioxobut-2-en-1-yl]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (4g). Yield 2.99 g (72%), orange crystals, mp 204°C. IR spectrum, ν, cm^{-1}: 3392 (NH), 1698 (C=O, ester), 1637 (C=O, amide). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.41 t (3H, Me, *J* = 7.1 Hz), 1.80 m (4H, CH_2), 2.38 s (3H, Me), 2.64 m (2H, CH_2), 2.80 m (2H, CH_2), 4.39 m (2H, OCH_2, *J* = 7.1 Hz), 7.27 and 7.88 (2H each, H_{arom}, *AA′BB′*, *J* = 8.1 Hz), 12.53 s (1H, NH), 15.43 br.s (1H, OH). Mass spectrum, *m*/*z* (I_{rel}, %): 413 (63) $[M]^+$, 179 (100), 225 (54), 69 (46) $[C_3H_3NO]^+$, 151 (35), 43 (24) $[NHCO]^+$. Found, %: C 69.89; H 5.62; N 3.41; S 7.73. $C_{22}H_{23}NO_5S$. Calculated, %: C 63.90; H 5.61; N 3.39; S 7.75. *M* 413.49.

Ethyl 2-{[2-hydroxy-1,4-dioxo-4-(thiophen-2-yl)-but-2-en-1-yl]amino}-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate (4h). Yield 3.37 g (83%), orange crystals, mp 191–192°C. IR spectrum, ν, cm^{-1}: 3119 (NH), 1684 (C=O, ester), 1668 (C=O, amide). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.40 t (3H, Me, *J* = 6.9 Hz), 1.80 m (4H, CH_2), 2.69 m (2H, CH_2), 2.80 m (2H, CH_2), 4.38 q (2H, OCH_2, *J* = 6.9 Hz), 7.10 s (1H, CH), 7.19 t (1H, H_{arom}, *J* = 4.2 Hz),

7.73 d.d (1H, H_{arom}, J = 1.1 Hz, 4.9 Hz), 7.87 d.d (1H, H_{arom}, J = 1.1, 3.9 Hz), 12.50 s (1H, NH), 15.01 br.s (1H, OH). Mass spectrum, m/z (I_{rel}, %): 405 (71) $[M]^+$, 179 (100), 225 (82), 69 (77) $[C_3H_3NO]^+$, 153 (60), 111 (43), 206 (42), 43 (19) $[NHCO]^+$. Found, %: C 56.30; H 4.72; N 3.44; S 15.80. $C_{19}H_{19}NO_5S_2$. Calculated, %: C 56.28; H 4.72; N 3.45; S 15.82. M 405.48.

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