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2-Acyl(aroyl)-1,1,3,3-tetracyanopropenides: II*. Synthesis of 2-[2-(Alkylsulfanyl)-5-amino-2-aryl-4-cyano-2,3-dihydrofuran-3-ylidenepropanedinitriles by Reaction with Thiols

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Abstract—Reactions of 2-aroyl-1,1,3,3-tetracyanopropenides with thiols in acid medium led to the formation of the corresponding 2-alkylsulfanyl-substituted 2-(5-amino-2-aryl-4-cyano-2,3-dihydrofuran-3-ylidene)propanedinitriles.

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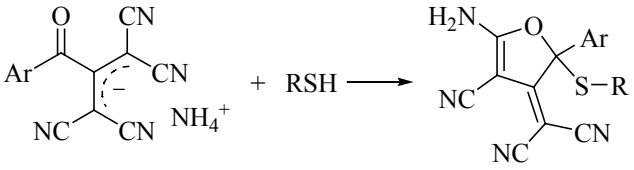
2-Aroyl-1,1,3,3-tetracyanopropenides **I** obtained from the corresponding tetracyanocyclopropyl ketones [2] are promising precursors for the synthesis of functionally substituted five-memebered heterocycles. In the previous paper on the reaction of propenides **I** with the hydrochloric acid we demonstrated that the chloride ion added to the protonated carbonyl group to give 2-chlorodihydrofurans [1]. Besides it was previously assumed that propenides **I** were intermediates in the process of tetracyanocyclopropyl ketones conversion into 2-alkoxydihydrofurans at the use as nucleophiles alcohols and ketoximes in the presence of the corresponding alcoholates and oximates [2, 3].

Thiols are close analogs of alcohols, and their involvement into the reaction with the 2-aroyl-1,1,3,3-tetra-cyanopropenides opens the way to the synthesis of previously unknown 2-alkylsulfanyl-substituted dihydrofurans. Therefore we studied the reactions of propenides **I** with mercaptans in various conditions. It was established that the expected 2-alkylsulfanyl derivatives of dihydrofurans formed at the use of an acid catalyst and water as a solvent. In these conditions the reaction of propenides **I** with alkylthiols afforded 2-[2-(alkylsulfanyl)-5-amino-2-aryl-4-cyano-2,3-dihydrofuran-3-ylidene] propanedinitriles **IIa–IIf**, and the reaction with ethyl mercaptoacetate provided ethyl 2-{[5-amino-2-aryl-3-(dicyanomethylidene)-4-cyano-2,3-dihydrofuran-2-yl]-sulfanyl}acetates **IIg–IIi** in up to 71–87% yields.



Ia–Ic **IIa–IIi**

I, Ar = C_6H_5 (**a**), 4-ClC_6H_4 (**b**), 4-$CH_3C_6H_4$ (**c**); **II**, R = C_2H_5, Ar = C_6H_5 (**a**), 4-ClC_6H_4 (**b**), 4-$CH_3C_6H_4$ (**c**);R = C_3H_7, Ar = C_6H_5 (**d**), 4-ClC_6H_4 (**e**), 4-$CH_3C_6H_4$, (**f**); R = $CH_2CO_2C_2H_5$, Ar = C_6H_5 (**g**), 4-ClC_6H_4 (h), 4-$CH_3C_6H_4$ (**i**).

The structure of compounds **IIa–IIi** was established with the use of the data of ^{1}H NMR, IR, and mass spectra. In the ^{1}H NMR spectra the signls of amino group are present at 10.28–10.31 ppm, and also the proton signal appeared of the aromatic ring and of the hydrocarbon substituents at the sulfur atom. The protons of the methylene group at the sulfur atom are diastereotopic, and their signal in the ^{1}H NMR spectrum is characteristic of the

* For Communication I, see [1].

spin system *AB*. Therefore the signal of the CH_2 group linked to sulfur in the spectra of compounds **IIg–IIi** gives rise to two doublets, and in the spectra of compounds **IIa–IIf**, a multiplet combined from two doublets of quartets (**IIa–IIc**) or from two doublets of triplets (**IId–IIf**). A similar pattern is observed also for the methylene group of the ester moiety of compounds **IIg–IIi**. The IR spectra contain the absorption bands of the conjugated cyano groups in the region 2200–2225 cm^{-1}, of the C=C bond of the dicyanomethylene moiety at 1669–1695 cm^{-1}, and of amino group at 3075–3280 cm^{-1}.

The catalyst role apparently consists in the activation of the carbonyl group by its protonation with the formation of an intermediate zwitter-ion **A**. The presumable scheme of transformations includes further the nucleophilic addition of the thiol giving a hemimercaptal **B** and the heterocyclization into dihydrofuran derivative **IIa–IIi** (see the scheme).

Water is not an optimal solvent due to the poor solubility of thiols, but the use of organic solvents or their additives in water completely inhibits the reaction, and we regard this fact as a confirmation of the zwitter-ionic character of intermediate **A**. We attained a sufficient success of the reaction at the use of the 5-fold excess of the thiol. Under these conditions the reaction apparently occurs at the interphase boundary, and the reaction product crystallizes in the thiol phase. We failed to obtain the desired result under the other conditions. The use of basic catalyst does not lead to the formation 2-alkylsulfanylfurans. Applying thiolates as catalysts in anhydrous solvents is accompanied with strong tarring impeding the isolation of individual products, and in the aqueous solvents the concurrent reaction with the hydroxide ion occurs resulting in the formation of pyrrolo[3,4-*C*]pyridine derivatives [4].

Today the 2-alkylsulfanyl-substituted 5-aminodihydrofurans are insufficiently described. The known method of preparation of 5-(methylsulfanyl)-3,4-diphenylfuran-2-(*N,N*-dimethyl)amine consisted in the reaction of diphenylcyclopropenone with *N,N*-dimethyl-1-(methylsulfanyl) ethyleneamine [5]. The method of the synthesis of 2-alkylsulfanyldihydrofurans **II** we developed is distinguished by the simplicity, high yield of the reaction products, and by the relative availability of the reagents.

EXPERIMENTAL

The monitoring of the reaction progress and checking the purity of compounds synthesized was carried out by TLC on Silufol UV-254 plates (spots visualized by UV irradiation, in iodine vapor, and by calcining). IR spectra were recorded on a spectrophotometer FSM 1201 from thin films or mulls in mineral oil. ^{1}H NMR spectra were registered on a spectrometer Bruker AM-500 at operating frequency 500.13 MHz, solvent DMSO-d_6, internal reference TMS. Mass spectra were measured on an instrument Finnigan MAT INCOS-50 (electron impact, 70 eV).

Ammonium 2-benzoyl-1,1,3,3-tetracyanopropenide (Ia) was obtained by method [5]. Yield 87%, mp 182–183°C (decomp.). IR spectrum, ν, cm^{-1}: 2225 (C≡N), 1675 (C=O).

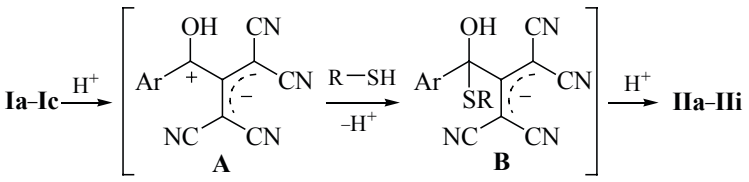
Compounds **Ib, Ic** were similarly prepared.

Ammonium 1,1,3,3-tetracyano-2-(4-chlorobenzoyl) propenide (Ib). Yield 91%, mp 165–167°C (decomp.). IR spectrum, ν, cm^{-1}: 2210 (C≡N), 1685 (C=O).

Ammonium 2-(4-methylbenzoyl)-1,1,3,3-tetracyanopropenide (Ic). Yield 85%, mp 176–178°C (decomp.). IR spectrum, ν, cm^{-1}: 2200 (C≡N), 1665 (C=O).

2-[5-Amino-2-phenyl-4-cyano-2-(ethylsulfanyl)-2,3-dihydrofuran-3-ylidene]propanedinitrile (IIa). To a solution of 2.63 g (10 mmol) of compound **Ia** in 20 ml of water was added dropwise at stirring 3.1 g (50 mmol) of ethanethiol. The emulsion obtained was acidified with two drops of concn. hydrochloric acid, and the mixture was stirred for 20 min. The separated precipitate was filtered off, washed with water, and recrystallized from methanol. Yield 2.25 g (73%), mp 165–166°C (decomp.). IR spectrum, ν, cm^{-1}: 3125 (NH_2), 2240 (C≡N), 1660 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.26 t (3H, CH_3, ^3J 7.4 Hz), 2.64 m (*ABX*$_2$ system) (2H, CH_2, ^2J 12.2,

Scheme.



^3J 7.5 Hz), 7.52–7.57 m (5H, Ph), 10.29 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 308 (30). Found, %: C 62.37; H 3.91; N 18.51. $C_{16}H_{12}N_4OS$. Calculated, %: C 62.32; H 3.92; N 18.17. *M* 308.36.

Compounds **IIb–IIi** were synthesized analogously.

2-[5-Amino-2-(4-chlorophenyl)-4-cyano-2-(ethylsulfanyl)-2,3-dihydrofuran-3-ylidene]propanedinitrile (IIb). Yield 81%, mp 196–198°C (decomp.). IR spectrum, ν, cm^{-1}: 3100 (NH_2), 2210 (C≡N), 1665 (C=C). ^1H NMR spectrum, δ, ppm: 1.25 t (3H, CH_3, ^3J 7.4 Hz), 2.65 m (*ABX*$_2$ system, 2H, CH_2, ^2J 12.2, ^3J 7.5 Hz), 7.57–7.62 m (4H, Ph), 10.32 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 342 (3), 344 (1). Found, %: C 57.1; H 3.31; N 16.84. $C_{16}H_{11}ClN_4OS$. Calculated, %: C 56.06; H 3.23; N 16.34. *M* 342.80.

2-[5-Amino-2-(4-methylphenyl)-4-cyano-2-(ethylsulfanyl)-2,3-dihydrofuran-3-ylidene]propanedinitrile (IIc). Yield 76%, mp 173–175°C (decomp.). IR spectrum, ν, cm^{-1}: 3200 (NH_2), 2215 (C≡N), 1655 (C=C). ^1H NMR spectrum, δ, ppm: 1.25 t (3H, $CH_2C\underline{H}_3$, ^3J 7.5 Hz), 2.28 s (3H, $PhC\underline{H}_3$), 2.63–2.71 m (2H, CH_2), 7.21 d (2H, C_6H_4, ^3J 8.3 Hz), 7.55 d (2H, C_6H_4, ^3J8.3 Hz), 10.29 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 322 (5), 307 (40). Found, %: C 64.81; H 4.65; N 16.9. $C_{17}H_{14}N_4OS$. Calculated, %: C 63.33; H 4.38; N 17.38. *M* 322.38.

2-[5-Amino-2-(propylsulfanyl)-2-phenyl-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (IId). Yield 71%, mp 165–166°C (decomp.). IR spectrum, ν, cm^{-1}: 3120 (NH_2), 2230 (C≡N), 1660 (C=C). ^1H NMR spectrum, δ, ppm: 1.00 t (3H, CH_3, ^3J 7.3 Hz), 1.57–1.67 m (2H, $SCH_2C\underline{H}_2CH_3$), 2.61 m (*ABX*$_2$ system, 2H, $SC\underline{H}_2CH_2CH_3$, ^2J 12.2, ^3J 7.2 Hz), 7.52–7.58 m (5H, Ph), 10.30 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 322 (23). Found, %: C 64.21; H 5.07; N 16.27. $C_{17}H_{14}N_4OS$. Calculated, %: C 63.33; H 4.38; N 17.38. *M* 322.38.

2-[5-Amino-2-(propylsulfanyl)-2-(4-chlorophenyl)-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (IIe). Yield 72%, mp 212–215°C (decomp.). IR spectrum, ν, cm^{-1}: 3180 (NH_2), 2220 (C≡N), 1650 (C=C). ^1H NMR spectrum, δ, ppm: 0.99 t (3H, CH_3, ^3J 7.3 Hz), 1.56–1.67 m (2H, $SCH_2C\underline{H}_2CH_3$), 2.62 m (*ABX*$_2$ system, 2H, $SC\underline{H}_2CH_2CH_3$, ^2J 12.2, ^3J 7.2 Hz), 7.57–7.63 m (4H, Ph), 10.32 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 356 (20), 358 (9). Found, %: C 57.3; H 3.71; N 14.70. $C_{17}H_{13}ClN_4OS$. Calculated, %: C 57.22; H 3.67; N 15.70. *M* 356.83.

2-[5-Amino-2-(4-methylphenyl)-2-(propylsulfanyl)-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (IIf). Yield 79%, mp 144–145°C (decomp.). IR spectrum, ν, cm^{-1}: 3180 (NH_2), 2220 (C≡N), 1665 (C=C). ^1H NMR spectrum, δ, ppm: 0.99 t (3H, CH_3, ^3J 7.3 Hz), 1.55–1.68 m (2H, $SCH_2C\underline{H}_2CH_3$), 2.34 s (3H, $PhC\underline{H}_3$), 2.53–2.65 m (2H, $SC\underline{H}_2CH_2CH_3$), 7.31 d (2H, Ph, ^3J 8.3 Hz), 7.44 d (2H, Ph, ^3J 8.3 Hz), 10.28 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 336 (18). Found, %: C 65.2; H 4.83; N 15.65. $C_{18}H_{16}N_4OS$. Calculated, %: C 64.26; H 4.79; N 16.65. *M* 336.41.

Ethyl 2-{[5-amino-3-(dicyanomethylidene)-2-phenyl-4-cyano-2,3-dihydrofuran-2-yl]sulfanyl}acetate (IIg). Yield 87%, mp 153–155°C (decomp.). IR spectrum, ν, cm^{-1}: 3210 (NH_2), 2200 (C≡N), 1650 (C=C). ^1H NMR spectrum, δ, ppm: 1.26 t (3H, CH_3, ^3J 7.1 Hz), 3.57 d (1H, SCH_2, ^2J 16.0 Hz), 3.62 d (1H, SCH_2, ^2J 16.0 Hz), 4.09–4.20 m ($OC\underline{H}_2CH_3$), 7.53–7.58 m (5H, Ph), 10.30 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 246 (33), 120 (30). Found, %: C 60.32; H 4.12; N 14.45. $C_{18}H_{14}N_4O_3S$. Calculated, %: C 59.01; H 3.85; N 15.29. *M* 366.39.

Ethyl 2-{[5-amino-3-(dicyanomethylidene)-2-(4-chlorophenyl)-4-cyano-2,3-dihydrofuran-2-yl]-sulfanyl}acetate (IIh). Yield 79%, mp 146–148°C (decomp.). IR spectrum, ν, cm^{-1}: 3190 (NH_2), 2210 (C≡N), 1660 (C=C). ^1H NMR spectrum, δ, ppm: 1.25 t (3H, CH_3, ^3J 7.1 Hz), 3.59 d (1H, SCH_2, ^2J 16.0 Hz), 3.64 d (1H, SCH_2, ^2J 16.0 Hz), 4.08–4.19 m (2H, $OC\underline{H}_2CH_3$), 7.58–7.62 m (4H, Ph), 10.33 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 400 (2), 402 (1), 280 (30), 282 (10), 245 (28). Found, %: C 54.21; H 4.12; N 12.77. $C_{18}H_{13}ClN_4O_3S$. Calculated, %: C 53.94; H 3.27; N 13.98. *M* 400.84.

Ethyl 2-{[5-amino-3-(dicyanomethylidene)-2-(4-methylphenyl)-4-cyano-2,3-dihydrofuran-2-yl]-sulfanyl}acetate (IIi). Yield 74%, mp 154–156°C (decomp.). IR spectrum, ν, cm^{-1}: 3210 (NH_2), 2250 (C≡N), 1665 (C=C). ^1H NMR spectrum, δ, ppm: 0.99 t (3H, CH_3, ^3J 7.1 Hz), 2.36 s (3H, $PhCH_3$), 3.60 d (1H, SCH_2, ^2J 16.0 Hz), 3.63 d (1H, SCH_2, ^2J 16.0 Hz), 4.07–4.20 m ($OC\underline{H}_2CH_3$), 7.36 d (2H, Ph, ^3J 8.2 Hz), 7.38 d (2H, Ph, ^3J 8.2 Hz), 10.18 s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 380 (13). Found, %: C 61.35; H 4.87; N 14.09. $C_{19}H_{16}N_4O_3S$. Calculated, %: C 59.99; H 4.24; N 14.73. *M* 380.42.

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