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SHORT COMMUNICATIONS

One-Pot Synthesis of 2-Alkylsulfanyldihydrofuran Derivatives from Tetracyanocyclopropyl Ketones

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Abstract—Successive treatment of 3-acylcyclopropane-1,1,2,2-tetracarbonitriles with sodium hydrogen carbonate and alkylmercaptan in water environment results in the formation of 2-(5-amino-2-aryl-2-alkylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene)propanedinitriles.

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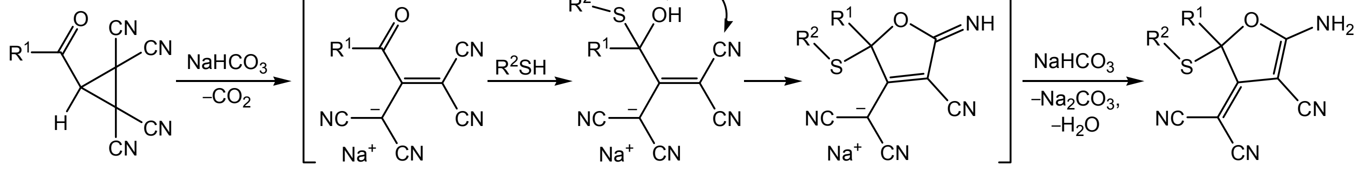
2-Acyltetracyanopropenides **2** are readily available [1] precursors for the synthesis of diverse polyfunctional heterocyclic compounds [2–4]. Formerly they were applied to the development of a synthesis method for 2-(5-amino-2-aryl-2-alkylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene)propanedinitriles **3** using hydrochloric acid as catalyst [5]. The disadvantages of this method consist in the necessity to apply a large excess of mercaptan and a low reproducibility at scaling the process. We established that the synthesis of dihydrofuran derivatives **3** could be performed at the catalysis with $NaHCO_3$ in water environment in good and high yields. Since propenides **2** are obtained at the reaction of tetracyanocyclopropyl ketones **1** with salts of weak acids in water solution we tested the possibility to combine the synthesis in a single process. The procedure of a multicomponent reaction did not provide the desired result probably due to the occurrence of competing reactions involving the cyano groups. The desired dihydrofurans **3** were prepared by successive treatment of cyclopropanes **1** first with $NaHCO_3$, and then after cooling the reaction mixture with equimolar quantity of alkylthiol. The presumed sequence of conversions includes the ring opening under the action of sodium hydrogen carbonate as a base with the formation of propenide **1**. Further thiol under catalysis with the base adds to the carbonyl group with subsequent heterocyclization. The reaction is completed by protonation to afford dihydrofurans **3**.

The refined procedure was tested by the example of several aryl tetracyanocyclopropyl ketones and alkylmercaptans which led to the preparation of 2-(5-amino-2-aryl-2-alkylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene)propanedinitriles **3a–3k**. The structure of compounds synthesized was proved by the data of



1a–1f **2a–2f** **3a–3k**

1, **2**, $R^1 = C_6H_5$ (**a**), $4\text{-}BrC_6H_4$ (**b**), $4\text{-}CH_3C_6H_5$ (**c**), $4\text{-}CH_3OC_6H_4$ (**d**), thien-2-yl (**e**), CH_3 (**f**); **3**, $R^2 = C_2H_5$, $R^1 = C_6H_5$ (**a**), $4\text{-}BrC_6H_4$ (**b**), $4\text{-}CH_3OC_6H_4$ (**c**), thien-2-yl (**d**); $R^2 = C_3H_7$, $R^1 = 4\text{-}BrC_6H_4$ (**e**), $4\text{-}CH_3OC_6H_4$ (**f**), thien-2-yl (**g**), CH_3 (**h**);

IR, ^{1}H and ^{13}C NMR, and mass spectra. Among the features of ^{1}H NMR spectra confirming the formation of dihydrofuran derivatives signals should be mentioned corresponding to the methylene unit of the alkylsulfanyl substituent linked directly to sulfur. Protons of this group are diastereotopic and appear as a multiplet built of two doublets of quartets or doublets of triplets.

2-(5-Amino-2-phenyl-4-cyano-2-ethylsulfanyl-2,3-dihydrofuran-3-ylidene)propanedinitrile (3a). A mixture of 0.246 g (0.001 mol) of 2,2,3,3-tetracyanocyclopropyl ketone **1a** and 0.168 g (0.002 mol) of sodium hydrogen carbonate in 2 mL of water was heated to boiling, and the boiling was continued till a transparent solution was obtained. The solution was cooled, 0.062 g (0.001 mol) of ethanethiol was added, and the mixture was stirred at room temperature to the completion of the reaction (TLC monitoring). Afterwards the separated precipitate was filtered off, washed with water, crystallized from acetic acid, and dried in air. Yield 0.265 g (86%). White crystalline powder, temp. decomp. 160–163°C (165–166°C [5]).

Compounds **3b–3k** were synthesized analogously.

2-[5-Amino-2-(4-bromophenyl)-4-cyano-2-ethylsulfanyl-2,3-dihydrofuran-3-ylidene]propanedinitrile (3b). Yield 0.306 g (79%), white powder, mp 155–158°C (decomp). IR spectrum, ν, cm^{-1}: 3260 (NH_2), 2214 (C≡N), 1683 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.23 t (3H, CH_3, ^3J 7.4 Hz), 2.53–2.73 m (2H, SCH_2), 7.51 d ($2H_{arom}$, ^3J 8.6 Hz), 7.70 d ($2H_{arom}$, ^3J 8.6 Hz), 10.32 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.9, 23.5, 54.7, 71.1, 103.4, 110.8, 113.6, 113.9, 124.5, 128.9, 132.2, 132.6, 168.0, 171.0. Mass spectrum, *m/z* (I_{rel}, %): 388/386 (1/1) $[M]^+$, 236 (9), 183/185 (6/9) $[ArCO]^+$, 157/155 (4.7/4.8) $[Ar]^+$, 62 (100). Found, %: C 49.44; H 2.87; N 14.42. $C_{16}H_{11}BrN_4OS$. Calculated, %: C 49.63; H 2.86; N 14.47. *M* 387.26.

2-[5-Amino-2-(4-methoxyphenyl)-4-cyano-2-ethylsulfanyl-2,3-dihydrofuran-3-ylidene]propanedinitrile (3c). Yield 0.274 g (81%), white powder, mp 162–164°C (decomp). IR spectrum, ν, cm^{-1}: 3165, 3250 (NH_2), 2207 (C≡N), 1670 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, CH_3, ^3J 7.4 Hz), 2.50–2.69 m (2H, SCH_2), 3.78 s (3H, OCH_3), 7.01 d ($2H_{arom}$, ^3J 8.9 Hz), 7.47 d ($2H_{arom}$, ^3J 8.9 Hz), 10.21 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.8, 23.5, 54.6, 55.3, 70.8, 104.2, 111.0, 113.8, 113.9, 114.0, 125.3, 128.2, 160.8, 168.7, 171.0. Mass spectrum, *m/z* (I_{rel}, %): 340 (41) $[M + 2]^+$, 338 (21) $[M]^+$, 322 (12), 296 (78), 268 (73), 236 (42), 134 (42), 107 (27), 88 (78), 62 (100). Found, %: C 60.55; H 4.16; N 16.48. $C_{17}H_{14}N_4O_2S$. Calculated, %: C 60.34; H 4.17; N 16.56. *M* 338.39.

2-[5-Amino-2-(thien-2-yl)-4-cyano-2-ethylsulfanyl-2,3-dihydrofuran-3-ylidene]propanedinitrile (3d). Yield 0.267 g (85%), white powder, mp 160–163°C (decomp). IR spectrum, ν, cm^{-1}: 3263 (NH_2), 2206 (C≡N), 1670 (C=C). ^{1}H NMR spectrum, δ, ppm: 1.22 t (3H, CH_3, ^3J 7.3 Hz), 2.53–2.74 m (2H, SCH_2), 7.12 d.d ($1H_{arom}$, ^3J 4.6, ^3J 4.0 Hz), 7.34–7.38 m ($1H_{arom}$), 7.76–7.82 m ($1H_{arom}$), 10.29 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 14.0, 24.3, 55.4, 70.5, 100.2, 110.8, 113.7, 113.8, 127.2, 128.7, 130.4, 136.3, 167.6, 170.3. Mass spectrum, *m/z* (I_{rel}, %): 316 (11) $[M + 2]^+$, 244 (32), 110 (27), 88 (87), 58 (100). Found, %: C 53.63; H 3.22; N 17.76. $C_{14}H_{10}N_4OS_2$. Calculated, %: C 53.49; H 3.21; N 17.82. *M* 314.38.

2-[5-Amino-2-(4-bromophenyl)-2-propylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (3e). Yield 0.309 g (77%), white powder, mp 181–184°C (decomp). IR spectrum, ν, cm^{-1}: 3360, 3255, 3155 (NH_2), 2216 (C≡N), 1682 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.96 t (3H, CH_3, ^3J 7.3 Hz), 1.49–1.67 m (2H, $SCH_2C\underline{H}_2$), 2.51–2.67 m (2H, SCH_2), 7.52 d ($2H_{arom}$, ^3J 8.7 Hz), 7.70 d ($2H_{arom}$, ^3J 8.7 Hz), 10.32 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.2, 21.7, 31.1, 54.7, 71.1, 103.3, 110.8, 113.6, 113.9, 124.5, 128.9, 132.2, 132.7, 168.0, 171.0. Mass spectrum, *m/z* (I_{rel}, %): 404/402/400 (6.2/9.2/5.3) $[M + 2]^+$ and $[M]^+$, 359 (12), 331 (21), 314 (31), 237 (42), 210 (72), 150 (98), 108 (100). Found, %: C 50.69; H 3.28; N 19.97. $C_{17}H_{13}BrN_4OS$. Calculated, %: C 50.88; H 3.27; N 13.96. *M* 401.28.

2-[5-Amino-2-(4-methoxyphenyl)-2-propylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (3f). Yield 0.278 g (79%), white powder, mp 150–153°C (decomp). IR spectrum, ν, cm^{-1}: 3150 (NH_2), 2214 (C≡N), 1652 (C=C). ^{1}H NMR spectrum, δ, ppm: 0.97 t (3H, CH_3, ^3J 7.3 Hz), 1.53–1.64 m (2H, $SCH_2C\underline{H}_2$), 2.49–2.63 m (2H, SCH_2), 3.78 s (3H, OCH_3), 6.99–7.04 m ($2H_{arom}$), 7.44–7.50 m ($2H_{arom}$), 10.21 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.2, 21.7, 31.1, 54.6, 55.2, 70.8, 104.1, 111.0, 113.9, 114.0, 114.5, 125.4, 128.1, 160.8, 168.8, 171.0. Mass spectrum, *m/z* (I_{rel}, %): 354 (31) $[M + 2]^+$, 352 (30) $[M]^+$, 310 (100), 268 (87), 236 (39), 134 (34), 88 (41), 76 (85). Found, %: C 61.12; H 4.59; N 15.96.

$C_{18}H_{16}N_4O_2S$. Calculated, %: C 61.35; H 4.58; N 15.90. *M* 352.41.

2-[5-Amino-2-propylsulfanyl-2-(thien-2-yl)-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (3g). Yield 0.272 g (83%), white powder, mp 137–140°C (decomp). IR spectrum, ν, cm^{-1}: 3260, 3342 (NH_2), 2209, 2212 (C≡N), 1673 (C=C). ^1H NMR spectrum, δ, ppm: 0.96 t (3H, CH_3, ^3J 7.3Hz), 1.52–1.63 m (2H, $SCH_2C\underline{H}_2$), 2.52–2.67 m (2H, SCH_2), 7.12 d.d (1H$_{arom}$, ^3J 5.0, ^4J 3.8 Hz), 7.36 d.d (1H$_{arom}$, ^3J 3.7, ^4J 1.0 Hz), 7.79 d.d (1H$_{arom}$, ^3J 5.1, ^4J 1.0 Hz), 10.28 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.2, 21.7, 31.8, 55.4, 70.5, 100.1, 110.8, 113.7, 113.8, 127.2, 128.7, 130.4, 136.2, 167.6, 170.3. Mass spectrum, *m/z* (I_{rel}, %): 330 (4) $[M]^+$, 287 (3), 245 (5), 111 (19) $[Ar]^+$, 88 (96), 58 (100). Found, %: C 55.01; H 3.69; N 17.11. $C_{15}H_{12}N_4OS_2$. Calculated, %: C 54.86; H 3.68; N 17.06. *M* 328.41.

2-(5-Amino-2-methyl-2-propylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene)propanedinitrile (3h). Yield 0.164 g (63%), white powder, mp 215–218°C (decomp). IR spectrum, ν, cm^{-1}: 3137, 3273, 3368 (NH_2), 2210, 2215 (C≡N), 1688 (C=C). ^1H NMR spectrum, δ, ppm: 0.91 t (3H, CH_3, ^3J 7.3 Hz), 1.42–1.54 m (2H, $SCH_2C\underline{H}_2$), 1.92 s (3H, CH_3), 2.36–2.54 m (SCH_2 + DMSO-d_6), 10.12 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.1, 21.9, 24.2, 30.9, 52.4, 70.3, 101.1, 111.1, 113.8, 114.6, 170.1, 171.2. Mass spectrum, *m/z* (I_{rel}, %): 260 (31) $[M]^+$, 217 (12), 201 (12), 185 (100), 75 (23). Found, %: C 55.16; H 4.66; N 21.44. $C_{12}H_{12}N_4OS$. Calculated, %: C 55.37; H 4.65; N 21.52. *M* 260.32.

2-[5-Amino-2-(4-bromophenyl)-2-butylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (3i). Yield 0.316 g (76%), white powder, mp 179–181°C (decomp). IR spectrum, ν, cm^{-1}: 3113, 3255 (NH_2), 2218 (C≡N), 1680 (C=C). ^1H NMR spectrum, δ, ppm: 0.87 t (3H, CH_3, ^3J 7.3 Hz), 1.32–1.47 m (2H, $SCH_2CH_2C\underline{H}_2$), 1.47–1.63 m (2H, $SCH_2C\underline{H}_2$), 2.52–2.70 m (2H, SCH_2), 7.52 d (2H$_{arom}$, ^3J 8.7 Hz), 7.69 d (2H$_{arom}$, ^3J 8.7 Hz), 10.32 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.3, 21.2, 28.8, 30.3, 54.7, 71.1, 103.3, 110.8, 113.6, 113.9, 124.5, 128.7, 132.2, 132.7, 168.0, 171.0. Mass spectrum, *m/z* (I_{rel}, %): 418/416 (2.2/3.6) $[M + 2]^+$, 374 (9), 237 (7), 211 (12), 57 (100). Found, %: C 52.26; H 3.65; N 19.17. $C_{18}H_{15}BrN_4OS$. Calculated, %: C 52.06; H 3.64; N 13.49. *M* 415.31.

2-[5-Amino-2-(*para*-tolyl)-2-butylsulfanyl-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (3j). Yield 0.280 g (80%), white powder, mp 160–163°C (decomp). IR spectrum, ν, cm^{-1}: 3166, 3250 (NH_2), 2208 (C≡N), 1656 (C=C). ^1H NMR spectrum, δ, ppm: 0.87 t (3H, CH_3, ^3J 7.3 Hz), 1.32–1.45 m (2H, $SCH_2CH_2C\underline{H}_2$), 1.49–1.61 m (2H, $SCH_2C\underline{H}_2$), 2.32 s (3H, CH_3), 2.51–2.67 m (2H, SCH_2), 7.29 d (2H$_{arom}$, ^3J 8.2 Hz), 7.42 d (2H$_{arom}$, ^3J 8.3 Hz), 10.24 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.3, 21.2, 28.6, 32.3, 54.7, 70.8, 104.2, 110.9, 113.8, 113.9, 126.5, 129.1, 130.3, 140.7, 168.6, 171.1. Mass spectrum, *m/z* (I_{rel}, %): 352 (27) $[M + 2]^+$, 350 (19) $[M]^+$, 335 (6) $[M - 15]^+$, 308 (40) $[M - C_3H_6]^+$, 293 (11) $[M - C_4H_9]^+$, 261 (26) $[M - SC_4H_9]^+$, 253 (81), 118 (43), 91 (75) $[Ar]^+$, 56 (100). Found, %: C 64.87; H 5.19; N 15.93. $C_{19}H_{18}N_4OS$. Calculated, %: C 65.12; H 5.18; N 15.99. *M* 350.44.

2-[5-Amino-2-butylsulfanyl-2-(*para*-tolyl)-4-cyano-2,3-dihydrofuran-3-ylidene]propanedinitrile (3k). Yield 0.277 g (81%), white powder, mp 144–146°C (decomp). IR spectrum, ν, cm^{-1}: 3116 (NH_2), 2210 (C≡N), 1673 (C=C). ^1H NMR spectrum, δ, ppm: 0.87 t (3H, CH_3, ^3J 7.3 Hz), 1.31–1.44 m (2H, $SCH_2CH_2C\underline{H}_2$), 1.48–1.60 m (2H, $SCH_2C\underline{H}_2$), 2.55–2.69 m (2H, SCH_2), 7.12 d.d (1H$_{arom}$, ^3J 5.0, ^3J 3.8 Hz), 7.39 d.d (1H$_{arom}$, ^3J 3.7, ^4J 1.1 Hz), 7.79 d.d (1H$_{arom}$, ^3J 5.1, ^4J 1.1 Hz), 10.28 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 13.3, 21.2, 29.5, 30.2, 55.4, 70.5, 100.1, 110.8, 113.7, 113.8, 127.2, 128.6, 130.3, 136.2, 167.8, 170.3. Mass spectrum, *m/z* (I_{rel}, %): 344 (7) $[M]^+$, 302 (8), 245 (17), 185 (9), 111 (16) $[Ar]^+$, 57 (100). Found, %: C 56.34; H 4.13; N 16.30. $C_{16}H_{14}N_4OS_2$. Calculated, %: C 56.12; H 4.12; N 16.36. *M* 342.44.

IR spectra were recorded on a Fourier spectrophotometer FSM-1202 from thin film (mull in mineral oil). ^1H and ^{13}C NMR spectra were registered on a spectrometer Agilent DDR2 400 at operating frequencies 400 and 101 MHz respectively, internal reference TMS. Mass spectra were taken on an instrument Shimadzu GCMS-QP 2010 SE (EI, 70 eV). Elemental analysis was carried out on a CHN-analyzer vario Micro cube. The homogeneity of compounds obtained was checked by TLC on plates Sorbfil PTCKh-AF-A-UF, development under UV irradiation and at heating.

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REFERENCES

1. Karpov, S.V., Grigor’ev, A.A., Kayukov, Ya.S., Karpova, I.V., Nasakin, O.E., and Tafeenko, V.A., *J. Org. Chem*., 2016, vol. 81, p. 6402.
2. Kayukov, Y.S., Karpov, S.V., Kayukova, O.V., Ershov, O.V., and Nasakin, O.E., *Russ. J. Org. Chem*., 2014, vol. 50, p. 1097. doi 10.1134/S1070428014080053
3. Grigor’ev, A.A., Karpov, S.V., Kayukov, Y.S., Nasakin, O.E., Gracheva, I.A., and Tafeenko, V.A., *Chem. Heterocycl. Compd*., 2017, vol. 53, p. 230. doi 10.1007/s10593-017-2044-6
4. Kayukov, Y.S., Karpov, S.V., Grigor’ev, A.A., Nikiforova, A.L., Nasakin, O.E., Shchegravina, E.S., Kayukova, O.V., and Tafeenko, V.A., *Chem. Heterocycl. Compd*., 2017, vol. 53, p. 568. doi 10.1007/s10593-017-2093-x
5. Karpov, S.V., Kayukov, Y.S., Bardasov, I.N., Ershov, O.V., Nasakin, O.E., and Kayukova, O.V., *Russ. J. Org. Chem*., 2011, vol. 47, p. 1161. doi 10.1134/S1070428011080070