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Synthesis of 2,3-Bis[allylsulfanyl(amino)methylidene]succinonitrile and Its Molecular and Crystal Structure

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Abstract—2,3-Bis[allylsulfanyl(amino)methylidene]succinonitrile was synthesized by alkylation of cyanothioacetamide with allyl bromide in DMF in the presence of aqueous potassium hydroxide, and its molecular and crystal structures were studied by X-ray analysis.

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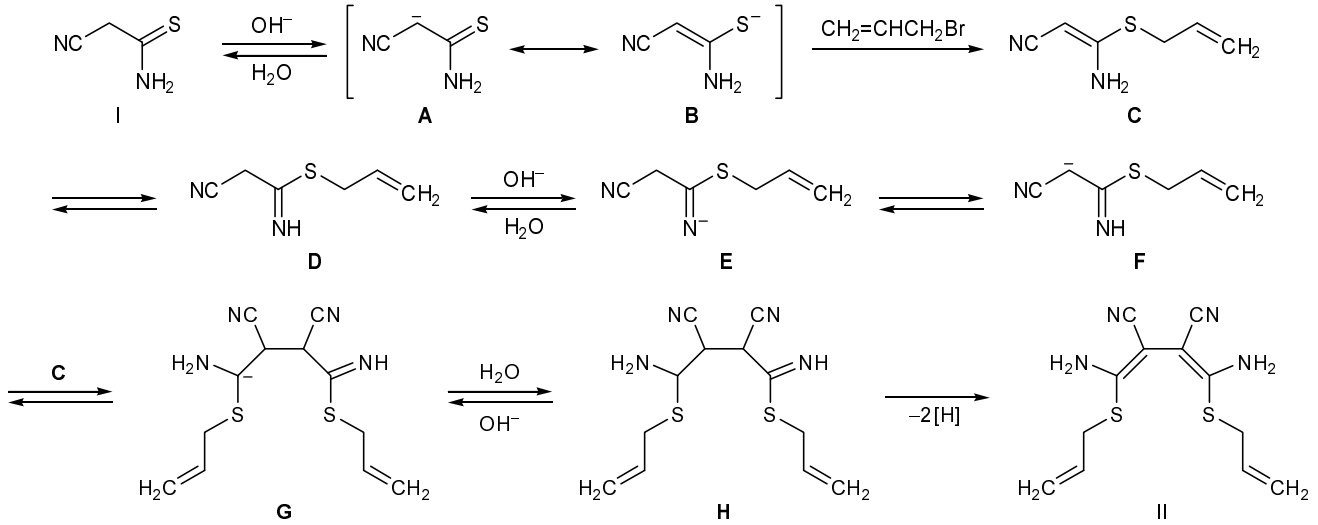
Cyanothioacetamide was synthesized for the first time in 1956 by the reaction of malononitrile with hydrogen sulfide [1]. At present, it is widely used in organic synthesis mainly as CH acid component in Knoevenagel condensations and Michael additions [2]. Cyanothioacetamide is also capable of undergoing dimerization to 4,6-diamino-3-cyanopyridine-2(1*H*)-thione according to Thorpe [3].

Reactions of cyanothioacetamide at the thioamide group are represented in the literature by several examples, including the reaction with phenacyl bromide and formation of thiazoles according to Hantzsch [4], S-alkylation with methyl iodide in the presence of sodium methoxide [5], and alkylation at the sulfur atom with ethyl bromide in the presence of sodium ethoxide [6]. In the two latter reactions, the resulting imidothioates were involved in heterocyclizations with anthranilic acid to obtain substituted 2-(4-oxo-3,4-dihydroquinazolin-2-yl)acetonitriles. We previously showed that 3,5-diaminothiophene-2-carbonitrile can be synthesized by alkylation of cyanothioacetamide with α-chloroacetonitrile [7].

Taking into account that the behavior of cyanothioacetamide (**I**) in reactions with alkyl halides has been studied relatively poorly, in the present work we examined its reaction with allyl bromide in DMF in the presence of alkali at 20°C. As a result, we isolated 2,3-bis[allylsulfanyl(amino)methylidene]succinonitrile

Scheme 1.



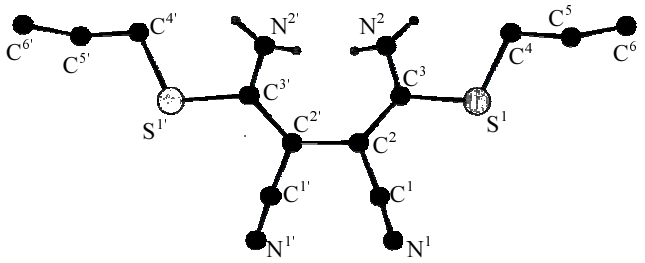


Fig. 1. Structure of the molecule of 2,3-bis[allylsulfanyl-(amino)methylidene]succinonitrile (**II**) according to the X-ray diffraction data. Hydrogen atoms (except for H^1 and H^2) are not shown.

(**II**) which attracts interest as potential protein kinase inhibitor [8]. A probable mechanism of formation of compound **II** is shown in Scheme 1. Deprotonation of cyanothioacetamide (**I**) by the action of aqueous potassium hydroxide gives carbanion **A** which can be stabilized as enethiolate **B**. Regioselective alkylation of intermediate **B** at the sulfur atom with allyl bromide leads to unsaturated sulfide **C** which undergoes prototropic rearrangement into imidothioate **D**. Deprotonation of the latter in basic medium yields anion **E** which is tautomeric to **F**. Carbanion **F** takes up molecule **C** according to the Michael addition pattern with formation of anionic adduct **G**, and proton addition to **G** gives intermediate **H**. The amine–imine tautomerization of **H** and subsequent dehydrogenation (presumably by the action of atmospheric oxygen) yields the final product, 2,3-bis[allylsulfanyl(amino)methylidene]-succinonitrile (**II**).

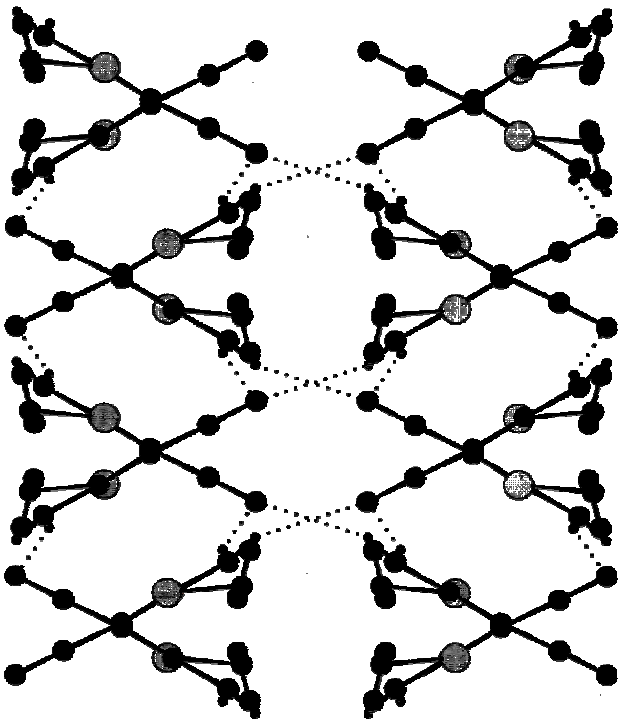


Fig. 2. A fragment of crystal packing of molecules **II**; intermolecular hydrogen bonds $N^2H^{1,2}\cdots N^1$ are shown with dotted lines.

The structure of compound **II** was proved by the X-ray diffraction data (Fig. 1). The N^2 atom adopts a configuration approaching planar–trigonal structure: the sum of the bond angles at that atom is 352.2°. Appreciable shortening of the N^2–C^3 bond [1.326(8) Å] and extension of the C^2=C^3 bond [1.365(8) Å] relative to the standard "purely" single N(sp^2)–C(sp^2) and double C(sp^2)=C(sp^2) bond lengths (1.43–1.45 [9, 10] and 1.30–1.33 Å [10–12], respectively) indicate essential conjugation between the lone electron pair on N^2 and π-electrons of the C^2=C^3 bond. The conformation of molecule **II** is quite favorable for such conjugation: the plane of the amino group N^2H^2 and the $C^{2'}C^1C^2C^3S^1N^2$ fragment are almost coplanar, the corresponding dihedral angle being 10.5°. On the other hand, the C^2=C^3 and $C^{2'}$=$C^{3'}$ π-bond systems are turned apart with respect to each other through an angle of 60.2° ($C^2C^3C^{2'}C^{3'}$); therefore, effective conjugation between these double bonds is hampered. In fact, the C^2–$C^{2'}$ bond length, 1.48(1) Å, coincides within the experimental error with the standard C(sp^2)–C(sp^2) bond length 1.476 Å [11]. The other geometric parameters of molecule **II** almost do not differ from their usual values (see table).

Molecules II in crystal give rise to a network (Fig. 2) via fairly weak intermolecular hydrogen bonds N^2–$H^1\cdots N^1$ and N^2–$H^2\cdots N^1$ with the following parameters: N^2–H^1 0.83(7), $N^2\cdots N^1$ 3.170(7), $N^1\cdots H^1$ 2.39(7) Å, $\angle N^2H^1N^1$ 156(5)°; N^2–H^2 0.83(7), $N^2\cdots N^1$ 3.128(7), $N^1\cdots H^2$ 2.37(7) Å, $\angle N^2H^2N^1$ 152(5)° (the average statistical N···N distance for hydrogen bonds like N–H···N is 2.98Å [13]).

EXPERIMENTAL

The X-ray diffraction data for a single crystal of compound **II** (0.22×0.28×0.56 mm) were acquired at 20°C on an Enraf–Nonius CAD-4 automatic four-circle diffractometer (MoK_α irradiation; scan rate ratio ω/2θ 1.2, θ_{max} 23°; spherical segment $0 \le h \le 14$, $0 \le k \le 17$, $-29 \le l \le 29$). Total of 2234 reflections were measured, 994 of which were symmetry-independent (averaging R factor 0.013). Rhombic crystals with the following unit cell parameters: a = 13.531(1), b = 15.535(3), c = 27.076(20) Å; V = 5691.2 $Å^3$;

Principal bond lengths *d* and bond angles ω in the molecule of 2,3-bis[allylsulfanyl(amino)methylidene]succinonitrile (**II**)

Bond	*d*, Å	Bond	*d*, Å	Angle	ω, deg	Angle	ω, deg	Angle	ω, deg
S^1–C^3	1.746(5)	C^1–C^2	1.410(9)	$C^3S^1C^4$	111.8(6)	$C^1C^2C^{2'}$	117.0(4)	$S^1C^3N^2$	117.7(5)
N^1–C^1	1.141(8)	C^2–$C^{2'}$	1.48(1)	$C^3S^1C^{14}$	108.1(6)	$C^1C^2C^3$	119.7(5)	$S^1C^3C^2$	118.3(4)
N^2–C^3	1.326(8)	C^2–C^3	1.365(8)	$N^1C^1C^2$	176.6(7)	$C^2C^{2'}C^3$	123.3(4)	$N^2C^3C^2$	124.1(5)

M 278.39; *Z* = 16, d_{calc} = 1.30 g/cm^3; μ = 3.47 cm^{-1}; space group *Fddd* (no, 70). The structure was solved by the direct method and was refined by the least-squares procedure in full-matrix anisotropic approximation using CRYSTALS software package [14]. The structure was refined using 541 reflections with $I > 2.5\sigma(I)$ (108 refined parameters, 5.0 reflections per parameter). The positions of the H^1 and H^2 atoms were determined from the difference synthesis of electron density and were refined in isotropic approximation; the positions of the other hydrogen atoms were set on the basis of geometry considerations, and they were included in the calculation with fixed positional and thermal parameters. Chebyshev's weight scheme [15] was used in the refinement with the following parameters: 0.97, 0.40, 0.69, 0.02, and 0.23. The final divergence factors were R = 0.073 and R_W = 0.073, GOF 1.127; residual electron density from the Fourier difference series 0.31 and –0.38 *e*/Å^3. The coordinates of atoms are available from the authors.

The IR spectrum of **II** was recorded on an IKS-40 spectrometer in mineral oil. The ^{1}H NMR spectrum was measured on a Bruker AM-300 instrument at 300.13 MHz in DMSO-d_6 using Me_4Si as internal reference. The melting point was determined on a Kofler melting point apparatus. The progress of the reaction was monitored by TLC on Silufol UV-254 plates using acetone–hexane (3:5) as eluent; spots were visualized by treatment with iodine vapor or under UV light.

2,3-Bis[allylsulfanyl(amino)methylidene]succinonitrile (II). Cyanothioacetamide (**I**), 1.0 g (10 mmol), was dissolved in 15 ml of DMF, 8.4 ml (10 mmol) of 10% aqueous potassium hydroxide and 0.85 ml (10 mmol) of allyl bromide were added in succession under stirring at 20°C, and the mixture was stirred for 3 h and left to stand for 2 days. The mixture was slowly diluted with an equal volume of water under stirring and was left to stand for 3 days at room temperature. The precipitate (brown rods) was filtered off and washed with water and propan-2-ol. Yield 46%, mp 167–168°C (from *i*-PrOH). IR spectrum, ν, cm^{-1}: 3212–3477 (NH_2), 2188 (C≡N), 1649 [δ(NH_2)]. ^{1}H NMR spectrum, δ, ppm: 3.67 d (4H, 2SCH_2, J = 6.55 Hz), 5.10 d (2H, 2CH_2=, J_{cis} = 9.48 Hz), 5.31 d (2H, 2CH_2=, J_{trans} = 17.39 Hz), 5.65–6.08 m (2H, 2CH=), 6.66 br.s (4H, 2NH_2). Found, %: C 51.64; H 4.89; N 20.02. $C_{12}H_{14}N_4S_2$. Calculated, %: C 51.77; H 5.07; N 20.13.

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