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SYNTHESIS AND STRUCTURE OF DIPYRIDO-1,4-DITHIINS[#]

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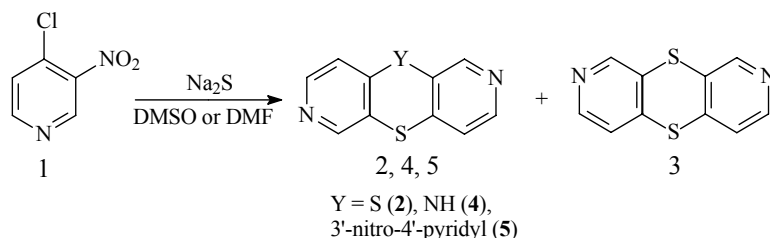
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Abstract – Synthesis, properties and reactions of two isomeric dipyrido-1,4-dithiins of the C_{2h} and C_{2v} symmetry are described. Their structure determination and identification are based on spectroscopic methods (¹H and ¹³C NMR, HETCOR, gHMBC and MS), physical properties (mp and R_f), the 1,4-dithiin ring opening reactions and finally X-Ray analysis. A very unusual type of the Smiles rearrangement (S→S, the pyridyl group migrates from one sulfur atom to another) during the 1,4-dithiin ring opening with sodium methanethiolate enabling isomerization of dithiin with the C_{2h} symmetry to dithiin with the C_{2v} symmetry is found.

INTRODUCTION

Diareno - and diheteroareno-1,4-dithiins are promising novel polyheterocyclic electron donors in the search of the organic materials with interesting electronic, optoelectronic and magnetic properties.¹⁻³ Our group found four fused pentacyclic diquino-1,4-dithiins that are useful substrates for obtaining various so far unknown quinoline derivatives of different types (disubstituted quinolines,^{4a,5} diquinoliny sulfides,^{4b,5-8} quinobenzothiazines^{4c} and their salts,^{4d} thiazinodiquinolines and related heterocyclodiquinolines^{4e} and quinoliny crown thioethers^{4f}). In our previous paper⁹ we described synthesis of the unknown dipyrido-1,4-dithiin (**3**) (systematic name: dipyrido[3,4-*b*;4',3'-*e*][1,4]dithiin) together with isomeric dipyrido-1,4-

dithiin (**2**) (systematic name: dipyrido[3,4-*b*;3',4'-*e*][1,4]dithiin) in the reaction of 4-chloro-3-nitropyridine (**1**) with sodium sulfide in DMSO at 140-150 °C for 10 h. The same reaction carried out in DMF led mainly to novel dipyrido-1,4-thiazines (**4**) and (**5**)⁹ (Scheme 1).



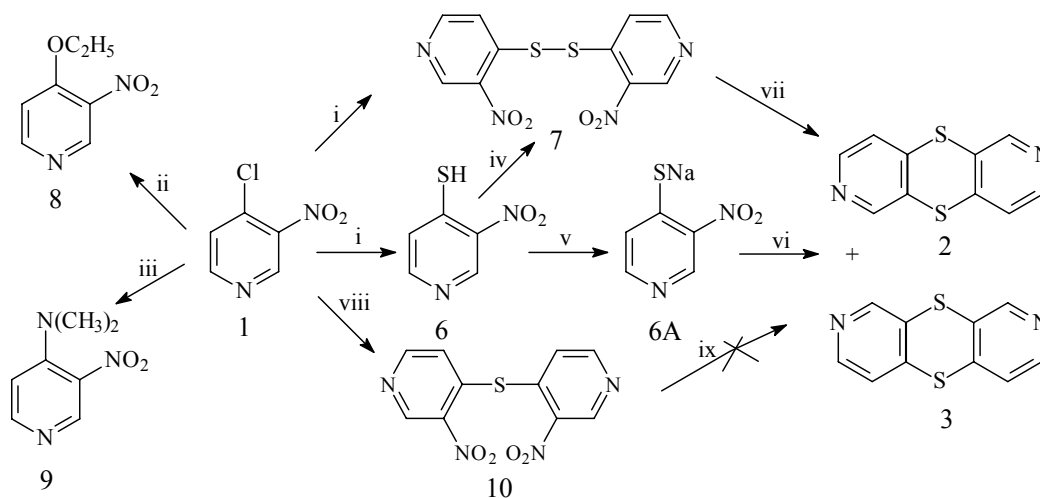
Scheme 1

Here, we report new synthetic methods of both dipyrido-1,4-dithiins (**2**) and (**3**), their structure determination and discrimination on the basis of the spectroscopical data, physical properties, chemical transformations and X-Ray analysis.

RESULTS AND DISCUSSION

Synthesis

In order to improve the yields of dipyrido-1,4-dithiins (**2**) and (**3**), we examined reactions of 4-chloro-3-nitropyridine (**1**) with sulfur reagents (sodium hydrosulfide, sodium sulfide, thiourea) in selected solvents (methanol, ethanol, HMPT) but we obtained only products of the chloro substitution: 4-mercapto-3-nitropyridine (**6**), 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**), 4-ethoxy-3-nitropyridine (**8**) and 4-dimethyl-amino-3-nitropyridine (**9**) (as a result of the action of ethanol and HMPT). Attempts of cyclization of compound (**6**) in MEDG (monomethyl ether of diethylene glycol) and sulfolane gave only disulfide (**7**). Only the cyclization of sodium 3-nitro-4-pyridinethiolate (**6A**) carried out in DMSO at 160 °C gave dipy-

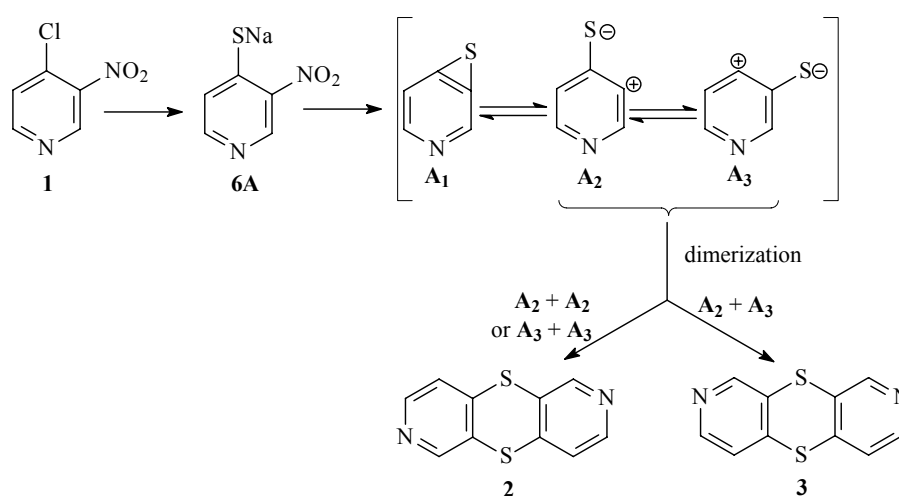


Scheme 2 Reagents: i, NaSH, Na₂S or thiourea, MeOH or EtOH; ii, Na₂S, EtOH, autoclave; iii, Na₂S, HMPT; iv, MEDG or sulfolane; v, MeONa, MeOH; vi, DMSO, vii, DMSO, NaOH; viii, (**6**), DMF; ix, Na₂S, DMSO.

rido-1,4-dithiins (**2**) and (**3**) in 28% and 21% yields. We also tried to transform disulfide (**7**) and sulfide

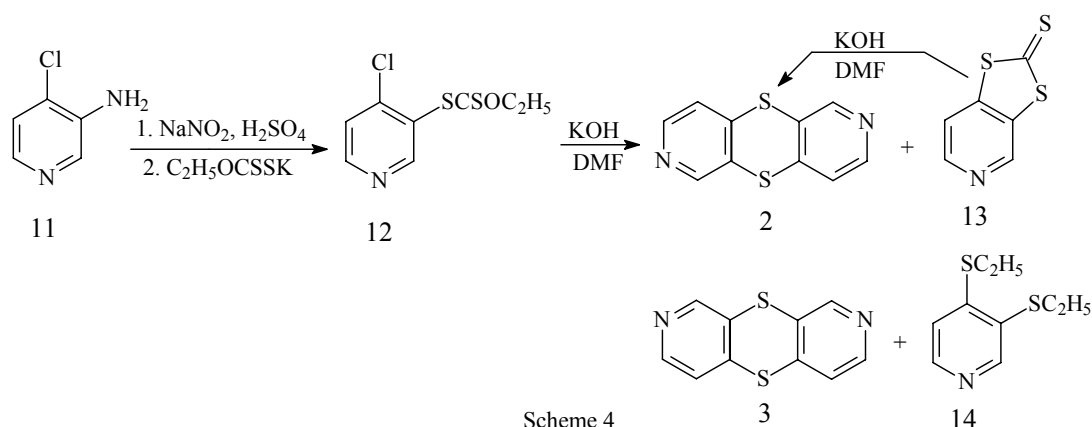
(10) (obtained from compounds (1) and (6)) into dithiins (2) and (3), respectively. Whereas the reaction of disulfide (7) with sodium hydroxide in DMSO at 160 °C gave both dithiins (2) and (3) in 28% and 28% yields, the reaction of sulfide (10) with sodium sulfide to form only dithiin (3) failed (giving only compound (6)) (Scheme 2).

The formation of both dipyrindodithiins (2) and (3) from compound (1) can be explained by analogy to the formation of substituted dipyridazodithiins.^{11,12} The reaction proceeds probably through active intermediates thiirene (**A**₁) and 1,3-dipolar species (**A**₂) and (**A**₃) which dimerize *per se* or crossed to give dithiins (2) and (3) respectively (Scheme 3).



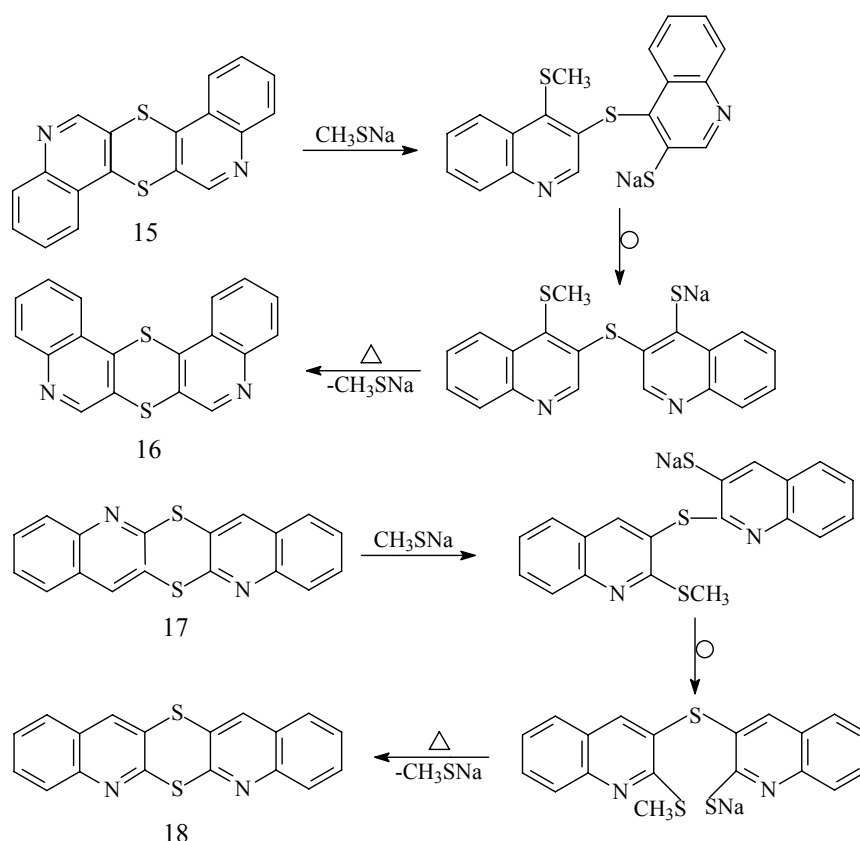
We also re-examined the procedure of the synthesis of dipyrido-1,4-dithiin (2) from 4-chloro-3-aminopyridine (11) *via* diazotization, substitution of the diazonium group by the xanthate group and hydrolysis of the obtained ethyl 4-chloro-3-pyridinedithiocarbonate (12) followed by cyclization, originally described by Krowicki and Nantka-Namirski,¹² giving dithiin (2) in 35 % yield. As we assumed the cyclization proceeds smoothly in aprotic solvents we changed boiling methanol into boiling DMF. In this way we obtained not only dithiin (2) in 40% yield but also small amounts of dithiin (3), pyridodithiolethione (13) and 3,4-diethylthiopyridine (14). We found dithiolethione (13) to be smoothly transformed into dithiin (2) in 92% yield in DMF in the presence of potassium hydroxide (Scheme 4).

As the yield of dithiin (3) was still unsatisfactory we decided to isomerize dithiin (2) via the 1,4-dithiin ring opening - ring closure reactions. In our previous papers^{8,13} we carried out isomerization of two diquino-1,4-dithiins with the C_{2h} symmetry (15) and (16) into diquino-1,4-dithiins with the C_{2v} symmetry (17) and (18). We found that the primary products of the 1,4-dithiin ring opening in dithiins (15) and (16) with sodium methanethiolate, sodium salts of 3'-mercapto-4-methylthio-3,4'-diquinoliny sulfide and of 3-mercapto-2'-methylthio-2,3'-diquinoliny sulfide, underwent an unprecedented S→S type of the Smiles rearrangement^{5,6,8,13} (the quinoliny groups migrate from one sulfur atom to another) to sodium salts of 4'-mercapto-4-methylthio-3,3'-diquinoliny sulfide and of 2-mercapto-2'-methylthio-3,3'-diquinoliny sulfi-

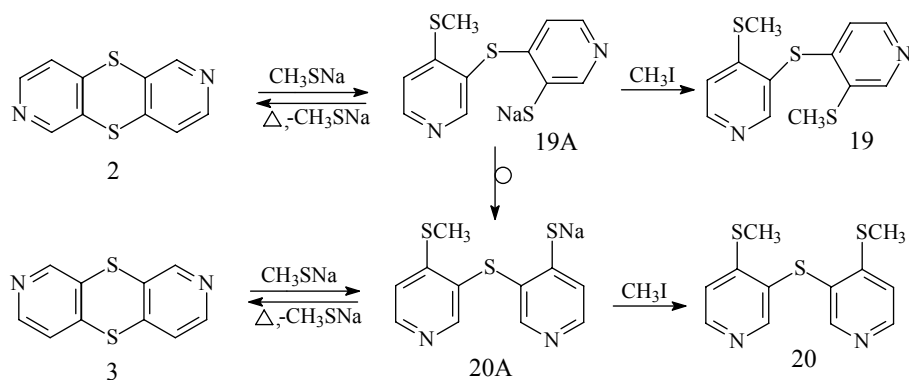


de in the reaction conditions (DMSO at 20 °C, 70 °C and 140 °C, respectively) (Scheme 5). Similar to the reactions of diquino-1,4-dithiins (**15-18**)^{5,6,8,13,14} the model reactions of dithiins (**2**) and (**3**) with sodium methanethiolate in DMSO at 70 °C followed by S-methylation with methyl iodide led to isomeric x,y-dimethylthio-3,4'- and 3,3'-dipyridinyl sulfides (**19**) and (**20**) (x,y = 3',4 and 4,4', respectively) in 79% yield. When the reaction of dithiin (**2**) was carried out at 170 °C the S→S type of the Smiles rearrangement was observed and after methylation 4,4'-dimethylthio-3,3'-dipyridinyl sulfide (**20**) was obtained.

In this case the primary product, sodium salt of 4-methylthio-3'-mercapto-3,4'-dipyridinyl sulfide (**19A**) underwent the rearrangement into sodium salt of 4-methylthio-4'-mercapto-3,3'-dipyridinyl sulfide (**20A**). The last sulfide heated instead of alkylation gave the 1,4-dithiin ring closure product, dithiin (**3**) in 50% yield. Since the unrearranged dithiin (**2**) was also recovered in 32% the efficiency of the rearrangement



was 74% taking into account the converted dithiin (**2**) (Scheme 6). The reverse isomerization of dithiin (**3**) to dithiin (**2**) was unsuccessful, dithiin (**3**) was isolated in 87% yield. The observed rearrangement is very unusual because the nucleophilic attack of the thiolate anion occurs at the position 3 in the pyridine ring, which is not susceptible as a rule for such attack. The more reactive position 2 remains unaffected. It is worth noting that *ab initio* calculations¹⁵ of all dipyridinyl sulfides showed possibility of the Smiles rearrangement for 2,2'-, 2,3'- and 2,4'-dipyridinyl sulfides and in fact, the rearrangement of the S→N type was observed only for 2,2'- and 2,4'-isomers.¹⁶ Our findings are the first examples of the Smiles rearrangement of 3,4'-dipyridinyl sulfide (the S→S type) observed during isomerization of dithiin (**2**) and of 4,4'-dipyridinyl sulfide (the S→N type) observed during synthesis of dipyrindo-1,4-thiazines (**4**) and (**5**).⁹



X-Ray analysis

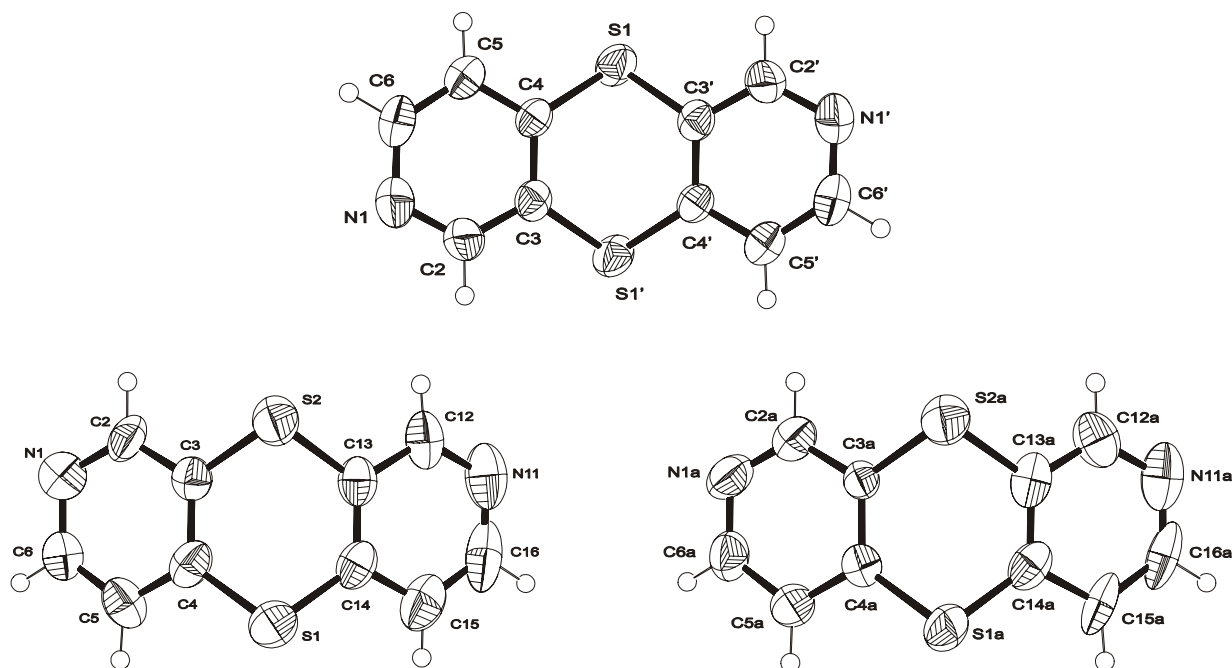


Figure 1. ORTEP drawings of dipyrindo-1,4-dithiins (**2**) and (**3**).

None of six isomeric dipyrido-1,4-dithiins has been X-Ray analyzed. Both isomeric dipyrido-1,4-dithiins (**2**) and (**3**) have pairs of the identical 3,4-pyridinediyl units, therefore they are difficult to distinguish. A problem in the determination of the correct structures of diazino-1,4-dithiins was put forward by some authors.¹⁷⁻¹⁹ The structure of dithiin (**2**) was determined until now on the basis of calculated and experimental dipole moment¹⁰ and *via* logical sequence of dimerization of the 4-pyridylthio radical resulted in thermolysis of 4,4'-dipyridinyl disulfide at 250 °C.²⁰ Since spectroscopic evidences are indirect and subtle, chemical ones sometimes dubious (with the regard to isomerization and rearrangement) only X-Ray analysis as a direct proof can give a final answer regarding the structure determination. Crystals of both dithiins for X-Ray analysis were grown from DMF, however, the crystals of dithiin (**3**) were twinned what makes the analysis difficult. Moreover synchrotron radiation was used to overcome the weakness of the diffracted intensities. Similarly to dithiin (**16**),⁸ dithiin (**3**) crystallized also with two molecules in the unit cell. This X-Ray study is the final confirmation of both compounds (**2**) and (**3**) as dipyrido[3,4-*b*;3',4'-*e*]-[1,4]dithiin and dipyrido[3,4-*b*;4',3'-*e*][1,4]dithiin, respectively. In contrast to planar dipyrazo-1,4-dithiin²¹ both dipyrido-1,4-dithiins (**2**) and (**3**) are folded mainly along the S...S axis and additionally along the C-C axes between the dithiin and pyridine rings (Figure 1). The central dithiin ring is in a boat conformation with the sulfur atoms deviating from the central CCCC plane. The 3-pyridinyl-sulfur bond is slightly longer than the 4-pyridinyl-sulfur bond in the both dithiins. Table 1 contains selected geometrical features of dithiins (**2**) and (**3**).

Table 1. Selected details of the molecular geometry of dithiins (**2**) and (**3**)

Geometrical feature	Dithiin (2)	Dithiin (3)	
		Molecule 1	Molecule 2
3-pyridinyl-sulfur bond (Å)	1.763(3)	1.768(3), 1.765(7)	1.777(7), 1.769(7)
4-pyridinyl-sulfur bond (Å)	1.757(3)	1.762(7), 1.755(8)	1.768(7), 1.755(8)
CSC angle (°)	101.41(14)	100.6(3), 100.9(3)	100.6(3), 100.6(3)
Dihedral angle between the pyridine rings (°)	43.91(8)	46.8(4)	42.6(3)
Dihedral angle between the halves of the dithiin ring (°)	48.08(7)	50.8(4)	48.8(4)
Displacement of the sulfur atoms from the central plane (Å)	0.607(2)	0.635(3)	0.589(3)
		0.647(3)	0.641(3)

¹H and ¹³C NMR spectral assignment dipyrido-1,4-dithiins (**2**) and (**3**).

The ¹H and ¹³C NMR spectra of both dipyrido-1,4-dithiins (**2**) and (**3**) revealed the symmetry of dithiins because the numbers of the proton and carbon signals were half the number of nuclei in the molecules.

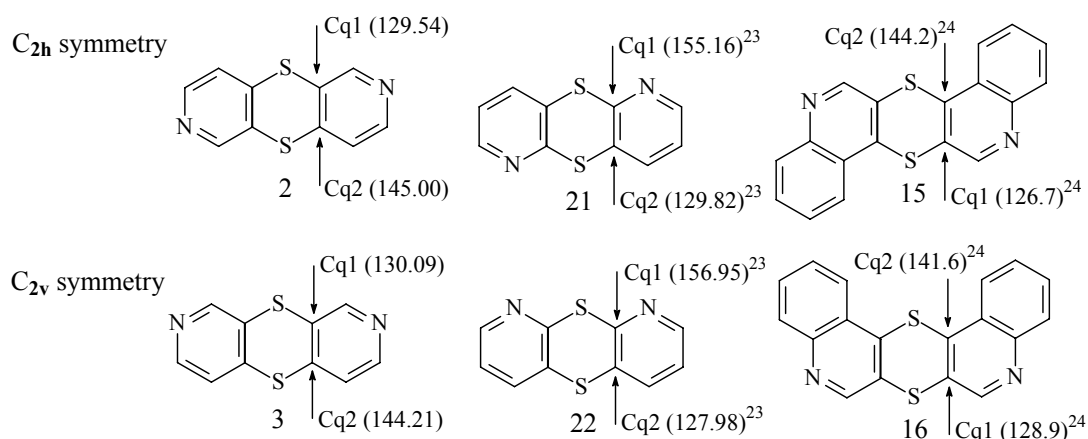
The ^1H NMR spectra showed one singlet signal at $\delta = 8.58$ ppm for dithiin (**2**) and at $\delta = 8.63$ ppm for dithiin (**3**) and two doublet signals with ortho coupling at $\delta = 7.39$ ppm and $\delta = 8.45$ ppm for dithiin (**2**), and at $\delta = 7.38$ ppm and $\delta = 8.46$ ppm for dithiin (**3**), easy to assign on the basis of the 3- and 4-pyridyl proton signals.²² The ^{13}C NMR spectra showed three tertiary carbon signals and two quaternary carbon signals. In order to assign unquestionably all these signals 2D NMR techniques: HETCOR and gHMBC were used. Whereas the HETCOR spectrum permitted the assignment of the tertiary carbon signals and the proton signals *via* one-bond correlations, the gHMBC spectrum made possible the assignment of the quaternary carbon signals *via* two-bond and three-bond correlations with the proton signals. These correlations allowed the unambiguous determinations of the proton and carbon signals in dithiins (**2**) and (**3**) (Table 2).

Table 2. The complete ^1H and ^{13}C NMR spectral assignment and summary of the HETCOR and gHMBC correlations for both dithiins (**2**) and (**3**)

Dithiin	^1H NMR spectral assignment δ (ppm)	^{13}C NMR spectral assignment δ (ppm)	HETCOR One-bond coupling δ (ppm)	g HMBC	
				two-bond coupling δ (ppm)	three- bond coupling δ (ppm)
(2)	H1/H6 (8.58, s)	C1/C6 (148.03)	8.58/148.03	8.58/129.54	8.58/145.00
	H3/H8 (8.45, d, J=5.0 Hz)	C3/C8 (148.50)	8.45/148.50	8.45/123.27	8.58/148.50
	H4/H9 (7.39, d, J=5.0 Hz)	C4/C9 (123.27)	7.39/123.27	7.39/148.50	8.45/145.00
		C4a/C9a (145.00)			8.45/148.03
		C5a/C10a (129.54)			7.39/129.54
(3)	H1/H9 (8.63, s)	C1/C9 (148.48)	8.63/148.48	8.63/130.09	8.63/144.21
	H3/H7 (8.46, d, J=5.0 Hz)	C3/C7 (148.42)	8.46/148.42	8.46/123.29	8.63/148.42
	H4/H6 (7.38, d, J=5.0 Hz)	C4/C6 (123.29)	7.38/123.29	7.38/148.42	8.46/144.21
		C4a/C5a (144.21)			8.46/148.48
		C9a/C10a (130.09)			7.38/130.09

Comparison of dipyrido-1,4-dithiins (**2**) and (**3**).

Tricyclic dipyrido-1,4-dithiins (**2**) and (**3**) represent two classes of symmetry: point groups C_{2h} and C_{2v} . We found in our previous paper⁸ pentacyclic diquino-1,4-dithiins (**15-18**) of the C_{2h} and C_{2v} symmetry to show some regularities in physical (mp, R_f) and spectroscopic data (^1H NMR and MS) which enabled their distinction. In this paper we would like to show some regularities in physical and spectroscopic data connected with the symmetry of dipyrido-1,4-dithiins (**2**) and (**3**). Similar to our previous findings dithiin



Scheme 7

with the C_{2h} symmetry (**2**) showed higher melting point and higher R_f values (a more mobile isomer) than the isomer with the C_{2v} symmetry (**3**) as a result of its higher thermal stability and less polarity (Table 3).

Table 3. Comparison of the physical and spectroscopic data of dipyrido-1,4-dithiins (**2**) and (**3**)

No	Physical and spectroscopic data	Dipyrido-1,4-dithiins	
		(2)	(3)
1	Melting point ($^{\circ}\text{C}$)	174-175 ¹²	146-147
2	TLC (R_f , spot colour)		
	a. silica gel, $\text{CHCl}_3\text{-C}_2\text{H}_5\text{OH}$ (10:1)	0.54 pale pink	0.50 pale pink
	b. aluminum oxide, CH_2Cl_2	0.55 pale pink	0.48 pale pink
3	^{13}C NMR, δ (ppm)		
	Cq1	129.54	130.09
	Cq2	145.00	144.21
4	MS 70 eV, m/z (%)		
	a. 218 (M)	100	100
	b. 191 (M-HCN)	48	37
	c. 186 (M-S)	6	5
	d. 174 (M-CS)	12	11

Analyzing quaternary carbon signals of the dithiin ring in the ^{13}C NMR spectra of dipyrido-1,4-dithiins (**2**) and (**3**), isomeric dipyrido-1,4-dithiins (**21**) and (**22**)²³ and the quinoline analogs (**15**) and (**16**),²⁴ we found regularity connected with an influence of the both electron-accepting nitrogen atoms on the chemical shift (Scheme 7). In all these pairs of isomers the carbon Cq1 signal is found more upfield and the carbon Cq2 signal more downfield for the isomers with C_{2h} symmetry in comparison to the isomers with C_{2v} symmetry. These data enable distinction both isomers.

MS spectra of dipyrindo-1,4-dithiins (**2**) and (**3**) showed formation of $[M-S]^+$, $[M-HCN]^+$ and $[M-CS]^+$ fragmentary ions but in contrast to diquino-1,4-dithiins (**15-18**) we could not find any differences between the isomers.

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Boetius melting point apparatus and are uncorrected. The ^1H and ^{13}C NMR spectra and the HETCOR correlations were recorded on a Varian Unity-Inova-300 spectrometer at 300.08 and 75.45 MHz in deuteriochloroform and dimethyl sulphoxide- d_6 with tetramethylsilane as the internal standard. The gHMBC correlations were recorded on a Bruker DRX spectrometer at 500.13 and 125.77 MHz. Electron impact mass spectra (EI MS) were run on a Finnigan MAT 95 spectrometer at 70 eV. The thin layer chromatography of dipyrindo-1,4-dithiins (**2**) and (**3**) were performed on silica gel 60 F₂₅₄ (Merck 1.05735) with chloroform-ethanol (10:1 v/v) and on aluminum oxide 60 F₂₅₄ neutral (type E) (Merck 1.05581) with methylene chloride as eluent.

Synthesis

4-Chloro-3-nitropyridine (**1**) and 3-amino-4-chloropyridine (**11**)

4(*1H*)-Pyridinone was nitrated with fuming nitric acid and 30% oleum to give 3-nitro-4(*1H*)-pyridinone according to described procedure²⁵ [mp 279-280 °C (water), lit.,²⁵ mp 280-281 °C]. As the published²⁵ ^1H NMR spectrum showed the acidic NH proton at a dubious region of $\delta = 3.60$ ppm, we re-examined the spectrum: ^1H NMR (DMSO- d_6) δ : 6.48 (d, $J = 7.5$ Hz, 1H, H5), 7.77 (dd, $J = 1.2$ and 7.5 Hz, 1H, H6), 8.79 (d, $J = 1.2$ Hz, 1H, H2), 12.3 (br s, 1H, NH). When nitration was performed with more concentrated acids the main product was 3,5-dinitro-4(*1H*)-pyridinone [mp > 300 °C (water), lit.,²⁶ mp 325 °C].

3-Nitro-4(*1H*)-pyridinone was chlorinated with phosphorus pentachloride and phosphorus oxychloride to give 4-chloro-3-nitropyridine (**1**) according to described procedure²⁷ (mp 43-45 °C, lit.,²⁷ mp 45 °C). ^1H NMR (CDCl₃) δ : 7.56 (d, $J = 5.4$ Hz, 1H, H5), 8.71 (d, $J = 5.4$ Hz, 1H, H6), 9.14 (s, 1H, H2).

3-Amino-4-chloropyridine (**11**) was obtained by reduction of 4-chloro-3-nitropyridine (**1**) with tin chloride according to described procedure²⁸ [mp 58-59 °C (petroleum ether), lit.,²⁹ mp 59.5-60.5 °C].

Reactions of 4-chloro-3-nitropyridine (**1**) with sulfur reagents

A. With sodium hydrogensulfide

To a solution of 4-chloro-3-nitropyridine (**1**) (0.32 g, 2 mmol) in ethanol (5 mL) sodium hydrogensulfide (NaSH \times $n\text{H}_2\text{O}$, Aldrich, 0.5 g, *ca.* 5 mmol) was added and the reaction mixture was boiled for 10 min. After cooling ethanol was evaporated in vacuo, water (2 mL) was added to the residue. An insoluble solid was filtered off, washed with water and air-dried to give 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**) (0.06 g, 19%); mp 234-235 °C (ethanol), lit.,²⁷ mp 235 °C. ^1H NMR (CDCl₃) δ : 7.74 (d, $J = 5.5$ Hz, 1H, H5), 8.70 (d, $J = 5.5$ Hz, 1H, H6), 9.49 (s, 1H, H2). The filtrate was acidified with 10% hydrochloric acid

to pH = 5. The resulting yellow solid was filtered off, washed with water and air-dried to give 4-mercapto-3-nitropyridine (**6**) (0.20 g, 64%); mp 152-154 °C, lit.,²⁷ mp 153 °C). ¹H NMR (DMSO-d₆) δ: 7.90 (d, J = 5.4 Hz, 1H, H5), 8.70 (d, J = 5.4 Hz, 1H, H6), 9.43 (s, 1H, H2), 13.2 (br s, 1H, SH).³⁰

When this reaction was carried out for 30 min. 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**) (0.22 g, 71%) and 4-mercapto-3-nitropyridine (**6**) (0.02 g, 6%) was isolated.

B. With thiourea

A solution of 4-chloro-3-nitropyridine (**1**) (0.159 g, 1 mmol) and thiourea (0.152 g, 2 mmol) in methanol (4 mL) was boiled for 2 h. After cooling the resulting solid was filtered off, washed with water and air-dried to give 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**) (0.11 g, 71%); mp 234-235 °C (ethanol), lit.,²⁷ mp 235 °C. The filtrate was diluted with water (8 mL), alkalized with 10% aqueous sodium hydroxide and next acidified with 15% hydrochloric acid to pH = 5. The resulting yellow solid was filtered off, washed with water and air-dried to give 4-mercapto-3-nitropyridine (**6**) (0.030 g, 19%); mp 152-154 °C, lit.,²⁷ mp 153 °C.

C. With sodium sulfide in ethanol

To a solution of 4-chloro-3-nitropyridine (**1**) (0.159 g, 1 mmol) in ethanol (5 mL) in an autoclave sodium sulfide (0.234 g, 3 mmol) was added and the reaction mixture was let with argon and next heated at 150 °C for 6 h. After cooling a resulting inorganic salt was removed by filtration, washed with ethanol and the filtrate was evaporated to dryness. The residue was purified by column chromatography (silica gel, chloroform) to give 4-ethoxy-3-nitropyridine (**8**) (0.140 g, 83%); mp 48-49 °C (ether), lit.,³¹ mp 46.5-48 °C.

D. With sodium sulfide in HMPT

To a solution of 4-chloro-3-nitropyridine (**1**) (0.159 g, 1 mmol) in HMPT (3 mL) sodium sulfide (0.234 g, 3 mmol) was added and the reaction mixture was heated under argon on an oil bath at 155 °C for 4 h. After cooling the reaction mixture was poured into water (15 mL) and extracted with chloroform (3 x 10 mL). The extract was dried with anhydrous calcium chloride and evaporated in vacuo. The residue was purified by column chromatography (silica gel, chloroform) to give 4-dimethylamino-3-nitropyridine (**9**) (0.160 g, 95%); mp 48-49 °C (ether), lit.,³² mp 48-49 °C.

3,3'-Dinitro-4,4'-dipyridinyl sulfide (**10**)

To a solution of 4-chloro-3-nitropyridine (**1**) (0.159 g, 1 mmol) in dry DMF (5 mL) 4-mercapto-3-nitropyridine (**6**) (0.156 g, 1 mmol) was added, the mixture was let with argon and kept at 5 °C for 48 h. The mixture was poured into water (15 mL) and the resulting solid was filtered off, washed with water and air-dried to give 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**) (0.03 g, 19%); mp 234-235 °C (ethanol), lit.,²⁷ mp 235 °C). The filtrate was extracted with chloroform (3 x 10 mL). The extract was dried with

anhydrous calcium chloride and evaporated in vacuo. The residue was purified by column chromatography (silica gel, chloroform) to give:

1. 3,3'-dinitro-4,4'-dipyridinyl sulfide (**10**) (0.11 g, 40%); mp 128-129 °C (ethanol), lit.,²⁷ mp 129-130 °C. ¹H NMR (CDCl₃) δ: 7.26 (d, J = 4.8 Hz, 1H, H5), 8.72 (d, J = 4.8 Hz, 1H, H6), 9.39 (s, 1H, H2).
2. 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**) (0.02 g, 13%); mp 234-235 °C (ethanol), lit.,²⁷ mp 235 °C.

Attempts of cyclization of 4-mercapto-3-nitropyridine (**6**)

A solution of 4-mercapto-3-nitropyridine (**6**) (0.156 g, 1 mmol) in MEDG (3 mL) or sulfolane (3 mL) was heated under argon on an oil bath at 160 °C for 2 h. After cooling the reaction mixture was poured into water (9 mL) and the resulting solid was filtered off, washed with water and air-dried to give 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**) (0.08 g, 52% in MEDG; 0.084 g, 54% in sulfolane); mp 234-235 °C (ethanol), lit.,²⁷ mp 235 °C.

Dipyrido-1,4-dithiins (**2**) and (**3**)

A. From sodium 3-nitro-4-pyridinethiolate (**6A**)

A solution of sodium 3-nitro-4-pyridinethiolate (**6A**) (0.18 g, 1 mmol) (obtained from equimolar amounts of 4-mercapto-3-nitropyridine and sodium methanolate in dry methanol followed by evaporation of the solvent) in dry DMSO (3 mL) was heated under argon on an oil bath at 160 °C for 20 h. After cooling the reaction mixture was poured into water (6 mL) and the resulting solid was filtered off, washed with water and air-dried. The filtrate was extracted with chloroform (3 x 20 mL). The extract was dried with anhydrous sodium sulfate and evaporated in vacuo to dryness. Combined solids were separated by column chromatography (silica gel, chloroform) to give:

1. dipyrido-1,4-dithiin (**2**) (0.031 g, 28%); mp 174-175 °C (ethanol), lit.,¹² mp 174-175 °C.
2. dipyrido-1,4-dithiin (**3**) (0.023 g, 21%); mp 146-147 °C (ethanol). Anal. Calcd for C₁₀H₆N₂S₂: C 55.02, H 2.77, N 12.83. Found: C 54.94, H 2.81, N 12.69.

B. From 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**)

To a solution of 3,3'-dinitro-4,4'-dipyridinyl disulfide (**7**) (0.31 g, 1 mmol) in dry DMSO (6 mL) sodium hydroxide (0.12 g, 3 mmol) was added. The reaction mixture was heated under argon on an oil bath at 160 °C for 20 h. After cooling the reaction mixture was poured into water (6 mL) and extracted with chloroform (3 x 20 mL). The extract was dried with anhydrous calcium chloride and evaporated in vacuo to dryness. Combined solids were separated by column chromatography (silica gel, chloroform) to give dipyrido-1,4-dithiin (**2**) (0.06 g, 28%) and dipyrido-1,4-dithiin (**3**) (0.06 g, 28%).

C. From 3-amino-4-chloropyridine (**11**)

To a solution of 3-amino-4-chloropyridine (**11**) (1.00 g, 7.8 mmol) in 20% solution of sulfuric acid (8 mL) at -10 °C aqueous solution (2 mL) of sodium nitrite (0.60 g, 8.7 mmol) was added dropwise keeping the temperature. Next aqueous solution (3 mL) of potassium xanthate (2.50 g, 15.6 mmol) was added

dropwise and the resulting solid was filtered off using chilled funnel. The filtrate was extracted with carbon tetrachloride (3 x 20 mL). Combined extracts (the solid was also dissolved in carbon tetrachloride) were dried with anhydrous calcium chloride and evaporated to half volume under vacuo, boiled for 10 min and next evaporated to the dryness to obtain an oil (1.3 g). The oil was dissolved in DMF (10 mL) and potassium hydroxide (0.5 g, 8.9 mmol) was added and the reaction mixture was boiled for 2.5 h. After cooling the solvent was evaporated and the residue was dissolved in chloroform (15 mL). The solution was washed with water, dried with calcium chloride and evaporated to the dryness. Separation by column chromatography (silica gel, chloroform) gave:

1. dipyrido-1,4-dithiin (**2**) (0.30 g, 36%),
2. dipyrido-1,4-dithiin (**3**) (0.03 g, 4%),
3. pyridodithiolethione (**13**) (0.06 g, 4%); mp 157-158 °C (ethanol), lit.,¹² mp 158 °C.
4. 3,4-diethylthiopyridine (**14**) (0.11 g, 7%); an oil. ¹H NMR (CDCl₃) δ: 1.29 (t, J = 7.4 Hz, 3H, CH₃), 1.43 (t, J = 7.5 Hz, 3H, CH₃), 2.94 (q, J = 7.5 Hz, 2H, CH₂), 2.99 (q, J = 7.4 Hz, 2H, CH₂), 7.03 (d, J = 5.3 Hz, 1H, H5), 8.32 (d, J = 5.3 Hz, 1H, H6), 8.44 (s, 1H, H2). EI MS (70 eV) 199 (M, 100), 177 (M-C₂H₄, 62). Anal. Calcd for C₉H₁₃NS₂: C 54.23, H 6.57, N 7.03. Found: C 54.09, H 6.62, N 6.97.

D. from pyridinedithiolethione (**13**)

To a solution of pyridodithiolethione (**13**) (0.185 g, 1 mmol) in dry DMF (5 mL) potassium hydroxide (0.11 g, 2 mmol) was added and the mixture was boiled for 3 h. After cooling the solvent was evaporated in vacuo and the residue was dissolved in chloroform (5 mL) and washed with water. The extract was dried with calcium chloride and evaporated in vacuo to give pure dipyrido-1,4-dithiin (**2**) (0.10 g, 92%).

Isomerization of dipyrido-1,4-dithiin (**2**) to dipyrido-1,4-dithiin (**3**)

To a suspension of dipyrido-1,4-dithiin (**2**) (0.218 g, 1 mmol) in dry DMSO (5 mL) at 70 °C sodium methanethiolate (0.084 g, 1.2 mmol) was added. The mixture was stirred at 170 °C for 30 min. After cooling the reaction mixture was poured into 15% aqueous sodium hydroxide (15 mL), diluted with water (40 mL) and boiled for 1 h. The resulting solid was filtered off, washed with water, air-dried and separated by preparative thin layer chromatography (aluminum oxide, methylene chloride) to give:

- (1) dipyrido-1,4-dithiin (**3**) (0.110 g, 50%).
- (2) dipyrido-1,4-dithiin (**2**) (0.070 g, 32%).

Attempts of isomerization of dipyrido-1,4-dithiin (**3**) to dipyrido-1,4-dithiin (**2**)

To a suspension of dipyrido-1,4-dithiin (**3**) (0.218 g, 1 mmol) in dry DMSO (5 mL) at 70 °C sodium methanethiolate (0.084 g, 1.2 mmol) was added. The mixture was stirred at 170 °C for 30 min. After cooling the reaction mixture was poured into 15% aqueous sodium hydroxide (15 mL), diluted with water (40 mL) and boiled for 1 h. The resulting solid was filtered off, washed with water, air-dried to give dipyrido-1,4-dithiin (**3**) (0.190 g, 87%).

3',4-Dimethylthio-3,4'-dipyridinyl sulfide (19)

To a suspension of dipyrido-1,4-dithiin (**2**) (0.218 g, 1 mmol) in dry DMSO (5 mL) at 70 °C sodium methanethiolate (0.084 g, 1.2 mmol) was added. The mixture was stirred for 30 min. After cooling the reaction mixture was poured into 15% aqueous sodium hydroxide (15 mL) and methyl iodide (0.1 mL, 1.6 mmol) was added. The resulting solid was filtered off, washed with water, air-dried and purified by column chromatography (silica gel, chloroform) to give 3',4-dimethylthio-3,4'-dipyridinyl sulfide (**19**) (0.220 g, 79%); mp 115-116 °C (ethanol). ¹H NMR (CDCl₃) δ: 2.60 (s, 3H, CH₃), 6.41 and 7.03 (2d, J = 5.3 and 5.4 Hz, 2H, H5 and H5'), 8.15 and 8.58 (2d, J = 5.3 and 6.4 Hz, 2H, H6 and H6'), 8.47 and 8.59 (2s, 2H, H2 and H2'). EI MS (70 eV) 280 (M, 100), 233 (M-SCH₃, 81.2), 218 (M-CH₃SCH₃, 82.3). Anal. Calcd for C₁₂H₁₂N₂S₂: C 51.40, H 4.31, N 9.99. Found: C 51.22, H 4.32, N 9.84.

4,4'-Dimethylthio-3,3'-dipyridinyl sulfide (20)

A. To a suspension of dipyrido-1,4-dithiin (**3**) (0.218 g, 1 mmol) in dry DMSO (5 mL) at 70 °C sodium methanethiolate (0.084 g, 1.2 mmol) was added. The mixture was stirred for 30 min. After cooling the reaction mixture was poured into 15% aqueous sodium hydroxide (15 mL) and methyl iodide (0.1 mL, 1.6 mmol) was added. The resulting solid was filtered off, washed with water, air-dried and purified by column chromatography (silica gel, chloroform) to give 4,4'-dimethylthio-3,3'-dipyridinyl sulfide (**20**) (0.22 g, 79%); 122-123 °C (ethanol). ¹H NMR (CDCl₃) δ: 2.48 (s, 3H, CH₃), 7.05 (d, J = 5.3 Hz, 1H, H5), 8.38 (d, J = 5.3 Hz, 1H, H6), 8.31 (s, 1H, H2). EI MS (70 eV) 280 (M, 70), 233 (M-SCH₃, 74), 218 (M-CH₃SCH₃, 100). Anal. Calcd for C₁₂H₁₂N₂S₂: C 51.40, H 4.31, N 9.99. Found: C 51.32, H 4.36, N 9.89.

B. To a suspension of dipyrido-1,4-dithiin (**2**) (0.218 g, 1 mmol) in dry DMSO (5 mL) at 70 °C sodium methanethiolate (0.084 g, 1.2 mmol) was added. The mixture was stirred at 170 °C for 30 min. After cooling the reaction mixture was poured into 15% aqueous sodium hydroxide (15 mL) and methyl iodide (0.1 mL, 1.6 mmol) was added. The resulting solid was filtered off, washed with water, air-dried and separated by column chromatography (silica gel, chloroform) to give:

1. 3',4-dimethylthio-3,4'-dipyridinyl sulfide (**19**) (0.105 g, 38%); mp 115-116 °C (ethanol).
2. 4,4'-dimethylthio-3,3'-dipyridinyl sulfide (**20**) (0.115 g, 41%); mp 122-123 °C (ethanol).

X-Ray analysis

A. Dipyrido-1,4-dithiin (**2**):

Data were measured on a Nonius KappaCCD diffractometer with graphite monochromated MoK α radiation ($\lambda = 0.70930$ Å). The structure was solved by direct methods (SHELXS-97)³³ and refined by full-matrix least-squares minimization based on all unique F^2 (SHELXL-97).³⁴

Crystal data: C₁₀H₆N₂S₂, M_r = 218.29, monoclinic, a = 17.219(2), b = 3.9414(4), c = 14.031(2), β = 99.366(5), space group C2/c, Z = 4, V = 939.6(2) Å³, μ = 0.520 mm⁻¹. 6106 reflections were collected of

which 664 were unique and 577 with $I > 2\sigma(I)$ ($R_{\text{int}} = 0.016$). The structure was refined to $R = 0.039$ and $R_w = 0.121$.

B. Dipyrido-1,4-dithiin (**3**):

The crystal was twinned and the twin law $[1\ 0\ 1; 0\ -1\ 0; 0\ 0\ -1]$ was applied during the refinement with a final fraction of 0.37(2) for the second component. Data were collected at the Swiss Norwegian Beamline at the European Synchrotron Radiation facility ($\lambda = 0.9250\ \text{\AA}$) in Grenoble (France). Data were integrated with the software CrysAlisCCD (Oxford Diffraction, 2004). The structure was solved by direct method using the SIR92³⁵ programs within the WINGX software suite³⁶. The structure was refined by full-matrix least-squares minimization on F^2 in the program Crystals.³⁷

Crystal data: $\text{C}_{10}\text{H}_6\text{N}_2\text{S}_2$, $M_r = 218.29$, monoclinic, $a = 18.9992(7)$, $b = 3.9440(2)$, $c = 13.522(1)$, $\beta = 110.902(6)$, space group Pc , $Z = 2$, $V = 946.6(1)\ \text{\AA}^3$, $\mu = 0.516\ \text{mm}^{-1}$. 36147 reflections were collected of which 5131 were unique ($R_{\text{int}} = 0.071$) and 2925 with $I > 2\sigma(I)$. The structure was refined to $R = 0.049$ and $R_w = 0.121$.

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