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Structure and base catalysed cyclization of methyl (2,6-disubstituted-4-nitrophenylsulphanyl)ethanoates

Valerio Bertolasi[a], Kateřina Dudová[b], Petr Šimůnek[b], Jiří Černý[b], Vladimír Macháček[b,*]

[a]*Dipartimento di Chimica and Centro di Strutturistica Diffrattometrica, Università degli Studi di Ferrara, Via Borsari 46, I-44100 Ferrara, Italy*
[b]*Department of Organic Chemistry, Faculty of Chemical Technology, University of Pardubice, Náměstí Legií 565, 53210 Pardubice, Czech Republic*

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Abstract

The conformation of side chain $-SCH_2COOCH_3$ in title compounds in crystal agrees with the reactivity of these compounds in base catalysed ring closure in solution. In the 2,4-dinitro derivative, the side chain is oriented towards the unsubstituted *ortho*-position of benzene ring, in the case of the 2-methoxycarbonyl derivative towards this substituent.

Keywords: Cyclization reactions; X-ray; NMR spectra; Methyl 4-nitrophenylsulphanylethanoates

1. Introduction

Preparation and properties of heterocyclic nitrones—*N*-oxides have been dealt with in literature rather extensively (for a survey see Refs. [1,2]). One of the methods of preparation of these compounds consists in an intramolecular attack of nitrogen atom of nitro group by a carbanion forming the respective *N*-oxide with five- or six-membered ring.

Wagner et al. [3] described a reaction of alkyl sulphanylethanoates with substituted 2-nitrochlorobenzenes catalysed by triethylamine giving the corresponding substituted benzo[*d*]thiazol-3-oxides (Scheme 1).

The presumed intermediate of this reaction, namely the substituted alkyl (2-nitrophenylsulphanyl) ethanoate, could only be prepared in a single case: ethyl (4-cyano-2,6-dinitrophenylsulphanyl)ethanoate [3]. However, a derivative not undergoing ring closure, methyl (2,4-dinitrophenylsulphanyl)ethanoate, was described as early as 1907 [4]. We developed a method of preparation of these substances [5]. We also studied the kinetics of ring closure of methyl (2,4,6-trinitrophenylsulphanyl)ethanoate (**1a**) and suggested the reaction mechanism [6]. The reaction proceeds in several steps: the first (rate-limiting) step consists in splitting off of the proton from the methylene group, the second step being an addition reaction of *ortho*-standing nitro group on the carbanion formed (Scheme 2).

Moreover, we found out [5] that, in contrast to the 2,4-dinitro derivative (which does not undergo ring

* Corresponding author. Tel.: +420-46-603-7506; fax: +420-46-603-7068.
E-mail address: vladimir.machacek@upce.cz (V. Macháček).

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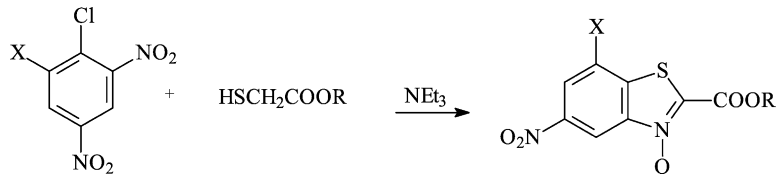


Scheme 1.

closure), the 2,4-dinitro-6-X derivatives containing the weakly electron-acceptor bromine or even electron-donor X substituents (such as CH_3, $CH(CH_3)_2$) undergo the ring closure.

The Dieckmann condensation of methyl 2-(methoxycarbonylmethylsulphanyl)-4,5-dinitrobenzoate, in which the intramolecular attack by carbanion takes place at the ester group, is an analogy of the above-mentioned formation of heterocyclic *N*-oxides. Beck [7] prepared a series of substituted methyl 3-hydroxybenzo[*b*]thiophen-2-carboxylates by nucleophilic substitution of activated nitro group in methyl 2-nitrobenzoates by methyl sulphanylethanoate with subsequent ring closure. The sequence of these two reactions was carried out with base catalysis (LiOH in DMF), and the structure of open-chain intermediates, i.e. methyl 2-(methoxycarbonylmethylsulphanyl)-benzoates, was only presumed but not proved.

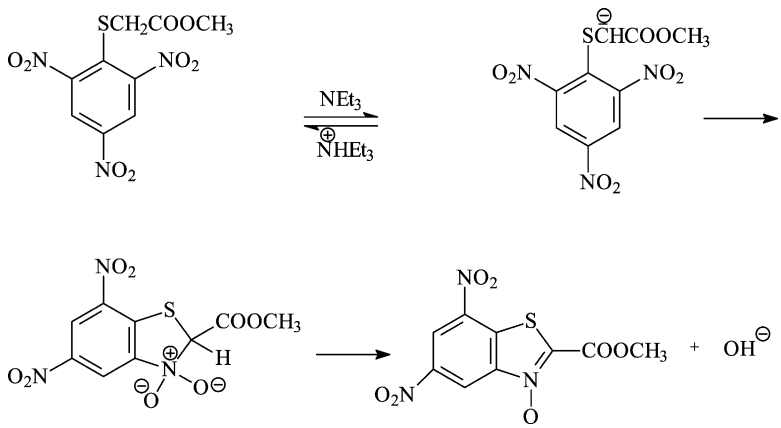
In analogy to esters, also methyl 2-(cyanophenylsulphanyl)ethanoates are cyclised via an intramolecular attack by carbanion. Beck [8] prepared a series of substituted methyl 3-aminobenzo[*b*]thiophen-2-carboxylates by the nucleophilic substitution reaction of activated nitro group in substituted 2-nitrobenzonitriles by methyl sulphanylethanoate. In another variant [8] the same author prepared substituted derivatives of 3-aminobenzo[*b*]thiophen-2-carboxylic acid from 2-sulphanylbenzonitrile. In both the variants the syntheses took place as base catalysed one-step reactions without isolation and identification of the open-chain intermediate. It was only possible to identify [9] 6-chloro-2-(2-cyanoethylsulphanyl)benzonitrile, which does not undergo ring closure at the reaction conditions used. These reactions and similar ones are summarised in Ref. [10].

The aim of this work was to prepare the open-chain intermediates and study their structure in detail in the context of the kinetic measurements being performed on their base catalysed ring closure [6]. The kinetics of ring closure reactions of the given compounds and the underlying relationships have not been studied yet.

2. Experimental

2.1. Methyl (2,4,6-trinitrophenylsulfanyl) ethanoate (*1a*)

Methyl sulfanylethanoate (1.1 g, 0.01 mol) was added to a solution of 2,4,6-trinitrochlorobenzene



Scheme 2.

(2.5 g, 0.01 mol) in 1,2-dimethoxyethane (10 ml) in a 50 ml flask at room temperature under an inert atmosphere of Ar. A solution of triethylamine (1.0 g, 0.01 mol) in 1,2-dimethoxyethane (5 ml) was added dropwise with magnetic stirring over cca 30 min. The mixture was stirred for an additional 1.5 h. The reaction course was monitored by thin layer chromatography. After the starting chloro derivative had reacted, the reaction mixture was poured into dilute hydrochloric acid (1:1; 20 ml). The product was extracted with chloroform (2 × 50 ml), the organic phase was dried over Na_2SO_4 and solvent was evaporated under reduced pressure. The raw product was separated by column chromatography (silica gel; chloroform/acetone 5:1 by vol.). The evaporation residue obtained from the fraction containing the product was recrystallised from methanol yielding 2.4 g (76%) of title product, mp 72–74 °C (Ref. [6], mp 72–73 °C).

In similar way, without chromatographic separation, the following substances were prepared from the corresponding chloro derivatives: methyl (2,4-dinitrophenylsulphanyl)ethanoate (**1b**), methyl (2-methyl-4,6-dinitrophenylsulphanyl)ethanoate (**1c**), methyl (2-isopropyl-4,6-dinitrophenylsulphanyl) ethanoate (**1d**) methyl (2-bromo-4,6-dinitrophenyl-sulphanyl)ethanoate (**1e**), methyl 2-(methoxycarbonylmethylsulphanyl)-3,5-dinitrobenzoate (**1f**), and methyl (2-cyano-4-nitrophenylsulphanyl)ethanoate (**1g**). The respective melting points, results of elemental analyses, chemical shifts $\delta(^1H)$ and $\delta(^{13}C)$ are presented in Tables 1–3.

2.2. 2-Methoxycarbonyl-5,7-dinitrobenzo[d]thiazol-3-oxide (*2a*)

2,4,6-Trinitrochlorbenzene (0.5 g, 2 mmol) was dissolved in methanol (50 ml), in three necked flask

Table 1
Elemental analyses and melting points of the compounds **1** and **2**

Comp.	Yield%	Formula (mw)	mp (°C) (solvent)	Elemental analysis calc./found				
				%C	%H	%N	%S	%Br
1a	65		72–74[a] (benzene–cyclohexane)					
1b	60		94–96[b] (benzene)					
1c	88	$C_{10}H_{10}N_2O_6S$ (286.3)	48–50 (methanol)	41.96	3.52	9.79	11.20	
				41.94	3.57	9.78	11.39	
1d	81	$C_{12}H_{14}N_2O_6S$ (314.3)	93–95 ($CHCl_3$–C_6H_{12})	45.86	4.49	8.91	10.20	
				45.66	4.72	8.68	10.26	
1e	78	$C_9H_7N_2O_6SBr$ (351.1)	103–104 (methanol)	30.79	2.01	7.98	9.13	22.76
				30.60	2.09	7.92	9.35	22.79
1f	81	$C_{11}H_{10}N_2O_8S$ (330.3)	76–77 (methanol)	40.00	3.05	8.48	9.71	
				40.27	3.02	8.37	9.49	
1g	49	$C_{10}H_8N_2O_4S$ (252.2)	120–123 (benzene–cyclohexane)	47.62	3.20	11.11	12.71	
				47.84	3.27	11.18	12.84	
2a	85		197–199[c] (toluene)					
2c	81	$C_{10}H_8N_2O_5S$ (268.2)	202–205 (methanol)	44.78	3.01	10.44	11.95	
				44.69	3.01	10.28	11.94	
2d	89	$C_{12}H_{12}N_2O_5S$ (296.3)	176–178 (methanol)	48.64	4.08	9.45	10.82	
				48.58	3.97	9.44	10.71	
2e	50	$C_9H_5N_2O_5SBr$ (333.1)	219–221 (methanol)	32.45	1.51	8.41	9.63	23.99
				32.49	1.48	8.22	9.78	23.83
2f	71	$C_{10}H_6N_2O_7S$ (298.2)	227–229 (toluene)	40.27	2.03	9.39	10.75	
				40.41	2.17	9.29	10.77	
2g	50	$C_{10}H_8N_2O_4S$ (252.2)	244–246 (methanol)	47.62	3.20	11.11	12.71	
				47.81	3.22	11.11	12.81	

[a] Ref. [6], mp 72–73 °C.
[b] Ref. [4], mp 93–94 °C.
[c] Ref. [6], mp 197–199 °C.

Table 2
^{1}H NMR parameters of the compounds **1** in $CDCl_3$

	X	Y	H-2	H-3	H-5	CH_2	CH_3	X
1a	NO_2	NO_2		8.76 s	8.76 s	3.73 s	3.68 s	
1b	H	NO_2	7.71 d, *J* 9.1	8.40 dd, *J* 2.5, 8.9	9.06 d, *J* 2.5	3.90 s	3.79 s	
1c	CH_3	NO_2		8.31 s	8.31 s	3.58 s	3.66 s	2.76 s
1d	iPr	NO_2		8.36 d, *J* 2.3	8.27 d, *J* 2.4	3.58 s	3.68 s	1.33 d (CH_3), *J* 6.9 3.91 sp (CH), *J* 6.8
1e	Br	NO_2		8.66 d, *J* 2.3	8.44 d, *J* 2.4	3.73 s	3.66 s	
1f	NO_2	$COOCH_3$		8.69 d, *J* 2.5	8.63 d, *J* 2.5	3.73 s	3.65 s	4.04 s
1g	H	CN	7.60 d, *J* 8.9	8.35 dd, *J* 2.4, 8.9	8.46 d, *J* 2.4	3.88 s	3.78 s	

with continuous stirring, whereupon methyl sulfanylethanoate (0.21 g, 2 mmol) and triethylamine (0.22 g, 2.2 mmol) were added at once. The mixture was stirred under argon atmosphere at room temperature 2 h. The suspension obtained was acidified with dilute hydrochloric acid (1:1), and the raw product was collected by suction. After column chromatography (silica gel, chloroform–acetone 10:1, v/v) and recrystallisation (toluene, alumina), product **2a** 0.4 g (85%) with mp 197–199 °C.

*2.3. 2-Methoxycarbonyl-7-methyl-5-nitrobenzo[d]thiazol-3-oxide (**2c**)*

Methyl (2-methyl-4,6-dinitrophenylsulphanyl) ethanoate (**1c**) (0.57 g, 2 mmol) was dissolved in methanol (50 ml). The mixture was stirred under argon atmosphere, and a solution of triethylamine (0.2 g, 2 mmol) in 5 ml methanol was added drop by drop. After 1 h stirring at room temperature, the suspension was acidified and further processed as in the case of the preparation of compound **2a**.

2-Methoxycarbonyl-7-isopropyl-5-nitrobenzo[*d*] thiazol-3-oxide (**2d**) was prepared from methyl (2-isopropyl-4,6-dinitrophenylsulfanyl)ethanoate (**1d**) in the same way.

*2.4. 2-Methoxycarbonyl-7-bromo-5-nitrobenzo[d]thiazol-3-oxide (**2e**)*

Methyl (2-bromo-4,6-dinitrophenylsulphanyl) ethanoate (0.5 g, 1.4 mmol) was dissolved in a mixture of methanol (20 ml) and methanolic buffer *N*-methylpiperidine–*N*-methylpiperidinium chloride (the base/acid ratio 1:4, the base concentration 0.025 M). After 35 min stirring at r.t. under argon, the mixture was poured into 15 ml dilute hydrochloric acid (1:1) and extracted with 2×20 ml chloroform. The evaporation residue obtained from the extract was submitted to column chroma-

Table 3
^{13}C chemical shifts of the compounds **1** in $CDCl_3$

	C-1	C-2	C-3	C-4	C-5	C-6	CH_2	CH_3	COO	X
1a	130.81	154.58	121.72	146.93	121.72	154.58	37.32	53.18	167.65	
1b	144.95	127.04	127.29	144.20	121.44	144.54	34.49	53.00	168.11	
1c	133.04	155.26	126.77	147.67	116.21	147.00	36.68	52.58	168.36	21.60
1d	131.20	158.24	123.04	147.98	115.81	155.53	38.10	52.47	168.25	23.42 (CH_3) 31.50 (CH)
1e	135.62	133.12	130.24	147.30	117.53	155.61	36.34	52.84	168.07	
1f	135.24	139.39	126.58	146.50	120.62	154.61	37.92	52.49	167.91	53.43 (CH_3) 164.01 (COO)
1g	112.05	127.08	127.36	145.03	128.44	149.46	34.12	53.13	167.98	114.42 (CN)

Table 4
^{1}H NMR parameters of the compounds **2** in DMSO-d6

	X	Y	H-4	H-6	CH_3	X
2a	NO_2	N^+-O^-	9.26 d, *J* 2.1	9.12 d, *J* 2.1	4.02 s	
2c	CH_3	N^+-O^-	8.60 d, *J* 2.3	8.51 d, *J* 2.2	3.99 s	2.72 s (CH_3)
2d	iPr	N^+-O^-	8.58 d, *J* 1.9	8.44 d, *J* 1.9	3.99 s	1.45 d, *J* 6.9 (CH_3) 3.37 sp, *J* 6.7 (CH)
2e	Br	N^+-O^-	8.78 d, *J* 2.0	8.91 d, *J* 2.0	4.01 s	
2f	NO_2	C–OH[a]	9.21 d, *J* 2.1	9.12 d, *J* 2.1	3.93 s	
2g	H	$C-NH_2$[b]	9.26 d, *J* 2.2	8.32 dd, *J* 8.9, 2.2	3.86 s	8.14 d, *J* 9.0

[a] OH not detected because of exchange with water.
[b] $\delta(NH_2)$ 7.50 br s.

tography as above, and the raw product was recrystallised from methanol.

2.5. 2-Methoxycarbonyl-3-hydroxy-5,7-dinitrobenzo[b]thiophene (*2f*)

A suspension of methyl 2-(methoxycarbonyl-methylsulphanyl)-3,5-dinitrobenzoate (**1f**) (0.66 g, 2 mmol) in 10 ml methanol was treated with triethylamine (0.2 g, 2 mmol) added in one portion. After 10 min, the suspension was poured in 100 ml ca. 5% hydrochloric acid. The separated raw product, 2-methoxycarbonyl-3-hydroxy-5,7-dinitrobenzo[*b*]thiophene (**2f**), was recrystallised from toluene.

2-Methoxycarbonyl-3-amino-5-nitrobenzo[*b*]thiophene (**2g**) was prepared from methyl (2-cyano-4-nitrophenylsulphanyl)ethanoate (**1g**) in the same way.

The respective melting points, results of elemental analyses, chemical shifts $\delta(^1H)$ and $\delta(^{13}C)$ are presented in Tables 1, 4 and 5.

2.5.1. NMR measurements

The ^{1}H and ^{13}C NMR spectra were measured with Bruker Avance 500 spectrometer at 500.13 and 125.77 MHz, respectively. The proton spectra were standardized by using hexamethyldisiloxane (δ : 0.05, in $CDCl_3$ solutions) and middle peak of solvent in hexadeuteriodimethylsulfoxide (δ : 2.55), respectively; the carbon spectra were referenced to the middle peak of solvent multiplet (δ : 77.0 in $CDCl_3$ and δ : 39.6 in hexadeuteriodimethylsulfoxide).

2.5.2. X-ray structure determinations

Data of compounds **1a**, **1b**, **1f** and **1g** were collected on a Nonius Kappa CCD diffractometer using graphite monochromated Mo Kα radiation ($\lambda = 0.7107$ Å) at room temperature (295 K). Data sets were integrated with the Denzo-SMN package [11] and corrected for Lorentz-polarization effects. The crystal parameters and other experimental details of the data collections are summarized in Table 6. The structures were solved by direct methods (SIR97) [12] and refined by full-matrix

Table 5
^{13}C chemical shifts of the compounds **2** in DMSO-d6

	C-2	C-4	C-5	C-6	C-7	C-8	C-9	COO	CH_3	X
2a	143.91	119.53	146.13	121.19	137.38	128.50	147.03	156.88	53.66	
2c	135.03	111.56	147.59	124.28	133.67	136.14	143.14	157.13	53.37	18.33
2d	132.28	111.79	147.83	120.64	145.88	132.28	144.13	157.02	53.31	21.81 (CH_3) 32.07 (CH)
2e	136.65	113.44	147.86	127.24	117.25	135.69	144.47	156.92	53.52	
2f	109.48	124.33	144.74	119.40	141.94	135.26	136.20	162.23	52.43	154.74 (C–OH)
2g	144.68	119.56	145.07	124.55	122.22	149.83	131.53	164.46	51.68	149.74 ($C-NH_2$)

Table 6
Crystallographic data

Compound	**1a**	**1b**	**1f**	**1g**
Formula	$C_9H_7N_3O_8S$	$C_9H_8N_2O_6S$	$C_{11}H_{10}N_2O_8S$	$C_{10}H_8N_2O_4S$
M	317.23	272.23	330.27	252.24
Space group	*P*-1	$Pna2_1$	*P*-1	*C2/c*
Crystal system	Triclinic	Orthorhombic	Triclinic	Monoclinic
a (Å)	5.6071(4)	12.7723(6)	8.3555(3)	18.9321(7)
b (Å)	8.8209(5)	4.5521(6)	9.0390(4)	7.4487(2)
c (Å)	13.3213(10)	19.4812(8)	9.5314(4)	15.6537(7)
α (degrees)	74.437(3)	90	94.464(2)	90
β (degrees)	82.417(2)	90	102.096(2)	94.447(2)
γ (degrees)	80.693(5)	90	94.091(2)	90
U (Å^3)	623.63(7)	1132.65(9)	698.90(5)	2200.8(1)
Z	2	4	2	8
D_c (g cm^{-3})	1.689	1.596	1.569	1.523
F(000)	324	560	340	1040
μ (Mo Kα) (cm^{-1})	3.074	3.089	2.758	2.985
Measured reflections	5083	6492	4995	4193
Unique reflections	2975	2271	3008	2475
R_{int}	0.025	0.058	0.031	0.02
Observed reflections [$I \geq 2\sigma(I)$]	2427	2075	2608	2150
$\theta_{min} - \theta_{max}$ (degrees)	3.2–28	5.3–27.5	2.95–27.5	4.36–28
hkl ranges	−7,7; −11,11; −16,17	−16,16; −5,5; −25,24	−10,10; −11,11; −12,12	−24,24; −9,9; −20,20
$R(F^2)$ (Observed reflections)	0.0427	0.0417	0.0475	0.0356
$wR(F^2)$ (All reflections)	0.1234	0.0987	0.1353	0.0973
Number of variables	218	194	239	186
Goodness of fit	1.083	1.047	1.052	1.084
ρ_{min}, ρ_{max} (eÅ^{-3})	−0.34, 0.37	−0.20, 0.16	−0.21, 0.24	−0.24, 0.19

least squares methods with all non-hydrogen atoms anisotropic. All hydrogens were refined isotropically. All calculations were performed using SHELXL-97 [13] and PARST [14] implemented in WINGX system of programs [15]. ORTEP [16] views of compounds are shown in Figs. 1–4. Selected bond distances and angles are given in Table 7. Table 8 reports the most significant intramolecular short contacts, and Table 9 the dihedral angles between the phenyl ring and the mean planes through the substituents.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications CCDC 204535-204538. Copies of the data can be obtained, free of charge on applications to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

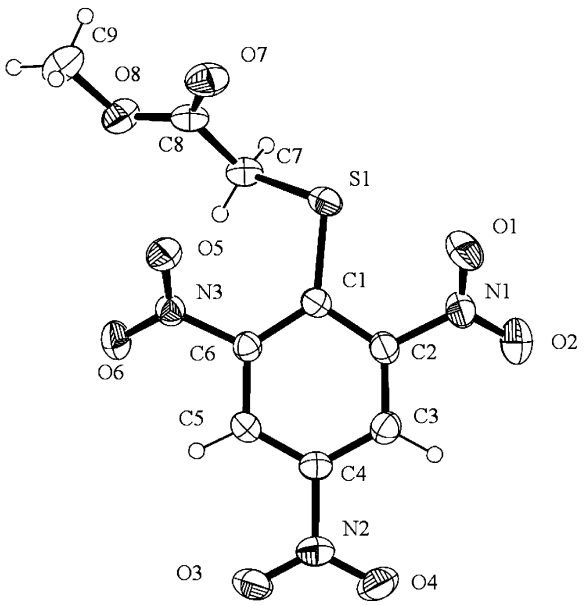


Fig. 1. ORTEP view and atom numbering of compound **1a** showing the thermal ellipsoids at 40% probability.

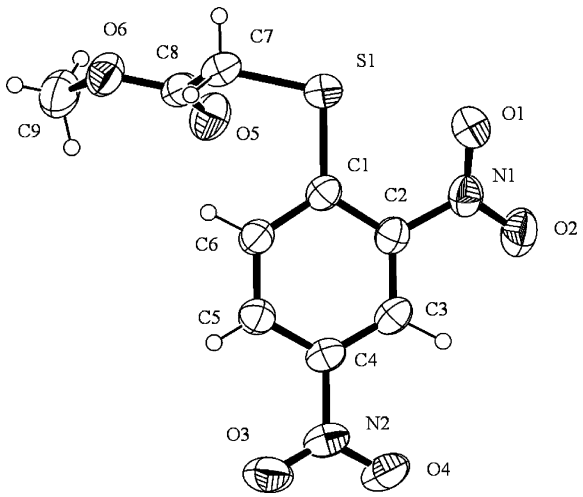


Fig. 2. ORTEP view and atom numbering of compound **1b** showing the thermal ellipsoids at 40% probability.

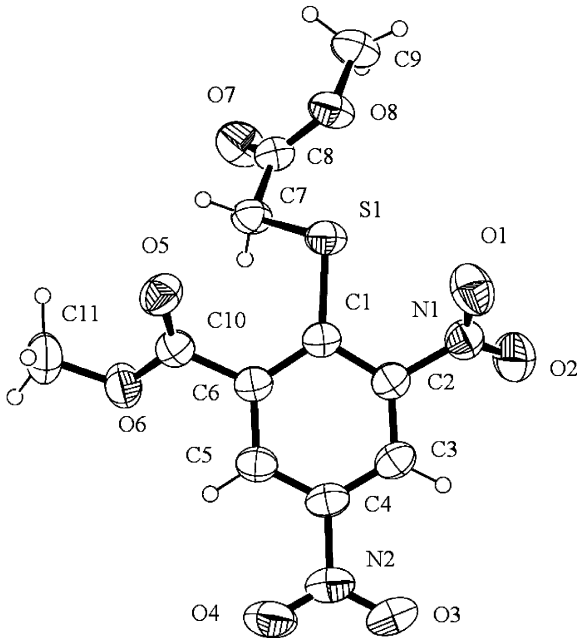


Fig. 3. ORTEP view and atom numbering of compound **1f** showing the thermal ellipsoids at 40% probability.

3. Results and discussion

Alkyl (2-X-4,6-dinitrophenylsulphanyl)ethanoates, where X is an electron-acceptor substituent (NO_2, CF_3, SO_2NH_2), very readily undergo

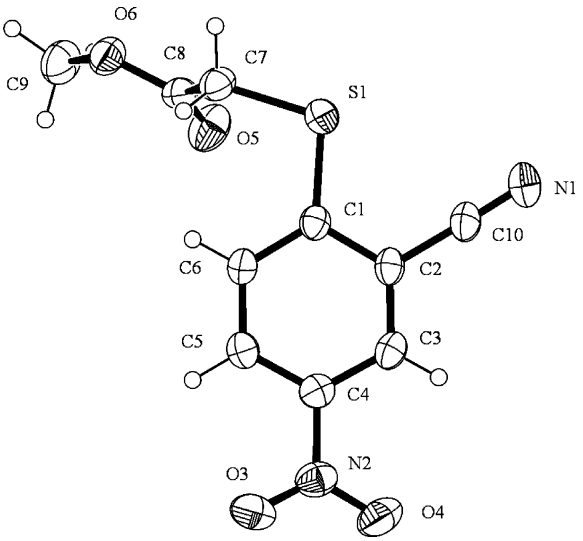


Fig. 4. ORTEP view and atom numbering of compound **1g** showing the thermal ellipsoids at 40% probability.

ring closure to give the respective 7-substituted-2-alkoxycarbonyl-5-nitrobenzo[*d*]thiazol-3-oxide [3]. Therefore, only in a single case it was possible to prepare the intermediate of this reaction. On the other hand, methyl (2,4-dinitrophenylsulphanyl)ethanoate has been known since 1907, thanks to the fact that it does not undergo the ring closure [4]. We have proved that this substance does not cyclise on heating in methanolic solution of triethylamine or methanolic sodium methoxide. The reactivity difference between 2,4-dinitro- and 2,4,6-trinitro derivatives in the cyclisation reaction must be more than 10 orders of magnitude. In contrast, the ring closure does take place with methyl (2-X-4,6-dinitrophenylsulphanyl)ethanoate having a weak electron-acceptor group (SO_3^-, Br) or even electron-donor group (CH_3, $(CH_3)_2CH$) at 2-position [3,5]. The presence of such groups should make the ring closure more difficult as compared with the 2,4-dinitro derivative, but in reality its effect is facilitating. This fact cannot be explained by the acidity of hydrogen atoms in $-SCH_2CO-$ grouping, but by operating of other factors. We presume that the presence of two nitro groups is sufficient for the protons of methylene group to be acidic enough. The third substituent at the other *ortho*-position is needed for restriction of number of possible conformations of the side chain, which

Table 7
Selected bond distances (Å), angles and torsion angles (degrees)

Compound	1a	1b	1f	1g
Distances				
C1–S1	1.757(2)	1.753(2)	1.767(2)	1.739(1)
C1–C2	1.408(2)	1.418(3)	1.398(3)	1.412(2)
C1–C6	1.405(2)	1.401(3)	1.410(2)	1.390(2)
C2–C3	1.376(2)	1.386(3)	1.377(3)	1.375(2)
C3–C4	1.371(2)	1.367(3)	1.362(3)	1.378(2)
C4–C5	1.375(2)	1.388(3)	1.379(3)	1.381(2)
C5–C6	1.384(2)	1.372(3)	1.390(3)	1.373(2)
N1–C2	1.470(2)	1.458(3)	1.467(2)	
N2–C4	1.470(2)	1.465(3)	1.470(3)	1.451(2)
N3–C6	1.470(2)			
C6–C10			1.500(3)	
C10–O5			1.201(3)	
C2–C10				1.439(2)
N1–C10				1.140(2)
Angles				
C1–S1–C7	105.2(1)	102.4(1)	102.0(1)	104.0(1)
S1–C1–C2	118.7(1)	122.0(2)	118.4(1)	117.0(1)
S1–C1–C6	127.6(1)	122.1(2)	125.3(1)	124.7(1)
C2–C1–C6	113.6(2)	115.9(2)	116.3(2)	118.3(1)
C1–C2–C3	124.4(2)	122.8(2)	124.0(2)	121.4(1)
C2–C3–C4	117.8(2)	118.2(2)	117.2(2)	118.0(1)
C3–C4–C5	122.0(2)	121.7(2)	122.6(2)	122.4(1)
C4–C5–C6	118.8(2)	119.4(2)	119.4(2)	119.2(1)
C1–C6–C5	123.7(2)	122.1(2)	120.5(2)	120.8(1)
Torsion angles				
C2–C1–S1–C7	145.4(1)	167.0(2)	135.1(2)	177.4(1)
C1–S1–C7–C8	117.6(1)	−66.5(2)	−139.2(1)	−78.3(1)

entropically facilitates the attack of electrophilic nitrogen atom of nitro group by the nucleophilic carbon atom. The three bulky groups present at mutual *ortho* positions are so close to each other and possess such a low degree of freedom that the geometry of starting molecule approaches the arrangement of the transition state of ring closure. This hypothesis formulated on the basis of behaviour of the substances studied cannot be directly verified by experiment. It is impossible to prepare X-ray-suitable crystals from the salts of readily cyclising substances, and even if this were possible, it would not be certain whether the structure of salts in crystal corresponds with that in solution during the ring closure reaction. Still more objectionable is the way of putting the structure of starting methyl (2-X-4,6-dinitrophenylsulphanyl)ethanoates into correspondence with the ability of their conjugated bases to undergo ring closure. Nevertheless, this is the only possibility to formulate a structure–reactivity relationship in this case.

Table 8
Intramolecular short contacts (Å) and (degrees)

Compound	1a	1b	1f	1g
Distances				
S1…O1	2.738(2)	2.634(2)	2.863(2)	
S1…O5	3.099(2)		3.178(2)	
S1…C10				2.914(2)
O5…C7	2.881(3)		3.022(2)	
O5…C8	2.750(2)			
N3…C7	3.016(3)			
C7…C10			3.028(2)	
Angles				
C7–S1…O1	166.7(2)	173.9(2)	157.2(2)	

3.1. X-ray structures of *1a* and *1b*

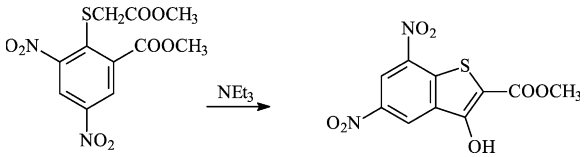
Molecules **1a** and **1b** (Figs. 1 and 2) exhibit short S···O intramolecular non-bonded interactions of 2.738(2) and 2.634(2) Å, which are much shorter than sum of van der Waals radii for S and O of 3.25 Å, and C–S···O angles of 166.7(2) and 173.9(2)° (Table 8). These data can been interpreted in terms of hypervalent interaction between a pair of electrons in a filled p-orbital from a nitro- or carbonyl-oxygen with an empty d_{x2-y2} sulfur orbital [17,18]. In agreement with this interpretation, several structures of similar compounds display short S···O distances and approximately linear C–S···O approach of the divalent sulfur to the oxygen [19–23]. The actual conformation of **1a** is controlled not only by intramolecular attractive S···O interaction but also

Table 9
Dihedral angles (degrees) between the mean planes: P1: (C1–C6 phenyl ring), P2: (O1–N1–O2 nitro group), P3: (O3–N2–O4 nitro group), P4: (O5–N3–O6 nitro group), P5 (O5–C10–O6 of methoxy carbonyl group)

Compound	1a	1b	1f	1g
Angles				
P1–P2	34.6(1)	15.2(1)	49.2(1)	
P1–P3	8.2(1)	8.3(1)	10.4(2)	15.1(1)
P1–P4	39.1(1)			
P1–P5			39.9(1)	

by short contacts between the $-S-CH_2-COOCH_3$ side chain and another nitro group in *ortho*' position displaying the following distances shorter than sum of van der Waals radii: O5···C7 of 2.881(3), O5···C8 of 2.750(2) and N3···C7 of 3.016(3) Å. The *ortho*' O5–N3–O6 nitro group is rotated by 39.1(2)° with respect the phenyl ring and makes an angle of 116.5(1)° with the C7···N3 direction of the attack of the nucleophile C7 carbon atom toward the electrophilic N3 nitrogen. This angle is very similar to the values, in the range 100–110°, obtained mapping the direction of the nucleophile addition of an amine nitrogen to a carbon atom of a ketone, from 97 entries in the Cambridge Structural Database pertaining to N···C=O interactions [24,25]. In order to maintain the C–S···O linearity, also the *ortho* O1–N1–O2 nitro groups is rotated with respect to the phenyl ring by 34.6(1)° (Table 9). At the same time, the S1–C1–C2 angle of 118.7(1)° become narrower than the adjacent one S1–C1–C6 of 127.6(1)° to reach a more suitable approach between S and O. Molecule **1b**, exhibits similar short intramolecular S···O interaction but the corresponding nitro group is rotated by only 15.2(1)°, while the S1–C1–C2 and S1–C1–C6 angles assume symmetric values of 122.0(2) and 122.1(2)°. In this molecule the absence of any substituent in *ortho*' position allows S atom to interact in the plane with the nitro group and form the C7–S1···O1 angle of 173.9(1)°, while the side chain displays its *trans-gauche* natural conformation as determined by the C2–C1–S1–C7 and C1–S1–C7–C8 torsion angles (Table 7). These structural data support the idea that there is a synergistic relationship between the rotations of *ortho* and *ortho*' nitro groups in **1a** to make the molecular conformation to be closer to the incipient transition state toward the formation of the benzothiazole derivative. In this reaction process the *ortho*-nitro group seems to be essential to put the $-S-CH_2-COOCH_3$ side chain in an orientation suitable to attack the second nitro group in *ortho*' position. Accordingly, compound **1b** which does not carry a second nitro group in *ortho*' position does not undergo any cyclization reaction.

We studied the base catalysed ring closure of methyl 2-(methoxycarbonylmethylsulphanyl)-3,5-dinitrobenzoate (**1f**) and found out [5], that the only product formed was benzo[*b*]thiophene derivative, which means that the carbanion primarily formed



Scheme 3.

exclusively attacks the carbonyl carbon atom of methoxycarbonyl group and not the nitrogen atom of nitro group (Scheme 3). The preference of the carbanion attack at methoxycarbonyl group to that at nitro group was confirmed by Beck [7], who isolated methyl 3-hydroxy-7-nitrobenzo[*b*]thiofen-2-carboxylate from reaction of methyl 2,3-dinitrobenzoate and methyl sulfanylethanoate.

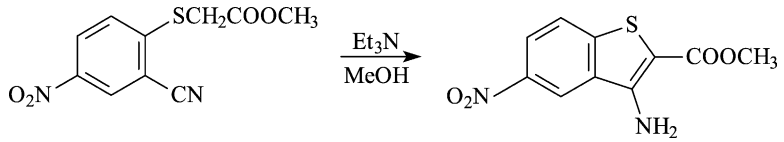
3.2. X-ray structure of *1f*

Compound **1f** (Fig. 3) displays similar features to those observed in **1a**: short S1···O1 contact distance of 2.863(2) Å, almost linear C1–S1···O1 angle of 157.2(2)°, rotation of *ortho*-nitro group by 49.2(1)° with respect to the phenyl ring and narrowing of S1–C1–C2 angle up to 118.4(1)°. Furthermore the $-S-CH_2-COOCH_3$ side chain is oriented toward the methoxy carbonyl group in *ortho*' position forming the non-bonding interactions O5–C7 of 3.022(7) and C7–C10 of 3.028(2) Å, shorter than van der Waals distances. In order to favour these interactions the methoxy carbonyl group mean plane is rotated by 39.9(1)° with respect to the phenyl ring and forms an angle of 113.80(2)° with the C7···C10 direction of the attack of the nucleophile C7 to the electrophile C10 toward the formation of the benzothiofene derivative.

3.3. X-ray structure of *1g*

In compound **1g** (Fig. 4) the $-S-CH_2-COOCH_3$ side chain conformation is similar to that observed in molecule **1b** (Table 7). The short non-bonded distance S1–C10 of 2.914(2) Å and the asymmetric external angles around C1 atom, S1–C1–C2 and S1–C1–C6 of 117.0(1) and 124.7(1)°, respectively, are indicative of the presence of an attractive interaction between S1 and C10 which should favour the subsequent CH_2 attack on the carbon of cyano group.

While the 2,4-dinitro derivative **1b** does not undergo ring closure even with sodium methoxide,



Scheme 4.

methyl (2-cyano-4-nitrophenylsulphanyl)ethanoate (**1g**) cyclises by action of triethylamine in methanol to give methyl 3-amino-5-nitrobenzo[*b*]thiophene-2-carboxylate (**2g**) (Scheme 4). This stands in accordance with the finding [9] that also 2-(cyanomethylsulphanyl)-5-nitrobenzonitrile and 2-(2-oxo-2-phenylethylsulphanyl)-5-nitrobenzonitrile undergo ring closure by action of KOH in aqueous DMF to give the corresponding derivatives of 3-amino-5-nitrobenzo[*b*]thiophene. This happens in spite of the fact that the side chain in compound **1g**, like in compound **1b**, is oriented towards the non-substituted *ortho*-position of the benzene ring. Obviously, the difference is in that the *ortho*-nitro group of compound **1b** is almost coplanar with the ring and the nucleophilic attack would necessitate a rotation of nitro group connected with a certain loss in resonance energy. On the other hand, the attack of the carbanion on nitrogen atom of linear cyano group is possible.

The fact that 2-cyano-4-nitro derivative undergoes ring closure whereas 2,4-dinitro derivative does not and the fact that in 2-methoxycarbonyl-4,6-dinitro derivative it is the methoxycarbonyl and not the nitro group that is attacked by the carbanion indicate that the nitro group is the least suitable for an attack by carbanion at the conditions used, and such an attack only takes place if there is no other, more suitable group available.

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