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Conversion of *N*-(1-Arylsulfonyl-2,2-dichloroethenyl)carboxamides into Derivatives of 4,5-Dimercaptooxazole

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Abstract—In reaction of excess thiols with α-arylsulfonyl-substituted enamides containing two chlorine atoms in β-position to the amide moiety the chlorine atoms and the arylsulfonyl group attached to the C=C bond are replaced by alkylthio or arylthio groups. The sulfur-containing enamides obtained undergo cyclization when treated with phosphorus pentachloride or thionyl chloride to furnish 4,5-dimercaptooxazoles used for preparation of the corresponding disulfonyl derivatives. The latter were also obtained by treating in succession the *N*-(1-arylsulfonyl-2,2-dichloroethenyl)carboxamides with sodium hydrosulfide, then with alkyl halides, and hydrogen peroxide in acetic acid.

We recently showed that with the use of chloral, carboxamides, and sodium arenesulfinates could be easily prepared sulfur-containing enamides **I** capable of versatile transformations [1–3]. In the present study we systematically investigated the condensation of electrophilic reagents I with various thiols and thus established a close relation of these enamides with quite a number of important acyclic and heterocyclic compounds **II**–**X** shown in a scheme.

First of all note that in reaction of enamides **I** with thiols in the presence of triethylamine we were able sometimes to isolate the expected products with chlorine atoms at the C=C bond substituted by the corresponding alkylthio or arylthio groups. However compounds **II** are not at all the final condensation products since at further action of thiols they readily afford sulfur-containing enamides **VI**. The substitution of arylsulfonyl group occurs apparently not at the C=C bond of intermediate compounds **II** but at C=N bond of prototropic tautomers thereof **V** that are likely to arise at least in a small amount in keeping with the general character of enamido–acylimine tautomerism [4]. The step-by-step performance of transformations **I** → **II** → **VI** provides a possibility to introduce various substituents to the sulfur atoms. If the desired compound **VI** should contain all substituents alike enamides **I** should be treated at once with excess thiol in the presence of triethylamine.

The specific feature of sulfur-containing enamides **VI** consists in their ability to cyclocondensation in the presence of phosphorus pentachloride or thionyl chloride. As a result arise previously unknown substituted 4,5-dimercaptooxazoles **VIII**. With the use of IR spectroscopy we confirmed the participation of the acylamine group in the formation of the oxazole ring, and the elimination of one alkylthio or arylthio group is in agreement with elemental analysis and ^{1}H NMR spectra (Table 1). The presence in compounds **VIII** of two substituted thiol groups was proved by their conversion into the corresponding disulfonyl derivatives of 2-alkyl or 2-aryloxazoles **IX**. It is also important that certain representatives of compounds **IX** were prepared by an independent procedure: the treatment of enamides **I** first with sodium hydrosulfide and then with alkyl halides and hydrogen peroxide in acetic acid [see transformations **I** → **VII** → **X** → **IX** on the scheme]. We discovered before the cyclocondensation of enamides **I** with sodium hydrosulfide [2] but the application of this reaction to the synthesis of 2-alkyl(aryl)-5-alkyl(aryl)-sulfonyl-4-arylsulfonyloxazoles was done for the first time.

It is obvious that the planned conversion of accessible enamides **I** into substituted 4,5-mercaptooxazoles **VIII** and their disulfonyl analogs **IX** is of considerable preparative interest. No approach was formerly developed to the synthesis of these promising compounds as showed the enumeration of the few preparation cases of sulfur-containing oxazoles in the recent fundamental monograph [5].

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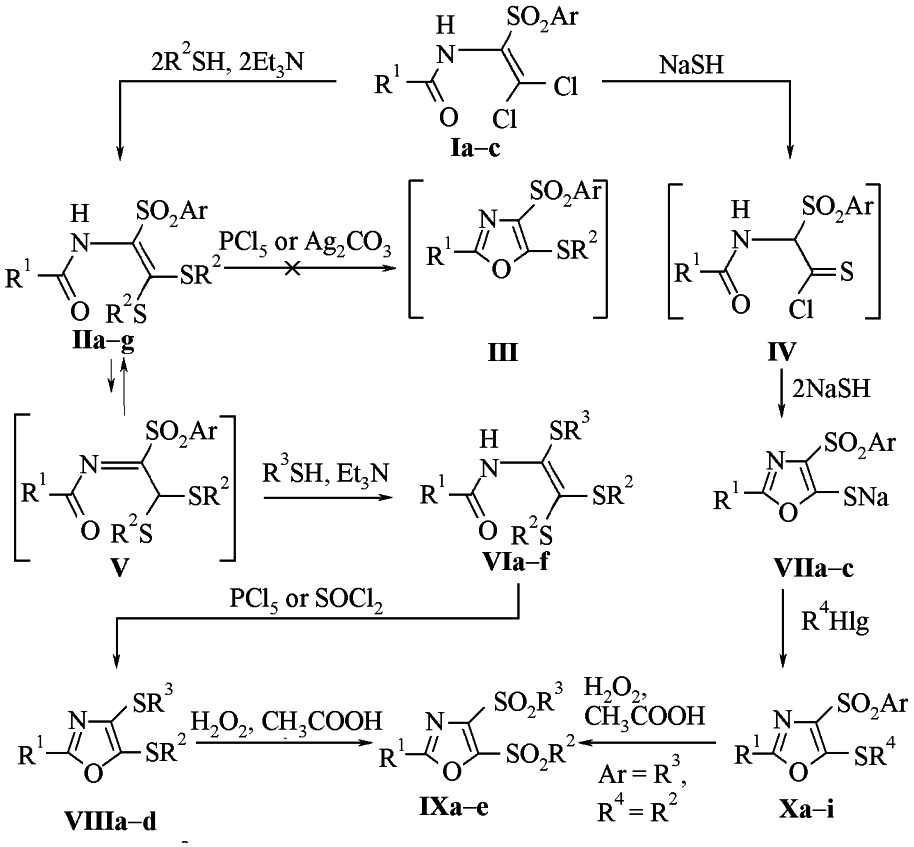

R^1 = CH_3 (**Ia, IIa–c, VIa, b, VIIa, IXa, Xa**), C_6H_5 (**Ib, IId–f, VIc–e, VIIb, VIIIa–c, IXb, c, Xb–e**), 4-$CH_3C_6H_4$ (**Ic, IIg, VIf, VIIc, VIIId, IXd, e, Xf–i**); R^2 = CH_3 (**IXb**), $C_6H_5CH_2$ (**IIa, g, VIf, VIIId, IXd, e**), 4-$NO_2C_6H_4CH_2$ (**IXa**), C_6H_5 (**IId, VIc, VIIIa**), 4-$CH_3C_6H_4$ (**IIb, e, VIa, b, d, VIIIb, IXc**), 4-ClC_6H_4 (**IIc, f, VIe, VIIIc**); R^3 = $C_6H_5CH_2$ (**VIf, VIIId, IXd**), C_6H_5 (**VIc, VIIIa, IXa, e**), 4-$CH_3C_6H_4$ (**VIa, d, VIIIb, IXb, c**), 4-ClC_6H_4 (**VIb, e, VIIIc**); R^4 = CH_3 (**Xb, f**), $C_6H_5CH_2$ (**Xc, g**), 4-$NO_2C_6H_4CH_2$ (**Xa, i**), 2-$FC_6H_4CH_2$ (**Xd**), $C_6H_5COCH_2$ (**Xh**), 4-$ClC_6H_4COCH_2$ (**Xe**); **Ar** = C_6H_5 (**Ia, c, IIa–c, g, VIIa, c, Xa, f–i**), 4-$CH_3C_6H_4$ (**Ib, IId–f, VIIb, Xb–e**).

Table 1. IR and ^1H NMR spectra of sulfur-containing enamides **II, VI** and oxazole derivatives **VIII–X**

Compd. no.	IR spectrum (CH_2Cl_2), ν, cm^{-1}	^1H NMR spectrum($CDCl_3$), δ, ppm
IIb	1130, 1310 (SO_2), 1700 (C=O), 3390 (NH)	2.16 s (3H, CH_3), 2.26 s (3H, CH_3), 2.31 s (3H, CH_3), 6.50–8.10 m (14H, Ar-H; 1H, NH)
VId	1685 (C=O), 3390 (NH)	2.25 s (3H, CH_3), 2.30 s (3H, CH_3), 2.33 s (3H, CH_3), 7.00–7.44 m (17H, Ar–H; 1H, NH)
VIIIb	No bands in 1600–2000 and 3200–3600 cm^{-1} regions	2.30 s (6H, $2CH_3$), 7.05–7.45 m (11H, Ar–H), 8.00–8.04 m (2H, Ar–H)
IXb	1150, 1340 (SO_2)	2.44 s (3H, CH_3), 3.60 s (3H, CH_3SO_2), 7.27–7.57 m (5H, Ar–H), 8.08–8.13 m (4H, Ar–H)
Xb	1150, 1310 (SO_2)	2.42 s (3H, CH_3), 2.67 s (3H, CH_3S), 7.26–7.45 m (5H, Ar–H), 7.95–8.01 m (4H, Ar–H)
Xh	1150, 1310 (SO_2), 1700 (C=O)	2.37 s (3H, CH_3), 4.61 s (2H, CH_2), 7.10–8.20 m (14H, Ar–H)

Table 2. Yields, melting points, and elemental analyses of sulfur-containing enamides **II, VI** and oxazole derivatives **VIII**–**X**

Compd. no.	Yield, %	mp,°C (solvent for crystallization)	Found, %		Formula	Calculated, %	
			N	S		N	S
IIa	52	145–146 (methanol)	2.95	20.19	$C_{24}H_{23}NO_3S_3$	2.98	20.48
IIb	78	207–208 (ethanol)	2.96	20.30	$C_{24}H_{23}NO_3S_3$	2.98	20.48
IIc	70	183–185 (ethanol)	2.70	18.76	$C_{22}H_{17}Cl_2NO_3S_3$[a]	2.74	18.84
VIa	98	110–111 (ethanol)	3.00	21.00	$C_{25}H_{25}NOS_3$	3.10	21.30
VIb	94	108–109 (ethanol)	2.91	20.30	$C_{24}H_{22}ClNOS_3$[b]	2.97	20.38
VIc	71	115–116 (ethanol)	2.92	20.37	$C_{27}H_{21}NOS_3$	2.97	20.40
VId	85	84–85 (ethanol)	2.72	18.67	$C_{30}H_{27}NOS_3$	2.73	18.72
VIe	87	150–151 (ethanol)	2.40	16.75	$C_{27}H_{18}Cl_3NOS_3$[c]	2.44	16.73
VIf	74	125–126 (ethanol)	2.63	18.20	$C_{31}H_{29}NOS_3$	2.65	18.23
VIIIa	52	93–94 (ethanol)	3.81	17.44	$C_{21}H_{15}NOS_2$	3.87	17.74
VIIIb	58	106–107 (ethanol)	3.65	16.03	$C_{23}H_{19}NOS_2$	3.60	16.46
VIIIc	61	121–122 (ethanol)	3.21	14.87	$C_{21}H_{13}Cl_2NOS_2$[d]	3.25	14.90
VIIId	66	50–51 (ethanol)	3.45	16.15	$C_{24}H_{21}NOS_2$	3.47	15.89
IXa	39	185–186 (ethanol)	6.59	15.10	$C_{17}H_{14}N_2O_7S_2$	6.63	15.18
IXb	63	179–180 (ethanol)	3.74	17.25	$C_{17}H_{15}NO_5S_2$	3.71	16.99
IXc	51	192–193 (acetonitrile)	3.12	14.10	$C_{23}H_{19}NO_5S_2$	3.09	14.14
IXd	40	132–134 (ethanol)	2.97	13.68	$C_{24}H_{21}NO_5S_2$	3.00	13.72
IXe	56	146–147 (ethanol)	3.10	14.23	$C_{23}H_{19}NO_5S_2$	3.09	14.14
Xa	76	68–69 (ethanol)	7.23	16.52	$C_{17}H_{14}N_2O_5S_2$	7.17	16.43
Xb[e]	84	153–154 (ethanol)	3.76	19.00	$C_{17}H_{15}NO_3S_2$	4.05	18.56
Xc	75	113–115 (ethanol)	3.20	15.18	$C_{23}H_{19}NO_3S_2$	3.32	15.21
Xd	57	109–110 (ethanol)	3.10	14.28	$C_{23}H_{18}FNO_3S_2$	3.19	14.59
Xe	85	140–143 (acetonitrile)	2.91	13.28	$C_{24}H_{18}ClNO_4S_2$[f]	2.89	13.25
Xf	81	157–159 (ethanol)	4.10	18.61	$C_{17}H_{15}NO_3S_2$	4.05	18.56
Xg	78	131–132 (ethanol)	3.27	15.19	$C_{23}H_{19}NO_3S_2$	3.32	15.21
Xh	85	140–141 (ethanol)	3.09	14.20	$C_{24}H_{19}NO_4S_2$	3.12	14.27
Xi	84	148–149 (ethanol)	6.08	13.80	$C_{23}H_{18}N_2O_5S_2$	6.00	$_1$3.75

[a] Found, %: Cl 13.81. Calculated, %: Cl 13.89.
[b] Found, %: Cl 7.56. Calculated, %: Cl 7.51.
[c] Found, %: Cl 18.40. Calculated, %: Cl 18.50.
[d] Found, %: C 58.30; H 2.29; Cl 16.45. Calculated, %: C 58.61; H 3.04; Cl 16.48.
[e] Compound **Xb** was formerly obtained under dissimilar conditions [2].
[f] Found, %: Cl 7.31. Calculated, %: Cl 7.33.

EXPERIMENTAL

IR spectra were recorded on spectrophotometer Specord 71IR. ^{1}H NMR spectra were registered on spectrometer Varian Gemini (200 MHz) in $CDCl_3$, internal reference TMS. Yields, melting points, and elemental analyses of the newly prepared compounds are given in Table 2.

***N*-[2,2-Di(benzylthio, arylthio)-1-phenylsulfonylethenyl]acetamides IIa–c.** To a dispersion of 0.01 mol of compound **Ia** in 30 ml of ethanol was added 0.02 mol of an appropriate thiol and 0.02 mol of triethylamine, the mixture was stirred for 0.5 h and left standing for 24 h at 20–25°C. The precipitate formed was filtered off, washed with water, and recrystallized.

***N*-[1-Arylthio-2,2-di(*p*-tolylthio)ethenyl]acetamides VIa, b.** A mixture of 2 mmol of compound **IIb**, 2 mmol of an appropriate thiol, 2 mmol of triethylamine, and 10 ml of ethanol was boiled for 2 h. On cooling the precipitate was filtered off, washed with water, and recrystallized.

***N*-[1,2,2-Tri(arylthio)ethenyl]benzamides VIc–e.** To a dispersion of 0.01 mol of compound **Ib** in 30 ml of ethanol was added 0.03 mol of an appropriate thiol and 0.03 mol of triethylamine. The mixture was stirred for 0.5 h and left standing for 24 h at 20–25°C. The precipitate formed was filtered off, washed with water, and recrystallized.

***N*-[1,2,2-Tri(benzylthio)ethenyl]-*p*-toluoylamide VIf** was prepared as above from compound **Ic** and benzylthiol.

4,5-Di(arylthio)-2-phenyloxazoles (VIIIa–c). To a solution of 6 mmol of one among compounds **VIc–e** in 10 ml of phosphorus oxychloride was added 6 mmol of phosphorus pentachloride. The mixture was left standing for 48 h, then the volatile substances were removed in a vacuum, the residue was treated with a little ethanol, filtered off, washed with ethanol, and recrystallized.

4,5-Di(benzylthio)-2-*p*-tolyloxazole VIIId. A solution of 6 mmol of compound **VIf** and 12 mmol of thionyl chloride in 10 ml of benzene was boiled for 1 h, then the volatile substances were removed in a vacuum, the residue was treated with a little ethanol, filtered off, washed with ethanol, and recrystallized.

2-Alkyl(aryl)-4-aryl(benzyl)sulfonyl-5-alkyl-(aryl)sulfonyloxazoles IXa–e. A mixture of 2 mmol of compound **VIIIb** or **VIIId** or **Xa, Xb**, or **Xg**, 10 ml of acetic acid and 1 ml of 33% water solution of hydrogen peroxide was boiled for 0.5 h, then 2 ml of 33% hydrogen peroxide solution was added, and the mixture was boiled for another 0.5 h. The solution was cooled, water and acetic acid removed in a vacuum. the residue was treated with ethanol, the precipitate was filtered off and recrystallized.

2-Alkyl(aryl)-4-arylsulfonyl-5-[alkyl(arylmethyl, acylmethyl)thio]oxazoles Xa–i. To a solution of 6 mmol of sodium hydrosulfide hydrate in 10 ml of ethanol was added at 10–15°C 2 mmol of compound **Ia, b**, or **c**. The mixture was stirred at 20–25°C for 15 h, the precipitate was filtered off, to the filtrate was added 2 mmol of an appropriate alkyl - or phenacyl halide, the mixture was stirred for 24 h at 20–25°C, the precipitate was filtered off, washed with ethanol, water, and recrystallized.

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