

## Vinyl Ethers with Isothiocyanate Group: XVIII.\* Reaction with Dicarboxylic Acids, an Easy Way to Bisacylals with Isothiocyanate Groups

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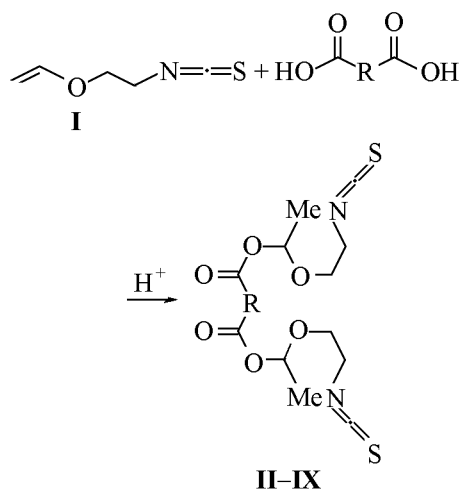
**Abstract**—Electrophilic reaction between 2-(vinylloxy)ethyl isothiocyanate and aliphatic and aromatic dicarboxylic acids (malonic, succinic, glutaric, sebacic, maleic, and phthalic) affords bisacylals with isothiocyanate groups in quantitative yield. The process is carried out at heating without solvent in the presence of catalytic quantities of trifluoroacetic acid.

Among important trends in the modern organic synthesis should be indicated the functionalization of organic compounds through selective modification of one reaction site in a polyfunctional substance. In this respect the substituted vinyl ethers (containing oxirane, thiirane, carbonate, cyclocarbonate, carbodiimide, isothiocyanate, and the other functional groups) are unique starting compounds for fine organic synthesis, unusual products, and promising materials for new technologies. We systematically develop the chemistry of these compounds for a long time [1–7].

Among the numerous reactions of this type that we successfully developed should be mentioned: The new strategy of epoxy resins synthesis based on regioselective addition of polyprotogenic compounds to the double bond of vinyl epoxyethers with conservation of the oxirane cycle [2], quantitative synthesis of previously unknown bisacetal bisisothiocyanates through regioselective addition of polyhydric phenols to 2-(vinylloxy)ethyl isothiocyanate (**I**) [1] that up till now remained the only accessible representative of vinyl ethers of isothiocyanatoalkanols, versatile anchor-type isothiocyanates and vinylloxy synthons [3, 4].

In the present report we describe the study of reaction between 2-(vinylloxy)ethyl isothiocyanate and aliphatic and aromatic dicarboxylic acids (malonic, succinic, glutaric, sebacic, maleic, and phthalic) as an easy and convenient way to functional diisocyanates that are now limited in number. Yet these compounds are valuable raw material for syntheses and are of

interest for production of bis-, poly-, and macrocyclic thiureas and amides, polymers with interpenetrating nets, cross-linking agents and modifiers of epoxy resins and hardeners, initial compounds for organic and heterocyclic synthesis.



The structure of R and the reaction conditions are listed in Table 1.

We showed formerly [8] that the electrophilic addition to 2-(vinylloxy)ethyl isocyanate of monocarboxylic acids (acetic, butyric, valeric, acrylic, methacrylic, and benzoic) occurred at room temperature or moderate heating in the presence of catalytic quantities (0.3–0.5 wt%) of perfluorobutyric acid. The reaction proceeded cleanly and highly selectively at the vinylloxy group resulting in semiacylals with isothiocyanate groups in virtually quantitative yield. In few cases from the reaction products were separat-

\* For communication XVII, see [1].

**Table 1.** Conditions of synthesis of bisacylals **II–IX** by reaction of 2-(vinylloxy)ethyl isothiocyanate (**I**) with dicarboxylic acids  $R(\text{COOH})_2$  [molar ratio ether (**I**):  $R(\text{COOH})_2 = 2:1$ , 0.01–0.02 mol]

Run no.	Compd. no.	R	Reaction temperature, °C <sup>a</sup>	Reaction time, h	Amount of $\text{CF}_3\text{CO}_2\text{H}$ , wt%	Yield, % bisacylal, <sup>b</sup> %
1	<b>II</b>	$\text{CH}_2$	65–100 <sup>c</sup>	~10 min	0	~100
2	<b>II</b>	$\text{CH}_2$	50–60 <sup>d</sup>	20–30 min	0.30 <sup>e</sup>	~100
3	<b>III</b>	$(\text{CH}_2)_2$	85–90 (122–125)	1	0.64 <sup>f</sup>	~100
4	<b>III</b>	$(\text{CH}_2)_2$	85–90 (122–125)	1	0.32 <sup>f</sup>	~100
5	<b>IV</b>	$(\text{CH}_2)_3$	55–60 (75–78)	1	0.62 <sup>f</sup>	~100
6	<b>IV</b>	$(\text{CH}_2)_3$	55–60 (75–78)	1.5	0.31 <sup>f</sup>	~100
7	<b>V</b>	$(\text{CH}_2)_4$	120–125	5	0	~80–85 <sup>g</sup>
8	<b>V</b>	$(\text{CH}_2)_4$	70–75 (80–85)	1	0.60 <sup>h</sup>	~100
9	<b>V</b>	$(\text{CH}_2)_4$	70–75 (95–100)	2 <sup>i</sup>	0.30 <sup>h</sup>	~100
10	<b>VI</b>	$(\text{CH}_2)_5$	85–90	5	0	~92–95 <sup>g</sup>
11	<b>VI</b>	$(\text{CH}_2)_5$	60–65 (75–77)	0.5	0.58 <sup>f</sup>	~100
12	<b>VI</b>	$(\text{CH}_2)_5$	60–65 (75–77)	1	0.29 <sup>f</sup>	~100
13	<b>VII</b>	$(\text{CH}_2)_8$	110–115	5	0	~80–85 <sup>g</sup>
14	<b>VII</b>	$(\text{CH}_2)_8$	70–75 (105–110)	1	0.50 <sup>j</sup>	~100
15	<b>VII</b>	$(\text{CH}_2)_8$	70–75 (105–110)	3 <sup>i</sup>	0.25 <sup>j</sup>	~100
16	<b>VIII</b>	$\text{CH}=\text{CH}$	90–100	1	0	~100
17	<b>VIII</b>	$\text{CH}=\text{CH}$	70–75	1	0.64 <sup>f</sup>	~100
18	<b>VIII</b>	$\text{CH}=\text{CH}$	70–80	1	0.32 <sup>e</sup>	~100
19	<b>IX</b>	<i>o</i> - $\text{C}_6\text{H}_4$	70–80 (120)	1	0.57 <sup>j</sup>	~100
20	<b>IX</b>	<i>o</i> - $\text{C}_6\text{H}_4$	70–80 (120)	1	0.29 <sup>j</sup>	~100

<sup>a</sup> The temperature given in parentheses was used for melting the acid (before addition of the catalyst).

<sup>b</sup> With respect to the amount of acid introduced into reaction.

<sup>c</sup> Self-heating of the reaction mixture from 65 to 100°C.

<sup>d</sup> Self-heating of the reaction mixture from 50 to 60°C.

<sup>e</sup> The catalyst added at room temperature.

<sup>f</sup> The catalyst added at 70–75°C.

<sup>g</sup> Estimated from IR and <sup>1</sup>H NMR spectra.

<sup>h</sup> The catalyst added at 40°C.

<sup>i</sup> After 1 h in the IR spectrum are observed only traces of  $\nu(\text{C}=\text{C})$ .

<sup>j</sup> The catalyst was added at ~100°C.

ed alongside the target acylals small amounts (5–7%) of 1,3-oxazolidine-2-thione or its polymer.

The experimental data obtained in this study evidenced that the dicarboxylic acids add to ether **I** also readily, very selectively, under fairly mild conditions (0.3–0.6 wt% of  $\text{CF}_3\text{COOH}$ , 50–90°C, 0.5–3 h) affording previously unknown bisacylal bisisothiocyanates **II–IX** in quantitative yield.

The reaction was monitored with the use of IR and <sup>1</sup>H NMR spectroscopy. The end of the process was judged by the complete disappearance from the IR spectrum of the reaction mixture of absorption bands belonging to carboxy [ $\nu(\text{OH})$  3500–2700  $\text{cm}^{-1}$ ] and vinylloxy groups (3100, 1620–1610, 1320, 1200, 820  $\text{cm}^{-1}$ ) and by simultaneous appearance of the

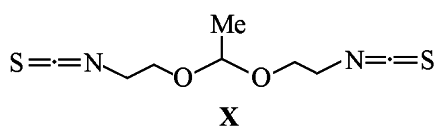
bands corresponding to the band of vibrations in the acylal moiety [ $\nu(\text{O}-\text{C}-\text{O})$  1200–1000  $\text{cm}^{-1}$ ,  $\nu(\text{C}=\text{O})$  1740–1700  $\text{cm}^{-1}$   $\ll$   $\nu(\text{Me})$  2990–2940  $\text{cm}^{-1}$ ] with retained absorption band of  $\nu(\text{N}=\text{C}=\text{S})$  at 2200–2100  $\text{cm}^{-1}$ .

In the <sup>1</sup>H NMR spectra of the reaction mixtures to the end of the process the signals of vinylloxy group (6.45 q, 4.19 d.d, 4.00 d.d ppm) were lacking, and instead appeared the signals from the acylal fragment  $\text{OCH}(\text{Me})\text{OC}(\text{O})$  in the region 6.17–5.93 q (CH) and 1.54–1.41 d ppm (Me).

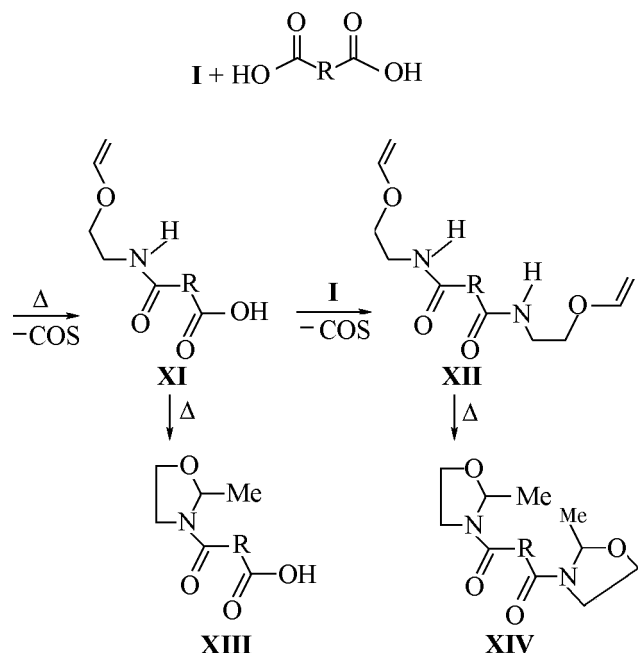
The reaction can proceed even with no catalyst at 65–125°C, but only relatively active malonic and maleic acids add to ether **I** quantitatively and virtually

without complications (Table 1, runs nos. 1 and 16). The reaction with malonic acid after heating the reaction mixture to 65°C further proceeds with self-heating to 100°C and completes during the spontaneous cooling to room temperature (~10 min).

In the  $^1\text{H}$  NMR spectrum of the product obtained in reaction with maleic acid alongside the signals of acylal **VIII** are observed weak resonances of an acetal moiety [4.80 q (OCHO) and 1.30 d ppm (Me)]. The latter probably appear due to formation under the reaction conditions of 2-[1-(2-isothiocyanatoethoxy)-ethoxy]ethyl isothiocyanate (**X**) that we have first identified in the reaction products of ether **I** with methacrylic acid [8].



Conversion of ether **I** at heating (120–125°C) with adipic acid (Table 1, run no. 7) for 1 h attained ~60–70% as evidenced by reduced intensity of the  $\nu(\text{C}=\text{C})$  absorption band in the IR spectrum at 1620–1610  $\text{cm}^{-1}$ . Further heating of the reaction mixture (4 h more) resulted only in a slight decrease in the intensity of the control absorption band and in respective small additional yield of acylal **V**. (The IR spectra were recorded every hour). At the same time was observed a weakening of the absorption bond of the isothiocyanate group (2200–2100  $\text{cm}^{-1}$ ) and



appearance of characteristic absorption bands of amide moiety  $\text{NHC}(\text{O})$  (3350, 1670–1660, 1530–1520  $\text{cm}^{-1}$ ). In the  $^1\text{H}$  NMR spectrum of the reaction products alongside the main signals of acylal **V** appeared weak resonances of vinyloxy group (~15–20% as showed the integration). These data indicate that in the absence of an acidic catalyst alongside the electrophilic addition to the  $\text{C}=\text{C}$  bond occurred to a small degree a parallel nucleophilic addition of the carboxylic acid to the isothiocyanate group affording mono- (**XI**) or bisamides (**XII**) [9].

Likewise behaved in the noncatalyzed reaction with ether **I** also pimelic and sebacic acids (Table 1, runs nos. 10 and 13). Also apparently cannot be excluded the possibility of nucleophilic addition of the dicarboxylic acid to the isothiocyanate group of the arising bisacylal, or the intramolecular cyclization of amides **XI** and **XII** into the corresponding oxazolidines **XIII** and **XIV**. At least the presence in the  $^1\text{H}$  NMR spectra of acylales **V** and **VII** of the trace signals from the other acylal [5.85 q, 5.70 q (OCHO), 1.50 d ppm (Me)] and presumably azaacetal [5.47 q (OCHN), 1.40 d, 1.38 d ppm (Me)] protons is not contradictory to these assumption. We previously observed numerous cases of thermal intramolecular acetalization of vinyl ethers containing in  $\beta$ -position with respect to the vinyloxy group amide, carbamide, thiocarbamide, carbamate, and thiocarbamate moieties (see [10] and references therein). The reaction resulted in 1,3-oxazolidines. In the  $^1\text{H}$  NMR spectra of the arising products the signals of the oxazolidine protons  $\text{OCH}(\text{Me})\text{N}$  usually appeared at 5.49–5.20 and 1.68–1.35 ppm [3, 10].

The noncatalytic reaction of ether **I** with pimelic acid was carried out at lower temperature than with adipic and sebacic acids (Table 1, runs nos. 7, 10, and 13). As a result the side processes were considerably suppressed, and the yield of the target acylal **VI** was higher. The content of amide **XII** in the reaction product was no more than 5–8% (according to  $^1\text{H}$  NMR spectrum). No signals from the other side products (acylals or oxazolidines) were detected.

In the presence of 0.5–0.6 wt% of trifluoroacetic acid the reaction proceeds cleanly and with no side transformations of the initial reagents and target products. The mixture of ether **I** and dicarboxylic acid was first heated to the melting of the acid (commonly to 75–125°C depending on the character of the acid). Therewith we observed as a rule self-heating by 10–30°C apparently due to the starting addition of the acid to ether **II**. Then the reaction mixture was

**Table 2.** Refractive indices and elemental analyses of bisacylals **II–IX**

Compd. no.	$n_D^{20}$	Found, %				Formula	Calculated, %			
		C	H	N	S		C	H	N	S
<b>II</b>	1.5236	43.54	4.36	7.83	17.48	$C_{13}H_{18}N_2O_6S_2$	43.08	5.01	7.73	17.70
<b>III</b>	1.5182	43.95	5.32	7.45	17.02	$C_{14}H_{20}N_2O_6S_2$	44.67	5.35	7.44	17.04
<b>IV</b>	1.5130	46.11	5.04	7.29	16.48	$C_{15}H_{22}N_2O_6S_2$	46.14	5.68	7.17	16.42
<b>V</b>	1.5128	47.50	6.35	6.77	15.37	$C_{16}H_{24}N_2O_6S_2$	47.51	5.98	6.93	15.85
<b>VI</b>	1.5094	48.65	6.16	6.84	15.66	$C_{17}H_{26}N_2O_6S_2$	48.79	6.26	6.69	15.32
<b>VII</b>	1.5050	52.16	6.81	6.11	13.61	$C_{20}H_{32}N_2O_6S_2$	52.15	7.00	6.08	13.92
<b>VIII</b>	1.5282	43.68	4.70	7.12	16.22	$C_{14}H_{18}N_2O_6S_2$	44.91	4.85	7.48	17.13
<b>IX</b>	1.5546	51.17	5.04	6.56	15.06	$C_{18}H_{20}N_2O_6S_2$	50.93	4.75	6.60	15.11

**Table 3.** Spectral characteristics of acylals **II–IX**

Compd. no.	R	IR spectrum, $\nu$ , $cm^{-1}$	$^1H$ NMR spectrum, $CDCl_3$ , $\delta$ , ppm			
			OCHO, q	$CH_3$ , d	$NCH_2$ , $OCH_2$ , m	R
<b>II</b>	$CH_2$	830, 935, 950 sh, 1035, 1070, 1140, 1190 sh, 1270, 1310, 1340, 1380, 1400, 1440, 1740, 2100–2200, 2880, 2940, 2990	5.98	1.45	3.94–3.72	3.47 s (2H)
<b>III</b>	$(CH_2)_2$	830, 930, 970, 1035, 1070, 1125, 1150, 1200 sh, 1250, 1340, 1360, 1400, 1440, 1720, 2100–2200, 2870, 2940, 2990	5.96	1.43	3.85, 3.73, 3.68	2.66 m (4H)
<b>IV</b>	$(CH_2)_3$	840, 940, 1000 sh, 1040, 1090, 1130, 1160, 1200 sh, 1250, 1270, 1310, 1340, 1390, 1410, 1440, 1730, 2100–2200, 2890, 2940, 3000	5.94	1.43	3.76–3.70	2.43 t (4H), 1.97 q (2H)
<b>V</b>	$(CH_2)_4$	840, 940, 1040, 1080, 1130, 1150 sh, 1240, 1340, 1370, 1400, 1440, 1730, 2100–2200, 2870, 2940, 2990	5.95	1.43	3.76–3.71	2.38 narrow m (4H), 1.70 narrow m (4H)
<b>VI</b>	$(CH_2)_5$	800, 900, 1000, 1050, 1090, 1120 sh, 1200, 1290, 1330, 1360, 1400, 1700, 2100–2200, 2850, 2940, 2990	5.93	1.42	3.84 (2H), 3.71 (2H), 3.66 (4H)	2.33 m (4H), 1.65 m (4H), 1.42 m (2H)
<b>VII</b>	$(CH_2)_8$	830, 930, 1030, 1070, 1120, 1150, 1230, 1340, 1370, 1400, 1440, 1720, 2100–2200, 2850, 2930, 2990	5.93	1.41	3.83 (2H), 3.75 (2H), 3.68 (4H)	2.32 m (4H), 1.61 m (4H), 1.31 narrow m (8H)
<b>VIII</b>	$CH=CH$	800 sh, 845, 860 sh, 910 sh, 940, 970, 1045, 1080, 1140, 1160, 1210, 1250, 1345, 1380, 1400, 1445, 1645, 1730, 2100–2200, 2880, 2940, 2990, 3050	5.99	1.43	3.89 (2H), 3.75 (2H), 3.64 (4H)	6.26 narrow m (2H)
<b>IX</b>	$o-C_6H_4$	700, 740, 840, 940, 1040, 1060, 1090, 1100, 1130 sh, 1150, 1280, 1345, 1390, 1440, 1570, 1600, 1730, 2100–2200, 2870, 2940, 2990, 3060	6.17	1.54 d.d	4.00 (2H), 3.83 (2H), 3.68 (4H)	7.73 narrow m (2H) 7.56 narrow m (2H)

cooled to 40–100°C, catalyst was added, and further the process was carried out under conditions described in Table 1. In all instances the quantitative yield of bisacylals was attained within 0.5–1 h.

The reaction is very fast (complete as a rule in ~1 h) also at lower catalyst concentration (~0.3 wt%, Table 1). The reaction with malonic acid is accompanied with mild heat evolution at heating the

reagents in the presence of the catalyst to 50°C and ends within 20–30 min (Table 1, run no. 2).

In contrast to reactions of ether **I** with some monocarboxylic acids [8], especially with halocarboxylic acids [11, 12] we did not observe in the reaction under study the formation of 1,3-oxazolidine-2-thione [originating from thermolysis or hydrolysis (commonly with moisture traces) of reaction products or ether **I**]. This fact however indirectly evidences the thermal and hydrolytic stability of the acylals obtained.

The synthesized compounds **II–IX** are viscous colored fluids, well soluble in the majority of organic solvents. Their composition and structure are in agreement with the elemental analyses, IR and <sup>1</sup>H NMR spectra (Tables 2 and 3).

### EXPERIMENTAL

IR spectra were recorded on spectrophotometer Specord 75IR from thin films (400–4000 cm<sup>-1</sup>). <sup>1</sup>H NMR spectra were registered on spectrometers Bruker DPX-400 (400 MHz, ~5–10% solution in CDCl<sub>3</sub>) and Jeol FX-90 Q (89.55 MHz, ~10% solution in CDCl<sub>3</sub>) at room temperature, internal reference HMDS.

2-(Vinylxy)ethyl isothiocyanate (**I**) we prepared by procedure [13], dicarboxylic acids were commercial products purified by recrystallization.

**General procedure for the synthesis of bisacylals II–IX.** A stirred mixture of 0.02 mol of ether **I** and 0.01 mol of dicarboxylic acid was heated till melting of the acid, then a catalyst (CF<sub>3</sub>COOH) was added, and the reaction was carried out under conditions described in Table 1. The reaction was monitored by IR and <sup>1</sup>H NMR spectra. The authors are grateful to Cand. Chem. Sci. G.I.Sarapulova for recording IR spectra.

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