

KINETICS OF NUCLEOPHILIC ADDITION REACTION OF PHENYL ISOSELENOCYANATES AND PHENYL ISOTHIOCYANATES*

P. KRISTIÁN, G. SUCHÁR and D. PODHRADSKÝ

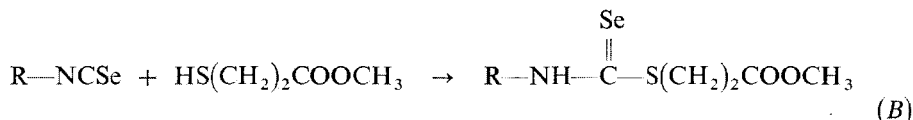
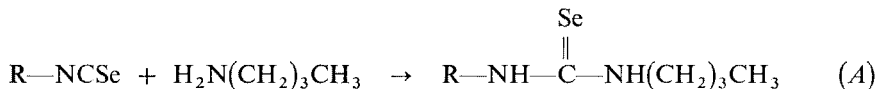
*Department of Organic Chemistry,
Šafárik University, 041 67 Košice*

Received October 22nd, 1974

Kinetics of nucleophilic addition reactions of phenyl isoselenocyanates and phenyl isothiocyanates with *n*-butylamine and methyl 3-mercaptopropionate and its dependence on temperature and solvents were studied by UV spectroscopic method. The rate and ρ constants indicate the greater reactivity of isoselenocyanates and their lesser sensitivity to substituent effects compared to corresponding sulphur analogues. On the basis of statistical treatment of the results, the reaction series were characterized with respect to their isokinetic behaviour. Mechanism of title reactions is proposed and based on observed solvent effects and the values of activation parameters.

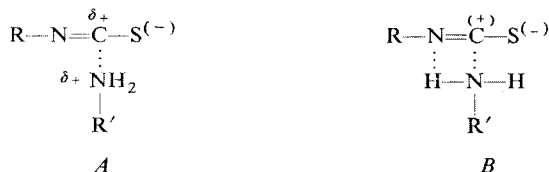
Although a number of studies were devoted to the kinetics of reactions of isothiocyanates with nucleophilic reagents, similar reactions of isoselenocyanates have not up to now been studied. Much attention has been paid to reactions of isothiocyanates with OH, NH₂ and SH groups¹⁻⁶. However, the studies concerned with mechanism of these reactions are still scarce^{7,8}.

In this work the kinetics of nucleophilic addition reactions of phenyl isoseleno- and isothiocyanates with *n*-butylamine and methyl 3-mercaptopropionate were studied in dependence on temperature and solvents with the aim of obtaining data on reactivity and isokinetic behaviour of these compounds. In this study we made use of reactions of phenyl isoselenocyanates with *n*-butylamine (Eq. (A)) and methyl 3-mercaptopropionate (Eq. (B)) that lead to corresponding selenoureas and selenocarbamoyl-3-mercaptopropionates, respectively.



* Part II in the series Synthesis, Chemical Properties and Reactions of Heterodienes; Part I: This Journal 37, 3066 (1972).

Reactions with *n*-butylamine were carried out in dry solvents with excess *n*-butylamine, which ensured pseudo-first order reaction⁶⁻⁸. The ester of 3-mercaptopropionic acid was well soluble in methanol and the addition of a small amount of sodium hydroxide ensured formation of the reactive anionic form⁽⁻⁾ S—CH₂—CH₂—COOCH₃ in sufficient concentration. In both cases parallel experiments were carried out in the absence of the reagent by which it was proved that under the conditions chosen side reactions did not occur. Kinetic study of reactions of phenyl isocyanates was abandoned because of the high reactivity of these compounds under the conditions mentioned (phenyl isocyanate reacted instantaneously with both *n*-butylamine and methyl 3-mercaptopropionate).



EXPERIMENTAL

Compounds studied. 4-Acetyl- (*I*), 4-chloro- (*II*), 4-methyl- (*III*), 4-ethoxy- (*IV*), 4-dimethylamino- (*V*), and 4-methoxyphenyl isoselenocyanate (*XI*) were reported in a previous work⁹. 4-Acetyl- (*VI*), 4-chloro- (*VII*), 4-methyl- (*VIII*), 4-ethoxy- (*IX*), 4-dimethylamino- (*X*), and 4-methoxyphenyl isothiocyanate (*XII*) were prepared by reported procedures¹⁰⁻¹². Phenyl isocyanate (Fluka A. G. Buchs) and *n*-butylamine were commercial samples. Methyl 3-mercaptopropionate was prepared by esterification¹³. The solvents — methanol, acetonitrile, chloroform, dichloromethane, dioxane, and *n*-heptane — were spectrograde preparations (Merck).

Products. *N,N'*-disubstituted selenoureas were prepared by reaction of equimolar amounts of *n*-butylamine and appropriate isoselenocyanate in diethyl ether. Crude products were recrystallized from a light petroleum–chloroform mixture. *N*-(4-Chlorophenyl), *N'*-(*n*-butyl)selenourea, m.p. 120–121°C. UV spectrum(methanol): $\lambda_{\max 1}$ 209 nm, $\log \epsilon_1$ 4.27; $\lambda_{\max 2}$ 286 nm, $\log \epsilon_2$ 4.07. For C₁₁H₁₅ClN₂Se (289.6) calculated: 45.61% C, 5.22% H, 9.67% N; found: 45.26% C, 5.11% H, 9.80% N. *N*-(4-Methoxyphenyl), *N'*-(*n*-butyl)selenourea, m.p. 95°C. UV spectrum(methanol): $\lambda_{\max 1}$ 208 nm, $\log \epsilon_1$ 4.29; $\lambda_{\max 2}$ 275 nm, $\log \epsilon_2$ 4.12. For C₁₂H₁₈N₂OSe (285.2) calculated: 50.52% C, 6.36% H, 9.28% N; found: 50.28% C, 6.43% H, 9.80% N. *N*-(Dimethylaminophenyl), *N'*-(*n*-butyl)selenourea, m.p. 104–105°C, UV spectrum(methanol): $\lambda_{\max 1}$ 207 nm, $\log \epsilon_1$ = 4.45; $\lambda_{\max 2}$ 273 nm, $\log \epsilon_2$ 4.37. For C₁₃H₂₁N₃Se (298.3) calculated: 52.34% C, 7.09% H, 14.08% N; found: 52.29% C, 7.07% H, 14.08% N. Methyl ester of *S*-[*N*-(4-chlorophenyl)-selenocarbamoyl]-3-mercaptopropionic acid was prepared by heating an equimolar mixture of *II* and methyl 3-mercaptopropionate for 0.5 h at 40°C. After standing for 10 h, the crude product was crystallized from a chloroform–light petroleum mixture (m.p. 161–162°C). UV spectrum(methanol): $\lambda_{\max 1}$ 287 nm, $\log \epsilon_1$ 4.28; $\lambda_{\max 2}$ 329 nm, $\log \epsilon_2$ 4.25. For C₁₁H₁₂ClNO₂SSe (336.7) calculated: 39.24% C, 3.59% H, 4.15% N; found: 38.80% C, 3.53% H, 4.29% N.

Procedure. Kinetics of reaction of phenyl isoselenocyanates or phenyl isothiocyanates with *n*-butylamine and methyl 3-mercaptopropionate was followed by UV spectroscopic method on a PE 402 spectrometer, measuring the loss of concentration of the heterocumulenes at an appropriate wavelength. Phenyl isoselenocyanates and phenyl isothiocyanates were used in $5 \cdot 10^{-5}$ M initial concentration and *n*-butylamine and methyl 3-mercaptopropionate in $5 \cdot 10^{-3}$ M initial

concentration. Kinetic measurements were carried out in thermostated 1 cm cells at a 25–45°C temperature range (a given temperature was kept within $\pm 0.2^\circ\text{C}$). Reactions of *n*-butylamine were carried out in single solvents, while in the case of methyl 3-mercaptopropionate a methanol–0.01M-NaOH mixture (100 : 1) was used. For rate constant calculations the first-order rate equation was employed, the actual rate constants k being obtained from the apparent rate constants k_{obs} by dividing them by the *n*-butylamine concentration. Corresponding k_{obs} 's were calculated from linear plots of $\log \Delta E$ vs time. With four derivatives, UV spectra of reaction products were compared with those of authentic samples to verify the identity of these products. Calculation of activation parameters and confirmation of the validity of isokinetic relation (by statistical method¹⁴) for series of compounds under study was performed on a Hewlett-Packard 9820 A digital computer. Linear dependences of $\log k_{\text{obs}}$ on Hammett σ_p constants were calculated by least squares method on an Olivetti 101 computer.

RESULTS AND DISCUSSION

For a comparative study of the reactivity of phenyl isoselenocyanates, analogous sulphur- and oxygen-containing compounds, it was first necessary to find a suitable reagent and reaction conditions. Very low stability of phenyl isoselenocyanates in aqueous media made it impossible to use the methods employed in reactions of isothiocyanates with OH, NH₂ and SH groups, which utilized buffer solutions^{1–7}.

Results of kinetic measurements of the reactions studied are given in Tables I and II. We attempted at classifying reaction series according to the relationship between activation parameters^{15,16} (Table III). Because of available experimental

TABLE I

Rate Constants (k_{obs} in s^{-1} and k in $\text{l mol}^{-1} \text{s}^{-1}$) and Activation Parameters (ΔH^\ddagger in kcal mol^{-1} and ΔS^\ddagger in $\text{cal grad}^{-1} \text{mol}^{-1}$) of Reactions for 4-Substituted Phenyl Isoselenocyanates I–V and Phenyl Isothiocyanates VI–X with *n*-Butylamine in Methanol

No	Group	$10^3 k_{\text{obs}}$ at				k at				ΔH^\ddagger	ΔS^\ddagger
		30°C	35°C	40°C	45°C	30°C	35°C	40°C	45°C		
I	CH ₃ CO	—	6.58	7.68	11.20	—	1.316	1.536	2.340	9.8	–26.1
II	Cl	—	3.05	4.76	5.91	—	0.610	0.958	1.188	12.3	–19.7
III	CH ₃	—	1.61	2.06	2.51	—	0.323	0.418	0.508	8.0	–34.9
IV	C ₂ H ₅ O	—	0.66	1.18	1.56	—	0.133	0.236	0.318	16.0	–10.5
V	(CH ₃) ₂ N	—	0.24	0.26	0.38	—	0.047	0.053	0.077	9.0	–35.4
VI	CH ₃ CO	1.80	2.28	3.08	4.25	0.360	0.450	0.616	0.850	10.4	–26.5
VII	Cl	0.93	1.30	1.58	2.03	0.186	0.260	0.316	0.406	9.1	–31.1
VIII	CH ₃	0.28	0.31	0.50	0.60	0.057	0.063	0.100	0.121	9.7	–27.9
IX	C ₂ H ₅ O	0.15	0.24	0.26	0.40	0.030	0.047	0.053	0.080	11.1	–33.1
X	(CH ₃) ₂ N	0.066	0.083	0.100	0.133	0.013	0.016	0.020	0.026	8.0	–40.7

facilities and solvents used, we were unable to follow these reactions over a broader temperature region which would have ensured the greater accuracy of statistical results. As it is seen from the results presented in Table III, single series can be

TABLE II

Rate Constants k_{obs} (in s^{-1}) and Activation Enthalpies ΔH^\ddagger (in kcal mol^{-1}) for Reactions of 4-Substituted Phenyl Isoselenocyanates *I–V* and Phenyl Isothiocyanates *VI*, *VIII–X* with Methyl 3-Mercaptopropionate in a Methanol-0.01M-NaOH Mixture (100 : 1)

No	Group	$10^3 k_{\text{obs}}$ at			ΔH^\ddagger
		25°C	30°C	35°C	
<i>I</i>	CH ₃ CO	6.21	8.75	10.28	8.6
<i>II</i>	Cl	4.86	5.86	8.13	8.7
<i>III</i>	CH ₃	1.40	1.55	2.35	8.8
<i>IV</i>	C ₂ H ₅ O	0.68	1.45	1.80	17.1
<i>V</i>	(CH ₃) ₂ N	0.31	0.45	0.85	17.4
<i>VI</i>	CH ₃ CO	4.10	4.48	5.53	4.8
<i>VIII</i>	CH ₃	0.35	0.55	1.06	19.7
<i>IX</i>	C ₂ H ₅ O	0.50	0.61	0.63	17.3
<i>X</i>	(CH ₃) ₂ N	0.066	0.150	0.216	16.8

TABLE III

Testing of Studied Reaction Series on the Validity of Isokinetic Relation

Symbols used: *l* degree of freedom, $\sum n$ number of measurements, ΔT temperature region (in K), *s* standard deviations; 00 without the condition of common point of intersection, 0 isokinetic; reactivity differences – R between reactions, ∞ isenthalpic; β isokinetic temperature (K), ψ the measure of values of isokinetic relation in a given region of *T*, ψ_n normalized with respect to the *T* region, and α level of significance.

Reaction	$l(\sum n)$ ΔT	s_{00}	s_R	ψ	β
		s_0	s_∞	ψ_n	α
<i>I–V</i> + <i>n</i> -C ₄ H ₉ NH ₂	5 (15)	0.038	0.564	0.083	5
	10	0.047	0.074	0.252	0.25
<i>VI–X</i> + <i>n</i> -C ₄ H ₉ NH ₂	5 (20)	0.029	0.587	0.052	105
	15	0.03	0.029	0.112	>0.25
<i>I–VI</i> , <i>VIII–X</i> + HSCH ₂ CH ₂ COOCH ₃	9 (27)	0.049	0.601	0.086	372
	10	0.052	0.072	0.244	>0.25

divided into two groups. The first one comprises reactions of isoselenocyanates and isothiocyanates with n-butylamine. The isoselenocyanate series appears as isenthalpic; this follows from the values of isokinetic temperature and standard deviation ($\beta \approx 0, s_0 \approx s_\infty$). Within the accuracy achieved, the isokinetic relation is nearly fulfilled (F-test) but the accuracy is low ($s_\infty = 0.038$). On the basis of this finding, this series can be considered as seemingly isenthalpic. Similarly, the reaction of isothiocyanates with n-butylamine appears as nearly isenthalpic ($s_0 \approx s_\infty$), even though $\beta = 105$ K. Also isokinetic relation is fulfilled within the accuracy given ($s_0 \approx s_\infty$). Due to the broader temperature region, the accuracy is also substantially greater compared to the preceding case ($s_\infty = 0.029$ and Ψ_n is close to the limit for statistically significant relations).

The second group comprises reactions of phenyl isoselenocyanates and phenyl isothiocyanates with methyl 3-mercaptopropionate. Within the accuracy achieved, which is comparatively low ($s_\infty = 0.049$), the isokinetic relation is fulfilled (Fig. 1, $\beta = 372$ K). According to Hinshelwood¹⁷, one can speak of a series with the so-called compensation, *i.e.* with changes of ΔH^\ddagger and ΔS^\ddagger in the same direction.

As isokinetic relation is fulfilled, for series under study these may be correlated by Hammett equation. By plotting $\log k_{\text{obs}}$'s vs Hammett σ_p constants¹⁸ we obtained linear correlation for reaction with both n-butylamine ($\rho_{\text{NCS}_e} = 1.09, r = 0.981$; $\rho_{\text{NCS}} = 1.13, r = 0.985$) and methyl 3-mercaptopropionate ($\rho_{\text{NCS}_e} = 0.91, r = 0.981$; $\rho_{\text{NCS}} = 1.06, r = 0.993$). As follows from comparison of the rate constants for isoselenocyanates and isothiocyanates and from the values of ρ_{NCS_e} and ρ_{NCS} , phenyl

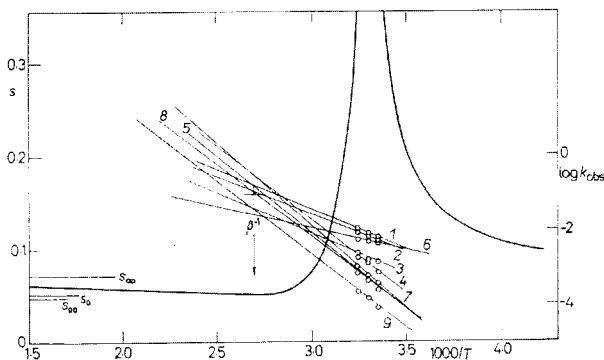


FIG. 1

Isokinetic Relation for Nucleophilic Addition Reaction of Phenyl Isoselenocyanates and Phenyl Isothiocyanates with Methyl 3-Mercaptopropionate

Lines 1—9 correspond to linear plots of $\log k_{\text{obs}}$ against $1/T$ for derivatives given in Table II. The curve represents the dependence of the standard deviation¹⁶ s_u on the presumed isokinetic temperature.

isoselenocyanates show enhanced reactivity but lesser sensitivity to substituent effects than analogous sulphur-containing derivatives. This finding agrees with results of our previous works^{9,19}.

With regard to reaction mechanism, the reactions studied thus far were the addition of *n*-butylamine to isothiocyanates in buffer solutions⁷ and additions of aromatic amines in tetrachloromethane⁸. Different mechanisms have been proposed for these reactions. While in the case of *n*-butylamine in water a two-step mechanism was suggested involving transition state *A*, the addition of aniline in CCl₄ was described by an electron donor – acceptor mechanism with transition state *B*.

Values of activation entropies ΔS^\ddagger and activation enthalpies ΔH^\ddagger obtained in the present work (Table I) correspond rather to a concerted addition mechanism²⁰. Similar values of activation enthalpies were obtained, however, also for the reaction of methyl 3-mercaptopropionate (Table II), for which compound concerted mechanism can be excluded, since the active form of the reagent is ⁽⁻⁾S—CH₂—CH₂—COOCH₃ anion.

As, according to statistical treatment, the reactions of *n*-butylamine with studied heterocumulenes are seemingly isoenthalpic, one can suppose that steric and solvent effects are operating in these reactions. For this reason we examined solvent effects in the reaction of 4-methoxyphenyl isoselenocyanate (*XI*) and 4-methoxyphenyl isothiocyanate (*XII*) with *n*-butylamine in six solvents of varying polarity (Table IV). It was found that in this case a linear correlation does not exist between solvent polarity constants E_T and $\log k_{\text{obs}}$. However, from Table IV it follows that reaction rate increases in polar solvents. This shows that the transition state is more polar

TABLE IV

Rate Constants k_{obs} (in s⁻¹) for Reactions of 4-Methoxyphenyl Isoselenocyanate (*XI*) and 4-Methoxyphenyl Isothiocyanate (*XII*) with *n*-Butylamine in Solvents of Varying Polarity at 35±0.2°C and Values of Empirical Parameters E_T (in kcal mol⁻¹)

Solvent	E_T^a	$10^3 k_{\text{obs}}$	
		<i>XI</i>	<i>XII</i>
Methanol	55.5	0.43	0.21
Acetonitrile	46.0	13.01	2.14
Dichloromethane	41.1	0.58	0.34
Chloroform	39.1	0.26	0.14
Dioxane	36.0	2.35	1.42
<i>n</i> -Heptane	(30.0)	0.25	0.07

^a Taken from ref.²¹.

than the initial state. From nonlinear correlation of $\log k_{\text{obs}}$ with E_T constants it follows further that the order of reactivity of individual compounds in different solvents is affected by additional factor, *i.e.* by mutual interaction of the solvent with *n*-butylamine. We therefore determined chemical shifts of protons of the amino group of *n*-butylamine in tetrachloromethane, acetonitrile, methanol- d_4 , and deuteriochloroform. Values of the chemical shifts in tetrachloromethane (τ 7.44) were used as standard in the estimation of the solvent-*n*-butylamine interaction ($\Delta\tau_{\text{CD}_3\text{OD}} = 0.07$; $\Delta\tau_{\text{CH}_3\text{CN}} = 0.05$; $\Delta\tau_{\text{CDCl}_3} = -0.06$). These chemical shifts result from bonding interactions of solvents with the amino group of *n*-butylamine. From the results it follows that there is no linear correlation of τ with E_T , which bears upon the possibility of bonding interactions of solvents with both nitrogen free electron pair and NH_2 group hydrogens of the butylamine. In conclusion, it seems likely that addition reaction of *n*-butylamine with phenyl isoselenocyanates and their sulphur analogues proceeds by non-synchronous mechanism.

We thank Professor O. Exner, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague, for valuable comments and programme for statistical calculations.

REFERENCES

1. Vlachová D., Zahradník R., Antoš R., Kristián P., Hulka A.: *This Journal* 27, 2826 (1962).
2. Drobnicová E., Augustin J.: *This Journal* 30, 99 (1965).
3. Drobnicová E., Augustin J.: *This Journal* 30, 1618 (1965).
4. Kristián P., Drobnicová E.: *This Journal* 31, 1333 (1966).
5. Kardoš A. M., Volke J., Kristián P.: *This Journal* 30, 931 (1965).
6. Zahradník R.: *This Journal* 24, 3047 (1959).
7. Zahradník R.: *This Journal* 24, 3422 (1959).
8. Akiyama H., Yoshida N., Araki Y., Ouchi K.: *J. Chem. Soc. B* 1968, 676.
9. Kristián P., Suchár G.: *This Journal* 37, 3066 (1972).
10. Dyson G. M., George H. J., Hunter R. F.: *J. Chem. Soc.* 1927, 442.
11. Dyson G. M., George H. J.: *J. Chem. Soc.* 125, 1702 (1924).
12. Houben - Weyl: *Methoden der Organischen Chemie*, Vol. X, p. 874. Thieme, Stuttgart 1955.
13. Drummond A. M., Gibson D. T.: *J. Chem. Soc.* 128, 3073 (1926).
14. Exner O., Beránek V.: *This Journal* 38, 781 (1973).
15. Exner O.: *This Journal* 29, 1094 (1964).
16. Exner O.: *Chem. Listy* 67, 135 (1973).
17. Blackadder D. A., Hinshelwood C.: *J. Chem. Soc.* 1958, 2720, 2728.
18. McDaniel D. H., Brown H. C.: *J. Org. Chem.* 23, 420 (1958).
19. Suchár G., Kristián P.: *This Journal*, in press.
20. Huisgen R., Feiler L. A., Otto O.: *Chem. Ber.* 102, 3444 (1969).
21. Reinhardt C.: *Lösungsmittel-Effekte in der Organischen Chemie*, p. 142. Verlag Chemie, Weinheim 1969.

Translated by J. Hetflejš.