# REACTIVITY OF PHENYLSULFONYL ISOTHIOCYANATES AND TRANSFER OF SUBSTITUENT EFFECTS THROUGH THE SULFONYL GROUP

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Kinetics of nucleophilic additions of butylamine to phenylsulfonyl isothiocyanate was investigated by the stopped-flow UV spectroscopic method and the transfer of electronic effects of substituents on the reaction centre through the $SO_2$ group was examined. The structure and the polar character of $SO_2NCS$, NCS and $SO_2$ groups is discussed.

Our preceding papers[1,2] concerning the dipole moments of –NCX group (X = O, S, Se) showed that the mesomeric effect of the –NCS group in phenyl, benzoyl and phenylsulfonyl isothiocyanates rises with the decreasing size of the positive charge at carbon atom. This dependence displayed the lowest mesomeric interaction of the –NCS group to be in phenylsulfonyl isothiocyanates.

To examine the substituent effects on the –NCS group in the above-mentioned isothiocyanates kinetics of their reactions with butylamine was measured by the stopped-flow method. Moreover, transfer of the substituent effects through the $SO_2$ group was investigated with a series of compounds of general formula $4\text{-RC}_6.\text{H}_4\text{MY}$ ($M = SO_2, CO$; $Y = NH_2$, NCS) using the stretching vibration of $\nu_{as}(NCS)$ wave numbers and chemical shift values $\delta(NH_2)$ as measured by IR and $^1$H NMR spectroscopies. The dissociation constant values of sulfonamides and the rate constants for nucleophilic additions of butylamine to phenyl and benzoyl isothiocyanates were taken from[3,4]. Data concerning the reactivity of phenylsulfonyl isothiocyanates and transfer of substituent effects have not been published as yet.

## EXPERIMENTAL

The IR spectra of chloroform solutions ($0{\cdot}05\ \text{mol l}^{-1}$) were measured with a Specord IR 75 (Zeiss, Jena) spectrometer in 0·17 mm-NaCl cells, the UV spectra of cyclohexane solutions ($5 \,.\, 10^{-5}\ \text{mol l}^{-1}$) were recorded with a Perkin–Elmer, model 402 spectrophotometer and the $^1$H NMR spectra of hexadeuterodimethyl sulfoxide solutions ($0{\cdot}3\ \text{mol l}^{-1}$), run with a Tesla BS 487 A apparatus, given on the $\delta$-scale, are relative to hexamethyldisiloxane as external reference.

*Chemicals*: Phenylsulfonyl isothiocyanate (b.p. 73—80°C/1 Pa), 4-chlorophenylsulfonyl isothiocyanate (b.p. 96—100°C/1 Pa) and 4-methylsulfonyl isothiocyanate (b.p. 116—120°C/1 Pa) were prepared by thermolysis of N-(phenylsulfonyl)dithiocarbamates according to ref.[5]. The series of 4-substituted benzenesulfonamides (R = $NO_2$, Ac, Cl, Br, H, Me, OMe, $NH_2$) were obtained from the corresponding benzenesulfonyl chlorides and ammonia[3], 4-substituted anilines were commercial products (Merck). N,N′-Disubstituted thioureas were prepared by reacting equimolar amounts of butylamine and phenylsulfonyl isothiocyanates in ether or benzene under cooling. The crude products were crystallized from benzene or ethanol.

N-(Phenylsulfonyl)-N′-butylthiourea: yield 85%, m.p. 114—115°C. For $C_{11}H_{16}N_2O_2S_2$ (272·4) calculated: 48·50% C, 5·92% H, 10·28% N; found: 48·52% C, 5·73% H, 10·41% N. UV spectrum, nm (log $\varepsilon$): 268 (3·02). IR spectrum, $cm^{-1}$: 3 319 (NH), 1 376 $(SO_2)_{as}$, 1 119 $(SO_2)_s$.

N-(4-Methylphenylsulfonyl)-N′-butylthiourea: yield 89%, m.p. 86—87°C. For $C_{12}H_{18}N_2O_2S_2$ (286·4) calculated: 50·32% C, 6·33% H, 9·78% N; found: 49·49% C, 6·24% H, 9·64% N. UV spectrum, nm (log $\varepsilon$): 264 (4·5). IR spectrum, $cm^{-1}$: 3 350 (NH), 1 376 $(SO_2)_{as}$, 1 119 $(SO_2)_s$.

N-(4-Chlorophenylsulfonyl)-N′-butylthiourea: yield 88%, m.p. 113—114°C. For $C_{11}H_{15}Cl.N_2O_2S_2$ (306·8) calculated: 43·06% C, 4·92% H, 9·13% N; found: 43·20% C, 4·61% H, 19·15% N. UV spectrum, nm (log $\varepsilon$): 235 (4·16). IR spectrum, $cm^{-1}$: 3 349 (NH), 1 369 $(SO_2)_{as}$, 1 141 $(SO_2)_s$.

*Kinetic measurements*. Kinetics of the reaction of phenylsulfonyl isothiocyanates with butylamine was measured on a UV Stopped-flow apparatus, model 1705 (Applied Photophysics) and the reaction course was monitored by a digital voltmeter, model 3437A (Hewlett–Packard) and evaluated by a HP-85 calculator connected with the voltmeter through interface 82937 A, HP-IB. This arrangement is described together with the testing procedure in[6,7]. Activation entropy values $\Delta S^{\ddagger}$ and activation enthalpy values $\Delta H^{\ddagger}$ could not be obtained with this apparatus. Kinetic measurements in cyclohexane were investigated at 25°C at initial concentrations of phenylsulfonyl isothiocyanates $2{\cdot}5 \,.\, 10^{-5}$ mol $l^{-1}$ and butylamine 2·4—2·5 mmol $l^{-1}$. The first order equation was applied for the calculation; the actual rate constants $k$ were obtained by dividing the apparent rate constants $k'$ by butylamine concentration. The apparent rate constants $k'$ were calculated from the linear equation $\log[\log(V_{\infty}/V_t)] = C - k't/2{\cdot}303$, where $V_t$ stands for the detector voltage in time $t$, and $V_{\infty}$ is the value at the end of the reaction (the voltage value is proportional to the intensity of light passing through the reaction vessel).

## RESULTS AND DISCUSSION

A suitable agent and conditions were necessary to find for comparison of results of kinetic measurements obtained with phenylsulfonyl isothiocyanates with those of phenyl and benzoyl isothiocyanates (Table I). The evaluated reactivity of the afore-mentioned isothiocyanates with butylamine in cyclohexane at 25°C showed that the reactions proceeded by 2·4 times faster with chloro derivatives of phenylsulfonyl and benzoyl isothiocyanates than those of the corresponding methyl derivatives. The reaction of chlorophenyl isothiocyanate is 6·5 times faster than that of the corresponding methyl derivative and therefore, it is of interest to compare reactivities of the unsubstituted isothiocyanates. Under the given reaction conditions the reaction of phenylsulfonyl isothiocyanate with butylamine is $10^5$ times faster than that of phenyl isothiocyanate and 10 times faster than that of benzoyl isothiocyanate. As seen in Table I, differences between logarithms of rate constants of chloro and methyl derivatives are equal with benzoyl and phenylsulfonyl isothiocyanates (0·39) and higher with phenyl isothiocyanates (0·81). These dependences let us conclude that reactions of phenylsulfonyl isothiocyanates with butylamine are characteristic of higher reactivity, but exhibit an approximately equal sensitivity against the substituent effects as the above-mentioned reactions of benzoyl isothiocyanates. Also the influence of dioxane ($E_T$ = 150·5 kJ mol$^{-1}$, ref.[8]) on the reaction rate of phenylsulfonyl isothiocyanate with butylamine was studied. The reaction under investigation proceeded, as follows from kinetic data ($k$ = 122 800 l mol$^{-1}$ . s$^{-1}$) in the more polar medium of dioxane 14 times faster than in cyclohexane ($E_T$ = 130·4 kJ mol$^{-1}$, ref.[8]). The by order increased reactivity of phenyl and benzoyl isothiocyanates with butylamine due to more polar solvents was reasoned in our preceding papers[4,9] by the mechanism of solvent effect involving a direct interaction between the reacting components and solvent in addition to solvation of the starting compounds and the transition state. Linear correlation with the $E_T$ values was not found with any of both reaction series.

The obtained results together with the published data let us conclude that reactions of phenylsulfonyl isothiocyanates with butylamine are second order nucleophilic additions leading to the corresponding N-phenylsulfonyl-N'-butylthioureas:

$$4\text{-}RC_6H_4SO_2NCS + CH_3(CH_2)_3NH_2 \rightarrow$$
$$\rightarrow 4\text{-}RC_6H_4SO_2NHCSNH(CH_2)_3CH_3 .$$

Physical properties of other sulfonyl compounds, especially from the standpoint of their correlation with constants of substituents, were examined besides the reactivity of sulfonyl isothiocyanates. Correlations presented in Table II were tried to employ for determination of the transfer effect of the $SO_2$ group. The transfer of electronic effects of substituents on the reaction centre Y through the $SO_2$ group was calculated according to Jaffe[10] from the reaction constant values $\varrho$; the com-

TABLE I

Rate constants $k$ (l mol$^{-1}$ s$^{-1}$) for reaction of 4-substituted phenylsulfonyl isothiocyanates, benzoyl isothiocyanates[a] and phenyl isothiocyanates[a] with butylamine in cyclohexane at 25°C

| R | $4\text{-}RC_6H_4SO_2NCS$ | $4\text{-}RC_6H_4CONCS$ | $4\text{-}RC_6H_4NCS$ |
|---|---|---|---|
| $CH_3$ | 6 586 | 520 | 0·0244 |
| H | 8 699 | 848 | 0·0549 |
| Cl | 16 240 | 1 270 | 0·1596 |

[a] Ref.[4].

TABLE II

Reaction constants ($\varrho$) and transfer factors of electronic effects ($\pi'_M$) for $SO_2$, CO and CH=CHCO groups in compounds 4-R–$C_6H_4$–M–Y

| Series | M | Y | Correlation (Solvent) | $n^a$ | $r^b$ | $\varrho$ | $\pi'_M{}^c$ |
|---|---|---|---|---|---|---|---|
| $A^d$ | $SO_2$ | $NH_2$ | $pK_a - \sigma_p$ ($H_2O$) | 7 | 0·997 | −1·00 | 0·42 |
| $B^d$ | $SO_2$ | $NH_2$ | $pK_a - X(R)$ ($H_2O$) | 7 | 0·973 | −2·70 | 0·48 |
| $C^e$ | — | $NH_2$ | $pK_a - \sigma_p$ ($H_2O$) | 7 | 0·990 | −2·40 | — |
| $D^e$ | — | $NH_2$ | $pK_a - X(R)$ ($H_2O$) | 7 | 0·965 | −5·56 | — |
| E | $SO_2$ | $NH_2$ | $\delta(NH_2)^f - \sigma_p$ ($CD_3SOCD_3$) | 8 | 0·995 | 0·56 | 0·40 |
| F | $SO_2$ | $NH_2$ | $\delta(NH_2)^f - X(R)$ ($CD_3SOCD_3$) | 8 | 0·994 | 1·61 | 0·42 |
| G | — | $NH_2$ | $\delta(NH_2)^g - \sigma_p$ ($CD_3SOCD_3$) | 6 | 0·983 | 1·39 | — |
| H | — | $NH_2$ | $\delta(NH_2)^g - X(R)$ ($CD_3SOCD_3$) | 6 | 0·996 | 3·79 | — |
| I | $SO_2$ | NCS | $\log k - \sigma_p$ (cyclohexane) | 3 | 0·990 | 1·00 | 0·45 |
| J | $SO_2$ | NCS | $\log k - X(R)$ (cyclohexane) | 3 | 0·935 | 2·79 | 0·47 |
| $K^h$ | CO | NCS | $\log k - \sigma_p$ (cyclohexane) | 7 | 0·944 | 0·64 | 0·3 |
| $L^h$ | CO | NCS | $\log k - X(R)$ (cyclohexane) | 7 | 0·983 | 2·89 | 0·48 |
| $M^h$ | — | NCS | $\log k - \sigma_p$ (cyclohexane) | 7 | 0·996 | 2·20 | — |
| $N^h$ | — | NCS | $\log k - X(R)$ (cyclohexane) | 7 | 0·980 | 5·97 | — |
| $O^i$ | CO | NCS | $\nu_{as}(NCS) - \sigma_p$ ($CHCl_3$) | 6 | 0·992 | −18·72 | 0·51 |
| $P^i$ | CO | NCS | $\nu_{as}(NCS) - X(R)$ ($CHCl_3$) | 6 | 0·967 | −52·00 | 0·45 |
| $Q^j$ | — | NCS | $\nu_{as}(NCS) - \sigma_p$ ($CHCl_3$) | 7 | 0·992 | −36·60 | — |

TABLE II
(*Continued*)

| Series | M | Y | Correlation (Solvent) | $n^a$ | $r^b$ | $\varrho$ | $\pi'^{c}_{M}$ |
|---|---|---|---|---|---|---|---|
| $R^j$ | – | NCS | $\nu_{as}$(NCS) – $X$(R) (CHCl$_3$) | 7 | 0·982 | –114·32 | – |
| $S^h$ | CH : CHCO | NCS | log $k$ – $\sigma_p$ (cyclohexane) | 7 | 0·995 | 0·64 | 0·29 |
| $T^{h,k}$ | CO | NCS | log $k$ – $\sigma_p$ (cyclohexane) | 7 | 0·985 | 0·94 | 0·43 |
| $U^{h,l}$ | CO | NCS | log $k$ – $\sigma_p$ (cyclohexane) | 7 | 0·994 | 1·05 | 0·47 |

[a] Number of compounds in correlation; [b] correlation coefficient; [c] $\pi'_M = \varrho_{4\text{-}RC_6H_4MY}/\varrho_{4\text{-}RC_6H_4Y}$; [d] ref.[3]; [e] ref.[19]; [f] R = $NO_2$ 8·06, Ac 7·86, Cl 7·81, Br 7·77, H 7·65, Me 7·63, OMe 7·56, $NH_2$ 7·08; [g] R = OEt 4·87, OMe 4·80, Me 4·98, H 5·31, Br 5·48, Cl 5·53; [h] ref.[4]; [i] ref.[15]; [j] ref.[20]; [k] reaction with benzylamine; [l] reaction with cyclohexylamine.

parison standards were 4-substituted phenyl isothiocyanates (series M, N, Q, R and 4-substituted anilines (C, D, G, H). Substituents were characterized by Hammet $\sigma_p$ constant[11] and constants $X$(R) derived from vibration frequencies of carbony groups[12]. Comparison of the transfer effects of $SO_2$ and CO groups (Table II) disclosed that the transfer factor of CO group calculated from the linear dependence of the rate constant logarithms with Hammett $\sigma_p$ constants (series K) is lower ($\pi'_{CO} = 0·30$, $r = 0·944$) than the average value we determined for the transfer factor of the $SO_2$ group ($\pi'_{SO_2} = 0·44$). This decrease could be explained by a worse correlation of the afore-mentioned dependence with regard to values of transfer factors of the CO group as obtained for reaction series of benzoyl isothiocyanates with benzylamine (series T, $\pi'_{CO} = 0·48$, $r = 0·985$) and with cyclohexylamine (series U, $\pi'_{CO} = 0·52$, $r = 0·994$).

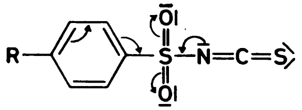
The average value for the transfer factor for the $SO_2$ binding centre $\varepsilon_{SO_2} = 0·59$ was calculated from linear dependences of dissociation constants p$K_a$ (in water) published so far for acids of 4-$RC_6H_4MCOOH$ type (M = $SO_2CH{=}CH_{trans}$, $SO_2CH_2$) with Hammett $\sigma_p$ constants[13] on the basis of additive scheme of transfer effects[14]

$$\pi' = \varepsilon_i^{n_i} \, . \, \varepsilon_j^{n_j} \, . \, \varepsilon_k^{n_k} \, . \, . \, . \, . \, ,$$

where $\varepsilon$ is the transfer factor for the individual binding centres and $n$ is the number of unitary groups. The almost concordant transfer factors for $SO_2CH{=}CH_{trans}$

group ($\pi'_{\mathrm{M}}$ = 0·33, series W in Table III) and COCH=$\mathrm{CH}_{trans}$ group ($\pi'_{\mathrm{M}}$ = 0·29, series S in Table II) evidence the equality between CO and $SO_2$ groups.

The transfer ability studies proved the $SO_2$ group of sulfonyl compounds to have negative transfer effect. The approximately equal average values of the $SO_2$ transfer factor determined by physical methods ($\pi'_{\mathrm{SO_2}}$ = 0·43) and that assessed from kinetic measurements ($\pi'_{\mathrm{SO_2}}$ = 0·46) indicate like configurations of these compounds in fundamental and transition states[14]. Analysis of transfer effects for $SO_2$ and CO groups (Table II) also revealed that the reaction rates of benzoyl and phenylsulfonyl isothiocyanates were equally, but not considerably influenced by substituents. Their influence on reactivity of the –NCS group bound to aromatic ring through $SO_2$ group is probably effected similarly as with benzoyl isothiocyanates, i.e. predominantly through the π-inductive effect[15].



For this reason, the higher reactivity of phenylsulfonyl isothiocyanates than that of benzoyl isothiocyanates resulted from the more electron-accepting effect of $SO_2$ group in comparison with the CO group.

To determine the Hammett constant for $SO_2NCS$ group, the substituent effects of 4-substituted toluene derivatives on chemical shift of aromatic ring protons were examined[16]. The Hammett constant value $\sigma_{\mathrm{p}}(\mathrm{SO_2NCS})$ = 0·63 was calculated from the linear relationship of chemical shifts for *ortho* protons on Hammett constants ($\delta_{\mathrm{H}}$ = 1·08$\sigma_{\mathrm{p}}$ + 7·08, $r$ = 0·977). The enhanced electron-accepting effect of $SO_2NCS$

TABLE III

Transfer factor values for the binding centre $SO_2$ ($\varepsilon_{\mathrm{SO_2}}$) in compounds 4-$\mathrm{RC_6H_4MCOOH}$[a] calculated from the additive scheme

| Series | M | Correlation (Solvent) | $\pi'_{\mathrm{M}}$ | $\varepsilon_{\mathrm{SO_2}}$ |
|---|---|---|---|---|
| V | $SO_2CH_2$ | p$K_a$ – $\sigma_p$ ($H_2O$) | 0·25[a] | 0·52[b] |
| W | $SO_2CH$=$\mathrm{CH}_{trans}$ | p$K_a$ – $\sigma_p$ ($H_2O$) | 0·33[a] | 0·66[c] |

[a] Ref.[13]; [b] $\varepsilon_{\mathrm{CH_2}}$ = 0·48 (ref.[14]); [c] $\varepsilon_{\mathrm{CH=CH}trans}$ = 0·5 (ref.[14]).

group with respect to that of CONCS ($\sigma_p = 0{\cdot}53$, ref.[17]) or NCS ($\sigma_p = 0{\cdot}38$, ref.[18]) groups can be real in spite of the restricted accuracy of this method.

## REFERENCES

1. Suchár G., Kristian P.: Collect. Czech. Chem. Commun. *40*, 2998 (1975).
2. Suchár G., Danihel I., Jasovská A.: Collect. Czech. Chem. Commun. *54*, 1437 (1989).
3. Ludwig M., Pytela O., Kalfus K., Večeřa M.: Collect. Czech. Chem. Commun. *48*, 1182 (1984).
4. Imrich J., Kristian P., Podhradský D., Dzurilla M.: Collect. Czech. Chem. Commun. *45*, 2334 (1980).
5. Gompper R., Hägele W.: Chem. Ber. *99*, 2885 (1966).
6. Hans M., Barnikol F., Imrich J., Suchár G.: Wiss. Z. Paedagog. Hochsch. "Liselotte Herrmann" Güstrow, Math.-Naturwiss. Fak. *27*, No. 1, 15 (1989).
7. Hans M., Imrich J., Barnikol F., Reinke H., Suchár G., Kristian P., Dehne H.: Z. Phys. Chem. (Leipzig) *270*, 1089, (1989).
8. Reichard C. in: *Lösungsmittel-Effekte in der organischen Chemie* (W. Foerst and H. Grünewald, Eds), p. 112. Verlag Chemie, Weinheim 1969.
9. Kristian P., Suchár G., Podhradský D.: Collect. Czech. Chem. Commun. *40*, 2838 (1975).
10. Jaffe H. M.: Chem. Rev. *53*, 191 (1953).
11. Exner O.: Collect. Czech. Chem. Commun. *31*, 65 (1966).
12. Senth-Paul W. A., Van Anyse A.: Spectrochim. Acta, A *28*, 211 (1972).
13. Shorter J. in: *The Chemistry of Sulphones and Sulphoxides* (S. Patai, P. Rappoport and C. J. M. Stirling, Eds), p. 517. Wiley, Chichester 1988.
14. Zhdanov Yu. A., Minkin V. I.: *Korrelyatsionnyi analiz v organicheskoi khimii.* Rostov Univ., Rostov 1966.
15. Kristian P., Hritzová O., Talán P.: Collect. Czech. Chem. Commun. *42*, 671 (1977).
16. Pouchert Ch. J., Campbell J. P. in: *The Aldrich Library of NMR Spectra*, Vol. 4—6. Aldrich Chemical Company, Milwaukee 1974.
17. Danihel I., Imrich J., Kristian P., Barančíková G.: Collect. Czech. Chem. Commun. *50*, 1422 (1985).
18. Kristian P., Antoš A., Vlachová D., Zahradník R.: Collect. Czech. Chem. Commun. *28*, 1651 (1963).
19. Nikolskii B. P. (Ed.): *Spravochnik khimika*, Vol. III, p. 98. Khimiya, Moscow 1964.
20. Kristian P., Suchár G.: Collect. Czech. Chem. Commun. *37*, 3066 (1972).

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