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ORIGINAL PAPER

Syntheses of *N*-alkyl, *N*,*N*-dialkyl, and *N*-(4-substituted phenyl) *O*-ethyl thioncarbamates: a kinetic study

Milutin M. Milosavljević · Aleksandar D. Marinković · Vlada B. Veljković · Dragan D. Milenković

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Abstract The kinetics of the syntheses of *N*-alkyl, *N*,*N*-dialkyl, and *N*-(4-substituted phenyl) *O*-ethyl thioncarbamates from sodium ethyl xanthogenacetate, ten alkylamines, and eight substituted anilines were studied at 25, 30, 35, and 40 °C. The reactions were found to follow second-order kinetics. The kinetic (Arrhenius) parameters, such as the activation energy and the frequency factor, as well as the Eyring parameters, such as the standard entropy, the standard Gibbs energy, and the standard enthalpy of activation, were calculated from the second-order rate constants. The mechanism of the reaction was postulated based on the kinetic studies presented and the optimization of the reaction mechanism using the MOPAC PM6 semi-empirical method.

Keywords Amines · Kinetics · Reaction mechanism · Synthesis · Thioncarbamates

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M. M. Milosavljević
Economics Institute, Kralja Milana 16, 11000 Belgrade, Serbia

A. D. Marinković
Faculty of Technology and Metallurgy, University of Belgrade, Karnegijeva 4, P.O. Box 3503, 11120 Belgrade, Serbia

V. B. Veljković
Faculty of Technology, University of Niš, 16000 Leskovac, Serbia

D. D. Milenković (✉)
High Chemical Technological School, Kosančićeva 36, 37000 Kruševac, Serbia
e-mail: milenkovic_dragan@yahoo.com

Introduction

Syntheses and properties of thio- and thioncarbamates have been attractive for many years because of their structural characteristics, such as the direct connection of the thiocarbonyl group to nitrogen, which contribute to their significant biological activity [1–7]. A general method for their preparation is the reaction of dithiocarbonic acid *O*,*S*-diesters in aqueous or alcoholic solution with primary or secondary amines, and the reaction of monothiocarbonic acid *O*-ester chloride with the corresponding amines [8]. Thioncarbamates can be prepared by the reaction of xanthogenates and amines in the presence of nickel and palladium catalysts [9], thiols and isothiocyanate in the presence of catalysts and without the use of solvent [10], as well as isocyanate and disulfide in the presence of $Zn/AlCl_3$ [11]. Syntheses of *N*-alkyl and *N*,*N*-dialkyl *O*-ethyl thioncarbamates have been performed from diethyl dixanthogenate and amines using different oxidants [12].

In addition, thioncarbamates can be prepared by reacting sodium ethyl xanthogenacetate (NaEtXAc) and alkyl- or dialkylamines [13]. It was found that the reactions follow second-order kinetics, and the formation of the transition state is probably the rate-determining step [13]. According to previous findings [13], the studied reactions were supposed to be thioacyl nucleophile substitutions of NaEtXAc by amines. The nucleophile, namely amine, "attacks" the thiocarbonyl carbon of NaEtXAc, forming a tetrahedral intermediate, as shown in Fig. 1, where R = alkyl, isoalkyl or cycloalkyl, and R′ = H for monoalkyl amines, R = alkyl and R′ = alkyl for dialkyl amines, and R = 4-substituted phenyl and R′ = H for 4-substituted anilines.

The structure of the amine is the most important factor affecting the reaction yield, and it was shown that lower

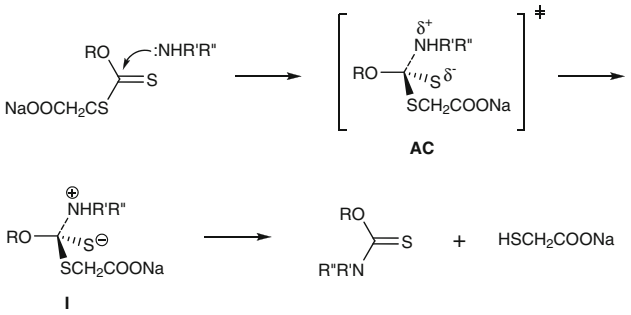

Fig. 1 The most probable reaction pathway (*AC* activated complex, *I* intermediate) [15, 16]

yields were obtained for amines with a bulkier alkyl group [14].

In the present study, we studied the kinetics of the syntheses of *N*-alkyl, *N*,*N*-dialkyl, and *N*-(4-substituted phenyl) *O*-ethyl thioncarbamates from NaEtXAc and a number of alkylamines with various alkyl groups [hexyl, *sec*-butyl (1-methylpropyl), isopropyl (1-methylethyl), isobutyl (2-methylpropyl), isopentyl (3-methylbutyl), cyclopropyl, cyclopentyl, cyclohexyl, as well piperidine and pyrrolidine] as well as aniline and 4-substituted anilines with various substituents [dimethylamino, methoxy, methyl, chloro, bromo, acetyl, and nitro groups]. The main goals of this study were to determine reaction rate constants and the reaction order with respect to the reactant, as well to elucidate the reaction mechanism. Based on the kinetics study, temperature-dependent Arrhenius parameters, such as the activation energy and frequency factor, and Eyring parameters, such as the standard entropy, the standard Gibbs energy, and the standard enthalpy of activation, were calculated.

Results and discussion

The aminolysis of NaEtXAc with a large excess of amine in water obeyed the simple kinetic law given by Eqs. 1 and 2. The linear dependence of $\ln[(A - A_\infty)/(A_0 - A_\infty)]$ on time indicates that the reactions of NaEtXAc with the amines were all first order with respect to NaEtXAc. Values of the apparent rate constant were calculated from the slope of the linear dependence of $\ln[(A - A_\infty)/(A_0 - A_\infty)]$ on time using the least-squares method; the value of the linear correlation coefficient for all reactions studied was higher than 0.98. In a previous study, the reaction was shown to be first order with respect to six alkylamines: ethyl, propyl, butyl, pentyl, diethyl, and dipropylamine [13]. Assuming first-order kinetics with respect to NaEtXAc, the second-order reaction rate constant was calculated according to Eq. 3 for the amines used in this work [hexyl, *sec*-butyl, isopropyl, isobutyl, isopentyl, cyclopropyl, cyclopentyl, cyclohexyl, as well piperidine and pyrrolidine] and for aniline and 4-substituted anilines with various substituents [dimethylamino, methoxy, methyl, chloro, bromo, acetyl, and nitro groups]. Kinetic results obtained in this and a previous study [13] are given in Table 1.

The order of reaction was confirmed by determining rate constants for the reactions between NaEtXAc (1.73×10^{-5} mol dm^{-3}) and amines at different initial concentrations (1.73×10^{-4}, 8.62×10^{-3}, 1.73×10^{-3}, and 1.73×10^{-2} mol dm^{-3}). The amines with propyl, hexyl, isopropyl, dipropyl, cyclopentyl, and piperidine groups were used, as well as aniline and 4-substituted anilines with methoxy, chloro, and nitro substituents. Plots of the calculated apparent first-order rate constants (k_{app}) versus initial amine concentrations gave correlations with slopes that correspond to the values of the second-order rate constants given in Table 1 (the relative error is less than 3%). This allowed the second-order rate law of the investigated reaction to be verified. As the reaction is first order with respect to both reactants, the proposed reaction

Table 1 Second-order reaction rate constants for the reactions of NaEtXAc with amines

Amine	$k_2 \times 10^3$/dm^3 mol^{-1} s^{-1}			
	25 °C	30 °C	35 °C	40 °C
Ethyl[a]	49.61	70.20	107.41	133.73
Propyl[a]	65.44	87.61	107.76	140.85
Butyl[a]	69.46	93.85	128.75	141.20
Pentyl[a]	70.56	97.50	119.14	179.61
Hexyl	69.90	96.80	131.59	165.03
Isopropyl	6.53	9.36	13.72	20.09
sec-Butyl	6.08	9.35	15.64	20.41
Isobutyl	31.47	40.50	58.68	90.69
Isopentyl	40.52	56.10	77.18	109.54
Diethyl[a]	6.12	8.07	9.85	16.39
Dipropyl[a]	5.48	6.48	7.43	9.63
Cyclohexyl	10.67	16.21	21.69	35.92
Cyclopentyl	17.43	26.10	32.72	55.48
Cyclopropyl	27.85	41.92	62.59	86.07
Piperidine	518.4	718.2	869.6	1121.4
Pyrrolidine	1036.7	1359.8	1645.0	2086.0
4-(Dimethylamino)aniline	2.28	4.06	6.24	9.10
4-Methoxyaniline	2.05	3.98	6.04	8.56
4-Methylaniline	1.95	3.94	5.97	8.49
Aniline	1.92	3.92	5.94	8.30
4-Chloroaniline	1.90	3.90	5.90	8.25
4-Bromoaniline	1.89	3.89	5.89	8.23
4-Aminoacetophenone	1.86	3.86	5.86	8.14
4-Nitroaniline	1.82	3.80	5.80	8.09

[a] From Milosavljević et al. [13]

Table 2 Thermodynamic parameters of investigated reactions

Amine	E_a/kJ mol^{-1}	A/dm^3 mol^{-1} s^{-1}	$\Delta S^{\#}_{25}$/J mol^{-1} K^{-1}	$\Delta G^{\#}_{25}$/kJ mol^{-1}
Ethyl	52.8 ± 4.1	9.10×10^7	−93.1	78.2
Propyl	38.9 ± 1.6	4.40×10^5	−137.5	77.5
Butyl	38.0 ± 5.4	3.33×10^5	−139.9	77.3
Pentyl	46.6 ± 4.5	1.01×10^7	−111.2	77.3
Hexyl	44.8 ± 2.1	5.06×10^6	−117.2	77.3
Isopropyl	58.2 ± 1.5	1.04×10^8	−91.8	83.2
sec-Butyl	64.5 ± 5.0	1.21×10^9	−71.6	83.4
Isobutyl	54.9 ± 5.1	1.26×10^8	−89.8	79.3
Isopentyl	51.1 ± 1.7	3.64×10^7	−100.6	78.7
Diethyl	48.7 ± 11	2.03×10^6	−124.3	83.4
Dipropyl	28.3 ± 4.4	4.82×10^2	−193.8	83.6
Cyclohexyl	61.0 ± 4.6	5.15×10^8	−78.5	82.0
Cyclopentyl	57.4 ± 6.4	1.93×10^8	−86.7	80.8
Cyclopropyl	58.8 ± 1.8	5.67×10^9	−77.9	79.6
Piperidine	39.3 ± 3.5	4.09×10^6	−119.1	72.4
Pyrrolidine	35.8 ± 1.8	2.02×10^6	−124.8	70.6
4-(Dimethylamino)aniline	71.2 ± 4.3	2.36×10^8	−72.41	21.64
4-Methoxyaniline	73.2 ± 7.2	4.36×10^8	−72.57	21.69
4-Methylaniline	74.1 ± 8.4	5.72×10^8	−72.67	21.73
Aniline	74.5 ± 8.9	6.62×10^8	−72.71	21.74
4-Chloroaniline	74.9 ± 9.0	7.74×10^8	−72.73	21.75
4-Bromoaniline	75.1 ± 9.1	8.35×10^8	−72.74	21.76
4-Acetylaniline	75.4 ± 9.4	8.87×10^8	−72.77	21.76
4-Nitroaniline	76.2 ± 9.5	1.14×10^9	−72.81	21.77

mechanism where the formation of the activated complex (AC, Fig. 1) is the rate-determining step was also verified.

By analyzing the kinetic data (Table 1), the influence of structural features of the reacting species on the reaction rate can be discerned. Considering the stereochemical aspects of the reacting species involved in creating the AC, a significant influence of the steric effect of the amine alkyl group on AC stability (i.e., on the reaction rate) could be expected. The isoalkylamines that branch at the α carbon have lower rate constants than those that branch at the β carbon, which indicates that the steric hindrance of the bulky group decreases with distance from the reaction center. A higher value of the rate constant for cyclic amines was noted compared to isopropyl amine. If we consider the highly strained cyclopropyl, the less strained cyclopentyl, and the almost strainless cyclohexyl ring, we can see that the rate constant decreases with increasing of hindrance of the amine group. The significantly lower rate constant for dialkylamines is an indication of the more pronounced steric repulsion of the groups in the AC. Piperidine and pyrrolidine show the highest reactivity due to the positive inductive effect of the two alkyl groups and the significantly reduced steric interference of the α-hydrogen atoms. It does seem reasonable that the increased reaction rates of piperidine and pyrrolidine can be attributed primarily to lower steric requirements that may favor the reaction. The polar effect (inductive/field effect) of the alkyl group has a role to play, too. The lower rate constants in a series of 4-substituted anilines are generally the consequence of their lower nucleophilicity, while differences in reaction constants are caused by electronic effects of the substituent.

The activation parameters, such as the activation energy and the frequency factor, as well as thermodynamic parameters, the standard entropy, the standard Gibbs energy and the standard enthalpy of activation, were calculated from the second-order rate constants [15], and the values are given in Table 2. By analyzing the relation between the nucleophile structure and the Eyring parameters, it could be possible to obtain information about the nature of the AC. A high negative value of the standard entropy of activation indicates that a high degree of arrangement is needed to create the activated amine–NaEtXAc complex. Standard entropies of activation for diethylamine, piperidine, and pyrrolidine were close to the values for alkylamines, while dipropylamine has a significantly more negative value, meaning a lower degree of freedom in the corresponding AC. In the series of cycloalkylamines, values of the standard entropies of activation

are more positive than in the isoalkyl series. There are two main factors that contribute to these entropy changes: the lower flexibility of the cycloalkylamine ring enables higher degrees of freedom for other constituents of the AC. The standard entropies of activation for 4-substituted anilines are more positive than those in the alkyl series, and show a low dependence on steric and electronic effects of the substituents present on the phenyl ring.

The values of the Eyring parameters $\Delta H^{\#}_{25}$ and $\Delta S^{\#}_{25}$ are in line with the proposed mechanism, where the expulsion of thioacetate anion is enhanced by the hydrogen bonding in AC, contributing to the highly structured nature of the AC and leading to the large negative standard entropies of activation.

Table 3 provides data on four series of amines that were used in the investigated reaction. All of the series have high correlation coefficients for the dependence of the standard enthalpy $\Delta H^{\#}_{25}$ on the standard entropy $\Delta S^{\#}_{25}$ of activation (Fig. 2), which indicates that steric effects have a similar qualitative influence on the reaction rate in all four series. However, the quantitative influence of the steric effects varies with the series.

Positive values of the correlation coefficient were noted for an alkyl series, a dialkyl series, and a cycloalkylamine series (Table 3). This result indicates the significance of the steric effects of the amine alkyl groups, as their electronic effects contribute in only a minor way to the values of the Eyring parameters. The large negative values of the proportionality constant observed for 4-substituted anilines (Table 3) indicate that the electronic effect of the substituent does have a pronounced effect on the kinetics. Generally, the correlations showed that amines with similar structures and electronic effects have a similar influence on the reaction rate.

In order to analyze the influence of the electronic substituent on the reactivities of *N*-(substituted phenyl) *O*-isobutyl thioncarbamates, a linear free-energy relationship (LFER) in the form of a single-substituent parameter equation (SSP), $s = h + \rho\sigma$, was applied. The substituent-dependent value s used in the SSP equation is k_2, where ρ is the proportionality constant that reflects the sensitivity of the s value to substituent effects, σ is the constant for the corresponding substituent [16], and h is the intercept (i.e., it describes the unsubstituted member of the series). Correlation results are presented in Table 4.

The results for SSP correlations of rate constants with σ at 25 and 30 °C show good precision, and at higher reaction temperatures (35 and 40 °C), the statistical parameters

Table 3 Correlation between standard enthalpies and standard entropies of activation for the investigated reaction, considering four series of amines

Amines	ρ	h	r	*s.d.*	F	n
Alkyl and isoalkyl	0.33 ± 0.01	81.35 ± 1.30	0.994	0.56	831	7
Dialkyl and *sec*-alkyl	0.30 ± 0.01	82.97 ± 0.18	0.999	0.13	44,106	4
Cycloalkyl, piperidine, and pyrrolidine	0.52 ± 0.03	98.72 ± 2.97	0.995	1.36	303	5
4-Substituted anilines	−12.12 ± 0.57	−809.18 ± 41.67	0.993	0.19	447	8

ρ Reaction constant, h intercept, r correlation coefficient, *s.d.* standard deviation, F Fisher test of significance; n number of data included in the correlation

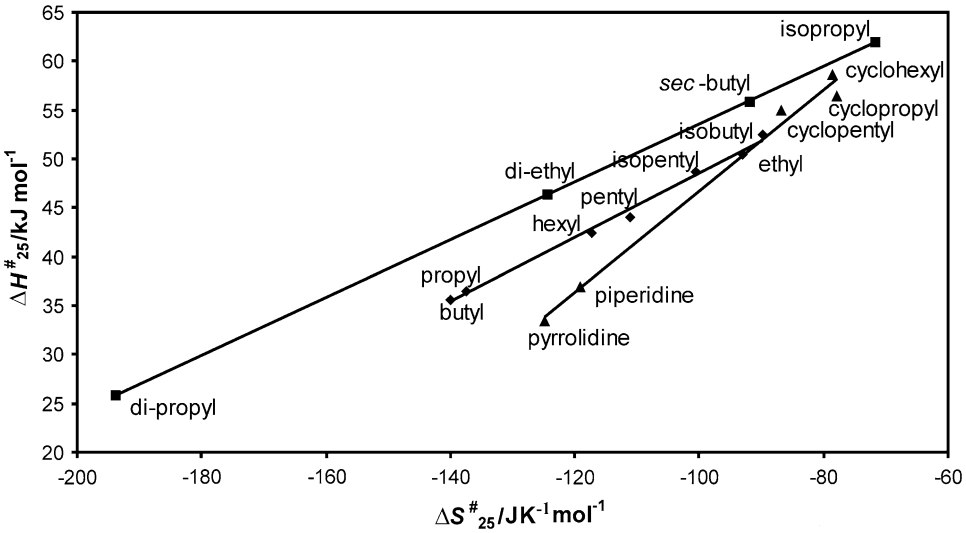

Fig. 2 Correlations between the standard enthalpy and the standard entropy of activation for reactions between NaEtXAc and amines

Table 4 Hammett SSP correlations of reaction rates for the synthesis of *N*-(4-substituted phenyl) *O*-ethyl thioncarbamates with substituent σ values

T/°C	ρ	*h*	*r*	*s.d.*	*F*	*n*
25	−0.16 ± 0.02	1.93 ± 0.01	0.989	0.02	277	8
30	−0.15 ± 0.01	3.93 ± 0.01	0.990	0.01	320	8
35	−0.26 ± 0.03	5.97 ± 0.02	0.967	0.04	86	8
	−0.37 ± 0.03	5.93 ± 0.02	0.993	0.02	148	4[a]
	−0.17 ± 0.02	5.92 ± 0.01	0.984	0.02	91	5[b]
40	−0.62 ± 0.08	8.44 ± 0.04	0.950	0.11	56	8
	−0.95 ± 0.03	8.31 ± 0.14	0.998	0.02	1,476	4[a]
	−0.28 ± 0.02	8.30 ± 0.01	0.994	0.01	273	5[b]

[a] Electron donor included

[b] Electron acceptor included

for separate correlations for electron donor and electron acceptor substituted compounds are excellent. These results show that reaction temperature has a significant influence on the reactivity of 4-substituted anilines that have substituents with different electronic properties. At increased temperature, electron donation from electron donors leads to higher amine nucleophilicity, or it may enable more effective stabilization/delocalization of the charges created during the formation of the AC.

To gain better insight into the mechanism of the reaction, the most probable intermediate structure in the reaction pathway was modeled by using a semi-empirical method. A difficulty was encountered during the optimization process, as the program could not simulate the charged sites of the reacting species, so part of the molecule (the sodium salt of the carboxylic acid) was fixed. The reaction pathway involves the out-of-plane nucleophilic attack of amine on the π orbital of the thiocarbonyl group (Fig. 3) to give the tetrahedral AC (Fig. 1).

The optimized structure of the AC (Fig. 3) was stabilized through the formation of a hydrogen bond between the partially positive hydrogen at the amino group or α-hydrogens and hydrogen bond accepting sites on NaEtXAc. A highly polarizable and dipolar water molecule could additionally stabilize polarizable sites on the AC through electrostatic interactions and hetero-intermolecular hydrogen bonding. It has been proposed that a hydrogen bond is created during the formation of a four-center type of AC in the reaction of aryl thiocarbamates with substituted benzylamines in acetonitrile, and the reaction follows second-order kinetics [17–19]. Castro et al. [20] reported that the reactions of pyrrolidine with *O*-ethyl *S*-(substituted phenyl) dithiocarbonates in aqueous ethanol [$w(C_2H_5OH) = 0.44$] at 25 °C occurred via a mechanism involving a tetrahedral intermediate, the formation of which is the rate-determining step.

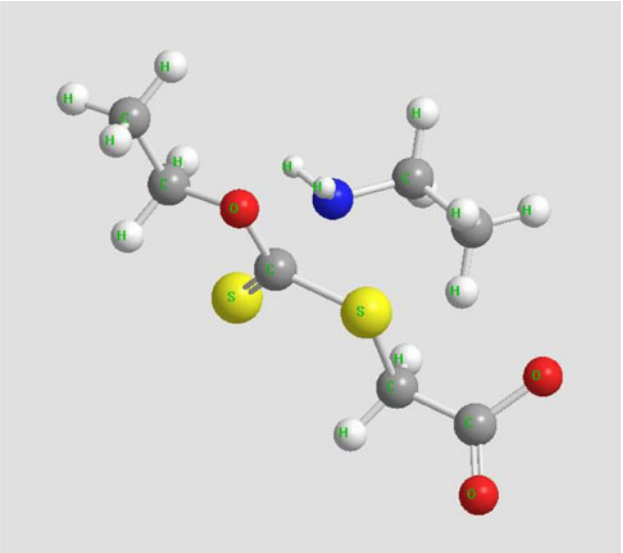

Fig. 3 Structure of the activated NaEtXAc–ethylamine complex with minimum potential energy, as calculated by the MOPAC PM6 method

The hydrogen bonding contributes to the stability of the AC, resulting in a more negative value of the standard entropy of activation. The significantly higher value of the standard entropy of activation for dipropylamine than that for diethylamine could be a consequence of its longer alkyl groups, which lead to higher steric repulsion and thereby a higher degree of AC order. The rigid structures of the piperidine and pyrrolidine rings can be arranged in a limited number of ways in the corresponding AC, which probably contributes to a greater extent than the hydrogen bonding.

Conclusion

The kinetic study of the syntheses of *N*-alkyl, *N*,*N*-dialkyl, and *N*-(4-substituted phenyl) *O*-ethyl thioncarbamates indicates that the steric effects of alkylamines as well as the electronic effects of substituents on aromatic amines exert significant influences on the reaction rate. The values of the thermodynamic activation parameters were in accord with the proposed reaction mechanism and the postulated second-order reaction rate law for all of the amines studied. The standard entropy of activation reflected the high degree of order in the AC, especially for amines that can create an intermolecular hydrogen bond and dialkylamines. The rather high values of the activation energies for 4-substituted anilines are a consequence of their low nucleophilicities, while the similar values of the standard entropy of activation indicate a high degree of order, but a very low sensitivity to electronic substituent effects was also noted.

Experimental

The ^{1}H and ^{13}C NMR spectral measurements were performed on a Bruker AC 250 spectrometer at 250 MHz for ^{1}H NMR and 62.89 MHz for ^{13}C NMR spectra. The spectra were recorded at room temperature in deuterated chloroform ($CDCl_3$) in 5 mm tubes. The chemical shifts are expressed in ppm (δ) values referenced to the TMS (tetramethylsilane) reference signal in ^{1}H NMR and the residual solvent signal in ^{13}C NMR spectra.

All mass spectra were recorded on a Thermo Finnigan Polaris Q ion trap mass spectrometer integrated with a Trace GC 2000 (ThermoFinnigan, Austin, TX, USA) to achieve a GC–MS/MS system. The DIP (direct insertion probe) mode was used to introduce the sample and the EI/MS/MS technique was employed to acquire the spectra. Ionization conditions were: ion source temperature 200 °C, maximum energy of electron excitation 70 eV, corona current 150 μA.

Gas chromatographic analysis (GC) was performed on a PerkinElmer 8700 equipped with a FID detector and a column filled with 5% OV-210 on Gas-Chrom Q [length 2 m, diameter 0.3175 cm (1/8″)]. Injector temperature was 250 °C; detector temperature was 270 °C; the column program was 50 °C (5 min), 10 °C/min, 130 °C (15 min); carrier gas was nitrogen (purity 99.99%), flow was 1 cm^3/min; air flow was 250 cm^3/min (purity 99.99%); and hydrogen flow was 25 cm^3/min (purity 99.99%).

Syntheses of N-alkyl and N,N-dialkyl O-ethyl thioncarbamates [13]

In a three-necked flask (500 cm^3) equipped with a magnetic stirrer, dropping funnel, condenser, and thermometer, 13.6 g of sodium hydroxide (0.34 mol) were dissolved in 150 cm^3 of water while being cooled in an ice bath, following by the addition of 32.1 g of chloroacetic acid (0.34 mol), which was added in small portions. Thereafter, a solution of 54.5 g of potassium ethyl xanthate (0.34 mol) in 200 cm^3 of water was added to the flask at ambient temperature, and the reaction mixture was gently mixed for 2 h. The prepared solution of sodium ethyl xanthogenacetate was then treated with 0.34 mol of the appropriate amine for 1 h, allowed to stand overnight, before being acidified with glacial acetic acid. The product was separated from the reaction mixture by three extractions with 150 cm^3 of ether, and the ether solutions were washed once with 10% aqueous sodium bicarbonate, twice with distilled water, and dried over anhydrous magnesium sulfate. Pure *N*-alkyl and *N,N*-dialkyl *O*-ethyl thioncarbamates were obtained by vacuum distillation.

The structures of known compounds were confirmed by comparing their physical and spectroscopic data with those reported in the literature [21–26]. These data can also be found in the Electronic supplementary material (ESM).

N-Isopentyl O-ethyl thioncarbamate ($C_8H_{17}NOS$)
Yield 90.5% (GC purity 98.5%); b.p.: 124–126 °C (2,000 Pa); MS: $m/z = 175.12$ (M^+); ^{1}H NMR ($CDCl_3$): $\delta = 0.92$ (6H, d, $N(CH_2)_2CH(C\underline{H}_3)_2$), 1.12 (3H, t, $OCH_2C\underline{H}_3$), 1.42 (2H, q, $NHCH_2C\underline{H}_2$), 1.68 (1H, m, C$\underline{H}$), 3.28 (2H, t, $NC\underline{H}_2$), 4.19 (2H, q, $OC\underline{H}_2CH_3$), 6.44 (1H, bs, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.6$, 22.6, 25.8, 36.7, 38.9, 67.9, 188.8 ppm.

N-Cyclopentyl O-ethyl thioncarbamate ($C_8H_{15}NOS$)
Yield 87.2% (GC purity 98.4%); b.p.: 124–128 °C (2,000 Pa); MS: $m/z = 173.06$ (M^+); ^{1}H NMR ($CDCl_3$): $\delta = 1.12$ (3H, t, $OCH_2C\underline{H}_3$), 1.52 (4H, m, $NCHCH_2C\underline{H}_2$), 1.75 (4H, m, $NCHC\underline{H}_2$), 2.68 (1H, q, $NC\underline{H}CH_2$), 4.31 (2H, q, $OC\underline{H}_2CH_3$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 14.4$, 22.8, 23.2, 32.6, 32.8, 55.2, 67.8, 188.7 ppm.

N-Cyclopropyl O-ethyl thioncarbamate ($C_6H_{11}NOS$)
Yield 89.4% (GC purity 99.1%); b.p.: 114–117 °C (2,000 Pa); MS: $m/z = 145.04$ (M^+); ^{1}H NMR ($CDCl_3$): $\delta = 0.68$ (4H, m, $NCHC\underline{H}_2$), 1.12 (3H, t, $OCH_2C\underline{H}_3$), 1.79 (1H, q, $NC\underline{H}CH_2$), 4.16 (2H, q, $OC\underline{H}_2CH_3$) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 7.2$, 14.4, 25.8, 67.3, 188.6 ppm.

Syntheses of N-(4-substituted phenyl) O-ethyl thioncarbamates

Syntheses of *N*-(4-substituted phenyl) *O*-ethyl thioncarbamates were performed analogously to the method described above, except that an ethanol solution (0.34 mol of 4-substituted aniline in 50 cm^3 of ethanol) was added to the aqueous solution of ethyl xanthogenacetic acid sodium salt. After heating the reaction mixture at 60 °C for 3 h, the ethanol was evaporated away and the crude reaction product was vacuum distilled, except for the nitro- and acetyl-substituted compounds, and crystallized from ethanol.

The structures were confirmed by comparing their physical and spectroscopic data with those reported in the literature [27–32]. These data can also be found in the ESM.

Study of the reaction kinetics

The reaction kinetics was followed spectrophotometrically (UV spectrophotometer, Shimadzu 1700) at 280 nm at four different temperatures (25, 30, 35, and 40 °C). The aqueous solutions of NaEtXAc and an amine or ethanol solution of substituted anilines were thermostated at the appropriate temperature for 30 min prior to performing measurements. The initial concentrations of NaEtXAc and the amines

were 1.73×10^{-5} and 4.68×10^{-2} mol dm^{-3}, respectively; exceptionally, the initial concentration of *n*-hexylamine was 2.34×10^{-2} mol dm^{-3}. The solutions (5 cm^3 of each) were mixed, and part of the mixture was poured into a measuring cell placed into the UV spectrophotometer with a thermostat.

Because the amines were in excess in all cases, the reactions became pseudo first order, corresponding to the following well-known kinetic equation:

$$-\ln(c_A/c_{A_0}) = k_{app}t, \quad (1)$$

where c_A and c_{A_0} are the actual and initial NaEtXAc concentrations.

Since $c_A \sim (A - A_\infty)$ and $c_{A_0} \sim (A_0 - A_\infty)$, Eq. 1 becomes

$$\ln[(A - A_\infty)/(A_0 - A_\infty)] = -k_{app}t, \quad (2)$$

where A_0, A, and A_∞ are the absorbances of the reaction system at the initial time, after some period of time, and after infinite time, respectively, and k_{app} is the apparent first-order reaction rate constant, defined as follows:

$$k_{app} = k_2 c_{B,0}, \quad (3)$$

where k_2 is the second-order reaction rate constant and $c_{B,0}$ is the initial amine concentration.

Determining the order of reaction

The reaction kinetics was followed at 30 °C, the initial concentration of NaEtXAc was 1.73×10^{-5} mol dm^{-3}, and initial amine concentrations were 1.73×10^{-4}, 8.62×10^{-3}, 1.73×10^{-3}, and 1.73×10^{-2} mol dm^{-3}.

Geometry optimization

The MNDO-PM6 method implemented in MOPAC2009™ was used to calculate the minimum potential energy of the AC. The initial structures of the compounds were generated by PC MODEL version 4.0 using an MMX force field [33, 34], and were saved as MOPAC input files for the MNDO-PM6 semi-empirical calculations [35, 36]. The geometries of all molecular species were optimized by the PM6 method to the root-mean-square gradient using eigenvector following below 0.042 kJ/mol. VEGA ZZ 2.3.2 was used as the graphical user interface (GUI). Simulation of the polar medium, with full geometry optimization, was performed using the COSMO facility [37, 38].

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