

Decomposition Rates of Some *trans*-2-Nitroso-1-phenylethane Dimers in Solution

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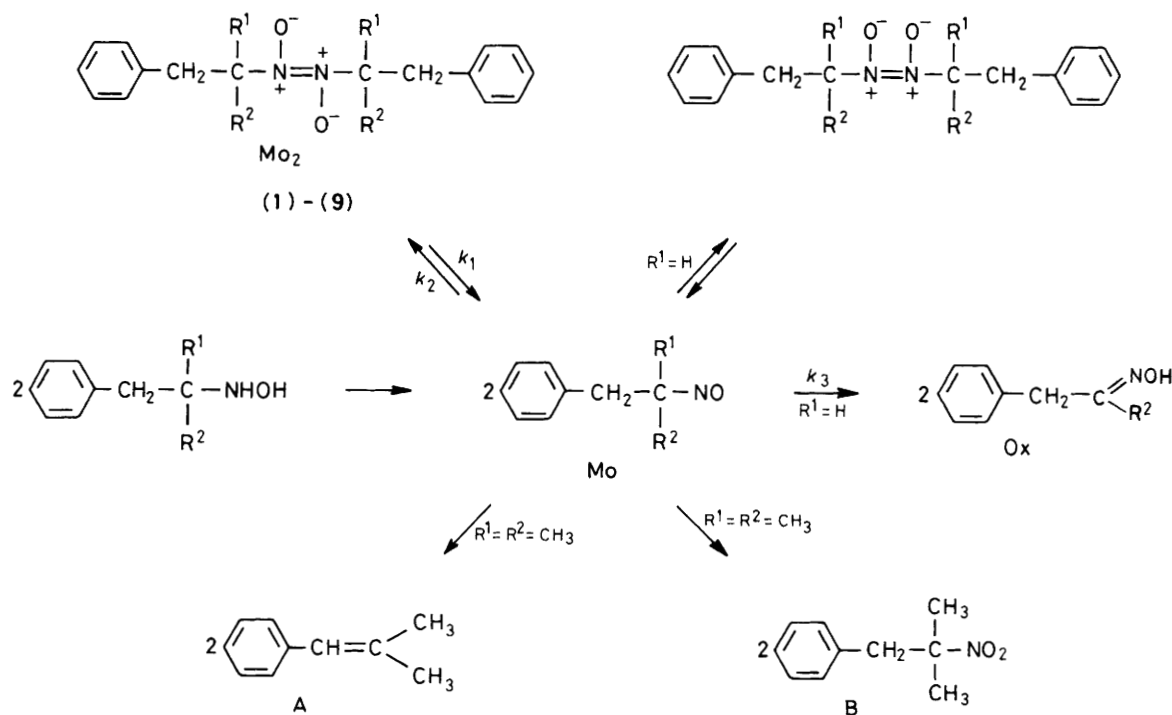
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The rate of decomposition of some *trans*- α -alkyl-substituted 2-nitroso-1-phenylethane dimers, including one deuterium-substituted analogue, has been measured spectrophotometrically in the temperature range 15–60 °C in ethanol, ethanol–water, cyclohexane, carbon tetrachloride, and chloroform. From studies in ethanol the rate constant of monomer formation, k_1 , the Arrhenius parameters, and the heat and entropy of activation were evaluated. The observed rate constant, k_{obs} , evaluated from a first-order plot of the decomposition of the secondary C-nitroso dimers decreased with increasing initial concentrations and with increasing size of the α -alkyl substituent. C-Nitroso dimers with one α -hydrogen decomposed up to 1 200 times faster in ethanol than in non-polar solvents. The decomposition rate of one dimer without α -hydrogens was comparatively independent of the solvent used. However, the addition of water to the ethanol solutions had a stabilizing effect on both types of dimers. The isotope effect, $k_{\text{H}}/k_{\text{D}}$, was shown to be 2–5 on k_1 , and 3–5 on k_{obs} for the dimer of 2-nitroso-1-phenylpropane.

We have previously reported^{1–3} on copper-catalysed autoxidation of some *N*-hydroxyphenylalkylamines which constitute primary metabolites to the drugs amphetamine and phentermine.^{4,5} Subsequent work has revealed that the same products are formed in the metal-catalysed autoxidation of these *N*-hydroxylamines as in their metabolic conversion in liver cytochrome P-450 enzyme systems.⁶ The initial oxidation products are C-nitroso compounds. If the *N*-hydroxylamine contains an α -hydrogen, the nitroso compound is ultimately converted into an oxime, whereas the lack of α -hydrogens results in oxidation of the nitroso to a nitro compound and the formation of a styrene (Scheme).

The C-nitroso monomers, which appear as metabolites to

phenylalkylamines, also act as strong ligands to the reduced iron of cytochrome P-450 enzymes, generating complexes characterized by difference spectra with a maximum at *ca.* 455 nm. However, comparative studies with synthetic C-nitroso compounds, which are available only as dimers, showed a slow and only partial formation of the 455 nm-absorbing complexes.^{7–9} This is certainly due to their very slow rate of dissociation, and to draw more definite conclusions from experiments with dimers included as substrates in enzyme reactions, detailed information on their chemistry was necessary. Some results obtained hitherto¹⁰ show that the formation of cytochrome P-455 nm complexes is directly related to the numerically predicted concentrations of the nitroso monomers.



Scheme.

Pioneering work on the chemistry of *C*-nitroso compounds has been performed by Gowenlock *et al.*^{11–14} Mechanistic and kinetic studies of different *cis* and *trans* *C*-nitroso dimers in various solvents have shown that the dimers first dissociate to the monomers. Then the monomers isomerize to the corresponding oxime, provided that a hydrogen atom is available on the α -carbon.^{11–17}

The present study deals with the complex reaction scheme for a series of ten α -substituted *trans*-2-nitroso-1-phenylethane dimers in solution (Scheme). The effects of different initial substrate concentrations, solvents, and temperatures on the decomposition rate of these dimers are presented. The rate constants of the monomer formation, and the Arrhenius and thermodynamic parameters, are discussed.

Experimental

Materials.—The various α -alkyl-substituted *trans*-2-nitroso-1-phenylethane dimers,^{1,10} and the corresponding oximes^{18,19} were prepared as cited. Deuteriated 2-nitroso-1-phenylpropane dimer [*cf.* compound (**2b**) in Table 1] was prepared by reduction of 2-nitro-1-phenylprop-1-ene with LiAlH_4 and subsequent oxidation with $\text{K}_3[\text{Fe}(\text{CN})_6]$ analogous to the preparation of the non-deuteriated one.¹⁰ A total yield of 53% of a diastereoisomeric mixture of the deuteriated nitroso dimer was obtained, m.p. 63–66 °C. Recrystallization from light petroleum yielded a racemic mixture of the pure (*R*)/(*S*)-diastereoisomer (see Table 1) with minimum isotopic purity 99.5% (n.m.r. and direct inlet mass spectroscopy).

The water used was redistilled in quartz vessels and other solvents were of spectroscopic grade. Except for specially synthesized substances all chemicals were of p.a. or equal quality. The LiAlH_4 used was obtained from E. Merck, Darmstadt, West Germany, and had a minimum isotopic purity of 99%.

Instrumentation.—Uncorrected m.p.s were determined in an electrically heated metal block. Elemental analyses were carried out at the Department of Chemistry, The Swedish University of Agricultural Sciences, Uppsala, and agreed within $\pm 0.4\%$ with the theoretical value. U.v. spectra were recorded on Beckman model 25 and Beckman Acta CIII spectrophotometers. I.r. and ^1H n.m.r. spectra were run for identification purposes on a Perkin-Elmer 157G spectrophotometer and a Perkin-Elmer R 12B spectrometer, respectively. Mass spectra were obtained on an LKB 9000 mass spectrometer, using the direct probe technique. The ionizing potential was 70 eV, the trap current 60 μA , the accelerating voltage 3–5 kV, and the temperature of the ion source 270 °C.

Thin Layer Chromatography.—The t.l.c. separations were performed on precoated silica gel plates (60 F₂₅₄; 0.25 mm; Merck). Before each experiment the plates were activated for 1 h at 100 °C. The plates were developed in chloroform–methanol (16:1 v/v) (system I), chloroform (system II), or chloroform–light petroleum (1:1 v/v) (system III).

Solubility Studies.—The solubility of some of the nitroso dimers in 99.5% or 30% ethanol (water as diluent) was determined in the following way. Amounts of the dimer to ca. 10–30% in excess of the expected solubility were added to test-tubes containing 8.00 ml of the solvent. The test-tubes were stoppered and agitated at 25.0 ± 0.1 °C for 2 h. A sample of the clear supernatant liquid was then withdrawn and, if necessary, appropriately diluted for spectrophotometric analysis.

Kinetic Studies.—The kinetic experiments were performed in volumetric thermostatted flasks. The temperature range was 15–60 °C and the settings were accurate to ± 0.1 °C. At a high

temperature and/or fast reaction rate the experiments were run directly in the thermostatted cuvettes of the spectrophotometer. The initial dimer concentration was varied between 0.02–7.6 mm for dimer (**2a**) (*cf.* Table 1) and between 0.01 and 0.30 mm for the other dimers. At low concentrations the dimers were dissolved within 1 min, but at the highest concentrations 5 min were needed for complete dissolution. The elapsed time was always determined from the moment the solvent was added. Although the solubility of dimers varied, which affected the true starting time of the experiment, the dissolution time was short in comparison with the period during which the reaction rate constant was determined. The samples were withdrawn at the times assumed appropriate and, if necessary, diluted to suitable concentration. The amount of dimers was determined by immediate recording of the u.v. spectra in the range 220–320 nm, where the reaction products showed no absorption, or alternatively, by measuring at the major absorbance band (see Table 1). A 50–95% decomposition was employed in the ethanol and ethanol–water mixtures, and mostly a lower percentage decomposition in the other solvents.

Theory

The rate equations of the reactants and products applicable to the model of decomposition (Scheme) of dimers (**1**)–(**8**) (*cf.* Table 1) are (1)–(4). If the monomer concentration is constant

$$d[\text{Mo}_2]/dt = -k_1[\text{Mo}_2] + k_2[\text{Mo}]^2 \quad (1)$$

$$d[\text{Mo}]/dt = 2k_1[\text{Mo}_2] - 2k_2[\text{Mo}]^2 - k_3[\text{Mo}] \quad (2)$$

$$d[\text{Ox}]/dt = k_3[\text{Mo}] \quad (3)$$

$$d[\text{Mo}_2]/dt + \frac{1}{2}d[\text{Mo}]/dt + \frac{1}{2}d[\text{Ox}]/dt = 0 \quad (4)$$

and low in comparison with the dimer and oxime concentrations a steady state is expected very soon after the start, *i.e.* $d[\text{Mo}]/dt = 0$. Applying this approximation equation (2) becomes (5). Insertion into equations (4) and (3) gives (6).

$$[\text{Mo}] = 2k_1[\text{Mo}_2]/(2k_2[\text{Mo}] + k_3) \quad (5)$$

$$-d[\text{Mo}_2]/dt = \frac{1}{2}d[\text{Ox}]/dt = \frac{1}{2}k_3[\text{Mo}] \quad (6)$$

Insertion of (5) into equation (6) gives (7). If this is valid a

$$-d[\text{Mo}_2]/dt = \frac{k_1k_3}{2k_2[\text{Mo}] + k_3}[\text{Mo}_2] = k_{\text{obs}}[\text{Mo}_2] \quad (7)$$

first-order rate constant, k_{obs} , for the overall reaction can be evaluated from the straight line obtained in the logarithmic plot of the absorbance *versus* time.

Inversion of k_{obs} gives equation (8). If the steady-state con-

$$\frac{1}{k_{\text{obs}}} = \frac{2k_2}{k_1k_3}[\text{Mo}] + \frac{1}{k_1} \quad (8)$$

centration of the monomer is assumed to be proportional to the initial concentration of the dimer, *i.e.* $[\text{Mo}]_{\text{ss}} \propto [\text{Mo}_2]_0$, equation (8) becomes (9) where a is a dimensionless propor-

$$\frac{1}{k_{\text{obs}}} = \frac{2k_2a}{k_1k_3}[\text{Mo}_2]_0 + \frac{1}{k_1} \quad (9)$$

tionality factor.

A plot of $1/k_{\text{obs}}$ against $[\text{Mo}_2]_0$ will give a straight line with an intercept $1/k_1$ and a slope proportional to k_2/k_3 .

Table 1. Physical data for the α -alkyl-substituted 2-nitroso-1-phenylethane dimers (Mo_2)

Compound	R ¹	R ²	M.p. (°C) ^a	Yield (%) ^b	$\lambda_{\text{max.}}$ /nm	$10^{-3}\epsilon^c/\text{l mol}^{-1}\text{ cm}^{-1}$	Solubility (mm)
(1)	H	H	88–92	26	290	7.7	
(<i>R</i>)(<i>S</i>)-(2a)	H	Me	92–94	52 ^g	293	7.9	2.4 ^c 1.0 ^h
(<i>R</i>)(<i>R</i>)-(2a) ^d	H	Me	96–98	35	293		
(<i>S</i>)(<i>S</i>)-(2a) ^d	H	Me	96–98	49	293		
(2b) ^e	² H	Me	90–96	53 ^g	293	7.6	
(3)	H	Et	106–108	56	297	7.3	
(4)	H	Pr ⁿ	108–110	28	297	7.7	1.1 ^c
(5)	H	Bu ⁿ	84–86	31	296	5.8	
(6)	H	Pr ⁱ	161–162	34	298	6.8	
(7)	H	Bu ^t	187–189 ^f	68	304	6.5	
(8)	H	Bu ⁱ	97–99	31	297	7.2	0.005 ^h
(9)	Me	Me	73–75	25	296	6	

^a Recrystallization solvent, light petroleum unless otherwise stated. ^b The yield applies to the total isomeric mixture for dimers (2)–(8). ^c 99.5% Ethanol, 25 °C. ^d $[\alpha]_D^{20}$ (CH_2Cl_2) for (*R*)(*R*)-(2a) is -104.9 and for (*S*)(*S*)-(2a) $+104.4^\circ$. ^e 2-Nitroso-1-phenyl[1,2-²H₂]propane dimer. ^f Recrystallization solvent, light petroleum–dichloromethane. ^g Consecutive recrystallizations yielded a racemic mixture of the pure (*R*)(*S*)-diastereoisomer. ^h 30% Ethanol, 25 °C.

Since compound (9) (*cf.* Table 1) is a tertiary dimer, no isomerization to the oxime occurs. Furthermore, the decomposition reaction of the dimer is irreversible at low concentrations,^{20,21} so, $k_{\text{obs}} = k_1$, for the dimer (9).

From the logarithmic form of the Arrhenius equation, the parameters E_a and A were evaluated for the monomer formation (k_1). By the use of the evaluated Arrhenius parameters, the heat of activation, ΔH^\ddagger , and the entropy of activation, ΔS^\ddagger , were obtained from the Eyring equation.²²

Results

Physical Properties of the Compounds Studied.—All the *trans* dimers showed absorption bands (Table 1), which were in accord with those in earlier reports.¹¹ A general characteristic of the dimers is that they are sparingly soluble in protic solvents. The solubility decreases with increasing size of the α -alkyl substituent (Table 1). However, competing decomposition reactions of the dimers render proper dissolution studies impossible. A slow rate of dissolution in combination with decomposition of the dimers in solution might introduce uncertainty of the numerical values of the absorptivity coefficients. Kinetic studies with most of the dimers could, due to their low solubility in ethanol, be performed only at low concentrations ($<0.3\text{mM}$).

Dimers (2) and (9) were chosen as model compounds and were studied in more detail. Dimer (9) lacks α -hydrogens and consequently oxime formation is impossible (Scheme).

Qualitative Identification of Products Formed.—The decomposition reactions were followed by t.l.c. for some of the dimers, and the corresponding oximes were thereby identified.^{1,2}

Order of Reaction.—The k_{obs} value was evaluated from the linear part of the logarithmic plot of the absorbance *versus* time. For dimers (9) and (1) the plots are linear during the whole time studied. For the other dimers the plots are linear only for about one half-life. The deviation from linearity is towards a lower order, and it appears earlier the higher the concentrations and the lower the temperatures.

Effect of Different Solvents on the Reaction Rate.—The decomposition of the nitroso dimers is sensitive to the solvent used. In ethanol and ethanol–water it initially follows first-order kinetics for compound (9) as well as for (2a), whereas in chloroform the decomposition of compound (2a) shows non-

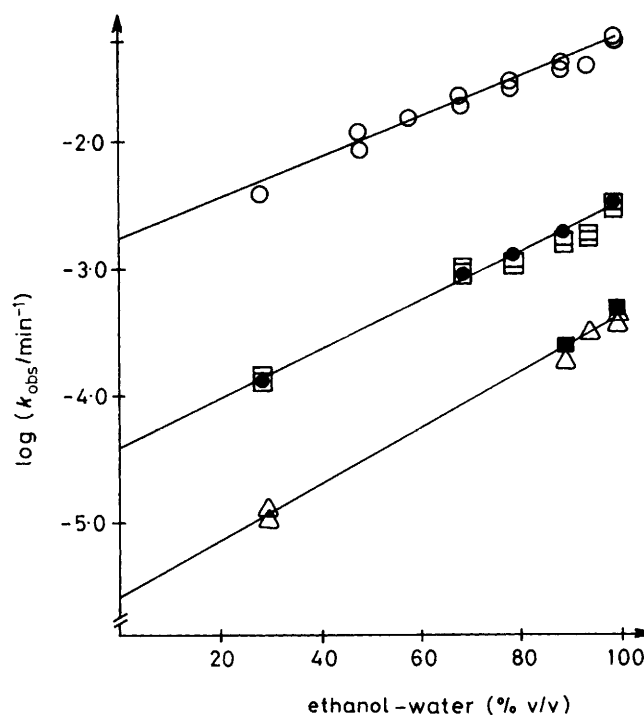


Figure 1. Plot of $\log k_{\text{obs}}$ versus percentage ethanol in water with $[\text{Mo}_2]_0$ ca. $70\mu\text{M}$: ○, 2-methyl-2-nitroso-1-phenylpropane dimer, (9), 25 °C; □, 2-nitroso-1-phenylpropane dimer, (*R*)(*S*)-(2a), 40 °C; △, (*R*)(*S*)-(2a), 25 °C; ●, (*S*)(*S*)-(2a), 40 °C; ■, (*S*)(*S*)-(2a), 25 °C

linear behaviour. Ethanol was therefore used as solvent in subsequent experiments.

The evaluated first-order rate constants k_{obs} for the decomposition of compounds (1)–(6) and (8), studied in 99.5% ethanol, are in Supplementary Publication No. SUP 56594 (7 pp.). Compound (7) was studied only in a few experiments due to its low solubility. These data show (1) a decrease in k_{obs} with increasing size of the α -alkyl substituents; (2) that the rate of decomposition of the enantiomers (*R*)(*R*)-(2a) and (*S*)(*S*)-(2a) is the same as for the *meso* isomer (*R*)(*S*)-(2a); (3) a considerably higher rate of decomposition for dimer (9); and (4) that k_{obs} increases with the temperature for all the dimers.

Water has a stabilizing effect on the dimers. In Figure 1 are shown the observed first-order rate constants for dimers (9),

(*R*)(*S*)-(2a), and (*S*)(*S*)-(2a) in different ethanol–water mixtures. The (*S*)(*S*)-isomer presents about the same k_{obs} value as the *meso*-isomer. The decomposition of compound (9), which lacks α -hydrogens, is comparatively independent of the kind of solvent used (Table 2). Dimer (2a) decomposes *ca.* 60 times faster in 99.5% ethanol than in cyclohexane or benzene and 1 200

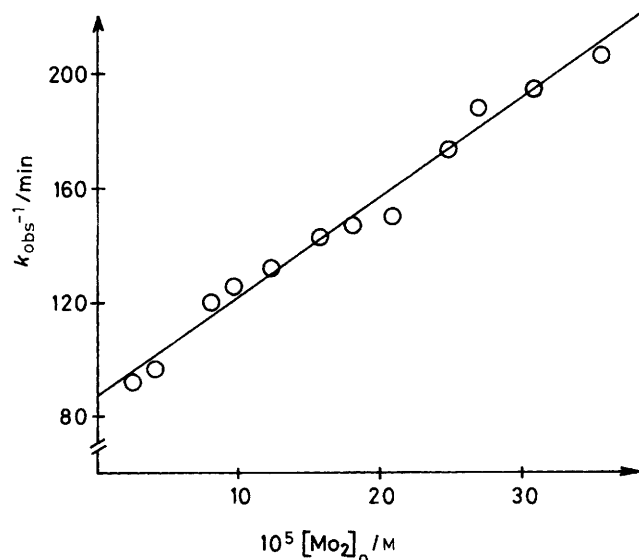


Figure 2. Plot of $1/k_{\text{obs}}$ versus $[\text{Mo}_2]_0$ for 2-nitroso-1-phenylpropane dimer, (*R*)(*S*)-(2a) in 99.5% ethanol at 50 °C

Table 2. The effect of different solvents on the evaluated first-order rate constant for the decomposition of compounds (9) and (*R*)(*S*)-(2a). $T/^\circ\text{C}$ in parentheses. $[\text{Mo}_2]_0$ *ca.* 70 μM

Solvent	Compound (9) $10^2 k_{\text{obs}}/\text{min}^{-1}$	Compound (2a) $10^5 k_{\text{obs}}/\text{min}^{-1}$
Ethanol, 99.5%	6.20 (25)	37.0 (25) 271 (40) 2 430 (60)
Benzene		0.838 (25)
Cyclohexane	22.2 (25)	42.2 (60)
Carbon tetrachloride	15.6 (25)	2.04 (60)
Dichloromethane	4.84 (25)	
Chloroform	0.991 (15)	0.67 ^a (25)
	4.28 (25)	0.75 ^a (40)
	4.12 (25)	5.8 ^a (60)

^a k_{obs} evaluated up to *ca.* 5% reacted substance.

times faster than in carbon tetrachloride. Moreover in chloroform compound (2a) shows deviation from both zero- and first-order kinetics even initially.

Effect of Initial Concentration on Reaction Rate.—The k_{obs} values (SUP 56594) also show that the decomposition of dimer (1) is essentially independent and that of dimer (9) clearly independent of the initial dimer concentration. For all other dimers studied the rate of decomposition is governed by the initial concentration as shown for the nitroso dimer (2a) in Figure 2 [*cf.* equation (9)]. The higher the initial concentration, $[\text{Mo}_2]_0$, the lower the k_{obs} value. From plots like that in Figure 2 the values of the rate constant for nitroso monomer formation, k_1 , were estimated. Only the linear part of the plots, *i.e.* $[\text{Mo}_2]_0 < 0.3 \text{ mm}$, was used. The k_1 values for the decomposition of some of the dimers in 99.5% ethanol are given in Table 3. The same variation as for k_{obs} is observed for k_1 , *i.e.* k_1 decreases with increasing size of the α -alkyl substituent, but to a lower degree. The deuterium-substituted 2-nitroso-1-phenylpropane dimer (2b) has a considerably lower k_1 value than the non-deuterated one (2a). This difference decreases with increasing temperature.

Arrhenius Plots and Thermodynamic Parameters for Monomer Formation in Ethanol.—The Arrhenius plots are linear in the temperature range studied (Figure 3) and the

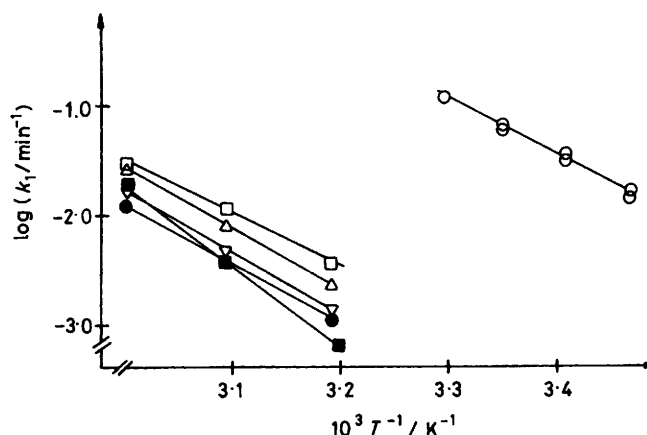


Figure 3. The Arrhenius plot of the monomer formation constant k_1 , in ethanol: Δ , compound (1); \square , compound (2a); \blacksquare , compound (2b); ∇ , compound (3); \bullet , compound (8); \circ , compound (9). For structures see Table 1

Table 3. The rate constant of monomer formation k_1 and thermodynamic parameters for the decomposition of some dimers in ethanol. The number of runs is shown in parentheses

Comp.	$10^3 k_1/\text{min}^{-1}$				E_a kJ mol^{-1}	$\log(A/\text{s}^{-1})$	$\Delta H^\ddagger(40^\circ\text{C})$ kJ mol^{-1}	$\Delta S^\ddagger(40^\circ\text{C})$ $\text{J K}^{-1} \text{mol}^{-1}$
	40 °C	50 °C	60 °C					
(2a)	3.53(5)	11.4(12)	29.3(5)		92.1	11.14	89.5	−40
(2b)	0.669(3)	3.76(4)	16.3(4)		139	18.25	136	96
(1)	2.18(4)	7.84(4)	26.0(3)		108	13.57	105	6.1
(3)	1.31(4)	4.45(5)	16.3(4)		110	13.62	107	7.0
(4)	1.22(4)	4.63(4)	15.7(3)		111	13.89	109	12
(8)	1.15(5)	3.82(4)	12.1(8)		103	12.40	100	−16
<hr/>								
(9)	15 °C	20 °C	25 °C	30 °C	99.7	14.47	97.1	23
	13.7	29.7	59.7	114				
	15.6	31.3	62.0					
		32.3						
		33.4						

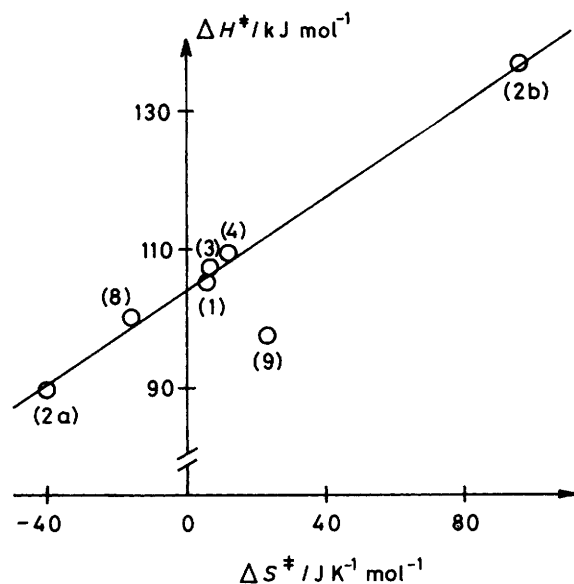


Figure 4. Plot of ΔH^\ddagger versus ΔS^\ddagger for data of Table 3

thermodynamic parameters are given in Table 3. The correlation between the heat of activation ΔH^\ddagger and the entropy of activation ΔS^\ddagger is shown in Figure 4. The dimers which have α -hydrogens follow very closely a linear relationship, whereas compound (9) deviates from this line.

Discussion

The results of this study are compatible with the mechanism of decomposition of the *trans*-nitroso dimers, illustrated in the Scheme. The *cis*-nitroso dimers generally show characteristic absorption bands at wavelengths 20 nm lower than the *trans*-nitroso dimers.^{3,11} No such absorption bands were observed in the experiments performed. The secondary oxidation products A and B are formed from dimer (9) in reactions which are slow compared with the formation of the monomer.² Consequently, these products were not detected in our studies.

That the k_{obs} values for the decomposition of compounds (1)–(8) decreased with increasing size of the alkyl group at the α -carbon is probably due to increased steric interaction between the alkyl and nitroso groups. Our previous studies¹⁰ have indicated that oxime formation (k_3) is the rate-determining step (*cf.* Scheme). Contrary to conclusions in other studies,²³ rearrangement of the nitroso monomer to the oxime tautomer was not found to be instantaneous in hydroxylic solvents. Our findings indicate that a rate-determining step in the tautomerization (k_3) would involve an attack on the α -carbon. In addition to the steric interaction, an increasing inductive effect with increasing size of the alkyl group would lead to decreased reactivity at the α -carbon. So, the little decrease in k_1 values together with a probable decrease in k_3 values could explain the decreasing k_{obs} values. Furthermore, increased k_2 values with increasing size of the alkyl substituent at the α -carbon would also lead to decreasing k_{obs} values.

The decomposition of dimer (2a) is very much dependent on the kind of solvent used (Table 2). In non-polar solvents the isomerization of the corresponding monomer is very slow compared with the dimerization. It has been shown^{1,24} by n.m.r. that there exists an equilibrium in chloroform between the monomer and the dimer (k_1/k_2) and oxime formation (k_3) was not observed. We can thus conclude that chloroform promotes monomer but not oxime formation, whereas ethanol promotes both.

Engberts *et al.*²⁵ suggest, from i.r. and n.m.r. studies, that *C*-nitroso compounds are proton acceptors in hydrogen bonding with the oxygen atom of the NO group as the hydrogen-bonding site. Moreover, the *trans*-dimeric *C*-nitroso compounds form stronger hydrogen bonds than do the corresponding monomers. This could explain the stabilizing effect of water on the rate of decomposition, *e.g.* that dimers (9) and (2a) decompose more slowly in water–ethanol mixtures than in absolute ethanol (Figure 1).

Since the evaluated first-order rate constants decrease with increasing initial dimer concentrations, first-order kinetics is not applicable to the overall reaction. According to the Scheme, k_1 and k_3 are first-order reaction constants whereas k_2 is second order. Steady-state treatment gives $k_{\text{obs}} = k_1 k_3 / (2k_2[\text{Mo}] + k_3)$ according to equation (7). This expression could be simplified to $k_{\text{obs}} = k_1 k_3 / 2k_2[\text{Mo}]$, if $k_2[\text{Mo}] \gg k_3$, *i.e.* if the recombination of the dimer is very fast compared with oxime formation.

If the recombination of the dimer is slow compared with the oxime formation and $k_3 \gg k_2[\text{Mo}]$ the result will be that $k_{\text{obs}} = k_1$. This is true of dimer (1), indicating that the k_2 value ought to be much smaller (at least 2–3 orders of magnitude) than for the other dimers (2)–(8). The results obtained with dimer (1) are consistent with those of Batt and Gowenlock.¹² For the other substances, however, none of these assumptions can be made, since the k_{obs} value changes with the initial dimer concentration $[\text{Mo}_2]_0$ and, consequently, with the steady-state concentration of the monomer $[\text{Mo}]_{\text{ss}}$.

Regarding the observed isotope effects for compound (2) (*cf.* Table 3), changes of vibration frequencies and zero-point energies which occur in reaching a non-linear transition state, as in an intramolecular or cyclic reaction, are different from those occurring with linear transition states, in which the loss of stretching vibrations is generally of primary importance. If there is only the loss of a bending frequency in the transition state, the isotope effect will be relatively small because of the smaller frequencies and zero-point energies of bending as compared with stretching vibrations. The magnitude of the isotope effects for such reactions is likely to be in the order of $k_{\text{H}}/k_{\text{D}}$ 2–3.²⁶ This is in accord with the results shown in Table 3. Comparison of k_1 for compound (2) shows an isotope effect, $k_{\text{H}}/k_{\text{D}}$, of *ca.* 5 at 40 °C which decreases to *ca.* 2 at 60 °C, *i.e.* dimer (2a) has a larger k_1 , and lower E_a , ΔH^\ddagger , and ΔS^\ddagger values as compared with (2b).

The k_{obs} values of compounds (2a and b) show an isotope effect of $k_{\text{H}}/k_{\text{D}}$ 3–5. Here the isotope effect is probably a contribution from both the dissociation of the dimer (a secondary isotope effect) and the isomerization of the monomer (a primary isotope effect). Since k_{obs} [*cf.* equation (7)] involves k_1 in the numerator and k_3 in both the numerator and the denominator the rate constants are too interwoven to permit of any firm conclusion.

Dimers (2a) and (8) have negative ΔS^\ddagger values. A negative entropy of activation implies that the activated complex for the unimolecular reaction has much less entropy than the reactant as would be the case if a linear molecule formed a cyclic activated complex.^{27,28}

Since in most of the experiments only the dimer concentration was monitored it is of some interest to obtain an expression for k_{obs} in terms of rate constants and dimer concentration. If steady-state approximation can be assumed, that is $d[\text{Mo}]/dt = 0$, equation (2) gives $[\text{Mo}]$ as a function of $[\text{Mo}_2]$. Solving equation (2) for $[\text{Mo}]$ and inserting this into equation (1) gives (10).

$$k_{\text{obs}} = -\frac{k_3}{2[\text{Mo}_2]} \left[\frac{k_3}{4k_2} \pm \sqrt{\frac{k_3^2}{16k_2^2} + \frac{k_1}{k_2}[\text{Mo}_2]} \right] \quad (10)$$

In the steady-state approximation, k_{obs} is thus related only to the rate constants and the dimer concentration. This equation being very complex, the approximate values of the rate constants have been determined from the experiments and are now further evaluated in a data program which will enable the estimation of each elementary rate constant.

Acknowledgements

We thank Professor L.-O. Sundelöf for discussions and Mr. M. Ashton, Miss B. Bergstrand, Miss H. Engvall, and Mrs. B. Johansson for technical assistance. One of us (G. L.) also thanks The Swedish Pharmaceutical Society and the IF Foundation for Pharmaceutical Research for grants.

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Received 18th June 1985; Paper 5/1028