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# Mechanochemically induced crossdimerizations of nitrosobenzenes. Kinetics and solid-state isotope effects

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Mechanical treatment (milling) of crystals of aromatic nitroso dimers (azodioxides) induces their dissociation and crossdimerizations. The mechanisms of these processes are discussed on the basis of kinetic studies and the solid-state <sup>15</sup> N kinetic isotope effect, which is measured for the first time. By comparison with analogous processes in cocrystals and in melts, it appears that the reactions follow similar mechanism in which the surface deformations play the crucial role. The system can also be used as a model for a more general conceptual study of solid-state reaction mechanisms. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: azodioxides; mechanochemistry; nitroso compounds; solid-state isotope effects; solid-state reaction mechanism

## INTRODUCTION

Interest in the reactions occurring in the solid phase, as well as on the solid-solid interface, has increased rapidly because of their application in the development of the solvent-free synthesis. Fast development of mechanochemical preparative methods has been successfully used in a series of organic reactions including imine condensations, cycloadditions, Michael addition, and especially organocatalytic reactions including also asymmetric catalysis.<sup>[1-7]</sup> In addition, we have recently reported the solvent-free preparation of aromatic nitroso compounds.<sup>[8e]</sup> However, in spite of the success in organic synthesis, our knowledge about the underlying mechanisms of the thermal solidstate chemical processes is still insufficient. Interpretations of the kinetic data of the solid-state processes, especially those occurring mechanochemically, have been focused mostly on the reactions of inorganic compounds. In our previous work,<sup>[8]</sup> we have demonstrated that the simple organic reaction, dimerization of C-nitroso compounds, can serve as a convenient model for studying kinetics and mechanisms of the reactions of organic molecules in crystals.

Majority of condensed-phase reactions were previously interpreted within the nucleation and growth concept by application of mathematical models such as the Avrami-Erofeev equations<sup>[9]</sup> or the recent mechanistic interpretations by Finke and Watzky,<sup>[10]</sup> as well as by M. E. Brown.<sup>[11]</sup> Measuring processes in the crystal or on the interface of two solid phases strongly depends on the experimental conditions, which vary from one experiment to another.<sup>[11,12]</sup> Every investigated crystalline or polycrystalline sample is specific because of its inhomogenity every crystal is characterized by its "individuality" because it has its own history of growth and formation. Number and distribution of defects in the crystal lattice, especially on its surface, critically influence the rate and nature of solid-state process. We have recently shown how the appearance of crystal defects caused by sublimating away of molecules from the surface can drastically affect the reaction rate of the chemical process in the crystal.<sup>[13]</sup> There is no doubt that surface defects could also play a crucial role during the mechanochemically induced reactions.

Because the observed rate constants,  $k_{obs}$ , are strongly dependent on the sample used in the experiment, their values are not sufficiently reproducible for rigorous mechanistic interpretations. Absence of experimental *ceteris paribus* condition, which is critical for the exact scientific explanation, requires an invention of new approach and new models in studying the reaction mechanisms and associated processes in solid-state chemistry. In principle, to avoid these sample-dependent effects, it is necessary to measure a set of reactions of structurally similar reactants simultaneously in the same experiment.

The model that we have previously developed<sup>[8]</sup> is based on the reactions of the substituted nitrosobenzenes in the crystal phase. The reaction system is in principle simple because it includes formation and/or breaking of only one chemical bond between two nitrogen atoms in dimerizations and dissociations of nitroso compounds<sup>[14]</sup> (Scheme 1).

It is already known for four decades that azodioxide (the nitroso dimer) dissociates in the gas phase and collects in the form of monomer crystals on the cold finger of the sublimer. Warming the crystals to room temperature causes the solid-state recombination of monomers to dimers. Monomers can also be obtained by the cryogenic photolysis<sup>[8b,8d,15]</sup> of dimers under 170 K. Only a slight warming greater than 170 K causes their redimerization. However, the thermal redimerization of the monomers obtained after sublimation follows quite a different mechanism than the redimerization of monomers obtained inside the single crystal by photolysis.<sup>[8d]</sup> While the former

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**Scheme 1.** Dimerization and dissociation of C-nitroso compounds under different conditions

process is relatively slow with the reaction half times between 10 and 45 min, the redimerization of the nitroso molecules produced by photolysis in the single crystal<sup>[8b,15]</sup> has been found to be a very fast process, such that it is very difficult to measure the reaction rate under the applied experimental setup.

In our previous papers we have shown that information about the processes that include both phase transformations and underlying chemical reactions could in principle be followed by the time resolved infrared (IR) (by measuring the signal at 1260 cm<sup>-1</sup>, assigned to the ON=NO asymmetric stretching) and by the time resolved XRPD.<sup>[8c]</sup> It has been demonstrated that, in some cases, if the process is measured by different methods, the diverse kinetic behaviors have been observed.

In this work, we wish to open a new approach to the study of the mechanisms of solid-state reactions by measuring the multicomponent parallel processes of dissociation and dimerization of the aromatic nitroso compounds in the same sample. Especially, this study is focused on the solid-state kinetic isotope effects and the comparison of the same chemical reaction under different solid-state environments.

Multicomponent solid-state processes are studied in the experiments with mechanochemically induced cross-dimerization (formations of *heterodimers*)<sup>[16,17]</sup> of two differently substituted nitrosobenzenes (A-NO + B-NO). Mechanochemical reactions are compared with the processes occurring in cocrystals and in the melts. In such system, we follow three simultaneous dimerizations in one experiment, the formations of A-A, B-B, and A-B dimers.

For identification of the heterodimer in the solid sample, as well as for measuring the isotope effect, one of the homodimer partners (*p*-bromonitrosobenzene) is labeled with <sup>15</sup> N isotope, and the cross-dimerized product can be easily identified by the appearance of the  $O^{14}N=^{15}NO$  stretching signal in the IR spectrum. The principle is shown in Scheme 2.

The model molecules selected in this study are the nitrosobenzenes with various substituents in *p*-position (Scheme 3).



Scheme 2. The principle of identification of heterodimers in solid samples

<sup>™</sup> N or <sup>15</sup>N) R = H, Br, Cl, NO<sub>2</sub>, I

Scheme 3. Compounds used in the study of solid-state cross-dimerization

## **EXPERIMENTAL SECTION**

#### Fourier transform infrared spectroscopy

Fourier transform infrared spectra by means of the attenuated total reflectance (ATR) were recorded on a Bruker Vector 22 spectrometer (Bruker Optics, Inc., Billerica, MA, USA) using the PIKE MIRacle ATR (PIKE Technologies, Inc., Madison, WI, USA) sampling accessory with a diamond/ZnS crystal plate. A pressure clamp was used for measurement of ATR of solid samples. The background spectrum was obtained by observing ambient air. The spectra were recorded in the single reflection configuration at room temperature in the spectral range between 4000 and  $600 \text{ cm}^{-1}$  at the resolution of 4 cm<sup>-1</sup>. Normally, 32 scans were averaged for a spectrum. The spectra were recorded every 0.5–2 min. Data were collected in a period of 1.5 h.

#### Preparation of nitrosobenzene derivatives

Nitrosobenzene and its *p*-Br, *p*-Cl, and *p*-NO<sub>2</sub> derivatives were prepared by oxidation of corresponding anilines with *Oxone*<sup>\*</sup> (K<sub>2</sub>SO<sub>5</sub>× K<sub>2</sub>SO<sub>4</sub>× KHSO<sub>4</sub>) analogously to the method previously described in the literature.<sup>[16,18,19]</sup> *p*-lodonitrosobenzene was prepared by mechanochemical grinding from corresponding aniline by standard procedure based on oxidation with Oxone.<sup>[8e] 15</sup> *N* isotopically labeled *p*-bromonitrosobenzene was prepared following the previously described method.<sup>[16,19]</sup> The prepared compounds were identified by comparison with the previously reported spectroscopic and analytical data.<sup>[8e,16,17]</sup>

#### **Preparation of heterodimers**

Heterodimers were prepared by mixing equimolar amounts of p-Cl, p-NO<sub>2</sub>, and p-l nitrosobenzene derivatives and <sup>15</sup>N isotope labeled p-bromonitrosobenzene at room temperature. Thus, the obtained mixture was sublimed, milled, or melted.

The freshly sublimed cocrystals were prepared under reduced pressure of around 10 mbar. The temperature of cooling water was around  $10 \,^{\circ}$ C. A green colored sublimate formed on the cold finger of the sublimator was transferred to ATR sampling accessory. In a period of 0.5–2 h at room temperature, depending on the compound, the color of the sublimate changed to yellow because of dimerization.

Ball mill experiments were performed in stainless steel jar of 10 ml volume using two stainless steel grinding balls, 7 mm in diameter with a yield of 50% in both cases. A Retsch MM200 (Retsch GmbH, Haan, Germany) grinder mill operating at 25 Hz frequency for 30 min was used for the synthesis. Cocrystals were transferred from jar to ATR sampling accessory.

Melt experiments were carried out in a test tube by heating in oil at temperatures varying from 80 to 120 °C depending on the compound. Melted crystals were put of oil, and in a short time, they underwent solid-ification. Subsequently, they were transferred to ATR sampling accessory.

## **Kinetics measurements**

The solid-state dimerization rate was measured by following the absorbance of the ON=NO asymmetric stretching signal. The spectra were baseline corrected using an automated algorithm in the oPUS software (Bruker Optics, Inc., Billerica, MA, USA). The IR intensities were extracted by integration of absorption bands using the oPUS software and exported into OriginPro 8<sup>\*</sup> (OriginLab, Northampton, MA, USA) for curve fitting and preparation of kinetic plots. Rate constants were obtained by fitting IR intensities into the exponential function of the form:

$$A = A_0 + A_{PF} e^{kt} \tag{1}$$

where A represents the absorbance in time t,  $A_0$  is the absorbance at the end of reaction,  $A_{PF}$  is pre-exponential factor, and k is the rate constant of

solid-state dimerization. Table 1 lists the values of obtained rate constants,  $k_{obs}(^{14}N^{-14}N)$  and  $k_{obs}(^{14}N^{-15}N)$ , along with the standard deviations for each measurement. Average values of rate constants and their standard deviations were also calculated and displayed in Table 1.

The kinetic isotope effects (*KIEs*) were calculated as a quotient of the rate constants for the formation of  ${}^{14}N/{}^{14}N$  and  ${}^{14}N/{}^{15}N$  dimers:

$$KIE = \frac{k_{obs}({}^{14}N - {}^{14}N)}{k_{obs}({}^{14}N - {}^{15}N)}$$
(2)

For each value of *KIE* standard errors (*S*) were calculated (Table 1) according to the following equation:

$$S = \frac{1}{k_{obs}({}^{14}N - {}^{15}N)} \left[ \sigma_{k_{obs}({}^{14}N - {}^{14}N)}^2 + (KIE)^2 \times \sigma_{k_{obs}({}^{14}N - {}^{15}N)}^2 \right]^{1/2}$$
(3)

where  $\sigma_{k_{obs}}({}^{^{14}}N{}^{^{-14}}N)$  and  $\sigma_{k_{obs}}({}^{^{14}}N{}^{^{-15}}N)$  are standard deviations of rate constants  $k_{obs}({}^{^{14}}N{}^{^{-15}}N)$  and  $k_{obs}({}^{^{14}}N{}^{^{-15}}N)$ , respectively.

In addition, average value of *KIEs* and standard deviation of average value were calculated and listed in Table 1.

## **RESULTS AND DISCUSSION**

### The solid-state kinetic isotope effect

Principle of measuring the solid-state kinetic isotope effect is represented in Scheme 4. Cosublimation of the equimolar mixture of the <sup>14</sup>*N*-nitrosobenzene and <sup>15</sup>*N*-nitrosobenzene precursors results in the formation of the <sup>14</sup>*N*/<sup>15</sup>*N* mixed crystals of monomers. Warming these cocrystals to room temperature causes formation of dimers with different isotope combinations (i.e., <sup>14</sup>*N*/<sup>14</sup>*N*, <sup>14</sup>*N*/<sup>15</sup>*N*, or <sup>15</sup>*N*/<sup>15</sup>*N*). Because all the isotope combinations appear in the same crystal, the effect of the molecular environment within the actual crystal on the variation in reaction rates is equal for all isotopomers. In this case, the isotope effect becomes the reproducible parameter relatively independent on the individual experimental conditions. The solid-state <sup>14</sup>*N*/<sup>15</sup>*N* kinetic isotope effects were measured in three media, in the monomer–dimer



ISOTOPE EFFECT: k<sup>14</sup>N/k<sup>15</sup>N

**Scheme 4**. The principle of measuring the solid-state kinetic isotope effect

exchange reaction triggered by the mechanochemical activation, in cocrystals obtained by cosublimation, and in the solid mixture prepared by melting the mixture of isotopomers.

The rate constants and corresponding <sup>14</sup> N/<sup>15</sup> N kinetic isotope effects were obtained by measuring the change in the intensity of the IR signals at 1259 cm<sup>-1</sup> (O<sup>14</sup>N=<sup>14</sup>NO stretching) and 1248 cm<sup>-1</sup> (O<sup>14</sup>N=<sup>15</sup>NO stretching) in different solid media. The processes are characterized by typical exponential kinetic curves (Fig. 1). The rate constants and the kinetic isotope effects are shown in Table 1. Because in most of the experiments the O<sup>15</sup>N=<sup>15</sup>NO absorption appears in the spectrum only as a shoulder, it was difficult to measure its intensity accurately, and the represented isotope effects were calculated only on the basis of the ratio of rate constants for the formation of <sup>14</sup> N/<sup>14</sup> N and <sup>14</sup> N/<sup>15</sup> N dimeric products.

Table	1.	The	solid-state	dimerization	rate	constants,	and	$^{14}N/^{13}N$	kinetic	isotope	effects	for	the	dimerization	of
p-brom	onit	rosol	oenzene in r	mechanically ir	nduce	d reactions,	in sub	olimed coc	rystals, a	nd in me	lts				

Method	$k_{\rm obs} {}^{14} N^{14} N \times 10^{-4}  {\rm s}^{-1}$	$k_{\rm obs} {}^{14} N^{15} N \times 10^{-4}  {\rm s}^{-1}$	KIE				
Sublimation	$5.76 \pm 0.23^{a}$	$4.94 \pm 0.15^{a}$	$1.17 \pm 0.06^{b}$				
Sublimation	8.39±0.64	$6.81 \pm 0.25$	$1.23 \pm 0.10$				
Sublimation	$2.14 \pm 0.70$	$1.98 \pm 0.25$	$1.08 \pm 0.38$				
Sublimation	3.37±0.13	$2.80 \pm 0.09$	$1.20 \pm 0.06$				
Sublimation	4.87±0.12	$4.41 \pm 0.14$	$1.10 \pm 0.04$				
Sublimation	$3.48 \pm 0.15$	$2.88 \pm 0.14$	$1.21 \pm 0.08$				
Mechanochemically	$18.2 \pm 0.99$	$16.0 \pm 0.99$	$1.14 \pm 0.09$				
Mechanochemically	11.7 ± 0.79	$10.4 \pm 0.69$	$1.13 \pm 0.1$				
Melt	$5.36 \pm 0.20$	$4.64 \pm 0.19$	$1.16 \pm 0.06$				
Average value of the rate constants and isotope effects $\overline{x}$	7.03	6.10	1.16				
Standard deviation of values of all rate constants and isotope effects $\sigma$	5.09	4.49	0.05				
KIE, kinetic isotope effect. <sup>a</sup> Standard deviation. <sup>b</sup> Standard error <sup>[22]</sup> was calculated according to Equation (3).							



**Figure 1.** Kinetics curves for dimerization of *p*-bromonitrosobenzene and its <sup>15</sup> N isotopomer. The curves were obtained by measuring the absorbances of  $O^{14}N=^{14}NO$  (1259 cm<sup>-1</sup>) and  $O^{14}N=^{15}NO$  (1248 cm<sup>-1</sup>) asymmetric stretching vibrations

Dissipation of rate constants (standard deviation 5.09) is higher than the dissipation of the values of  $k^{14} N/k^{15} N$  kinetic isotope effects (standard deviation is 0.05). Hence, the isotope effect is to the high degree independent not only on the particular experiment but also on the method by which the reaction is activated (i.e., by mechanical triggering, by melting, or by sublimation). In such a way, the kinetic isotope effect, rather than the reaction rate constant  $k_{obs}$ , becomes the convenient observable that could be used in mechanistic studies of solid-state reactions.

Because the average value of the effect, 1.16, is higher than the observed <sup>15</sup>N isotope effects for the enzyme catalyzed reactions in solution (1.01 or less),<sup>[20]</sup> its interpretation can be at the moment only tentative. One of possible explanations could be derived from solid-state physics. It has been observed on the simple model<sup>[21]</sup> that molecular vibrations of the excited individual isotopomer can decay by strong interaction with phonon vibrations. Consequently, the lifetime of this isotopomer is shorter than the lifetimes of other isotopomers that have vibrational frequencies different from the phonon frequency. Analogously, phonons could also change lifetime of the transition state of only one isotopomer. However, it must be a scope of further investigations to see whether such effect can be operative in complex organic molecular crystals.

Possible interpretation of the effect within the concept of the transition state configuration can be based on the crystal and molecular structure of reactants and products. In our earlier studies of the mechanisms of dimerizations of nitrosobenzenes in crystal phase, we have found that the reaction occurs because the nitroso groups of neighboring molecules are close to each other with relative short distance between the nitrogen atoms (i.e., the topochemical condition is satisfied).<sup>[8b,8c]</sup> From the observed change in the molecular and crystal structure in going from monomers to dimers, it follows that the transition state can inter alia have azodioxide-like structure (green in Fig. 2). This molecular transformation includes reorientation of nitrogenoxygen bonds relative to the benzene ring plane. Such rearrangement of the reactant to the transition state noticeably changes the nature of the N–O bonds. Consequently, the normal isotope effect  $(k^{14}_{N}/k^{15}_{N} > 1)$  may be explained by the change in the force constants of  $O^{-14}N$  or  $O^{-15}N$  stretching vibrations. Weakening of force constants on going from the nitroso reactants to the azodioxide-like transition state is remarkable



**Figure 2.** Superposition of crystal structures of the sublimed monomer reactant (gray) and dimer product (green) of *p*-bromonitrosobenzene (reproduced with permission from ref. <sup>[8b]</sup>)

because the NO bond-length is elongated from 1.223 Å in monomers to 1.284 Å in azodioxides.<sup>[8a]</sup> However, in spite of such difference in the force constant, the observed effect is still too large to be explained only on the basis of the classical theory of kinetic isotope effects. Because the equivalent experiments in solution still failed because it is very difficult to follow the concentration of different isotopomers spectroscopically, the detailed study of this isotope effect requires rigorous calculations of molecular vibrations. The work is in progress in our group.

#### **Cross-dimerizations and multicomponent reactions**

Because in cross-dimerization experiments (Scheme 2), one of the partners, *p*-bromonitrosobenzene, is labeled with the <sup>15</sup> N isotope, the appearance of all product dimers in the reaction mixture can be identified by IR spectra as (O)<sup>14</sup> N=<sup>14</sup> N(O) signal of *p*-x-Ph<sup>14</sup>NO homodimer in the 1260 cm<sup>-1</sup> region, (O)<sup>15</sup> N=<sup>14</sup> N(O) signal of *p*-BrPh<sup>15</sup>NO-x-Ph<sup>14</sup>NO heterodimer at nearly 1245 cm<sup>-1</sup>, and (O)<sup>15</sup> N—<sup>15</sup> N(O) signal of *p*-Br-Ph<sup>15</sup>NO homodimer close to 1235 cm<sup>-1</sup> (Fig. 3). Simultaneous temporal changes in intensities of these three signals were used for the kinetic measurements. For instance, with *p*-Cl-Ph<sup>14</sup>NO as a partner, it was possible to measure three rates simultaneously, formation of the heterodimer *p*-Br (O)<sup>15</sup> N-*p*-Cl<sup>14</sup>N(O) and formation of two homodimers, *p*-Cl (O)<sup>14</sup> N-*p*-Cl<sup>14</sup>N(O), and *p*-Br(O)<sup>15</sup> N-*p*-Br<sup>15</sup>N(O), respectively.

The observed rate constants for all the combinations of the nitroso derivatives with  ${}^{15}$  *N*-*p*-bromonitrosobenzene are represented in Tables 2–4. The reference reaction rate constants for the formations of *p*-chloro- and *p*-nitro- homodimers in all the investigated media are shown in Table 5 (data for the *p*-bromohomodimer were already represented in Table 1).



**Figure 3.** The infrared spectra (ON=NO asymmetric stretching) of pure homodimers of *p*-nitronitrosobenzene-<sup>14</sup> *N* (red), *p*-bromonitrosobenzene-<sup>15</sup> *N* (black), and products after cross-dimerization induced by milling (blue). The heterodimer is characterized by <sup>14</sup> *N*-<sup>15</sup> *N* signal

**Table 2.** Observed average rate constants (reactions triggered mechanochemically, in sublimates, and after melting) for the crossdimerization of p-bromo<sup>15</sup> N with p-chloro<sup>14</sup> N nitrosobenzenes in solid-state

Reaction	p-Cl <sup>14</sup> N – $p$ -Br <sup>15</sup> N heterodimer formation	p-Cl <sup>14</sup> $N$ – $p$ -Cl <sup>14</sup> $N$ homodimer formation	Experimental method
<i>p</i> -BrPh <sup>15</sup> NO + <i>p</i> -CIPh <sup>14</sup> NO	$k_{obs} = 2.06 \times 10^{-3} \text{ s}^{-1}$	$k_{obs} = 2.24 \times 10^{-3} \text{ s}^{-1}$	Sublimation
	$k_{obs} = 3.23 \times 10^{-3} \text{ s}^{-1}$	$k_{obs} = 3.63 \times 10^{-3} \text{ s}^{-1}$	Mechanochemically
	$k_{obs} = 1.40 \times 10^{-3} \text{ s}^{-1}$	$k_{obs} = 1.68 \times 10^{-3} \text{ s}^{-1}$	After melting

**Table 3.** Observed average rate constants (reactions triggered mechanochemically, in sublimates, and after melting) for the crossdimerization of p-bromo<sup>15</sup> N with p-nitro<sup>14</sup> N nitrosobenzenes in solid-state

Reaction	p-NO <sub>2</sub> <sup>14</sup> $N$ – $p$ -Br <sup>15</sup> $Nheterodimer formation$	$p-NO_2^{14}N - p-NO_2^{14}N$ homodimer formation	Experimental method				
p-BrPh <sup>15</sup> NO + $p$ -NO <sub>2</sub> Ph <sup>14</sup> NO	$k_{obs} = 2.17 \times 10^{-3} s^{-1}$ $k_{obs} = 3.63 \times 10^{-3} s^{-1}$ $k_{obs} = 2.38 \times 10^{-3} s^{-1}$	$k_{obs} = 1.64 \times 10^{-3} \text{ s}^{-1}$ $k_{obs} = 3.64 \times 10^{-3} \text{ s}^{-1}$ $k_{obs} = 2.20 \times 10^{-3} \text{ s}^{-1}$	Sublimation Mechanochemically After melting				
For formation of $p$ -Br <sup>15</sup> $N$ – $p$ -Br <sup>15</sup> $N$ homodimer in sublimate $k_{obs} = 1.12 \times 10^{-3} \text{ s}^{-1}$ .							

**Table 4.** Observed average rate constants (reactions triggered mechanochemically, in sublimates, and after melting) for the crossdimerization of p-bromo<sup>15</sup> N with p-iodo<sup>14</sup> N nitrosobenzenes in solid-state

Reaction	p-I <sup>14</sup> N – $p$ -Br <sup>15</sup> N heterodimer formation	p-l <sup>14</sup> $N$ – $p$ -l <sup>14</sup> $Nhomodimer formation$	Experimental method
<i>p</i> -BrPh <sup>15</sup> NO + <i>p</i> -IPh <sup>14</sup> NO	No reaction	No reaction	Sublimation
	$k_{obs} = 0.67 \times 10^{-3} s^{-1}$	$k_{obs} = 0.68 \times 10^{-3} s^{-1}$	Mechanochemically
	$k_{obs} = 0.19 \times 10^{-3} s^{-1}$	Not measured	After melting

Table	5.	The	rate	consta	nts	of	homodimerizatio	ons	of
<i>p</i> -nitronitrosobenzene and <i>p</i> -chloronitrosobenzene under									
different solid-state conditions									

	$p\text{-CIC}_6\text{H}_4\text{NO}$ $k_{\text{obs}} \times 10^{-3} \text{s}^{-1}$	$p-NO_2C_6H_4NO$ $k_{obs}  imes 10^{-3} s^{-1}$
Sublimation Mechanical	3.72 8.16	1.58 Not measured
Melt	2.46	Not measured

The represented data can be interpreted as the following. Heterodimers are formed by mixing and mechanical treatment of crystals of two homodimers. Because the cross-dimerization continues after the reaction mixture is removed from the mill, we can conclude that the mechanical treatment serves mostly for triggering the reaction. The rates of the mechanochemical reactions are slightly faster than the processes in cocrystals and in melts.

Rates of formation of homodimers and heterodimers have close values, and they do not depend highly on the molecular structures of substrates (Tables 2–4). Hence, the rate constants,  $k_{obs}$ , are parameters, which reflect mostly combinations of different and complex processes more or less associated to phase changes, diffusion, and surface effects. Events on the molecular

level (the classical mechanistic interpretation) are only one of the components, perhaps minor, that contribute to the value of the rate constant.

Solid-state dissociation and subsequent redimerization of *p*-iodonitrosobenzene are observed only under the mechanochemical conditions. In the sublimed crystal, *p*-iodonitrosobenzene appears exclusively as monomer.

# CONCLUSIONS

- (i) Mechanochemical stress triggers dissociation and redimerization of the aromatic nitrosobenzene molecules. Such a mechanochemically induced bond breaking and bond formation enables formation of cross-dimerized azodioxides.
- (ii) While the observed rate constant,  $k_{obs}$ , strongly depends on the individual experimental conditions, it cannot be taken as an exact parameter for mechanistic interpretation of solid-state reactions. In contrast, the kinetic isotope effect is much less dependent on the particular experiment, and its future interpretation can be used for the detailed study of the solid-state processes and reaction mechanisms. Kinetic isotope effects  $k^{14} N/k^{15} N$ for the dimerization of nitroso compounds have the similar values, independently whether the reaction proceeds in the crystal (triggered by sublimation), in mechanochemical mill, or in the melt.

- (iii) If the solid-state dimerization occurs in the mixture of differently substituted nitrosobenzenes in the multicomponent reaction systems, all of the observed rate constants have the values within the same range. This observation confirms the statement that the kinetic observable,  $k_{obs}$ , is predominantly a consequence of the different types of phase transformation. No correlations between the measured rate constants and the molecular structure variation have been found.
- (iv) Resemblance of the kinetics of the reactions in mechanical mill with the kinetics of the thermal reactions in the freshly sublimed crystals of monomers implies that the mechanisms of two processes are similar. In both cases, the process is triggered by formation of vacancies on the crystal surface. The only difference is in the way the surface defects are obtained, mechanically, or by sublimating away of monomer molecules from the outer crystal plane. Slightly higher reaction rates in mechanochemical systems are another argument that the reaction depends on the surface damage.

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