Nitrosobenzene Library: A Model for Studying Selectivity in the Solid State Nitroso-Azodioxide Dimerization*

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Cross-linking of nitroso benzenes to heterodimers (azodioxides), in the case when they are not sterically crowded with large groups in *ortho*-position, was studied by NMR, UV-VIS, and Raman spectroscopy as well as by powder X-ray crystallography. Dimerization of nitroso compounds to azodioxides can, in principle, be used for the construction of novel supramolecular structures. As a preliminary investigation, the selectivity of nitrosobenzenes to form dimers in the solid state was studied. Observations by NMR and vibrational spectroscopy show that selectivity for cross-linking is quite different in the solid state from that in solution. This is explained by a considerable influence of packing factors in the former. Selectivities for cross-linking in the solid state in a complex chemical library of monomers were formulated and measured using simple spectroscopic and diffraction methods. For every member of such a nitrosobenzene chemical library it is possible to measure and, using the Tanimoto similarity coefficients, calculate two selectivity parameters, *chemical selectivity* and *packing selectivity*. While *packing selectivity* is correlated with total dipole moments of nitroso monomer molecules, *chemical selectivity* is in correlation with the x-component of the molecular dipole, i.e., the axis that is nearly collinear with the C-N bond in nitroso group. The method developed in this work could, in principle, be proposed for more general use in investigations of similar chemical libraries with binary combined components.

INTRODUCTION

Broad literature already exists on the dimerization of nitroso compounds to azodioxides (Scheme 1).[1] Such a monomer-dimer equilibrium in solution was studied in detail from kinetic and thermodynamical aspects. In our recent studies, we found that azodioxides (nitroso dimers) afford photochromic behavior not only in solution but also in the solid state.[2] Although this photochromism is not immediately applicable because photodissociation only occurs under cryogenic conditions, we have found that the formation of dimers and their dissociation can be achieved either by UV irradiation under controlled mild conditions or even by using high pressure (piezochromism).[3]
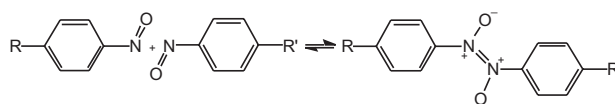
Scheme 1.

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Taking into account the discovered possibilities of OFF-ON (monomer-dimer) manipulations with nitroso compounds and the evidence that the RON=NOR bond strength is nearly of the same order of magnitude as a hydrogen bond,[4] investigations of this system can be directed to applications in molecular logic or in the development of a novel type of supramolecular self-organization, or both. Small nitroso molecules interconnected with (O)N=N(O) bonds can be used as building blocks for the construction of supramolecular structures. A study of the selectivity of nitroso monomers for cross-linking, *i.e.,* formation of *heterodimers* (R ≠ R' in Scheme 1), must be one of the first preliminary investigations. (Later in this work, the technical term *homodimer* will be used for azodioxides with equal substituents, R = R'). It is known from previous work that cross-linked dimers are formed only if a nitroso group is sterically crowded by substituents in *ortho* position in one of the monomer partners.[5] On the other hand, there is still no systematic knowledge about the influence of electronic factors on the cross-linking selectivity. Moreover, since most dimerizations appear in the solid state, it is also necessary to investigate the influence of crystal packing, *i.e.,* topochemical effects, on the formation of different homo- and/or heterodimers. Such effect on the cross-linking of nitrosobenzenes is the central point in this paper. As it will be seen later, in many examples it will be very difficult to make an unequivocal distinction between these two effects, *i.e.,* whether packing is induced by electronically preferred dimerization, or if crystal self-organization is responsible for the formation of heterodimers.

Such a *chicken-or-egg problem* is even more general, and it appears in all cases where the final organized structure is an interplay between chemical and topochemical factors. For instance, if there is a series of compounds which can dimerize to different *homo-* or *hetero-* azodioxides, the number of possible binary combinations can be very large. Consequently, it becomes necessary to develop a simple and fast method of searching for a new phase, *i.e.,* appearance of different *hetero-combinations*. In this work, we report on our combinatorial approach where such screening, applied to the nitroso compound dimerization, is based on Raman spectroscopy and on powder X-ray diffraction method, respectively. In solution, where packing factors are absent and the dimerization is governed mostly by electronic effects, the possible formation of cross-linked dimers was investigated by low temperature ^{1}H NMR.

EXPERIMENTAL

Powder X-ray diffraction data were collected on a Philips PW 1700 automated diffractometer with a control unit PW3710 using the scanning method with the following parameters: monochromatic Cu $K\alpha 1$ radiation (λ = 1.5406 Å), observation range 5 ° – 2θ – 35 °, continuous scan mode, step scan with 0.025 °, counting time per step 0.5 s. With this choice of parameters, one circle lasts 10 minutes. We collected data in a period of 4 hours. Data collection was performed by the Expert Software Suite 1.2, *Program package for measuring and analysis of diffraction data on Philips X-ray diffraction equipment*, Analytical, Lamely, Netherlands 1999. For background correcting, $K\alpha 2$ stripping and integration of intensity were performed using X'Pert Plus 1.0, *Program for Crystallography and Rietveld Analysis*, Panalytical, Almelo, Netherlands 1999.

FT-IR and Raman spectra were recorded on Bruker Equinox 55 and Bruker FRA 106/S spectrometers, respectively, under 2 cm^{-1} resolution. Physical mixtures were obtained by gently grinding equimolar amounts of homodimers. The Raman spectrum of such a sample is compared to the computer sum of the spectra recorded for individual homodimers. Only those spectra of the prepared physical mixtures which agree with such a computer sum were used in this study. In the control experiment, equimolar amounts of homodimers were ground with the excess of KBr and the FT-IR spectra were recorded and compared with the computer sum of the spectra of individual components.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker SP 600 MHz spectrometer. Solid-state CP MAS ^{13}C NMR spectra were recorded at 125.77 MHz on a Bruker Avance DRX-500 NMR spectrometer using a BL-4 CP MAS probehead and a high resolution/high performance (HPHP) ^{1}H preamplifier for solids. The rotor frequency for VACP experiments was 5 kHz. CP TOSS pulse sequence was used to obtain carbon spectra with a spectral width of 40000 Hz and two pulse phase modulation for proton decoupling. Contact time was 2 ms. All spectra were acquired with 2 k data points in the time domain and zero-filling to 16 k and were then transformed by using 10 Hz of line broadening. Recycle delay in all experiments was 6.0 ms. 500 scans per each experiment were used. Digital resolution was 14.32 Hz.

UV-VIS spectra were taken on a Cary 5 spectrometer. Solid samples were prepared in KBr pellets and recorded in a special homemade holder.

Synthetic Procedures

Nitrosobenzenes **6**, **7**, **8**, and **9**, were prepared from nitrobenzenes by standard procedures based on Zn reduction followed by oxidations with FeCl$_3$[10] or Na$_2$Cr$_2$O$_7$ [11] oxidations. For compounds **1–5**, and **10–13**, an alternative procedure of H$_2$O$_2$ oxidations of aminobenzenes with [MoO(O$_2$)$_2$(H$_2$O)]-hmpa catalyst was used.[12]

Computational Methods

Molecular geometries of the *m*- and *p*-substituted nitrosobenzenes were fully optimized using the Hartree-Fock method, with the 6-31G(d) basis set,[12] implemented in the programs GAUSSIAN 98[14] and GAUSSIAN 03.[15] The calculations also predict dipole moments, which are the first derivatives of energy with respect to the applied electric field. The dipole moment is a measure of the asymmetry in the molecular charge distribution, and is given as a vector in three di-

mensions. For Hartree-Fock calculations, *X*, *Y* and *Z* components and total dipole moments are the quantities reported in the output (Debye), referring to the standard orientation for the molecule.

RESULTS AND DISCUSSION

Formation of Heterodimers

The main problem of studying the possible formation of cross-linked dimers is how to find the method by which heterodimers can be quickly, and with relatively high certainty, distinguished from the mixture of homodimers. Our approach is based on the comparison of the spectra or X-ray diffractograms, or both, of two different types of mixtures. The first is called *physical mixture*, and it consists of equimolar amounts of solid samples of homodimers. This mixture is prepared by careful grinding of both components. Since grinding can result in formation of multicomponent molecular crystals,[6] the Raman spectrum of such a mixture is compared with the computer sum of the spectra extra recorded for individual homodimers. All the spectra of the prepared physical mixtures agree with such computer sums. The second is a *chemical mixture*, obtained by dissolving the physical mixture and evaporating the solvent. As only monomers are present in solution, after evaporation of the solvent they can recombine with each other either by forming the same mixture of homodimers, or by cross-linking into heterodimers (Scheme 2).

If the spectra of such physical and chemical mixtures are identical or very similar, then this could be an indication that only homodimers were present (**A-A** or **B-B** combinations in Scheme 2). In contrast, if spectra of the chemical mixture differ from those of the physical mixture, then we can suspect either a possible formation of
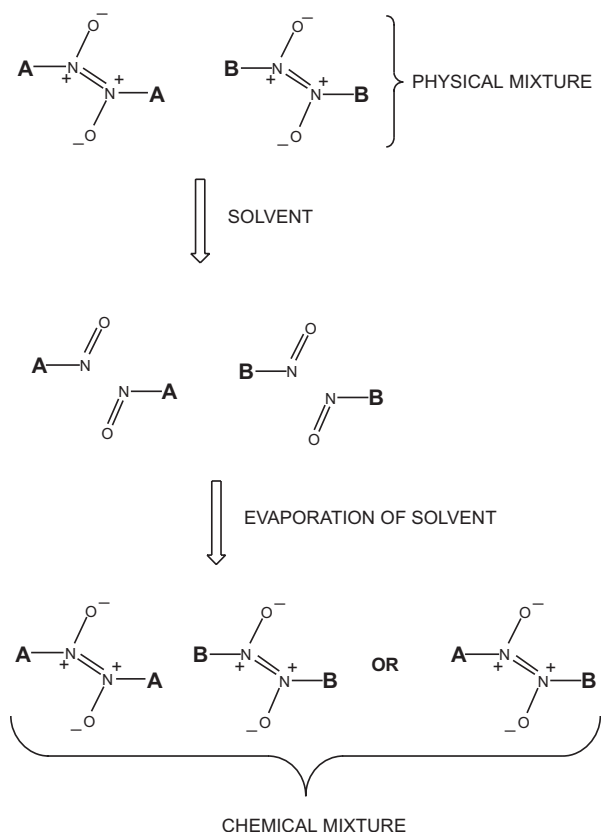
Scheme 2.

heterodimers (**A-B** combination in Scheme 2), or the appearance of a new crystal phase, perhaps a sort of mixed crystals consisting, for instance, of **A-A** and **B-B** layers.

NMR Spectra.

As an example of the formation of heterodimers, we prepared physical and chemical mixtures of *p*-nitronitroso-
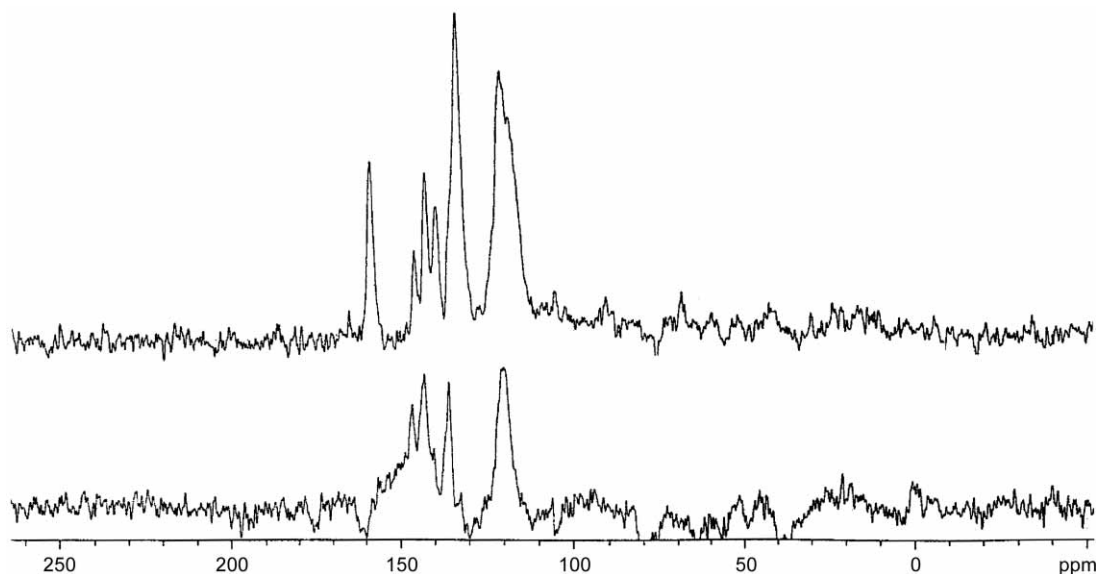

Figure 1. [13]C CP-MAS spectra of a *physical mixture* (top) and a *chemical mixture* (bottom) of *p*-nitronitrosobenzene and *p*-iodonitrosobenzene.

benzene and *p*-iodonitrosobenzene and investigated them by solid state CP-MAS ^{13}C NMR. The spectra of the corresponding physical and chemical mixtures (chemical mixtures were obtained after dissolving in CHCl$_3$ and successive evaporation of the solvent) are shown in Figure 1.

The spectrum of the physical mixture corresponds to the direct sum of signals from the spectra of individual homodimers (for detailed spectral data see Supporting material S2 and S3). On the other hand, the spectrum of the chemical mixture is noticeably different. For instance, the signal at 158 ppm is completely absent in the chemical mixture. Evidently, *p*-nitronitrosobenzene and *p*-iodonitrosobenzene form heterodimers in the solid state. Since we must know whether the formation of this heterodimer is a consequence of crystal packing or merely a consequence of electronic factors in monomer molecules, we repeated the experiment in solution, *i.e.*, in the medium not influenced by crystal packing. To achieve efficient dimerization, the ^{1}H NMR spectra were recorded at –60 °C.
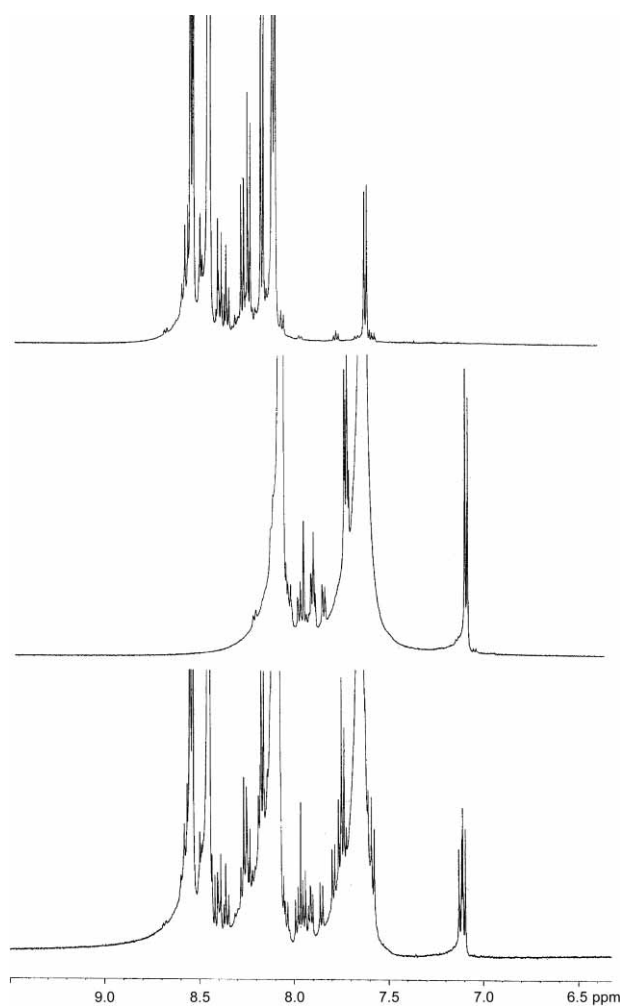

Figure 2. ^{1}H NMR spectra of *p*-nitronitrosobenzene (top), *p*-iodonitrosobenzene (middle), and their mixture (bottom), all recorded in CHCl$_3$ at –60 °C.

	p-Br	*p*-I	*p*-CH$_3$	*p*-CF$_3$	*p*-NO$_2$
p-Br				μ	μ
p-I				μ	μ
p-CH$_3$					μ
p-CF$_3$	μ	μ			μ
p-NO$_2$	μ	μ	μ	μ	

Figure 3. Combinatorial matrix for the selectivity of the formation of heterodimers in solution, based on ^{1}H NMR spectra. μ label combinations of nitroso monomers, which form heterodimers.

The equimolar solution of *p*-nitronitrosobenzene and *p*-iodonitrosobenzene in CHCl$_3$ cooled to –60 °C affords the ^{1}H NMR spectrum, which is different from the sum of ^{1}H NMR spectra recorded for the solutions of individual components under the same conditions (Figure 2). Accordingly, *p*-nitronitrosobenzene and *p*-iodonitrosobenzene form the corresponding heterodimer also in solution.

This ^{1}H NMR study of the possible formation of heterodimers in solution was extended to a series of *p*-substituted nitrosobenzenes. The results are summarized in the combinatorial matrix in Figure 3, in which combinations of nitroso monomers that form heterodimers are labeled with μ. It is evident that the compounds differ in selectivity. For instance, *p*-nitronitrosobenzene binds with all partners, *i.e.*, it is nonselective in the formation of heterodimers. On the other hand, *p*-methylnitrosobenzene is most selective, and it forms a heterodimer only with *p*-nitronitrosobenzene.

Solid-state UV VIS Spectra

From the results shown in Figure 3 it follows that *p*-bromonitrosobenzene and *p*-methylnitrosobenzene do not form heterodimers with each other in solution. In the solid state, both compounds exist mostly as dimers, but with some »impurity« of monomer molecules.[7] Consequently, samples of both compounds absorb at 765 nm, *i.e.,* in the VIS spectral region in which only the monomer nitroso group absorbs. However, in the spectrum of a chemical mixture of *p*-bromonitrosobenzene and *p*-methylnitrosobenzene, the 765 nm absorption is drastically reduced (spectrum b in Figure 4). It is possible to speculate that in the case of a solid *chemical mixture*, packing factors are such that they induce dimerization and decrease the amount of monomers.

In reality, the system could be even much more complex because it may also include mixtures of heterodimers, homodimers, monomers, and also numerous possible combinations of co-crystals between these components.
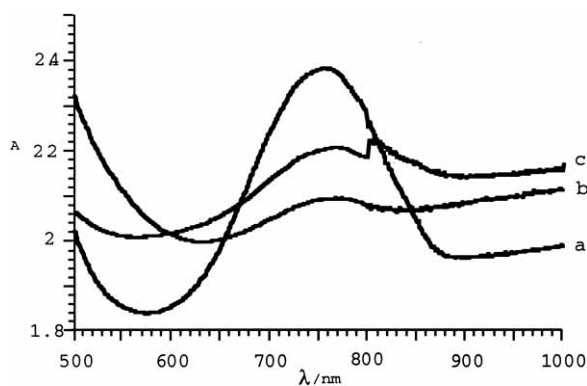
Figure 4. Solid state VIS spectra of a) 4-methylnitrosobenzene, b) *chemical mixture* of 4-methylnitrosobenzene and 4-bromonitrosobenzene, c) 4-bromonitrosobenzene.

Even a small »impurity« of one component in the mixture can change the interaction between molecules and influence the extent of dimerization.

Combinatorial Approach and Selectivity for Cross-linking

Formation of an azodioxide (O)N=N(O) bond from two nitroso groups could, in principle, be applied to generate supramolecular structures based on nitroso compounds as building blocks. To estimate such a possibility, it becomes necessary to perform systematic studies of the cross-linking *ability* of nitroso compounds in the formation of azodioxide dimers or oligomers in condensed systems. This can be done *inter alia* by formulating and measuring particular characteristic numerical selectivity parameters. Comprehensive investigation of such selectivity in the case of a large number of pairs of nitroso monomers by the methods described in previous sections is extremely time-consuming and also expensive because it requires large amounts of synthesized compounds.

In this study, we use a kind of combinatorial method, investigating the chemical library that consists of 13 different nitrosobenzenes (Scheme 3), which could combine with each other in 78 combinations of possible cross-linked dimers (heterodimers). From such a 13 x 13 combinatorial matrix, it is possible to obtain an *overview* of the correlation of cross-linking selectivity with the structure of nitrosobenzene molecules, which are differently substituted in *para* position. The main experimental problem is how to find a relatively fast method for screening all the combinations. Although the best method of structure elucidation is the single crystal X-ray diffraction, it is too time-consuming, and we have used a simpler and faster method based on Raman spectroscopy combined with powder X-ray diffraction. The principle of finding the possibility of heterodimer formation is the same as described in previous sections. If *chemical* and *physical mixtures* afford very similar or equal Raman spectra, there are only homodimers in the mixture, and

oppositely, if the spectra are different, this may be an indication of the appearance of heterodimers or of some other new phase. On the same principle, if the X-ray powder diffractograms of physical and chemical mixtures are compared, we can get information about the possible appearance of a new crystal phase. It must be pointed out that origins of the appearance of the new crystal phase could be also quite different, not only the formation of heterodimers. By summarizing the observations obtained from Raman and X-ray data, we were able to calculate the two selectivity factors that influence self-organization of the nitroso building blocks, *i.e.,* the *chemical factor* and the *packing factor.* While the vibrational Raman spectrum is more sensitive to the change in the nature of chemical bonding between nitroso monomers (*i.e.,* formation of the new (O)N=N(O) bond), the X-ray diffractogram informs about the emergence of a new plane in the crystal lattice, that is, it informs about changes in molecular packing.
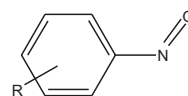
1, R = *p*-NO$_2$
2, R = *p*-CF$_3$
3, R = *p*-CO$_2$Me
4, R = *m*-Cl
5, R = *m*-Br
6, R = *p*-Br
7, R = *p*-Cl
8, R = *p*-I
9, R = *p*-F
10, R = *m*-OCH$_3$
11, R = *p*-OCH$_3$
12, R = *p*-C$_2$H$_5$
13, R = *p*-CH$_3$

Scheme 3.

The 13 x 13 chemical library formed from structures **1–13** (Scheme 3) was organized so that every point, let's say »matrix element«, of the combinatorial matrix represents one of the possible cross-linked combinations of investigated nitroso compounds (Figure 5). The color of each matrix element represents the degree of similarity between the Raman spectra of chemical and physical mixtures for the corresponding combination. As a criterion for estimating the extent of spectral agreement, we have calculated the Tanimoto coefficients for all points (Table I), *i.e.,* the parameters that have a wide application in the evaluation of structural or spectral similarity.[8] If spectra are similar, the Tanimoto coefficient is close to zero, and it is represented in red color in Figure 5. In contrast, blue color means a high Tanimoto coefficient close to 1, which corresponds to very different spectra. Actually, we speak about the dissimilarity in the same way as it was applied in the study of polymorph library in Ref. 8b. In summary, blue colored zones of the matrix belong to combinations in which formation of heterodimers predominates, and reddish regions belong to combinations that avoid cross-linking and prefer association of nitroso molecules in homodimers.

A similar 9 x 9 combinatorial matrix was constructed on the basis of the resemblance of X-ray powder diffractograms of physical and chemical mixtures. The same

TABLE I. Tanimoto coefficients for similarity between the Raman spectra of physical and chemical mixtures (0 = high similarity; 1= low similarity)

|	1	2	3	4	5	6	7	8	9	10	11	12	13
1	•	0.172	0.514	0.743	0.593	0.513	0.269	0.606	0.448	0.500	0.476	0.217	0.648
2	0.172	•	0.272	0.500	0.194	0.333	0.382	0.240	0.593	0.310	0.411	0.333	0.615
3	0.514	0.272	•	0.333	0.268	0.333	0.200	0.272	0.102	0.114	0.108	0.206	0.378
4	0.743	0.500	0.333	•	0.410	0.511	0.400	0.387	0.500	0.555	0.262	0.585	0.614
5	0.593	0.194	0.268	0.410	•	0.243	0.171	0.320	0.264	0.555	0.200	0.172	0.578
6	0.513	0.333	0.333	0.511	0.243	•	0.361	0.583	0.615	0.702	0.631	0.613	0.500
7	0.269	0.382	0.200	0.400	0.171	0.361	•	0.538	0.100	0.371	0.294	0.302	0.457
8	0.606	0.240	0.272	0.387	0.320	0.583	0.538	•	0.286	0.291	0.115	0.154	0.500
9	0.448	0.593	0.102	0.500	0.264	0.615	0.100	0.286	•	0.093	0.285	0.470	0.512
10	0.500	0.310	0.114	0.555	0.555	0.702	0.371	0.291	0.093	•	0.172	0.125	0.697
11	0.476	0.411	0.108	0.262	0.200	0.631	0.294	0.115	0.285	0.172	•	0.178	0.486
12	0.217	0.333	0.206	0.585	0.172	0.613	0.302	0.154	0.470	0.125	0.178	•	0.675
13	0.648	0.615	0.378	0.614	0.578	0.500	0.457	0.500	0.512	0.697	0.486	0.675	•
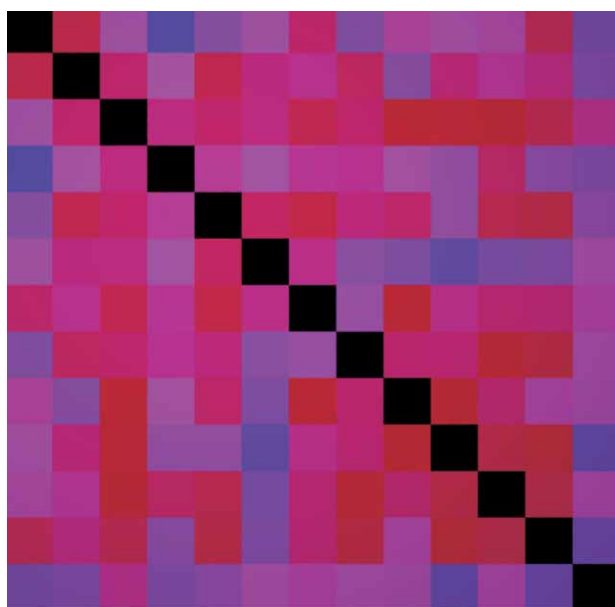
Figure 5. Combinatorial matrix obtained from the Tanimoto coefficients calculated by comparing the Raman spectra of physical and chemical mixtures. Values close to 0 are visually represented by the red part of the spectra, and those close to 1 by the blue spectral limit.

color labeling of Tanimoto values (Table II) as in the case of Raman spectra was used to visualize similarity between the mixtures (Figure 6).

For every nitroso monomer studied in one of the two combinatorial matrices, it is possible to calculate the average Tanimoto coefficient ($T_{average}$). In the Raman matrix, the highest value ($T_{average.max} = 0.555$) belongs to *p*-methylnitrosobenzene, and the maximal average coefficient in the X-ray matrix was calculated for *p*-nitronitrosobenzene ($T_{average.max} = 0.513$). Using these numbers as limiting values, we can calculate selectivities of all the studied nitroso monomers using the formula:

$$\text{Selectivity: } S = 1 - T_{average} / T_{average.max}$$

While selectivities calculated from the Raman data are more sensitive to the chemical nature of intermolecular interactions (in our case especially to the formation of a (O)N=N(O) bond), we call them *chemical selectivity* (S_{Ch}), the values obtained from the powder X-ray matrix are more influenced by the packing, and we call them *packing selectivity* (S_{Pac}, Table III). It is very important to note that these two numerical characteristics of nitroso monomers are not correlated with each other.

TABLE II. Tanimoto coefficients (T_m) for similarity between the powder X-ray diffractograms of physical and chemical mixtures (0 = high similarity; 1= low similarity)

|	1	2	3	4	5	6	7	8	13
1	•	0.361	0.870	0.344	0.167	0.393	0.698	0.550	0.868
2	0.361	•	0.129	0.214	0.167	0.297	0.111	0.204	0.269
3	0.870	0.129	•	0.349	0.219	0.361	0.286	0.378	0.091
4	0.344	0.214	0.349	•	0.244	0.273	0.391	0.520	0.156
5	0.167	0.167	0.219	0.244	•	0.375	0.333	0.324	0.429
6	0.393	0.297	0.361	0.273	0.375	•	0.711	0.780	0.870
7	0.698	0.111	0.286	0.391	0.333	0.711	•	0.729	0.308
8	0.550	0.204	0.378	0.520	0.324	0.780	0.729	•	0.205
13	0.868	0.269	0.091	0.156	0.429	0.870	0.308	0.205	•
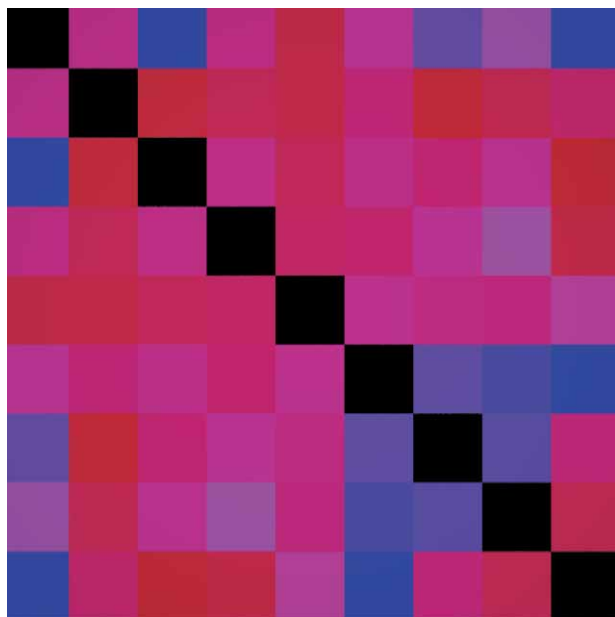
Figure 6. Combinatorial matrix obtained from the Tanimoto coefficients calculated by comparing the powder X-ray diffractograms of physical and chemical mixtures. Values close to 0 are visually represented by the red part of the spectra, and those close to 1 by the blue spectral limit.

As can be seen from these numbers, while *p*-methyl-nitrosobenzene is very unselective in solid-state dimerization, and can form many heterodimers, nitrosobenzenes with *p*-CF$_3$ or *p*-CO$_2$Me groups afford substantial selectivity.

One of the most important intermolecular forces responsible for the process of crystal packing is the dipole-dipole interaction,[9] and we believe that it also influences the cross-linking selectivity. Following this fact, we made a series of correlations between calculated selectivities (S_{Ch} and S_{Pac}) and dipole moments of the corresponding monomers (r^2 values for all the possible correlations are

TABLE III. Chemical and packing selectivities for cross-linking of nitrosobenzenes

Group	Chemical Selectivity S_{Ch}	Packing Selectivity S_{Pac}
p-NO$_2$	0.137	0.000
p-CF$_3$	0.346	0.588
p-CO$_2$Me	0.535	0.369
m-Cl	0.130	0.414
m-Br	0.445	0.469
p-Br	0.108	0.043
p-Cl	0.423	0.160
p-I	0.355	0.132
p-F	0.359	
m-OCH$_3$	0.326	
p-OCH$_3$	0.456	
p-C$_2$H$_5$	0.395	
p-CH$_3$	0.000	0.247

listed in Table IV). Indeed, we found that there is a correlation between total dipole moments and *packing selectivity* (S_{Pac}) (Table IV).[9] On the other hand, *chemical selectivity* (S_{Ch}) is not correlated with the total dipole moment, but correlates relatively satisfactorily with the *x*-component of the dipole moment (Table IV). Perhaps, it could be speculated that the sensitivity of such *chemical reactivity* to the *x*-component of the molecular dipole is a consequence of mutual interactions of polar nitroso groups situated on neighboring dimerizing molecules. Namely, the C-N bond in the nitroso group is almost collinear with the *x*-axis (Figure 7, see also Supporting material).
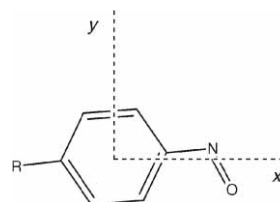

Figure 7. Molecular orientation used in the dipole moment calculation. The C-N bond is almost collinear with the *x*-component of the dipole moment.

TABLE IV. Comparison of the r^2 coefficients for all correlations of chemical and packing selectivities with the *x*- and *y*- components of the molecular dipole, as well as with the total dipole moments

	Total dipole moment	*x* – component	*y* – component
S_{Ch}	0.11	0.86	0.07
S_{Pac}	0.63	0.02	0.05

The presented combinatorial approach can, in principle, be applied to any other binary chemical library where hetero-combinations between building blocks are formed in the solid state, quite independently of whether the main chemical interaction is a chemical bond such as (O)N=N(O) in azodioxides or a hydrogen bond, like for instance in combinations of nucleotides.

CONCLUSIONS

Nitroso benzenes can cross-link into heterodimers (azodioxides) even if they are sterically not crowded with large groups in *ortho*-position. As it was observed by NMR and vibrational spectroscopy, selectivity for cross-linking is quite different in the solid state than in solution because of a considerable influence of packing factors in the former. Selectivities for cross-linking in the solid state can, in the complex chemical library of monomers, be formulated and measured by simple spectroscopic and diffraction methods. For every chemical unit that is a member of such a chemical library it is possible to measure and, by using the Tanimoto spectral similarity coefficients, calculate two selectivity parameters, *chemical selectivity* and *packing selectivity*. Of the two types of

selectivities, *packing selectivity* is correlated with the total dipole moments of nitroso monomers, exactly as predicted by the theory of crystal packing, and *chemical selectivity* is in correlation with the *x*-component of the molecular dipole. *x*-Axis is nearly aligned with the C-N bond of the nitroso group. This method may be proposed for a more general use in investigations of similar chemical libraries with binary combined components.

Supporting material. – S1: HF/6-31G(d) calculated dipole moments for nitroso compounds **1–13**. S2: ^{13}C NMR CP MAS chemical shifts (in ppm) of *p*-iodonitrosobenzene, *p*-nitronitrosobenzene and their physical mixture. S3: ^{13}C NMR CP MAS spectra of a) *p*-nitronitrosobenzene, b) *p*-iodonitrosobenzene, c) their physical mixture, d) their chemical mixture.

REFERENCES

1. a) B. G. Gowenlock and W. Lütke, *Quart. Rev.* **12** (1958) 321–341. b) Th. A. J. Wajer and Th. J. De Boer, *Recueil* **91** (1972) 565–577. c) F. D. Greene and K. E. Gilbert, *J. Org. Chem.* **40** (1975) 1409–1415. d) J. P. Snyder, M. H. Heyman, and E. Suciu, *J. Org. Chem.* **40** (1975) 1395–1404. e) M. L. Greer, H. Sarker, M. E. Medicino, and S. C. Blackstock, *J. Am. Chem. Soc.* **117** (1995) 10460–10467. f) P. Singh, *ibid.* 1405–1408. g) D. A. Fletcher, B. G. Gowenlock, and K. G. Orrell, *J. Chem. Soc., Perkin Trans.* **2**, (1998) 797–803.

2. H. Vančik, V. Šimunić-Mežnarić, I. Čaleta, E. Meštrović, S. Milovac, K. Mlinarić Majerski, and J. Veljković, *J. Phys. Chem. B* **106** (2002) 1576–1580.

3. Vančik, H.; Lukić, K. *unpublished results.*

4. R. Glaser, R. K. Murmann, and Ch. L. Barnes, *J. Org. Chem.* **61** (1996) 1047–1058.

5. V. A. Batyuk, T. I. Shabatina, Yu. N. Morozov, S. V. Ryapisov, and G. B. Sergeev, *Vestn. Mos. Univ. Ser. 2*: *Khim.* **29** (1988) 270–274.

6. a) E. Y. Cheung, S. J. Kitchin, K. D. M. Harris, Y. Imai, N. Tajima, and R. Kuroda, *J. Am. Chem. Soc.* **125** (2003) 14658–14659. b) R. Kuroda, Y. Imai, and N. Tajima, *J. Chem. Soc. Chem. Commun.* **23** (2002) 2848–2849. c) V. R. Pedireddi, W. Jones, A. P. Chorlton, and R. Docherty, *J. Chem. Soc., Chem. Commun.* **8** (1996) 987–988.

7. H. Vančik, V. Šimunić-Mežnarić, E. Meštrović, and I. Halasz, *J. Org. Chem.* **69** (2004) 4829 – 4834.

8. Tanimoto coefficients were calculated by the formula: $T_{\mathrm{m}} = 1 - [N_{\mathrm{ab}} / (N_{\mathrm{a}} + N_{\mathrm{b}} - N_{\mathrm{ab}})]$, where N_{ab} is the number of peaks coincident within a user defined range in both spectra a and b, N_{a} is the number of peaks in spectrum a, and N_{b} is the number of peaks in spectrum b. See also: a) A. R. Leach, *Molecular Modeling. Principles and applications*, 2nd Ed., Prentice Hall, London, 2001, pp. 676–678. b) M. L. Peterson, Sh. L. Morissette, Ch. McNulty, A. Goldsweig, P. Shaw, M. LeQuesne, J. Monagle, N. Encina, J. Marchionna, A. Johnson, J. Gonzalez-Zugasti, A. V. Lemmo, S. J. Ellis, M. J. Cima, and Ö. Almarsson, *J. Am. Chem. Soc.* **124** (2002) 10958–10959.

9. G. R. Desiraju, *Crystal Engineering*, Elsevier, Amsterdam, 1989.

10. K. G. Orrell, D. Stephenson, and J. H. Velarque, *J. Chem. Soc, Perkin Trans* **2** (1990) 1297–1303.

11. a) G. H. Coleman, C. M. McCloskey, and F. A. Stuart, *Org. Synth.* **3** (1955) 668–669. b) B. S. Furniss, A. J. Hannaford, V. Rogers, P. W. Smith, and A. R. Tatchel, *Vogel's Textbook of Practical Organic Chemistry*, 4th Ed., Longman, London, 1978, pp. 723–724.

12. a) S. Tollari, M. Cuscela, and F. Porta, *J. Chem. Soc., Chem., Commun.* (1993) 1510–1511. b) H. Mimoun, I. Seree de Roch, and L. Sajus, *Bull. Soc. Chim. Fr.* (1969) 1481–1492. c) H. Mimoun, *Angew. Chem., Int. Ed.* **21** (1982) 734–750.

13. J. B. Foresman and F. Frisch, *Exploring Chemistry with Electronic Structure Methods: A Guide to Using Gaussian*, Gaussian, Inc., Pittsburgh, 1993.

14. F. Frisch and M. J. Frisch, *Gaussian 98 User's Reference*, Gaussian, Inc., Pittsburgh, 1999.

15. F. Frisch, M. J. Frisch, and G. W. Trucks, *Gaussian 03 User's Reference*, Gaussian, Inc., Pittsburgh, 2003.

SAŽETAK

Nitrozobenzenska biblioteka: Model za proučavanje selektivnosti dimerizacije nitrozo-azodioksida u čvrstom stanju

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Dimerizacija različito supstituiranih nitrozobenzena, do koje dolazi kristalizacijom, rabljena je kao model za kvantificiranje reaktivnosti i selektivnosti u čvrstome stanju. Predloženi parametri selektivnosti dobiveni su na temelju IR spektroskopije i difrakcije X-zraka na prahu za kemijsku biblioteku nitrozobenzena supstituiranih u *m*- i *p*- položaju.