



Nitrosobenzene cross-dimerization: Structural selectivity in solution and in solid state

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ABSTRACT

Possibility of nitrosobenzenes to form dimeric molecular structures (azodioxides) is used as a model for intermolecular selectivity investigations in solution as well as in solid state. Cross-dimerization of different combinations of *p*- and *m*-substituted nitrosobenzene pairs was studied by variable temperature ¹H NMR, solid-state NMR (CP MAS), IR, and *ab initio* calculations. It is evident that *p*-nitronitrosobenzene behaves nonselectively because it forms dimers with all the studied nitrosobenzene partners. In contrast, *p*-methoxynitrosobenzene in most cases does not form dimers. The evidence that ability to form dimers is different in solution than in the solid state can be explained by influence of molecular arrangements in the crystal lattice.

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1. Introduction

Nitrosobenzenes and their dimers (azodioxides) exist in solution in equilibrium, in which monomers are dominant at the room temperature [1]. Appearance of dimers, either with (*Z*) or with (*E*) stereochemistry, can be observed by NMR only if the solution temperature is lowered to 225 K [2]. However, the ability of nitrosobenzenes to dimerize is structure dependent, and it was proposed that strong electron-donating *para*-substituents diminish proportion of dimers. For instance, *p*-methoxynitrosobenzene does not dimerize at all. The influence of substituents on the degree of dimerization was previously explained by contribution of the quinoid resonance structure (Scheme 1) [3].

In solid state, dimerization is dependent not only on the electronic factors but also on the molecular arrangement in the crystal lattice (topochemical effect). In principle, if nitroso molecules are well oriented with their nitroso groups in the vicinity, formation of azodioxides is strongly preferred [4a].

In our recent paper we found that the mixture of *p*-bromo- and *p*-nitronitrosobenzene can combine by forming the cross-linked dimer (*heterodimer*), which was observed by NMR in solution. In solid state, the same heterodimer appears as a solid solution

together with dimers of *p*-bromo- and *p*-nitronitrosobenzene (*homodimers*) [4b].

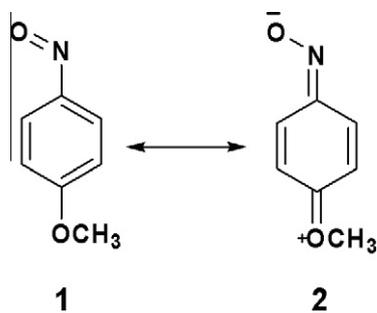
Cross-linking selectivity in solid state between different nitrosobenzene pairs has been investigated previously by combinatorial method [5], but without looking in the details of molecular structures of heterodimers. In this work we analyze the selectivity in formation of corresponding *heterodimers* from dimerizations of *para*- and *meta*-substituted nitrosobenzenes with parent nitrosobenzene in solution and in solid state. The nitrosobenzenes are chosen on the basis of the different electron effects of *meta*- and *para*-substituents (Scheme 2). Their selectivity in forming dimers was studied in solution by low temperature ¹H NMR, and in the solid state by ¹³C CP MAS NMR as well as by IR spectroscopy of the ¹⁵N-isotopomers. Experimental results are compared with the results of *ab initio* calculations.

2. Experimental

2.1. Preparation of nitrosobenzenes

Nitrosobenzenes **1**, **2**, **4**, **5**, **7**, **9**, **10** and **11** were prepared by oxidation of corresponding anilines with Oxone® (K₂SO₅ × K₂SO₄ × KHSO₄) analogously to a method previously described in the literature [6]. Compounds **3**, **6** and **8** were prepared from corresponding nitrobenzenes by standard procedures based on Zn reduction followed by oxidation with FeCl₃ [7].

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Scheme 1.

2.2. Preparation of crystals of heterodimers

Heterodimers were prepared by dissolving equimolar quantities of nitrosobenzenes **2–10** and ^{15}N -nitrosobenzene (**11**) in cold ($5\text{ }^\circ\text{C}$) and dry chloroform. Green solutions were left to evaporate in a refrigerator at $5\text{ }^\circ\text{C}$.

2.3. IR spectroscopy

IR spectra were recorded on a Bruker Equinox FT-IR spectrometer under 2 cm^{-1} resolution.

2.4. NMR spectroscopy

The liquid-state one- and two-dimensional ^1H NMR spectra (600.13 MHz) were measured in CDCl_3 at 298 K and 218 K on a Bruker AV600 spectrometer equipped with 5 mm TBI and 5 mm BBO probes with z -gradients. Chemical shifts, in ppm, were referred to TMS as the internal standard. The standard ^1H and COSY experiments were used. The FID resolution in ^1H NMR was 0.29 Hz per point. The COSY technique with a standard two $\pi/2$ pulse sequence (cosygpqf) in the pulsed field gradient mode (z -gradient) was applied using 2 k data points in F2 dimension and 512 increments in F1 dimension. The latter was subsequently zero-filled to 1024 points. Increments were obtained by four scans each, 8 kHz sweep width and pulse spacing was 1.0 s. The FID resolution was 4.1 Hz/point and 16.4 Hz/point in F2 and F1 dimensions, respectively.

Solid-state NMR experiments were performed on a 14.1 T Varian NMR System equipped with a 3.2 mm MAS probe. ^1H - ^{13}C CPMAS spectra were recorded using a standard ramped cross-polarization pulse sequence with high-power proton decou-

pling during acquisition. Contact time for cross-polarization was 5 ms, repetition delay was 10 s and sample rotation frequency was 10 kHz for all samples. Number of scans for different samples varied between 1000 and 6000. Chemical shifts of ^{13}C signals were referenced to the signal of tetramethylsilane.

2.5. Methods of calculations

Structures, natural charges and natural bond orders were calculated by the NBO-NRT analysis using the NBO 5.0 program package [8a] incorporated into the Gaussian 03 program package [8b].

3. Results and discussion

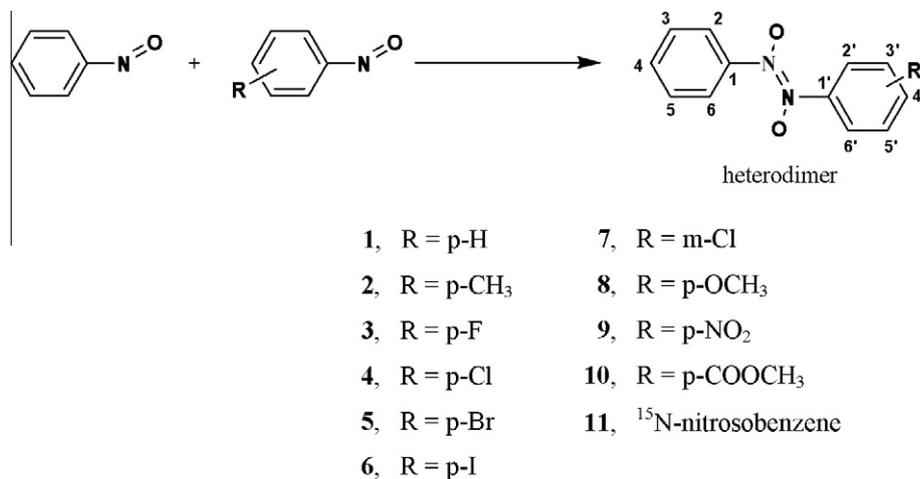
3.1. Cross-dimerization in solution

The 1D and 2D ^1H NMR spectra were recorded in chloroform- d solution for all the heterodimer combinations in which the referent partner was always the parent nitrosobenzene, and the other partner was one of the substituted nitrosobenzenes. While at the room temperature only the mixtures of monomers were observed, lowering the temperature to 218 K enabled us to observe signals assigned to dimers. Heterodimers were recognized on the basis of the extra signals, which neither belong to nitroso monomers nor to any of homodimers.

Because of the spectral complexity, we were not able to determine the ratio of (*Z*)- and (*E*)-dimers, but we successfully estimated the extent to which heterodimers appear. The results are collected in Table 1. Looking at the intensity of the heterodimer signals, we could observe that the most reactive partner for dimerization with the parent nitrosobenzene is *p*-nitronitrosobenzene (**9**). On the other side, *p*-methoxy- (**8**), *p*-methyl (**2**), *p*-fluoro (**3**), *p*-chloro (**4**), and *p*-methylformyl nitrosobenzene (**10**) do not form heterodimers at all. In frame of the selectivity concept, **9** is quite unselective, and **8** affords maximal selectivity: the formation of heterodimer was observed only in its combination with **9**. It means that **8** selects only one of the studied partners for cross-dimerization.

3.2. Cross-dimerization in solid state

To study cross-dimerization in solid state we have mixed equimolar solutions of different nitrosobenzenes and left the solvent to evaporate. The composition of the remaining crystals can consist from the mixture of homodimers and/or the heterodimer. To distinguish heterodimer from the mixture of homodimers, we have la-



Scheme 2.

Table 1¹H NMR shifts of aromatic protons of compounds (**1–10**) and their combinations recorded at 218 K in CDCl₃.

Compound	Dominant species ^{a,b}	$\delta_{\text{H}}^{\text{c}}$					Combination	New signals ^e	$\delta_{\text{H}}^{\text{c}}$						
		2	3	4	5	6			2,6	3,5	4	2',6'	3',5'		
1	(Z)-D	7.35–7.45 complex multiplet					1 + 2								
	M	7.96	7.69	7.80	7.69	7.96									
2	(Z)-D	7.26	7.16		7.16	7.26	1 + 3								
	M	~7.90	7.45		7.45	~7.90									
3	(Z)-D	7.43	7.13		7.13	7.43	1 + 4								
	M	~8.00	7.36		7.36	~8.00									
4	(Z)-D	7.40	7.36		7.36	7.40	1 + 5	+	7.42–7.50		7.29	7.52			
	M	7.89	7.65		7.65	7.89									
5	(Z)-D	7.31	7.56		7.56	7.31	1 + 6	+	7.40–7.50		7.15	7.72			
	M	~7.80	~7.80		~7.80	~7.80									
6	(Z)-D	7.14	7.76		7.76	7.14	1 + 7^f	+	?		?	?			
	M	7.68	8.08		8.08	7.68									
7	(Z)-D	7.57		7.47	7.36	7.19	1 + 8								
	M	7.59		7.72–7.77	8.26										
8^d	M	6.58	6.88		7.30	9.39	1 + 9	+	7.42–7.56		7.72	8.37			
9	(Z)-D	7.65	8.29		8.29	7.65	1 + 10								
	(E)-D	8.27	8.51		8.51	8.27									
10	M	8.61	8.16		8.16	8.61	8 + 9	+	7.35	6.89	-	7.64	8.30		
	(Z)-D	7.50	8.07		8.07	7.50									
	M	8.03	8.36		8.36	8.03									

^a M = monomer and D = dimer.^b Assignment was based in accordance with the previous study which suggested that (Z)-dimers were more abundant over (E)-dimers in solution of nitrosobenzenes at low temperatures [2].^c CDCl₃ solutions measured at 218 K.^d Ref. [3b].^e New signals that appeared in five combinations are attributed to heterodimers, presumably the (Z)-dimers.^f Six additional signals were detected at $\delta = 7.56, 7.45, 7.43, 7.31, 7.29, 7.20$ but could not be assigned with certainty.

beled the NO group of the parent nitrosobenzene with ¹⁵N isotope. Since all the other nitroso partners have only ¹⁴N nitroso group, the appearance of the ¹⁵N–¹⁴N signal of the asymmetric ON=NO vibration in the IR spectrum of the solid mixture is an indication that a heterodimer is formed in solid state. Note, that while the parent nitrosobenzene homodimer must have ¹⁵N–¹⁵N signal, other homodimers must have only ¹⁴N–¹⁴N signals. The ¹⁵N–¹⁵N signals which belong to homodimers of parent nitrosobenzene are at higher wavenumbers than ¹⁴N–¹⁴N signals because it crystallizes as Z-dimer. The only exception is combination **11 + 9** where position of the ¹⁵N–¹⁵N signal of nitrosobenzene homodimer is really at lower frequency (1233 cm⁻¹). This could be an indication that nitrosobenzene homodimer cocrystallizes with **9** in form of E-dimer. Such cocrystallization was described previously [4b]. The combination **11 + 6** is somewhat different because *p*-iodonitrosobenzene can crystallize in both forms, as monomer as well as dimer [1j]. From the results represented in Table 2, most of the combinations are able to form heterodimers with the exception of *p*-methoxynitrosobenzene (**8**) and *p*-methylformylnitrosobenzene (**10**). As it could be seen in Table 3, the ability to form heterodimers in solid state is higher than in solution and the derivatives which do not form heterodimers in solid state also are not able to form heterodimers in solution too.

Table 2Wavenumbers and assignments of bands in the IR spectra of ¹⁵N-nitrosobenzene (**11**) combined with compounds (**2–10**).

Combinations	$\bar{\nu}(\text{}^{14}\text{N=O})/\text{cm}^{-1}$	$\bar{\nu}(\text{}^{14}\text{N}^{14}\text{N})/\text{cm}^{-1}$	$\bar{\nu}(\text{}^{15}\text{N}^{15}\text{N})/\text{cm}^{-1}$	$\bar{\nu}(\text{}^{14}\text{N}^{15}\text{N})/\text{cm}^{-1}$
11 + 2		1255	1365, 1382 ^a	1248
11 + 3		1266	1357, 1365, 1382 ^a	1248
11 + 4		1259	1357, 1365, 1382 ^a	1247
11 + 5		1260	1357, 1382 ^a	1248
11 + 6	1482	1260	1357, 1365, 1382 ^a	1248
11 + 7		1413	1363 ^a	1394
11 + 8	1506		1357, 1365, 1382 ^a	
11 + 9		1266	1233 ^b	1248
11 + 10		1266	1357, 1382 ^a	

^a Z-dimer.^b E-dimer.**Table 3**

Appearance of heterodimers in solution and in solid state.

Combination	Solution	Solid state
1 + 2		●
1 + 3		●
1 + 4		●
1 + 5	◆	●
1 + 6	◆	●
1 + 7	◆	●
1 + 8		●
1 + 9	◆	●
1 + 10		

◆ Labels heterodimers formed in solution.

● Labels heterodimers formed in solid state.

Evidently, the topochemical factors are crucial for the ON=NO bond formation in these combinations.

For three combinations (*p*-methylformyl- (**10**), *p*-nitro- (**9**), and *m*-chloronitrosobenzenes (**7**)) with the parent nitrosobenzene we have recorded and analyzed the ¹³C NMR CP MAS spectra. Solid-state NMR spectroscopy can provide a wealth of information on different solid forms and their mixtures and is now considered as one of the

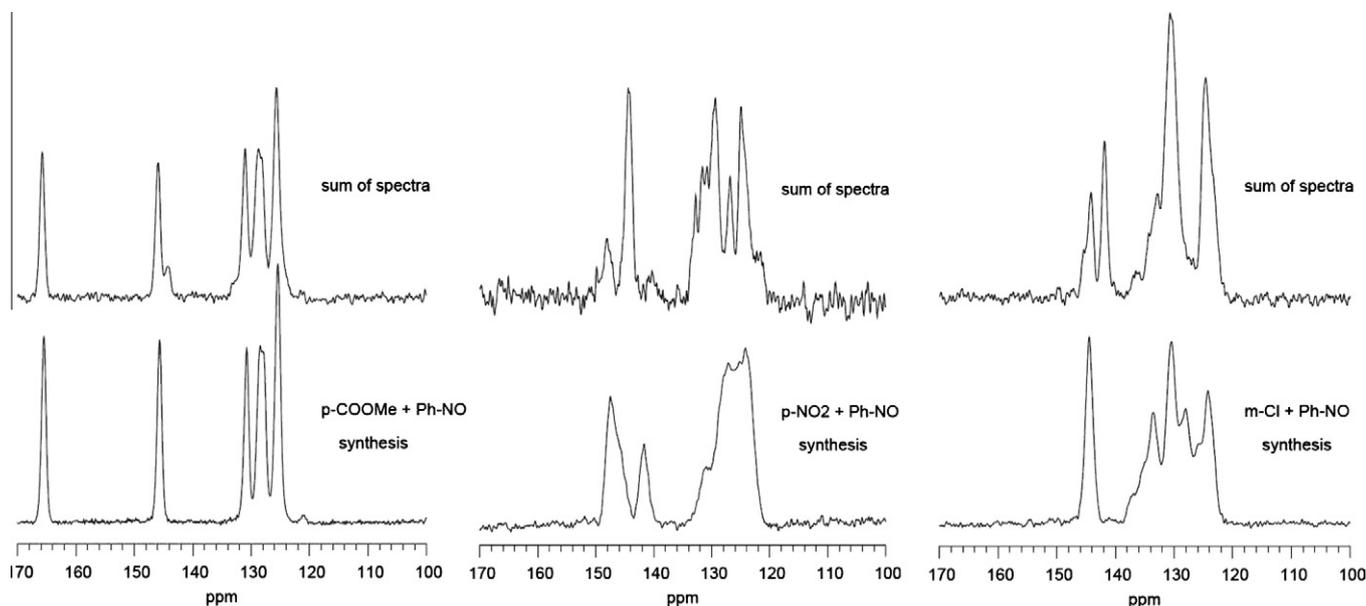


Fig. 1. ^{13}C NMR CP MAS spectra of solids obtained after mixing the equimolar solutions of two different nitrosobenzenes and evaporation of the solvent (labeled as “synthesis”) and the sum of the spectra of pure homodimers.

most powerful tool in characterization of solid samples. This technique has already proven useful to differentiate homo- and heterodimers of nitrosobenzenes [4b]. In Fig. 1 are shown the spectra of solids obtained after mixing the equimolar solutions of different nitrosobenzenes and evaporation of the solvent (labeled as “synthesis”) together with the sum of the spectra of pure homodimers. In the case of *p*-methylformylnitrosobenzene (**10**) no new signals have appeared in the spectra indicating no heterodimer formation. On the other hand, the other two derivatives provided the spectra which were different from the sum of the spectra of pure homodimers. New signals which appeared have aroused as a consequence of heterodimer formation either as co-crystals or as solid solutions. Our previous investigations suggested that a solid solution of heterodimer together with two homodimers was preferred over the co-crystals [4b].

3.3. Quantum-chemical calculations

Structures and energies of all the possible dimers of nitrosobenzenes and their hetero-partners were calculated by B3LYP/6-311++G** method [8]. The stability of hetero- versus homodimers was estimated by calculating $\Delta\Delta G_r$ for the corresponding isodesmic reaction (Scheme 3, Fig. 2).

In principle, for all dimers, hetero combination is more stable than homo combination. As in experiments in solution, *p*-nitronitrosobenzene (**9**) forms the most stable heterodimer with the parent

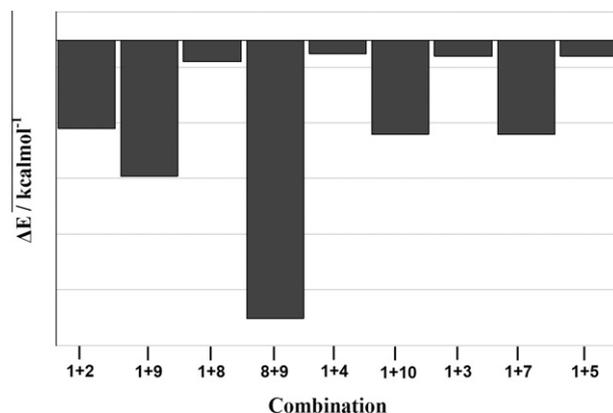
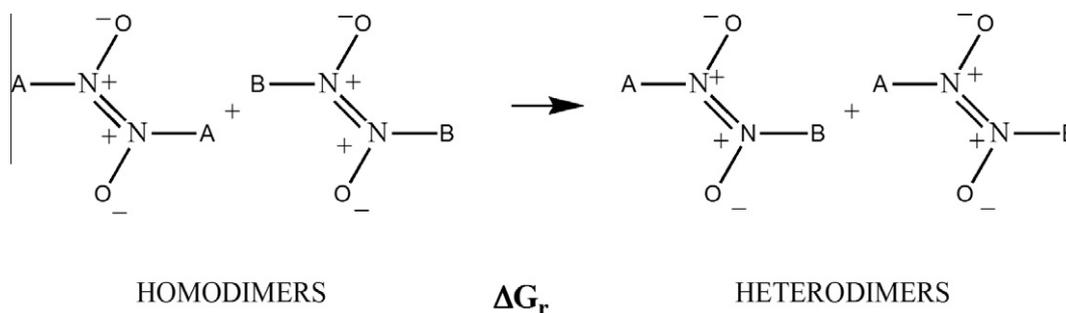


Fig. 2. Relative stabilities of hetero- versus homodimers calculated by B3LYP/6-311++G** method.

nitrosobenzene, and almost negligible affinity to dimerization affords *p*-methoxy- (**8**), and *p*-halonitrosobenzenes.

The difference in ability of **8** and **9** to form dimers can be explained by comparison of the calculated group natural charges and the bond orders in going from nitrosobenzene to **8** or to **9**, respectively (Table 4). It is evident that while *p*-NO₂ group in the benzene ring increases the positive charge on the nitroso group,



Scheme 3.

Table 4
Natural charges and bond orders of **1**, **8**, and **9**.

	<i>p</i> -Nitronitroso-benzene 9	Nitroso-benzene 1	<i>p</i> -Methoxy-nitrosobenzene 8
C–N natural bond order	1.049	1.026	1.005
Nitroso group	1.955	1.933	1.916
N–O natural bond order			
Nitroso group natural charge change relative to unsubstituted nitrosobenzene	0.033	0.000	–0.034

the *para*-substitution of –OCH₃ group makes the nitroso group more negative in accordance with the earlier explanation by influence of the resonance structure **2** in Scheme 1.

4. Conclusions

Nitrosobenzenes afford different chemical affinity to form cross-dimerized azodioxides. While *p*-nitronitrosobenzene is not selective because it yields heterodimers with all the investigated nitroso partners, *p*-methoxynitrosobenzene behaves quite oppositely: it affords high selectivity and in most cases it does not form dimers. We have also found that ability to form dimers and the selectivity in these reactions is different in solution than in the solid state what can be explained by topochemical factors of molecular arrangements in the crystal lattice. To resolve the details of the solid-state structures it is necessary to do systematic X-ray diffraction investigations, but as we know from our previous research, it is possible that heterodimers are incorporated in the crystal lattice of one of homodimer probably as a solid solution.

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