

Cyanamide Nitrosation

Nitrosation of Cyanamide: Preparation and Properties of the Elusive *E*- and *Z*-*N'*-CyanodiazohydroxidesThomas Guethner,^{*,[a]} Evi Huber,^[a] Juergen Sans,^[a] and Franz Thalhammer^[a]*This work is dedicated to Dr. Stefan Weiss who developed the chemistry of cyanamide at SKW Trostberg.*

Abstract: Nitrosation of cyanamide leads to unstable *E/Z*-cyanodiazohydroxides that easily deprotonate to *E/Z*-cyanodiazotates. Pursuing observations of E. Drechsel 145 years ago, the structure and reactivity of those products was determined,

mainly in aqueous solution. Depending on the pH, three different thermal decomposition pathways give either $N_2O + HCN$ or $N_2 + HNCO$. They were evaluated experimentally and by quantum mechanical calculations.

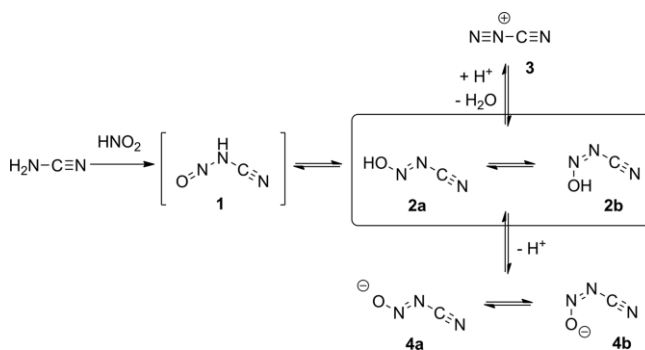
Diazotation of typical amines has high relevance in organic chemistry, not only for preparation of azo dyes, but also for aromatic substitution reactions as those invented by Sandmeyer and Balz/Schiemann. From cyanamide, one of the simplest molecules bearing a primary amino group, however, reaction with nitrite or nitrosation agents is only very scarcely known. As early as 1875, E. Drechsel^[1a,1b] reported an intense gas evolution reacting cyanamide with potassium nitrite, without identifying the products formed. In 1915, E. A. Werner^[1c] reported a nitrogen gas evolution from reacting cyanamide with sodium nitrite and sulfuric acid, but not with acetic acid. He drew conclusions about the tautomeric structure of cyanamide. Besides MO calculations suggesting stability of cyanodiazonium^[2a] and its experimental observation in the gas phase formed from cyanamide and NF_3 ,^[2b] Olah^[3] reported a reaction between cyanamide and nitrosyl tetrafluoroborate. He postulated cyanodiazonium tetrafluoroborate as an unstable intermediate that reacts with toluene under N_2 abstraction to form a mixture of isomeric tolunitriles. The lack of citations or younger literature suggests, that this reaction had not been tried to reproduce it or generalize it since 1985. Köhler^[4a] obtained the silver salt of "cyanamido-nitrite" by reacting $NaHCN$ with $NOCl$ and precipitation by silver nitrate. The product had low stability and was characterized only by IR. Fuchigami^[4b] reduced nitrosocyanamide electrochemically to form "nitrosocyanamide" that was isolated as K or Ag salt and only sparsely characterized.

Our investigations started from the findings, that aqueous cyanamide solutions, upon reaction with nitrosating agents, release nitrous oxide (N_2O) gas and give cyanide in solution. To understand this unexpected behaviour, we started investiga-

tions on stoichiometric reactions of cyanamide with nitrosation reagents.

We herein report new findings about the structure, properties and stability of nitrosated cyanamide, pathways and kinetics of its decomposition into gaseous products, and some ideas for its preparative use in organic synthesis.

Reaction of cyanamide with nitrous acid or other nitrosation agents leads to stereoisomeric *E*- and *Z*-*N'*-cyanodiazohydroxides **2a** and **2b**, most probably via the unverified *N*-nitrosocyanamide **1**. The cyanodiazohydroxides are acidic molecules that dissociate forming *E*- and *Z*-cyanodiazotate anions **4a/b** in aqueous solution. Further protonation and water abstraction seems to give the cyanodiazonium cation **3** as an intermediate or transition state (see Scheme 1).



Scheme 1. Nitrosation products of cyanamide.

We found, that the simple reaction between aqueous cyanamide, sodium nitrite and acetic acid in equimolar amounts below 0 °C gives a solution containing a mixture of **2a** and **2b** sufficiently stable to be handled for at least 24 hours. Typically, we prepared 1 molar solutions (see experimental section and supplement S1). Reagent addition sequence can be altered in many ways giving identical results, as long as nitrite is prevented from reacting with acid without cyanamide being present.

[a] Alzchem Trostberg GmbH, IM-2-F+E
Dr.-Albert-Frank-Strasse 32, 83308 Trostberg, Germany
E-mail: thomas.guethner@alzchem.com
<https://www.alzchem.com>

Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under <https://doi.org/10.1002/ejoc.202000181>.

Mineral acids with sodium nitrite give a similar product, although at lower yield because the unbuffered solution is more prone to decomposition. The same molecules are formed by passing an equimolar mixture of NO and NO₂ gas into an aqueous cyanamide solution. Non-aqueous nitrosation, e.g. in dichloromethane or diethyl ether is also possible, using sodium nitrite and acid or alkyl nitrites (see supplement S1.5 to S1.6). The product **2a/b** is less stable in organic solvents and can be easily extracted into water.

Aqueous solutions of **2a/b** are slightly yellowish to greenish and show first gas bubbles through thermal decomposition after about 15 minutes at 20 °C.

When heated to above 50 °C, a continuous and controllable gas evolution occurs. The total gas volume is about the 30-fold volume compared to that of the solution. We therefore alert all readers, not to store a solution of **2a/b** in a closed bottle, as it might explode. During gas evolution, the pH raises from 3 to about 6. Preliminary gas analysis gave a varying composition, beginning with mainly nitrogen (N₂) and ending up with mainly nitrous oxide (N₂O). The remaining solution contains large amounts of hydrogen cyanide (HCN, caution!). Ion chromatography detected significant amounts of dicyanamide in solution. GC/MS found small amounts of cyanogen (CN)₂ in the evolved gas mixture. We suppose, these products form by electrophilic cyanation of cyanamide and HCN respectively.

We determined the pH dependent UV spectra of a freshly prepared solution of **2a/b** (see supplement S2). An intense UV absorption at 260 nm ($\epsilon_{260} = 726 \text{ m}^2\text{mol}^{-1}$ at pH 4.0 or higher) shows, that the cyanodiazotate anions **4a/b** are present. Lowering the pH, ϵ_{260} diminishes, indicating protonation to the neutral species **2a/b** with a pK_a of 1.8. A second, much weaker UV absorption band at 370 nm ($\epsilon_{370} = 2.96 \text{ m}^2\text{mol}^{-1}$ at pH 4.0), responsible for the visual color, is almost independent of the pH.

Titration solutions of **2a/b** with NaOH gives the expected assay. Solutions prepared from sodium nitrite and mineral acids are partly dissociated to the ion pair H₃O⁺ ⁻O=N=N-CN, even in presence of excess mineral acid. Acetate-based solutions consist of the diazotate anions **4a/b** and equimolar acetic acid, thus titration just measures the acetate content. Decomposition of **2a/b**, forming much less acidic products, can be monitored by titration (see supplement S3).

Upon addition of silver nitrate a light yellow silver salt is formed between pH 1 and pH 5. It decomposes slowly even at 0 °C and is very impact sensitive, but not highly energetic. Obviously, this silver salt was prepared and described years ago.^[4a,4b] The FTIR spectrum of the silver salt shows a strong C≡N band at 2177, a N=N band at 1441 and a N-O band at 1168 cm⁻¹ (see supplement S4.1).

FTIR measurement of the aqueous solution did not show the C≡N absorption. Raman measurements in solution (see supplement S4.3) showed a sharp C≡N band at 2185, a N=N band at 1364 and a N-O band at 1201 cm⁻¹. Those bands disappeared upon thermal decomposition.

To our astonishment, solutions of **2a/b** can easily be chromatographed on a Hydrosphere C18 column at 20 °C (see Figure 1). Aqueous phosphate or acetate buffers of pH 4.0 gave a

well-formed peak at a detection wavelength of 260 nm. The DAD spectra are identical to UV data mentioned above, including the weak absorbance at 370 nm. The chromatographic peak consists of two overlapping signals with identical UV spectra, always in a peak ratio of about 9:1. We interpret this as a partial separation of the interconverting *E/Z*-isomers **4a/b**.

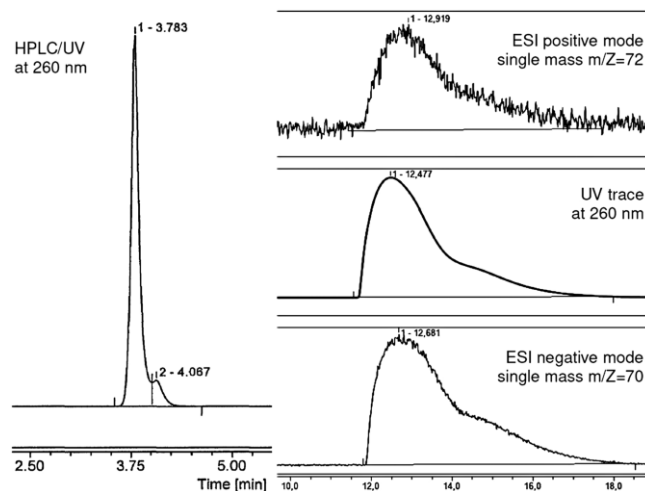


Figure 1. Left: HPLC of **2a/b** at pH 4 on Hydrosphere C18 with UV detection at 260 nm. Right: LC/MS SIM traces in positive/negative mode with aqueous formic acid as eluent on Hydrosphere C18 compared to a parallel UV trace at 260 nm.

HPLC was used to compare the assay of solutions of **2a/b** prepared by different methods (acids, solvents) and to monitor decomposition. An absolute assay however was not possible, because no stable reference standard could be defined. We therefore took a freshly prepared acetate solution as the 100 % reference and calculated concentrations of **2a/b** based on that reference. The double peak **2a/b** was always integrated as a whole.

LC/MS experiments were successful on Hydrosphere C18 using 50 mM aqueous formic acid as eluent, as ammonium acetate at pH 4 did not give a good ionization. In mass spectra of positive mode, $m/Z + 1 = 72$ was found. In the negative mode, $m/Z - 1 = 70$ could be detected as well. SIM mode traces in positive and negative mode correlated exactly to the UV trace at 260 nm. We therefore are confident, that the neutral molecules **2a/b** have a molecular mass of 71 and are interconverting isomers, both absorbing at $\lambda_{\text{max}} = 260 \text{ nm}$.

For NMR experiments, we reacted equimolar amounts of sodium nitrite, cyanamide and acetic acid, all dissolved in D₂O at 0 °C. The sample solution was measured at 25 °C. ¹³C NMR spectra gave – besides the acetate signals – only two sharp peaks at 122.0 and 114.4 ppm in an intensity ratio of about 2:1, being distinctly different from traces of remaining cyanamide signaling at 117.9 ppm. We interpret those as C≡N signals of the stereoisomers **4a** and **4b** (see Figure 2).

Because ¹⁵N enriched materials were not available, we tried ¹⁴N NMR experiments, despite the naturally very broad signals. As chemical shifts in ppm scale are independent of the nucleus measured, ¹⁴N data are comparable to ¹⁵N reference data. Peaks at –172 and –160 ppm in the ratio 2:1 are interpreted as cyano

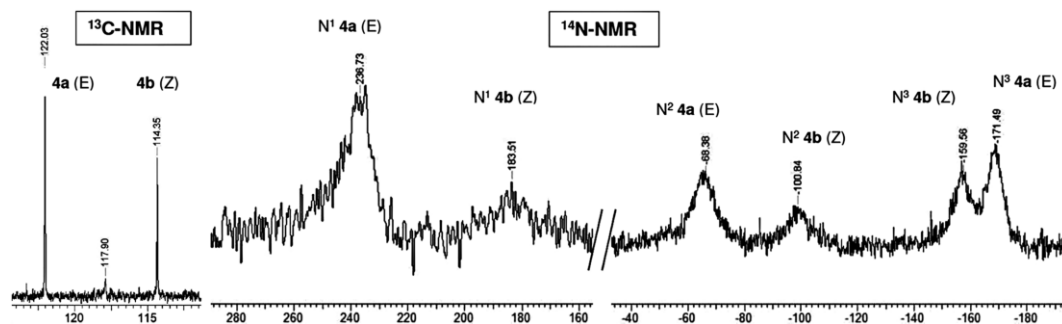


Figure 2. Extracts of the ^{13}C -NMR and ^{14}N -NMR spectra of **4a/b**. Full scale spectra can be found in supplement S7.

nitrogen atoms of the anions **4a/b**, signals at -68 and -103 ppm and at 237 and 183 ppm respectively (both also in the ratio 2:1) are interpreted as the azo N atoms.

As direct reference spectra are missing, the most similar substances found were aryldiazocyanides and aryldiazotates. Their reported NMR data clearly correlate to our assignment with the *E*-stereoisomer **4a** being the major compound (see table S7.1). The tautomeric *N*-nitrosocyanamide **1** seems not to be present in significant amounts, as no further ^{13}C absorption and no ^{14}N nitroso signals were found.

HPLC was used to monitor thermal decomposition of **2a/b** without pH control (see Figure 3). A sample of the acetate-based solution was heated to $80\text{ }^\circ\text{C}$. The evolved gas volume was measured and liquid samples were withdrawn, cooled down immediately, diluted and analyzed by HPLC. The evolved gas volume clearly correlates with the vanishing HPLC signal, thus the species absorbing at 260 nm is the gas evolving species. pH rose from 3.0 to 6.3 during the decomposition reaction. The greenish-yellow color of the solution vanished during reaction giving a clear, colorless solution. It got brownish during further 2 hours at $80\text{ }^\circ\text{C}$ after gas evolution ended, probably due to polymerization of HCN formed. The gas composition varied over time (and thus over pH) from $4.0\text{ }\%v/v$ N_2O at the beginning to $77\text{ }\%v/v$ N_2O in the last gas sample.

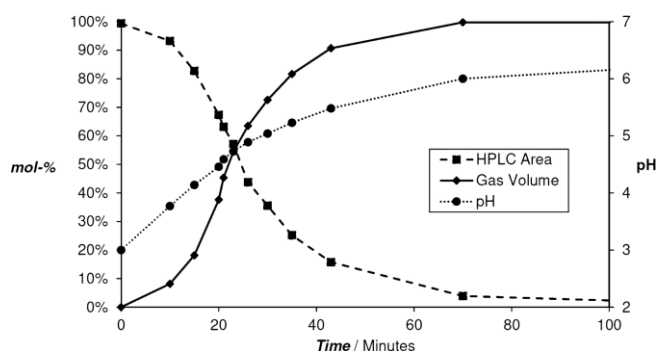


Figure 3. Decomposition of an acetate solution of **2a/b** without pH control.

During the whole decomposition reaction, the HPLC peak ratio of **2a/2b** always remained at 9:1, thus indicating, that decomposition forming gaseous compounds is slower than the interconversion of **2a** into **2b**. The ratio here is different to that found by NMR (2:1), most probable because the NMR timescale is different.

Next, we tried to decompose **2a/b** at constant pH. Because the synthesis from cyanamide was limited to a pH range of 2 to 4 (see supplement S8.1), we gradually added an acetate-based solution to excess hot buffer solution. Now, at constant pH, the gas composition remained constant during the whole reaction (see Figure 4 and supplement S8.2). 1 mol of N_2 and 0.5 mol of CO_2 evolved per mole of **2a/b** at $\text{pH} \leq 1$ together with 0.5 mol of urea formed. Cyanide formation in this pathway **A** was almost zero. In the range pH 4 to 6, nearly stoichiometric amounts of nitrous oxide (N_2O) and almost no N_2 and CO_2 were detected, together with high amounts of hydrocyanic acid (pathway **B**). In the range of $\text{pH} 2 \pm 1$, correlating to the pK_a of **2a/b**, a mixture of those products, thus a competition between pathways **A** and **B** was found.

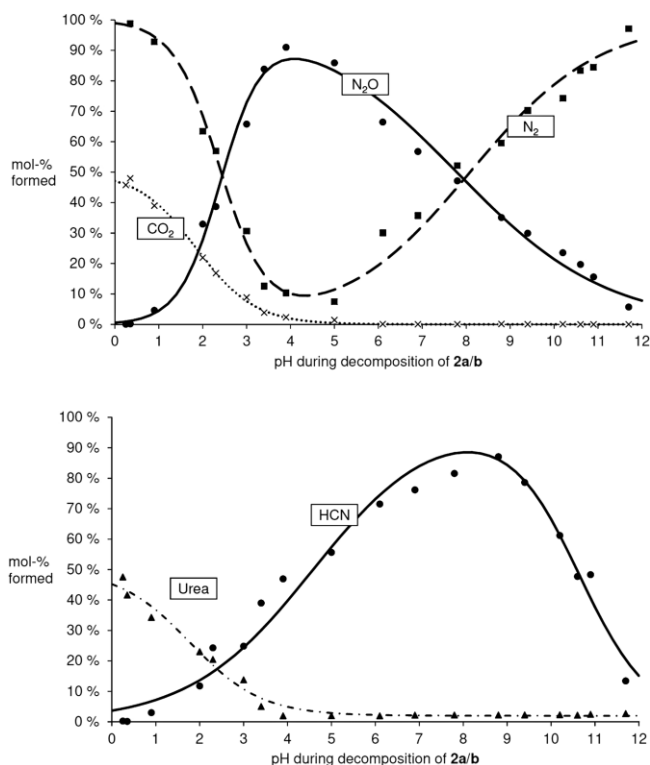
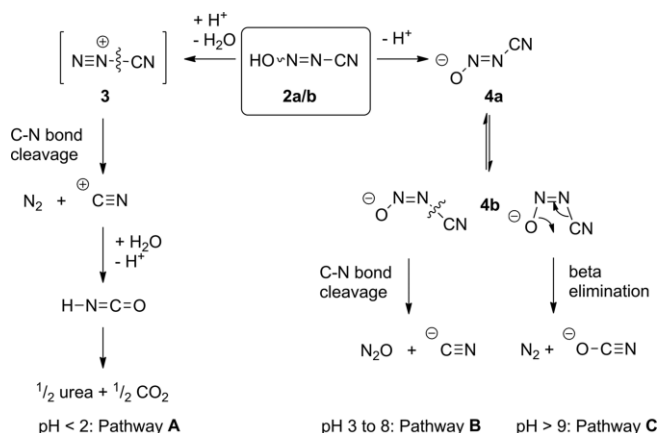


Figure 4. Product quantification relative to the pH of decomposition of **2a/b**.

To our astonishment, at higher pH above 9, cyanide (and thus N_2O) formation diminishes again with almost exclusively releasing N_2 gas at pH 12 or higher. We unambiguously de-

ected cyanate anions stoichiometrically formed in this pathway **C**.

We explain this pH dependent 3-way decomposition (see Scheme 2) by the pK_a of **2a/b**. Below pH 2, protonation leads to the cyanodiazonium cation **3** whose bond cleavage to N_2 and a CN^+ cation is obvious. In aqueous media, the CN^+ cation stabilizes forming CO_2 and urea as detected.



Scheme 2. Thermal decomposition pathways at different pH.

In neutral media, at pH 3 to 8, the diazotate anions **4a/b** are predominant. Simple bond cleavage via pathway **B** leads to N_2O gas and a CN^- anion or HCN respectively. At pH 9 and above, the anions **4a/b** do not have any possibility for further deprotonation. Thus, the gradual change of the decomposition products from N_2O and cyanide to N_2 and cyanate must have a mechanistic background. We suppose that at higher pH a beta elimination process, possibly with contribution of water or OH^- anions takes place via pathway **C**.

Activation energies for all three pathways are low. We measured the first order gas evolution speed rate at pH 0, 5, 7 and 10 for different temperatures. An Arrhenius plot (see supplement S9) gave the very low activation energy $\Delta G^\ddagger = 54 \text{ kJ mol}^{-1}$ for pathway **A** at pH 0 and values around 110 kJ mol^{-1} for both pathways **B** and **C**. Thus pathways **B** and **C**, though leading to different products, seem to proceed via transition states of equal enthalpy.

Comprehensive thermodynamic calculations including the synthesis of **2a/b** from cyanamide and nitrous acid, were estimated based on tabulated enthalpies of formation (see supplement S10).

Pathway **A** or **C** (to isocyanic acid):
 $H_2NCN + HNO_2 \rightarrow HOCN + H_2O + N_2$
 $\Delta H_{\text{react}}^0 = -401.5 \text{ kJ mol}^{-1}$

Pathway **A** (to CO_2 and urea):
 $H_2NCN + HNO_2 \rightarrow \frac{1}{2} CO_2 + \frac{1}{2} H_2N-CO-NH_2 + \frac{1}{2} H_2O + N_2$
 $\Delta H_{\text{react}}^0 = -493.4 \text{ kJ mol}^{-1}$

Pathway **B**:
 $H_2NCN + HNO_2 \rightarrow HCN + H_2O + N_2O$
 $\Delta H_{\text{react}}^0 = -82.6 \text{ kJ mol}^{-1}$

Pathway **B** leading to N_2O formation thus has a much lower exotherm, but is preferred at moderate pH for kinetic reasons.

Quantum mechanical calculations on the anionic species **4a/b** (see supplement S11) gave evidence of *E/Z* stereoisomers as enthalpy surface minima with the *Z*-isomer **4b** being slightly more energetic. The *E/Z* isomerisation activation enthalpy is around 87 kJ mol^{-1} , thus low enough to take place at 0°C . Bond cleavage of the anions to form N_2O and cyanide anion was calculated to be slightly endothermic (between $+20$ and $+40 \text{ kJ mol}^{-1}$) with an enthalpy barrier around 113 kJ mol^{-1} from the *Z* isomer **4b**, the same activation energy as found experimentally. Thus, decomposition via pathway **B** is an entropy driven mechanism. The decomposition barrier from **4a** is much higher, so the predominant **4a** is assumed to isomerize to **4b** that decomposes to cyanide and nitrous oxide. Estimated frequency factors coincide with the observed experimental lifetimes of **2a/b**.

Ab initio calculations on the neutral species gave only minor enthalpy differences between the O- and N-protonated species **1** and **2a/b**. Transitions of the neutral species to form N_2O and HCN have high enthalpy barriers, thus decay of **2a/b** via pathway **B** should proceed via deprotonation to **4a** and isomerization to **4b**.

Summarizing these findings, *N'*-cyanodiazohydroxides exist in two stereoisomeric forms *E* (**2a**) and *Z* (**2b**). They isomerize easily in aqueous solution. The concentration of the tautomer *N*-nitrosocyanamide **1** is too low to be detected.

The cyanodiazohydroxides **2a/b** are medium strong acids with a pK_a around 1.8, dissociate in aqueous solution to form the stereoisomeric cyanodiazotate anions **4a/b**. Protonation and dehydration to the cyanodiazonium cation **3** cannot be observed in aqueous solution but is postulated as a transition state. All species are thermally unstable and decompose with gas evolution. As anticipated by their structure, **4a/b** decompose to form N_2O and hydrocyanic acid at ambient conditions. It is noteworthy, that nitrosation (oxidation) of cyanamide is able to reduce a C^{4+} derivative (cyanamide) to a C^{2+} compound (HCN). Hydrocyanic acid formed can react with excess cyanamide forming a new carbon-carbon bond, finally leading to oxalate (see supplement S12). In strongly alkaline environment, the mechanism gradually changes to a beta elimination pathway that ends up with N_2 and cyanate. In strongly acidic media however, **2a/b** are protonated to the cyanodiazonium cation **3** that splits off nitrogen leaving a CN^+ cation. In aqueous environment, HNCO and CO_2 are formed thereof.

Diazotation of cyanamide in aprotic acidic environment however opens new synthetic pathways for electrophilic cyanation by generating reactive CN^+ cations from cyanamide. Besides the observed formation of $(CN)_2$ and dicyanamide, we got first results in cyanating electron-rich aromatic compounds, e.g. *p*-xylene and mesitylene to the corresponding benzonitriles (see supplement S1.9 to S1.11). This will be subject for an upcoming publication.

Experimental Section

Warning! Nitrosation reactions of cyanamide give intermediates that easily decompose into gaseous products. We recommend not

to synthesize larger amounts, especially not in dry state. All experiments have to be done in open glassware, because gas evolution might rupture any container.

6.00 g (0.1 mol) glacial acetic acid was dissolved in 50 mL of demineralized water and cooled to $-5\text{ }^{\circ}\text{C}$. 4.20 g (0.1 mol) of solid Cyanamide F1000 (Alzchem) and 6.90 g (0.1 mol) of sodium nitrite were separately dissolved in 20 mL of water each. Using two dropping funnels, the cyanamide solution and the sodium nitrite solution were dosed parallel over 30 minutes. The solution became greenish-yellow, the pH dropped from 3.5 to 2.9 during postreaction over another 30 minutes at $-5\text{ }^{\circ}\text{C}$. This solution contains approximately 1 mol per liter of **2a/b** and can be stored at $0\text{ }^{\circ}\text{C}$ for at least 24 hours without significant assay losses.

Supporting Information (see footnote on the first page of this article): Further experimental details can be found in supporting information S1.

Conflict of Interest

There are no conflicts to declare.

Acknowledgments

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Keywords: Cyanamide · Thermochemistry · Cyanodiazohydroxides · Nitrous oxide · Diazo compounds

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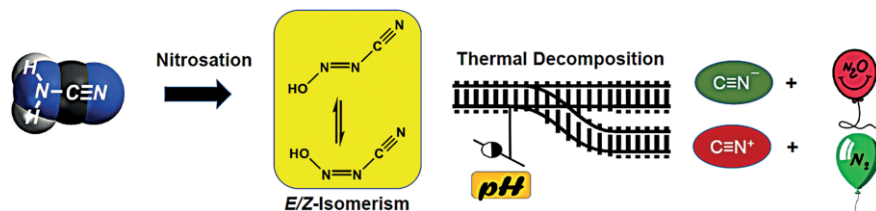
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T. Guethner,* E. Huber, J. Sans,
F. Thalhammer 1–6



Nitrosation of Cyanamide: Preparation and Properties of the Elusive *E*- and *Z*-*N'*-Cyanodiazohydroxides



The simple reaction between cyanamide and nitrous acid in aqueous solution leads to unstable azo intermediates that easily decompose into gaseous products. Principally known for 145 years, the elusive intermediates

and complex reaction pathways were identified and characterized for the first time. Depending on pH conditions, either N₂O + HCN or N₂ + HNCO are formed by three different decomposition pathways.

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