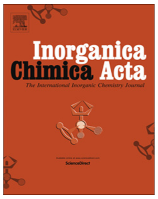
Inorganica Chimica Acta 425 (2015) 114–117

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica



Metal-mediated cyanamide–hydroxyguanidine coupling

Marina Ya. Demakova [a], Dmitrii S. Bolotin [a], Nadezhda A. Bokach [a,*], Galina L. Starova [a], Vadim Yu. Kukushkin [a,b,*]

[a] *Institute of Chemistry, Saint Petersburg State University, Universitetskiy Pr., 26, 198504 Saint Petersburg, Russian Federation*
[b] *Institute of Macromolecular Compounds of Russian Academy of Sciences, V.O. Bolshoi Pr. 31, 199004 Saint Petersburg, Russian Federation*

ARTICLE INFO

Article history:
Received 11 August 2014
Received in revised form 11 October 2014
Accepted 14 October 2014
Available online 4 November 2014

Keywords:
Hydroxyguanidine
Cyanamide
Zinc(II) complexes
Metal-mediated reaction
Molecular structures

ABSTRACT

Reaction of the cyanamides R_2NCN (R = Me **2a**, Et **2b**) with the hydroxyguanidine $OC_4H_8NC(=NOH)NH_2$ (**1**) in the presence of zinc halides leads to $[ZnX_2\{HN{=}C(NR_2)ON{=}C(NH_2)NC_4H_8O\}]$ derived from the Zn^{II}-mediated cyanamide–hydroxyguanidine coupling. This reaction is the first observation of interplay between any nitrile group and any hydroxyguanidine both in metal-involving and metal-free chemistry. Complexes **3a**,**b**–**5a**,**b** rather rapidly degrade in solutions at RT, but solvates **3a**,**b**·MeOH and **4a**·MeOH are sufficiently stable in the solid state and they were characterized by IR, HRESI$^+$-MS, solid state CP-MAS TOSS ^{13}C NMR, and X-ray crystallography (for **3a**,**b**). Complexes **4b** and **5a**,**b** were identified in solutions by HRESI$^+$-MS.

1. Introduction

One of the most efficient methods for activation of rather inert nitrile substrates toward nucleophilic addition or dipolar cycloaddition is coordination of RCN species to a metal center [1–3]. Although the nucleophilic addition of *N*-nucleophiles to metal-activated nitriles was thoroughly studied for a century, the addition of HON-type nucleophiles – for instance oximes, amidoximes, and hydroxylamines – become subject of research rather recently [2].

Besides basic interest, the coupling between nitriles and HON-systems conducted at Ni^{II} [4], Co^{II} [5], and Zn^{II} [6,7] centers has some practical implications insofar as these reactions open up facile routes to amidines [5], 1,3,5-triazapentadienes [4], phthalocyanines [8], and carboxamides [6,7], viz. the compounds exhibiting a broad range of various applications.

The current trend in the field of nitrile moiety–HON group integration includes various functionalizations of oximes (Fig. 1, A; R = Alk, Ar, H) and use of species relevant to oximes such as, for instance, amidoximes (B) [9] that in accord with IUPAC nomenclature are not derived from ketones or aldehydes and therefore do not belong to the category of oximes.

These structure modifications either leads to a substantial alteration of nucleophilicity of HON groups (that in turn, strongly affect some synthetic procedures, e.g. the synthesis of phthalocyanines [8]) or direct the coupling to unexplored directions thus giving libraries of novel species originating from the nitrile–HON integration followed by, in some instances, secondary reactions.

If reactions of ket- or aldoximes $R^1RC{=}NOH$ (**A**) and amidoximes $R^1C(NR_2){=}NOH$ (**B**) with nitriles RCN were studied in both organic [10] and coordination chemistry [2], nothing is known on interplay between hydroxyguanidines $(R_2N)_2C{=}NOH$ (**C**) with any of CN groups. In this work, we report on the first observation of such reaction that includes zinc(II)-mediated coupling between dialkylcyanamides and a hydroxyguanidine.

2. Experimental

2.1. Instrumentation

Melting points were measured on a Stuart SMP30 apparatus in capillaries and are not corrected. Microanalyses were carried out on a Euro EA3028-HT instrument. Electrospray ionization mass-spectra were obtained on a Bruker micrOTOF spectrometer equipped with an electrospray ionization (ESI) source. The instrument was operated both in positive and in negative ion mode using a *m*/*z* range 50–3000. The capillary voltage of the ion source was set at −4500 V (ESI$^+$-MS) and the capillary exit at ±(70–150) V. The nebulizer gas flow was 0.4 bar and the drying gas flow 4.0 L/

---

* Corresponding authors at: Institute of Macromolecular Compounds of Russian Academy of Sciences, V.O. Bolshoi Pr. 31, 199004 Saint Petersburg, Russian Federation (V.Yu. Kukushkin).

E-mail addresses: n.bokach@spbu.ru (N.A. Bokach), kukushkin@VK2100.spb.edu (V.Yu. Kukushkin).

http://dx.doi.org/10.1016/j.ica.2014.10.015
0020-1693/© 2014 Elsevier B.V. All rights reserved.

min. For ESI, complexes were dissolved in MeOH. In the isotopic pattern, the most intensive peak is reported. The solid state CP-MAS TOSS ^{13}C NMR spectra were measured on Bruker Avance III WB 400 with magic angle spinning at 10 kHz frequencies. Infrared spectra (4000–400 cm^{-1}) were recorded on a Shimadzu IR Prestige-21 instrument in KBr pellets.

2.2. Materials

Solvents and the dialkylcyanamides were obtained from commercial sources and used as received. The *N*-morpholinecarbamidoxime (**1**) and also $R_2NC(=NOH)NH_2$ ($R_2 = C_5H_{10}$, Ph_2) were synthesized according to the literature methods [11].

2.3. X-ray structure determinations

Single crystals of **3a**·EtOH and **3b**·MeOH were grown from an EtOH/ethyl acetate 1:1 (v/v) mixture and MeOH, respectively. A crystal suitable for X-ray diffraction was mounted on Xcalibur, Eos diffractometer and it was kept at 100(2) K during data collection. Using OLEX2 [12], the structure was solved with the Superflip [13] structure solution program using Charge Flipping and refined with the SHELXL [14] refinement package using Least Squares minimization. Crystal data for **3a**·EtOH: $C_{10}H_{23}N_5O_3Cl_2Zn$, $M = 395.59$, triclinic, $a = 8.4794(3)$ Å, $b = 8.6365(3)$ Å, $c = 12.5146(4)$ Å, $\alpha = 95.846(3)$, $\beta = 107.638(3)$, $\gamma = 106.815(3)°$, $V = 817.80(5)$ Å^3, $T = 100(2)$, space group $P\bar{1}$ (No. 2), $Z = 2$, μ(Cu Kα) = 5.248, 16944 reflections measured, 3240 unique ($R_{int} = 0.0917$), which were used in all calculations. The final wR_2 was 0.1721 (all data) and R_1 was 0.0596 (>2$\sigma(I)$). Crystal data for **3b**·MeOH: $C_{11}H_{25}N_5Cl_2O_3Zn$, $M = 788.19$, triclinic, $a = 8.5625(7)$ Å, $b = 9.1343(11)$ Å, $c = 12.3374(14)$ Å, $\alpha = 110.392(11)°$, $\beta = 97.707(8)$, $\gamma = 98.570(8)$, $V = 876.17(16)$ Å^3, $T = 100(2)$, space group $P\bar{1}$ (No. 2), $Z = 1$, μ(Mo Kα) = 1.719, 7461 reflections measured, 3753 unique ($R_{int} = 0.0964$), which were used in all calculations. The final wR_2 was 0.1769 (all data) and R_1 was 0.0834 (>2$\sigma(I)$).

2.4. Synthetic work

Powder of $OC_4H_8NC(=NOH)NH_2$ (0.55 mmol) was added to a stirred solution of ZnX_2 (X = Cl, Br, I; 0.55 mmol) in MeOH (5 mL), whereupon $NCNR_2$ (0.66 mmol for R = Me; 0.83 mmol for R = Et) was added to the mixture. Colorless powder was released after 2 min (R = Me), it was separated by centrifugation, washed with CH_2Cl_2 (two 2-mL portions) and dried in air at RT overnight. For system with R = Et 8-fold excess of EtOAc was added to the reaction mixture after 2 min, whereupon the formed colorless precipitate was treated as described for R = Me. Yields 73% (**3a**·MeOH), 69% (**3b**·MeOH), and 67% (**4a**·MeOH).

2.4.1. $[ZnCl_2\{HN=C(NMe_2)ON=C(NH_2)NC_4H_8O\}]\cdot MeOH$ (3a·MeOH)

M.p. 153 °C (dec.). *Anal.* Calc. for $C_9H_{21}N_5Cl_2O_3Zn$: C, 28.18; H, 5.52; N, 18.26. Found: C, 28.45; H, 5.59; N, 19.01%. HRESI$^+$-MS (MeOH, *m/z*): 216.1452 (calc. 216.1461) $[C_8H_{17}N_5O_2+H]^+$ ($[L+H]^+$), 314.0343 (calc. 314.0331) $[C_9H_{21}N_5ClO_3Zn]^+$ ($[M-Cl]^+$), 667.0332 (calc. 667.0332) $[C_{18}H_{34}N_{10}Cl_3O_4Zn_2]^+$ ($[2M-Cl]^+$). IR (KBr, selected bands, cm^{-1}): 3419(vs), 3331(m), 3231(m), 3182(m) [ν(N—H)]; 2961(w), 2919(w), 2899(vw), 2852(vw) [ν(C—H)]; 1619(s) [ν(C=N)]; 1558(w) [δ(N—H), ν(C=N)]; 552(m) [δ(C—H)]. ^{13}C NMR (CP-MASS TOSS, δ): 36.84 (Me^1 and Me^2), 49.31 (CH_2–N), 64.65 (CH_2–O), 160.54 (C_1 and C_4); the signal of MeOH (46.21 ppm) was also detected.

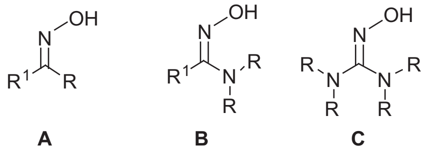


Fig. 1. Structural types of HON-systems for the coupling (R = Alk, Ar or H; R^1 = Alk, Ar): (A) – oximes, (B) – amidoximes, (C) – hydroxyguanidines.

2.4.2. $[ZnCl_2\{HN=C(NEt_2)ON=C(NH_2)NC_4H_8O\}]\cdot MeOH$ (3b·MeOH)

M.p. 149 °C (dec.). *Anal.* Calc. for $C_{11}H_{25}N_5Cl_2O_3Zn$: C, 32.10; H, 6.12; N, 17.01. Found: C, 32.45; H, 6.09; N, 17.23%. HRESI$^+$-MS (MeOH, *m/z*): 244.1776 (calc. 244.1774) $[C_{10}H_{21}N_5O_2+H]^+$ ($[L+H]^+$), 342.0684 (calc. 342.0686) $[C_{10}H_{21}N_5ClO_2Zn]^+$ ($[M-Cl]^+$), 725.1148 (calc. 725.1142) $[C_{20}H_{42}N_{10}Cl_3O_4Zn_2]^+$ ($[2M-Cl]^+$). IR (KBr, selected bands, cm^{-1}): 3429(vs), 3332(m), 3226(m) [ν(N—H)]; 2975(w), 2901(w), 2861(vw) [ν(C—H)]; 1625(s) [ν(C=N)]; 1560(w) [δ(N—H), ν(C=N)]; 552(m) [δ(C—H)]. ^{13}C NMR (CP-MASS TOSS, δ): 15.31 (Me^1 and Me^2), 42.61 (CH_2^1 and CH_2^2), 47.79 (CH_2–N), 66.50 (CH_2–O), 161.67 (C_1 and C_4); the signal of MeOH (46.72 ppm) was also detected.

2.4.3. $[ZnBr_2\{HN=C(NMe_2)ON=C(NH_2)NC_4H_8O\}]\cdot MeOH$ (4a·MeOH)

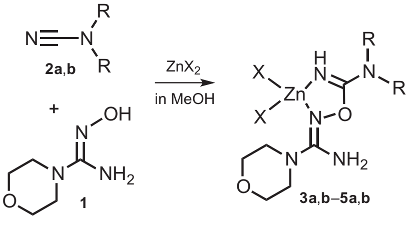
M.p. 151 °C (dec.). *Anal.* Calc. for $C_9H_{21}N_5Br_2O_3Zn$: C, 22.88; H, 4.48; N, 14.82. Found: C, 22.65; H, 4.74; N, 15.01%. HRESI$^+$-MS (MeOH, *m/z*): 216.1454 (calc. 216.1461) $[C_8H_{17}N_5O_2+H]^+$ ($[L+H]^+$), 389.0225 (calc. 389.0221) $[C_9H_{21}N_5BrO_3Zn]^+$ ($[M-Br]^+$), 858.9615 (calc. 858.9611) $[C_{18}H_{34}N_{10}Br_3O_4Zn_2]^+$ ($[2M-Br]^+$). IR (KBr, selected bands, cm^{-1}): 3514(vs), 3439(m), 3336(m), 3230(m) [ν(N—H)]; 2967(w), 2917(w), 2896(vw), 2858(vw) [ν(C—H)]; 1628(s) [ν(C=N)]; 1560(w) [δ(N—H), ν(C=N)]; 551(m) [δ(C—H)]. ^{13}C NMR (CP-MASS TOSS, δ): 37.93 (Me^1 and Me^2), 47.68 (CH_2–N), 67.73 (CH_2–O), 160.00 and 161.56 (C_1 and C_4); the signal of MeOH (46.13 ppm) was also detected.

Complexes **4b** and **5a**,**b** were detected in MeOH in solutions by HRESI$^+$-MS. **4b**, *m/z*: 244.1766 (calc. 244.1768) $[C_{10}H_{21}N_5O_2+H]^+$ ($[L+H]^+$), 388.6810 (calc. 388.6814) $[C_{10}H_{21}N_5BrO_2Zn]^+$ ($[M-Br]^+$). **5a**, *m/z*: 216.1455 (calc. 216.1455) $[C_8H_{17}N_5O_2+H]^+$ ($[L+H]^+$), 405.9707 (calc. 405.9712) $[C_9H_{21}N_5IO_3Zn]^+$ ($[M-I]^+$). **5b**, *m/z*: 244.1765 (calc. 244.1768) $[C_{10}H_{21}N_5O_2+H]^+$ ($[L+H]^+$), 434.0023 (calc. 434.0026) $[C_{10}H_{21}N_5IO_2Zn]^+$ ($[M-I]^+$).

3. Results and discussion

In our work, we observed the reaction between the dialkylcyanamides R_2NCN (R = Me **2a**, Et **2b**) and a hydroxyguanidine, viz. *N*-morpholinecarbamidoxime (**1**) [11] in the presence of ZnX_2 (X–Cl, Br, I), which leads to zinc(II) chelates **3a**,**b**–**5a**,**b** (Scheme 1).

Thus, complexes **3a**,**b**·MeOH and **4a**·MeOH were obtained as colorless solids in the reaction of anyone of ZnX_2 with **1** equiv $OC_4H_8NC(=NOH)NH_2$ (**1**) [11] in the presence of excess $NCNR_2$ (1.1-fold for R = Me **2a**; 1.5-fold for R = Et **2b**) in MeOH (R = Me) or in a mixture of MeOH and ethyl acetate (R = Et) at RT for 2 min. Complex **4b** was not isolated from the reaction mixture, but it was identified by HRESI$^+$-MS. Analogously, for the systems $ZnI_2/NCNR_2/$



Nos	R	X	Yield (%)
3a	Me	Cl	73
3b	Et	Cl	69
4a	Me	Br	67
4b	Et	Br	Not isolated
5a	Me	I	Not isolated
5b	Et	I	Not isolated

Scheme 1. The observed coupling.