Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2019, **29**, 111–113

Mendeleev Communications

Uncommon condensations of 1,2,3-triketone 2-oximes with *o*-phenylenediamine

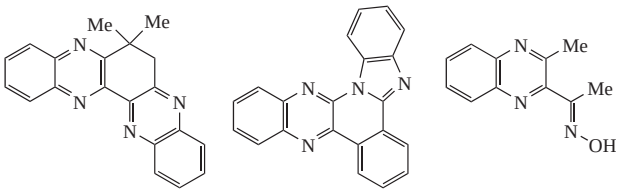
Lev Yu. Ukhin,*[a] Lyudmila G. Kuz'mina,[b] Danil V. Alexeenko,[a] Lyudmila V. Belousova,[a] Anatolii S. Morkovnik,[a] Gennadii S. Borodkin[a] and Tatyana N. Gribanova[a]

[a] *Institute of Physical and Organic Chemistry, Southern Federal University, 344090 Rostov-on-Don, Russian Federation. E-mail: lyukhin@ipoc.sfedu.ru*

[b] *N. S. Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: kuzmina@igic.ras.ru*

DOI: 10.1016/j.mencom.2019.01.038

A condensation of 2-hydroxyimino-5,5-dimethylcyclohexane-1,3-dione, ninhydrin oxime and 3-hydroxyiminopentane-2,4-dione with *o*-phenylenediamine in the presence of CF_3COOH provided 6,6-dimethyl-6,7-dihydroquinoxalino-[2,3-*a*]phenazine, benzimidazo[2′,1′:1,2]isoquino[3,4-*b*]quinoxaline, and 2-acetyl-3-methylquinoxaline oxime, respectively. An ability to form stacking dimers was found for the second product.



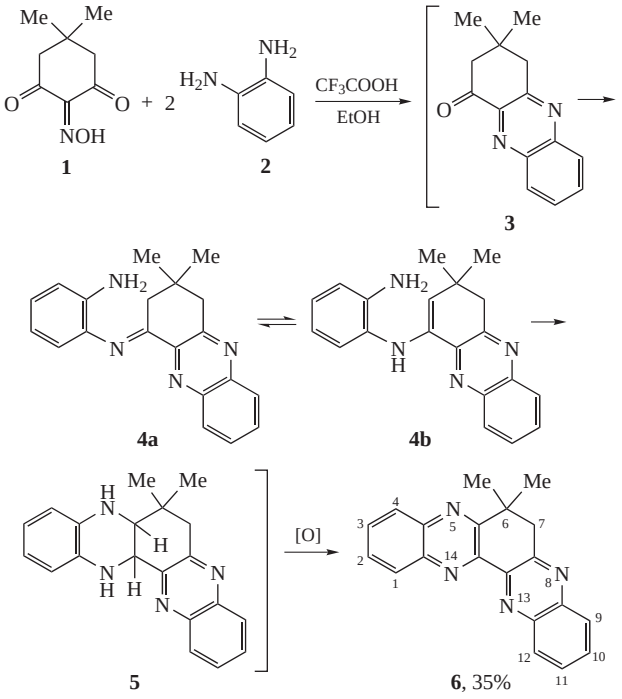
A conjugation with oxygen of OH groups in oximes suppresses the electrophilic properties of oxime carbon, which prevents a nucleophilic addition to C=N bonds.[1] Oxime carbon exhibits weak electrophilic properties only when the oxime group is protonated.[2] Lewis acids are used as catalysts along with proton acids in the reactions of oximes with nucleophiles,[3] otherwise high pressure accelerated their cycloaddition reactions without catalysts.[4]

Here, we assumed that the condensation of oximes of polycarbonyl compounds with 1,2-diamine derivatives in acidic media could differ from that of the polycarbonyl compounds. This may be caused by changing reaction sites towards the amino functions as well as by the inclusion of electrophilic steps into the process, *e.g.*, the Beckmann rearrangement.

We have recently reported on the synthesis of new spiro compounds from ninhydrin and mercapto carboxylic acids in the presence of CF_3COOH.[2] This study was aimed at the condensation of oximes of some 1,2,3-triketones with *o*-phenylenediamine catalyzed by CF_3COOH.

An addition of CF_3COOH to a solution of 2-hydroxyimino-5,5-dimethylcyclohexane-1,3-dione **1**[5] and *o*-phenylenediamine **2** in EtOH (Scheme 1) caused an exothermic reaction with a sharp coloration. A colourless precipitate of new 6,6-dimethyl-1,2-dihydroquinoxalino[2,3-*a*]phenazine **6**† was obtained upon cooling of the black-violet reaction mass. The proposed reaction mechanism includes intermediate **3** bearing a quinoxaline moiety. The oxime protonation should facilitate transamination at this step. After that (or simultaneously), Schiff base **4a** is formed, whose tautomeric form **4b** cyclizes into tetrahydro derivative **5**. The ultimate dehydrogenation (probably, with air oxygen) leads to final product **6** (see Scheme 1).

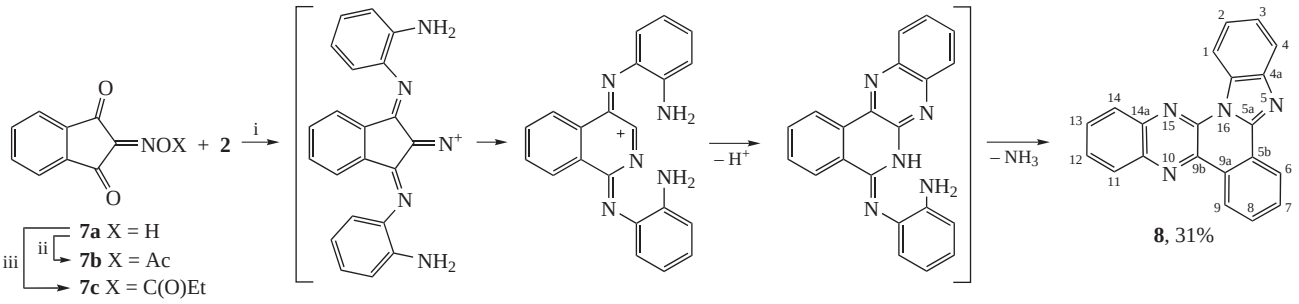
The reaction between ninhydrin oxime **7a** and diamine **2** gives benzimidazo[2′,1′:1,2]isoquino[3,4-*b*]quinoxaline **8**‡ (Scheme 2). The reaction proceeded with an extension of five-membered



Scheme 1

† *6,6-Dimethyl-6,7-dihydroquinoxalino[2,3-a]phenazine* **6**. *o*-Phenylenediamine **2** (0.22 g, 2 mmol) was dissolved under heating in EtOH (3 ml), oxime **1** (0.17 g, 1 mmol) was added. The mixture was heated to boiling, and CF_3COOH (2 drops) was added. The dark mixture formed in the exothermic reaction was kept until jelling (1.5 h), filtered and washed with Et_2O to isolate the colourless substance. The yield of crude product was 0.11 g (35%), mp 217–218 °C (EtOH). IR (Nujol, ν/cm^{-1}): 1611, 1557, 1491 (arom.). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.58 (s, 6H, Me), 3.54 (s, 2H, CH_2), 7.83 (m, 4H, H_{Ar}), 8.15 (m, 2H, H_{Ar}), 8.45 (m, 2H, H_{Ar}). MS (EI, 70 eV), *m*/*z* (%): 312 (70) [M$^+$], 297 (100) [M–Me], 284 (40) [M–C_2H_4].

‡ *Benzimidazo[2′,1′:2,1]isoquino[3,4-b]quinoxaline* **8**. Ninhydrin oxime **7** (0.35 g, 2 mmol) was dissolved under heating in a mixture of AcOH (2 ml) and EtOH (4 ml), *o*-phenylenediamine **2** (0.44 g, 4 mmol) was added. The



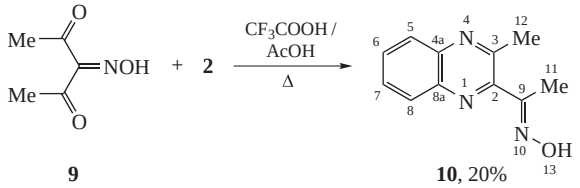
Scheme 2 *Reagents and conditions:* i, CF_3COOH, EtOH, Δ; ii, Ac_2O, Δ; iii, $(EtCO)_2O$, Δ.

cycle of oxime, which indicates an inclusion of the Beckmann rearrangement step. It is of note that ninhydrin itself reacts quickly with compound **2** in MeOH at room temperature yielding another product, 11*H*-indeno[1,2-*b*]quinoxaline.[6] Similarly to compound **7a** and probably, *via* the same mechanism, its *O*-acyl derivatives **7b**,**c** react under the same conditions providing product **8** (see Scheme 2).

The preparation of ester **7b** from **7a** has already been reported,[7] but it involves a complicated and time-consuming mixed anhydride method. In our work, we discovered that esters **7b**,**c** are smoothly produced upon dissolving ninhydrin oxime in the corresponding boiling anhydrides (see Scheme 2). Compounds **7b**,**c** were also synthesized from ninhydrin in a three-component one-pot synthesis when oxime **7** was formed from ninhydrin and $H_2NOH \cdot HCl$ in boiling H_2O (see Online Supplementary Materials for the synthetic procedures).

Compound **8** has been recently synthesized *via* a Pd-catalyzed tandem N–H/C–H arylation of 2-phenylbenzimidazole by 2,3-dichloroquinoxaline.[8] During the recording of ^{1}H NMR spectra of compound **8**, it was discovered that an increase in its concentration in $CDCl_3$ causes an upfield shift of signals by 0.3 ppm. A formation of complex between the molecules in solution is known to affect the position of signals.[9] Calculations by the M06-2X/6-311++G(d,p) method revealed that the non-valent interaction between two monomers **8** leads to the formation of stacking dimer **8′** (Figure 1) with the stabilization energy of 24.3 kcal mol^{-1} (see Online Supplementary Materials).

The similar processing of 3-hydroxyiminopentane-2,4-dione **9**[5] and diamine **2** gave 2-acetyl-3-methylquinoxaline oxime **10** (Scheme 3). This compound has already been reported[10] as one of



9 **10**, 20%

Scheme 3

mixture was refluxed for 1 min, CF_3COOH (0.2 ml) was added, and the resulting mixture was refluxed for 1 min. The mixture solidified upon cooling on ice, transferred onto a filter, washed with cold Pr^{i}OH and light petroleum, and dried. The yield of the crude product was 0.2 g (31%). Yellow needles, mp 257–259 °C (lit.,[6] mp 250–253 °C). ^{1}H NMR (300 MHz, $CDCl_3$, 2 mg) δ: 7.51–7.54 (m, 2H, H_{Ar}), 7.76–7.87 (m, 4H, H_{Ar}), 7.97–8.00 (m, 1H, H_{Ar}), 8.20–8.25 (m, 2H, H_{Ar}), 8.73–8.76 (m, 1H, H_{Ar}), 9.03–9.07 (m, 1H, H_{Ar}), 9.16–9.19 (m, 1H, H_{Ar}). ^{1}H NMR (300 MHz, $CDCl_3$, 20 mg) δ: 7.36–7.38 (m, 2H, H_{Ar}), 7.57–7.67 (m, 4H, H_{Ar}), 7.81–7.84 (m, 1H, H_{Ar}), 7.91–7.98 (m, 2H, H_{Ar}), 8.52–8.55 (m, 1H, H_{Ar}), 8.73–8.76 (m, 1H, H_{Ar}), 8.85–8.88 (m, 1H, H_{Ar}). ^{13}C NMR (150 MHz, $CDCl_3$, 20 mg) δ: 116.01, 119.26, 123.70, 124.38, 124.63, 124.79, 124.81, 127.31, 128.18, 128.63, 128.93, 130.02, 130.06, 130.83, 131.28, 136.16, 139.31, 139.44, 140.04, 143.34, 146.33. MS (EI, 70 eV), *m*/*z* (%): 320 (100) [M$^+$], 230 (25), 102 (30), 90 (60).

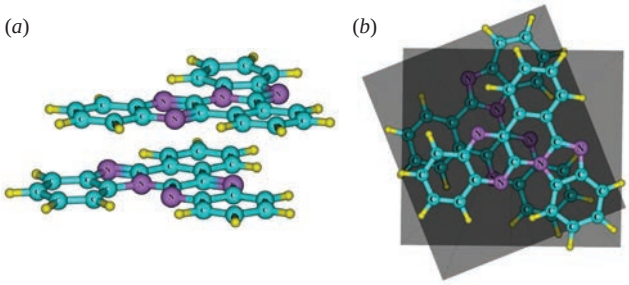


Figure 1 Stacking dimer **8′** predicted by the M06-2X/6-311++G(d,p) method: (*a*) side view and (*b*) top view.

the products of acid hydrolysis of 3-hydroxyimino-2,4-dimethyl-1,5-benzodiazepine. The synthesis of product **10** starting from compounds **9** and **2** with HCl as the acid reagent is also known.[11] The published procedure provides a higher yield than that achieved in our work, but it is also significantly more time and reagents consuming. In the reports[10,11] the mechanisms of considered reactions are discussed in details, but there are no spectral data other than UV-VIS spectra. The quick method of synthesis and spectral data for oxime **10** (including the full assignment of signals in its NMR spectra) are given in Online Supplementary Materials.

The structures of compounds **6** and **7c** were confirmed by the single crystal X-ray diffraction (Figures 2 and 3).[§]

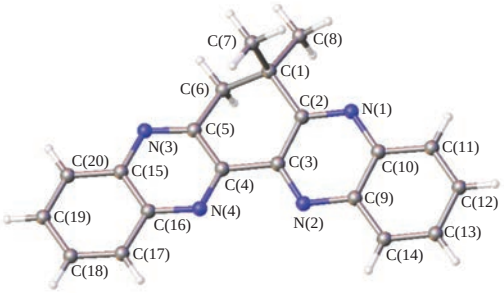


Figure 2 Molecular structure of compound **6**.

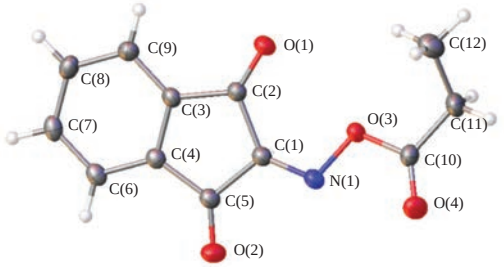


Figure 3 Molecular structure of compound **7c**.

§ Crystals of **6** and **7c** were mounted at a SMART APEX II diffractometer under a stream of cooled nitrogen (graphite monochromated MoKα radiation, λ = 0.71073 Å, ω-scan technique). Structures were solved by

In conclusion, condensation of polycarbonyl compound oximes with 1.2-diamines in acidic media can serve as a route to new interesting and unexpected compounds.

This work was supported by the Ministry of Education and Science of the Russian Federation (base part of a state task for scientific activity of Southern Federal University, no. 4.5821. 2017/8.9). The authors are grateful to the 'Molecular Spectroscopy' Center of the Institute of Physical and Organic Chemistry of Southern Federal University, Rostov-on-Don.

direct methods and refined by least squares in the anisotropic approximation for non-hydrogen atoms. Hydrogen atoms were placed at the calculated positions and refined using riding model. All the calculations were performed in the SHELXTL-Plus and OLEX-2 software packages.[12]

Crystal data for **6**. $C_{20}H_{16}N_4$ (M = 312.37), monoclinic, space group $P2_1/n$ (no. 14), a = 7.0722(9), b = 22.864(3) and c = 9.9034(13) Å, β = = 106.961(2)°, V = 1531.7(3) Å^3, Z = 4, T = 150 K, μ(MoKα) = 0.083 mm^{-1}, d_{calc} = 1.355 g cm^3, 15497 reflections measured (4.66° ⩽ 2θ ⩽ 56°), 3696 unique (R_{int} = 0.0716, R_σ = 0.0676) which were used in all calculations. The final R_1 = 0.0787 [$I > 2\sigma(I)$] and wR_2 = 0.2249 (all data).

Crystal data for **9b**. $C_{12}H_9NO_3$ (M = 215.20), monoclinic, space group $P2_1/c$ (no. 14), a = 10.1252(9), b = 15.8716(15) and c = 6.6820(6) Å, β = 100.608(2)°, V = 1055.47(17) Å^3, Z = 4, T = 150.0(2) K, μ(MoKα) = = 0.099 mm^{-1}, d_{calc} = 1.354 g cm^{-3}, 11527 reflections measured (4.1° ⩽ ⩽ 2θ ⩽ 58°), 2795 unique (R_{int} = 0.0270, R_σ = 0.0226) which were used in all calculations. The final R_1 = 0.0421 [$I > 2\sigma(I)$] and wR_2 = 0.1174 (all data).

CCDC 1856186 and 1540185 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2019.01.038.

References

1 C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, NY, 1969.
2 L. Yu. Ukhin, L. G. Kuz'mina, D. V. Alexeenko, L. V. Belousova, E. N. Shepelenko, V. A. Podshibyakin and A. S. Morkovnik, *Mendeleev Commun.*, 2018, **28**, 300.
3 Yu. P. Ustimenko, A. M. Agafontsev, V. Yu. Komarov and A. V. Tkachev, *Mendeleev Commun.*, 2018, **28**, 584.
4 S. V. Baykov, A. A. Zharov, G. A. Stashina, I. V. Zavarzin and E. R. Kofanov, *Mendeleev Commun.*, 2016, **26**, 264.
5 M. A. Zolfigol, *Molecules*, 2001, **6**, 694.
6 V. B. Nishtala, J. B. Nanubolu and S. Basavoju, *Res. Chem. Intermed.*, 2017, **43**, 1365.
7 S. Minchev, H. Nedev and V. Enchev, *Liebigs Ann. Chem.*, 1987, 375.
8 L. Yan, D. Zhao, J. Lan, Y. Cheng, Q. Guo, X. Li, N. Wu and J. You, *Org. Biomol. Chem.*, 2013, **11**, 7966.
9 A. Sygula, F. R. Fronczek, R. Sygula, P. W. Rabideau and M. M. Olmstead, *J. Am. Chem. Soc.*, 2007, **129**, 3842.
10 J. A. Barltrop, C. G. Richards, D. M. Russel and G. Ryback, *J. Chem. Soc.*, 1959, 1132.
11 C. N. O'Callaghan and D. Twomey, *J. Chem. Soc. C*, 1969, 600.
12 (*a*) *SAINT, v. 6.02A*, Bruker AXS, Madison, WI, 2001; (*b*) *SHELXTL Plus, v. 5.10*, Bruker AXS, Madison, WI, 2001; (*c*) O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339.

Received: 20th July 2018; Com. 18/5650