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Colloid and Nanosized Catalysts in Organic Synthesis: XIII.[1] Synthesis of 2-R-2-Imidazolines Catalyzed by Copper and Iron Oxide Nanoparticles

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Abstract—The reaction of carboxylic acids with ethylenediamine catalyzed by copper or iron oxide nanoparticles proceeds at 80°C with azeotropic water distilling off during 2–8 h to form 2-*R*-2-imidazolines. Acyl and diacyl derivatives of ethylenediamine are formed in the reaction as side products.

Keywords: catalysis, nanoparticles, copper, Fe_3O_4, ethylenediamine, imidazoline

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2-Alkyl substituted imidazolines have been used as corrosion inhibitors [2, 3], components of detergents [4], additives for lubricating oil [5], components of nonpolar solvents for hydrophobization of wood, concrete, metal, and tissue softeners and antistatic agents [6]. Furthermore, 2-imidazolines have been widely used in pharmaceutical industry. In particularly, well known drugs such as Naphthyzin [2-(1-naphthyl-methyl)-2-imidazoline nitrate], Galazolin, Clophelin, and some others contain imidazoline fragment in their structure [7].

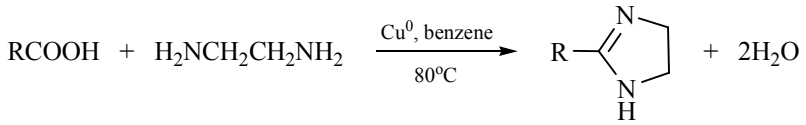
A number of methods for preparation of imidazolines have been developed [8–15]. The main approach towards their preparation is the reaction of nitriles of with ethylenediamine monohydrochloride or other salts at high temperature [8, 9] or under microwave irradiation [10]. In addition, imidazolines can be obtained starting from carboxylic acids esters or amides [11, 12], aldehydes [13], imidates [14], and other compounds [8, 15]. A significant limitation of these methods is a requirement to use the carboxylic acids derivatives rather than better available carboxylic acids.

However, the methods of preparation of imidazolines from aliphatic carboxylic acids and ethylenediamine have been also reported. For example, nitrogen-containing heterocyclic derivatives have been obtained via the reaction of the saturated acids or their esters with 1,2-diamines or polyethylene-polyamines [16]. The reaction has been performed without any catalyst at evelated temperature (120–220°C) at equimolar ratio of the reagents. It has been shown that the yield of side products increases with the increase of the alkyl chain of the carboxylic acid. In particular, in the case of acetic acid yield of the high-boiling side products was of about 33%, but it increased to 92% in the case of myristic acid; yield of the target imidazolines do not exceed 30% [16]. Later it has been shown that non-catalytic synthesis provides a number of compounds besides imidazolines, such as amine soaps, amidoamines, and diamides [17]. Formation of amidoamines and diamines started at 120–180°C; further increase of temperature promotes cyclization of amidoamines to form imidazolines. Diamides are not involved in any further conversions. To reduce the fraction of diamines in the prepared product, a large excess of ethylenediamine has been applied, β-oxyethylethylenediamine or polyethylene-polyamine have been alternatively used as starting materials [17]. The main drawbacks of the catalyst-free synthesis are high temperature of the process and formation of the side products.

When esters have been used instead of the acids at the ester : ethylenediamine molar ratio of 1:3 and 100–250°C, yield of imidazolines has reached 85%, the reaction duration being of 12–20 h [18]. High reaction

[1] For communication XII, see [1].

Scheme 1.



1a–1c **2** **3a–3c**

R = Me (**a**), *i*-Pr (**b**), *i*-Bu (**c**).

temperature, its long duration, and the multi-stage character (the synthesis proceeds via initial monoamide formation followed by its cyclization to give 2-alkyl-2-imidazoline) are among the disadvantages of this method.

Over the recent years, significant efforts have been concentrated on preparation of novel derivatives of 2-imidazoline [19–21]. For example, the reaction of ethylenediamine with carboxylic acids at 120–140°C in toluene or in bulk has led to the formation of amides; their heating under argon at 180–220°C has resulted in the cyclization affording 2-alkylimidazolines in 70–75% yield [19]. Moderate yield of the target compounds can be explained by the formation of 1,2-disubstituted amides along with the monosubstituted acid amides as a result of rapid reaction between ethylenediamine and the acids; 1,2-disubstituted amides undergo cyclization at 180–220°C to form 3-amidoalkylimidazolines.

Another procedure for imidazolines preparation utilizes cation exchange resin KU-2 as a catalyst; this allows for the mild reaction conditions, but the yield of the products was as low as 65–75% [20].

2-Imidazolines can be also prepared from technical grade stearin, soy-bean fatty acids, and flax oil as well as bisimidazolines of the fatty acid dimers, via condensation of the corresponding fatty acids with diethylenetriamines [17], however the process requires high-temperature heating.

To sum up, the simplest (and, at the same time, the least suitable) method for 2-imidazolines preparation is heating of an organic acid and diamine in the presence of acidic agent. To increase the process efficiency, the attempts to use of orthophosphoric and hydrochloric acids as catalysts have been made. The acid presence blocks one of ethylenediamine amine groups, and the yield of diamides has been decreased [21].

Nowadays, the application of the catalysts based on nanoparticles or their colloidal solutions is of great interest, enhancing the possibilities of organic synthesis. However, data on the synthesis of 2-alkyl-2-imidazolines catalyzed by metal nanoparticles have been absent.

The procedure for direct amidation of carboxylic acids with amines and transamidation of carboxamides under catalysis with copper nanoparticles has been earlier described [22]. In this work we investigated the possibility to apply this catalyst in condensation of carboxylic acids with ethylenediamine as a novel approach towards synthesis of imidazolines.

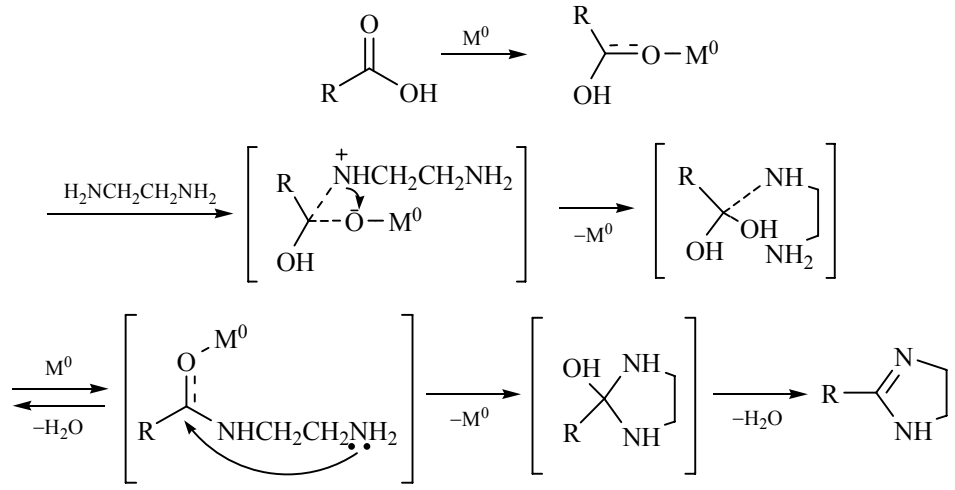
We performed the synthesis of 2-alkyl-2-imidazolines via reaction of carboxylic acids with ethylenediamine in the presence of neutral colloidal copper catalyst for the first time. Acetic acid **1a**, 2-methylpropionic acid **1b**, and isovaleric acid **1c** were used as the starting materials. The reactions were performed in benzene at 80°C using the acid and ethelenediamine in the molar ratio of 1 : 1–1.2 in the presence of copper nanoparticles, upon distilling off water as azeotropic mixture with benzene. Yield of 2-alkyl-2-imidazolines **3a–3c** was of 70–88% (Scheme 1).

Gas chromatography–mass spectrometry analysis data showed that two side products were also formed: monoacylethylenediamines (8–15 wt %) and *N*,*N*′-diacylethylenediamines (5–12 wt %). It was found that addition of fresh portions of the catalyst to the reaction mixture enhanced the water release, thus confirming the catalytic action of colloidal copper.

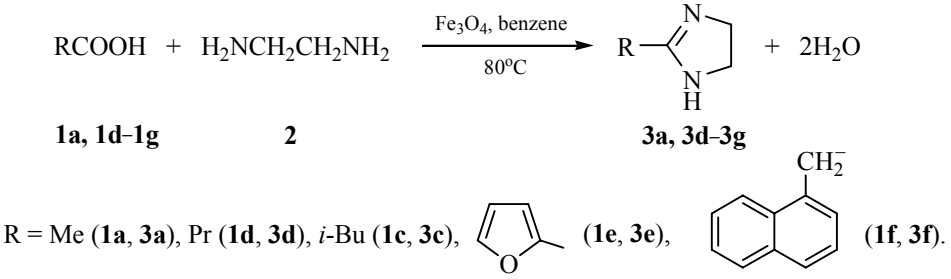
The effect of carboxylic acid structure on the reaction outcome was discovered: the linear acids reacted with ethylenediamine faster than their branched analogs. It should be noted that the reaction of ethylenediamine with 1-adamantanecarboxylic acid and 1-naphthylacetic acid did not proceed under the studied conditions [22], that could be explained by the steric effect hindering the interaction of the C=O bond with surface of large copper nanoparticles (70 nm).

Formation of imidazolines in the neutral medium at relatively low temperature is interesting in view of elucidation of the possible reaction mechanism.

Scheme 2.



Scheme 3.



Presumably, the mechanism of catalysis in imidazolines synthesis is similar to that in the carboxylic acids amidation [22] (Scheme 2).

The catalytic effect of copper nanoparticles could be explained by appearance of significant fraction of metal atoms (M^0) with lower coordination number at the edges or apexes of the crystal, increasing the ability of those sites to coordinate at polar groups of organic molecules. Based on the reference data [23], it might be supposed that the catalyst coordination occurred through the oxygen of carbonyl fragment of the acid. At the second step, the coordination of the carbonyl oxygen with the nanoparticle surface occurred, accompanied by attack of the amino group of monoamide at the carbonyl carbon atom followed by the ring closure.

It was supposed that enhancement of the nanocatalyst acidic properties accelerated the reaction and increased the yield of the target imidazolines. Of a number of the opportunities, we selected nanosized iron oxide Fe_3O_4 to be used as the catalyst; the methods of its preparation have been described in Ref. [24]. Our choice was based on the easy removal of the catalyst from the reaction mixture and the possibility of its recovery, owing to the ferromagnetic (or paramagnetic) properties.

Fe_3O_4 nanoparticles were prepared via gel precipitation in the course of ammonia solution addition to the solution of a mixture of Fe^{2+} and Fe^{3+} salts. Aqueous colloid solution was used in the further synthesis without isolation of the nanoparticles. When mixing the catalyst with ethylenediamine, a stable solution was formed, probably stabilized by the diamine. Moreover, the use of diamine excess prevented the undesired reaction of the catalyst particles with carboxylic acids.

Acetic, butyric, isovaleric, 2-furoic, and 1-naphthylacetic acids were used as the starting materials (Scheme 3).

It was found that the reaction catalyzed by the iron oxide proceeded faster than that catalyzed by copper nanoparticles. Moreover, even acids **1e** and **1f** (inert in the latter case) participated in the reaction with ethylenediamine catalyzed by the iron oxide. Water was distilled off in the form of the azeotrope with

benzene. The yield of imidazolines reached 70%. The GC–MS data revealed the formation of mono- and diacyl derivatives of ethylenediamine as side products in the reaction.

All the prepared compounds were isolated by vacuum distillation. The structure of the obtained imidazolines **3a–3f** was confirmed by means of mass spectrometry data. The spectral characteristics of the compounds matched the reference data.

In summary, a suitable preparative method for the synthesis of imidazolines in high yield under mild conditions of catalysis with copper or iron oxides nanoparticles was elaborated.

EXPERIMENTAL

GC–MS analysis was performed using a Saturn 2100 T/GC3900 (EI, 70 eV) instrument. Copper nanoparticles were prepared by as described in [22].

Synthesis of Fe_3O_4 nanoparticles. A solution of $FeSO_4 \cdot 7H_2O$ (7 g, 0.0583 mol) and $FeCl_3 \cdot 6H_2O$ (5 g, 0.0292 mol) in 40 mL of distilled water was stirred during 60 min, and then aqueous 10% ammonia solution was added to slightly basic pH. The obtained colloidal solution was used as the catalyst without isolation of the nanoparticles.

2-Methyl-2-imidazoline (3a). *a*. A mixture of ethylenediamine (12 g, 0.2 mol), acetic acid (12 g, 0.2 mol), 15 mL of benzene, and 0.1 g of copper nanoparticles was refluxed during 5 h with water distillation off (7.2 mL, 0.4 mol). After the reaction was complete, the solvent was distilled off, and the residue was distilled in vacuum. Yield 12.6 g (0.15 mol, 74%), bp 110–114°C (100 mmHg), mp 86–88°C {bp 144°C (140 mmHg), mp 87°C [25]}. Mass spectrum, *m*/*e* (I_{rel}, %): 85.0 (100) [*M* + 1], 83 (25), 55.0 (49), 42.0 (22).

b. A mixture of ethylenediamine (10.5 g, 0.18 mol), acetic acid (7 g, 0.12 mol), 15 mL of benzene, and 1 mL of aqueous 50% suspension of nanosized iron oxide Fe_3O_4 was refluxed during 3 h with water distillation off (4.7 mL, 0.26 mol). After the reaction was complete, the solvent was removed, and the residue was distilled in vacuum. Yield 8.3 g (0.1 mol, 85%).

2-Isopropyl-2-imidazoline (3b) was prepared similarly by procedure *a* from ethylenediamine (9.6 g, 0.16 mol) and 2-methylbutanoic acid (13.2 g, 0.15 mol). Yield 14.8 g (0.132 mol, 88%), bp 150°C (30 mmHg), mp 40–43°C (mp 42°C [25]). Mass spectrum, *m*/*e* (I_{rel}, %): 112.0 (33) $[M]^+$, 97.0(80), 83.0 (58), 41.0 (100).

2-Isobutyl-2-imidazoline (3c) was prepared similarly by procedure *a* from ethylenediamine (12 g, 0.2 mol) and isovaleric acid (20.4 g, 0.2 mol); the reaction duration was 7 h. Yield 17.6 g (0.14 mol, 70%), bp 167–170°C (30 mmHg). Mass spectrum, *m*/*e* (I_{rel}, %): 128.0 (8.0) [*M* + 1], 127.0 (100) $[M]^+$, 97.1 (64.0), 82.0 (12), 41.0 (25).

b. Similarly, by method *b* from ethylenediamine (7.1 g, 0.12 mol) and isovaleric acid (8 g, 0.078 mol); the reaction duration was 4 h. Yield 6.9 g (0.055 mol, 70%).

2-Propyl-2-imidazoline (3d) was prepared similarly to method *b* from ethylenediamine (7.2 g, 0.12 mol) and butyric acid (7 g, 0.08 mol); the reaction duration was 4 h. Yield 6.2 g (0.056 mol, 70%), bp 145–150°C (30 mmHg), mp 40–43°C (mp 42°C [25]). Mass spectrum, *m*/*e* (I_{rel}, %): 112.0 (33) $[M]^+$, 97.0 (80), 83.0 (58), 41.0 (100).

2-(2-Furyl)-2-imidazoline (3e) was prepared similarly to method *b* from ethylenediamine (5.6 g, 0.094 mol) and 2-furoic acid (7 g, 0.063 mol); the reaction duration was 3 h. Yield 3.43 g (0.025 mol, 40%), bp 168–170°C (30 mmHg) (decomp.). Mass spectrum, *m*/*e* (I_{rel}, %): 136.9 (80.3) [*M* + 1], 135.0 (79.9) [*M* – 1], 107.0 (100), 79.0 (72), 52.0 (38).

2-(Naphthylmethyl)-2-imidazoline (3f) was prepared similarly to method *b* from ethylenediamine (3.4 g, 0.057 mol) and 1-naphthylacetic acid (7 g, 0.038 mol); the reaction duration was 4 h. Yield 2.4 g (0.0114 mol, 30%), bp 308–310°C (30 mmHg) (decomp.), mp 117–119°C {bp 230°C (10 mmHg), mp 119°C [26]}. Mass spectrum, *m*/*e* (I_{rel}, %): 211.0 (8.0) [*M* + 1], 210.0 (35) $[M]^+$, 209.0 (100) [*M* – 1], 141.0 (22), 115.0 (15).

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REFERENCES

1. Mokhov, V.M., Popov, Yu.V., and Shcherbakova, K.V., *Russ. J. Gen. Chem*., 2016, vol. 86, no. 2, p. 273. DOI: 10.1134/S1070363216020110.

2. Frolov, V.I., *Tr. Ros. Gos. Univ. Nefti i Gaza*, 2009, no. 2, p. 165.
3. Kuznetsov, S.A., Belyaeva, N.A., and Kol'tsov, N.I., *Khim. i Tekhnol. Topliv i Masel*, 2009, no. 3, p. 48.
4. Peregudova, A.S., Kruzhilin, A.A., Perelygina, I.E., Falaleev, A.V., and Stolpovskaya, N.V., *Sorbts. Khromatograf. Protsessy*, 2015, vol. 15, no. 3, p. 464.
5. Kuznetsov, S.A., and Kol'tsov, N.I., *Russ. J. Appl. Chem*., 2010, vol. 83, no. 11, p. 1993. DOI: 10.1134/S1070427210110194.
6. *Khimicheskaya entsiklopediya* (Chemical Encyclopedia), Knunyants, I.L., Ed., Moscow: Sovetskaya Entsiclopediya, 1990, vol. 2, p. 413.
7. Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Kharkov: Torsing, 1998.
8. Crouch, R.D., *Tetrahedron*, 2009, vol. 65, no. 12, p. 2387. DOI: 10.1016/j.tet.2008.12.022.
9. Ferm, R.J., and Riebsomer, J.L., *Chem. Rev*., 1954, vol. 54, p. 593. DOI: 10.1021/cr60170a002.
10. de la Hoz, A., Diaz-Ortiz, A., Mateo, M.d.C., Moral, M., Moreno, A., Elguero, J., Foces-Foces, C., Rodriguez, M.L., and Sanchez-Migallon, A., *Tetrahedron*, 2006, vol. 62, no. 26, p. 5868. DOI: 10.1016/j.tet.2006.04.020.
11. Sperber, N., and Fricano, R., *J. Am. Chem. Soc*., 1953, vol. 75, no. 12, p. 2986. DOI: 10.1021/ja01108a058.
12. Hill, A.J., and Aspinall, S.R., *J. Am. Chem. Soc*., 1939, vol. 61, no. 4, p. 822. DOI: 10.1021/ja01873a015.
13. Fujioka, H., Murai, K., Ohba, Y., Hiramatsu, A., and Kita, Y., *Tetrahedron Lett*., 2005, vol. 46, no. 13, p. 2197. DOI: 10.1016/j.tetlet.2005.02.025.
14. Lauwagie, S., Millet, R., Pommery, J., Depreux, P., and Henichart, J.-P., *Heterocycles*, 2006, vol. 68, p. 1149. DOI: 10.3987/COM-06-10708.
15. Liua, H., and Du, D.-M., *Adv. Synth. Catal*., 2009, vol. 351, p. 489. DOI: 10.1002/adsc.200800797.
16. Riebsomer, J.L., *J. Am. Chem. Soc*., 1948, vol. 70, no. 4, p. l629. DOI: 10.1021/ja01184a095.
17. Chebaksarov, A.I., Chebaksarova, L.V., and Pak, Kh.S., RF Patent 2487122, 2013.
18. Verolainen, N.V., Petrova, V.E., and Temnikova, S.A., *Vestn. TvGU. Khimiya*, 2014, vol. 8, no. 1, p. 36.
19. Zagidullin, R.N., Rakhmankulov, D.L., Rysaev, U.Sh., Rysaev, D.U., Kozyreva, Yu.P., and Mazitova, I.Sh., *Bash. Khim. Zh*., 2007, vol. 14, no. 4, p. 21.
20. Isagulyants, V.I., Bova, R.S., and Belov, P.S., Author's Certificate no. 189437, 1967; *Byull. Izobret.*, 1966, no. 24.
21. Baganz, H., Domaschke, L., and Fock, J., *Chem. Ber*., 1962, vol. 95, no. 7, p. 1832. DOI: 10.1002/cber.19620950740.
22. Mokhov, V.M., Popov, Yu.V., and Budko, I.I., *Russ. J. Gen. Chem*., 2015, vol. 85, no. 4, p. 820. DOI: 10.1134/S1070363215040088.
23. Xie, Y.-X., Song, R.-J., Liu, Y., Liu, Y.-Y., Xiang, J.-N., Li, J.-H., *Adv. Synth. Catal*., 2013, vol. 355, p. 3387. DOI: 10.1002/adsc.201300630.
24. Mahdavi, M., Ahmad, M.B., Haron, M.J., Namvar, F., and Nadi, B., *Molecules*, 2013, vol. 18, p. 7533. DOI: 10.3390/molecules 18077533.
25. *Alfa Aesar, Research Chemicals, Metals and Materials*, 2006–2007.
26. Carlsson, S., US Patent 2441867, 1948.