Periodica Polytechnica
Chemical Engineering

59(1), pp. 72-81, 2015
DOI: 10.3311/PPch.7343

RESEARCH ARTICLE

Supported Metal Catalysts in Organic Syntheses

Árpád KISS[1], János NÉMETH[1], Anna FODOR[1], Zoltán HELL[1 *]

Received 10 February 2014; accepted after revision 05 May 2014

Abstract
The importance of heterogeneous catalytic methods in organic syntheses is growing dynamically. Among the methods developed the supported metal catalysts take up an outstanding role. In this paper the results of the research group obtained in this field are reviewed.

Keywords
heterogeneous catalysis, supported metal catalysts, organic syntheses

1 Introduction

Most organic syntheses require a catalyst for good conversion. With the exception of heterogeneous oxidation and reduction, these catalysts are mostly acids or bases. The traditional acids and bases have several disadvantageous properties, they are often dangerous, flammable, corrosive, or toxic, the workup of the reaction mixture is often tedious, producing high amounts of waste water, and the catalyst often decomposes during the workup procedure. These compounds or even their preparation is often harmful for the environment. Therefore in recent decades the development of heterogeneous catalytic methods became one of the main synthetic goals. The heterogeneous catalysts can eliminate the problems arising from the use of a homogeneous catalyst; they can be filtered out from the reaction mixture, simplifying this way the workup procedure, reducing the energy costs and decreasing the operation time as well as the amount of waste water. They are generally non-corrosive, non-toxic and often reusable or simply recyclable materials, and in some cases they can induce a considerable regio- even stereoselectivity. There were several minerals found in nature which showed excellent catalytic avtivity in organic syntheses. Based on these materials numerous mineral-based heterogeneous catalysts were developed in recent years not only for laboratory but also for industrial use. Thus, *e.g.* in a review published in 1999 about the heterogeneous catalytic industrial processes, 71 methods were presented which used natural, modified or artificial zeolites [1].

These materials can also serve as supports of different metals. The acidic or basic properties of the support, their great surface as well as the fine dispersity of the metal on the support's surface can significantly increase the efficiency of these catalysts. Furthermore, the ligands which are often required for a homogeneous catalytic process, can be omitted in the heterogeneous methods, which can increase the atom efficiency of the process and make the workup of the reaction mixture easier.

2 Palladium-catalyzed reactions

Our research group works on the elaboration of different heterogeneous catalysts and on the examination of their reactivity

[1] Department of Organic Chemistry and Technology, Faculty of Chemical Technology and Biotechnology, Budapest University of Technology and Economics, H-1521 Budapest, Hungary

[*] Corresponding author, e-mail: zhell@mail.bme.hu

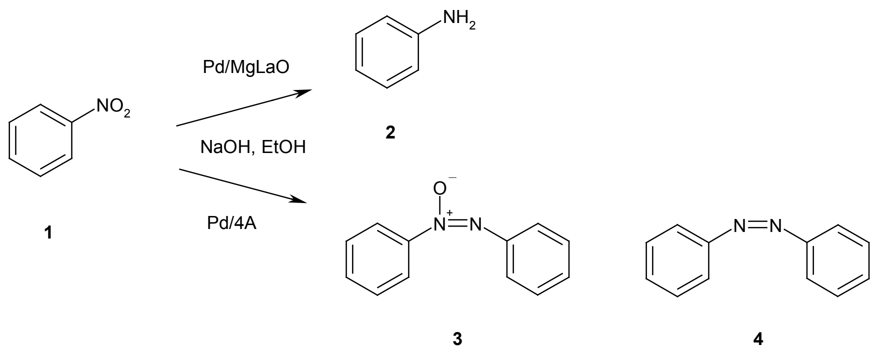


Fig. 1

in different organic syntheses. During this work we applied successfully palladium(0) on Mg-La mixed oxide (Pd^0/MgLaO) in the Heck- [2], Sonogashira- [3] and Suzuki-reaction [4]. Continuing the examination of the palladium-catalyzed cross-coupling reaction we found an interesting transfer hydrogenation process when nitrobenzene derivatives were reacted in the presence of supported palladium catalysts in alkaline alcohols. GC-MS examination of the reaction mixture detected the presence of aldehyde and acid derivatives, showing that the alcohol was the hydrogen source in the process. Depending on the support, the products of the reactions were different. Thus, in the presence of Pd^0/MgLaO the appropriate aniline derivative was obtained quantitatively, while in the presence of palladium(0) on 4 Å molecular sieve (Pd^0/4A) the known intermediates of the base-catalyzed reduction of nitrobenzene, azoxy- (**3**) or azobenene (**4**, Fig. 1) could be obtained with high yield and selectivity [5].

When 4-nitroacetophenone (**5**) was reacted in boiling ethanol, in the presence of 3 equiv. of sodium hydroxide and Pd^0/MgLaO, a new compound was detected. Based on the mass spectrum and ^{1}H NMR examination this compound was 4-aminobutyrophenone (**6a**, Fig. 2). This means that in the reaction the nitro group was reduced and the alkyl chain of the acetophenone was extended with two carbon atoms while the carbonyl function remained intact.

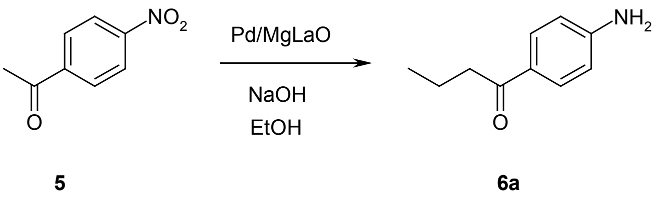


Fig. 2

The following mechanism is proposed for this reaction (Fig. 3). After the reduction of the nitro group, an aldol-type reaction between the acetophenone and the aldehyde derived from the alcohol occurs. This is followed by the dehydration of β-keto-alcohol (**A**), and the final product is formed by reduction of the olefinic double bond of **B**. In the GC-MS spectra of the reaction mixtures a small amount of **B** was also found, which further supported this mechanism.

Similar results were obtained with other primary alcohols (Table 1), but in methanol, as well as in secondary alcohols such as isopropanol only the reduction of the nitro group occurred. In *n*-propanol a significant amount of 1-(4-aminophenyl)-2-propylpentan-4-one (**8**) was also formed via the coupling of two propyl groups onto 4-aminoacetophenone [6].

We investigated the reaction of other acetophenones as well as benzaldehyde derivatives in ethanol, too, but the formation of the appropriate chain elongated products was not significant. Among the products of the reaction of 2-nitroacetophenone and 2-nitrobenzaldehyde, 4-methylquinoline and quinoline,

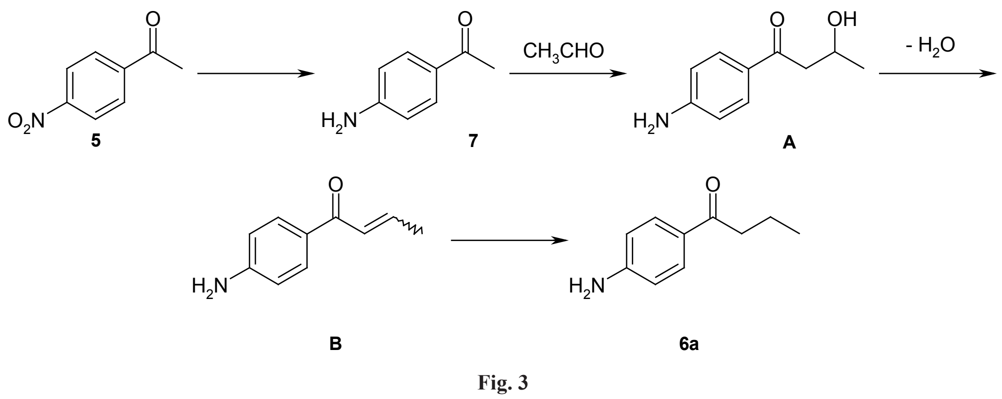


Fig. 3

Table 1 Reaction of 4-nitroacetophenone with alcohols.

Entry	ROH	Reaction time (h)	Yield (%)[b]
1	methanol	24	**6b** (16), **7** (84)
2	propanol	24	**6c** (42), **7** (20), **8** (33)
3	isopropanol	12	**7** (~100)
4	butanol	24	**6d** (73), **7** (25)
5	isobutanol	24	**6e** (75), **7** (16)

[a] 5 mmol **5**, 0.2 g catalyst, 0.6 g NaOH, 10 ml alcohol, reflux

[b] Based on GC-MS analysis of the product

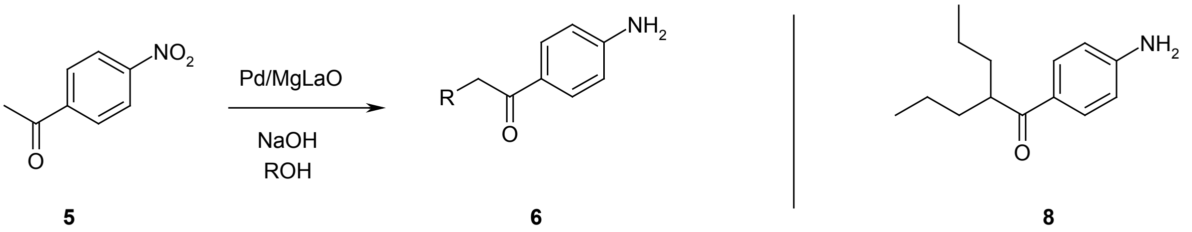


Fig. 4

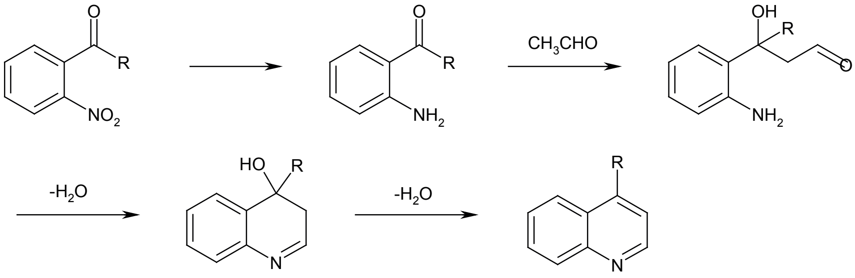


Fig. 5

respectively, were found. The formation of these quinoline derivatives can be explained by the reaction of the intermediate amino-carbonyl compound with acetaldehyde, which then will undergo an intramolecular cyclization (Fig. 5).

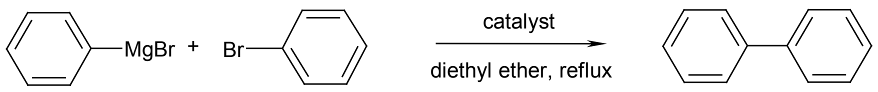
3 The Kumada-coupling

The reaction of organomagnesium halides with carbonyl compounds discovered by Barbier [7] and improved by Grignard [8] has became a very important synthetic method even in industrial syntheses. Among the methods developed the coupling of Grignard reagents in a homogeneous, nickel complex-catalyzed reaction (Kumada-coupling) proved to be a useful tool for the preparation of non-symmetrical biaryl derivatives [9]. The classical methods used bidentate phosphines as ligands [9] but acetylacetone [10] was also described.

The known disadvantage of the homogeneous catalytic methods, that the metal or the ligand can contaminate the product, induced a considerable research effort to develop new, heterogeneous catalytic systems for the Kumada-coupling. Lipshutz described the use of Ni on activated charcoal (DARCO). He obtained good conversions even with aryl chlorides, but only in the presence of equimolar amount of anhydrous LiBr, and only the addition of a large amount of triphenyl phosphine (free or polymer-bound) could suppress the formation of the homocoupled product [11]. In another method a nickel chelate complex bound to Merrifield-resin was used as catalyst. The disadvantage of this method was that a great excess (3 moles) of Grignard compound was necessary to obtain good yield [12]. Very recently Richardson examined the coupling of phenylmagnesium chloride and 4-bromoanisole using nickel(II) acetylacetonato complex supported on either polymer-bound ethylenediamine or on modified mesoporous silica. He found that the leached nickel promoted the catalysis [13].

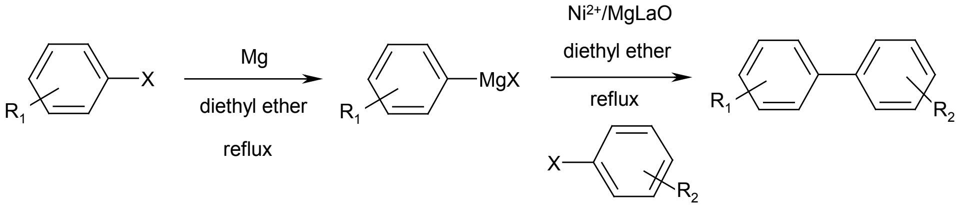
Based on these results we examined whether our supported metal catalysts developed could be used efficiently in the Kumada-coupling. Four different supports; Mg-Al 2:1 and 3:1 hydrotalcite (HT 2:1 and HT 3:1, respectively), Mg-La 3:1 mixed oxide (MgLaO) and 4Å molecular sieve (4A), and the metals mentioned in the literature (Pd^{2+}, Pd^0, Co^{2+}, Cu^{2+}, Cu^0, Ni^{2+}, Fe^{3+}) were tested in the reaction of phenylmagnesium bromide and bromobenzene (Fig. 6). The catalysts were prepared by the impregnation of the support with the appropriate metal salt [14].

The best result was obtained with Ni^{2+}/MgLaO (86 % isolated yield). The support had a significant role on the yield, HT 2:1 and 4A gave lower yield, 72 and 66 %, respectively. The other metals



9a **10a** **11a**

Fig. 6



9 **10** **12** **11**

Fig. 7

Table 2 Effect of the nature of the halogen, and results of the cross-coupling reactions

Entry	**R_1, X**	**R_2, X**	**Yield (%)**[a]
1	H, Br	H, Br	**86**
2	H, Br	H, Cl	**50**
3	H, Br	H, I	**99**
4	H, I	H, I	**94**
5	H, Br	*p*-Me, Br	**86**
6	H, Br	*o*-OMe, Br	**73**
7	H, Br	*m*-OMe, Br	**81**
8	H, Br	*p*-OMe, Br	**83**
9	H, Br	*o*-CF_3, Br	**23**
10	H, Br	*m*-CF_3, Br	**78**
11	H, Br	*p*-CF_3, Br	**84**
12	*p*-Me, Br	*o*-CF_3, Br	**25**
13	*p*-Me, Br	*m*-CF_3, Br	**69**
14	*p*-Me, Br	*p*-CF_3, Br	**29**
15	*p*-Me, Br	*p*-OMe, Br	**55**
16	*p*-OMe, Br	*p*-Me, Br	**11**

[a]Isolated yield, the purity was checked by GC-MS. The raw product contained about 15 % R_1-homo-coupled product.

examined gave only moderate yield, moreover, in the presence of iron only 1,1-diphenylethanol could be isolated from the reaction mixture, which could be formed in the reaction of phenylmagnesium bromide with the solvent diethyl ether. Thus, the determination of the optimal reaction conditions were made with Ni^{2+}/MgLaO. Above 3 h reaction time the yield did not increase, and 0.16 mol% Ni^{2+} gave the best result. In the published experiments the amount of nickel varied between 0.3 and 3 mol%. Thus, our catalyst requires smaller amount of nickel for better yield than the published methods. The optimal reagent ratio was also determined. It has to be mentioned, that the Grignard-compounds are susceptible to self-coupling in solution. This means that during the preparation of an arylmagnesium halogenide about 15 % of homo-coupled product is always forming. Thus, magnesium remains in the reaction mixture, which will form a Grignard-compound with the second aryl halide, which leads to the formation of the homo-coupled product from this second halide. We established that this side reaction can be avoided with the addition of excess magnesium in the first step.

This optimized reaction conditions (13 mmol of R_1 aryl halide, 11.5 mmol of Mg, diethyl ether, then 10 mmol of R_2 aryl halide, 0.2 g of Ni^{2+}/MgLaO, 3 h, reflux) served to investigate the cross-coupling reaction of aryl halides (Fig. 7, Table 2).

The nature of the halogen, especially in the R_2-compound, influenced the yield (see entries 1-4). From practical point of view (availabilty, price, reactivity) the cross-coupling experiments were made with bromides. The results varied strongly with the structure of the reactants. Surprisingly, when the coupling aryl halide was *o*-trifluoromethylbromobenzene, the yield was very low. The Grignard reagent obtained from *p*-bromotoluene had poorer reactivity than the bromobenzene derivative. Entries 15 and 16 also gave weak results. When the reaction of *p*-tolylmagnesium bromide with *p*-bromoanisole (entry 15) was investigated by GC-MS the presence of a great amount of unreacted *p*-bromoanisole and the lack of *p*-bromotoluene showed that the formation of the Grignard compound occurred, but the coupling took place weakly. Contrarily when the Grignard compound was formed from *p*-bromoanisole and this was coupled with *p*-bromotoluene (entry 16), GC-MS of the product showed the presence of a lot of anisole, which was formed from the unreacted Grignard compound during the workup of the reaction mixture. These results show that the methoxy group can inhibit the reaction, although this is not verified by the results obtained in entries 6–8.

The use of this type of solid catalyst system generally induces dispute over whether the reaction takes place on the solid surface or with the metal leached into the solution. We used the hot filtration test to choose from these two possibilities. Thus, after 2 h the reaction mixture was filtered, and the filtrate was examined by X-ray fluorescence. This showed that there was about 1–2 ppm nickel in the solution which might verify a capture–release mechanism. The X-ray fluorescence investigation of the isolated products showed the absence of nickel.

The recyclability of the catalyst was investigated in the reaction of bromobenzene and *p*-bromotoluene. Thus in the first reaction the yield obtained was 86 %. The catalyst was filtered out from the mixture and after washing it with toluene and drying at 120°C for 1 h it was reused in the same reaction. In the second run the yield obtained was 70 %. The quite big decrease in the yield can be explained with the precipitation of magnesium bromide – which is formed in the reaction of necessity – onto the surface of the catalyst. Its separation from the catalyst cannot be effected easily because of its low solubility in organic solvents.

4 Copper-catalyzed reactions

In recent years the metal-catalyzed carbon-carbon coupling reactions became more and more important in the preparative organic chemistry. Some metal such as palladium and ruthenium have an outstanding importance, but the significance of nickel, iron or copper increase rapidly.

Propargylamines are important synthons in the syntheses of organic compounds, especially N-heterocycles. There are a number of homogeneous catalytic methods for their preparation, but these processes require metallorganic compounds, exact reaction conditions and the sensitive functional groups (*e.g.* aldehydes) have to be protected. In recent years transiton metal-catalyzed methods were developed, where the role of the metals is to activate the terminal alkyne C-H bond.

A possible method for the synthesis of propargylamines is the A^3 reaction, a multicomponent reaction between **a**lkynes, **a**mines and **a**ldehydes. Among the number of methods developed, an efficient homogeneous gold-catalyzed process was developed in water, but the expensive and unrecoverable catalyst and the tedious workup made the method unfavourable [15]. Later heterogeneous catalytic methods were also described using *e.g.* a gold-based complex [16], silver-tungstenphosphoric acid [17], Cu(I) compound on silica [18] or on USY zeolite [19], Cu(II)-salt on hydroxyapatite [20].

We examined the possibility of the development of a heterogeneous copper catalyst, which would be appropriate for the catalysis of the A^3-coupling. Three basic supports, MgLaO, HT 2:1, and 4A were impregnated in ion-exchanged water with copper(II)-chloride. The catalyst thus obtained were tested in the reaction of phenylacetylene, paraformaldehyde and morpholine (Fig. 8). We found that Cu^{2+}/4A proved to be an efficient catalyst, without solvent, at room temperature stirring for 24 h the desired *N*-(3-phenylprop-2-ynyl)morpholine was formed with 92 % preparative yield. Under these reaction conditions a numerous compounds were prepared (Table 3).

The results showed that phenylacetylene, aliphatic aldehydes (formaldehyde, butyraldehyde) and secondary amines gave the appropriate propargylamines with good yield. Primary amines (*n*-butylamine) gave poor yield. Aromatic amines did not react. In case of methyl acetylenecarboxylate instead of the coupling the addition of the amine to the C≡C bond occurred. Aromatic aldehydes at room temperature without solvent did not react, but in boiling toluene, using 50 % excess of alkyne the compounds presented in Table 3 were prepared with good to excellent yield.

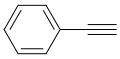
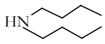
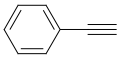
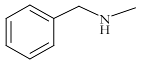
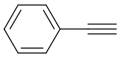
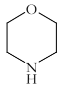
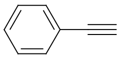
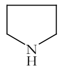
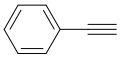
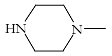
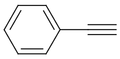
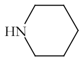
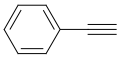
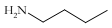
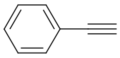
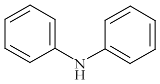
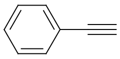
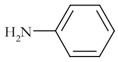
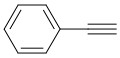
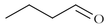
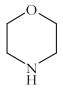
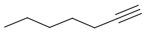
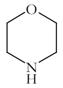
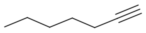
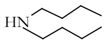
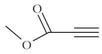
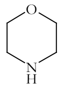
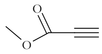
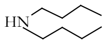
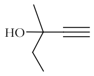
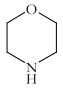
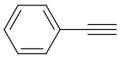
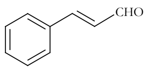
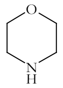
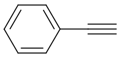
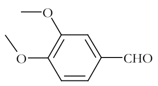
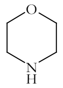
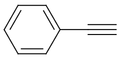
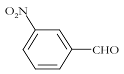
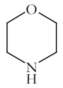
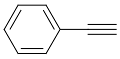
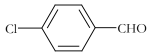
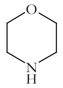
X-ray fluorimetry showed that the products contained less than 1 ppm copper, thus our method is suitable in pharmaceutical and fine chemical syntheses.

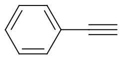
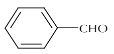
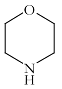
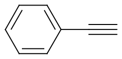
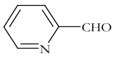
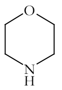
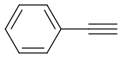
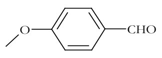
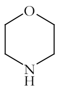
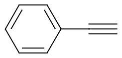
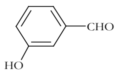
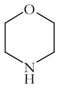
Nitriles are important intermediates in pharmaceutical and fine chemical syntheses. A number of method was developed to their preparation, but they generally use dangerous reagents, mostly cyanides. The preparation of different aldehydes is simplier, their transformation to oximes is a known reaction, so the transformation of oximes into nitriles, especially in the case of aromatic compounds, can be a good alternative to take out the dangerous cyanides. Thus, a number of methods were developed using different organic or inorganic reagents. Among them transition metal-catalyzed methods were also described using cobalt [21], ruthenium [22], rhenium [23], platinum [24], palladium [25], indium and zinc [26] as well as other metal compounds or complexes. The big disadvantage of

13 14 15 16

Fig. 8

Table 3 A^3-coupling in the presence of Cu^{2+}/4A[a]

Alkyne	Aldehyde	Amine	Yield[b] (%)
	CH_2O		96
	CH_2O		93
	CH_2O		92
	CH_2O		76
	CH_2O		72
	CH_2O		70
	CH_2O		40
	CH_2O		1[c,d]
	CH_2O		7[d]
			98
	CH_2O		2[d] (27)[e]
	CH_2O		4[d]
	CH_2O		-
	CH_2O		-
	CH_2O		-(94[f])
			99[f]
			70[g,h]
			99[g,h]
			96[g,h]

			$90^{g,h}$
			$70^{g,h}$
			$89^{g,h}$
			$54^{g,h}$

[a] Alkyne (6 mmol), aldehyde (5 mmol), amine (5 mmol), Cu^{2+}/4A (0.5 g), neat, room temperature, 24 h

[b] Isolated yield, the purity of the product was checked by GC-MS and ^{1}H NMR spectroscopy

[c] At 60°C

[d] Conversion based on GC-MS data

[e] in acetonitrile (2 ml) at 82°C

[f] in toluene (2 ml) at 110°C

[g] Phenylacetylene (7.5 mmol), aldehyde (5 mmol), morpholine (5 mmol), Cu^{2+}/4A (0.5 g), toluene (2 ml), 110°C, 15 h.

[h] 7.5 mmol phenylacetylene

these homogeneous catalytic method is that the residue of the reagents are difficult to separate from the product. The metal contaminates the product which is generally unacceptable.

Continuing our work we tested whether the supported metal catalysts used in the A^3-coupling are suitable for the oxime – nitrile conversion. In these reactions we examined only 4A-supported catalysts. and found that in the benzaldoxime → benzaldehyde reacion, in boiling acetonitrile, Cu^{2+} and Pd^{2+} gave excellent results (within 8 h 100 and 98 % conversion, respectively), while Pd^0 showed significantly less activity (26 % conversion), Ag^+, Fe^{3+}, Co^{2+} and Ni^{2+} were inactive. Based on these results we chose copper for the further experiments, not only for the complete conversion it showed but because the common byproduct of these transformations, the acid amide was not detectable in the copper-catalyzed experiments (GC-MS showed ca. 2 % benzamide in the Pd-catalyzed reaction). The solvent acetonitrile had determinant role in the transformation, without acetonitrile the conversion decreased dramatically even with longer reaction time, too [27].

Different mechanisms are described in the literature for the transition metal-catalyzed conversion of oximes into nitriles. The authors proposed a water transfer from the aldoxime to the solvent - mostly acetonitrile - C≡N bond, which produces equimolar amount of acetamide byproduct. The key step is complex formation among the metal, the aldoxime, and the C≡N group. GC-MS examination of the reaction mixture showed the presence of lage amount of acetamide. Treating Cu^{2+}/4A in boiling aqueous acetonitrile no product was observed, this verifies the concerted mechanism. Thus our investigations supported that the mechanism of the copper-catalyzed reaction can be described with the cyclic process represented in Fig. 9. As a consequence of this mechanism if the amount of the acetonitrile is increased, the reaction time can be decreased significantly, and even the formation of the amide byproduct can be strongly suppressed, since the product nitrile can replace the place of acetonitrile and taking up the water from the oxime can form the amide. The large amount of acetonitrile can largely suppresses this side reaction.

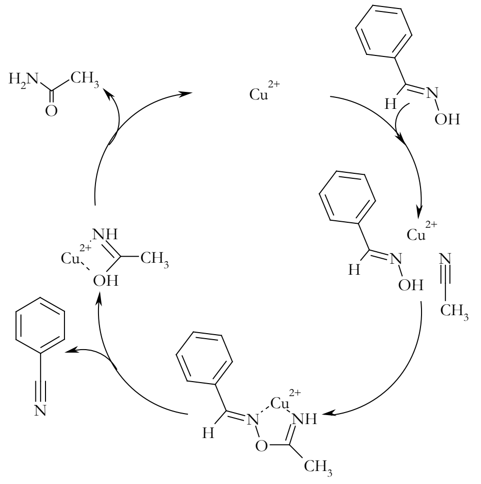
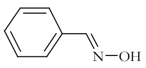
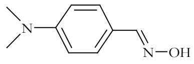
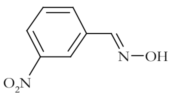
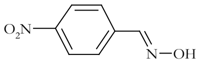
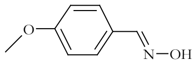
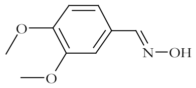
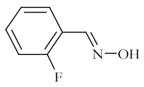
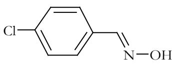
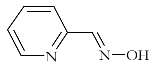
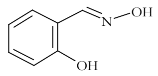
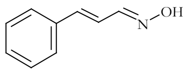
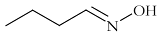


Fig. 9

The optimized reaction conditions were used to synthesize a series of nitrile derivatives (Table 4).

As shown in Table 4, 2-hydroxy-benzaldoxime (salicylaldoxime) gave a very poor yield and near salicylonitrile we also detected the formation of benzisoxazole. It is well known that in salicylaldoxime there is a strong intramolecular hydrogen bond between the aldoxime nitrogen and the o-hydroxyl group. This hydrogen bond can hinder the complex formation of the oxime group with copper, which can explain the weak reactivity of salicylaldoxime. We tried to break this hydrogen bond by adding different bases. The best result was obtained using triethylamine; the conversion was complete after 16 h. The compounds given in Table 5 was prepared with this modified method.

Table 4 Conversion of aldoximes into nitriles[a]

Aldoxime	Conversion[b] (%)	Nitrile[b,c] (%)	Amide[b] (%)
	100	99	0
	100	98(91)	1
	100	96(90)	4
	100	96(87)	4
	100	95(88)	4
	100	86(78)	14
	100	90(82)	10
	100	83(76)	17
	87	25	62
	15[d]	6	0
	100	96(87)	4
	100	100	0

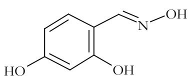
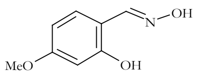
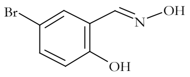
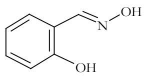
[a]Aldoxime (5 mmol), Cu^{2+}/4[a] (0.5 g), acetonitrile (10 ml), 82°C, 8 h.

[b]Based on GC-MS

[c]Isolated yields in parentheses, the purity of the products were checked with GC-MS és ^{1}H NMR

[d]9 % benzisoxazole was also formed.

Table 5 Conversion of salicylaldoximes[a]

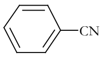
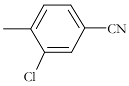
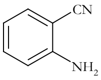
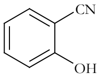
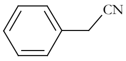
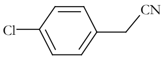
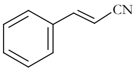
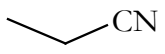
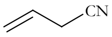
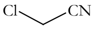
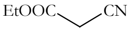
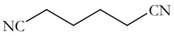
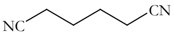
Salicylaldoximes	Conversion[b] (%)	Nitrile[b, c] (%)	Amide[b] (%)
	100	100(98)	0
	100	99(91)	1
	100	99(90)	1
	100	93(85)	7

[a]Salicyaldoxime (5 mmol), triethylamine (5 mmol), Cu^{2+}/4[a] (0.5 g), acetonitrile (10 ml), 82°C, 16 h

[b]Based on GC-MS

[c]Isolated yields in parentheses, the purity of the products were checked with GC-MS and ^{1}H NMR

Table 6 Conversion of nitriles into amides in the presence of Cu^{2+}/4A[a]

Nitrile	Conversion[b] (%)	Amide[b, c] (%)
	100	100(98)
	100	100(98)
	96	71(62)
	81	58(50)
	100	100(97)
	100	100(97)
	100	100(96)
	100	100(94)
	100	100(95)
	98	98(93)
	97	97(95)
	100	54[46][d]
	100	73[27][d,e]

[a] Nitril (2 mmol), acetaldoxime (6 mmol), Cu^{2+}/4A (0,2 g), MeOH (4 ml), 65°C, 4h

[b] Based on GC-MS

[c] Isolated yields in parentheses, the purity of the products were checked with GC-MS and ^1H NMR

[d] The amount of the monoamide in brackets – calculed from the ^1H NMR spectrum

[e] Adiponitrile (2 mmol), acetaldoxime (12 mmol), Cu^{2+}/4A (0.4 g), MeOH (8 ml), 4 h, 65°C.

The reusability of the catalyst was also tested. We found that its activity did not decreased significantly even after the 10th run (98 vs. 95 % in the reaction of benzaldoxime).

Acid amides are valuable synthons in organic syntheses. Numerous methods were developed for their preparation, but these are mostly acid- or base-catalyzed hydrolytic processes which can lead to undesired side reactions. Thus a mild procedure with big functional group tolerancy may have great synthetic importance. We examined the adaptability of the method developed for the oxime – nitrile conversion to the non-hydrolytic transformation of nitriles into amides. Of course, acetonitrile could not be used as solvent, but another compound was also required for the transformation. For this purpose the cheap and easily accesible acetaldoxime was chosen, 3 mol has to be added for the good conversion. Methanol and ethanol proved to be appropriate solvent, from technical reasons methanol was chosen. While Pd^{2+}/4A and Cu^{2+}/4A showed almost the same activity in the oxime – nitrile transformation, in this case only Cu^{2+}/4A was suitable.

The optimised reaction conditions were used to prepare the compounds represented in Table 6 [28].

As can see from Table 6, aromatic, aralkyl and aliphatic nitriles gave generally excellent result. In the case of 2-amino- and 2-hydroxybenzonitrile an unidentified side product debased the results. In case of adiponitrile even 6 mol acetaldoxime was not enough for the conversion of both nitrile groups, a significant amount of monoamide was formed. It is important to note that in the case of ethyl cyanoacetate the ester function remained intact. The products were examined by XRF and found that they contained no detectable amount of copper.

References

[1] Tanabe, K. "Industrial application of solid acid-base catalysts." *Applied Catalysis A: General*. 181 (2) pp. 399-434. 1999. DOI: 10.1016/s0926-860x(98)00397-4

[2] Cwik, A., Hell, Z., Figueras, F. "Palladium/Magnesium-Lanthanum Mixed Oxide Catalyst in the Heck Reaction." *Advanced Synthesys & Catalysis*. 348. pp. 523-530. 2006. DOI: 10.1002/adsc.200505225

[3] Cwik, A., Hell, Z., Figueras, F. "A copper-free Sonogashira reaction using a Pd/MgLa mixed oxide." *Tetrahedron Letters*. 47 (18). pp. 3023-3026. 2006.
DOI: 10.1016/j.tetlet.2006.03.015

[4] Cwik, A., Hell, Z., Figueras, F. "Suzuki–Miyaura cross-coupling reaction catalyzed by Pd/MgLa mixed oxide." *Organic & Biomolecular Chemistry*. 3 (24). pp. 4307-4309. 2005.
DOI: 10.1039/b512767j

[5] Németh, J., Kiss, Á., Hell, Z. "Palladium-catalyzed transfer hydrogenation of nitrobenzenes: investigation of the selectivity." *Reaction Kinetics, Mechanisms Catalysis*. 111 (1). pp. 115-121. 2014.
DOI: 10.1007/s11144-013-0633-7

[6] Németh, J., Kiss, Á., Hell, Z. "Palladium-catalysed transfer hydrogenation of aromatic nitro compounds — an unusual chain elongation." *Tetrahedron Letters*. 54 (45). pp. 6094-6096. 2013.
DOI: 10.1016/j.tetlet.2013.08.123

[7] Barbier, P. "Synthèse du diéthylhepténol." *Comptes Rendus de l'Académie des Sciences*. 128. 110. 1899.

[8] Grignard, V. "Sur quelques nouvelles combinaisons organométalliques du magnésium et leur application à des synthèses d'alcools et d'hydrocarbures." *Comptes Rendus Chimie*. 130. 1322. 1900.

[9] Tamao, K., Sumitani, K., Kumada, M. "Selective carbon-carbon bond formation by cross-coupling of Grignard reagents with organic halides. Catalysis by nickel-phosphine complexes." *Journal of the American Chemical Society*. 94 (12). pp. 4374-4376. 1972.
DOI: 10.1021/ja00767a075

[10] Corriu, R. J. P., Masse, J. P. "Activation of Grignard reagents by transition-metal complexes. A new and simple synthesis of trans-stilbenes and polyphenyls." *Journal of the Chemical Society, Chemical Communications*. 3. p. 144a. 1972.
DOI: 10.1039/c3972000144a

[11] (a) Lipshutz, B. H., Tomioka, T., Blomgren, P. A., Sclafani, J. A. "Kumada couplings catalyzed by nickel on charcoal (Ni/C)." *Inorganica Chimica Acta*. 296 (1). pp. 164-169. 1999.
DOI: 10.1016/s0020-1693(99)00388-6

[11] (b) Lipshutz, B. H., Tasler, S., Chrisman, W., Spliethoff, B., Tesche, B. "On the Nature of the 'Heterogeneous' Catalyst: Nickel-on-Charcoal." *The Journal of Organic Chemistry*. 68 (4). pp. 1177-1189. 2003.
DOI: 10.1021/jo020296m

[12] Styring, P., Grindon, C., Fisher, C. M. "A Polymer-Supported Nickel(II) Catalyst for Room Temperature Tamao–Kumada–Corriu Coupling Reactions." *Catalysis Letters*. 77 (4). pp. 219-225. 2001.
DOI: 10.1023/A:1013209202418

[13] Richardson, J. M., Jones, C. W. "Leached nickel promotes catalysis using supported Ni(II) complex precatalysts in Kumada-Corriu reactions." *Journal of Molecular Catalysis A: Chemical*. 297 (2). pp. 125-134. 2009.
DOI: 10.1016/j.molcata.2008.09.021

[14] Kiss, Á., Hell, Z., Bálint, M. "Nickel/magnesium–lanthanum mixed oxide catalyst in the Kumada-coupling." *Organic, Biomolecular Chemistry*. 8 (2). pp. 331-335. 2010.
DOI: 10.1039/b919246h

[15] Wei, C., Li, C.-J. "A Highly Efficient Three-Component Coupling of Aldehyde, Alkyne, and Amines via C−H Activation Catalyzed by Gold in Water." *Journal of the American Chemical Society*.125 (32). pp. 9584-9585. 2003.
DOI: 10.1021/ja0359299

[16] Lo, V. K.-Y., Kung, K. K.-Y., Wong, M.-K., Che, C.-M. "Gold(III) (C^N) complex-catalyzed synthesis of propargylamines via a three-component coupling reaction of aldehydes, amines and alkynes." *Journal of Organometallic Chemistry*. 694 (4). pp. 583-591. 2009.
DOI: 10.1016/j.jorganchem.2008.12.008

[17] Reddy, K. M., Babu, N. S., Suryanarayana, I., Prasad, P. S. S., Lingaiah, N. "The silver salt of 12-tungstophosphoric acid: an efficient catalyst for the three-component coupling of an aldehyde, an amine and an alkyne." *Tetrahedron Letters*. 47 (43). pp. 7563-7566. 2006.
DOI: 10.1016/j.tetlet.2006.08.094

[18] Sreedhar, B., Reddy, P. S., Krishna, C. S. V., Babu, P. V. "An efficient synthesis of propargylamines using a silica gel anchored copper chloride catalyst in an aqueous medium." *Tetrahedron Letters*. 48 (44). pp. 7882-7886. 2007.
DOI: 10.1016/j.tetlet.2007.08.116

[19] Patil, M. K., Keller, M., Reddy, B. M., Pale, P., Sommer, J. "Copper Zeolites as Green Catalysts for Multicomponent Reactions of Aldehydes, Terminal Alkynes and Amines: An Efficient and Green Synthesis of Propargylamines." *European Journal of Organic Chemistry*. 2008 (26). pp. 4440-4445. 2008.
DOI: 10.1002/ejoc.200800359

[20] Choudary, B. M., Sridhar, C., Kantam, M. L., Sreedhar, B. "Hydroxyapatite supported copper catalyst for effective three-component coupling." *Tetrahedron Letters*. 45 (39). pp. 7319-7321. 2004.
DOI: 10.1016/j.tetlet.2004.08.004

[21] Attanasi, O., Palma, P., Serra-Zanetti, F. "Effect of Metal Ions in Organic Synthesis; XVII. Mild, Easy, and High-Yield Conversion of Aldoximes into Nitriles under Copper(II) Acetate-Catalysis." *Synthesis*. 1983 (9). pp. 741-742. 1983.
DOI: 10.1055/s-1983-30495

[22] (a) Yang, S. H., Chang, S. "Highly Efficient and Catalytic Conversion of Aldoximes to Nitriles." *Organic Letters*. 3 (26). pp. 4209-4211. 2001.
DOI: 10.1021/ol0168768

[22] (b) Choi, E., Lee, C., Na, Y., Chang, S. "[RuCl$_2$(*p*-cymene)]$_2$ on Carbon: An Efficient, Selective, Reusable, and Environmentally Versatile Heterogeneous Catalyst." *Organic Letters*. 4 (14). pp. 2369-2371. 2002.
DOI: 10.1021/ol0260977

[23] Ishihara, K., Furuya, Y., Yamamoto, H. "Rhenium(VII) Oxo Complexes as Extremely Active Catalysts in the Dehydration of Primary Amides and Aldoximes to Nitriles." *Angewandte Chemie International Edition*. 41 (16). pp. 2983-2986. 2002.

[24] Makarycheva-Mikhailova, A. V., Bokach, N. A., Haukka, M., Kukushkin, V. Y. "The first example of ligand-mediated dehydration of aldoximes." *Inorganica Chimica Acta*. 356. pp. 382-386. 2003
DOI: 10.1016/s0020-1693(03)00275-5

[25] Kim, H. S., Kim, S. H., Kim, J. N. "Highly efficient Pd-catalyzed synthesis of nitriles from aldoximes." *Tetrahedron Letters*. 50 (15). pp. 1717-1719. 2009.
DOI: 10.1016/j.tetlet.2009.01.150

[26] Allen, C. L., Burel, C., Williams, J. M. J. "Cost efficient synthesis of amides from oximes with indium or zinc catalysts." *Tetrahedron Letters*. 51 (20). pp. 2724-2726. 2010.
DOI: 10.1016/j.tetlet.2010.03.048

[27] Kiss, Á., Hell, Z. "Heterogeneous Catalytic Method for the Conversion of Aldoximes into Nitriles Using Molecular Sieve Modified with Copper(II)." *Synthetic Communications*. 43 (13). pp. 1778-1786. 2013.
DOI: 10.1080/00397911.2012.667861

[28] (a) Kiss, Á., Hell, Z. "A heterogeneous catalytic method for the conversion of nitriles into amides using molecular sieves modified with copper(II)." *Tetrahedron Letters*. 52 (45). pp. 6021-6023. 2011.
DOI: 10.1016/j.tetlet.2011.09.012

[28] (b) Kiss, Á., Hell, Z. "Cu^{II}-MS-4Å for Hydration of Nitriles into Amides. *Synfacts*." 8 (1). p. 0105. 2012.
DOI: 10.1055/s-0031-1289493