Development of reusable supported catalysts for carbonylation reactions

In the past two decades we used carbonylation reactions effectively for the synthesis of several new compounds, especially for the functionalisation of steroids and ferrocene derivatives. Carbonylation reactions of aryl/alkenyl halides involve the formation of carbonyl compounds and carboxylic acid derivatives using carbon monoxide as the source of the C=O group. Application of amines as the nucleophilic partner leads to amides and α-ketoamides, via mono- and double carbonylation processes, respectively. Both types of the products have practical importance: the amide functionality is an important motif in a lot of biologically active molecules [1] and some α-ketoamides also show interesting pharmacological properties, such as anti-HIV activity [2] or HCV protease inhibition. [3]

These reactions usually require the use of a relatively large amount of the palladium catalyst (2-10%) that contaminates the products. When the reactions are carried out in homogeneous phase, catalyst recirculation is not possible with the exception of some special cases, *e.g.* the application of biphasic solvent systems. Ionic liquids (ILs) supported on solid phases may stabilise catalytically active palladium complexes or nanoparticles, and their use may result in the formation of heterogeneous catalysts. The latter had been used for various cross-couplings before, but when our proposal was submitted, there was only one example for their application in carbonylations. [4] Moreover, other heterogeneous systems were rarely used in such reactions and there were only two examples for double carbonylation reactions carried out with a heterogeneous catalyst [5-6] (It should be mentioned that during the course of the present project several research groups started to develop their own catalytic system for mono- [7] and double carbonylation. [8]) The aim of our research was twofold: *i*) to develop new, reusable SILP (supported ionic liquid phase) catalysts for carbonylation reactions and *ii*) to evaluate their efficiency in the synthesis of molecules with practical importance.

In case of these heterogeneous catalysts, the catalytic systems can really be very complicated, as palladium either adsorbed on the surface of the support or dissolved in the reaction mixture (or both) may play a role in the carbonylation. Moreover, both palladium nanoparticles and palladium complexes formed under catalytic conditions may be involved. According to our own results, modification of the support, that of the palladium precursor or conditions of immobilisation may affect considerably the selectivity and recyclability of the catalysts.

1. Methods

1.1. Preparation and characterisation of SILP phases

First, kaolinite and silica (silica gel) was used as the solid support for the preparation of SILP phases. During the test reactions both types of supports led to recyclable catalysts, but the heterogeneous phase could be removed only by centrifugation in case of catalysts supported on kaolinite, while in the other case the two phases could be separated by simple filtration or decantation. So silica was chosen as the suitable support for further investigations.

Imidazolium, phosphonium and pyridinium ILs were immobilised on silica by physisorption (Fig. 1, A) or grafting (B). To achieve a better stabilisation of palladium, supports with dicationic moieties (C) were also prepared. An organic/inorganic hybrid material was obtained by the polymerisation of an IL monomer in the presence of silica (D). (Again, the use of the polymer alone as support led to heterogeneous catalysts that could be removed only by centrifugation. Moreover, efficiency of the catalysts derived from the latter material fell behind those obtained from the polymer/silica support.)

The supports were characterised by solid phase NMR (^{13}C-, ^{29}Si-, ^{31}P- CP MAS NMR) and FTIR measurements.

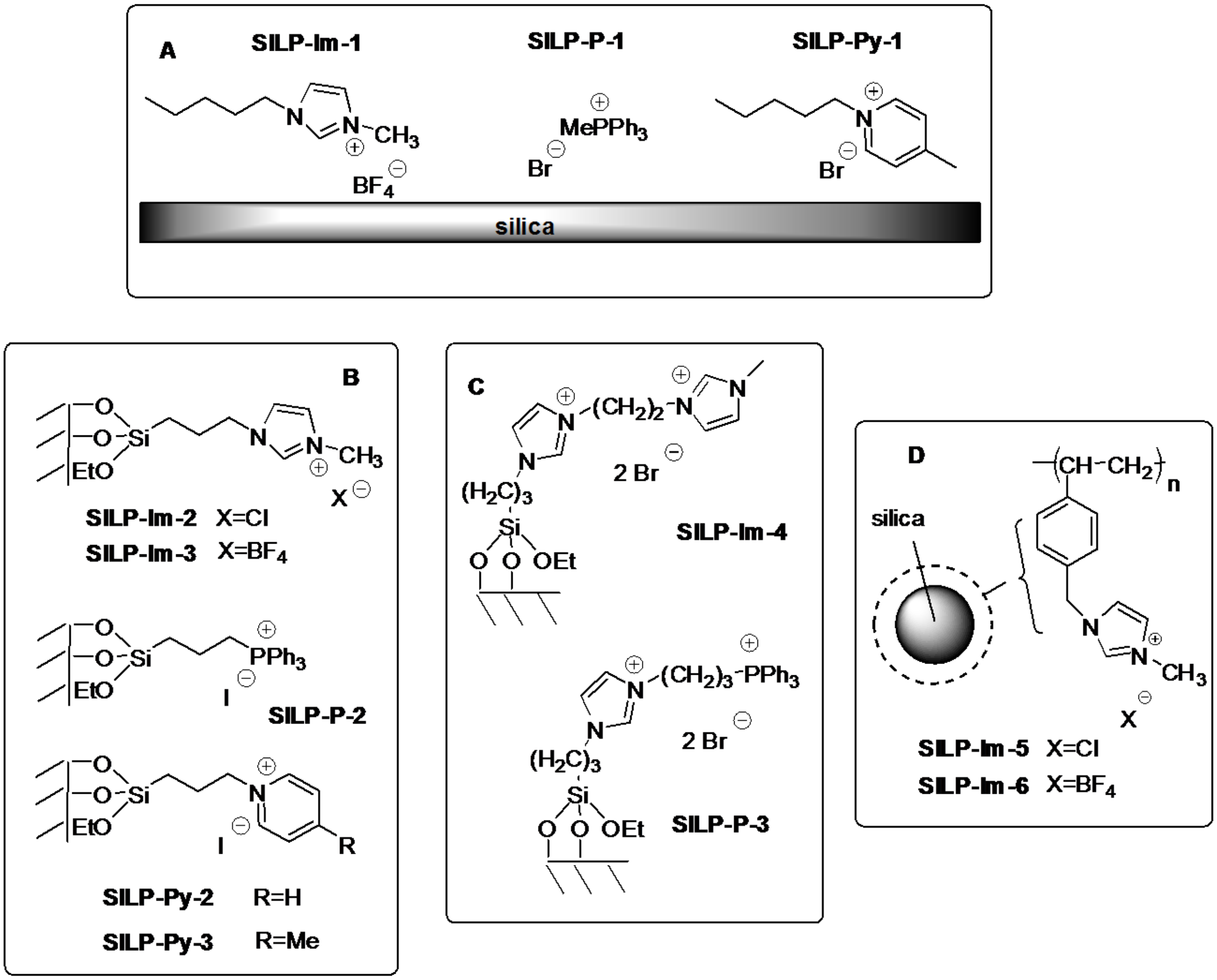


Figure 1. SILP phases used as supports in catalytic reactions

1.2. Preparation, characterisation and evaluation of catalysts

Catalysts were obtained using various Pd(0) and Pd(II) precursors including Pd-phosphine and Pd-carbene complexes in different solvents (*e.g.* THF, acetonitrile, ethanol). Among the precursors tested, $Pd_2(dba)_3$ and $Pd(OAc)_2$ were proved to lead to the most efficient catalysts. [9] (Main features of the catalysts discussed in the present report are summarised in Table 1.) The fresh and spent catalysts were characterised by solid phase NMR, TEM, XPS and FTIR measurements. Pd-content was determined by ICP and the amount of heterogeneous catalysts used in carbonylations was calculated accordingly. Their efficiency was tested in model reactions of iodobenzene with simple aliphatic and aromatic amines, such as morpholine and aniline. Reaction conditions, choice of solvent, base, pressure, temperature and reaction time were optimised to achieve highest conversion together with optimal selectivity. Recyclability of the catalysts was investigated. Palladium leaching was determined by ICP analysis of the reaction mixtures. Hot filtration and mercury poisoning tests were carried out to obtain information about the homogeneous or heterogeneous nature of the reaction mixture and leached species. The best catalysts and optimal conditions were used to prepare amides and α-ketoamides from different aryl halides and amines. The products were characterised by ^{1}H-, ^{13}C NMR and MS.

Table 1. Preparation conditions of the catalysts discussed in this report

	support	precursor	conditions for immobilisation	metal content (m/m%)
CAT-0	silica	$Pd_2(dba)_3$	$THF+CH_3CN$	0.55
CAT-1	**SILP-Im-1**	$Pd_2(dba)_3$	$THF+CH_3CN$	0.40
CAT-2	**SILP-P-1**	$Pd_2(dba)_3$	$THF+CH_3CN$	0.93
CAT-3	**SILP-Py-1**	$Pd_2(dba)_3$	$THF+CH_3CN$	0.48
CAT-4	**SILP-Im-2**	$Pd(OAc)_2$	$EtOH/KO^tBu$	0.60
CAT-5	**SILP-Im-3**	$Pd_2(dba)_3$	$THF+CH_3CN$	0.29
CAT-6	**SILP-Im-3**	$Pd_2(dba)_3$	EtOH	0.75
CAT-7	**SILP-Im-3**	$Pd(OAc)_2$ +DPPBA	$THF+CH_3CN$	0.44
CAT-8	**SILP-P-2**	$Pd_2(dba)_3$	$THF+CH_3CN$	0.58
CAT-9	**SILP-Py-2**	$Pd_2(dba)_3$	$THF+CH_3CN$	0.79
CAT-10	**SILP-Im-4**	$Pd_2(dba)_3$	$THF+CH_3CN$	2.64
CAT-11	**SILP-Im-4**	$Pd(OAc)_2$	$EtOH/KO^tBu$	1.66
CAT-12	**SILP-P-3**	$Pd_2(dba)_3$	$THF+CH_3CN$	1.95
CAT-13	**SILP-Im-5**	$Pd_2(dba)_3$	$THF+CH_3CN$	0.89
CAT-14	**SILP-Im-5**	$Pd(OAc)_2$	$EtOH/KO^tBu$	1.20
CAT-15	**SILP-Im-5**	CuI	CH_3CN/DMF	3.50
CAT-16	**SILP-Im-5**	CuI	THF/KO^tBu	10.3
CAT-17	**SILP-Im-5**	CuI	THF/KO^tBu	3.06

Copper catalysts obtained by supporting CuI on the **SILP-Im-5** (Fig.1.) material (**CAT-15** — **CAT-17**, Table 1) were characterised by similar methods as mentioned above and were used in azide-alkyne cycloadditions. After optimisation of the reaction conditions in a model reaction, various 1,4-substitued-1,2,3-triazoles were prepared with some steroid and ferrocene derivatives among them.

2. Results

2.1. Palladium-catalysed carbonylation reactions of aryl halides

The main requirements that an optimal supported catalyst should fulfil include activity, selectivity, recyclability and small loss of palladium.

These parameters are influenced not only by the preparation method of the heterogeneous catalysts but also on the reaction conditions. Some general effects of the latter are as follows. The use of polar solvents accelerated the reaction, favoured the formation of double carbonylated products and promoted reusability in spite of somewhat higher palladium leaching. In apolar solvents, such as toluene, the added base had a decisive effect both on selectivity and recyclability. In the presence of DBU, double carbonylation was the main reaction and most of the catalysts could be recycled, while the application of Et_3N resulted in lower reaction rates, poor selectivity and quickly decreasing activity of catalysts upon reuse. Similarly to homogeneous phase reactions, high CO pressure was proved to favour double carbonylation. For efficient recycling, 5-30 bar pressure was necessary. With the exception of one catalyst, low catalytic activity was observed under atmospheric conditions and practically no recyclability could be achieved.

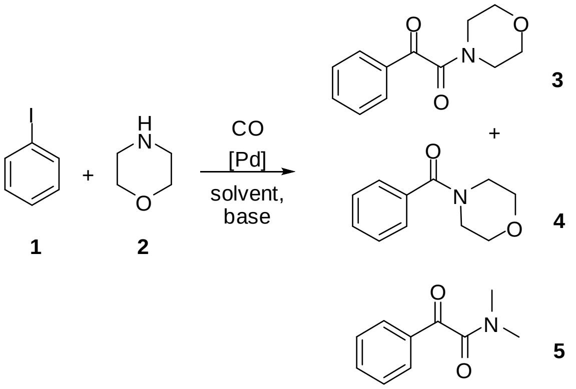
Reaction time also influences catalyst reuse. In most cases, incomplete reactions resulted in quickly decreasing activity in the next cycles. According to our results, the presence of unreacted starting material increased palladium leaching. After completion of the reaction, the active species re-precipitated on the support [10] so the catalyst could better preserve its activity. In case of catalysts with lower activity, relatively long reaction time (8-12h) was used during carbonylations to enhance recyclability. [11]

It should be mentioned that although some efficient catalysts were obtained from SILP phases incorporating $[BF_4]^-$ anions (**CAT-1** from **SILP-Im-1** and **CAT-5**—**CAT-7** from **SILP-Im-3**), the results proved that halide containing supports were more suitable. Especially marked differences were observed in the performance of the catalysts obtained from the polymeric phases **SILP-Im-5** and **SILP-Im-6**. **CAT-13**, obtained from **SILP-Im-5** was proved to be one of the systems with excellent activity and lowest loss of palladium upon recycling, while a catalyst prepared from the latter showed much lower activity and poor reusability.

Due to the limited size of the report, only a few examples will be shown here, to highlight the main differences between the efficiency of the catalysts obtained from various SILP phases.

2.1.1. Double carbonylations

As heterogeneous phase double carbonylation had been less explored before, first we focussed on the selective synthesis of α-ketoamides. The model reaction was carbonylation of iodobenzene with morpholine (Scheme 1). In DMF, beside the awaited α-ketoamide (**3**) and amide (**4**), a side product (**5**), formed from the decomposition product of DMF, could also be detected. In spite of this, DMF was proved to be the solvent of choice in most cases. The use of acetonitrile led to somewhat lower α-ketoamide/amide ratios.



Scheme 1. The model reaction for carbonylation experiments

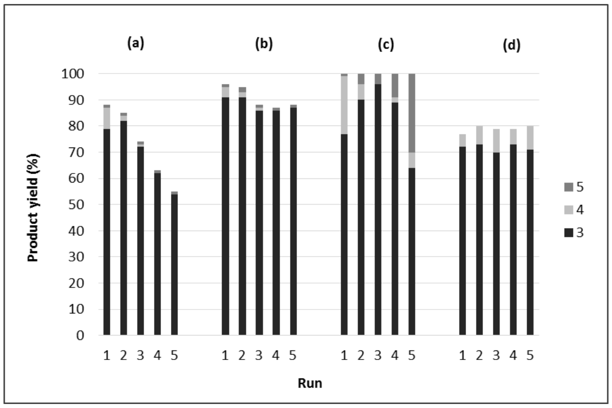


Figure 2. Recycling experiments with catalysts obtained from $Pd_2(dba)_3$ and (a) silica (**CAT-0**), (b) **SILP-Im-1** (**CAT-1**) (c) **SILP-P-1** (**CAT-2**) and (d) **SILP-Py-1** (**CAT-3**)

Interestingly, even the use of SILPs with physisorbed ILs led to catalysts that could be reused several times, despite the fact that the majority of the adsorbed IL was washed off by the polar solvent in the first run. The decisive role of the IL on the formation of the catalyst is well demonstrated by the differences observed during recycling of catalysts obtained from simple silica, **SILP-Im-1**, [11] **SILP-P-1** [12] and **SILP-Py-1** as supports (Fig. 2.). **CAT-0** lost its activity quickly. Highest activity and recyclability was shown by the catalyst obtained from **SILP-P-1** (**CAT-2**), but the amount of side product **5** increased considerably upon reuse. Best selectivity was observed in the reaction of **CAT-1**. **CAT-3**, obtained from **SILP-Py-1** retained its activity throughout several cycles in spite of incomplete conversion.

ILs can be grafted on silica by a condensation reaction between the solid phase and triethoxysilyl groups of the cations (Fig. 1. B). All of the catalysts derived from these phases were recyclable, but again, great differences could be observed in their performance. In case of catalysts obtained from pyridinium-type phases (**SILP-Py-2** and **SILP-Py-3**), the catalytically active species were formed only during the carbonylation reaction, so an increase in the activity was observed in the second run (Fig. 3, c). Palladium leaching was around 4% of the original load in case of imidazolium and phosphonium-type catalysts (**CAT-5** and **CAT-8**) [11, 12] while it remained under detection limit (< 5 ppm) with those obtained from **SILP-Py-2** (**CAT-9**) and **SILP-Py-3**.

By a change of the solvent used during the deposition of palladium on the solid support from THF/CH_3CN to EtOH, a very active catalyst (**CAT-6**) could be obtained from **SILP-Im-3**, too. Although a relatively high amount of side product **5** was formed (up to 10 %) in DMF, the catalyst could be reused readily in at least 7 cycles in acetonitrile with a loss of palladium around 1.5%. [9]

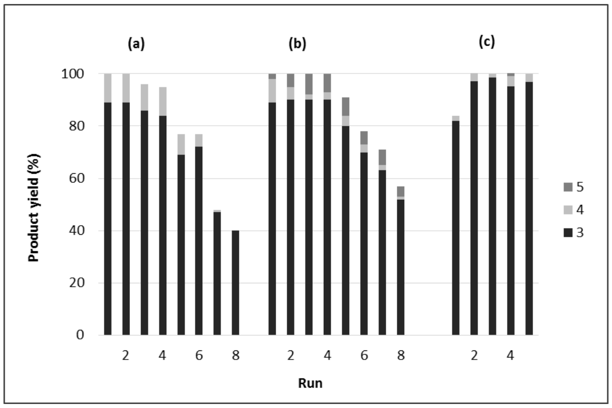


Figure 3. Three hour-long recycling experiments with catalysts obtained from $Pd_2(dba)_3$ and (a) **SILP-Im-3** (**CAT-5**) (b) **SILP-P-2** (**CAT-8**) and (c) **SILP-Py-2** (**CAT-9**)

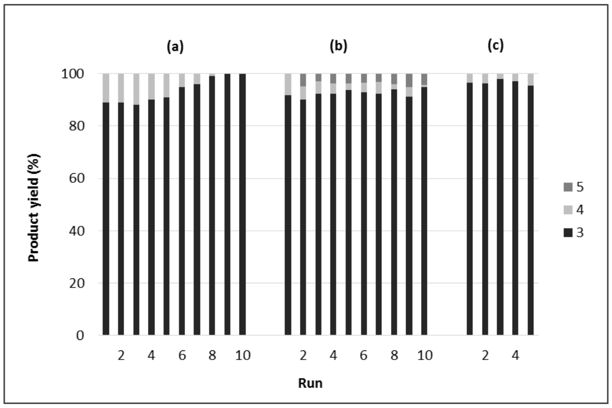


Figure 4. Eight hour-long recycling experiments with catalysts obtained from $Pd_2(dba)_3$ and (a) **SILP-Im-3** (**CAT-5**) (b) **SILP-P-2** (**CAT-8**) and (c) **SILP-Py-2** (**CAT-9**)

Palladium leaching could also be reduced by the application of dicationic phases **SILP-Im-4** [9] or **SILP-P-3** [12] under well-chosen reaction conditions.

From the catalysts obtained from the $Pd_2(dba)_3$ precursor, the use of the one derived from **SILP-P-3** (**CAT-12**) was proved to be more advantageous. It could be reused more efficiently in three hour-long reactions (Fig.5, b and Fig. 6, c).

Carbonylations carried out in toluene together with DBU as base resulted in a loss of palladium below the detection limit (<1.1-1.2% of the original load) in case of both catalysts.

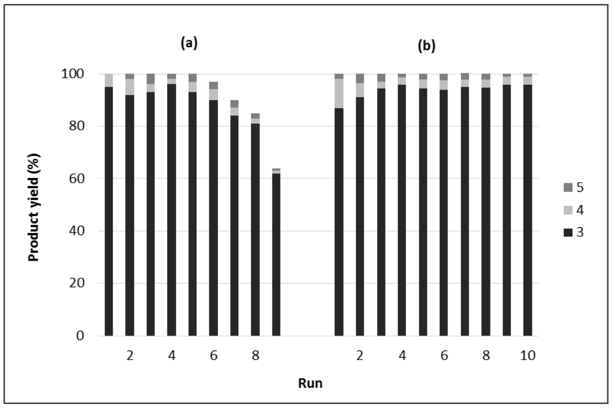


Figure 5. Three hour-long recycling experiments with catalysts obtained from $Pd_2(dba)_3$ and (a) **SILP-Im-4** (**CAT-10**) (b) **SILP-P-3** (**CAT-12**), (solvent: DMF, base: Et_3N)

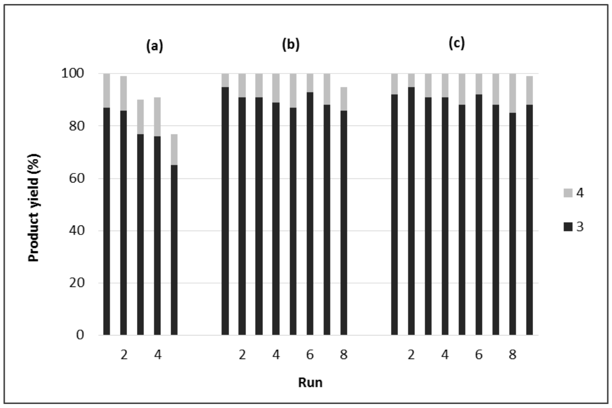


Figure 6. Recycling experiments with catalysts obtained from $Pd_2(dba)_3$ and (a) **SILP-Im-4** (**CAT-10**), 3h (b) **SILP-Im-4** (**CAT-10**), 8h (c) **SILP-P-3** (**CAT-12**), 3h (solvent: toluene, base: DBU)

The most efficient catalyst was obtained from **SILP-Im-4** by the immobilisation of $Pd(OAc)_2$ in the presence of KO^tBu in EtOH solvent (**CAT-11**). (The addition of KO^tBu may facilitate deprotonation of the C2-H of the imidazolium ring and formation of Pd-NHC complexes. Such derivatives were proved to be only precatalysts and the active species were shown to be released into the medium as soluble nanoclusters in Heck reactions by Burguete *et al*. [13]. The presence of nanoparticles both on the heterogeneous support and in the reaction mixture was also detected during the present work.)

In three hour-long reactions carried out in DMF, total conversion could be achieved in 10 consecutive cycles. The α-ketomide was obtained with 97-99% selectivity and no formation of side product **5** could be detected (Fig.7, a). Palladium leaching remained below the detection limit (1.3-1.6%). Excellent results could be obtained even by reducing the pressure to 20 bar (Fig.7, b).

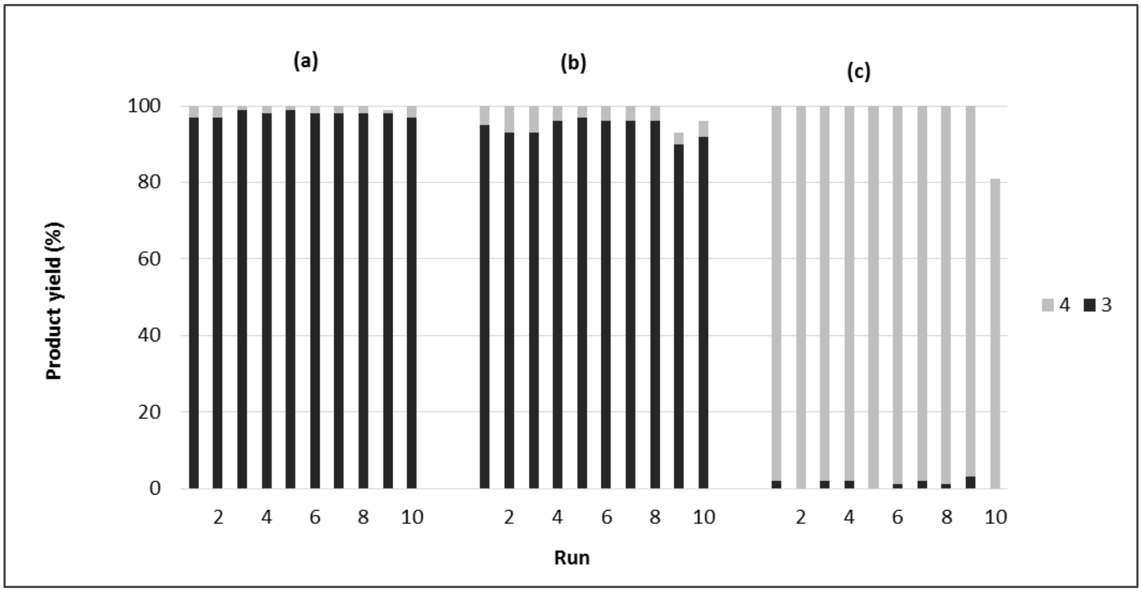


Figure 7. Recycling experiments with **CAT-11** obtained from $Pd(OAc)_2$ and **SILP-Im-4** (a) 30 bar, 100 °C, DMF, Et_3N, 3h (b) 20 bar, 100 °C, DMF, Et_3N, 3h (c) 5 bar, 120 °C, solvent-free, DABCO, 3h

Interestingly, efficiency of catalysts obtained from the same precursors ($Pd_2(dba)_3$ and $Pd(OAc)_2$) was found to be completely reversed when they were deposited on **SILP-Im-5** (**CAT-13** and **CAT-14**). The use of the former resulted in efficient recycling (in at least 6 successive runs) and Pd leaching below the detection limit (<0.1%) while the latter was proved to be less stable with a palladium loss around 4%.

Beside the model reaction, double carbonylation was carried out with other iodoarenes and amines with the most successful catalytic systems (**CAT-1**, **CAT-5**, **CAT-6**, **CAT-9**, **CAT-11**, **CAT-12** and **CAT-13**). The products are shown in Figure 8. The possibility of catalyst recycling was also checked in 2-4 runs. Most of the reactions were carried out in DMF. The applicability of the toluene/DBU system was restricted because solubility problems of the products (*e.g.* in the reaction of 4-iodoanisole or 4-iodo-nitrobenzene) that hindered separation of catalysts from the reaction mixtures.

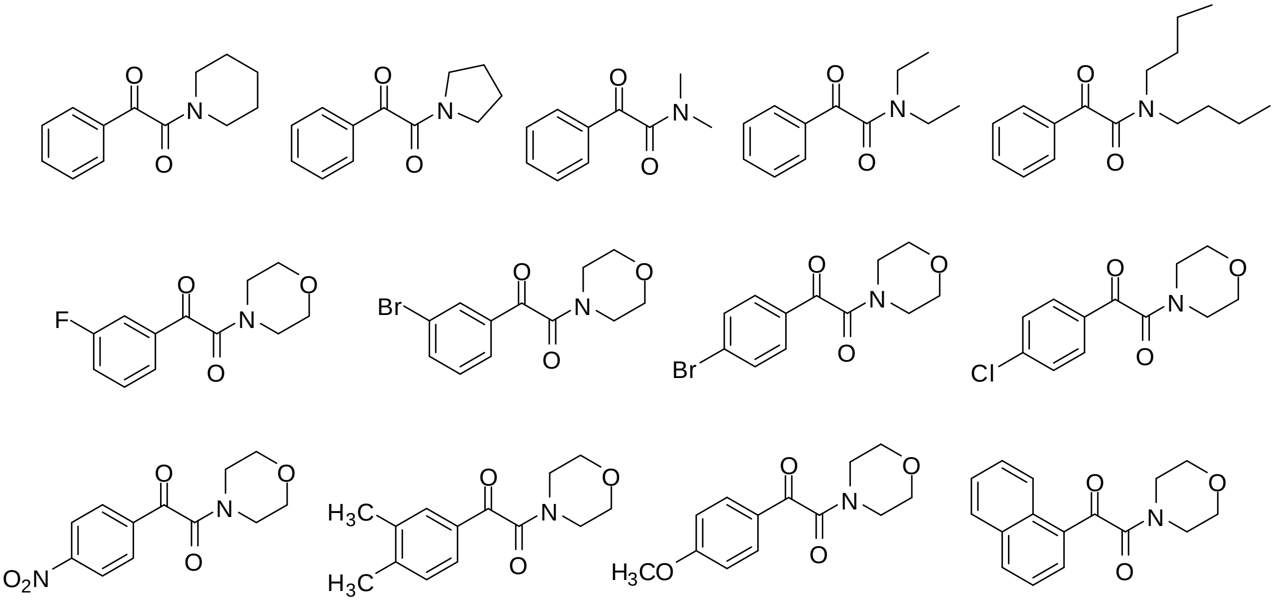
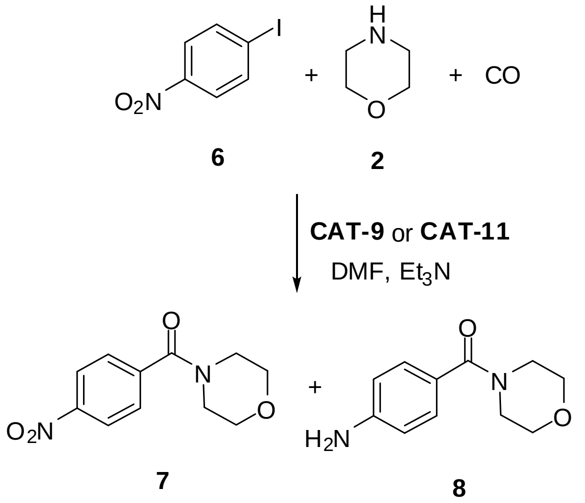


Figure 8. Some ketoamide products obtained during double carbonylations

α-Ketoamides could be produced with good selectivity in most cases, starting from iodobenzene derivatives with either electron withdrawing or -donating groups. At the same time, a considerable amount of amide side product was formed starting from 1-iodonaphtalene. Another exception is the conversion of 4-iodo-nitrobenzene where only monocarbonylation took place and the nitro group of the product underwent reduction to produce approximately equal amounts of the awaited amide (**7**) and morpholino(4-aminophenyl)methanone (**8**, Scheme 2) in the presence of **CAT-9** and **CAT-11**.



Scheme 2. Carbonylation of 4-iodo-nitrobenzene in the presence of **CAT-9** and **CAT-11**

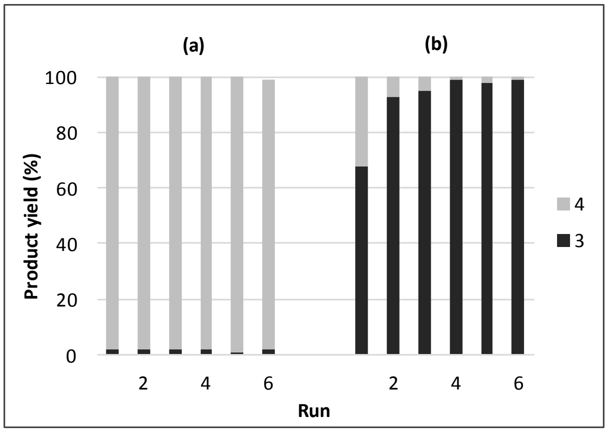


Figure 9. Recycling experiments with **CAT-7** obtained from $Pd(OAc)_2$, DPPBA and **SILP-Im-3** (a) 5 bar, 120 °C, solvent-free, Et_3N, 8h (b) 30 bar, 100 °C, DMF, Et_3N, 8h

Cyclic amines (piperidine and pyrrolidine) and secondary amines with short alkyl chains (Me_2NH, Et_2NH) could be converted to the corresponding α-ketoamides with good selectivity. Exclusive formation of the amide was observed starting from the bulky diisopropylamine and the corresponding amide could be obtained with acceptable yield. It should be mentioned that this amine had been reported to produce neither mono-, nor double carbonylated products before, during aminocarbonylation of iodobenzene carried out in the presence of a palladium-phosphine complexes grafted onto mesoporous silica. [8a] Poor selectivity was observed in the reactions of 2-ethylpiperidine and longer-chain amines, such as *n*-butylamine resulting in the formation of similar amounts of amides and α-ketoamides. Also, a marked loss of catalyst activity was detected in the last two reactions.

2.1.2. Monocarbonylation with aliphatic amines

The synthesis of amides with the help of the catalysts mentioned above turned out to be a more problematic task. With the exception of higher temperature, all of the reaction conditions that usually promote monocarbonylation (low pressure, apolar solvent, Et_3N as base), decreased the recyclability of the catalysts considerably. Even if activity and selectivity of some of the systems were found to be satisfactory, a marked loss of conversion was observed upon reuse in most cases. After a careful optimisation of reaction conditions of our model reaction (Scheme 1) (pressure, temperature, solvent, added base), two catalytic systems were found to show good recyclability together with a preferred formation of amides. The addition of a polar phosphine ligand, 4-diphenylphosphino benzoic acid (DPPBA) to the precursor $Pd(OAc)_2$ upon deposition to **SILP-Im-3** resulted in a catalyst (**CAT-7**) with good selectivity towards monocarbonylation when the reaction was carried out under solvent-free conditions (Fig.9, a). [14] By the change in the reaction conditions, this catalyst was proved to be suitable for the synthesis of α-ketoamides (Fig. 9, b), too. To the best of our knowledge, there had been only one report in the literature before for a heterogeneous catalyst that could be used flexibly for the selective synthesis of either amides or α-ketoamides. [15] A simple change in the reaction conditions when using the most efficient catalyst for double carbonylation (**CAT-6**, see Fig. 7, a), namely application of solvent-free conditions, DABCO as base, lower pressure and higher temperature resulted in selective monocarbonylation together with good recyclability (Fig. 7, c). [10] That means that we succeeded in developing a phosphine-free, recyclable catalyst that can be used for the synthesis of either amides or α-ketoamides under relatively mild conditions.

Several amides were obtained under solvent-free conditions with **CAT-6** and **CAT-7** starting from iodobenzene and other aliphatic amines, as well as from different iodoarenes and morpholine (Fig. 10). Recyclability of the catalysts was proved in at least 2 cycles. The antidepressant agent Moclobemide (**9**) could be produced with 90 % isolated yield.

In case of 3-Br- and 4-Br-iodobenzene, the Br substituent could also be converted to the amide functionality in a consecutive reaction with this catalyst. With the more active catalyst **CAT-6**, the bis-amides (**10** and **11**) were the main products when longer reaction time (8h) was applied. Unfortunately, the Br substituent of bromobenzene and its derivatives with different electron-withdrawing atoms/groups (3-Cl-, 4-Cl-, 4-F-, 4-Ac) remained intact under similar conditions even in the presence of KI. So the unique reactivity of 3-Br- and 4-Br-iodobenzene requires further investigation.

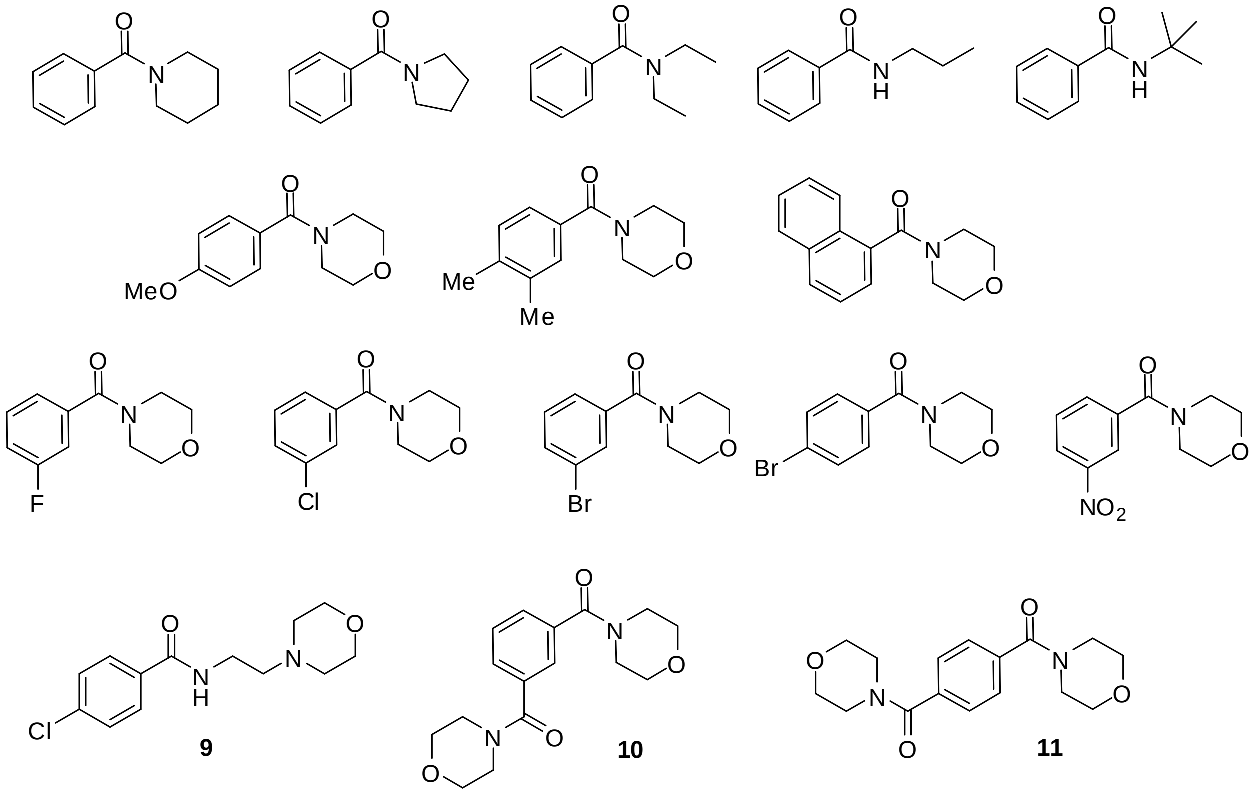


Figure 10. Amide products obtained from aliphatic amines under solvent-free conditions

2.1.3. Carbonylations with aromatic amines

Contrary to aliphatic amines, the use of aniline derivatives as nucleophiles led to the selective formation of amides in all cases, the presence of no double carbonylated products could be detected. Good catalyst recycling could be achieved under a number of conditions applied in mono- or double carbonylations of aliphatic amines. Some examples include the use of **CAT-1** (30 bar, 100 ^{o}C, DMF, Et_3N, 4h) [9], **CAT-7** (5 bar, 120 ^{o}C, solvent-free, Et_3N) [14] **CAT-9** (30 bar, 100 ^{o}C, DMF, Et_3N, 3h), **CAT-11** (5 bar, 120 ^{o}C, solvent-free, DABCO, 3h) **CAT-12** (30 bar, 100 ^{o}C, DMF, Et_3N, 3h) [12] and **CAT-13** (30 bar, 100 ^{o}C, DMF, Et_3N, 3h).

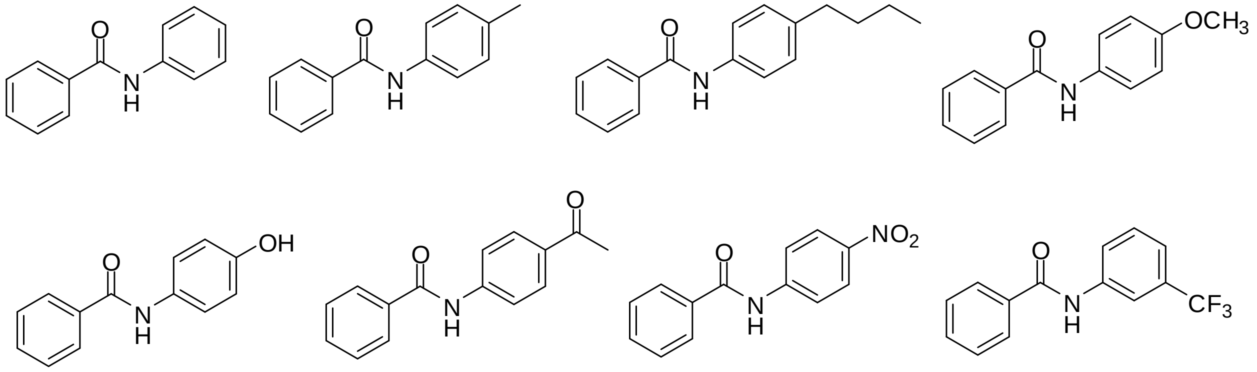


Figure 11. Amide products obtained from aromatic amines in the presence of **CAT-1**, **CAT-7**, **CAT-9**, **CAT-11**, **CAT-13** under 5-30 bar pressure, and with **CAT-4** at atmospheric CO

As it was mentioned before, a number of catalysts were tested in carbonylations at atmospheric conditions. The only catalyst that was found to be recyclable under a CO atmosphere was **CAT-4**, obtained from **SILP-Im-2**. [16] The catalyst could be reused efficiently in at least 3 cycles in the reaction of a number of aromatic amines both with electron donating and -withdrawing substituents, as well as with amino groups in sterically hindered position. Beside the amides depicted in Figure 11, other derivatives were also produced (Fig. 12.). Different iodoarenes were also converted successfully to the products with aniline as nucleophile (Fig. 12.).

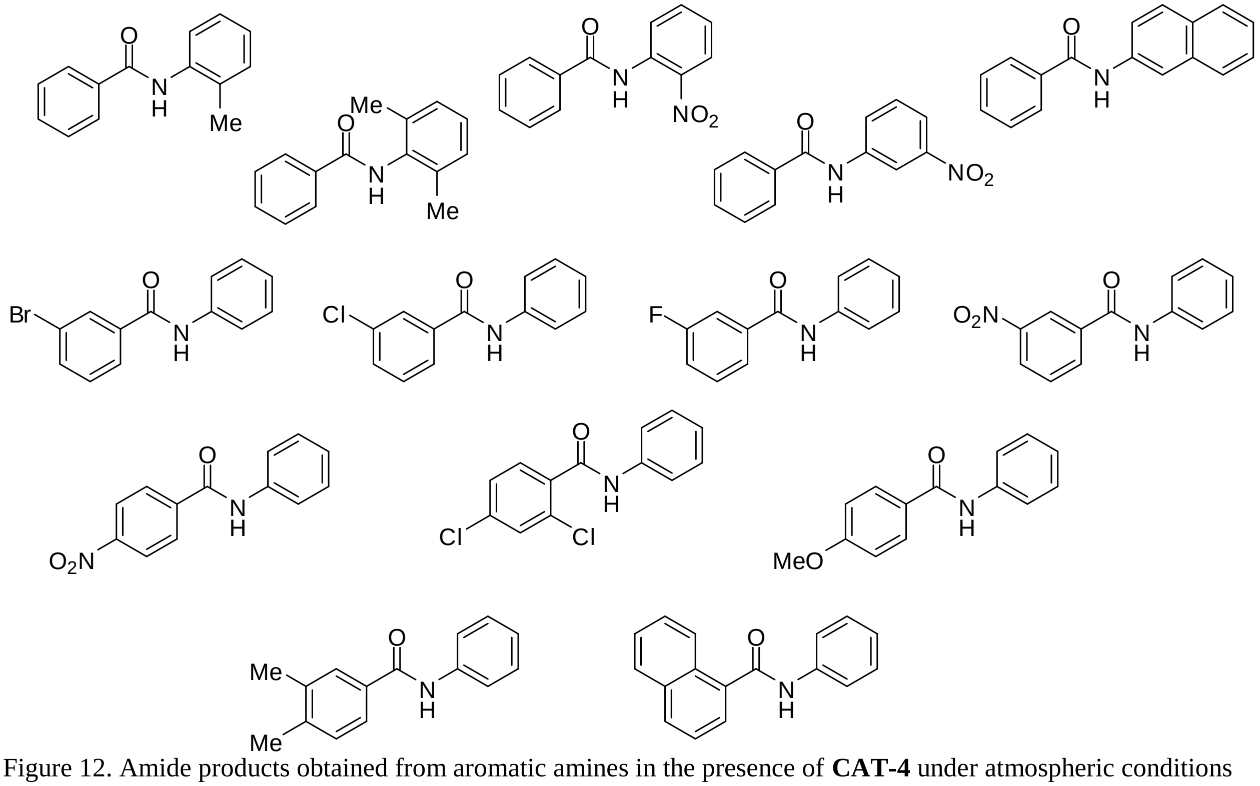


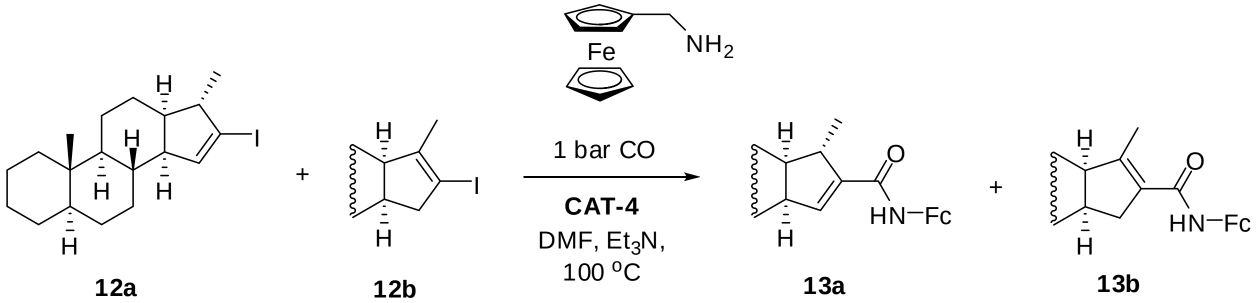
Figure 12. Amide products obtained from aromatic amines in the presence of **CAT-4** under atmospheric conditions

Unfortunately, low conversion and poor amide selectivity, due to competing double carbonylation, was observed with aliphatic amines under similar conditions.

2.2. Application of the palladium catalysts in other reactions

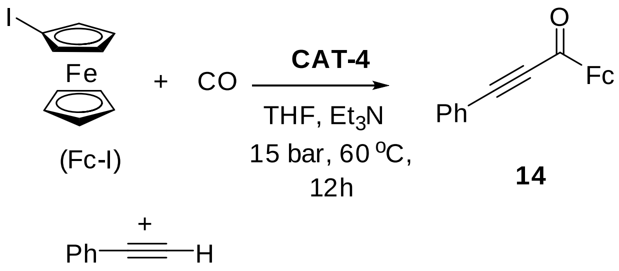
CAT-4, obtained from the **SILP-Im-2** phase, was proved to be very efficient in a number of carbonylation and coupling reactions and its performance was compared with that of homogeneous catalysts.

During aminocarbonylation of a mixture of steroidal substrates **12a** and **12b** (Scheme 3), somewhat lower yields were obtained with **CAT-4** than with the homogeneous system [17] under atmospheric conditions. At the same time, the catalyst could be recycled with only a little decrease in the amount of the isolated products. [18] Also, a greater difference in the reactivity of alkenyl iodides **12a** and **12b** was observed compared to the homogeneous reaction that facilitated separation of the main product **13a** from **13b**. Lower rate of conversion of **12b** in the presence of bulky nucleophiles had been explained by a steric hindrance caused by the planar disposition and close proximity of the 17-methyl and 16-iodo groups. [17] In case of **CAT-4**, the greatest bulk of the heterogeneous catalyst may enhance the difference between the reactivity of **12b** and the sterically less hindered **12a**.

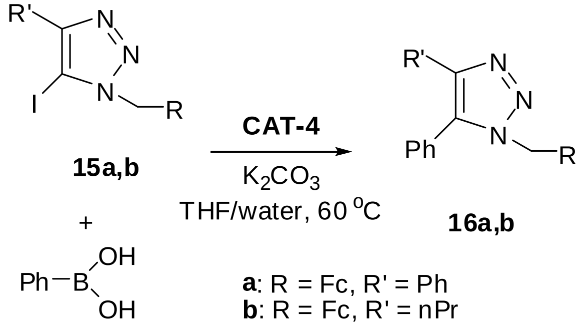


Scheme 3. Aminocarbonylation of steroidal alkenyl iodides **12a** and **12b** with ferrocenylmethylamine

During the carbonylative Sonogashira reaction of iodoferrocene, the product ketone **14** (Scheme 4.) could be obtained in 83 %, 86 % and 76 % yields in three subsequent runs with the recycling of **CAT-4**. Although these yields were a bit lower than those obtained by the homogeneous system, the TON was much higher (a total of 153 for the three cycles compared to TON=9 for $PdCl_2(PPh_3)_2$) because of the lower palladium/substrate ratio (**CAT-4**:1.6%, $PdCl_2(PPh_3)_2$:10%). As another advantage, the heterogeneous reaction was carried out under copper-free conditions, while 4% of CuI co-catalyst had to be added to the mixture in the homogeneous reaction. [19] The products were converted to 2-ureido-4-ferrocenyl pyrimidine derivatives, promising candidates for molecular detection of appropriate guest molecules, such as 2,6-diaminopyridine.



Scheme 4. Carbonylative Sonogashira coupling of iodoferrocene



Scheme 5. Suzuki coupling of 5-iodotriazoles **15a,b**

Suzuki coupling of 5-iodo-triazoles **15a** and **15b** with phenylboronic acid (Scheme 5) gave 1**6a** and 1**6b** in 95% and 96% yields, respectively, in the presence of **CAT-4**. The catalyst could be recycled with a small loss of activity leading to 1**6a** in 93% and 88% yield in the second and third runs. [20]

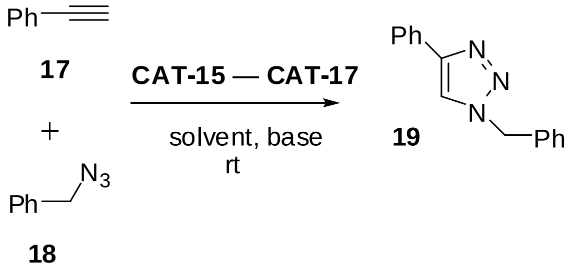
Heck reaction of aryl iodides and methyl acrylate was carried out in an X-Cube^{TM} reactor in the presence of supported catalysts. Different palladium precursors were immobilised on **SILP-Im-2**. Similarly to the results in carbonylation reactions, activity and selectivity of the catalysts were found to depend greatly on the conditions used during heterogenisation. **CAT-4** was proved to be the most efficient catalyst showing stable performance for hours on stream. [21]

2.3. Copper-catalysed azide-alkyne cycloaddition

Originally, preparation of heterogeneous catalysts for cobalt-catalysed carbonylations was also planned. Cobalt catalysts were deposited on SILPs but they were found to be not stable enough for further carbonylation experiments.

Instead, copper catalysts were immobilised on SILPs with imidazolium cations and were tested in azide-alkyne cycloaddition reactions. Among them, catalysts obtained by the deposition of CuI on **SILP-Im-5** in the absence (**CAT-15**) and in the presence of KO^{t}Bu (**CAT-16**, **CAT-17**) were found to be active in the synthesis of 1,2,3-triazoles. [22] In the presence of KO^{t}Bu, a higher amount of copper could be immobilized under identical conditions (Table 1, **CAT-15** and **CAT-16**).

The catalysts were tested in the cycloaddition reaction of phenylacetylene (**17**) with benzyl-azide (**18**) (Scheme 6). The reactions were carried out until total conversion of substrates was observed by GC. **CAT-15** and **CAT-16** gave similar results in catalytic reactions under identical conditions, but copper leaching was lower in case of **CAT-16**. The use of polar solvents (such as acetonitrile) and the addition of a base (*e. g.* DIPEA) accelerated the reaction considerably, but increased loss of copper. In CH_2Cl_2 a low metal leaching (0.8% of the original load) was observed with **CAT-16** but the reaction was completed in only 4 days at room temperature. An increase in the catalyst/substrate ratio and especially the use of a higher temperature led to a decrease in the necessary reaction time but it was accompanied by high copper content of the filtrate. Filtration and mercury poisoning tests showed the presence of copper nanoparticles in the reaction mixture. To prevent aggregation of the latter on the surface of the support, **CAT-17** with a lower copper/imidazolium ion ratio was prepared. With its use, the starting materials were fully converted to the product (**19**) in 24 h, besides, copper leaching was below the detection limit (<0.14% of the original load). During recycling tests, a slight increase in the reaction time, necessary to achieve total conversion, could be observed only after the 7th run (Fig.13). In the 10 cycles, a total loss of only 8% of the original load of copper was detected.



Scheme 6. Azide-alkyne cycloaddition of phenylacetylene (**17**) with benzyl-azide (**18**)

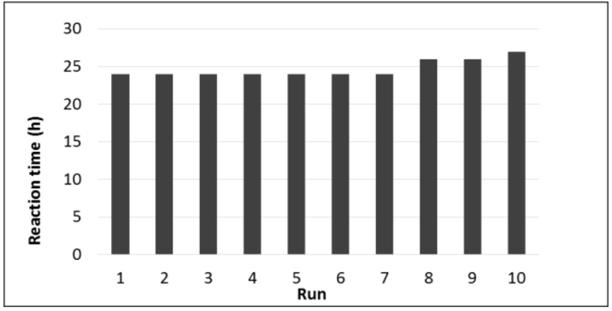
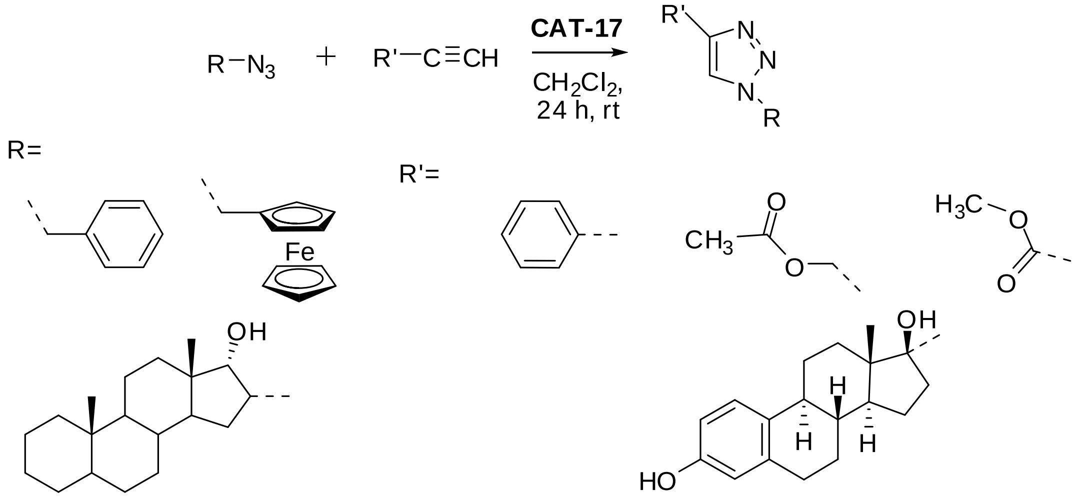


Figure 13. Recirculation experiments with **CAT-17**: reaction time necessary for total conversion

The efficiency of **CAT-17** was tested during the preparation of 11 further derivatives (Scheme 7), using simple azides and alkynes, as well as ferrocene and steroid derivatives. Good recyclability of the catalyst was observed in each case in 3 successive runs. At the same time, bulky substituents on either the alkyne or the azide components were found to retard the reaction. It should be mentioned that, with the exception of two derivatives, similar results could be achieved to those obtained under homogeneous conditions.



Scheme7. Copper-catalysed azide-alkyne cycloaddition of different substrates

3. Concluding remarks

During the project, we succeeded in developing new, efficient SILP-catalysts for palladium-catalysed mono- and double carbonylation reactions and shedding some light on the effect of the structure of the ionic liquid component on the performance of the catalysts. The most significant achievements are the development of the phosphine-free, recyclable catalysts **CAT-4** and **CAT-11**. The former made it possible to synthesise amides from iodoarenes and aromatic amines under atmospheric conditions and the latter can be used for the synthesis of either amides or α-ketoamides under relatively mild conditions.

The applicability of pyridinium ionic liquids and new dicationic phases surely deserves further investigations. Also, the substitution of Br in certain cases in the presence of **CAT-11** promises the possibility to prepare a catalyst that can be used in the conversion of bromoarenes instead of the more expensive iodo-derivatives. The test of the heterogeneous copper catalyst in other copper catalysed reactions (carbonylation, synthesis of heterocycles, etc.) is also planned.

Besides the publications that have already appeared, the drafts of three manuscripts are almost ready and will be submitted soon. [10, 12, 22] Also, two manuscripts concerning the use of catalysts with palladium deposited on pyridinium phases and the polymer/silica material are under construction.

The results formed the basis of 5 BSc and 2 MSc thesis projects. Part of the work was presented by undergraduate students at the conferences of the Scientific Students' Associations. An MSc student, Máté Papp was awarded the Pro Scientia Gold Medal for his work on the present topic.

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